

Suspected Cancer:

recognition and referral

NICE Guideline

Appendix F: Evidence review

Developed for NICE by the National Collaborating Centre for Cancer

© 2015 National Collaborating Centre for Cancer

This guideline updates and replaces NICE guideline CG27

This Evidence Review updates and replaces that in NICE guideline CG27 (published June 2005).

Evidence has been reviewed on the recognition and management of suspected cancer in children, young people and adults. New evidence which has been included as part of this update is highlighted in peach.

Contents

PATIENT INFORMATION

8

What are the information needs of: 1) patients who are referred for suspected cancer and their carers/families, and 2) patients who are being monitored (for suspected cancer) in primary care and their carers/families? 8

SAFETY-NETTING

26

What safety-netting strategies are effective in primary care for patients being monitored for suspected cancer? 26

LUNG AND PLEURAL CANCERS

39

LUNG CANCER 39

What is the risk of lung cancer in patients presenting in primary care with symptom(s)? 39

Which investigations of symptoms of suspected lung cancer should be done with clinical responsibility retained by primary care? 81

MESOTHELIOMA 124

What is the risk of mesothelioma in patients presenting in primary care with symptom(s)? 124

Which investigations of symptoms of suspected mesothelioma should be done with clinical responsibility retained by primary care? 127

UPPER GASTRO-INTESTINAL TRACT CANCERS

135

OESOPHAGEAL 135

What is the risk of oesophageal cancer in patients presenting in primary care with symptom(s)? 135

Which investigations of symptoms of suspected oesophageal cancer should be done with clinical responsibility retained by primary care? 204

PANCREATIC CANCER 231

What is the risk of pancreatic cancer in patients presenting in primary care with symptom(s)? 231

Which investigations of symptoms of suspected pancreatic cancer should be done with clinical responsibility retained by primary care? 274

STOMACH CANCER 306

What is the risk of stomach cancer in patients presenting in primary care with symptom(s)? 306

Which investigations of symptoms of suspected stomach cancer should be done with clinical responsibility retained by primary care? 379

SMALL INTESTINAL CANCER 402

What is the risk of small intestine cancer in patients presenting in primary care with symptom(s)? 402

Which investigations of symptoms of suspected small intestine cancer should be done with clinical responsibility retained by primary care?	415
GALL BLADDER CANCER	425
What is the risk of gall bladder cancer in patients presenting in primary care with symptom(s)?	425
Which investigations of symptoms of suspected gall bladder cancer should be done with clinical responsibility retained by primary care?	442
LIVER CANCER	456
What is the risk of liver cancer in patients presenting in primary care with symptom(s)?	456
Which investigations of symptoms of suspected liver cancer should be done with clinical responsibility retained by primary care?	475
LOWER GASTRO-INTESTINAL TRACT CANCERS	504
COLORECTAL CANCER	504
What is the risk of colorectal cancer in patients presenting in primary care with symptom(s)?	504
Which investigations of symptoms of suspected colorectal cancer should be done with clinical responsibility retained by primary care?	616
ANAL CANCER	657
What is the risk of anal cancer in patients presenting in primary care with symptom(s)?	657
Which investigations of symptoms of suspected anal cancer should be done with clinical responsibility retained by primary care?	667
BREAST CANCER	675
What is the risk of breast cancer in patients presenting in primary care with symptom(s)?	675
Which investigations of symptoms of suspected breast cancer should be done with clinical responsibility retained by primary care?	714
GYNAECOLOGICAL CANCERS	763
ENDOMETRIAL CANCER	763
What is the risk of endometrial cancer in patients presenting in primary care with symptom(s)?	763
Which investigations of symptoms of suspected endometrial cancer should be done with clinical responsibility retained by primary care?	786
CERVICAL CANCER	803
What is the risk of cervical cancer in patients presenting in primary care with symptom(s)?	803
Which investigations of symptoms of suspected cervix cancer should be done with clinical responsibility retained by primary care?	814

VULVAL CANCER	835
What is the risk of vulval cancer in patients presenting in primary care with symptom(s)?	835
Which investigations of symptoms of suspected vulval cancer should be done with clinical responsibility retained by primary care?	848
VAGINA CANCER	856
What is the risk of vagina cancer in patients presenting in primary care with symptom(s)?	856
Which investigations of symptoms of suspected vaginal cancer should be done with clinical responsibility retained by primary care?	863
UROLOGICAL CANCERS	868
PROSTATE CANCER	868
What is the risk of prostate cancer in patients presenting in primary care with symptom(s)?	868
Which investigations of symptoms of suspected prostate cancer should be done with clinical responsibility retained by primary care?	901
BLADDER CANCER	939
What is the risk of bladder cancer in patients presenting in primary care with symptom(s)?	939
Which investigations of symptoms of suspected bladder cancer should be done with clinical responsibility retained by primary care?	983
RENAL CANCER	997
What is the risk of renal cancer in patients presenting in primary care with symptom(s)?	997
Which investigations of symptoms of suspected renal cancer should be done with clinical responsibility retained by primary care?	1033
TESTICULAR CANCER	1051
What is the risk of testicular cancer in patients presenting in primary care with symptom(s)?	1051
Which investigations of symptoms of suspected testicular cancer should be done with clinical responsibility retained by primary care?	1070
PENILE CANCER	1080
What is the risk of penile cancer in patients presenting in primary care with symptom(s)?	1080
Which investigations of symptoms of suspected penile cancer should be done with clinical responsibility retained by primary care?	1087
SKIN CANCERS	1092
MELANOMA	1092
What is the risk of melanoma in patients presenting in primary care with symptom(s)?	1092
Which investigations of symptoms of suspected melanoma should be done with clinical responsibility retained by primary care?	1109

SQUAMOUS CELL CARCINOMA 1153

What is the risk of squamous cell carcinoma in patients presenting in primary care with symptom(s)? 1153

Which investigations of symptoms of suspected squamous cell carcinoma should be done with clinical responsibility retained by primary care? 1175

BASAL CELL CARCINOMA 1203

What is the risk of basal cell carcinoma in patients presenting in primary care with symptom(s)? 1203

Which investigations of symptoms of suspected basal cell carcinoma should be done with clinical responsibility retained by primary care? 1222

HEAD AND NECK CANCERS 1250

LARYNGEAL CANCER 1250

What is the risk of laryngeal cancer in patients presenting in primary care with symptom(s)? 1250

Which investigations of symptoms of suspected laryngeal cancer should be done with clinical responsibility retained by primary care? 1261

ORAL CANCER 1268

What is the risk of oral cancer in patients presenting in primary care with symptom(s)? 1268

Which investigations of symptoms of suspected oral cancer should be done with clinical responsibility retained by primary care? 1283

THYROID CANCER 1304

What is the risk of thyroid cancer in patients presenting in primary care with symptom(s)? 1304

Which investigations of symptoms of suspected thyroid cancer should be done with clinical responsibility retained by primary care? 1325

BRAIN AND CENTRAL NERVOUS SYSTEM CANCERS 1345

What is the risk of brain and CNS cancer in patients presenting in primary care with symptom(s)? 1345

Which investigations of symptoms of suspected brain and CNS cancer should be done with clinical responsibility retained by primary care? 1384

HAEMATOLOGICAL CANCERS 1399

LEUKEMIA 1399

What is the risk of leukaemia in adults and children presenting in primary care with symptom(s)? 1399

Which investigations of symptoms of suspected leukemia should be done with clinical responsibility retained by primary care? 1414

MYELOMA	1421
What is the risk of myeloma in patients presenting in primary care with symptom(s)?	1421
Which investigations of symptoms of suspected myeloma should be done with clinical responsibility retained by primary care?	1443
NON-HODGKIN'S LYMPHOMA	1455
What is the risk of Non-Hodgkin's lymphoma in patients presenting in primary care with symptom(s)?	1455
Which investigations of symptoms of suspected Non-Hodgkin's lymphoma cancer should be done with clinical responsibility retained by primary care?	1485
HODGKIN'S LYMPHOMA	1500
What is the risk of Hodgkin's lymphoma in patients presenting in primary care with symptom(s)?	1500
Which investigations of symptoms of suspected Hodgkin's lymphoma should be done with clinical responsibility retained by primary care?	1515
SARCOMAS	1521
BONE SARCOMA	1521
What is the risk of bone sarcoma in patients presenting in primary care with symptom(s)?	1521
Which investigations of symptoms of suspected bone sarcoma should be done with clinical responsibility retained by primary care?	1545
SOFT TISSUE SARCOMA	1565
What is the risk of soft tissue sarcoma in patients presenting in primary care with symptom(s)?	1565
Which investigations of symptoms of suspected soft tissue sarcoma should be done with clinical responsibility retained by primary care?	1579
CHILDHOOD CANCERS	1587
NEUROBLASTOMA, RETINOBLASTOMA, WILM'S TUMOUR	1587
What is the risk of neuroblastoma, retinoblastoma and Wilm's tumour in children presenting in primary care with symptom(s)?	1587
Which investigations of symptoms of suspected retinoblastoma, neuroblastoma and Wilm's tumour in children should be done with clinical responsibility retained by primary care?	1618
NON-SITE SPECIFIC SYMPTOMS	1631

PATIENT INFORMATION

Review question:

What are the information needs of: 1) patients who are referred for suspected cancer and their carers/families, and 2) patients who are being monitored (for suspected cancer) in primary care and their carers/families?

Results

Literature search

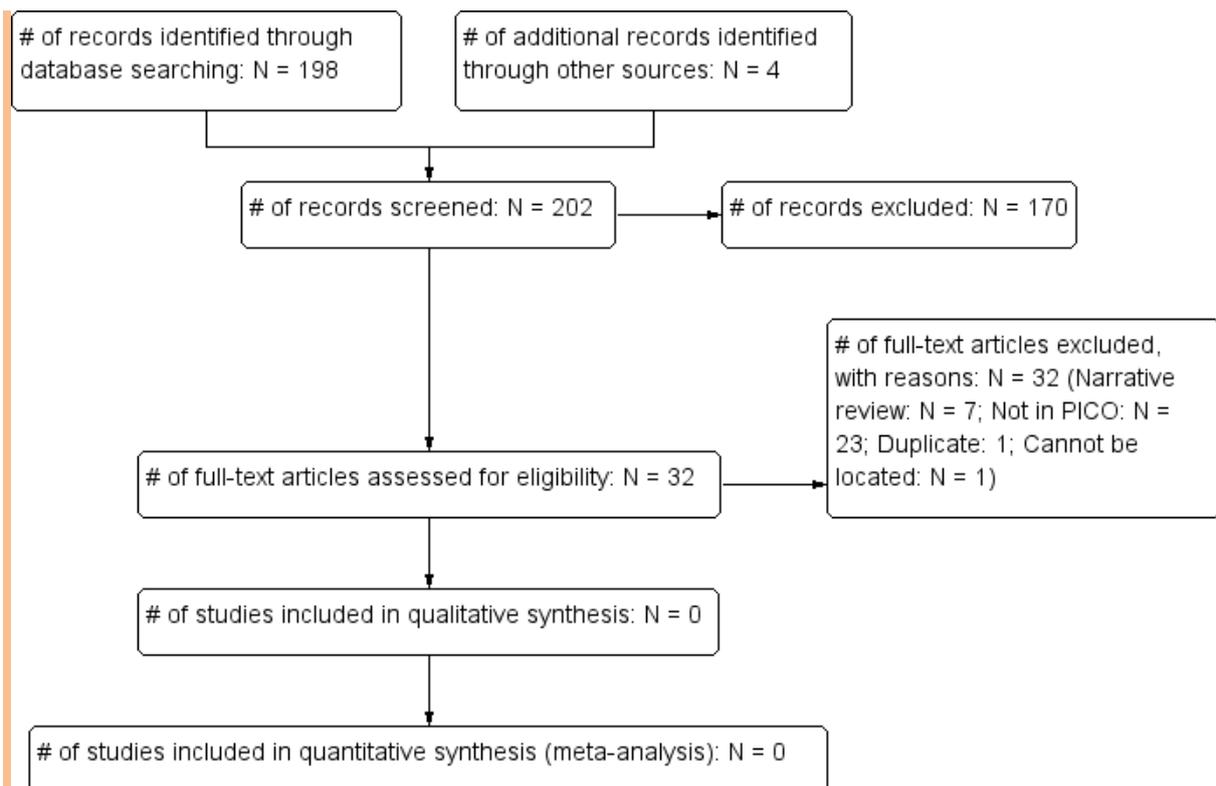
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	1575	93	11/07/2013
<i>Premedline</i>	1980-2013	95	3	11/07/2013
<i>Embase</i>	1980-2013	799	33	09/09/2013
<i>Cochrane Library</i>	1980-2013	874	0	09/09/2013
<i>Psychinfo</i>	1980-2013	133	3	09/09/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	38	0	09/09/2013
<i>Websites etc</i>			18	09/09/2013

Total References retrieved (after de-duplication): 142

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-27/082014	70	24	27/082014
<i>Premedline</i>	2013-27/082014	89	22	27/082014
<i>Embase</i>	2013-27/082014	125	31	27/082014
<i>Cochrane Library</i>	2013-27/082014	279	1	27/082014
<i>Psychinfo</i>	2013-27/082014	22	7	27/082014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-27/082014	4	1	27/082014

Total References retrieved (after de-duplication): 56



Study results

No evidence was found pertaining to the information needs of primary care patients who are referred for suspected cancer and their carers/families, or of patients who are being monitored (for suspected cancer) in primary care and their carers/families.

References

Included studies

None

Excluded studies (with reason)

(2005) Information from your family doctor. Early prostate cancer: what you should know. *American Family Physician*, 71: 1929-1930.

Information leaflet, not study data

(2007). *Cancer Tales: Communicating in Cancer* . Haymarket Medical Publications .

Not in PICO which is about information, not communication as such, and about what information patients/carers/families want/need or don't want/need during referral and monitoring.

PATIENT PARTICIPATION Cancer Care Focus Group at Caen Medical Centre. 2013.

Not in PICO

Why have I been referred urgently to the hospital. 2013.

Information, not study data

Abdolmohammadi, A., Sears, W., Rai, S., Pan, J., Alexander, J. & Kloecker, G. (2014) - Survey of primary care physicians on therapeutic approaches to lung and breast cancers. - *Southern Medical Journal*, 107: 437-442.

Not in PICO

- Abel, G. A., Friese, C. R., Neville, B. A., Richardson, L. C., Wilson, K. M., Hastings, B. T., Earle, C. C. & Soiffer, R. J. (2010) Primary care referrals for suspected hematologic malignancies: Incidence, factors affecting choice of specialist, and flow of referral information. *Blood*, 116.
Not in PICO
- Akiba, T., Yamashita, M., Sato, S., Nagata, T. & Yamazaki, Y. (2002) Requests for second opinions through the Internet reveal the feelings and concerns of patients with lung cancer and their families. [Japanese]. *Japanese Journal of Lung Cancer*, 42: 589-593.
Not in PICO
- Albert, U. S., Schulz, K. D., Alt, D., Beck, V., Doherty, J., Holsteg, K., Kalbheim, E., Muller, J., Nass-Griegoleit, I., Nill, J., Nioduschewski, G., Schulte, H., von, W. A. & Kopp, I. (2003) [A guideline for guidelines--methodological report and use of the guideline women's information]. [Review] [62 refs] [German][Erratum appears in Zentralbl Gynakol. 2004 Feb;126(1):41]. *Zentralblatt fur Gynakologie*, 125: 484-493.
Not in PICO
- Altman, D. G. (1985) Utilization of a telephone cancer information program by symptomatic people. *Journal of Community Health*, 10: 156-171.
Not in PICO
- Anglia Cancer Network . Patient Information Prescriptions Strategy 2012-2013. 2012.
Information, not study data
- Badger, T., Segrin, C., Pasvogel, A. & Lopez, A. M. (2013) - The effect of psychosocial interventions delivered by telephone and videophone on quality of life in early-stage breast cancer survivors and their supportive partners. - *Journal of Telemedicine & Telecare*, 19: 260-265.
Not in PICO
- Bain, N. S., Campbell, N. C., Ritchie, L. D. & Cassidy, J. (2002) Striking the right balance in colorectal cancer care--a qualitative study of rural and urban patients. *Family Practice*, 19: 369-374.
Not in PICO
- Ballal, M. S., Selvachandran, S. N. & Maw, A. (2010) Use of a patient consultation questionnaire and weighted numerical scoring system for the prediction of colorectal cancer and other colorectal pathology in symptomatic patients: a prospective cohort validation study of a Welsh population. *Colorectal Disease*, 12: 407-414.
Not in PICO
- Barnato, A. E., Llewellyn-Thomas, H. A., Peters, E. M., Siminoff, L., Collins, E. D. & Barry, M. J. (2007) Communication and decision making in cancer care: setting research priorities for decision support/patients' decision aids. *Medical Decision Making*, 27: 626-634.
Not in PICO
- Bashari, D. R., Sharma, R., Wijeyakuhan, N., Butt, S., Frankenthaler, M., Akerman, M., Kline, M., Nouryan, C. N. & Wolf-Klein, G. P. (2013) Differences between primary care physicians and oncologists in initiating advance directives in older adults: When is the optimal time? *Journal of the American Geriatrics Society*, 61: S55-S56.
Not in PICO
- Bergholdt, S. H., Hansen, D. G., Larsen, P. V., Kragstrup, J. & Sondergaard, J. (2013) - A randomised controlled trial to improve the role of the general practitioner in cancer rehabilitation: effect on patients' satisfaction with their general practitioners. - *BMJ Open*, 3.
Not in PICO
- Bergholdt, S. H., Hansen, D. G., Larsen, P. V., Kragstrup, J. & Sondergaard, J. (2013) A randomised controlled trial to improve the role of the general practitioner in cancer rehabilitation: Effect on patients' satisfaction with their general practitioners. *BMJ Open*, 3.
Not in PICO
- Blumenthal-Barby, J. S., Cantor, S. B., Russell, H. V., Naik, A. D. & Volk, R. J. (2013) - Decision aids: when 'nudging' patients to make a particular choice is more ethical than balanced, nondirective

- content. - *Health Affairs*, 32: 303-310.
Not in PICO
- Booth-Clibborn, N., Milne, R. & Oliver, S. (2001) Searching for high-quality evidence to prepare patient information. *Health Information & Libraries Journal*, 18: 75-82.
Not in PICO
- Bredal, I. S., Karesen, R., Smeby, N. A., Espe, R., Sorensen, E. M., Amundsen, M., Aas, H. & Ekeberg, O. (2014) Effects of a psychoeducational versus a support group intervention in patients with early-stage breast cancer: Results of a randomized controlled trial. *Cancer Nursing*, 37: 198-207.
Not in PICO
- Bright, M. A. (2007) The National Cancer Institute's Cancer Information Service: a premiere cancer information and education resource for the nation. *Journal of Cancer Education*, 22: Suppl-7.
Not in PICO
- Bruera, E., Sweeney, C., Calder, K., Palmer, L. & Benisch-Tolley, S. (2001) Patient preferences versus physician perceptions of treatment decisions in cancer care. *Journal of Clinical Oncology*, 19: 2883-2885.
Not in PICO
- Budden, L. M., Hayes, B. A. & Buettner, P. G. (2014) - Women's decision satisfaction and psychological distress following early breast cancer treatment: a treatment decision support role for nurses. - *International Journal of Nursing Practice*, 20: 8-16.
Not in PICO
- Burgess, C., Hunter, M. S. & Ramirez, A. J. (2001) A qualitative study of delay among women reporting symptoms of breast cancer. *British Journal of General Practice*, 51: 967-971.
Not in PICO
- Capirci, C., Feldman-Stewart, D., Mandoliti, G., Brundage, M., Belluco, G. & Magnani, K. (2005) Information priorities of Italian early-stage prostate cancer patients and of their health-care professionals. *Patient Education & Counseling*, 56: 174-181.
Not in PICO
- Chandrasekhar, S. S., Randolph, G. W., Seidman, M. D., Rosenfeld, R. M., Angelos, P., Barkmeier-Kraemer, J., Benninger, M. S., Blumin, J. H., Dennis, G., Hanks, J., Haymart, M. R., Kloos, R. T., Seals, B., Schreibstein, J. M., Thomas, M. A., Waddington, C., Warren, B. & Robertson, P. J. (2013) Clinical practice guideline: Improving voice outcomes after thyroid surgery. *Otolaryngology - Head and Neck Surgery (United States)*, 148: S1-S37.
Not in PICO
- Chin, J. Y., Goldstraw, E., Lunniss, P. & Patel, K. (2012) Evaluation of the utility of abdominal CT scans in the diagnosis, management, outcome and information given at discharge of patients with non-traumatic acute abdominal pain. *British Journal of Radiology*, 85: e596-e602.
Not in PICO
- Chubak, J., Aiello Bowles, E. J., Tuzzio, L., Ludman, E., Rutter, C. M., Reid, R. J. & Wagner, E. H. (2014) - Perspectives of cancer survivors on the role of different healthcare providers in an integrated delivery system. - *Journal of Cancer Survivorship*, 8: 229-238.
Not in PICO
- Clicsargent . More than my illness.
http://www.clicsargent.org.uk/sites/files/clicsargent/field/field_document/More%20Than%20My%20Illness%20to%2018%202008.pdf . 2014.
Not in PICO (no original data)
- Cooper, C. P., Gelb, C. A., Rodriguez, J. & Hawkins, N. A. (2014) - Promoting gynecologic cancer awareness at a critical juncture--where women and providers meet. - *Journal of Cancer Education*, 29: 247-251.
Not in PICO
- Coory, M., Gkolia, P., Yang, I. A., Bowman, R. V. & Fong, K. M. (2008) Systematic review of multidisciplinary teams in the management of lung cancer. [Review] [41 refs]. *Lung Cancer*, 60:

14-21.

Not in PICO

Cornford, C. S., Harley, J. & Oswald, N. (2004) The '2-week rule' for suspected breast carcinoma: a qualitative study of the views of patients and professionals. *British Journal of General Practice*, 54: 584-588.

Methods underspecified. The only mention of information preferences in the results cannot be evaluated or related to any absolute starting point (information level). Input as not in PICO

Culligan, M., Hesdorffer, M., Lai, Y.-H., Yates, P., White, J. & Broderick, C. (2013) Negative. *Journal of Thoracic Oncology*, 8: S122.

Not in PICO

Davies, E., van der Molen, B. & Cranston, A. (2007) Using clinical audit, qualitative data from patients and feedback from general practitioners to decrease delay in the referral of suspected colorectal cancer. *Journal of Evaluation in Clinical Practice*, 13: 310-317.

Not in PICO

Davison, B. J., Goldenberg, S. L., Gleave, M. E. & Degner, L. F. (2003) Provision of individualized information to men and their partners to facilitate treatment decision making in prostate cancer. *Oncology Nursing Forum*, 30: 107-114.

Not in PICO

Davison, B. J., Keyes, M., Elliott, S., Berkowitz, J. & Goldenberg, S. L. (2004) Preferences for sexual information resources in patients treated for early-stage prostate cancer with either radical prostatectomy or brachytherapy. *BJU International*, 93: 965-969.

Not in PICO

de Bekker-Grob, E. W., Bliemer, M. C., Donkers, B., Essink-Bot, M. L., Korfage, I. J., Roobol, M. J., Bangma, C. H. & Steyerberg, E. W. (2013) - Patients' and urologists' preferences for prostate cancer treatment: a discrete choice experiment. - *British Journal of Cancer*, 109: 633-640.

Not in PICO

Delva, F., Marien, E., Fonck, M., Rainfray, M., Demeaux, J. L., Moreaud, P., Soubeyran, P., Sasco, A. J. & Mathoulin-Pelissier, S. (2011) Factors influencing general practitioners in the referral of elderly cancer patients. *BMC Cancer*, 11: 5.

Not in PICO

Deutsch, L., King, E., Sinclair, S., Hastings, P., Mazza, D., Chakraborty, S., Southern, D. & Zorbas, H. (2013) Investigating symptoms of lung cancer: An evidence-based guide for general practitioners. *Journal of Thoracic Oncology*, 8: S980-S981.

Guideline

Devbhandari, M. P., Quennell, P., Krysiak, P., Shah, R. & Jones, M. T. (2008) Implications of a negative bronchoscopy on waiting times to treatment for lung cancer patients: results of a prospective tracking study. *European Journal of Cardio-Thoracic Surgery*, 34: 479-483.

Not in PICO

Diefenbach, M., Mohamed, N. & Hall, S. (2011) Examining an interactive, multimedia education and decision program for early-stage prostate cancer patients. *Journal of Urology*, 185: e404.

Not in PICO

Diefenbach, M. A., Dorsey, J., Uzzo, R. G., Hanks, G. E., Greenberg, R. E., Horwitz, E., Newton, F. & Engstrom, P. F. (2002) Decision-making strategies for patients with localized prostate cancer. *Seminars in Urologic Oncology*, 20: 55-62.

Not in PICO

Diefenbach, M. A., Mohamed, N. E., Butz, B. P., Bar-Chama, N., Stock, R., Cesaretti, J., Hassan, W., Samadi, D. & Hall, S. J. (2012) Acceptability and preliminary feasibility of an internet/CD-ROM-based education and decision program for early-stage prostate cancer patients: randomized pilot study. *Journal of Medical Internet Research*, 14: e6.

Not in PICO

- Dionigi, G., Tanda, M. L., Piantanida, E., Boni, L., Rovera, F., Dionigi, R. & Bartalena, L. (2009) Time interval in diagnosis and treatment of papillary thyroid cancer: a descriptive, retrospective study. *American Journal of Surgery*, 197: 434-438.
Not in PICO
- Dyrop, H. B., Safwat, A., Vedsted, P., Maretty-Nielsen, K., Hansen, B. H., Jorgensen, P. H., Baad-Hansen, T., Bungler, C. & Keller, J. (2013) - Cancer Patient Pathways shortens waiting times and accelerates the diagnostic process of suspected sarcoma patients in Denmark. - *Health Policy*, 113: 110-117.
Not in PICO
- Early, D. S., Janec, E., Azar, R., Ristvedt, S., Gao, F. & Edmundowicz, S. A. (2006) Patient preference and recall of results of EUS-guided FNA. *Gastrointestinal Endoscopy*, 64: 735-739.
Not in PICO
- Eicher, M., De, M. J., Dubey, C., Hoeppli, C. & Betticher, D. (2013) Unmet supportive care needs and resilience in cancer patients under early treatment: A descriptive study. *European Journal of Cancer*, 49: S375.
Not in PICO
- Ellis, P. M., Thannikkotu, C., Van, D. A., Chambers, S., Hapke, S., Martelli-Reid, L. & Goffin, J. R. (2013) Educating community health professionals about lung cancer: A pilot evaluation of a web-based educational tool. *Journal of Thoracic Oncology*, 8: S873-S874.
Not in PICO
- Elustondo, S. G., Padilla, E. S., Aleson, V. R., Hernandez, M., Navarro, A. G. & Gomez, C. L. (2008) Opinion and participation in the regional early breast cancer detection program in 2007 on the part of family physicians from a health district in the autonomous community of Madrid, Spain. [Spanish]. *Revista Espanola de Salud Publica*, 82: 201-208.
Not in PICO
- Enel, C., Matte, A., Berchi, C., Binquet, C., Cormier, L. & Lejeune, C. (2013) - [Prostate cancer: how do patients choose their treatment?]. [French]. - *Bulletin du Cancer*, 100: 191-199.
Not in PICO
- Enel, C., Matte, A., Berchi, C., Binquet, C., Cormier, L. & Lejeune, C. (2013) [Prostate cancer: how do patients choose their treatment?]. [French]. *Bulletin du Cancer*, 100: 191-199.
Not in PICO
- Ersig, A. L., Ayres, L., Hadley, D. W. & Koehly, L. M. (2010) Explanations of risk in families without identified mutations for hereditary nonpolyposis colorectal cancer. *Journal of Nursing Scholarship*, 42: 139-146.
Not in PICO
- Evans, R. E., Morris, M., Sekhon, M., Buszewicz, M., Walter, F. M., Waller, J. & Simon, A. E. (2014) - Increasing awareness of gynaecological cancer symptoms: a GP perspective. - *British Journal of General Practice*, 64: e372-e380.
Not in PICO
- Evans, R. E. C., Morris, M., Sekhon, M., Buszewicz, M., Walter, F. M., Waller, J. & Simon, A. E. (2014) Increasing awareness of gynaecological cancer symptoms: A GP perspective. *British Journal of General Practice*, 64: e372-e380.
Duplicate
- Fagerlin, A., Rovner, D., Stableford, S., Jentoft, C., Wei, J. T. & Holmes-Rovner, M. (2004) Patient education materials about the treatment of early-stage prostate cancer: a critical review. *Annals of Internal Medicine*, 140: 721-728.
Not in PICO
- Fallowfield, L. J., Solis-Trapala, I. & Jenkins, V. A. (2012) Evaluation of an educational program to improve communication with patients about early-phase trial participation. *The Oncologist*, 17: 377-383.
Not in PICO

- Feldman-Stewart, D., Brundage, M. D., Hayter, C., Groome, P., Nickel, J. C., Downes, H. & MacKillop, W. J. (2000) What questions do patients with curable prostate cancer want answered? *Medical Decision Making*, 20: 7-19.
Not in PICO
- Feldman-Stewart, D., Brundage, M. D., Nickel, J. C. & MacKillop, W. J. (2001) The information required by patients with early-stage prostate cancer in choosing their treatment. *BJU International*, 87: 218-223.
Not in PICO
- Feldman-Stewart, D., Capirci, C. & Brundage, M. D. (2003) Information for patients with early-stage prostate cancer: a comparison of professionals' attitudes in Canada and Italy. *Supportive Care in Cancer*, 11: 472-480.
Not in PICO
- Feldman-Stewart, D., Brundage, M. D., Van, M. L., Skarsgard, D. & Siemens, R. (2003) Evaluation of a question-and-answer booklet on early-stage prostate-cancer. *Patient Education & Counseling*, 49: 115-124.
Not in PICO
- Feldman-Stewart, D. & Brundage, M. D. (2004) Challenges for designing and implementing decision aids. *Patient Education & Counseling*, 54: 265-273.
Not in PICO
- Feldman-Stewart, D., Brundage, M. D., Van, M. L. & Svenson, O. (2004) Patient-focussed decision-making in early-stage prostate cancer: insights from a cognitively based decision aid. *Health Expectations*, 7: 126-141.
Not in PICO
- Feldman-Stewart, D., Brundage, M. D., Siemens, R. & Skarsgard, D. (2006) A randomized controlled trial comparing two educational booklets on prostate cancer. *Canadian Journal of Urology*, 13: 3321-3326.
Not in PICO
- Feldman-Stewart, D., Brennenstuhl, S. & Brundage, M. D. (2007) A purpose-based evaluation of information for patients: an approach to measuring effectiveness. *Patient Education & Counseling*, 65: 311-319.
Not in PICO
- Feldman-Stewart, D., Brennenstuhl, S. & Brundage, M. D. (2008) The information needed by Canadian early-stage prostate cancer patients for decision-making: stable over a decade. *Patient Education & Counseling*, 73: 437-442.
Not in PICO
- Feldman-Stewart, D., Brennenstuhl, S., Brundage, M. D. & Siemens, D. R. (2009) Overall information needs of early-stage prostate cancer patients over a decade: highly variable and remarkably stable. *Supportive Care in Cancer*, 17: 429-435.
Not in PICO
- Feldman-Stewart, D., Brundage, M. D. & Tong, C. (2011) Information that affects patients' treatment choices for early stage prostate cancer: a review. [Review]. *Canadian Journal of Urology*, 18: 5998-6006.
Not in PICO
- Feldman-Stewart, D., Tong, C., Siemens, R., Alibhai, S., Pickles, T., Robinson, J. & Brundage, M. D. (2012) The impact of explicit values clarification exercises in a patient decision aid emerges after the decision is actually made: evidence from a randomized controlled trial. *Medical Decision Making*, 32: 616-626.
Not in PICO
- Feldman-Stewart, D., Madarnas, Y., Mates, M., Tong, C., Grunfeld, E., Verma, S., Carolan, H. & Brundage, M. (2013) - Information for decision making by post-menopausal women with hormone receptor positive early-stage breast cancer considering adjuvant endocrine therapy. -

- Breast*, 22: 919-925.
Not in PICO
- Forrest, G., Plumb, C., Ziebland, S. & Stein, A. (2006) Breast cancer in the family-children's perceptions of their mother's cancer and its initial treatment: Qualitative study. *British Medical Journal*, 332: 998-1001.
Not in PICO
- Forrest, L. F., Sowden, S., Rubin, G., White, M. & Adams, J. (2014) - Socio-economic inequalities in patient, primary care, referral, diagnostic, and treatment intervals on the lung cancer care pathway: protocol for a systematic review and meta-analysis. - *Systems Review*, 3: 30.
Protocol
- Gaertner, J., Weingartner, V., Wolf, J. & Voltz, R. (2013) Early palliative care for patients with advanced cancer: How to make it work? *Current Opinion in Oncology*, 25: 342-352.
Not in PICO
- Gafni, A., Charles, C. & Whelan, T. (1998) The physician-patient encounter: the physician as a perfect agent for the patient versus the informed treatment decision-making model. *Social Science & Medicine*, 47: 347-354.
Not in PICO
- Gjengsto, P., Eide, J., Frugard, J., Bakke, A. & Hoisaeter, P. A. (2004) The potentially curable prostate cancer patient and the pathways leading to diagnosis and treatment. *Scandinavian Journal of Urology & Nephrology*, 38: 15-18.
Not in PICO
- Gorman, D. R., Mackinnon, H., Storrie, M., Wilson, G. S. & Parker, S. (2000) The general practice perspective on cancer services in Lothian. *Family Practice*, 17: 323-328.
Not in PICO
- Graydon, J., Galloway, S., Palmer-Wickham, S., Harrison, D., Rich-van der Bij, L., West, P., Burlein-Hall, S. & Evans-Boyden, B. (1997) Information needs of women during early treatment for breast cancer. *Journal of Advanced Nursing*, 26: 59-64.
Not in PICO
- Greater Midlands cancer Network . Primary Care Audit. 2009.
Not in PICO
- Greenhalgh, J., Abhyankar, P., McCluskey, S., Takeuchi, E. & Velikova, G. (2013) - How do doctors refer to patient-reported outcome measures (PROMS) in oncology consultations? - *Quality of Life Research*, 22: 939-950.
Not in PICO
- Greenhalgh, J., Abhyankar, P., McCluskey, S., Takeuchi, E. & Velikova, G. (2013) - How do doctors refer to patient-reported outcome measures (PROMS) in oncology consultations? [References]. - *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation*, Vol.22: 939-950.
Duplicate
- Hacking, B., Wallace, L., Scott, S., Kosmala-Anderson, J., Belkora, J. & McNeill, A. (2013) Testing the feasibility, acceptability and effectiveness of a 'decision navigation' intervention for early stage prostate cancer patients in Scotland - A randomised controlled trial. *Psycho-Oncology*, 22: 1017-1024.
Not in PICO
- Hall, S. E., Holman, C. D. 'A., Threlfall, T., Sheiner, H., Phillips, M., Katriss, P. & Forbes, S. (2008) Lung cancer: An exploration of patient and general practitioner perspectives on the realities of care in rural Western Australia. *Australian Journal of Rural Health*, 16: 355-362.
Not in PICO
- Hamaker, M. E., Hamelinck, V. C., van Munster, B. C., Bastiaannet, E., Smorenburg, C. H., Achterberg, W. P., Liefers, G. J. & de Rooij, S. E. (2012) Nonreferral of nursing home patients with suspected

- breast cancer. *Journal of the American Medical Directors Association*, 13: 464-469.
Not in PICO
- Hamilton, W. (2009) The CAPER studies: five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients. *British Journal of Cancer*, 101: Suppl-6.
Not in PICO
- Harder, H., Ballinger, R., Langridge, C., Ring, A. & Fallowfield, L. J. (2013) - Adjuvant chemotherapy in elderly women with breast cancer: patients' perspectives on information giving and decision making. - *Psycho-Oncology*, 22: 2729-2735.
Not in PICO
- Hashim, S. M., Fah, T. S., Omar, K., Rashid, M. R., Shah, S. A. & Sagap, I. (2011) Knowledge of colorectal cancer among patients presenting with rectal bleeding and its association with delay in seeking medical advice. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 12: 2007-2011.
Not in PICO
- Hiramanek, N. & McAvoy, B. R. (2005) Meeting the needs of patients with cancer--a GP guide to support services. [Review] [9 refs]. *Australian Family Physician*, 34: 365-367.
Narrative review
- Hitchins, C. R., Lawn, A., Whitehouse, G. & McFall, M. R. (2014) - The straight to test endoscopy service for suspected colorectal cancer: meeting national targets but are we meeting our patients' expectations? - *Colorectal Disease*, 16: 616-619.
Not in PICO
- Hoekstra-Weebers JE, J. J. K. W. K. E. (2001) Psychological adaptation and social support of parents of pediatric cancer patients: a prospective longitudinal study. *J Pediatr Psycho*, 26: 225-235.
Not in PICO
- Holmes, B. C. (1987) Psychological evaluation and preparation of the patient and family. *Cancer*, 60: 2021-2024.
Narrative review
- Hunt, N., Allcock, R., Sharma, A. & Myers, M. (2014) Diagnostic performance of faecal calprotectin in primary care. *Gut*, 63: A159.
Test not in PICO
- Ishibashi A. (2001) The needs of children and adolescents with cancer for information and social support. *Cancer Nursing*, 24: 61-67.
Narrative review
- Jenkins V, F. L. S. J. (2001) Information needs of patients with cancer: results from a large study in UK cancer centres. *Br J Cancer.*, 84: 48-51.
Not in PICO (population)
- Jensen, H., Topping, M. L., Larsen, M. B. & Vedsted, P. (2014) - Existing data sources for clinical epidemiology: Danish Cancer in Primary Care cohort. - *Clinical Epidemiology*, 6: 237-246.
Not in PICO
- Jensen, H., Topping, M. L., Larsen, M. B. & Vedsted, P. (2014) Existing data sources for clinical epidemiology: Danish cancer in primary care cohort. *Clinical Epidemiology*, 6: 237-246.
Duplicate
- Jiwa, M., McManus, A. & Dadich, A. (2013) The impact of knowledge, attitudes and beliefs on the engagement of primary and community-based healthcare professionals in cancer care: A literature review. *Current Medical Research and Opinion*, 29: 1475-1482.
Not in PICO
- Jones, J. M., Lewis, F. M., Griffith, K., Cheng, T., Secord, S., Walton, T., Bernstein, L. J., Maheu, C. & Catton, P. (2013) - Helping Her Heal-Group: a pilot study to evaluate a group delivered educational intervention for male spouses of women with breast cancer. - *Psycho-Oncology*, 22: 2102-2109.
Not in PICO

- Junod, A. F. (2005) [Early detection in prostate cancer and shared decision making]. [German]. *Praxis*, 94: 1525-1529.
Narrative review
- Juraskova, I., Hegedus, L., Butow, P., Smith, A. & Schofield, P. (2010) Discussing complementary therapy use with early-stage breast cancer patients: exploring the communication gap. *Integrative Cancer Therapies*, 9: 168-176.
Not in PICO
- Kahan, Z., Varga, K., Dudas, R., Nyari, T. & Thurzo, L. (2006) Collaborative/active participation per se does not decrease anxiety in breast cancer. *Pathology Oncology Research*, 12: 93-101.
Not in PICO
- Kazer, M. W., Psutka, S. P., Latini, D. M. & Bailey, D. E., Jr. (2013) - Psychosocial aspects of active surveillance. [Review]. - *Current Opinion in Urology*, 23: 273-277.
Narrative review
- Kazer, M. W., Psutka, S. P., Latini, D. M. & Bailey, J. (2013) Psychosocial aspects of active surveillance. *Current Opinion in Urology*, 23: 273-277.
Narrative review
- Keeney, S., McKenna, H., Fleming, P. & McIlpatrick, S. (2011) An exploration of public knowledge of warning signs for cancer. *European Journal of Oncology Nursing*, 15: 31-37.
Not in PICO
- Khong, T., Naik, K., Sivakumar, R. & Shah, S. (2014) United kingdom national bowel cancer awareness programme - More pain, no gain? *Gut*, 63: A241-A242.
Not in PICO
- King, E., Deutsch, L., Sinclair, S., Evans, A., Hirst, S. & Zorbas, H. (2013) Developing an optimal best practice model of care for the management of lung cancer in Australia: A national approach. *Journal of Thoracic Oncology*, 8: S1021.
Not in PICO
- Klabunde, C. N., Han, P. K., Earle, C. C., Smith, T., Ayanian, J. Z., Lee, R., Ambs, A., Rowland, J. H. & Potosky, A. L. (2013) - Physician roles in the cancer-related follow-up care of cancer survivors. - *Family Medicine*, 45: 463-474.
Not in PICO
- Knight, J. A. (2007) Change management in cancer care: a one-stop gynaecology clinic. *British Journal of Nursing*, 16: 1122-1126.
Not in PICO
- Knobf, M. T. (328) Treatment options for early stage breast cancer. [Review] [61 refs]. *Medsurg Nursing*, 3: 249-257.
Not in PICO
- Kunkel, E. J., Myers, R. E., Lartey, P. L. & Oyesanmi, O. (2000) Communicating effectively with the patient and family about treatment options for prostate cancer. *Seminars in Urologic Oncology*, 18: 233-240.
Narrative review
- Kyle, G. & Prynne, P. (2004) Guidelines for patients undergoing faecal occult blood testing. [Review] [7 refs]. *Nursing Times*, 100: 62-64.
Narrative review
- Laryionava, K., Sklenarova, H., Heussner, P., Hartmann, M. & Winkler, E. C. (2013) Quality or Length of Life? What are the preferences of patients with advanced cancer? *Onkologie*, 36: 108-109.
Not in PICO
- Letton, C., Cheung, C. & Nordin, A. (2013) - Does an enhanced recovery integrated care pathway (ICP) encourage adherence to prescribing guidelines, accelerate postoperative recovery and reduce the length of stay for gynaecological oncology patients? - *Journal of Obstetrics & Gynaecology*, 33: 296-297.
Not in PICO

Leydon G. The Information preferences of people with cancer, Final Research Report. 2001.
Not in PICO

Leydon, G. (2000) Cancer patients' information needs and information seeking behaviour: in depth interview study. *BMJ*, 320: 909-913.
Not in PICO

Liao, M. N., Chen, P. L., Chen, M. F., Chen, S. C. & Chen, Y. H. (2009) Supportive care for Taiwanese women with suspected breast cancer during the diagnostic period: effect on healthcare and support needs. *Oncology Nursing Forum*, 36: 585-592.
Not in PICO

Liao, M. N., Chen, P. L., Chen, M. F. & Chen, S. C. (2010) Effect of supportive care on the anxiety of women with suspected breast cancer. *Journal of Advanced Nursing*, 66: 49-59.
Not in PICO

Liao, M. N., Chen, P. L., Chen, M. F., Chen, S. C. & Chen, Y. H. Supportive care for Taiwanese women with suspected breast cancer during the diagnostic period: Effect on healthcare and support needs. [References]. *Oncology Nursing Forum* 36[5], 585-592. 2009.
Not in PICO

Liersch, S., Davis, H., Fox, J. & Lewis, H. (2011) National breast and ovarian cancer centre: Shared care national demonstration project at southern health. *Asia-Pacific Journal of Clinical Oncology*, 7: 137-138.
Not in PICO

Liew, Y., De, B. D. & Sansom, J. (2014) Rapid clinical review of patients assessed by a teledermatology service: Analysis of pathways and outcomes. *British Journal of Dermatology*, 171: 138.
Not in PICO

Ling, R. E., Capsomidis, A. & Patel, S. R. (2014) Identifying childhood cancer: How is the urgent suspected cancer referral pathway performing? *Archives of Disease in Childhood*, 99: A108.
Not in PICO

Livaudais, J. C., Franco, R., Fei, K. & Bickell, N. A. (2013) - Breast cancer treatment decision-making: are we asking too much of patients? - *Journal of General Internal Medicine*, 28: 630-636.
Not in PICO

Loiselle, C. G., Peters, O., Haase, K. R., Girouard, L., Korner, A., Wiljer, D. & Fitch, M. (2013) - Virtual navigation in colorectal cancer and melanoma: an exploration of patients' views. - *Supportive Care in Cancer*, 21: 2289-2296.
Not in PICO

Luschin, G. & Habersack, M. (2014) - Oral information about side effects of endocrine therapy for early breast cancer patients at initial consultation and first follow-up visit: an online survey. - *Health Communication*, 29: 421-426.
Not in PICO

Lyratzopoulos, G., Abel, G. A., McPhail, S., Neal, R. D. & Rubin, G. P. (2013) - Gender inequalities in the promptness of diagnosis of bladder and renal cancer after symptomatic presentation: evidence from secondary analysis of an English primary care audit survey. - *BMJ Open*, 3.
Not in PICO

Lyratzopoulos, G., Abel, G. A., McPhail, S., Neal, R. D. & Rubin, G. P. (2013) Gender inequalities in the promptness of diagnosis of bladder and renal cancer after symptomatic presentation: Evidence from secondary analysis of an English primary care audit survey. *BMJ Open*, 3.
Not in PICO

Macmillan Cancer Support . Improving cancer patient experience. A top tips guide. 2012.
Not in PICO (patient information material)

Macmillan Cancer Support . Cancer in the UK 2014.
<http://www.macmillan.org.uk/Documents/AboutUs/WhatWeDo/CancerintheUK2014.pdf> . 2014.
Not in PICO/Narrative review

- Madarnas, Y., Joy, A. A., Verma, S., Sehdev, S., Lam, W. & Sideris, L. (2011) Models of care for early-stage breast cancer in Canada. *Current Oncology*, 18: Suppl-9.
Not in PICO
- Malli, G. (2013) - [Early detection of prostate cancer by PSA testing: the results of a qualitative study on barriers caused by physicians in Austria implementing informed decision making]. [German]. - *Gesundheitswesen*, 75: 22-28.
Not in PICO
- Mann, G. B., Pitcher, M., Shanahan, K., Storer, L., Rio, I., Bell, B., Hookey, S., Hickey, M., Kennedy, L., Curwen-Walker, R., Vij, S., Park, A. & Bell, C. (2013) Survivorship care involving a nurse-led survivorship consultation, community support and shared care with primary practitioners. *Cancer Research*, 73.
Not in PICO
- Marengi, C., Bellardita, L., Rancati, T., Villani, D., Avuzzi, B., Nicolai, N., Villa, S., Donegani, S., Magnani, T., Bedini, N., Salvioni, R., Catania, S. & Valdagni, R. (2011) Active surveillance in patients with low-risk prostate cancer: PRIAS experience at the national cancer institute (Milan). *Anticancer Research*, 31: 1944-1945.
Not in PICO
- Marshall, T., Lancashire, R., Sharp, D., Peters, T. J., Cheng, K. K. & Hamilton, W. (2011) The diagnostic performance of scoring systems to identify symptomatic colorectal cancer compared to current referral guidance. *Gut*, 60: 1242-1248.
Not in PICO
- Martin, T. A., Moran-Kelly, R. M., Concert, C. M., Roberts, L. M., Powe, J. G., Farrell, S. N. & Singleton, J. (2013) Effectiveness of individualized survivorship care plans on quality of life of adult female breast cancer survivors: A systematic review. *JBI Database of Systematic Reviews and Implementation Reports*, 11: 258-309.
Not in PICO
- Martinez, J. A. (1111) - Exploring variations in knowledge, decision making and information inquiry among minority women with breast cancer. - *Dissertation Abstracts International Section A: Humanities and Social Sciences*, Vol.74.
Not in PICO
- Masera G, C. M. J. M. A. A. B. A. M. B. F. SIOP Working Committee on psychosocial issues in pediatric oncology: guidelines for communication of the diagnosis. *Med Pediatr Oncol*. 28[5], 382. 1997.
Guideline
- Mazur, D. J. & Hickam, D. H. (1996) Patient preferences for management of localized prostate cancer. *Western Journal of Medicine*, 165: 26-30.
Not in PICO
- Mazur, D. J., Hickam, D. H. & Mazur, M. D. (1999) How patients' preferences for risk information influence treatment choice in a case of high risk and high therapeutic uncertainty: asymptomatic localized prostate cancer. *Medical Decision Making*, 19: 394-398.
Not in PICO
- McComas, K. A., Trumbo, C. W. & Besley, J. C. (2007) Public meetings about suspected cancer clusters: the impact of voice, interactional justice, and risk perception on attendees' attitudes in six communities. *Journal of Health Communication*, 12: 527-549.
Not in PICO
- Metcalfe, A., Werrett, J., Burgess, L., Chapman, C. & Clifford, C. (2009) Cancer genetic predisposition: information needs of patients irrespective of risk level. *Familial Cancer*, 8: 403-412.
Not in PICO
- Mileshkin, L., Robins-Browne, K., Aranda, S., Marven, M., Gough, K. & Sheeran, L. (2011) A national survey of support and information needs of women with advanced breast cancer. *Asia-Pacific Journal of Clinical Oncology*, 7: 61.
Not in PICO

- Mitchell, E. D., Rubin, G. & Macleod, U. (2013) - Understanding diagnosis of lung cancer in primary care: qualitative synthesis of significant event audit reports. - *British Journal of General Practice*, 63: e37-e46.
Not in PICO
- Mohammadzadeh, N. & Safdari, R. (2014) - The intelligent clinical laboratory as a tool to increase cancer care management productivity. - *Asian Pacific Journal of Cancer Prevention: Apjcp*, 15: 2935-2937.
Narrative review
- Molassiotis, A., Wilson, B., Brunton, L. & Chandler, C. (2010) Mapping patients' experiences from initial change in health to cancer diagnosis: a qualitative exploration of patient and system factors mediating this process. *European Journal of Cancer Care*, 19: 98-109.
Not in PICO
- Mosko, J., Timmouth, J. M., Tomlinson, G. A. & Bernstein, M. (2013) Barriers to effective physician-patient communication following endoscopic procedures. *Gastrointestinal Endoscopy*, 77: AB473.
Not in PICO
- Moss, E. L., Moran, A., Reynolds, T. M. & Stokes-Lampard, H. (2013) - Views of general practitioners on the role of CA125 in primary care to diagnose ovarian cancer. - *BMC Women's Health*, 13: 8.
Not in PICO
- Mount Vernon Cancer Centre . Referral Routes and Forms. 2013.
Patient information/not study data
- Murchie, P., Raja, E. A., Brewster, D. H., Campbell, N. C., Ritchie, L. D., Robertson, R., Samuel, L., Gray, N. & Lee, A. J. (2014) - Time from first presentation in primary care to treatment of symptomatic colorectal cancer: effect on disease stage and survival. - *British Journal of Cancer*, 111: 461-469.
Not in PICO
- Myers, R. E. & Kunkel, E. J. (2000) Preparatory education for informed decision-making in prostate cancer early detection and treatment. [Review] [52 refs]. *Seminars in Urologic Oncology*, 18: 172-177.
Narrative review
- Nagler, R. H., Gray, S. W., Romantan, A., Kelly, B. J., DeMichele, A., Armstrong, K., Schwartz, J. S. & Hornik, R. C. (2010) Differences in information seeking among breast, prostate, and colorectal cancer patients: results from a population-based survey. *Patient Education & Counseling*, 81: Suppl-62.
Not in PICO
- National Guideline Clearinghouse, N. Psychosocial support and information needs. In: Suspected cancer in primary care: guidelines for investigation, referral and reducing ethnic disparities. 2004. Agency for Healthcare Research and Quality (AHRQ).
Guideline
- Ndukwe, N., Borowski, D. W., Lee, A., Orr, A., Dexter-Smith, S. & Agarwal, A. K. (2012) The two-week rule for suspected colorectal cancer: patient experience and psychological impact. *International Journal of Health Care Quality Assurance*, 25: 75-85.
Not in PICO
- Nielsen, T. N., Hansen, R. P. & Vedsted, P. (2010) [Symptom presentation in cancer patients in general practice]. [Danish]. *Ugeskrift for Laeger*, 172: 2827-2831.
Not in PICO
- O'Brien, M. A., Ellis, P. M., Whelan, T. J., Charles, C., Gafni, A., Lovrics, P., Mukherjee, S. D. & Hodgson, N. (2013) - Physician-related facilitators and barriers to patient involvement in treatment decision making in early stage breast cancer: perspectives of physicians and patients. - *Health Expectations*, 16: 373-384.
Not in PICO

- O'Conner-Von, S. (2009) Coping with cancer: a Web-based educational program for early and middle adolescents. *Journal of Pediatric Oncology Nursing*, 26: 230-241.
Not in PICO
- O'Leary, K. A., Estabrooks, C. A., Olson, K. & Cumming, C. (2007) Information acquisition for women facing surgical treatment for breast cancer: influencing factors and selected outcomes. [Review] [71 refs]. *Patient Education & Counseling*, 69: 5-19.
Not in PICO
- Obeidat, R. F. & Lally, R. M. (2014) - Health-related information exchange experiences of Jordanian women at breast cancer diagnosis. - *Journal of Cancer Education*, 29: 548-554.
Not in PICO
- Onyeka, B. A. & Martin-Hirsch, P. (2003) Information leaflets, verbal information and women's knowledge of abnormal cervical smears and colposcopy. *Journal of Obstetrics & Gynaecology*, 23: 174-176.
Not in PICO
- Orlando, L. A., Wu, R. R., Beadles, C., Himmel, T., Buchanan, A. H., Powell, K. P., Hauser, E. R., Henrich, V. C. & Ginsburg, G. S. (2014) - Implementing family health history risk stratification in primary care: impact of guideline criteria on populations and resource demand. - *American Journal of Medical Genetics, Part C, Seminars in Medical Genetics*. 166C: 24-33.
Not in PICO
- Padwick, R. T., Bajwa, A. A., Shaw, A., Leung, E., Francombe, J. & Stellakis, M. L. (2013) - The Two-Week Referral System for colorectal cancer--not fit for purpose. - *International Journal of Colorectal Disease*, 28: 1531-1534.
Not in PICO
- Pan, X. F., Fei, M. D., Zhang, K. Y., Fan, Z. L., Fu, F. H. & Fan, J. H. (2013) - Psychopathological profile of women with breast cancer based on the symptom checklist-90-R. - *Asian Pacific Journal of Cancer Prevention: Apjcp*, 14: 6579-6584.
Not in PICO
- Patient Information Forum . Making the case for information. <http://www.pifonline.org.uk/wp-content/uploads/2012/09/PIF-Case-for-Information-full-report-FINAL-Sept2013.pdf> . 2014.
Not in PICO
- Patistea E, B. (2003) Parents' perceptions of the information provided to them about their child's leukaemia. *Eur J Oncol Nurs*, 7: 172-181.
Not in PICO
- Paul, S. P., Debono, R. & Walker, D. (2013) Clinical update: recognising brain tumours early in children. *Community Practitioner*, 86: 42-45.
Narrative review
- Payne, H., Bahl, A., Mason, M., Troup, J. & De, B. J. (2012) Optimizing the care of patients with advanced prostate cancer in the UK: current challenges and future opportunities. *BJU International*, 110: 658-667.
Not in PICO
- Pieterse, A. H., Henselmans, I., de Haes, H. C., Koning, C. C., Geijsen, E. D. & Smets, E. M. (2011) Shared decision making: prostate cancer patients' appraisal of treatment alternatives and oncologists' eliciting and responding behavior, an explorative study. *Patient Education & Counseling*, 85: e251-e259.
Not in PICO
- Poon, E. G., Kachalia, A., Puopolo, A. L., Gandhi, T. K. & Studdert, D. M. (2012) Cognitive errors and logistical breakdowns contributing to missed and delayed diagnoses of breast and colorectal cancers: a process analysis of closed malpractice claims. *Journal of General Internal Medicine*, 27: 1416-1423.
Not in PICO

- Ptacek JT, E. T. Breaking bad news. A review of the literature. *JAMA* 27[6], 496--502. 1996.
Not in PICO/Narrative review
- Quin, J., Stams, V., Phelps, B., Boley, T. & Hazelrigg, S. (2010) Interest in Internet Lung Cancer Support Among Rural Cardiothoracic Patients. *Journal of Surgical Research*, 160: 35-39.
Not in PICO
- Raptis, D. A., Graf, R., Peck, J., Mouzaki, K., Patel, V., Skipworth, J., Oberkofler, C. & Boulos, P. B. (2011) Development of an electronic web-based software for the management of colorectal cancer target referral patients. *Informatics for health & social care*, 36: 117-131.
Not in PICO
- Redwood, D., Holman, L., Zandman-Zeman, S., Hunt, T., Besh, L. & Katinszky, W. (2011) Collaboration to increase colorectal cancer screening among low-income uninsured patients. *Preventing chronic disease*, 8: A69.
Not in PICO
- Rees, C. E. & Bath, P. A. (2000) The psychometric properties of the Miller Behavioural Style Scale with adult daughters of women with early breast cancer: a literature review and empirical study. *Journal of Advanced Nursing*, 32: 366-374.
Not in PICO
- Renton, J. P., Twelves, C. J. & Yuille, F. A. (2002) Follow-up in women with breast cancer: the patients' perspective. *Breast*, 11: 257-261.
Not in PICO
- Royal College of Physicians . Improving communication between doctors and patients report of a working party of the Royal College of Physicians. 1997.
Not in PICO
- Ruesch, P., Schaffert, R., Fischer, S., Feldman-Stewart, D., Ruzsat, R., Sporri, P., Zurkirchen, M. & Schmid, H.-P. (2014) Information needs of early-stage prostate cancer patients: Within- and between-group agreement of patients and health professionals. *Supportive Care in Cancer*, 22: 999-1007.
Not in PICO
- Russo, P., Szczech, L. A., Torres, G. S. & Swartz, M. D. (2013) Patient and caregiver knowledge and utilization of partial versus radical nephrectomy: Results of a national kidney foundation survey to assess educational needs of kidney cancer patients and caregivers. *American Journal of Kidney Diseases*, 61: 939-946.
Not in PICO
- Sada, Y. H., Street, R. L., Jr., Singh, H., Shada, R. E. & Naik, A. D. (2011) Primary care and communication in shared cancer care: a qualitative study. *American Journal of Managed Care*, 17: 259-265.
Not in PICO
- Salminen, E., Vire, J., Poussa, T. & Knifund, S. (2004) Unmet needs in information flow between breast cancer patients, their spouses, and physicians. *Supportive Care in Cancer*, 12: 663-668.
Not in PICO
- Savory, S., Richardson, A., Darlison, L. & Macdonald, J. (2014) A lung cancer and mesothelioma patient focus group. *Lung Cancer*, 83: S37-S38.
Not in PICO
- Schaffert, R., Ruesch, P., Gugler, R., Fischer, S., Schmid, H. P., Sporri, P., Zurkirchen, M. & Ruzsat, R. (2011) [Information needs of patients with prostate cancer. Pronounced differences between individuals after diagnosis of localised prostate carcinoma]. [German]. *Urologe (Ausg.A)*, 50: 1089-1094.
Not in PICO
- Scheel, B. I., Ingebrigtsen, S. G., Thorsen, T. & Hortedahl, K. (2013) - Cancer suspicion in general practice: the role of symptoms and patient characteristics, and their association with subsequent cancer. - *British Journal of General Practice*, 63: e627-e635.

- Not in PICO for patient information, and for S & S topics: Symptoms not linked to specific cancers, only to cancer overall
- Schichtel, M., Rose, P. W. & Sellers, C. (2013) Educational interventions for primary healthcare professionals to promote the early diagnosis of cancer: a systematic review. *Education for primary care : an official publication of the Association of Course Organisers, National Association of GP Tutors, World Organisation of Family Doctors*, 24: 274-290.
Not in PICO
- Schjolberg, T. K., Dodd, M., Henriksen, N., Asplund, K., Cvancarova, S. M. & Rustoen, T. (2014) - Effects of an educational intervention for managing fatigue in women with early stage breast cancer. - *European Journal of Oncology Nursing*, 18: 286-294.
Not in PICO
- Schou, B., I, Karesen, R., Smeby, N. A., Espe, R., Sorensen, E. M., Amundsen, M., Aas, H. & Ekeberg, O. (2014) - Effects of a psychoeducational versus a support group intervention in patients with early-stage breast cancer: results of a randomized controlled trial. - *Cancer Nursing*, 37: 198-207.
Not in PICO
- Scott JT, H. M. P. M. S. A. W. I. (2003) Interventions for improving communication with children and adolescents about their cancer. *Cochrane Database*.
Not in PICO
- Scott, S. E., Khwaja, M., Low, E. L., Weinman, J. & Grunfeld, E. A. (2012) A randomised controlled trial of a pilot intervention to encourage early presentation of oral cancer in high risk groups. *Patient Education & Counseling*, 88: 241-248.
Not in PICO
- Semple CJ, M. B. Need for appropriate written information for patients, with particular reference to head and neck cancer. *J Clin Nurs*. 11[5], 585-593. 2002.
Narrative review
- Shaffer, V. A., Owens, J. & Zikmund-Fisher, B. J. (2013) - The effect of patient narratives on information search in a web-based breast cancer decision aid: an eye-tracking study. - *Journal of Medical Internet Research*, 15: e273.
Not in PICO
- Shahmirzadi, L., Chao, E. C., Palmaer, E., Parra, M. C., Tang, S. & Gonzalez, K. D. (2014) - Patient decisions for disclosure of secondary findings among the first 200 individuals undergoing clinical diagnostic exome sequencing. - *Genetics in Medicine*, 16: 395-399.
Not in PICO
- Shapley, M., Mansell, G., Jordan, J. L. & Jordan, K. P. (2010) Positive predictive values of $\geq 5\%$ in primary care for cancer: systematic review. [Review]. *British Journal of General Practice*, 60: e366-e377.
Not in PICO
- Smith, S. G., Petrides, K. V., Green, J. S. & Sevdalis, N. (2012) The role of trait emotional intelligence in the diagnostic cancer pathway. *Supportive Care in Cancer*, 20: 2933-2939.
Not in PICO
- Smith, S. M., Murchie, P., Devereux, G., Johnston, M., Lee, A. J., Macleod, U., Nicolson, M. C., Powell, R., Ritchie, L. D., Wyke, S. & Campbell, N. C. (2012) Developing a complex intervention to reduce time to presentation with symptoms of lung cancer. *British Journal of General Practice*, 62: e605-e615.
Not in PICO
- Snow, S. L., Panton, R. L., Butler, L. J., Wilke, D. R., Rutledge, R. D., Bell, D. G. & Rendon, R. A. (2007) Incomplete and inconsistent information provided to men making decisions for treatment of early-stage prostate cancer. *Urology*, 69: 941-945.
Not in PICO

- Somov, P. & Irwin, P. (2013) Analysis of referral pathways in patients diagnosed with urological cancer. *Journal of Clinical Urology*, 6: 10-14.
Not in PICO
- Spiegel, W., Zidek, T., Karlic, H., Maier, M., Vutuc, C., Isak, K. & Micksche, M. (2010) Cancer patients' perception of information exchange between hospital-based doctors and their general practitioners. *Journal of Evaluation in Clinical Practice*, 16: 1309-1313.
Not in PICO
- Stacey, D., Legare, F., Col, N. F., Bennett, C. L., Barry, M. J., Eden, K. B., Holmes-Rovner, M., Llewellyn-Thomas, H., Lyddiatt, A., Thomsom, R., Trevena, L. & Wu, J. H. C. (2014) **Decision aids for people facing health treatment or screening decisions (Review)**. *Cochrane Database of Systematic Reviews 2014, Issue 1*. Art.No.: CD001431. DOI: 10.1002/14651858.CD001431.pub4..
Not in PICO
- Stanbridge, S. & Osborne, S. (2013) New prostate cancer diagnoses-improving timeliness of communication with patients general practitioners. *BJU International*, 112: 56.
Not in PICO
- Steginga, S. K., Pinnock, C., Jackson, C. & Gianduzzo, T. (2005) Shared decision-making and informed choice for the early detection of prostate cancer in primary care. *BJU International*, 96: 1209-1210.
Narrative review
- Step, M. M., Rose, J. H., Albert, J. M., Cheruvu, V. K. & Siminoff, L. A. (2009) Modeling patient-centered communication: oncologist relational communication and patient communication involvement in breast cancer adjuvant therapy decision-making. *Patient Education & Counseling*, 77: 369-378.
Not in PICO
- Stewart MA. Effective physician-patient communication and health outcomes: a review. *CMAJ*. 152[9], 1423-1433. 1995.
Not in PICO
- Tentzeris, V., Lake, B., Cherian, T., Milligan, J. & Sigurdsson, A. (2011) Poor awareness of symptoms of oesophageal cancer. *Interactive Cardiovascular & Thoracic Surgery*, 12: 32-34.
Not in PICO
- The University of York, N. C. f. R. a. D. Informing, communicating and sharing decisions with people who have cancer. *Effective Health*, 6. 2000.
Narrative review
- Thewes, B., Butow, P., Bell, M. L., Beith, J., Stuart-Harris, R., Grossi, M., Capp, A., Dalley, D. & FCR Study Advisory Committee (2012) Fear of cancer recurrence in young women with a history of early-stage breast cancer: a cross-sectional study of prevalence and association with health behaviours. *Supportive Care in Cancer*, 20: 2651-2659.
Not in PICO
- Thompson, J., Coleman, R., Colwell, B., Freeman, J., Greenfield, D., Holmes, K., Mathers, N. & Reed, M. (2014) - Preparing breast cancer patients for survivorship (PREP) - a pilot study of a patient-centred supportive group visit intervention. - *European Journal of Oncology Nursing*, 18: 10-16.
Not in PICO
- Thomson, H. (2000) Information needs in the early detection phase of colorectal cancer. [Review] [18 refs]. *Canadian Oncology Nursing Journal*, 10: 22-25.
Narrative review
- Thygesen, M. K., Pedersen, B. D., Kragstrup, J., Wagner, L. & Mogensen, O. (2012) Gynecological cancer patients' differentiated use of help from a nurse navigator: a qualitative study. *BMC Health Services Research*, 12: 168.
Not in PICO
- van, H. M., Ranke, G. M., van Nes, J. G., Stiggelbout, A. M., de Bock, G. H. & van de Velde, C. J. (2011) Patients' needs and preferences in routine follow-up for early breast cancer; an evaluation of the

- changing role of the nurse practitioner. *European Journal of Surgical Oncology*, 37: 765-773.
Not in PICO
- Van, M. L., Feldman-Stewart, D. & Brundage, M. D. (2006) Men considering a hypothetical treatment for prostate cancer: a comparison to patients. *Patient Education & Counseling*, 61: 33-42.
Not in PICO
- Vasen, H. F., Haites, N. E., Evans, D. G., Steel, C. M., Moller, P., Hodgson, S., Eccles, D., Morrison, P., Stoppa, L. D., Chang-Claude, J. & Caligo, M. (1998) Current policies for surveillance and management in women at risk of breast and ovarian cancer: a survey among 16 European family cancer clinics. European Familial Breast Cancer Collaborative Group. *European Journal of Cancer*, 34: 1922-1926.
Not in PICO
- Wahba, J., Cherfan, L. & Nicholas, N. (2013) Referrals to colposcopy with clinical indications-the Hillingdon experience. *BJOG: An International Journal of Obstetrics and Gynaecology*, 120: 232-233.
Not in PICO
- Wahlberg, H., Valle, P. C., Malm, S. & Broderstad, A. R. (2013) - Practical health co-operation - the impact of a referral template on quality of care and health care co-operation: study protocol for a cluster randomized controlled trial. - *Trials [Electronic Resource]*, 14: 7.
Protocol
- Walter, F., Webster, A., Scott, S. & Emery, J. (2012) The Andersen Model of Total Patient Delay: a systematic review of its application in cancer diagnosis. [Review]. *Journal of Health Services & Research Policy*, 17: 110-118.
Not in PICO
- Wang, J. H., Adams, I. F., Pasick, R. J., Gomez, S. L., Allen, L., Ma, G. X., Lee, M. X. & Huang, E. (2013) - Perceptions, expectations, and attitudes about communication with physicians among Chinese American and non-Hispanic white women with early stage breast cancer. - *Supportive Care in Cancer*, 21: 3315-3325.
Not in PICO
- Wilson, K., Lydon, A. & Amir, Z. (2013) - Follow-up care in cancer: adjusting for referral targets and extending choice. - *Health Expectations*, 16: 56-68.
Not in PICO
- Wilson, K., Lydon, A. & Amir, Z. (2013) Follow-up care in cancer: adjusting for referral targets and extending choice. *Health expectations : an international journal of public participation in health care and health policy*, 16: 56-68.
Not in PICO
- Wilt, T. J. (2002) Clarifying uncertainty regarding detection and treatment of early-stage prostate cancer. [Review] [23 refs]. *Seminars in Urologic Oncology*, 20: 10-17.
Narrative review
- Winter, J. A. (2000) Doctor, can we talk? Physician-patient communication issues that could jeopardize patient trust in the physician. *South Dakota Journal of Medicine*, 53: 273-276.
Narrative review/Not in PICO
- Xu, J., Neale, A. V., Dailey, R. K., Eggly, S. & Schwartz, K. L. (2012) Patient perspective on watchful waiting/active surveillance for localized prostate cancer. *Journal of the American Board of Family Medicine: JABFM*, 25: 763-770.
Not in PICO
- Ziebland, S., Chapple, A., Dumelow, C., Evans, J., Prinjha, S. & Rozmovits, L. (2004) How the internet affects patients' experience of cancer: a qualitative study. *BMJ*, 328: 564.
Not in PICO

SAFETY-NETTING

Review question:

What safety-netting strategies are effective in primary care for patients being monitored for suspected cancer?

Results

Literature search

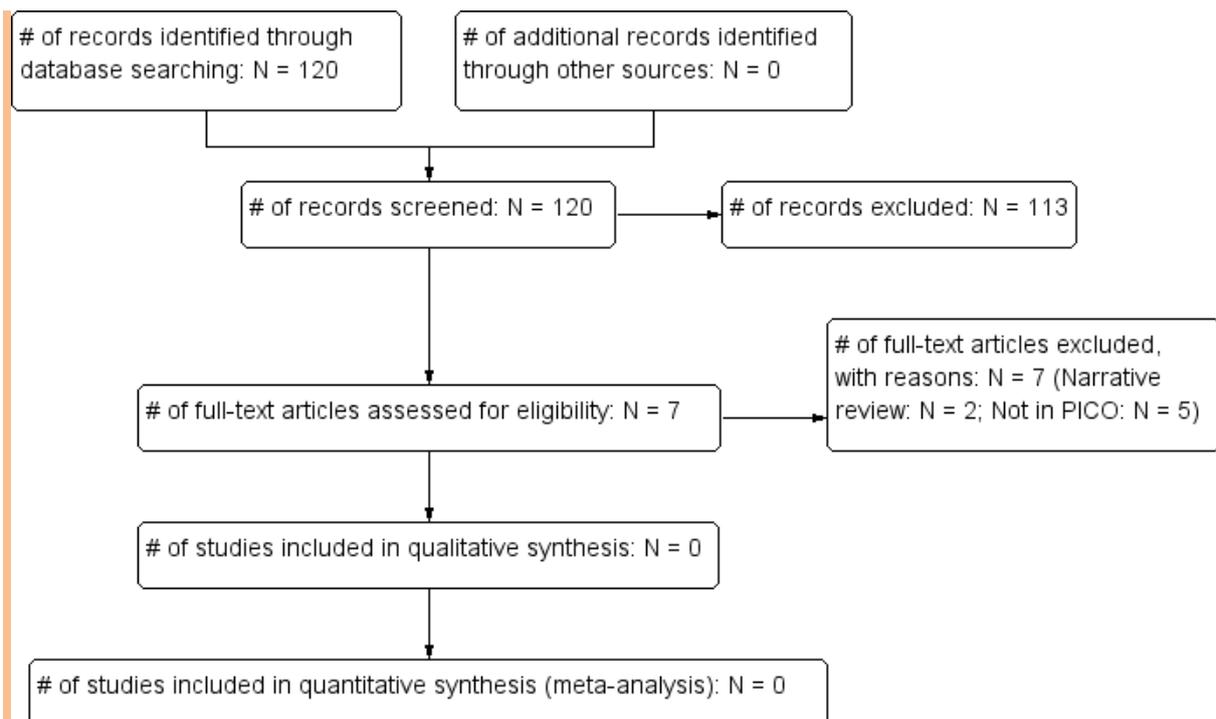
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	362	51	03/07/2013
<i>Premedline</i>	1980-2013	79	9	04/07/2013
<i>Embase</i>	1980-2013	548	21	04/07/2013
<i>Cochrane Library</i>	1980-2013	27	1	04/07/2013
<i>Psychinfo</i>	1980-2013	35	3	04/07/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	567	8	04/07/2013
<i>Websites, Cancer networks</i>			12	08/07/2013

Total References retrieved (after de-duplication): 85

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-27/08/2014	49	5	27/08/2014
<i>Premedline</i>	2013-27/08/2014	67	5	27/08/2014
<i>Embase</i>	2013-27/08/2014	98	10	27/08/2014
<i>Cochrane Library</i>	2013-27/08/2014	4	0	27/08/2014
<i>Psychinfo</i>	2013-27/08/2014	13	3	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-27/08/2014	132	24	27/08/2014
<i>Websites, Cancer networks</i>			7	27/08/2014

Total References retrieved (after de-duplication): 35



Study results

No evidence was found pertaining to the effectiveness of any safety-netting strategies in primary care for patients being monitored for suspected cancer.

References

Included studies

None

Excluded studies (with reason)

Pancreatic UK's Early Diagnosis Summit. 2012.

Not in PICO

<http://www.phc.ox.ac.uk/research/crg/primary-care-cancer-diagnostics/safety-netting-to-improve-early-diagnosis-in-primary-care>. 2014.

Narrative review/guideline

<http://www.angcn.nhs.uk/primary-care/awareness-and-early-diagnosis-primary-care-pack/safety-netting.aspx>. 2014.

Narrative review/guideline

<http://www.ncbi.nlm.nih.gov/pubmed/23818159>. 2014.

Not in PICO

http://cancer.northwestern.edu/press_releases/auto.cfm?fn=safetynet. 2014.

Not in PICO

<http://what-when-how.com/cancer-disparities/partnering-with-safety-net-primary-care-clinics-a-model-to-enhance-screening-in-low-income-populationsprinciples-challenges-and-key-lessons-cancer-disparities-part-2/>. 2014.

Not in PICO

Ahrensberg, J. M., Olesen, F., Hansen, R. P., Schroder, H. & Vedsted, P. (2013) Childhood cancer and factors related to prolonged diagnostic intervals: a Danish population-based study. *British Journal*

- of Cancer*, 108: 1280-1287.
Not in PICO
- Aizer, A. A., Paly, J. J., Zietman, A. L., Nguyen, P. L., Beard, C. J., Rao, S. K., Kaplan, I. D., Niemierko, A., Hirsch, M. S., Wu, C. L., Olumi, A. F., Michaelson, M. D., D'Amico, A. V. & Efstathiou, J. A. (2013) Models of Care and NCCN Guideline Adherence in Very-Low-Risk Prostate Cancer. *Journal of the National Comprehensive Cancer Network*, 11: 1364-1372.
Not in PICO
- Al-Hakami, H. A., Makis, W., Anand, S., Mlynarek, A., Black, M. J., Stern, J., Payne, R. J. & Hier, M. P. (2011) Head and neck incidentalomas on positron emission tomographic scanning: ignore or investigate? *Journal of Otolaryngology: Head and Neck Surgery*, 40: 384-390.
Not in PICO
- Albert, R. H. & Russell, J. J. (2009) Evaluation of the solitary pulmonary nodule. [Review] [25 refs]. *American Family Physician*, 80: 827-831.
Narrative review
- Alho, O. P., Teppo, H., Mantyselka, P. & Kantola, S. (2006) Head and neck cancer in primary care: presenting symptoms and the effect of delayed diagnosis of cancer cases. *CMAJ Canadian Medical Association Journal*, 174: 779-784.
Not in PICO
- Almond S, M. D. T. M. (2009) Diagnostic safety-netting. *Br J Gen Pract.*, 59: 872-874.
Narrative review
- Ambeba, E. & Linkov, F. (2011) Advancements in the use of blood tests for cancer screening in women at high risk for endometrial and breast cancer. [Review]. *Future Oncology*, 7: 1399-1414.
Narrative review
- Aubin, M., Giguère, A., Martin, M., Verreault, R., Fitch, M., I, Kazanjian, A. & Carmichael, P. (2012) Interventions to improve continuity of care in the follow-up of patients with cancer. *Cochrane Database of Systematic Reviews.*
Not in PICO
- Bae, J. S., Lee, J. H., Ryu, K. W., Kim, Y. W. & Bae, J. M. (2006) Characteristics of synchronous cancers in gastric cancer patients. *Cancer Research & Treatment*, 38: 25-29.
Not in PICO
- Bailey, D. E. Jr. & Wallace, M. Critical review: Is watchful waiting a viable management option for older men with prostate cancer? [References]. *American Journal of Men's Health* 1[1], 18-28. 2007.
Narrative review
- Bankhead, C. & Carl Heneghan, P. H. M. T. o. o. t. C. S. N. D. T. Safety netting to improve early cancer diagnosis in primary care: development of consensus guidelines. *Final Report*. 2011. Department of Primary Health Care University of Oxford.
Narrative review/guideline
- Barnes, A. S. (2013) Prescribing pedometers in a safety-net health system: Pilot and feasibility study results. *Journal of General Internal Medicine*, 28: S155.
Not in PICO
- Bellwood, A., Hanson, J., Gulley, K., Brain, K. & Neal, R. D. GP and practice determinants of safety netting in cancer diagnosis: findings from the International Cancer Benchmarking Partnership (ICBP) Module 3 for Wales . 2014.
Not in PICO
- Bergholdt, S. H., Hansen, D. G., Larsen, P. V., Kragstrup, J. & Sondergaard, J. (2013) - A randomised controlled trial to improve the role of the general practitioner in cancer rehabilitation: effect on patients' satisfaction with their general practitioners. - *BMJ Open*, 3.
Not in PICO
- Bertaccini, A., Giampaoli, M., Cividini, R., Gattoni, G. L., Sanseverino, R., Realfonso, T., Napodano, G., Fandella, A., Guidoni, E., Prezioso, D., Galasso, R., Cicalese, C., Scattoni, V., Armenio, A., Conti, G.,

- Corinti, M., Spasciani, R., Liguori, G., Lampropoulou, N. & Martorana, G. (2012) Observational database serenoa repens (DOSSER): overview, analysis and results. A multicentric SIUrO (Italian Society of Oncological Urology) project. *Archivio Italiano di Urologia, Andrologia*, 84: 117-122.
Not in PICO
- Bessen, T., Chen, G., Street, J., Elliott, J., Karnon, J., Keefe, D. & Ratcliffe, J. (2014) What sort of follow-up services would Australian breast cancer survivors prefer if we could no longer offer long-term specialist-based care? A discrete choice experiment. *British Journal of Cancer*, 110: 859-867.
Not in PICO
- Blanch-Hartigan, D., Forsythe, L. P., Alfano, C. M., Smith, T., Nekhlyudov, L., Ganz, P. A. & Rowland, J. H. (2014) Provision and Discussion of Survivorship Care Plans Among Cancer Survivors: Results of a Nationally Representative Survey of Oncologists and Primary Care Physicians. *Journal of Clinical Oncology*, 32: 1578-1585.
Not in PICO
- Bornhak, S., Heidemann, E., Herschlein, H. J., Simon, W., Merkle, E., Widmaier, G., Ernst, R., Greulich, M., Bittner, R., Kieninger, G., Merkle, P., Strosche, H., Karg, C., Wellhaeusser, U., Aulitzky, W., Schmidt, B., Metzger, H., Hahn, M., Stauch, A., Meisner, C., Selbmann, H. K., Regelmann, C. & Brinkmann, F. (2007) Symptom-oriented follow-up of early breast cancer is not inferior to conventional control. Results of a prospective multicentre study. *Onkologie*, 30: 443-449.
Not in PICO
- Brennan, M. E. & Houssami, N. (2006) Image-detected 'probably benign' breast lesions: A significant reason for referral from primary care. *Breast*, 15: 683-686.
Not in PICO
- Brett, T. (2001) Prostate cancer in general practice. Results of a five year prospective clinical study in one practice. *Australian Family Physician*, 30: 717-723.
Not in PICO
- Bridges, J. F., Gallego, G., Kudo, M., Okita, K., Han, K. H., Ye, S. L. & Blauvelt, B. M. (2011) Identifying and prioritizing strategies for comprehensive liver cancer control in Asia. *BMC Health Services Research*, 11: 298.
Not in PICO
- Brower, V. (2008) Watchful waiting beats androgen deprivation therapy in early prostate cancer. *Journal of the National Cancer Institute*, 100: 1494-1496.
Narrative review
- Buntinx, F., Mant, D., Van den Bruel, A., Donner-Banzhof, N. & Dinant, G. J. (2011) Dealing with low-incidence serious diseases in general practice. *British Journal of General Practice*, 61: 43-46.
Narrative review
- Calderwood, A. H., Schroy, P. C., Cabral, H. & Burgess, J. F. (2014) Predictors of adherence to post-polypectomy surveillance. *Gastroenterology*, 146: S-547.
Not in PICO
- Campion-Smith, C. Top tips for safety netting. 2013. MacMillan Cancer Support.
Ref Type: Report
Ref ID: 77
Reprint: In File
- Carpentier, M. Y., Vernon, S. W., Bartholomew, L. K., Murphy, C. C. & Bluethmann, S. M. (2013) Receipt of recommended surveillance among colorectal cancer survivors: a systematic review. *Journal of Cancer Survivorship*, 7: 464-483.
Not in PICO
- Chargari, C., Kirova, Y., Bollet, M., Sigal-Zafrani, B., Dendale, R., Rizand, P., de la Rochefordiere, A., Fourquet, A. & Campana, F. (2008) Shared responsibility for follow-up of breast cancer patients. Experience of the Institut Curie. *Bulletin du Cancer*, 95: 1047-1051.
Not in PICO

- Cheung, W. Y., Aziz, N., Noone, A. M., Rowland, J. H., Potosky, A. L., Ayanian, J. Z., Virgo, K. S., Ganz, P. A., Stefanek, M. & Earle, C. C. (2013) Physician preferences and attitudes regarding different models of cancer survivorship care: a comparison of primary care providers and oncologists. *Journal of Cancer Survivorship*, 7: 343-354.
Not in PICO
- Chin, M., Romalis, D., Doorley, S., Bymaster, A., Tsai, H., Kamal, A. & Ho, C. (2013) Colorectal cancer screening in a vulnerable population: Can providers predict who is likely to complete fecal occult blood testing? *Journal of General Internal Medicine*, 28: S45-S46.
Not in PICO
- Colt, H. G., Murgu, S. D., Korst, R. J., Slatore, C. G., Unger, M. & Quadrelli, S. (2013) Follow-up and surveillance of the patient with lung cancer after curative-intent therapy: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*, 143: Suppl-54S.
Not in PICO
- Cooperberg, M. R., Moul, J. W. & Carroll, P. R. (2005) The changing face of prostate cancer. [Review] [54 refs]. *Journal of Clinical Oncology*, 23: 8146-8151.
Narrative review
- Cowens-Alvarado, R., Sharpe, K., Pratt-Chapman, M., Willis, A., Gansler, T., Ganz, P. A., Edge, S. B., McCabe, M. S. & Stein, K. (2013) Advancing survivorship care through the National Cancer Survivorship Resource Center Developing American Cancer Society Guidelines for Primary Care Providers. *Ca-A Cancer Journal for Clinicians*, 63: 147-150.
Not in PICO
- Dalton-Fitzgerald, E., Tiro, J. A., Kandunoori, P., Yopp, A. & Singal, A. G. (2014) Primary care provider practice patterns for hepatocellular carcinoma surveillance in patients with cirrhosis. *Gastroenterology*, 146: S-998.
Not in PICO
- Dannecker, C., Strnad, V. & Hegewisch-Becker, S. (2014) Follow-up care for vulvar and vaginal cancer. *Onkologie*, 20: 355-357.
Not in PICO
- de Raaf, P. J., de Klerk, C., Timman, R., Busschbach, J. J. V., Oldenmenger, W. H. & van der Rijt, C. C. D. (2013) Systematic Monitoring and Treatment of Physical Symptoms to Alleviate Fatigue in Patients With Advanced Cancer: A Randomized Controlled Trial. *Journal of Clinical Oncology*, 31: 716-723.
Not in PICO
- Demers, R. Y., Neale, A. V., Budev, H. & Schade, W. J. (1990) Pathologist agreement in the interpretation of colorectal polyps. *American Journal of Gastroenterology*, 85: 417-421.
Not in PICO
- Devbhandari, M. P., Quennell, P., Krysiak, P., Shah, R. & Jones, M. T. (2008) Implications of a negative bronchoscopy on waiting times to treatment for lung cancer patients: results of a prospective tracking study. *European Journal of Cardio-Thoracic Surgery*, 34: 479-483.
Not in PICO
- Diefenbach, M. A., Mohamed, N. E., Butz, B. P., Bar-Chama, N., Stock, R., Cesaretti, J., Hassan, W., Samadi, D. & Hall, S. J. (2012) Acceptability and preliminary feasibility of an internet/CD-ROM-based education and decision program for early-stage prostate cancer patients: randomized pilot study. *Journal of Medical Internet Research*, 14: e6.
Not in PICO
- Dominguez-Ayala, M., Diez-Vallejo, J. & Comas-Fuentes, A. (2012) Missed opportunities in early diagnosis of symptomatic colorectal cancer. *Revista Espanola de Enfermedades Digestivas*, 104: 343-349.
Not in PICO

- Elit, L., Fyles, A. W., Oliver, T. K., Devries-Aboud, M. C., Fung-Kee-Fung, M. & members of the Gynecology Cancer Disease Site Group of Cancer Care Ontario's Program in Evidence-Based Care (2010) Follow-up for women after treatment for cervical cancer. *Current Oncology*, 17: 65-69.
Not in PICO
- Evans, D. G., Gaarenstroom, K. N., Stirling, D., Shenton, A., Maehle, L., Dorum, A., Steel, M., Lalloo, F., Apold, J., Porteous, M. E., Vasen, H. F., van Asperen, C. J. & Moller, P. (2009) Screening for familial ovarian cancer: poor survival of BRCA1/2 related cancers. *Journal of Medical Genetics*, 46: 593-597.
Not in PICO
- Evans, J., Ziebland, S. & McPherson, A. (2007) Minimizing delays in ovarian cancer diagnosis: an expansion of Andersen's model of 'total patient delay'. *Family Practice*, 24: 48-55.
Not in PICO
- Fader, A. N., Alward, E. K., Niederhauser, A., Chirico, C., Lesnock, J. L., Zwiesler, D. J., Guido, R. S., Lofgren, D. J., Gold, M. A. & Moore, K. N. (2010) Cervical dysplasia in pregnancy: a multi-institutional evaluation. *American Journal of Obstetrics & Gynecology*, 203: 113-116.
Not in PICO
- Fehniger, J., Livaudais-Toman, J., Karliner, L., Kerlikowske, K., Tice, J. A., Quinn, J., Ozanne, E. & Kaplan, C. P. (2014) Perceived versus objective breast cancer, breast cancer risk in diverse women. *Journal of Women's Health*, 23: 420-427.
Not in PICO
- Feldman-Stewart, D., Brundage, M. D., Van, M. L. & Svenson, O. (2004) Patient-focussed decision-making in early-stage prostate cancer: insights from a cognitively based decision aid. *Health Expectations*, 7: 126-141.
Not in PICO
- Fiscella, K., Humiston, S., Hendren, S., Winters, P., Idris, A., Li, S. X. L., Ford, P., Specht, R. & Marcus, S. (2011) A Multimodal Intervention to Promote Mammography and Colorectal Cancer Screening in a Safety-Net Practice. *Journal of the National Medical Association*, 103: 762-768.
Not in PICO
- Forsythe, L. P., Arora, N., Alfano, C. M., Weaver, K. E., Hamilton, A. S., Aziz, N. & Rowland, J. H. (2014) Role of oncologists and primary care physicians in providing follow-up care to non-Hodgkin lymphoma survivors within 5 years of diagnosis: a population-based study. *Supportive Care in Cancer*, 22: 1509-1517.
Not in PICO
- Friese, C. R., Martinez, K. A., Abrahamse, P., Hamilton, A. S., Graff, J. J., Jagsi, R., Griggs, J. J., Hawley, S. T. & Katz, S. J. (2014) Providers of follow-up care in a population-based sample of breast cancer survivors. *Breast Cancer Research and Treatment*, 144: 179-184.
Not in PICO
- Ganz, P. A., Yip, C. H., Gralow, J. R., Distelhorst, S. R., Albain, K. S., Andersen, B. L., Bevilacqua, J. L. B., de Azambuja, E., El Saghir, N. S., Kaur, R., McTiernan, A., Partridge, A. H., Rowland, J. H., Singh-Carlson, S., Vargo, M. M., Thompson, B. & Anderson, B. O. (2013) Supportive care after curative treatment for breast cancer (survivorship care): Resource allocations in low- and middle-income countries. A Breast Health Global Initiative 2013 consensus statement. *Breast*, 22: 606-615.
Not in PICO
- Glancy, D. G., Card, M., Sylvester, P. A., Thomas, M. G., Durdey, P., Callaway, M. & Virjee, J. (2005) Fast-track barium enema: meeting the two-week wait rule for patients with suspected colorectal cancer. *Colorectal Disease*, 7: 241-244.
Not in PICO
- Goff, B. A. (2012) Ovarian cancer: screening and early detection. *Obstetrics & Gynecology Clinics of North America*, 39: 183-194.
Narrative review

- Greater Manchester and Cheshire Cancer Network . Safety Netting Guide. 2013.
Narrative review/guideline
- Gupta, D., Mishra, S. & Bhatnagar, S. (2007) Somatization disorder, a cause of difficult pain: a case report. *American Journal of Hospice & Palliative Medicine*, 24: 219-223.
Not in PICO
- Gupta, S., Halm, E. A., Rockey, D. C., Hammons, M., Koch, M., Carter, E., Valdez, L., Tong, L., Ahn, C., Kashner, M., Argenbright, K., Tiro, J., Geng, Z., Pruitt, S. & Skinner, C. S. (2013) Comparative effectiveness of fecal immunochemical test outreach, colonoscopy outreach, and usual care for boosting colorectal cancer screening among the underserved a randomized clinical trial. *JAMA Internal Medicine*, 173: 1725-1732.
Not in PICO
- Hahn, E. E., Ganz, P. A., Melisko, M. E., Pierce, J. P., von Friederichs-Fitzwater, M., Lane, K. T. & Hiatt, R. A. (2013) Provider perceptions and expectations of breast cancer posttreatment care: a University of California Athena Breast Health Network project. *Journal of Cancer Survivorship*, 7: 323-330.
Not in PICO
- Haneuse, S., Buist, D. S., Miglioretti, D. L., Anderson, M. L., Carney, P. A., Onega, T., Geller, B. M., Kerlikowske, K., Rosenberg, R. D., Yankaskas, B. C., Elmore, J. G., Taplin, S. H., Smith, R. A. & Sickles, E. A. (2012) Mammographic interpretive volume and diagnostic mammogram interpretation performance in community practice. *Radiology*, 262: 69-79.
Not in PICO
- Heikkinen, M., Rasanen, H. & Farkkila, M. (2005) Clinical value of ultrasound in the evaluation of dyspepsia in primary health care. *Scandinavian Journal of Gastroenterology*, 40: 980-984.
Not in PICO (Patients with dyspepsia and negative endoscopy, received follow up US after 6-7 years)
- Hendren, S., Winters, P., Humiston, S., Idris, A., Li, S. X. L., Ford, P., Specht, R., Marcus, S., Mendoza, M. & Fiscella, K. (2014) Randomized, controlled trial of a multimodal intervention to improve cancer screening rates in a safety-net primary care practice. *Journal of General Internal Medicine*, 29: 41-49.
Not in PICO
- Hoekstra, J., van Duijn, N. P., Bindels, P. J. E. & Schade, E. (2002) Symptom monitoring in palliative treatment of patients with cancer; a comparative population-based study in primary and ambulatory care. *International Journal of Cancer*, 488.
Not in PICO
- Houzar, S., Dubot, C., Fridmann, S., Dagousset, I., Rousset-Jablonski, C., Callet, N., Nos, C., Villet, R., Thoury, A., Delalogue, S., Crockett, F. B. & Fourquet, A. (2014) Out-of-hospital follow-up after low risk breast cancer within a care network: 14-year results. *Breast*, 23: 407-412.
Not in PICO
- Hudson, S. V., Miller, S. M., Hemler, J., Ferrante, J. M., Lyle, J., Oeffinger, K. C. & Dipaola, R. S. (2012) Adult cancer survivors discuss follow-up in primary care: 'not what i want, but maybe what i need'. *Annals of Family Medicine*, 10: 418-427.
Not in PICO
- Isebaert, S., Van, A. C., Haustermans, K., Junius, S., Joniau, S., De, R. K. & Van, P. H. (2008) Evaluating a decision aid for patients with localized prostate cancer in clinical practice. *Urologia Internationalis*, 81: 383-388.
Not in PICO
- Jacobs, B. L., Tan, H. J., Montgomery, J. S., Weizer, A. Z., Wood, D. P., Miller, D. C., Wolf, J. S., Jr. & Hafez, K. S. (2012) Understanding criteria for surveillance of patients with a small renal mass. *Urology*, 79: 1027-1032.
Not in PICO

- James, A. S., Richardson, V., Wang, J. S., Proctor, E. K. & Colditz, G. A. (2013) Systems intervention to promote colon cancer screening in safety net settings: protocol for a community-based participatory randomized controlled trial. *Implementation Science*, 8: 58.
Protocol/Not in PICO
- Kaplan, C. P., Livaudais-Toman, J., Tice, J. A., Kerlikowske, K., Gregorich, S. E., Perez-Stable, E. J., Pasick, R. J., Chen, A., Quinn, J. & Karliner, L. S. (2014) A randomized, controlled trial to increase discussion of breast cancer in primary care. *Cancer Epidemiology Biomarkers and Prevention*, 23: 1245-1253.
Not in PICO
- Kasperzyk, J. L., Shappley, W. V., III, Kenfield, S. A., Mucci, L. A., Kurth, T., Ma, J., Stampfer, M. J. & Sanda, M. G. (2011) Watchful waiting and quality of life among prostate cancer survivors in the Physicians' Health Study. *Journal of Urology*, 186: 1862-1867.
Not in PICO
- Kazimierczak, K. A., Skea, Z. C., Dixon-Woods, M., Entwistle, V. A., Feldman-Stewart, D., N'Dow, J. M. O. & MacLennan, S. J. (2013) Provision of cancer information as a "support for navigating the knowledge landscape": Findings from a critical interpretive literature synthesis. *European Journal of Oncology Nursing*, 17: 360-369.
Not in PICO
- Kennedy, A. M., Aziz, A., Khalid, S. & Hurman, D. (2012) Do GP referral guidelines really work? Audit of an electronic urgent referral system for suspected head and neck cancer. *European Archives of Oto-Rhino-Laryngology*, 269: 1509-1512.
Not in PICO
- Kernick, D. P., Ahmed, F., Bahra, A., Dowson, A., Elrington, G., Fontebasso, M., Giffin, N. J., Lipscombe, S., MacGregor, A., Peatfield, R., Weatherby, S., Whitmarsh, T. & Goadsby, P. J. (2008) Imaging patients with suspected brain tumour: guidance for primary care. *British Journal of General Practice*, 58: 880-885.
Narrative review
- Khatcheressian, J. L., Hurley, P., Bantug, E., Esserman, L. J., Grunfeld, E., Halberg, F., Hantel, A., Henry, N. L., Muss, H. B., Smith, T. J., Vogel, V. G., Wolff, A. C., Somerfield, M. R. & Davidson, N. E. (2013) Breast Cancer Follow-Up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update. *Journal of Clinical Oncology*, 31: 961-965.
Not in PICO
- Kirchhoff, A. C., Montenegro, R. E., Warner, E. L., Wright, J., Fluchel, M., Stroup, A. M., Park, E. R. & Kinney, A. Y. (2014) Childhood cancer survivors' primary care and follow-up experiences. *Supportive Care in Cancer*, 22: 1629-1635.
Not in PICO
- Klabunde, C. N., Han, P. K., Earle, C. C., Smith, T., Ayanian, J. Z., Lee, R., Ambs, A., Rowland, J. H. & Potosky, A. L. (2013) - Physician roles in the cancer-related follow-up care of cancer survivors. - *Family Medicine*, 45: 463-474.
Not in PICO
- Kramer, J. R., Arney, J., Chen, J., Richardson, P., Duan, Z., Street, R. L., Jr., Hinojosa-Lindsey, M., Naik, A. D. & El-Serag, H. B. (2012) Patient-centered, comparative effectiveness of esophageal cancer screening: protocol for a comparative effectiveness research study to inform guidelines for evidence-based approach to screening and surveillance endoscopy. *BMC Health Services Research*, 12: 288.
Not in PICO
- Kunkel, E. J., Myers, R. E., Lartey, P. L. & Oyesanmi, O. (2000) Communicating effectively with the patient and family about treatment options for prostate cancer. *Seminars in Urologic Oncology*, 18: 233-240.
Not in PICO

- Kwast, A. B. G., Drossaert, C. H. C. & Siesling, S. (2013) - Breast cancer follow-up: From the perspective of health professionals and patients. [References]. - *European Journal of Cancer Care*, Vol.22: 754-764.
Not in PICO
- Kwon, J. H., Hui, D., Chisholm, G., Ha, C., Yennurajalingam, S., Kang, J. H. & Bruera, E. (2013) - Clinical characteristics of cancer patients referred early to supportive and palliative care. [References]. - *Journal of Palliative Medicine*, Vol.16: 148-155.
Not in PICO
- Levi, Z., Baris, H. N., Kedar, I., Niv, Y., Geller, A., Gal, E., Gingold, R., Morgenstern, S., Baruch, Y., Leach, B. H., Bronner, M. P. & Eng, C. (2011) Upper and Lower Gastrointestinal Findings in PTEN Mutation-Positive Cowden Syndrome Patients Participating in an Active Surveillance Program. *Clinical and Translational Gastroenterology*, 2: e5.
Not in PICO
- Lim, W. S., Macfarlane, J. T., Deegan, P. C., Manhire, A., Holmes, W. F. & Baldwin, D. R. (1999) How do general practitioners respond to reports of abnormal chest X-rays? *Journal of the Royal Society of Medicine*, 92: 446-449.
Not in PICO
- Loomer, L., Brockschmidt, J. K., Muss, H. B. & Saylor, G. (1991) Postoperative follow-up of patients with early breast cancer. Patterns of care among clinical oncologists and a review of the literature. [Review] [18 refs]. *Cancer*, 67: 55-60.
Not in PICO
- Luschin, G. & Habersack, M. (2014) - Oral information about side effects of endocrine therapy for early breast cancer patients at initial consultation and first follow-up visit: An online survey. - *Health Communication*, Vol.29: 421-426.
Not in PICO
- Lynch, H. T., Smyrk, T., Lynch, J., Fitzgibbons, R., Jr., Lanspa, S. & McGinn, T. (1995) Update on the differential diagnosis, surveillance and management of hereditary non-polyposis colorectal cancer. [Review] [43 refs]. *European Journal of Cancer*, 31A: 1039-1046.
Narrative review
- Maldonado, M. (2013) In the safety net: A tale of ticking clocks and tricky diagnoses. *Health Affairs*, 32: 1501-1504.
Not in PICO
- Marghoob, A. A. (146) Basal and squamous cell carcinomas. What every primary care physician should know. [Review] [20 refs]. *Postgraduate Medicine*, 102: 139-142.
Narrative review
- Mathew, A. & Desai, K. M. (2009) An audit of urology two-week wait referrals in a large teaching hospital in England. *Annals of the Royal College of Surgeons of England*, 91: 310-312.
Not in PICO
- Matro, J. M. & Goldstein, L. J. (2014) - How do I follow patients with early breast cancer after completing adjuvant therapy. - *Current Treatment Options in Oncology*, 15: 63-78.
Not in PICO
- Mccabe, M. S., Partridge, A. H., Grunfeld, E. & Hudson, M. M. (2013) Risk-Based Health Care, the Cancer Survivor, the Oncologist, and the Primary Care Physician. *Seminars in Oncology*, 40: 804-812.
Narrative review
- Meister, T., Heinzow, H. S., Woestmeyer, C., Lenz, P., Menzel, J., Kucharzik, T., Domschke, W. & Domagk, D. (2013) Intraductal ultrasound substantiates diagnostics of bile duct strictures of uncertain etiology. *World Journal of Gastroenterology*, 19: 874-881.
Not in PICO

- Mikulin, T. & Hardcastle, J. D. (1987) Gastric cancer--delay in diagnosis and its causes. *European Journal of Cancer & Clinical Oncology*, 23: 1683-1690.
Not in PICO
- Mitchell, E. Improving diagnosis of cancer A TOOLKIT FOR GENERAL PRACTICE. 2012.
Not in PICO
- Mitchell, E. D., Rubin, G. & Macleod, U. (2013) Understanding diagnosis of lung cancer in primary care: qualitative synthesis of significant event audit reports. *British Journal of General Practice*, 63: e37-e46.
Not in PICO
- Molassiotis, A., Wilson, B., Brunton, L. & Chandler, C. Mapping patients' experiences from initial change in health to cancer diagnosis: A qualitative exploration of patient and system factors mediating this process. [References]. *European Journal of Cancer Care* 19[1], 98-109. 2010.
Not in PICO
- Nekhlyudov, L. (2009) "Doc, Should I See You or My Oncologist?" A Primary Care Perspective on Opportunities and Challenges in Providing Comprehensive Care for Cancer Survivors. *Journal of Clinical Oncology*, 27: 2424-2426.
Not in PICO
- Nordin, A. J. & National Group of Gynaecology NSSG Leads (2006) Mode of detection of recurrent gynecological malignancy: Does routine follow-up delay diagnosis and treatment? *International Journal of Gynecological Cancer*, 16: 1746-1748.
Not in PICO
- O'Malley, A. S., Beaton, E., Yabroff, K. R., Abramson, R. & Mandelblatt, J. (2004) Patient and provider barriers to colorectal cancer screening in the primary care safety-net. *Preventive Medicine*, 39: 56-63.
Not in PICO
- Omeragic, F. & Ljuca, D. (2007) [Early detection of ovarian cancer in FB&H--role of family medicine]. [Bosnian]. *Medicinski Arhiv*, 61: 77-81.
Not in PICO
- Oxford University . Working with general practice on safety netting – FAQ based on the experience of cancer network GP leads. 2012.
Narrative review/guideline
- Pagh, A., Vedtofte, T., Lynggaard, C. D., Rubek, N., Lonka, M., Johansen, J., Andersen, E., Kristensen, C. A., von Buchwald, C., Andersen, M., Godballe, C., Overgaard, J. & Grau, C. (2013) The value of routine follow-up after treatment for head and neck cancer. A National Survey from DAHANCA. *Acta Oncologica*, 52: 277-284.
Not in PICO
- Payne, H. & Cornford, P. (2011) Prostate-specific antigen: an evolving role in diagnosis, monitoring, and treatment evaluation in prostate cancer. [Review]. *Urologic Oncology*, 29: 593-601.
Narrative review
- Peninsula Cancer Network . Safety-netting guidance for general practice ClearonCancer. 2012.
Narrative review/guideline
- Pingali, S. R., Jewell, S. W., Havlat, L., Bast, M. A., Thompson, J. R., Eastwood, D. C., Bartlett, N. L., Armitage, J. O., Wagner-Johnston, N. D., Vose, J. M. & Fenske, T. S. (2014) Limited Utility of Routine Surveillance Imaging for Classical Hodgkin Lymphoma Patients in First Complete Remission. *Cancer*, 120: 2122-2129.
Not in PICO
- Puglisi, F., Fontanella, C., Numico, G., Sini, V., Evangelista, L., Monetti, F., Gori, S. & Del, M. L. (2014) Follow-up of patients with early breast cancer: Is it time to rewrite the story? *Critical Reviews in Oncology/Hematology*, 91: 130-141.
Not in PICO

- Raje, D., Mukhtar, H., Oshowo, A. & Ingham, C. C. (2007) What proportion of patients referred to secondary care with iron deficiency anemia have colon cancer? *Diseases of the Colon & Rectum*, 50: 1211-1214.
Not in PICO
- Ray, P. & Kaul, V. (2008) Prevalence of high-grade squamous intraepithelial neoplasia (HiSIL) in symptomatic women referred to the colposcopy clinic with negative cytology. *Archives of Gynecology & Obstetrics*, 277: 501-504.
Not in PICO
- Reid, B. C. & Rozier, R. G. (2006) Continuity of care and early diagnosis of head and neck cancer. *Oral Oncology*, 42: 510-516.
Not in PICO
- Renton, J. P., Twelves, C. J. & Yuille, F. A. (2002) Follow-up in women with breast cancer: the patients' perspective. *Breast*, 11: 257-261.
Not in PICO
- Rojas, M. P., Telaro, E., Russo, A., Fossati, R., Confalonieri, C. & Liberati, A. (2000) Follow-up strategies for women treated for early breast cancer. [Review] [22 refs][Update in Cochrane Database Syst Rev. 2005;(1):CD001768; PMID: 15674884]. *Cochrane Database of Systematic Reviews*.(4):CD001768, 2000., CD001768.
Not in PICO
- Roorda, C., Berendsen, A. J., Groenhof, F., van der Meer, K. & de Bock, G. H. (2013) - Increased primary healthcare utilisation among women with a history of breast cancer. - *Supportive Care in Cancer*, 21: 941-949.
Not in PICO
- Roorda, C., Berendsen, A. J., Groenhof, F., van der Meer, K. & de Bock, G. H. (2013) Increased primary healthcare utilisation among women with a history of breast cancer. *Supportive Care in Cancer*, 21: 941-949.
Not in PICO
- Sabatino, S. A., Thompson, T. D., Smith, J. L., Rowland, J. H., Forsythe, L. P., Pollack, L. & Hawkins, N. A. (2013) Receipt of cancer treatment summaries and follow-up instructions among adult cancer survivors: results from a national survey. *Journal of Cancer Survivorship-Research and Practice*, 7: 32-43.
Not in PICO
- Shaw, A. G., Simpson, J., Tierney, G., Goddard, A. F., Reynolds, J. R. & Lund, J. N. (2008) Referral of patients with iron deficiency anaemia under the lower gastrointestinal two-week wait rule. *Colorectal Disease*, 10: 294-297.
Not in PICO
- Shockney, L. D. (2013) Perspectives on Surveillance and Survivorship: When to Make the Transition. *Journal of the National Comprehensive Cancer Network*, 11: 1298-1302.
Not in PICO
- Simon, M. S., Hoff, M., Hussein, M., Martino, S. & Walt, A. (1993) An evaluation of clinical follow-up in women with early stage breast cancer among physician members of the American Society of Clinical Oncology. *Breast Cancer Research & Treatment*, 27: 211-219.
Not in PICO
- Skolarus, T. A., Wolf, A. M. D., Erb, N. L., Brooks, D. D., Rivers, B. M., Underwood, W., Salner, A. L., Zelefsky, M. J., Aragon-Ching, J. B., Slovin, S. F., Wittmann, D. A., Hoyt, M. A., Sinibaldi, V. J., Chodak, G., Pratt-Chapman, M. L. & Cowens-Alvarado, R. L. (2014) American Cancer Society Prostate Cancer Survivorship Care Guidelines. *Ca-A Cancer Journal for Clinicians*, 64: 226-249.
Not in PICO
- Smith, I. E. & Schiavon, G. (2013) - Follow-up tests to detect recurrent disease: patient's reassurance or medical need?. [Review]. - *Breast*, 22 Suppl 2: S156-S160.
Not in PICO

- Stapley, S., Sharp, D. & Hamilton, W. (2006) Negative chest X-rays in primary care patients with lung cancer. *British Journal of General Practice*, 56: 570-573.
Not in PICO
- Taggart, F., Donnelly, P. & Dunn, J. (2012) Options for early breast cancer follow-up in primary and secondary care - a systematic review. *BMC Cancer*, 12: 238.
Not in PICO
- Thompson, J., Coleman, R., Colwell, B., Freeman, J., Greenfield, D., Holmes, K., Mathers, N. & Reed, M. (2014) - Preparing breast cancer patients for survivorship (PREP) - a pilot study of a patient-centred supportive group visit intervention. - *European Journal of Oncology Nursing*, 18: 10-16.
Not in PICO
- Thygesen, M. K., Pedersen, B. D., Kragstrup, J., Wagner, L. & Mogensen, O. (2012) Gynecological cancer patients' differentiated use of help from a nurse navigator: a qualitative study. *BMC Health Services Research*, 12: 168.
Not in PICO
- Tonini, G. P., Nakagawara, A. & Berthold, F. (2012) Towards a turning point of neuroblastoma therapy. [Review]. *Cancer Letters*, 326: 128-134.
Not in PICO
- van Wayenburg, C. A., Rasmussen-Conrad, E. L., van den Berg, M. G., Merks, M. A., van Staveren, W. A., van, W. C. & van Binsbergen, J. J. (2010) Weight loss in head and neck cancer patients little noticed in general practice. *Journal of Primary Health Care*, 2: 16-21.
Not in PICO
- van, H. M., van den Akker, M. E., van de Velde, C. J., Scholten, A. N. & Hille, E. T. (2012) Costs of different follow-up strategies in early breast cancer: a review of the literature. [Review]. *Breast*, 21: 693-700.
Not in PICO
- Vrooman, O. P. & Witjes, J. A. (2010) Follow-up of patients after curative bladder cancer treatment: guidelines vs. practice. *Current Opinion in Urology*, 20: 437-442.
Not in PICO
- Weight, C. J., Kim, S. P., Jacobson, D. J., McGree, M. E., Boorjian, S. A., Thompson, R. H., Leibovich, B. C., Karnes, R. J. & St, S. J. (2013) The effect of benign lower urinary tract symptoms on subsequent prostate cancer testing and diagnosis. *European Urology*, 63: 1021-1027.
Not in PICO for safety netting or prostate cancer
- Wilson, K., Lydon, A. & Amir, Z. (2013) - Follow-up care in cancer: adjusting for referral targets and extending choice. - *Health Expectations*, 16: 56-68.
Not in PICO
- Wilson, K., Lydon, A. & Amir, Z. (2013) Follow-up care in cancer: adjusting for referral targets and extending choice. *Health Expectations*, 16: 56-68.
Not in PICO for safety netting
- Wirtz, H. S., Boudreau, D. M., Gralow, J. R., Barlow, W. E., Gray, S., Bowles, E. J. & Buist, D. S. (2014) - Factors associated with long-term adherence to annual surveillance mammography among breast cancer survivors. - *Breast Cancer Research & Treatment*, 143: 541-550.
Not in PICO
- Wujcik, D. (2002) Help patients from slipping through the holes of the healthcare "safety net". *ONS News*, 17: 2.
Not in PICO
- Yorkshire Cancer Network . Safety Netting in Primary Care. 2013.
Narrative review/guideline
- Yorkshire Cancer Network . Safety-netting in primary care. 2014.
Narrative review/guideline
- Zelle, S. G., Nyarko, K. M., Bosu, W. K., Aikins, M., Niens, L. M., Lauer, J. A., Sepulveda, C. R., Hontelez, J. A. & Baltussen, R. (2012) Costs, effects and cost-effectiveness of breast cancer

control in Ghana. *Tropical Medicine & International Health*, 17: 1031-1043.
Not in PICO

LUNG AND PLEURAL CANCERS

LUNG CANCER

Review question:

What is the risk of lung cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

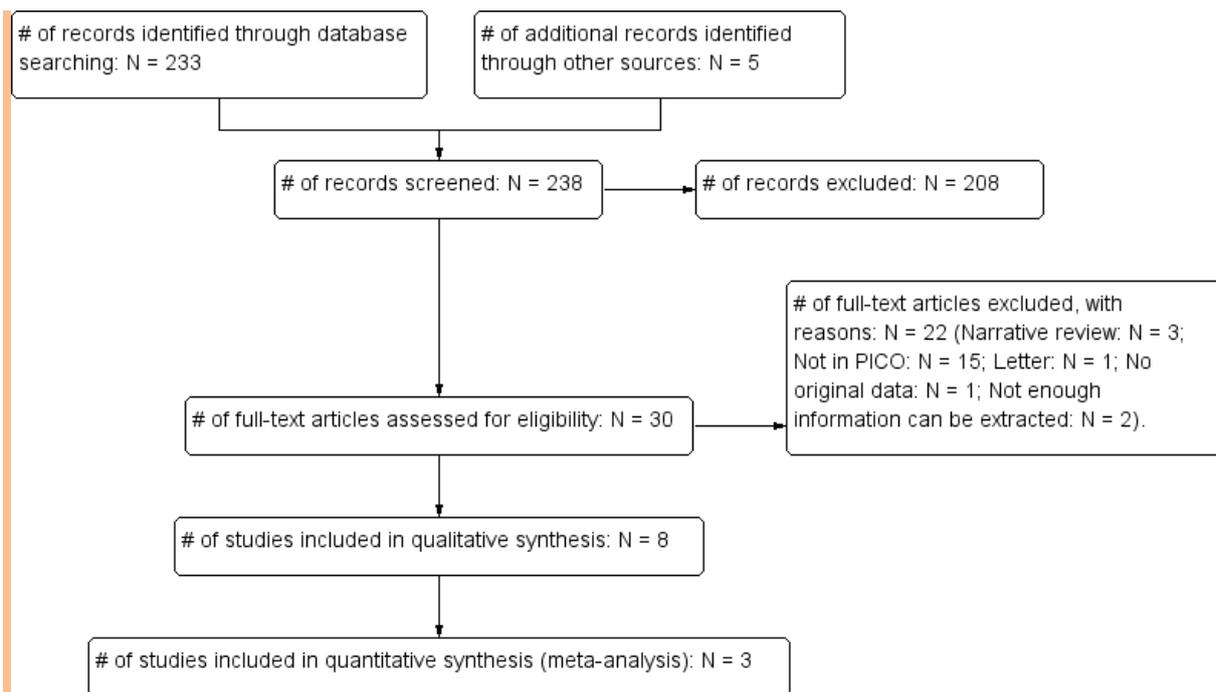
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	1520	57	06/02/2013
<i>Premedline</i>	All-2012	19	3	06/02/2013
<i>Embase</i>	All-2012	4958	100	12/02/2013
<i>Cochrane Library</i>	All-2012	419	3	12/02/2013
<i>Psychinfo</i>	All-2012	21	3	12/02/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	784	65	13/02/2013
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search

Total References retrieved (after de-duplication): 208

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-19/08/2014	109	2	19/08/2014
<i>Premedline</i>	2013-19/08/2014	195	9	19/08/2014
<i>Embase</i>	2013-19/08/2014	298	13	19/08/2014
<i>Cochrane Library</i>	2013-19/08/2014	140	0	19/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-19/08/2014	178	6	19/08/2014

Total References retrieved (after de-duplication): 25



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main bias and validity issues to note are that patient sampling was not based on a consecutive or random series of patients in a number of the studies, some of which were also not conducted in a population directly relevant to the current question. Studies employing non-consecutive/random sampling are at high risk of bias because, for example, case-control studies have been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection. Studies conducted in other settings than UK-based primary care are only applicable to the extent that the study populations and settings are comparable to a UK GP population as defined for the current purposes. Other bias and applicability threats to the results concern missing data, symptom coding and specification as well as suboptimal reference standard.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Deyo (1988)	?	+	?	+	-	+	+
Hallissey (1990)	+	+	+	+	?	+	+
Hamilton (2005)	-	+	+	+	+	+	+
Hippisley-Cox (2011)	+	+	+	-	+	+	+
Iyen-Omofoman (2013)_deri	-	+	+	+	+	+	+
Iyen-Omofoman (2013)_vali	+	+	+	+	+	+	+
Jones (2007)	+	+	+	+	+	+	+
Muris (1995)	-	+	+	+	-	-	+
Oudega (2006)	+	+	+	+	?	+	+

 High	 Unclear	 Low
---	--	--

Study results

Table 1: Lung cancer: Meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Jones (2007, at 6 months), Hippisley-Cox (2011), Iyen-Omofoman (2013)	Haemoptysis	All patients (N = 14516)	3.51 (1.61-7.5)
Jones (2007, at 3 years), Hippisley-Cox (2011), Iyen-Omofoman (2013)	Haemoptysis	All patients (N = 14516)	3.83 (1.66-8.62)

Please note that the data from Hamilton (2005) are not included in these meta-analyses due to the case-control design of the study. These data are instead reported in the second table below.

Table 2: Lung cancer: Individual positive predictive values from the meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Hippisley-Cox (2011)	Haemoptysis	All patients (N = 7861)	6.4 (5.9-7)
Iyen-Omofoman (2013)	Haemoptysis	All patients (N = 1843)	1.3 (0.9-2)
Jones (2007, at 6 months),	Haemoptysis	All patients (N =4822)	4.8 (4.2-5.5)

Jones (2007, at 3 years),	Haemoptysis	All patients (N = 4822)	6.3 (6-7)
---------------------------	-------------	-------------------------	-----------

Table 3: Lung cancer: Additional results reported by the individual papers: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Deyo (1988)	Back pain	All patients	0.05 (0.003-0.3) 1/1975
Muris (1995)	Non-acute abdominal complaints	All patients	0.2 (0.04-0.9) 2/933
Oudega (2006)	Deep vein thrombosis	All patients	0.7 (0.2-2.2) 3/430
Hallissey (1990)	Dyspepsia	All patients	0.3 (0.1-0.6) 8/2585
Jones (2007)	Haemoptysis	Men (all ages) at 6 months	5.8 (5-6.7) 169/2930
Jones (2007)	Haemoptysis	Men (all ages) at 3 years	7.5 (6.6-8.5) 220/2930
Jones (2007)	Haemoptysis	Men < 45 years at 3 years	0.21 (0.03-7.55) 9/954
Jones (2007)	Haemoptysis	Men 45-54 years at 3 years	1.65 (0.67-3.37) 7/424
Jones (2007)	Haemoptysis	Men 55-64 years at 3 years	8.37 (6.12-11.1) 43/514
Jones (2007)	Haemoptysis	Men 65-74 years at 3 years	14.86 (12-18.1) 82/552
Jones (2007)	Haemoptysis	Men 75-84 years at 3 years	17.05 (13.5-21.1) 67/393
Jones (2007)	Haemoptysis	Men ≥ 85 years at 3 years	20.43 (12.8-30.1) 19/93
Jones (2007)	Haemoptysis	Women (all ages) at 6 months	3.3 (2.6-4.3) 63/1882
Jones (2007)	Haemoptysis	Women (all ages) at 3 years	4.3 (3.4-5.3) 81/1882
Jones (2007)	Haemoptysis	Women < 45 years at 3 years	0.36 (0.04-1.3) 2/553
Jones (2007)	Haemoptysis	Women 45-54 years at 3 years	1.84 (0.6-4.24) 5/272
Jones (2007)	Haemoptysis	Women 55-64 years at 3 years	4.12 (2.32-6.71) 15/364
Jones (2007)	Haemoptysis	Women 65-74 years at 3 years	8.38 (5.73-11.8) 30/358
Jones (2007)	Haemoptysis	Women 75-84 years at 3 years	10.47 (7.01-14.9) 27/258
Jones (2007)	Haemoptysis	Women ≥ 85 years at 3 years	2.6 (0.32-9.07) 2/77
Hamilton (2005)	Haemoptysis	All patients	2.4 (1.4-4.1) Cases: 50/247 Controls: 19/1235
Hamilton (2005)	Haemoptysis	All smokers	4.5 (NR)

Hamilton (2005)	Haemoptysis (reported twice)	All patients	17 (NR)
Hamilton (2005)	Haemoptysis (reported twice)	All smokers	12 (NR)
Hamilton (2005)	Haemoptysis	Patients \geq 70 years	7.1 (NR)
Hamilton (2005)	Cough	All patients	0.4 (0.3-0.5)
Hamilton (2005)	Cough	All smokers	0.9 (NR)
Hamilton (2005)	Cough (reported twice)	All patients	0.58 (0.4-0.8)
Hamilton (2005)	Cough (reported twice)	All smokers	1.3 (NR)
Iyen-Omofoman (2013)	Haemoptysis 4-12 months prior to diagnosis	Derivation cohort	Cases: 247/12074 Controls: 125/120731
Iyen-Omofoman (2013)	Haemoptysis 13-24 months prior to diagnosis	Derivation cohort	Cases: 133/12074 Controls: 191/120731
Hamilton (2005)	Cough (reported 3 times)	All patients	0.77 (0.54-1.1)
Iyen-Omofoman (2013)	Cough	Validation cohort	0.24 (0.2-0.3) 413/175290
Iyen-Omofoman (2013)	Cough 4-12 months prior to diagnosis	Derivation cohort	Cases: 1938/12074 Controls: 7088/120731
Iyen-Omofoman (2013)	Cough 13-24 months prior to diagnosis	Derivation cohort	Cases: 1774/12074 Controls: 9087/120731
Iyen-Omofoman (2013)	Voice hoarseness	Validation cohort	0.17 (0.08-0.3) 9/5209
Iyen-Omofoman (2013)	Voice hoarseness 4-12 months prior to diagnosis	Derivation cohort	Cases: 66/12074 Controls: 219/120731
Iyen-Omofoman (2013)	Voice hoarseness 13-24 months prior to diagnosis	Derivation cohort	Cases: 56/12074 Controls: 326/120731
Hamilton (2005)	Fatigue	All patients	0.43 (0.3-0.6) Cases: 87/247 Controls: 186/1235
Hamilton (2005)	Fatigue	All smokers	0.8 (NR)
Hamilton (2005)	Fatigue (reported twice)	All patients	0.57 (0.4-0.9)
Hamilton (2005)	Fatigue (reported twice)	All smokers	1.2 (NR)
Hamilton (2005)	Dyspnoea	All patients	0.66 (0.5-0.8) Cases: 139/247 Controls: 192/1235
Hamilton (2005)	Dyspnoea	All smokers	1.2 (NR)
Hamilton (2005)	Dyspnoea (reported twice)	All patients	0.88 (NR)
Hamilton (2005)	Dyspnoea (reported twice)	All smokers	1.5 (NR)
Iyen-Omofoman (2013)	Dyspnoea	Validation cohort	0.51 (0.5-0.6) 315/61631
Iyen-Omofoman	Dyspnoea 4-12 months	Derivation cohort	Cases: 1091/12074

(2013)	prior to diagnosis		Controls: 2479/120731
Iyen-Omofoman (2013)	Dyspnoea 13-24 months prior to diagnosis	Derivation cohort	Cases: 992/12074 Controls: 3047/120731
Hamilton (2005)	Chest pain	All patients	0.82 (0.6-1.1) Cases: 100/247 Controls: 150/1235
Hamilton (2005)	Chest pain	All smokers	1.3 (NR)
Hamilton (2005)	Chest pain (reported twice)	All patients	0.95 (0.7-1.4)
Hamilton (2005)	Chest pain (reported twice)	All smokers	1.4 (NR)
Iyen-Omofoman (2013)	Chest/shoulder pain	Validation cohort	0.18 (0.15-0.21) 192/107753
Iyen-Omofoman (2013)	Chest/shoulder pain 4-12 months prior to diagnosis	Derivation cohort	Cases: 1002/12074 Controls: 4880/120731
Iyen-Omofoman (2013)	Chest/shoulder pain 13-24 months prior to diagnosis	Derivation cohort	Cases: 959/12074 Controls: 6540/120731
Hamilton (2005)	Weight loss	All patients	1.1 (0.8-1.6) Cases: 67/247 Controls: 54/1235
Hamilton (2005)	Weight loss	All smokers	2.1 (NR)
Hamilton (2005)	Weight loss (reported twice)	All patients	1.2 (0.7-2.3)
Hamilton (2005)	Weight loss (reported twice)	All smokers	1.7 (NR)
Iyen-Omofoman (2013)	Weight loss	Validation cohort	0.34 (0.23-0.5) 26/7679
Iyen-Omofoman (2013)	Weight loss 4-12 months prior to diagnosis	Derivation cohort	Cases: 197/12074 Controls: 323/120731
Iyen-Omofoman (2013)	Weight loss 13-24 months prior to diagnosis	Derivation cohort	Cases: 139/12074 Controls: 416/120731
Hamilton (2005)	Appetite loss	All patients	0.87 (0.6-1.3) Cases: 47/247 Controls: 49/1235
Hamilton (2005)	Appetite loss	All smokers	1.8 (NR)
Hamilton (2005)	Appetite loss	Patients 40-69 years	1.1 (NR)
Hamilton (2005)	Appetite loss (reported twice)	All patients	1.7 (NR)
Hamilton (2005)	Appetite loss (reported twice)	All smokers	2.7 (NR)
Iyen-Omofoman (2013)	Constipation 4-12 months prior to diagnosis	Derivation cohort	Cases: 423/12074 Controls: 1469/120731
Iyen-Omofoman (2013)	Constipation 13-24 months prior to	Derivation cohort	Cases: 421/12074 Controls:

	diagnosis		1848/120731
Hamilton (2005)	Thrombocytosis	All patients	1.6 (0.8-3.1) Cases: 34/247 Controls: 19/1235
Hamilton (2005)	Thrombocytosis	All smokers	4.2 (NR)
Hamilton (2005)	Thrombocytosis	Patients 40-69 years	3 (NR)
Hamilton (2005)	Abnormal spirometry	All patients	1.6 (0.9-2.9) Cases: 24/247 Control: 14/1235
Hamilton (2005)	Abnormal spirometry	All smokers	4 (NR)
Hamilton (2005)	Abnormal spirometry	Patients ≥ 70 years	4.1 (NR)
Hamilton (2005) also reports that the PPVs for all the variables reported for this study apart from thrombocytosis were higher for patients aged ≥ 70 years than patients aged 40-69 years. In patients aged ≥ 70 years the PPVs ranged from 0.9-2.2% apart from for haemoptysis and abnormal spirometry (see separate entry)			
Iyen-Omofoman (2013)	Depressive disorders 4-12 months prior to diagnosis	Derivation cohort	Cases: 365/12074 Controls: 3365/120731
Iyen-Omofoman (2013)	Depressive disorders 13-24 months prior to diagnosis	Derivation cohort	Cases: 449/12074 Controls: 4705/120731
Iyen-Omofoman (2013)	Upper respiratory tract infections 4-12 months prior to diagnosis	Derivation cohort	Cases: 426/12074 Controls: 3082/120731
Iyen-Omofoman (2013)	Upper respiratory tract infections 13-24 months prior to diagnosis	Derivation cohort	Cases: 497/12074 Controls: 4274/120731
Iyen-Omofoman (2013)	Lower respiratory tract infections 4-12 months prior to diagnosis	Derivation cohort	Cases: 516/12074 Controls: 1585/120731
Iyen-Omofoman (2013)	Lower respiratory tract infections 13-24 months prior to diagnosis	Derivation cohort	Cases: 566/12074 Controls: 2218/120731
Iyen-Omofoman (2013)	Non-specific chest infections 4-12 months prior to diagnosis	Derivation cohort	Cases: 1398/12074 Controls: 4350/120731
Iyen-Omofoman (2013)	Non-specific chest infections 13-24 months prior to diagnosis	Derivation cohort	Cases: 1356/12074 Controls: 5856/120731
Iyen-Omofoman (2013)	Chronic obstructive pulmonary disease 4-12 months prior to diagnosis	Derivation cohort	Cases: 978/12074 Controls: 1349/120731
Iyen-Omofoman (2013)	Chronic obstructive pulmonary disease 13-24 months prior to diagnosis	Derivation cohort	Cases: 1024/12074 Controls: 1553/120731
Iyen-Omofoman (2013)	Outcome of blood tests 4-12 months prior to diagnosis	Derivation cohort	
	No blood test record		Cases: 6406/12074

			Controls: 84997/120731
	Test without results		Cases: 5431/12074 Controls: 34295/120731
	Abnormal		Cases: 107/12074 Controls: 528/120731
	Normal		Cases: 130/12074 Controls: 911/120731
Iyen-Omofoman (2013)	Outcome of blood tests 13-24 months prior to diagnosis	Derivation cohort	
	No blood test record		Cases: 6136/12074 Controls: 79446/120731
	Test without results		Cases: 5632/12074 Controls: 39255/120731
	Abnormal		Cases: 127/12074 Controls: 752/120731
	Normal		Cases: 179/12074 Controls: 1278/120731
Iyen-Omofoman (2013)	Number of GP consultations 4-12 months prior to diagnosis	Derivation cohort	
	0-10		Cases: 4316/12074 Controls: 77720/120731
	11-20		Cases: 4373/12074 Controls: 29327/120731
	≥21		Cases: 3385/12074 Controls: 13684/120731
Iyen-Omofoman (2013)	Number of GP consultations 13-24 months prior to diagnosis	Derivation cohort	
	0-10		Cases: 3491/12074 Controls: 64881/120731
	11-20		Cases: 3492/12074 Controls: 29296/120731
	≥21		Cases: 5091/12074 Controls:

26554/120731

NR = Not reported, TP = true positives, FP = false positives. Please note the calculations of the positive predictive values differ between the studies with Deyo (1988), Hippisley-Cox (2011), Jones (2007), Iyen-Omofoman (2013), Muris (1995) and Oudega (2003) using $(TP)/(TP+FP)$ and Hamilton (2005) using Bayesian statistics due to the case-control design of this study.

Table 4: Lung cancer: Additional results reported by the individual papers: Pairs of signs/symptoms

Hippisley-Cox (2011)	Haemoptysis + current/ex-smoking	Patients \geq 40 years	9.7 (8.9-10.7)
Hamilton (2005)	Haemoptysis + cough	All patients	2 (1.1-3.5)
Hamilton (2005)	Haemoptysis + cough	All smokers	3.9 (NR)
Hamilton (2005)	Haemoptysis + fatigue	All patients	3.3 (NR)
Hamilton (2005)	Haemoptysis + fatigue	All smokers	6.1 (NR)
Hamilton (2005)	Haemoptysis + dyspnoea	All patients	4.9 (NR)
Hamilton (2005)	Haemoptysis + dyspnoea	All smokers	6.9 (NR)
Hamilton (2005)	Haemoptysis + chest pain	All patients	5 (NR)
Hamilton (2005)	Haemoptysis + chest pain	All smokers	4.1 (NR)
Hamilton (2005)	Haemoptysis + weight loss	All patients	9.2 (NR)
Hamilton (2005)	Haemoptysis + weight loss	All smokers	*
Hamilton (2005)	Haemoptysis + appetite loss	All patients	> 10 (NR)
Hamilton (2005)	Haemoptysis + appetite loss	All smokers	*
Hamilton (2005)	Haemoptysis + thrombocytosis	All patients	> 10 (NR)
Hamilton (2005)	Haemoptysis + thrombocytosis	All smokers	NR
Hamilton (2005)	Haemoptysis + abnormal spirometry	All patients	> 10 (NR)
Hamilton (2005)	Haemoptysis + abnormal spirometry	All smokers	*
Hamilton (2005)	Fatigue + cough	All patients	0.63 (0.5-0.9)
Hamilton (2005)	Fatigue + cough	All smokers	1 (NR)
Hamilton (2005)	Fatigue + dyspnoea	All patients	0.89 (0.6-?)
Hamilton (2005)	Fatigue + dyspnoea	All smokers	1.4 (NR)
Hamilton (2005)	Fatigue + chest pain	All patients	0.84 (0.5-1.3)
Hamilton (2005)	Fatigue + chest pain	All smokers	1.3 (NR)
Hamilton (2005)	Fatigue + weight loss	All patients	1 (0.6-1.7)
Hamilton (2005)	Fatigue + weight loss	All smokers	2 (NR)
Hamilton (2005)	Fatigue + appetite loss	All patients	1.2 (0.7-2.1)
Hamilton (2005)	Fatigue + appetite loss	All smokers	2.3 (NR)
Hamilton (2005)	Fatigue + thrombocytosis	All patients	1.8 (NR)
Hamilton (2005)	Fatigue +	All smokers	2.4 (NR)

	thrombocytosis		
Hamilton (2005)	Fatigue + abnormal spirometry	All patients	4 (NR)
Hamilton (2005)	Fatigue + abnormal spirometry	All smokers	>10 (NR)
Hamilton (2005)	Cough + dyspnoea	All patients	0.79 (0.6-1)
Hamilton (2005)	Cough + dyspnoea	All smokers	1.4 (NR)
Hamilton (2005)	Cough + chest pain	All patients	0.76 (0.6-1)
Hamilton (2005)	Cough + chest pain	All smokers	0.9 (NR)
Hamilton (2005)	Cough + weight loss	All patients	1.8 (1.1-2.9)
Hamilton (2005)	Cough + weight loss	All smokers	2.3 (NR)
Hamilton (2005)	Cough + appetite loss	All patients	1.6 (0.9-2.7)
Hamilton (2005)	Cough + appetite loss	All smokers	2.8 (NR)
Hamilton (2005)	Cough + thrombocytosis	All patients	2 (1.1-3.5)
Hamilton (2005)	Cough + thrombocytosis	All smokers	6.5 (NR)
Hamilton (2005)	Cough + abnormal spirometry	All patients	1.2 (0.6-2.6)
Hamilton (2005)	Cough + abnormal spirometry	All smokers	3.6 (NR)
Hamilton (2005)	Dyspnoea + chest pain	All patients	1.2 (0.9-1.8)
Hamilton (2005)	Dyspnoea + chest pain	All smokers	2.2 (NR)
Hamilton (2005)	Dyspnoea + weight loss	All patients	2 (1.2-3.8)
Hamilton (2005)	Dyspnoea + weight loss	All smokers	3.1 (NR)
Hamilton (2005)	Dyspnoea + appetite loss	All patients	2 (1.2-3.8)
Hamilton (2005)	Dyspnoea + appetite loss	All smokers	5.5 (NR)
Hamilton (2005)	Dyspnoea + thrombocytosis	All patients	2 (NR)
Hamilton (2005)	Dyspnoea + thrombocytosis	All smokers	2.4 (NR)
Hamilton (2005)	Dyspnoea + abnormal spirometry	All patients	2.3 (NR)
Hamilton (2005)	Dyspnoea + abnormal spirometry	All smokers	>10 (NR)
Hamilton (2005)	Chest pain + weight loss	All patients	1.8 (1-3.4)
Hamilton (2005)	Chest pain + weight loss	All smokers	4.4 (NR)
Hamilton (2005)	Chest pain + appetite loss	All patients	1.8 (0.9-3.9)
Hamilton (2005)	Chest pain + appetite loss	All smokers	7.6 (NR)
Hamilton (2005)	Chest pain + thrombocytosis	All patients	2 (NR)
Hamilton (2005)	Chest pain + thrombocytosis	All smokers	>10 (NR)
Hamilton (2005)	Chest pain + abnormal spirometry	All patients	1.4 (NR)
Hamilton (2005)	Chest pain + abnormal spirometry	All smokers	>10 (NR)
Hamilton (2005)	Weight loss + appetite	All patients	2.3 (1.2-4.4)

	loss		
Hamilton (2005)	Weight loss + appetite loss	All smokers	5 (NR)
Hamilton (2005)	Weight loss + thrombocytosis	All patients	6.1 (NR)
Hamilton (2005)	Weight loss + thrombocytosis	All smokers	>10 (NR)
Hamilton (2005)	Weight loss + abnormal spirometry	All patients	1.5 (NR)
Hamilton (2005)	Weight loss + abnormal spirometry	All smokers	>10 (NR)
Hamilton (2005)	Appetite loss + thrombocytosis	All patients	0.9 (NR)
Hamilton (2005)	Appetite loss + thrombocytosis	All smokers	*
Hamilton (2005)	Appetite loss + abnormal spirometry	All patients	2.7 (NR)
Hamilton (2005)	Appetite loss + abnormal spirometry	All smokers	*
Hamilton (2005)	Thrombocytosis + abnormal spirometry	All patients	3.6 (NR)
Hamilton (2005)	Thrombocytosis + abnormal spirometry	All smokers	NR

TP = true positives, FP = false positives, NR = Not reported. * "The original study was not able to calculate figures for these boxes, but they are almost certainly worthy of a red shade [2 week wait referral]", * effectively means >2%. Please note the calculations of the positive predictive values differ between the studies with Hippisley-Cox (2011) using (TP)/(TP+FP) and Hamilton (2005) using Bayesian statistics due to the case-control design of this study.

Evidence statement(s):

Haemoptysis (4 studies, N = 15998) presenting in a primary care setting is associated with overall positive predictive values of 2.4-17% for lung cancer, which tended to increase with age in men and women (1 study, N = 4822). The studies were associated with 0-1 bias or applicability concern (see also Tables 1-3).

Single symptoms other than haemoptysis presenting in a primary care setting is associated with overall positive predictive values from 0.05% (for back pain) to 1.6% (for abnormal spirometry and thrombocytosis) for lung cancer (6 studies, N = 1833698), and with positive predictive values from 0.9% (for cough) to 4.2% (for thrombocytosis) for smokers for lung cancer (1 study, N = 1482). The studies were associated with 1-3 bias or applicability concerns (see also Table 3).

Two symptoms presenting in combination in a primary care setting were associated with overall positive predictive values from 0.63% (for fatigue and cough) to > 10% (for haemoptysis with appetite loss, abnormal spirometry or thrombocytosis) for lung cancer (2 studies, N = 6030), and with positive predictive values from 0.9% (for chest pain and cough) to > 10% (for abnormal spirometry with fatigue, dyspnoea, chest pain or loss of weight, and for thrombocytosis with chest pain or loss of weight) for smokers for lung cancer (1 study, N = 1482). The studies were each associated with 1 bias concern (see also Table 4).

Evidence tables

Deyo (1988)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive? patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 1975, mean (SD; range) age = 39.5 (15.4; 15-86) years, 62% females. 54% of the patients were seeking medical care for back pain for the first time and 76% of the patients had had back pain for < 3 months. 3% had a history of back pain surgery. Maximal back pain in the low back (84%) or in the upper back (16%).</p> <p><u>Inclusion criteria:</u> Patients who sought treatment between March 1982 and September 1984 in the walk-in clinic of a public hospital where virtually all patients are self-referred. In each case back pain was part of the chief complaint.</p> <p><u>Exclusion criteria:</u> Neck pain.</p> <p><u>Clinical setting:</u> Walk-in clinic of a public hospital; this clinic is a source of primary care for indigent persons in a county in the USA with a population of approximately 1 million.</p>
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	Back pain; not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	The reference standard consisted of a search on each patient name in the institutional tumour registry ≥ 6 months after the index visit. The registry included every patient with a histological diagnosis of cancer made in the authors' hospital system regardless of site of care. The authors point out that "while this method might fail to identify cancer patients who sought care elsewhere, it is likely that most patients sought follow-up for a particular illness at the same facility.
Is the reference standard likely to correctly classify the	Unclear

target condition?	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	It is a concern that some patients with cancer might have been missed due to the choice of reference standard because this would result in an underestimation of the positive predictive value. 38/1975 patients were found in the tumour registry. Of those 38, 13 patients had tumours that were probable causes of back pain, and 4 of these 13 patients already had a diagnosis of cancer at presentation. The 9/1975 patients who had undiagnosed cancer that the back pain could be attributed to had: Lymphoma (NOS; 2), cancer of unknown primary (1), prostate cancer (1), retroperitoneal liposarcoma (1), lung cancer (1), renal cell (1), multiple myeloma (1), mucinous adenocarcinoma (of gallbladder?; 1)

Hallissey (1990)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Propective consecutive patient series from a group of 10 general practices in England.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia. <u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, England.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern

INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia of any degree
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	2659 patients were seen and 2585 attended for investigation
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), circinomatosis of unknown primary (7).
Hamilton (2005)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based matched case-control study involving all 21 general practices in Exeter, Devon, UK.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes

<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?		Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?		Yes
Could the selection of patients have introduced bias?		High risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p><u>Cases:</u> N = 247 (170 males/77 females), age at diagnosis: < 60 years: N = 35, 60-69 years: N = 60, 70-79 years: N = 118, 80+ years: N = 34.</p> <p><u>Controls:</u> N = 1235 (850 males/385 females), age at diagnosis: < 60 years: N = 178, 60-69 years: N = 310, 70-79 years: N = 575, 80+ years: N = 174.</p> <p><u>Inclusion criteria:</u> Cases: All patients aged ≥ 40 years with a primary lung cancer, diagnosed from 1998 to 2002, were identified from the cancer registry at the Royal Devon and Exeter Hospital combined with computerised searches at every practice in Devon to identify any cases missing from the cancer register. Controls: Five controls were matched to each case on sex, general practice, and age. Controls were eligible if they were alive at the time of diagnosis of their case.</p> <p><u>Exclusion criteria:</u> Cases and controls: Unobtainable records; no consultations in the 2 years before diagnosis; previous lung cancer; or residence outside Exeter at the time of diagnosis. Clinical setting: Primary care, UK.</p>	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	Anonymised photocopies of the full primary care records for 2 years before diagnosis were coded (blinded to case/control status) for all entries using the International Classification of Primary Care-2. Additional codes were created to incorporate all possible clinical features. Only variables occurring in ≥ 2.5% of cases or controls were analysed.	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference	Lung cancer diagnosis in the cancer registry at the Royal Devon and Exeter	

standard(s)	Hospital or practice notes.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All the patients are accounted for.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES		
Hippisley-Cox (2011)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>A total of 1267151 patients were identified from 189 practices (632522 males, 634629 females), mean (SD) age = 49.6 (14.8) years, mean (SD) Townsend score = -0.1 (3.6).</p> <p><u>Current symptoms and symptoms in the preceding year:</u> Current haemoptysis (N = 8010), current appetite loss (N = 6303), current weight loss (N = 17355), cough in the last year (N = 30298), dyspnoea in the last year (N = 5887), tiredness in the last year (N = 12854), hoarseness (N = 966), haemoglobin recoded in the last year (N = 189945), haemoglobin < 11 g/dl in the last year (N = 8010).</p> <p><u>Incident cases of lung cancer during the 2-year follow up period:</u> N = 2196.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ 1 year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from</p>	

	<p>patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months' registration prior to study entry. For patients with haemoptysis, appetite loss, or weight loss, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of lung cancer at baseline, and patients with a recorded 'red-flag' (see "Definition of symptom" below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of lung cancer; that is, symptoms of haemoptysis, loss of appetite, or weight loss.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Lung tract cancer during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 codes or ICD-10 diagnostic codes.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	The numbers of patients in the validation cohort reported in text/Table 5 do not correspond to those reported in Table 1, both on terms of total numbers of patients (1243329/1342329 versus 1267151) and number of patients with

	haemoptysis (7861 v 8010). The missing data does not appear to include any of the cancer cases, but it is unclear what the effect of the missing data is on the PPVs as clearly some of the false positives are missing.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	
Iyen-Omofoman (2013)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Case-control study using The Health Improvement Network (THIN) database, which had data from 446 UK general practices with a total of 8.2 million patients.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No (for derivation cohort) Yes (for validation cohort)
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk (for derivation cohort) Low risk (for validation cohort)
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> N = 12074 (7154 males/4920 females), age at diagnosis: 40-45 years: N = 95, 45-50 years: N = 220, 50-55 years: N = 469, 55-60 years: N = 896, 60-65 years: N = 1488, 65-70 years: N = 1750, 70-75 years: N = 2212, 75-80 years: N = 2305, > 80 years: N = 2639.</p> <p><u>Controls:</u> N = 120731 (58034 males/62697 females), age at diagnosis (of cases): 40-45 years: N = 18969, 45-50 years: N = 16756, 50-55 years: N = 15963, 55-60 years: N = 15439, 60-65 years: N = 13475, 65-70 years: N = 11201, 70-75 years: N = 9940, 75-80 years: N = 8191, > 80 years: N = 10797.</p> <p><u>Validation cohort:</u> N = 1826293 (886994 males/939299 females). Age: Not reported. Incident cases of lung cancer during the 1-year follow up: N = 1728.</p> <p><u>Inclusion criteria:</u> Cases: All incident cases of lung cancer diagnosed between 1 January 2000 and 28 July 2009 in patients aged ≥ 40 years. Controls: Ten randomly selected controls aged ≥ 40 years with ≥ 1 year of active records were matched to each case on general practice. Validation cohort: All THIN patients aged > 39 years, free from lung cancer on</p>

	29 July 2009, and ≥ 1 year general practice follow up. Exclusion criteria: Cases: Patients with < 1 year of active records prior to their first diagnosis of lung cancer. Clinical setting: Primary care, UK.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Cough, chest/shoulder pain, dyspnoea, weight loss, hoarseness, upper and lower respiratory tract infections, non-specific chest infections, constipation, depressive disorders, and chronic obstructive pulmonary disease (COPD), recorded over the 2-year period before lung cancer diagnosis.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Lung cancer diagnosis in THIN database
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	

Jones (2007)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective consecutive patient series using patients in the UK's General Practice Research Database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 923605 patients were identified, of whom 762325 were aged ≥ 15 years.</p> <p><u>Number of first occurrences in patients with no previous diagnosis of cancer:</u></p> <p><u>Haematuria:</u> N = 11138, mean (SD) age at first symptom = 58.5 (18.9) years. Patients excluded due to incomplete dates for their first symptom: N = 30. Sex (of final sample): 6385 males, 4723 females.</p> <p><u>Haemoptysis:</u> N = 4822, mean (SD) age at first symptom = 61.6 (18) years. Patients excluded due to incomplete dates for their first symptom: N = 10. Sex (of final sample): 2930 males, 1882 females.</p> <p><u>Dysphagia:</u> N = 6003, mean (SD) age at first symptom = 54.5 (19.4) years. Patients excluded due to incomplete dates for their first symptom: N = 4. Sex (of final sample): 2628 males, 3371 females.</p> <p><u>Rectal bleeding:</u> N = 15314, mean (SD) age at first symptom = 52.5 (18.8) years. Patients excluded due to incomplete dates for their first symptom: N = 25. Sex (of final sample): 7523 males, 7766 females.</p> <p><u>Inclusion criteria:</u> All patients from 128 general practices that provided data of a sufficient standard from 1 January 1994 to 31 December 2000 and which provided exclusively Read coded data, who were aged between 15 and 100 years, whose first ever recorded occurrence of each alarm symptom (haematuria, haemoptysis, dysphagia, or rectal bleeding) was after 31 December 1994 and who had not previously been diagnosed as having any cancer.</p> <p><u>Exclusion criteria:</u> Patients whose date of first symptom or first relevant diagnosis of cancer was before 1 January 1995 and patients with a diagnosis of any other cancer than the ones of interest before the date of the first recorded symptom or before the index cancer diagnosis date if the related symptom was not recorded.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Identification of all patients who ever had symptoms recorded for haematuria, haemoptysis, dysphagia, or rectal bleeding.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Cancer code in the UK's General Practice Research Database: <u>Haematuria</u> : Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs. <u>Haemoptysis</u> : Respiratory tract neoplasms. <u>Dysphagia</u> : Oesophageal neoplasms. <u>Rectal bleeding</u> : Colorectal neoplasms.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Diagnoses of cancer were most often made in the first three months after the onset of alarm symptoms; very few diagnoses of cancer were made later than three years after symptom onset. In the 4th and 5th years of study, the small number of observed occurrences of cancer was similar to the number expected from background incidence rates. Secondary analyses evaluating whether the incidence of neoplasms other than those prespecified was increased after the occurrence of alarm symptoms showed for: <u>Haematuria</u> : Inclusion of cancers of the reproductive organs yielded 21 additional cancers in women and 158 cancers in men, mostly cancers of the prostate. Inclusion of these cancers in the analysis would give a positive predictive value of 3.9% in women and 9.9% in men. <u>Dysphagia</u> : Inclusion of gastric cancers yielded 17 additional cancer diagnoses in women and 30 in men. Inclusion of these cancers gave positive predictive values of 5.2% in women and 6.9% in men. <i>Estimates based on the pre-specified cancers may be thus conservative for these symptoms.</i> <u>Haemoptysis</u> : Extension of the diagnostic criteria yielded 6 additional cancers. <u>Rectal bleeding</u> : Extension of the diagnostic criteria yielded 2 additional

	cancers.
Muris (1995)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 80/460 general practitioners in Limburg (The Netherlands)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 933; 335 males, 598 females; age range = 18-75, aged > 30 years: N = 712, aged > 40 years: N = 517, aged > 60 years: N = 171. <u>Inclusion criteria:</u> Patients who in 1989 consulted one of the participating GPs for new abdominal complaints lasting ≥ 2 weeks and with whom the GPs had a diagnostic problem. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> GPs in The Netherlands
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	New abdominal complaints lasting ≥ 2 weeks. Not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up for ≥ 12 months (mean = 18 months).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	

A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Other cancers diagnosed in these patients were: Stomach (2/933), pancreas (2/933), trachea/bronchus/lung (2/933), kidney (1/933), cervix (1/933), other cancer of the female genital system (2/933), and other and unspecified sites (2/933).

Oudega (2006)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective study of all primary care physicians (N = 50) within a catchment area (ca 130000 inhabitants) of a non-teaching hospital in The Netherlands.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 430; 162 males, 268 females; mean age (SD) = 60.7 (18.2) years. <u>Inclusion criteria:</u> Consecutive patients who consulted their GP between January 1996 and July 2002 and who, after investigation (not referral) was confirmed to have deep vein thrombosis. <u>Exclusion criteria:</u> Patients with a known malignancy or a malignancy detected within 2 weeks of deep vein thrombosis diagnosis. <u>Clinical setting:</u> Primary care, The Netherlands.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Deep vein thrombosis (suspicion based on painful swollen leg \leq 30 days). Patients were classified as having secondary deep vein thrombosis if \geq 1 of the following risk factors for deep vein thrombosis were present: Recent surgery, prolonged immobilisation, use of oral contraceptives or hormonal replacement therapy. If no risk factors were present patients were classified as having idiopathic deep vein thrombosis.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2 years follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 19 had cancer: 3 colorectal, 5 urogenital (not further subgrouped), 4 breast, 3 lung and 4 other. The urogenital data is added to the renal cancer evidence review.

References

Included studies

- Deyo, R. A. & Diehl, A. K. (1988) Cancer as a cause of back pain: Frequency, clinical presentation, and diagnostic strategies
185. *Journal of General Internal Medicine*, 3: 230-238.
- Hallissey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.
- Hamilton, W., Peters, T. J., Round, A. & Sharp, D. (2005) What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. *Thorax*, 60: 1059-1065.
The data split by smoking status is available from:
<http://webarchive.nationalarchives.gov.uk/20130513211237/http://www.ncat.nhs.uk/sites/default/files/work-docs/ncl%20lung%20guide.pdf>
- Hippisley-Cox, J. & Coupland, C. (2011) Identifying patients with suspected lung cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice*, 61: e715-e723.
- Iyen-Omofoman, B., Tata, L. J., Baldwin, D. R., Smith, C. J. P. & Hubbard, R. B. (2013) Using socio-demographic and early clinical features in general practice to identify people with lung cancer earlier. *Thorax*, 68, 451-9.
- Jones, R., Latinovic, R., Charlton, J. & Gulliford, M. C. (2007) Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *British Medical Journal*, 334: 1040-1044.

Muris, J. W., Starmans, R., Fijten, G. H., Crebolder, H. F., Schouten, H. J. & Knottnerus, J. A. (1995) Non-acute abdominal complaints in general practice: diagnostic value of signs and symptoms. *British Journal of General Practice*, 45: 313-316.

Oudega, R. (2006) Deep vein thrombosis in primary care: Possible malignancy? *British Journal of General Practice*, 56: 693-696.

Excluded studies (with excl reason)

Abraham, P. J., Capobianco, D. J. & Cheshire, W. P. (2003) Facial pain as the presenting symptom of lung carcinoma with normal chest radiograph. *Headache*, 43: 499-504.

Not in PICO

Ajanovic, E. & Ajanovic, E. (1995) [Symptomatology in bronchial carcinoma]. [Croatian]. *Medicinski Arhiv*, 49: 33-35.

Not in PICO

Alberg, A. J., Brock, M. V., Ford, J. G., Samet, J. M. & Spivack, S. D. (2013) Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American college of chest physicians evidence-based clinical practice guidelines. *Chest*, 143: e1S-e29S.

Narrative review

Albert, R. H. R. (2009) Evaluation of the solitary pulmonary nodule. *American Family Physician*, 80: 827-831+834.

Narrative review

Ali, M. H. B. (2011) Do we need a "two week rule" referral pathway for lung cancer? *Thorax*, Conference: December.

Not in PICO

Allgar, V. L. & Neal, R. D. (2005) Delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS Patients: Cancer. *British Journal of Cancer*, 92: 1959-1970.

Not in PICO

Allgar, V. L., Neal, R. D., Ali, N., Leese, B., Heywood, P., Proctor, G. & Evans, J. (2006) Urgent GP referrals for suspected lung, colorectal, prostate and ovarian cancer. *British Journal of General Practice*, 56: 355-362.

Not in PICO

Alpert, J. B., Fantauzzi, J. P., Melamud, K., Greenwood, H., Naidich, D. P., Ko, J. P., Alpert, J. B., Fantauzzi, J. P., Melamud, K., Greenwood, H., Naidich, D. P. & Ko, J. P. (2012) Clinical significance of lung nodules reported on abdominal CT. *AJR, American Journal of Roentgenology*. 198: 793-799.

Not in PICO

Alwan, Y. (2010) Lung cancer and delay in diagnosis. *Lung Cancer*, Conference: Conference.

Not in PICO

Antler, A. S., Ough, Y., Pitchumoni, C. S., Davidian, M., Thelmo, W., Antler, A. S., Ough, Y., Pitchumoni, C. S., Davidian, M. & Thelmo, W. (1982) Gastrointestinal metastases from malignant tumors of the lung. *Cancer*, 49: 170-172.

Not in PICO

Aoe, K. (2003) Gingival Metastasis as Initial Presentation of Small Cell Carcinoma of the Lung. *Anticancer Research*, 23: 4187-4189.

Not in PICO

Arenberg, D. A. (2004) Evaluating the patient with suspected lung cancer. *Journal of Respiratory Diseases*, 25: 266-272.

Narrative review

Balbo, P. E., Bodini, B. D., Patrucco, F., Della, C. F., Zanaboni, S., Bagnati, P., Andorno, S. & Magnani, C. (2013) Electromagnetic navigation bronchoscopy and rapid on site evaluation added to fluoroscopy-guided assisted bronchoscopy and rapid on site evaluation: improved yield in

- pulmonary nodules. *Minerva Chirurgica*, 68: 579-585.
Not in PICO
- Barchuk, A. S. L. (1987) Bronchoscopy in the outpatient examination of patients. *Voprosy Onkologii*, 33: 75-78.
Paper in Russian. Unclear whether relevant, but unlikely based on the short abstract there available in English.
- Barnard, S. (2009) Delays in the lung cancer pathway in South Auckland - And author response. *New Zealand Medical Journal*, 122: 88-89.
Not in PICO
- Barraclough, K. (2010) The predictive value of cancer symptoms in primary care. *British Journal of General Practice*, 60: 639-640.
Narrative review
- Barrett, J. & Hamilton, W. (2008) Pathways to the diagnosis of lung cancer in the UK: a cohort study. *BMC Family Practice*, 9.
Not in PICO
- Baughan, P. (2009) Auditing the diagnosis of cancer in primary care: The experience in Scotland. *British Journal of Cancer*, 101: S87-S91.
Not in PICO
- Baughan, P., Keatings, J., O'Neill, B., Baughan, P., Keatings, J. & O'Neill, B. (2011) Urgent suspected cancer referrals from general practice: audit of compliance with guidelines and referral outcomes. *British Journal of General Practice*, 61: e700-e706.
Not in PICO
- Beaune, D. & Caron, R. (2006) Lung cancer and delay with consultations associated with the precariousness in the north and the region of Pas de Calais. [French]. [References]. *Revue Francophone de Psycho-Oncologie*, 5: 109-114.
Not in PICO
- Bechtel, J. J., Kelley, W. A., Coons, T. A., Mohler, P., Mohler, A., James, D. & Petty, T. L. (2009) Five-year outcome of lung cancer detection in patients with and without airflow obstruction in a primary care outpatient practice. *Journal of Thoracic Oncology*, 4: 1347-1351.
Not in PICO
- Bellamy, D., Peake, M. & Williams, A. (2013) The role of primary care as part of the multidisciplinary team (MDT) in the management of lung cancer: the "Dream MDT" report - new guidance from the UK Lung Cancer Coalition. *Primary Care Respiratory Journal*, 22: 3-4.
Not in PICO
- Bidwell, J. L. & Pachner, R. W. (2005) Hemoptysis: Diagnosis and management. *American Family Physician*, 72: 1253-1260.
Narrative review
- Bjerager, M., Palshof, T., Dahl, R., Vedsted, P., Olesen, F., Bjerager, M., Palshof, T., Dahl, R., Vedsted, P. & Olesen, F. (2006) Delay in diagnosis of lung cancer in general practice. *British Journal of General Practice*, 56: 863-868.
Not in PICO
- Bodh, A., Kaushal, V., Kashyap, S. & Gulati, A. (2013) Cytohistological correlation in diagnosis of lung tumors by using fiberoptic bronchoscopy: Study of 200 cases. *Indian Journal of Pathology and Microbiology*, 56: 84-88.
Not in PICO
- Booth, S. (2003) Breathlessness in cancer and chronic obstructive pulmonary disease: using a qualitative approach to describe the experience of patients and carers. *Palliative & supportive care*, 1: 337-344.
Not in PICO

- Bowen, E. F. R. (2002) Patient and GP led delays in the recognition of symptoms suggestive of lung cancer [1]. *Lung Cancer*, 37: 227-228.
Not in PICO
- Brindle, L., Pope, C., Corner, J., Leydon, G. & Banerjee, A. (2012) Eliciting symptoms interpreted as normal by patients with early-stage lung cancer: could GP elicitation of normalised symptoms reduce delay in diagnosis? Cross-sectional interview study. *BMJ Open*, 2.
Not in PICO
- Brocken, P., Kiers, B. A. B., Looijen-Salamon, M. G., Dekhuijzen, P. N. R., Smits-van der Graaf, C., Peters-Bax, L., de Geus-Oei, L. F. & van der Heijden, H. F. M. (2012) Timeliness of lung cancer diagnosis and treatment in a rapid outpatient diagnostic program with combined (18)FDG-PET and contrast enhanced CT scanning. *Lung Cancer*, 75: 336-341.
Not in PICO
- Brocken, P., van der Heijden, H. F., Dekhuijzen, P. N., Peters-Bax, L. & de Geus-Oei, L. F. (2014) High Performance of F-Fluorodeoxyglucose Positron Emission Tomography and Contrast-Enhanced CT in a Rapid Outpatient Diagnostic Program for Patients with Suspected Lung Cancer. *Respiration*, 87: 32-37.
Not in PICO
- Bruno, P., Ricci, A., Esposito, M. C., Scozzi, D., Tabbi, L., Sposato, B., Falasca, C., Giarnieri, E., Giovagnoli, M. R. & Mariotta, S. (2013) Efficacy and cost effectiveness of rapid on site examination (ROSE) in management of patients with mediastinal lymphadenopathies. *European Review for Medical & Pharmacological Sciences*, 17: 1517-1522.
Not in PICO
- Buccheri, G. (2004) Lung cancer: Clinical presentation and specialist referral time. *European Respiratory Journal*, 24: 898-904.
Not in PICO
- Bugalho, A., Ferreira, D., Eberhardt, R., Dias, S. S., Videira, P. A., Herth, F. J. & Carreiro, L. (2013) Diagnostic value of endobronchial and endoscopic ultrasound-guided fine needle aspiration for accessible lung cancer lesions after non-diagnostic conventional techniques: a prospective study. *BMC Cancer*, 13: 130.
Not in PICO
- Campbell, J. H. R. (1991) Symptomatic hypercalcaemia in lung cancer. *Respiratory Medicine*, 85: 223-227.
Not in PICO
- Campos-Santiago, Z. (2012) An unusual presentation of pulmonary nocardiosis. *Infectious Diseases in Clinical Practice*, 20: 213-215.
Not in PICO
- Capell, S., Comas, P., Piella, T., Rigau, J., Pruna, X., Martiinez, F. & Montull, S. (2004) Quick and early diagnostic outpatient unit: an effective and efficient assistential model. Five years experience. *Medicina Clinica*, 123: 247-250.
Not in PICO
- Carlsson, L., Hakansson, A. & Nordenskjold, B. (2001) Common cancer-related symptoms among GP patients - Opportunistic screening in primary health care. *Scandinavian Journal of Primary Health Care*, 19: 199-203.
Not in PICO
- Carpenter, L., Beral, V., Strachan, D., Ebi-Kryston, K. L., Inskip, H., Carpenter, L., Beral, V., Strachan, D., Ebi-Kryston, K. L. & Inskip, H. (1989) Respiratory symptoms as predictors of 27 year mortality in a representative sample of British adults. *BMJ*, 299: 357-361.
Not in PICO
- Chakraborty, S. P., Jones, K. M. & Mazza, D. (2014) Adapting lung cancer symptom investigation and referral guidelines for general practitioners in Australia: Reflections on the utility of the ADAPTE

- framework. *Journal of Evaluation in Clinical Practice*, 20: 129-135.
Not in PICO
- Chandra, S., Mohan, A., Guleria, R., Singh, V. & Yadav, P. (2009) Delays during the Diagnostic Evaluation and Treatment of Lung Cancer. *Asian Pacific Journal of Cancer Prevention*, 10: 453-456.
Not in PICO
- Chatwin, J., Kennedy, A., Firth, A., Povey, A., Rogers, A. & Sanders, C. (2014) How potentially serious symptom changes are talked about and managed in COPD clinical review consultations: A micro-analysis. *Social Science & Medicine*, 113: 120-136.
Not in PICO
- Christiaans, M. H., Kelder, J. C., Arnoldus, E. P., Tijssen, C. C., Christiaans, M. H., Kelder, J. C., Arnoldus, E. P. J. & Tijssen, C. C. (2002) Prediction of intracranial metastases in cancer patients with headache. *Cancer*, 94: 2063-2068.
Not in PICO
- Colice, G. L. (2009) Haemoptysis with a normal chest radiograph: How concerned should we be? *Thorax*, 64: 829-830.
Narrative review
- Connolly, G. C., Menapace, L., Safadjou, S., Francis, C. W. & Khorana, A. A. (2013) Prevalence and clinical significance of incidental and clinically suspected venous thromboembolism in lung cancer patients. *Clinical Lung Cancer*, 14: 713-718.
Not in PICO
- Cooley, M. E., Lobach, D. F., Johns, E., Halpenny, B., Saunders, T. A., Del, F. G., Rabin, M. S., Calarese, P., Berenbaum, I. L., Zaner, K., Finn, K., Berry, D. L. & Abrahm, J. L. (2013) Creating computable algorithms for symptom management in an outpatient thoracic oncology setting. *Journal of Pain & Symptom Management*, 46: 911-924.
Not in PICO
- Cooper, S. J. & Mandal, S. (2011) Gp Education of the Early Symptoms of Lung Cancer: Does It Improve Our Earlier Diagnosis Or Staging of Lung Cancer? *Thorax*, 66: A130-A131.
Not in PICO
- Corner, J., Hopkinson, J., Fitzsimmons, D., Barclay, S. & Muers, M. (2005) Is late diagnosis of lung cancer inevitable? Interview study of patients' recollections of symptoms before diagnosis. *Thorax*, 60: 314-319.
Not in PICO
- Corner, J. & Brindle, L. (2011) The influence of social processes on the timing of cancer diagnosis: a research agenda. *Journal of Epidemiology and Community Health*, 65: 477-482.
Not in PICO
- Cortes Sancho, R. (2003) Diagnostic and therapeutic attitude in patient with hemoptysis. *MEDIFAM - Revista de Medicina Familiar y Comunitaria*, 13: 258-264.
Narrative review
- Costa, G. (1980) Weight loss and cachexia in lung cancer. *Nutrition and Cancer*, 2: 98-103.
Not in PICO
- Currow, D. C., Plummer, J. L., Crockett, A., Cert, G. & Abernethy, A. P. (2009) A Community Population Survey of Prevalence and Severity of Dyspnea in Adults. *Journal of Pain and Symptom Management*, 38: 533-545.
Not in PICO
- Dalton, S. O., Frederiksen, B. L., Jacobsen, E., Steding-Jessen, M., Osterlind, K., Schuz, J., Osler, M. & Johansen, C. (2011) Socioeconomic position, stage of lung cancer and time between referral and diagnosis in Denmark, 2001-2008. *British Journal of Cancer*, 105: 1042-1048.
Not in PICO
- Damron, T. A., Heiner, J., Damron, T. A. & Heiner, J. (2000) Distant soft tissue metastases: a series of 30 new patients and 91 cases from the literature. [Review] [55 refs]. *Annals of Surgical Oncology*,

7: 526-534.

Not in PICO

Darwiche, K., Zarogoulidis, P., Krauss, L., Oezkan, F., Walter, R. F., Werner, R., Theegarten, D., Sakkas, L., Sakkas, A., Hohenforst-Schmidt, W., Zarogoulidis, K. & Freitag, L. (2013) "One-stop shop" spectral imaging for rapid on-site diagnosis of lung cancer: a future concept in nano-oncology. *International Journal of Nanomedicine*, 8: 4533-4542.

Not in PICO

Davies, C. (2012) A breathlessness aid simple helpful hints for patients. *Lung Cancer*, Conference: January.

Not in PICO

de Torres, J. P., Marin, J. M., Casanova, C., Cote, C., Carrizo, S., Cordoba-Lanus, E., Baz-Davila, R., Zulueta, J. J., Aguirre-Jaime, A., Saetta, M., Cosio, M. G. & Celli, B. R. (2011) Lung Cancer in Patients with Chronic Obstructive Pulmonary Disease Incidence and Predicting Factors. *American Journal of Respiratory and Critical Care Medicine*, 184: 913-919.

Not in PICO

De, F. D., Turner, R. D. & Rogers, T. K. (2013) Evaluation of an expedited referral pathway for suspected lung cancer. *Lung Cancer*, 79: S18-S19.

Not in PICO

Demetriou, J., Demetriou, G. J., Demetriou, J. & Demetriou, G. J. (2008) Lung cancer metastasis to the scapula and spine: a case report. *Chiropractic & Osteopathy [Electronic Resource]*, 16: 8.

Not in PICO

Dodds, W. (2004) Implementing the 2-week wait rule for cancer referral in the UK: General practitioners' views and practices. *European Journal of Cancer Care*, 13: 82-87.

Not in PICO

Dong, X., Qiu, X., Liu, Q. & Jia, J. (2013) Endobronchial ultrasound-guided transbronchial needle aspiration in the mediastinal staging of non-small cell lung cancer: a meta-analysis. *Annals of Thoracic Surgery*, 96: 1502-1507.

Not in PICO

Dregan, A., Moller, H., Murray-Thomas, T. & Gulliford, M. C. (2012) Validity of cancer diagnosis in a primary care database compared with linked cancer registrations in England. Population-based cohort study. *Cancer Epidemiology*, 36: 425-429.

Not in PICO

Dregan, A., Moller, H., Charlton, J. & Gulliford, M. C. (2013) Are alarm symptoms predictive of cancer survival? Population-based cohort study. *British Journal of General Practice*, 63: E807-E812.

Duplicate

Dregan, A., Moller, H., Charlton, J. & Gulliford, M. C. (2013) Are alarm symptoms predictive of cancer survival? Population-based cohort study. *British Journal of General Practice*, 63: e807-e812.

Not in PICO

Dunn, M. (1997) Unilateral pulmonary edema: When to suspect, what to do. *Journal of Respiratory Diseases*, 18: 657-666.

Narrative review

El Ouazzani, H., Menchafou, I., Achachi, L., El Ftouh, M. & Fihry, M. T. E. (2010) Delay in the diagnosis of primary bronchial cancer. Study carried out in the pneumology unit of Ibn Sina university hospital, Rabat (Morocco). *Revue de Pneumologie Clinique*, 66: 335-341.

Not in PICO

Eremeishvili, K. (2011) Timeliness of referral of patients with abnormal chest X-ray suggestive of lung cancer. *European Journal of Cancer*, Conference: September.

Not in PICO

Evison, M., Crosbie, P., Martin, J., Barber, P. & Booton, R. (2013) EBUS-TBNA in the diagnosis of non-primary lung cancers. *Lung Cancer*, 79: S24.

Not in PICO

- Ezzie, M. E., Janssen, W. J., O'Brien, J. M., Fox, C. C. & Schwarz, M. I. (2008) Clinical problem-solving. Failure to respond--a 52-year-old man presented to his primary care physician with dyspnea and cough. *New England Journal of Medicine*, 358: 70-74.
Not in PICO
- Fox, R. (2007) Alarm symptoms in primary care. *British Medical Journal*, 334: 1013-1014.
Narrative review
- Fuchs, F. S., Zirlik, S., Hildner, K., Schubert, J., Vieth, M. & Neurath, M. F. (2013) Confocal laser endomicroscopy for diagnosing lung cancer in vivo. *European Respiratory Journal*, 41: 1401-1408.
Not in PICO
- Geraghty, C. B. O. (2011) Time is vital: Exploring delays in referral to a rapid access lung cancer clinic. *Irish Journal of Medical Science*, Conference: November.
Not in PICO
- Gilbert, R., Franks, G., Watkin, S., Gilbert, R., Franks, G. & Watkin, S. (2005) The proportion of general practitioner referrals to a hospital Respiratory Medicine clinic suitable to be seen in a GPWSI Respiratory Clinic. *Primary Care Respiratory Journal*, 14: 314-319.
Not in PICO
- Girolami, A., Prandoni, P., Zanon, E., Bagatella, P., Girolami, B., Girolami, A., Prandoni, P., Zanon, E., Bagatella, P. & Girolami, B. (1999) Venous thromboses of upper limbs are more frequently associated with occult cancer as compared with those of lower limbs. *Blood Coagulation & Fibrinolysis*, 10: 455-457.
Not in PICO (referred patients)
- Godden, D. J. K. (2011) Rational development of telehealth to support primary care respiratory medicine: Patient distribution and organisational factors. *Primary Care Respiratory Journal*, 20: 415-420.
Not in PICO
- Gonzalez-Barcala, F. J., Falagan, J. A., Garcia-Prim, J. M., Valdes, L., Carreira, J. M., Pose, A., Canive, J. C., Anton, D., Garcia-Sanz, M. T., Puga, A., Temes, E. & Lopez-Lopes, R. (2014) - Symptoms and reason for a medical visit in lung cancer patients. - *Acta Medica Portuguesa*, 27: 318-324.
Not in PICO
- Gonzalez, J. M., de Castro, F. J., Barrueco, M., Cordovilla, R., Fernandez, J. L., Gomez, F. P., de Vega, B. M., Ramos, J. & Serrano, A. R. (2003) Delays in the diagnosis of lung cancer. *Archivos de Bronconeumologia*, 39: 437-441.
Not in PICO
- Gruning, W., Ammenwerth, W., Wurps, H., Kollmeier, J., Blum, T., Schonfeld, N., Griff, S. & Bauer, T. T. (2013) [Diagnostic yield and safety of bronchoscopic cryotechnique in routine diagnostics for suspected lung cancer]. [German]. *Pneumologie*, 67: 676-682.
Not in PICO
- Haidl, P., Kohler, D., Haidl, P. & Kohler, D. (2007) [How much pulmonary diagnostics does the family physician need?]. [Review] [0 refs] [German]. *MMW Fortschritte der Medizin*, 149: 28-31.
Narrative review
- Hamilton, W. & Sharp, D. (2004) Diagnosis of lung cancer in primary care: a structured review. [Review] [83 refs]. *Family Practice*, 21: 605-611.
Narrative review
- Hamilton, W. (2009) The CAPER studies: five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients. *British Journal of Cancer*, 101: S80-S86.
Narrative review
- Hamilton, W. (2009) Five misconceptions in cancer diagnosis. *British Journal of General Practice*, 59: 441-447.
Narrative review

- Hamilton, W. (2010) Cancer diagnosis in primary care. *British Journal of General Practice*, 60: 121-128.
Narrative review
- Hansen, R. P., Vedsted, P., Sokolowski, I., Sondergaard, J. & Olesen, F. (2011) Time intervals from first symptom to treatment of cancer: a cohort study of 2,212 newly diagnosed cancer patients. *Bmc Health Services Research*, 11.
Not in PICO
- Harkness, H. (2012) Downgrading red flag referrals for lung cancer. *Lung Cancer*, Conference: January.
Not in PICO
- Harris, J. (2012) The Colchester fast-track chest X-ray referral pathway. *Lung Cancer*, Conference: January.
Not in PICO
- Herth, F., Ernst, A. & Becker, H. D. (2001) Long-term outcome and lung cancer incidence in patients with hemoptysis of unknown origin. *Chest*, 120: 1592-1594.
Not in PICO
- Hill, K. M., Amir, Z., Muers, M. F., Connolly, C. K. & Round, C. E. (2003) Do newly diagnosed lung cancer patients feel their concerns are being met? *European Journal of Cancer Care*, 12: 35-45.
Not in PICO
- Ho, K. K. M. (2008) Two Chinese gentlemen with lung cancer presented with chest pain. *Hong Kong Practitioner*, 30: 100-104.
Not in PICO
- Hodgson, L. (2011) Reducing emergency admissions to hospital through the introduction of an acute lung cancer clinic. *Lung Cancer*, Conference: January.
Not in PICO
- Holmes, R. L. F. (2004) Evaluation of the Patient with Chronic Cough. *American Family Physician*, 69: 2159-2166+2169.
Narrative review
- House, J. (2010) Evaluation and management of shoulder pain in primary care clinics. *Southern Medical Journal*, 103: 1129-1135.
Narrative review
- Hsieh, C.-C. (2009) Incidental solitary knee mass as the first manifestation of hidden lung cancer. *Knee*, 16: 161-164.
Not in PICO
- Hsieh, M. J., Liu, H. P., Chang, J. P., Chang, C. H., Hsieh, M. J., Liu, H. P., Chang, J. P. & Chang, C. H. (1993) Thoracic actinomycosis. *Chest*, 104: 366-370.
Not in PICO
- Huq, S. (2010) Inappropriate referrals to the rapid access lung clinic (RALC). *Thorax*, Conference: December.
Not in PICO
- Huq, S. (2011) Wording of chest X-rays coded as possible lung cancer and their predictive value in confirming the diagnosis. *American Journal of Respiratory and Critical Care Medicine*, Conference.
Not in PICO
- Huq, S. (2011) Accuracy of coded chest X-rays and grade of reporter in diagnosis of lung cancer - A 9 year comparative study. *American Journal of Respiratory and Critical Care Medicine*, Conference.
Not in PICO
- Iyen-Omofoman, B. (2011) How long do patients in the united kingdom get treated for non-specific respiratory symptoms by general practitioners before they are diagnosed with lung cancer? *American Journal of Respiratory and Critical Care Medicine*, Conference.
Only published as abstract which doesn't allow the extraction of relevant data. Hopefully, the study will be published in full by the time the outdate search is done.

- Iyen-Omofoman, B., Hubbard, R. B., Smith, C. J. P., Sparks, E., Bradley, E., Bourke, A. & Tata, L. J. (2011) The distribution of lung cancer across sectors of society in the United Kingdom: A study using national primary care data. *BMC Public Health*, 11: 857-865.
Not in PICO
- Iyer, S., Roughley, A., Rider, A. & Taylor-Stokes, G. (2014) The symptom burden of non-small cell lung cancer in the USA: a real-world cross-sectional study. *Supportive Care in Cancer*, 22: 181-187.
Not in PICO
- Jett, J. R. M. (2011) Screening for lung cancer: For patients at increased risk for lung cancer, it works. *Annals of Internal Medicine*, 155: 540-542.
Not in PICO
- Jin, G. Y., Kim, Y. S., Han, Y. M., Lee, Y. C. & Kim, S. R. (2013) Combined pulmonary fibrosis and emphysema: Comparison of CT findings in symptomatic vs. Asymptomatic subjects. *Journal of Thoracic Imaging*, 28: W113.
Not in PICO
- Jiwa, M., Arnet, H., Halkett, G., Smith, M., O'Connor, M., Rhodes, J., Poland, K., Bulsara, M., Jiwa, M., Arnet, H., Halkett, G., Smith, M., O'Connor, M., Rhodes, J., Poland, K. & Bulsara, M. (2009) Does smoking status affect the likelihood of consulting a doctor about respiratory symptoms? A pilot survey in Western Australia. *BMC Family Practice*, 10: 16.
Not in PICO
- Johnson, M. (2003) Research into practice: The reality of implementing a non-pharmacological breathlessness intervention into clinical practice. *European Journal of Oncology Nursing*, 7: 33-38.
Not in PICO
- Jones, R. V. H. & Dudgeon, T. A. (1992) Time Between Presentation and Treatment of 6 Common Cancers - A Study in Devon. *British Journal of General Practice*, 42: 419-422.
Not in PICO
- Jordan, K. P., Hayward, R. A., Blagojevic-Bucknall, M. & Croft, P. (2013) Incidence of prostate, breast, lung and colorectal cancer following new consultation for musculoskeletal pain: a cohort study among UK primary care patients. *International Journal of Cancer*, 133: 713-720.
Cannot extract outcome in PICO (PPVs) as cancer data only reported in total for 10-year follow up
- Kanashiki, M., Satoh, H., Ishikawa, H., Yamashita, Y. T., Ohtsuka, M. & Sekizawa, K. (2003) Time from finding abnormality on mass-screening to final diagnosis of lung cancer. *Oncology Reports*, 10: 649-652.
Not in PICO
- Kane, B. (2009) Impact of implementing a local cancer awareness campaign on referrals to secondary care for suspected lung cancer. *Thorax*, Conference: December.
Not in PICO
- Kanemoto, K., Matsuno, Y., Kagohashi, K., Satoh, H., Ohtsuka, M., Sekizawa, K., Kanemoto, K., Matsuno, Y., Kagohashi, K., Satoh, H., Ohtsuka, M. & Sekizawa, K. (2002) [Thromboembolism in lung cancer patients]. [Japanese]. *Nihon Kokyuki Gakkai Zasshi*, 40: 863-868.
Not in PICO
- Kardos, P. (2006) Complaint, symptom and reflex - Diagnostic of cough in adults. *Notfall und Hausarztmedizin*, 32: 482-485.
Narrative review
- Kawamura, T. (1996) Clinical study of patients with bloody sputum. *Japanese Journal of Lung Cancer*, 36: 753-757.
Not in PICO
- Kennington, E. J. A. (2012) Early detection of lung cancer symptoms - A role for community for pharmacy. *International Journal of Pharmacy Practice*, Conference: May.
Not in PICO

- Khan, D. (2010) Lymphoma presenting to respiratory medicine at a district general hospital in the UK. *Lung Cancer*, Conference: Conference.
Not in PICO
- Kino, A., Boiselle, P. M., Raptopoulos, V. & Hatabu, H. (2006) Lung cancer detected in patients presenting to the Emergency Department studies for suspected pulmonary embolism on computed tomography pulmonary angiography. *European Journal of Radiology*, 58: 119-123.
Not in PICO
- Klabunde, C. N., Marcus, P. M., Silvestri, G. A., Han, P. K., Richards, T. B., Yuan, G., Marcus, S. E. & Vernon, S. W. (2010) U.S. primary care physicians' lung cancer screening beliefs and recommendations. *American Journal of Preventive Medicine*, 39: 411-420.
Not in PICO
- Klabunde, C. N., Marcus, P. M., Han, P. K., Richards, T. B., Vernon, S. W., Yuan, G., Silvestri, G. A., Klabunde, C. N., Marcus, P. M., Han, P. K. J., Richards, T. B., Vernon, S. W., Yuan, G. & Silvestri, G. A. (2012) Lung cancer screening practices of primary care physicians: results from a national survey. *Annals of Family Medicine*, 10: 102-110.
Not in PICO
- Kontos, M. C. D. (2010) Emergency Department and office-based evaluation of patients with chest pain. *Mayo Clinic Proceedings*, 85: 284-299.
Narrative review
- Koyi, H., Hillerdal, G. & Branden, E. (2002) Patient's and doctors' delays in the diagnosis of chest tumors. *Lung Cancer*, 35: 53-57.
Not in PICO
- Krishnasamy, M., Wilkie, E., Haviland, J., Krishnasamy, M., Wilkie, E. & Haviland, J. (2001) Lung cancer health care needs assessment: patients' and informal carers' responses to a national mail questionnaire survey. *Palliative Medicine*, 15: 213-227.
Not in PICO
- Kubik, A., Zatloukal, P., Boyle, P., Robertson, C., Gandini, S., Tomasek, L., Gray, N., Havel, L., Kubik, A., Zatloukal, P., Boyle, P., Robertson, C., Gandini, S., Tomasek, L., Gray, N. & Havel, L. (2001) A case-control study of lung cancer among Czech women. *Lung Cancer*, 31: 111-122.
Not in PICO
- Kubík, A. & Polák, J. (1986) Lung cancer detection. Results of a randomized prospective study in Czechoslovakia. *Cancer*, 57: 2427-2437.
Not in PICO
- Kupeli, E. (2012) Transbronchial needle aspiration: A tool for a community bronchoscopist. *Journal of Bronchology and Interventional Pulmonology*, 19: 115-120.
Not in PICO
- Lafontaine, M. (2012) Awareness about the signs and symptoms of lung cancer in at risk populations in NSW. *Journal of Thoracic Oncology*, Conference: S175.
Not in PICO
- Lamm, G. (2004) Dyspnea with multiple causes and fatal evolution. *Internistische Praxis*, 44: 777-782.
Not in PICO
- Lawson, M. (2012) Early diagnosis of lung cancer initiative in North East Essex. *Lung Cancer*, Conference: January.
Not in PICO
- Le Jeune, I. R., Lewis, N. R. & Baldwin, D. R. (2003) Presenting symptoms and chest radiographic features in urgent referrals for suspected lung cancer: How well do they discriminate? *Thorax*, 58: 48.
Not in PICO
- Lee, D. K. C. (2007) Suspected lung cancer: Its initial management and staging. *Primary Care Respiratory Journal*, 16: 106-111.
Narrative review

- Lee, M. & Tariq, A. (2014) How many doctors does it take . . .? *HIV Medicine*, 15: 109.
Not in PICO
- Lehto, R. H. (2011) Identifying Primary Concerns in Patients Newly Diagnosed With Lung Cancer. *Oncology Nursing Forum*, 38: 440-447.
Not in PICO
- Lewis, N. R., Le, J., I & Baldwin, D. R. (2005) Under utilisation of the 2-week wait initiative for lung cancer by primary care and its effect on the urgent referral pathway. *British Journal of Cancer*, 93: 905-908.
Not in PICO
- Leyakath Ali, K. S., Anwar, N., Nuttal, E., Clarke, S. & Zaman, F. (2014) Lung cancer from symptoms to referral across the Lancashire and South Cumbria Network. *Lung Cancer*, 83: S50.
Not in PICO
- Li, M., Peng, Z., Liu, Q., Sun, J., Yao, S. & Liu, Q. (2013) Value of 11C-choline PET/CT for lung cancer diagnosis and the relation between choline metabolism and proliferation of cancer cells. *Oncology Reports*, 29: 205-211.
Not in PICO
- Liedekerken, B. M., Hoogendam, A., Buntinx, F., van der Weyden, T., de Vet, H. C., Liedekerken, B. M., Hoogendam, A., Buntinx, F., van der Weyden, T. & de Vet, H. C. (1997) Prolonged cough and lung cancer: the need for more general practice research to inform clinical decision-making. *British Journal of General Practice*, 47: 505.
Review identifying no papers in PICO
- Lim, W. S. M. (1999) How do general practitioners respond to reports of abnormal chest X-rays? *Journal of the Royal Society of Medicine*, 92: 446-449.
Not in PICO
- Lovgren, M., Levealahti, H., Tishelman, C., Runesdotter, S., Hamberg, K., Lovgren, M., Levealahti, H., Tishelman, C., Runesdotter, S. & Hamberg, K. (2008) Time spans from first symptom to treatment in patients with lung cancer--the influence of symptoms and demographic characteristics. *Acta Oncologica*, 47: 397-405.
Not in PICO
- Lowry, B. (2009) Experiences of direct access CT scanning for general practitioners and implications for investigation of possible lung cancer. *Thorax*, Conference: December.
Not in PICO
- Lyon, D., Knowles, J., Slater, B., Kennedy, R., Lyon, D., Knowles, J., Slater, B. & Kennedy, R. (2009) Improving the early presentation of cancer symptoms in disadvantaged communities: putting local people in control. *British Journal of Cancer*, 101 Suppl 2: S49-S54.
Not in PICO
- Lyratzopoulos, G., Neal, R. D., Barbiere, J. M., Rubin, G. P. & Abel, G. A. (2012) Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. *Lancet Oncology*, 13: 353-365.
Not in PICO
- Mabry, L. M., Ross, M. D. & Tonarelli, J. M. (2014) - Metastatic cancer mimicking mechanical low back pain: a case report. - *Journal of Manual & Manipulative Therapy*, 22: 162-169.
Not in PICO
- Maeda, J., Hamanaka, W., Sakata, Y., Yoshida, K., Honda, H., Kakihana, M., Kajiwara, N., Ohira, T. & Ikeda, N. (2013) Effectiveness of cytological diagnosis of small-cell lung carcinoma by bronchoscopic examination. *Acta Cytologica*, 57: 116.
Not in PICO
- Maji, A., Maikap, M. K., Jash, D., Saha, K., Kundu, A., Saha, D., Banerjee, S. & Patra, A. (2013) Role of common investigations in aetiological evaluation of exudative pleural effusions. *Journal of Clinical and Diagnostic Research*, 7: 2223-2226.
Not in PICO

- Malatani, T. S., Batouk, A., Teklu, B., Irani, C., Dewan, M., Softah, A. H., al-Ghamdi, B. H., Grillo, I. A., Malatani, T. S., Batouk, A., Teklu, B., Irani, C., Dewan, M., Softah, A. H., al-Ghamdi, B. H. & Grillo, I. A. (1997) Bronchial carcinoid tumours in southern Saudi Arabia. *Indian Journal of Chest Diseases & Allied Sciences*, 39: 221-227.
Not in PICO
- Mandaliya, R., Hughes, L., Auerbach, H. & LePar, F. (2014) - Small cell lung cancer presenting as severe thrombocytopenia and refractory hypokalemia. - *Case Reports in Oncological Medicine*, 2014: 874831.
Not in PICO
- Mandigers, L., Houterman, S. & Van Den Borne, B. (2014) Tumor-specific diagnostic values of the diagnostics in lung cancer. *Journal of Clinical Oncology*, 32.
Not in PICO
- Mansell, G., Shapley, M., Van Der Windt, D., Sanders, T. & Little, P. (2014) Critical items for assessing risk of lung and colorectal cancer in primary care: A Delphi study. *British Journal of General Practice*, 64: e509-e515.
Duplicate
- Mansell, G., Shapley, M., Van Der Windt, D., Sanders, T. & Little, P. (2014) - Critical items for assessing risk of lung and colorectal cancer in primary care: a Delphi study. - *British Journal of General Practice*, 64: e509-e515.
Not in PICO
- Mansson, J., Bengtsson, C., Mansson, J. & Bengtsson, C. (1994) Pulmonary cancer from the general practitioner's point of view. Experience from the health centre area of Kungsbacka, Sweden. *Scandinavian Journal of Primary Health Care*, 12: 39-43.
Not in PICO
- Mansson, J., Bjorkelund, C., Hultborn, R., Mansson, J., Bjorkelund, C. & Hultborn, R. (1999) Symptom pattern and diagnostic work-up of malignancy at first symptom presentation as related to level of care. A retrospective study from the primary health care centre area of Kungsbacka, Sweden. *Neoplasma*, 46: 93-99.
Not in PICO
- Mansson, J. (2001) The diagnosis of cancer in the "roar" of potential cancer symptoms of patients in primary health care. Research by means of the computerised journal. *Scandinavian Journal of Primary Health Care*, 19: 83-89.
Not in PICO (outcome)
- Mansson, J. (2006) Costs in primary care of investigating symptoms suspicious of cancer in a defined population. *Scandinavian Journal of Primary Health Care*, 24: 243-250.
Not in PICO
- Mantri, S. (2003) Pattern of lung cancer in elderly. *The Journal of the Association of Physicians of India*, 51: Oct.
Not in PICO
- Marino, C., Zoppi, M., Morelli, F., Buoncristiano, U., Pagni, E., Marino, C., Zoppi, M., Morelli, F., Buoncristiano, U. & Pagni, E. (1986) Pain in early cancer of the lungs. *Pain*, 27: 57-62.
Not in PICO
- Mazel, J. A. D. (2001) With a view to vocal cords; general practitioner and hoarseness. *Nederlands Tijdschrift Voor Geneeskunde*, 145: 985-989.
Not in PICO
- Meyer, R. J. (2009) Respiratory services in New Zealand: A breath of fresh air is needed. *New Zealand Medical Journal*, 122.
Not in PICO
- Miser, W. F. (2007) Cancer screening in the primary care setting - The role of the primary care physician in screening for breast, cervical, colorectal, lung, ovarian, and prostate cancers. *Primary*

- Care, 34: 137-+.
Not in PICO
- Mitchell, E. (2009) Analysis of significant event audits of lung cancer diagnosis in primary care. *Thorax*, Conference: December.
Not in PICO
- Mitchell, E. D., Rubin, G. & Macleod, U. (2013) Understanding diagnosis of lung cancer in primary care: qualitative synthesis of significant event audit reports. *British Journal of General Practice*, 63: 37-46.
Not in PICO
- Mitchell, G., Mitchell, C., Mitchell, G. & Mitchell, C. (2004) Lung cancer. [Review] [14 refs]. *Australian Family Physician*, 33: 321-325.
Narrative review
- Molassiotis, A., Wilson, B., Brunton, L. & Chandler, C. (2010) Mapping patients' experiences from initial change in health to cancer diagnosis: a qualitative exploration of patient and system factors mediating this process. *European Journal of Cancer Care*, 19: 98-109.
Not in PICO
- Molina, R., Marrades, R. M., Auge, J. M., Escudero, J. M., Vinolas, N., Reguart, N., Ramirez, J., Filella, X., Molins, L. & Agusti, A. (2014) Tumor markers in lung cancer: A tool for early diagnosis? *Clinical Chemistry and Laboratory Medicine*, 52: S113.
Not in PICO
- Mortensen, E. M., Copeland, L. A., Pugh, M. J., Fine, M. J., Nakashima, B., Restrepo, M. I., de Molina, R. M. & Anzueto, A. (2010) Diagnosis of Pulmonary Malignancy after Hospitalization for Pneumonia. *American Journal of Medicine*, 123: 66-71.
Not in PICO
- Mulka, O. (2005) NICE suspected cancer guidelines. *British Journal of General Practice*, 55: 580-581.
Editorial
- Mustfa, N., Bain, A. & Allen, M. B. (2000) An audit of suspected lung cancer referrals (LC) to clinic and their impact on other urgent (OU) referrals. *Thorax*, 55: A13.
Not in PICO
- Nakajima, T. & Yasufuku, K. (2013) Early Lung Cancer. Methods for Detection. *Clinics in Chest Medicine*, 34: 373-383.
Narrative review
- Neal, R. D., Allgar, V. L., Ali, N., Leese, B., Heywood, P., Proctor, G., Evans, J., Neal, R. D., Allgar, V. L., Ali, N., Leese, B., Heywood, P., Proctor, G. & Evans, J. (2007) Stage, survival and delays in lung, colorectal, prostate and ovarian cancer: comparison between diagnostic routes. *British Journal of General Practice*, 57: 212-219.
Not in PICO
- Neal, R. D., Pasterfield, D., Wilkinson, C., Hood, K., Makin, M. & Lawrence, H. (2008) Determining patient and primary care delay in the diagnosis of cancer - lessons from a pilot study of patients referred for suspected cancer. *BMC Family Practice*, 9.
Not in PICO
- Neal, R. D. (2009) Do diagnostic delays in cancer matter? *British Journal of Cancer*, 101: S9-S12.
Not in PICO
- Nielsen, T. N., Hansen, R. P., Vedsted, P., Nielsen, T. N., Hansen, R. P. & Vedsted, P. (2010) [Symptom presentation in cancer patients in general practice]. [Danish]. *Ugeskrift for Læger*, 172: 2827-2831.
Not in PICO
- Nordin, F. (2012) Airway obstruction and respiratory ill-health in a population at increased lung cancer risk. *Journal of Thoracic Oncology*, Conference: S26.
Not in PICO

- Oki, M., Saka, H., Kitagawa, C., Kogure, Y., Murata, N., Adachi, T. & Ando, M. (2013) Rapid on-site cytologic evaluation during endobronchial ultrasound-guided transbronchial needle aspiration for diagnosing lung cancer: a randomized study. *Respiration*, 85: 486-492.
Not in PICO
- Onishi, H., Onose, M., Yamada, T., Mizuno, Y., Ito, M., Sato, H., Sato, H. & Kosaka, K. (2003) Post-traumatic stress disorder associated with suspected lung cancer and bereavement: 4-year follow-up and review of the literature. *Supportive Care in Cancer*, 11: 123-125.
Not in PICO
- Ost, D. E., Yeung, S. C., Tanoue, L. T. & Gould, M. K. (2013) Clinical and organizational factors in the initial evaluation of patients with lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*, 143: Suppl-41S.
Guideline/not in PICO
- Paneesha, S. (2010) Frequency, demographics and risk (according to tumour type or site) of cancer-associated thrombosis among patients seen at outpatient DVT clinics. *Thrombosis and Haemostasis*, 103: 338-343.
Not in PICO
- Patel, A. M., Peters, S. G., Patel, A. M. & Peters, S. G. (1993) Clinical manifestations of lung cancer. [Review] [51 refs]. *Mayo Clinic Proceedings*, 68: 273-277.
Narrative review
- Patel, P. (2004) Clinical course of lung cancer in patients with chronic kidney disease. *Lung Cancer*, 43: 297-300.
Not in PICO
- Patrick, H. (1995) Chronic cough. *Medical Clinics of North America*, 79: 361-372.
Narrative review
- Pavic, M., Debourdeau, P., Vacelet, V., Rousset, H., Pavic, M., Debourdeau, P., Vacelet, V. & Rousset, H. (2008) [Sarcoidosis and sarcoid reactions in cancer]. [Review] [93 refs] [French]. *Revue de Medecine Interne*, 29: 39-45.
Narrative review
- Peavie S. (2012) A patient's presentation of persistent sweet taste in her mouth leads to a diagnosis of small cell lung cancer. *Journal of Hospital Medicine*, Conference: March.
Not in PICO
- Petty, T. L. & Petty, T. L. (133) The predictive value of spirometry. Identifying patients at risk for lung cancer in the primary care setting. [Review] [14 refs]. *Postgraduate Medicine*, 101: 128-130.
Narrative review
- Piers, R. D., Benoit, D. D., Schrauwen, W. J. & Van den Noortgate, N. J. (2010) Factors influencing ICU referral at the end of life in the elderly. *Zeitschrift fur Gerontologie und Geriatrie*, 43: 376-380.
Not in PICO
- Prasad, R. (2009) Lessons from patients with hemoptysis attending a chest clinic in India. *Annals of Thoracic Medicine*, 4: 10-12.
Not in PICO
- Puolijoki, H. (1992) Symptomatic hypercalcaemia in lung cancer [5]. *Respiratory Medicine*, 86: 359-360.
Not in PICO
- Rahim, M. A., Sarma, S. K., Rahim, M. A. & Sarma, S. K. (1984) Pulmonary and extrapulmonary manifestations in delayed diagnosis of lung cancer in Bangladesh. *Cancer Detection & Prevention*, 7: 31-35.
Not in PICO
- Raza, T. J. (2009) Pulmonary telemedicine-A model to access the subspecialist services in underserved rural areas. *International Journal of Medical Informatics*, 78: 53-59.
Not in PICO

- Rivera, M. P., Detterbeck, F., Mehta, A. C. & American College of Chest Physicians. (2003) Diagnosis of lung cancer: the guidelines. *Chest*, 123: 129S-136S.
Guideline
- Rivera, M. P., Mehta, A. C. & Wahidi, M. M. (2013) Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*, 143: Suppl-65S.
Not in PICO
- Rogers, T. K. (2010) Primary care radiography in the early diagnosis of lung cancer. *Cancer Imaging*, 10: 73-76.
Narrative review
- Rolke, H. B. (2007) Delays in the diagnostic pathways for primary pulmonary carcinoma in Southern Norway. *Respiratory Medicine*, 101: 1251-1257.
Not in PICO
- Rolston, K. V., Rodriguez, S., Dholakia, N., Whimbey, E., Raad, I., Rolston, K. V., Rodriguez, S., Dholakia, N., Whimbey, E. & Raad, I. (1997) Pulmonary infections mimicking cancer: a retrospective, three-year review. [Review] [29 refs]. *Supportive Care in Cancer*, 5: 90-93.
Not in PICO
- Romankiewicz, K. (2006) Hospitalizations caused by pneumonia non-efficiently treated by GPs. *Family Medicine and Primary Care Review*, 8: 743-746.
Not in PICO
- Ruffatti, S., Zanchin, G. & Maggioni, F. (2008) A case of intractable facial pain secondary to metastatic lung cancer. [References]. *Neurological Sciences*, 29: 117-119.
Not in PICO
- Ryan, J. (2010) Comparison of clinical outcomes from chest X-rays of smokers and non-smokers in a general practice population. *Irish Medical Journal*, 103.
Letter
- Safe, A. (2011) Naedi lung cancer awareness campaign in London. *Thorax*, Conference: December.
Not in PICO
- Saha, A., Ghosh, S., Saha, K. & Biswas, A. (1111) Relationship between chest X-ray and pathological cell types of lung cancer. *Lung India*, 30: S34-December.
Not in PICO
- Sahn, S. A. & Sahn, S. A. (1998) Malignancy metastatic to the pleura. [Review] [101 refs]. *Clinics in Chest Medicine*, 19: 351-361.
Not in PICO
- Salzman, B. E., Lamb, K., Olszewski, R. F., Tully, A. & Studdiford, J. (2009) Diagnosing Cancer in the Symptomatic Patient. *Primary Care*, 36: 651-+.
Narrative review
- Scherrer, M., Tschumi, H. J., Zeller, C., Zimmermann, C., Scherrer, M., Tschumi, H. J., Zeller, C. & Zimmermann, C. (1980) [Subjective early symptoms of bronchial neoplasms. Retrospective computer analysis of case histories, written in free prose]. [Review] [42 refs] [German]. *Schweizerische Medizinische Wochenschrift*, Journal Suisse de Medecine. 110: 715-721.
Not in PICO
- Schiff, G. D., Hasan, O., Kim, S., Abrams, R., Cosby, K., Lambert, B. L., Elstein, A. S., Hasler, S., Kabongo, M. L., Krosnjar, N., Odwazny, R., Wisniewski, M. F. & Mcnutt, R. A. (2009) Diagnostic Error in Medicine Analysis of 583 Physician-Reported Errors. *Archives of Internal Medicine*, 169: 1881-1887.
Not in PICO
- Schildge, J., Cegla, M., Ortlieb, H., Schulte-Monting, J., Schildge, J., Cegla, M., Ortlieb, H. & Schulte-Monting, J. (1989) [The effect of mass chest x-ray on early detection of bronchial cancer]. [German]. *Pneumologie*, 43: 500-506.
Not in PICO

- Schramm, N., Rominger, A., Schmidt, C., Morelli, J. N., Schmid-Tannwald, C., Meinel, F. G., Reiser, M. F. & Rist, C. (2013) Detection of underlying malignancy in patients with paraneoplastic neurological syndromes: Comparison of 18F-FDG PET/CT and contrast-enhanced CT. *European Journal of Nuclear Medicine and Molecular Imaging*, 40: 1014-1024.
Not in PICO
- Scott, N., Donato-Hunt, C., Crane, M., Lafontaine, M., Varlow, M., Seale, H. & Currow, D. (2014) Knowledge, attitudes and beliefs about lung cancer in three culturally and linguistically diverse communities living in Australia: a qualitative study. *Health promotion journal of Australia : official journal of Australian Association of Health Promotion Professionals*, 25: 46-51.
Not in PICO
- Seek, A. & Hogle, W. P. (2007) Modeling a better way: navigating the healthcare system for patients with lung cancer. *Clinical Journal of Oncology Nursing*, 11: 81-85.
Not in PICO
- Sekine, Y., Katsura, H., Koh, E., Hiroshima, K., Fujisawa, T., Sekine, Y., Katsura, H., Koh, E., Hiroshima, K. & Fujisawa, T. (2012) Early detection of COPD is important for lung cancer surveillance. [Review]. *European Respiratory Journal*, 39: 1230-1240.
Narrative review
- Shapley, M., Mansell, G., Jordan, J. L., Jordan, K. P., Shapley, M., Mansell, G., Jordan, J. L. & Jordan, K. P. (2010) Positive predictive values of $\geq 5\%$ in primary care for cancer: systematic review. [Review]. *British Journal of General Practice*, 60: e366-e377.
Systematic Review. The included studies are also included in our review.
- Sharma, S. C. (1995) Delay in diagnostic biopsies in suspected cancer. *Indian journal of pathology & microbiology*, 38: 81-89.
Not in PICO
- Sheridan, E. A., Stephenson, J., McHugh, P., Chrystyn, H., Philip, B. & Airley, R. (2014) Pharmacist-led lung cancer biomarker detection. *Journal of Clinical Oncology*, 32.
Not in PICO
- Shim, J., Brindle, L., Simon, M. & George, S. (2014) A systematic review of symptomatic diagnosis of lung cancer. *Family Practice*, 31: 137-148.
Duplicate
- Shim, J., Brindle, L., Simon, M. & George, S. (2014) - A systematic review of symptomatic diagnosis of lung cancer. - *Family Practice*, 31: 137-148.
Duplicate
- Shim, J., Brindle, L., Simon, M. & George, S. (2014) A systematic review of symptomatic diagnosis of lung cancer. *Family Practice*, 31: 137-148.
Systematic review, included studies checked for relevance.
- Silva, P. P., Pereira, J. R., Ikari, F. K., Minamoto, H., Silva, P. P., Pereira, J. R., Ikari, F. K. & Minamoto, H. (1992) [Lung cancer and the delay in the diagnosis: analysis of 300 cases]. [Portuguese]. *Revista da Associação Médica Brasileira*, 38: 145-149.
Not in PICO
- Singh, H. (2010) Characteristics and predictors of missed opportunities in lung cancer diagnosis: an electronic health record-based study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 28: 3307-3315.
Not in PICO
- Sinnakirouchenan, R. & Ramalingam, V. (2012) All that wheezes is not asthma! *Journal of Hospital Medicine*, Conference: March.
Not in PICO
- Smith, S., Fielding, S., Murchie, P., Johnston, M., Wyke, S., Powell, R., Devereux, G., Nicolson, M., Macleod, U., Wilson, P., Ritchie, L., Lee, A. J. & Campbell, N. C. (2013) Reducing the time before consulting with symptoms of lung cancer: a randomised controlled trial in primary care. *British*

Journal of General Practice, 63: 47-54.

Not in PICO

Smith, S. M., Campbell, N. C., Macleod, U., Lee, A. J., Raja, A., Wyke, S., Ziebland, S. B., Duff, E. M., Ritchie, L. D. & Nicolson, M. C. (2009) Factors contributing to the time taken to consult with symptoms of lung cancer: a cross-sectional study. *Thorax*, 64: 523-531.

Not in PICO

Smith, S. M., Murchie, P., Devereux, G., Johnston, M., Lee, A. J., Macleod, U., Nicolson, M. C., Powell, R., Ritchie, L. D., Wyke, S. & Campbell, N. C. (2012) Developing a complex intervention to reduce time to presentation with symptoms of lung cancer. *British Journal of General Practice*, 62: e605-e615.

Not in PICO

Souza, F. F. O. (2009) Venous thrombosis in an outpatient oncologic center: Distribution, type, and comorbidities. *Ultrasound Quarterly*, 25: 145-150.

Not in PICO

Speets, A. M. (2006) Chest radiography in general practice: Indications, diagnostic yield and consequences for patient management. *British Journal of General Practice*, 56: 574-578.

Not in PICO (for S&S or for tests)

Squerzanti, A., Basteri, V., Antinolfi, G., D'agostino, F., Scutellari, P. N., Ravenna, F., Ghirardi, R., Cavallesco, G., Squerzanti, A., Basteri, V., Antinolfi, G., D'agostino, F., Scutellari, P. N., Ravenna, F., Ghirardi, R. & Cavallesco, G. (2002) Bronchial carcinoid tumors: clinical and radiological correlation. *Radiologia Medica*, 104: 273-284.

Not in PICO

Stapley, S., Sharp, D. & Hamilton, W. (2006) Negative chest X-rays in primary care patients with lung cancer. *British Journal of General Practice*, 56: 570-573.

Not in PICO

Steer, H. J., Bowie, E. & Masani, V. (2007) Presenting symptoms, chest radiograph abnormalities and FEV1 in GP referrals for suspected lung cancer: How well do they discriminate? *Thorax*, 62: A135-A136.

Not in PICO

Stenqvist, C. & Majed, A. (2013) [Shoulder pain as the first sign of disseminated lung cancer.]. *Ugeskrift for Laeger*, 175: 287-288.

Not in PICO

Strauss, G. M., Gleason, R. E., Sugarbaker, D. J., Strauss, G. M., Gleason, R. E. & Sugarbaker, D. J. (1995) Chest X-ray screening improves outcome in lung cancer. A reappraisal of randomized trials on lung cancer screening. [Review] [58 refs]. *Chest*, 107: 270S-279S.

Not in PICO

Sulu, E., Tasolar, O., Takir, H. B., Tuncer, L. Y., Karakurt, Z. & Yilmaz, A. (2011) Delays in the diagnosis and treatment of non-small-cell lung cancer. *Tumori*, 97: 693-697.

Not in PICO

Sun Young Kim Hae Jeong Cho Geun Hwa Kim Dong Seok Ko Jae Chul Suh Kyoung Sang Shin Seong Su Jeong Ju Ock Kim (1998) Delayed diagnosis of primary lung cancer. *Tuberculosis and Respiratory Diseases*, 45: 754-759.

Not in PICO

Sun, Y. Y. & Knobf, M. T. (2008) Concept Analysis of Symptom Disclosure in the Context of Cancer. *Advances in Nursing Science*, 31: 332-341.

Not in PICO

Suteanu, S., Rohan, C., Gherasim, E., Stoica, V., Suteanu, S., Rohan, C., Gherasim, E. & Stoica, V. (1992) Hypertrophic osteoarthropathy secondary to bronchopulmonary cancer (our experience). *Romanian Journal of Internal Medicine*, 30: 281-284.

Not in PICO

- Svendson, R. P., Stovring, H., Hansen, B. L., Kragstrup, J., Sondergaard, J. & Jarbol, D. E. (2010) Prevalence of cancer alarm symptoms: A population-based cross-sectional study. *Scandinavian Journal of Primary Health Care*, 28: 132-137.
Not in PICO
- Tadros, M. B. C. (2011) Lower extremity edema, Could it be cancer? *Journal of General Internal Medicine*, Conference: May.
Narrative review
- Tammemagi, C. M., Neslund-Dudas, C., Simoff, M., Kvale, P., Tammemagi, C. M., Neslund-Dudas, C., Simoff, M. & Kvale, P. (2004) Lung carcinoma symptoms--an independent predictor of survival and an important mediator of African-American disparity in survival. *Cancer*, 101: 1655-1663.
Not in PICO
- Tammemagi, M. C., Freedman, M. T., Pinsky, P. F., Oken, M. M., Hu, P., Riley, T. L., Ragard, L. R., Berg, C. D. & Prorok, P. C. (2009) Prediction of true positive lung cancers in individuals with abnormal suspicious chest radiographs: a prostate, lung, colorectal, and ovarian cancer screening trial study. *Journal of Thoracic Oncology*, 4: 710-721.
Not in PICO
- Tanner, K., Roden, K., Hancock, J. & Morgan, A. (2014) Haemoptysis referrals with a normal CT scan can be seen safely in a monthly haemoptysis clinic results of a retrospective audit. *Lung Cancer*, 83: S33.
Not in PICO
- Tejerina, G. E., Lopez, G. A., Martin, L. J. & Perez, A. R. (2013) Intramuscular metastases as the initial presentation of non-small cell pulmonary carcinoma: Report of three cases diagnosed by fine needle aspiration cytology. *Virchows Archiv*, 463: 273.
Not in PICO
- Thirkill, C. E. & Thirkill, C. E. (1996) Lung cancer-induced blindness. [Review] [79 refs]. *Lung Cancer*, 14: 253-264.
Not in PICO
- Tod, A. M., Craven, J. & Allmark, P. (2008) Diagnostic delay in lung cancer: a qualitative study. *Journal of Advanced Nursing*, 61: 336-343.
Not in PICO
- Tod, A. M. J. (2010) Overcoming delay in the diagnosis of lung cancer: a qualitative study. *Nursing standard (Royal College of Nursing (Great Britain) : 1987)*, 24: 35-43.
Not in PICO
- Triller, N., Beres, V. & Rozman, A. (2010) Delays in the diagnosis and treatment of lung cancer: can the period between the onset of symptoms and the diagnosis and treatment be shortened? *Zdravniški Vestnik-Slovenian Medical Journal*, 79: 618-622.
Not in PICO
- Turkington, P. M., Kennan, N., Greenstone, M. A., Turkington, P. M., Kennan, N. & Greenstone, M. A. (2002) Misinterpretation of the chest x ray as a factor in the delayed diagnosis of lung cancer. *Postgraduate Medical Journal*, 78: 158-160.
Not in PICO
- Vakil, A., Abubaker, A., Upadhyay, H., Patel, V., Cervellione, K. & Shalanov, A. (2013) Soft tissue mass above the knee as the initial presentation of metastatic NSCLC in an asymptomatic patient. *Chest*, 144.
Not in PICO
- Valdes, S., Garcia, E., Perez, H. & Hernandez, M. (2010) Length of Diagnostic Delay in Patients with Non-small-cell Lung Cancer. *Medicc Review*, 12: 29-32.
Not in PICO
- van Veenendaal, L. M., de, K. G. & van, d., V (2014) - A painful finger as first sign of a malignancy. - *Geriatric Orthopaedic Surgery & Rehabilitation*, 5: 18-20.
Not in PICO

- Vergnon, J.-M. (2014) The bronchoscopy in the diagnosis of lung cancer. [French]. *Revue des Maladies Respiratoires Actualites*, 5: 339-345.
Narrative review
- Vieira, T., Duruisseaux, M., Ruppert, A. M., Cadranel, J., Antoine, M., Wislez, M., Vieira, T., Duruisseaux, M., Ruppert, A. M., Cadranel, J., Antoine, M. & Wislez, M. (2012) [Pulmonary sarcomatoid carcinoma]. [Review] [French]. *Bulletin du Cancer*, 99: 995-1001.
Narrative review
- Vigg, A., Mantri, S., Vigg, A., Vigg, A., Vigg, A., Mantri, S., Vigg, A. & Vigg, A. (2003) Pattern of lung cancer in elderly. *Journal of the Association of Physicians of India*, 51: 963-966.
Not in PICO
- Wagland, R. (2011) How standard is 'standard care' in the symptom management of patients with lung cancer? The example of the 'respiratory distress' symptom cluster. *European Journal of Oncology Nursing*, 15: 1-2.
Not in PICO
- Wai, E. S., Mackinnon, M., Hooker, R., Moccia, P., Perry, K. R. & Truong, P. T. (2012) Wait Times in Diagnostic Evaluation and Treatment for Patients With Stage III Non-Small Cell Lung Cancer in British Columbia. *American Journal of Clinical Oncology-Cancer Clinical Trials*, 35: 373-377.
Not in PICO
- Wallace, G. M., Winter, J. H., Winter, J. E., Taylor, A., Taylor, T. W., Cameron, R. C., Wallace, G. M. F., Winter, J. H., Winter, J. E., Taylor, A., Taylor, T. W. & Cameron, R. C. (2009) Chest X-rays in COPD screening: are they worthwhile? *Respiratory Medicine*, 103: 1862-1865.
Not in PICO (for S7S and for tests)
- Walters, J., Sr. (2010) The epidemiology of pleural effusions referred to a pleural procedures clinic. *American Journal of Respiratory and Critical Care Medicine*, Conference.
Not in PICO
- Wang, F., Zhang, Y., Feng, Y.-C. & Huang, Y.-C. (2013) Comparison between FISH and cytology of sputum samples in detection of lung cancer. [Chinese]. *Journal of Practical Oncology*, 28: 197-199.
Not in PICO
- Ward, S. (2010) Is the increase in number of referrals to the fast track lung cancer service the result of an increase in the number of inappropriate referrals? *American Journal of Respiratory and Critical Care Medicine*, Conference.
Not in PICO
- Watanabe, Y. (1990) Clinical analyses of early hilar lung cancer. *Japanese Journal of Lung Cancer*, 30: 175-181.
Not in PICO
- Weiser, M. A. C. (2005) Diagnostic evaluation of patients with a high suspicion of malignancy: Comorbidities and clinical predictors of cancer. *American Journal of the Medical Sciences*, 330: 11-18.
Not in PICO
- Weldon, C. B., Shamberger, R. C., Weldon, C. B. & Shamberger, R. C. (2008) Pediatric pulmonary tumors: primary and metastatic. [Review] [171 refs]. *Seminars in Pediatric Surgery*, 17: 17-29.
Narrative review
- Whitten, S. E. (2006) Hypertension, hypokalemia and edema in a patient with cough. *Advance for Nurse Practitioners*, 14: 24-25.
Not in PICO
- Winter, H. (2012) Lung cancer referrals in new zealand-the experience of one regional cancer service. *Journal of Thoracic Oncology*, Conference: S188.
Not in PICO

Yacoub, M. (1980) Shoulder pain as an early symptom of pancoast tumor. *The Journal of the Medical Society of New Jersey*, 77: 583-586.

Not in PICO

Yaman, N., Ozgen, A., Celik, P., Ozyurt, B. C., Nese, N., Coskun, A. S. & Yorgancioglu, A. (2009) Factors affecting the interval from diagnosis to treatment in patients with lung cancer. *Tumori*, 95: 702-705.

Not in PICO

Yelland, M. (2010) An Algorithm for the Diagnosis and Management of Chest Pain in Primary Care. *Medical Clinics of North America*, 94: 349-374.

Narrative review

Zaric, B., Perin, B., Stojic, V., Carapic, V., Matijasevic, J., Andrijevic, I. & Eri, Z. (2013) Detection of premalignant bronchial lesions can be significantly improved by combination of advanced bronchoscopic imaging techniques. *Annals of Thoracic Medicine*, 8: 93-98.

Not in PICO

Zhao, H., Xie, Z., Zhou, Z. L., Sui, X. Z. & Wang, J. (2013) Diagnostic value of endobronchial ultrasound-guided transbronchial needle aspiration in intrapulmonary lesions. *Chinese Medical Journal*, 126: 4312-4315.

Not in PICO

Review question:

Which investigations of symptoms of suspected lung cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

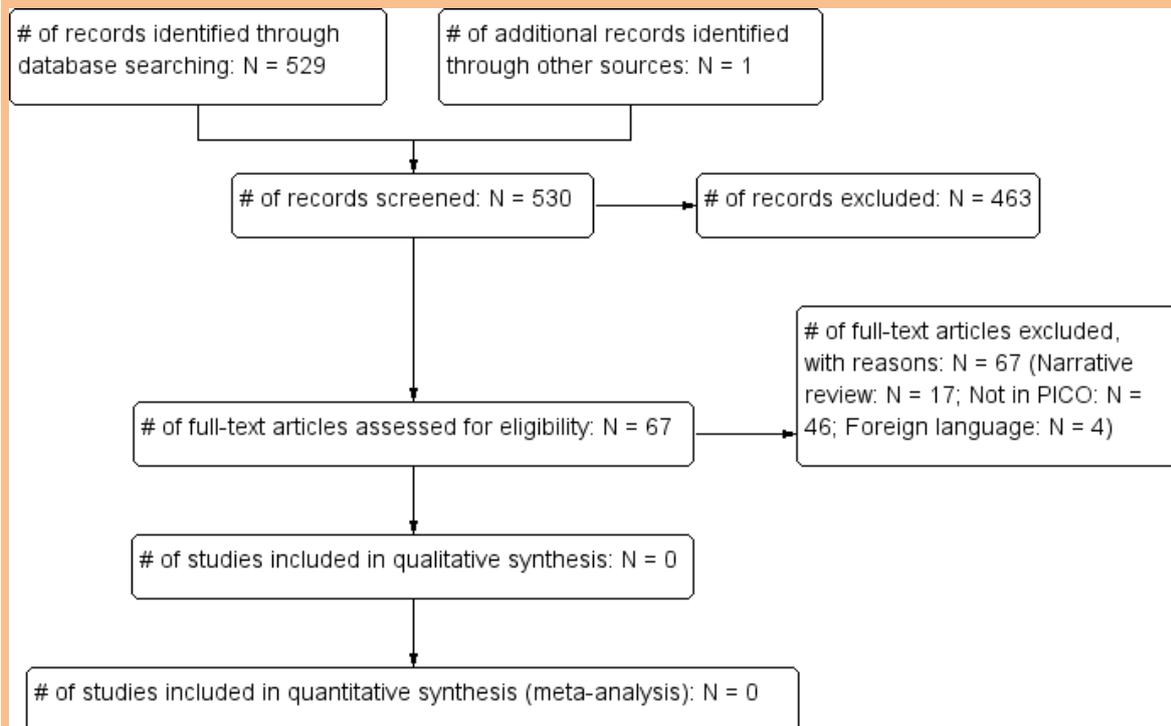
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	958	180	28/02/2013
<i>Premedline</i>	1980-2013	136	25	28/02/2013
<i>Embase</i>	1980-2013	1481	339	06/03/2013
<i>Cochrane Library</i>	1980-2013	175	2	06/03/2013
<i>Psychinfo</i>	1980-2013	14	4	06/03/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	224	26	06/03/2013

Total References retrieved (after de-duplication): 487

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-19/08/2014	105	6	19/08/2014
<i>Premedline</i>	2013-19/08/2014	133	14	19/08/2014
<i>Embase</i>	2013-19/08/2014	164	31	19/08/2014
<i>Cochrane Library</i>	2013-19/08/2014	70	0	19/08/2014
<i>Web of Science (SCI &</i>	2013-	47	3	19/08/2014

Total References retrieved (after de-duplication): 42



Study results

No evidence was identified pertaining to the diagnostic accuracy of chest x-ray, CT, sputum cytology, or bronchoscopy in patients with suspected lung cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

(1984) Early lung cancer detection: summary and conclusions. *American Review of Respiratory Disease*, 130: 565-570.

Narrative review

(2001) Promoting self-referral for advanced imaging. *Effective Clinical Practice*, 4: 93-94.

Not in PICO

(2011) Finding lung cancer early. CT scans may break the impasse over lung cancer screening, although many questions remain. *Harvard health letter / from Harvard Medical School*, 36: 1-3.

Not in PICO

Ahn, M. I. (2004) Lung cancer screening with low-dose chest CT: current issues. *Cancer Research & Treatment*, 36: 163-166.

Not in PICO

- Akira, C., Sakurada, E. & Kondo, T. (2012) Early central airways lung cancer. *General Thoracic and Cardiovascular Surgery*, 60: 557-560.
Narrative review
- Alberg, A. J., Brock, M. V., Ford, J. G., Samet, J. M. & Spivack, S. D. (2013) Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American college of chest physicians evidence-based clinical practice guidelines. *Chest*, 143: e1S-e29S.
Narrative review
- Albert, R. H. & Russell, J. J. (2009) Evaluation of the solitary pulmonary nodule. [Review] [25 refs]. *American Family Physician*, 80: 827-831.
Narrative review
- Allah, M. F., Hussein, S. R., El-Asmar, A. B., Zoair, H. M., Mohamed, G. A., Metwaly, A. M., Abboud, M. A. & Shalan, I. M. (2012) Role of virtual bronchoscopy in the evaluation of bronchial lesions. *Journal of Computer Assisted Tomography*, 36: 94-99.
Not in PICO
- Alpert, J. B., Fantauzzi, J. P., Melamud, K., Greenwood, H., Naidich, D. P. & Ko, J. P. (2012) Clinical significance of lung nodules reported on abdominal CT. *AJR.American Journal of Roentgenology*, 198: 793-799.
Not in PICO
- Ammanagi, A. S., Dombale, V. D., Miskin, A. T., Dandagi, G. L. & Sangolli, S. S. (2012) Sputum cytology in suspected cases of carcinoma of lung (Sputum cytology a poor man's bronchoscopy!). *Lung India*, 29: 19-23.
Not in PICO
- Ang, T. L., Tee, A. K. H., Fock, K. M., Teo, E. K. & Chua, T. S. (2007) Endoscopic ultrasound-guided fine needle aspiration in the evaluation of suspected lung cancer. *Respiratory Medicine*, 101: 1299-1304.
Not in PICO
- Ardissone, F., Rapellino, M., Obert, R., Baldi, S., Scappaticci, E., Pecchio, F. & Borasio, P. (1989) Lung cancer in patients under 40 years of age. [Italian]. *Minerva Medica*, 80: 1301-1304.
Not in PICO
- Arenberg, D. A. (2004) Evaluating the patient with suspected lung cancer. *Journal of Respiratory Diseases*, 25: 266-272.
Narrative review
- Arroliga, A. C. & Matthay, R. A. (1993) The role of bronchoscopy in lung cancer. *Clinics in Chest Medicine*, 14: 87-98.
Narrative review
- Asamura, H., Nakayama, H., Kondo, H., Tsuchiya, R. & Naruke, T. (1997) Thoracoscopic evaluation of histologically/cytologically proven or suspected lung cancer: A VATS exploration. *Lung Cancer*, 16: 183-190.
Not in PICO
- Athey, V. L., Suckling, R. J., Tod, A. M., Walters, S. J. & Rogers, T. K. (2012) Early diagnosis of lung cancer: evaluation of a community-based social marketing intervention. *Thorax*, 67: 412-417.
Not in PICO
- Aydin, E., Yazici, U., Gulgosteren, M., Agackiran, Y., Kaya, S., Gulhan, E., Tastepe, I. & Karaoglanoglu, N. (2011) Long-term outcomes and prognostic factors of patients with surgically treated pulmonary carcinoid: Our institutional experience with 104 patients. *European Journal of Cardio-Thoracic Surgery*, 39: 549-554.
Not in PICO
- Bakir, B., Tuzun, U., Terzibasoglu, E., Dursun, M., Guven, K., Salmaslioglu, A. & Tunaci, A. (2008) The diagnostic efficiency of multislice CT virtual bronchoscopy in detecting endobronchial tumors. [Turkish]. *Tuberkuloz ve Toraks*, 56: 43-49.
Not in PICO

- Bakris, G. L., Mulopulos, G. P., Korchik, R., Ezdinli, E. Z., Ro, J. & Yoon, B. H. (1983) Pulmonary scar carcinoma. A clinicopathologic analysis. *Cancer*, 52: 493-497.
Not in PICO
- Balbo, P. E., Bodini, B. D., Patrucco, F., Della, C. F., Zanaboni, S., Bagnati, P., Andorno, S. & Magnani, C. (2013) Electromagnetic navigation bronchoscopy and rapid on site evaluation added to fluoroscopy-guided assisted bronchoscopy and rapid on site evaluation: improved yield in pulmonary nodules. *Minerva Chirurgica*, 68: 579-585.
Not in PICO
- Barchuk, A. S., Loviagin, E. V., Moerman, B. A. & Lemekhov, V. G. (1987) [Bronchoscopy in the outpatient examination of patients]. [Russian]. *Voprosy Onkologii*, 33: 75-78.
Paper in Russian. Unclear whether relevant based on the short abstract there available in English.
- Barlesi, F., Doddoli, C., Greillier, L., Dutau, H. & Astoul, P. (2006) [Bronchoscopy in the diagnosis of lung cancer: an evaluation of current practice]. [Review] [72 refs] [French]. *Revue des Maladies Respiratoires*, 23: Suppl-4S26.
Narrative review
- Barrett, J. & Hamilton, W. (2008) Pathways to the diagnosis of lung cancer in the UK: a cohort study. *BMC Family Practice*, 9: 31.
Not in PICO
- Barschuk, A. S., Maximov, J. A., Prigov, A. I., Polak, J., Podubnyi, B. K., Rotte, K. H., Sally-Dobrai, G., Stein, F. M., Widow, W. & Wilde, J. (1982) [Theses for the diagnosis of lung cancer]. [German]. *Archiv fur Geschwulstforschung*, 52: 83-86.
Narrative review
- Batra, P., Brown, K. & Steckel, R. (1987) Diagnostic imaging techniques in lung carcinoma. *American Journal of Surgery*, 153: 517-524.
Narrative review
- Battista, R. N. (1983) Adult cancer prevention in primary care: patterns of practice in Quebec. *American Journal of Public Health*, 73: 1036-1039.
Not in PICO
- Beattie, E. J. & Raskin, N. M. (1987) Progress in lung cancer: Non-oat cell (non-small cell lung cancer). *Japanese Journal of Surgery*, 17: 313-322.
Not in PICO
- Bechtel, J. J., Kelley, W. R., Petty, T. L., Patz, D. S. & Saccomanno, G. (1994) Outcome of 51 patients with roentgenographically occult lung cancer detected by sputum cytologic testing: A community hospital program. *Archives of Internal Medicine*, 154: 975-980.
Not in PICO
- Bechtel, J. J., Kelley, W. A., Coons, T. A., Klein, M. G., Slagel, D. D. & Petty, T. L. (2005) Lung cancer detection in patients with airflow obstruction identified in a primary care outpatient practice. *Chest*, 127: 1140-1145.
Not in PICO
- Bechtel, J. J., Kelley, W. A., Coons, T. A., Mohler, P., Mohler, A., James, D. & Petty, T. L. (2009) Five-year outcome of lung cancer detection in patients with and without airflow obstruction in a primary care outpatient practice. *Journal of Thoracic Oncology*, 4: 1347-1351.
Not in PICO
- Bergner, A. & Huber, R. M. (2011) [Interventional bronchoscopy in lung cancer]. [German]. *Internist*, 52: 155-157.
Narrative review
- Bernal, S. D. & Elias, A. D. (1988) Early lung cancer detection: Monoclonal antibody staining of exfoliated cells in sputum. *Journal of Clinical Oncology*, 6: 1676-1678.
Not in PICO

- Bidwell, J. L. & Pachner, R. W. (2005) Hemoptysis: Diagnosis and management. *American Family Physician*, 72: 1253-1260.
Narrative review
- Biggi, A., Buccheri, G., Ferrigno, D., Viglietti, A., Farinelli, M. C., Comino, A., Leone, A., Quaranta, M. & Taviani, M. (1991) Detection of suspected primary lung cancer by scintigraphy with indium-111-anti-carcinoembryonic antigen monoclonal antibodies (type F023C5). *Journal of Nuclear Medicine*, 32: 2064-2068.
Not in PICO
- Bilaceroglu, S., Kumcuoglu, Z., Alper, H., Osma, E., Cagirici, U., Gunel, O., Bayol, U., Celikten, E., Perim, K. & Kose, T. (1998) CT bronchus sign-guided bronchoscopic multiple diagnostic procedures in carcinomatous solitary pulmonary nodules and masses. *Respiration*, 65: 49-55.
Not in PICO
- Bilicky, J. & Belan, P. (1994) Contribution of X-ray supported bronchoscopy with taking of bioptic specimen in the diagnosis of bronchogenic carcinoma. [Slovak]. *Studia Pneumologica et Phtiseologica*, 54: 95-98.
Not in PICO
- Bjerager, M., Palshof, T., Dahl, R., Vedsted, P. & Olesen, F. (2006) Delay in diagnosis of lung cancer in general practice. *British Journal of General Practice*, 56: 863-868.
Not in PICO
- Bjornsson, J., Goellner, J. R., Williams, D. E. & Scheiber, M. V. (1986) Cytologic findings in stage I adenocarcinoma of the lung: implications for the detection of early lung cancer. *Journal of Cancer Research & Clinical Oncology*, 111: 289-290.
Not in PICO
- Blanchon, T., Brechot, J. M., Grenier, P. A., Ferretti, G. R., Lemarie, E., Milleron, B., Chague, D., Laurent, F., Martineti, Y., Beigelman-Aubry, C., Blanchon, F., Revel, M. P., Friard, S., Remy-Jardin, M., Vasile, M., Santelmo, N., Lecalier, A., Lefebure, P., Moro-Sibilot, D., Breton, J. L., Carette, M. F., Brambilla, C., Fournel, F., Kieffer, A., Frija, G. & Flahault, A. (2007) Baseline results of the Depiscan study: A French randomized pilot trial of lung cancer screening comparing dose CT scan (LDCT) and chest X-ray (CXR). *Lung Cancer*, 58: 50-58.
Not in PICO
- Blondal, T. & Bengtsson, A. (1982) Diagnostic application of nuclear DNA measurements on bronchial secretions. *Analytical and Quantitative Cytology*, 4: 269-274.
Not in PICO
- Bocking, A., Biesterfeld, S., Chatelain, R., Gien-Gerlach, G. & Esser, E. (1992) Diagnosis of bronchial carcinoma on sections of paraffin-embedded sputum: Sensitivity and specificity of an alternative to routine cytology. *Acta Cytologica*, 36: 37-47.
Not in PICO (secondary care)
- Bodh, A., Kaushal, V., Kashyap, S. & Gulati, A. (2013) Cytohistological correlation in diagnosis of lung tumors by using fiberoptic bronchoscopy: Study of 200 cases. *Indian Journal of Pathology and Microbiology*, 56: 84-88.
Not in PICO
- Boiselle, P. M., Ernst, A. & Karp, D. D. (2000) Lung cancer detection in the 21st century: potential contributions and challenges of emerging technologies. [Review] [75 refs]. *AJR.American Journal of Roentgenology*, 175: 1215-1221.
Narrative review
- Bolliger, C. T. & Haeussinger, K. (1998) Early detection of lung cancer. *European Respiratory Monograph*, 3: 22-35.
Not in PICO
- Brady, M. J., Thomas, J., Wong, T. Z., Franklin, K. M., Ho, L. M. & Paulson, E. K. (2009) Adrenal nodules at FDG PET/CT in patients known to have or suspected of having lung cancer: a proposal

- for an efficient diagnostic algorithm. *Radiology*, 250: 523-530.
Not in PICO
- Brindle, L., Pope, C., Corner, J., Leydon, G. & Banerjee, A. (2012) Eliciting symptoms interpreted as normal by patients with early-stage lung cancer: could GP elicitation of normalised symptoms reduce delay in diagnosis? Cross-sectional interview study. *BMJ Open*, 2: 2012.
Not in PICO
- Brocken, P., Prins, J. B. & van der Heijden, H. F. (2009) A two-day rapid outpatient diagnostic program decreases anxiety in suspected lung cancer patients. *European Journal of Cancer, Supplement*, 7: 189.
Not in PICO
- Brocken, P., Kiers, B. A. B., Looijen-Salamon, M. G., Dekhuijzen, P. N. R., Smits-van der Graaf, C., Peters-Bax, L., de Geus-Oei, L. F. & Van Der Heijden, H. F. M. (2012) Timeliness of lung cancer diagnosis and treatment in a rapid outpatient diagnostic program with combined (18)FDG-PET and contrast enhanced CT scanning. *Lung Cancer*, 75: 336-341.
Not in PICO
- Brocken, P., Van Der Heijden, H. F. M., Dekhuijzen, P. N. R., Peters-Bax, L. & De Geus-Oei, L.-F. (2014) High performance of f-fluorodeoxyglucose positron emission tomography and contrast-enhanced ct in a rapid outpatient diagnostic program for patients with suspected lung cancer. *Respiration*, 87: 32-37.
Not in PICO
- Brocken, P., van der Heijden, H. F., Dekhuijzen, P. N., Peters-Bax, L. & de Geus-Oei, L. F. (2014) - High performance of F-fluorodeoxyglucose positron emission tomography and contrast-enhanced CT in a rapid outpatient diagnostic program for patients with suspected lung cancer. - *Respiration*, 87: 32-37.
Duplicate
- Brocken, P., van der Heijden, H. F., Dekhuijzen, P. N., Peters-Bax, L. & de Geus-Oei, L. F. (2014) High Performance of F-Fluorodeoxyglucose Positron Emission Tomography and Contrast-Enhanced CT in a Rapid Outpatient Diagnostic Program for Patients with Suspected Lung Cancer. *Respiration*, 87: 32-37.
Not in PICO
- Broderick, L. S., Tarver, R. D. & Conces, D. J., Jr. (1997) Imaging of lung cancer: old and new. [Review] [53 refs]. *Seminars in Oncology*, 24: 411-418.
Narrative review
- Bruno, P., Ricci, A., Esposito, M. C., Scozzi, D., Tabbi, L., Sposato, B., Falasca, C., Giarnieri, E., Giovagnoli, M. R. & Mariotta, S. (2013) Efficacy and cost effectiveness of rapid on site examination (ROSE) in management of patients with mediastinal lymphadenopathies. *European Review for Medical & Pharmacological Sciences*, 17: 1517-1522.
Not in PICO
- Bugalho, A., Ferreira, D., Eberhardt, R., Dias, S. S., Videira, P. A., Herth, F. J. & Carreiro, L. (2013) Diagnostic value of endobronchial and endoscopic ultrasound-guided fine needle aspiration for accessible lung cancer lesions after non-diagnostic conventional techniques: a prospective study. *BMC Cancer*, 13: 130.
Not in PICO
- Bundgaard, N., Eriksen, H. & Greisen, O. (1989) [Bronchoscopy in monosymptomatic hemoptysis--hemoptysis in bronchial carcinoma]. [Danish]. *Nordisk Medicin*, 104: 52-53.
Not in PICO
- Bungay, H. K., Pal, C. R., Davies, C. W., Davies, R. J. & Gleeson, F. V. (2000) An evaluation of computed tomography as an aid to diagnosis in patients undergoing bronchoscopy for suspected bronchial carcinoma. *Clinical Radiology*, 55: 554-560.
Not in PICO

- Burbank, D. N. (1983) The evaluation of the patient for lung cancer. *Cancer*, 51: 2453-2455.
Narrative review
- Burguete, S. R. & Levine, S. (2010) Bronchogenic carcinoma? A fat chance. *American Journal of Respiratory and Critical Care Medicine*, 181.
Not in PICO
- Byers, T., Wolf, H. J., Franklin, W. A., Braudrick, S., Merrick, D. T., Shroyer, K. R., Hirsch, F. R., Zeng, C., Baron, A. E., Bunn, P. A., Miller, Y. E. & Kennedy, T. C. (2008) Sputum cytologic atypia predicts incident lung cancer: Defining latency and histologic specificity. *Cancer Epidemiology Biomarkers and Prevention*, 17: 158-162.
Not in PICO
- Callol, S. L. & Gomez, d. T. (1999) [Early diagnosis of cancer of the lung]. [Review] [112 refs] [Spanish]. *Archivos de Bronconeumologia*, 35: 395-403.
Narrative review
- Cao, J., Pan, Q. J., Li, Z. L. & Liu, S. F. (2006) Value of ThinPrep bronchial brushing cytology in the diagnosis of lung cancers. [Chinese]. *Zhonghua zhong liu za zhi [Chinese journal of oncology]*, 28: 536-538.
Not in PICO
- Caputi, M., Sessa, E., Esposito, E. & Speranza, A. (1995) Current role of imaging technique is the early diagnosis of lung cancer. [Italian]. *Lotta Contro la Tuberculosis e le Malattie Polmonari Sociali*, 65: 5-23.
Not in PICO
- Carr, D. T. (1990) Histopathology of lung cancer. *International Journal of Epidemiology*, 19: Suppl-10.
Narrative review
- Carvalho, L. M., Duarte, I. F., Rocha, C. M., Barros, A. S., Gil, A. M., Goodfellow, B. J., Gomes, A. I., Oliveira, D. M., Sousa, V. M. & Bernardo, J. (2010) Lung tumors' biomarker profiles of malignancy and histological type assessed by nuclear magnetic resonance (NMR) spectroscopy. *Histopathology*, 57: 226.
Not in PICO
- Cecener, G., Tunca, B., Egeli, U., Karadag, M., Vatan, O., Uzaslan, E. & Tolunay, S. (2008) Mutation analysis of the FHIT gene in bronchoscopic specimens from patients with suspected lung cancer. *Tumori*, 94: 845-848.
Not in PICO
- Chan, H. P., Lewis, C. & Thomas, P. S. (2009) Exhaled breath analysis: Novel approach for early detection of lung cancer. *Lung Cancer*, 63: 164-168.
Narrative review
- Charig, M. J. & Phillips, A. J. (2000) CT-guided cutting needle biopsy of lung lesions--safety and efficacy of an out-patient service. *Clinical Radiology*, 55: 964-969.
Not in PICO
- Cheah, P. L., Liam, C. K., Yap, S. F. & Looi, L. M. (1994) Squamous cell carcinoma antigen as an adjunct tumour marker in primary carcinoma of the lung. *Journal of Clinical Pathology*, 47: 535-537.
Not in PICO
- Chen, B. & Li, W. (2010) Comparative values of different imaging methods in lung cancer screening. [Chinese]. *Chinese Journal of Lung Cancer*, 13: 992-998.
Not in PICO
- Chen, L.-H., Chen, Y.-F., Zhang, J.-Q., Wang, W.-W., Xia, Y.-B. & Wang, J. (2012) Application value of apparent diffusion coefficient in diagnosis of different histological subtypes of lung cancers. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 28: 1541-1545.
Not in PICO

- Chen, Y. (1993) [Bronchiectasis with concomitant lung cancer--a report of 7 cases]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 15: 461-463.
Not in PICO
- Cheyne, L., Milton, R., Fear, J. & Callister, M. E. J. (2012) Variability in Gp Referral Rates for Chest X-Ray Does Not Appear to Affect Stage Or Performance Status of Patients Diagnosed with Lung Cancer. *Thorax*, 67: A90.
Not in PICO
- Chien, C.-R., Lai, M.-S. & Chen, T. H. H. (2008) Estimation of mean sojourn time for lung cancer by chest X-ray screening with a Bayesian approach. *Lung Cancer*, 62: 215-220.
Not in PICO
- Chin, T., Yano, T., Akusawa, K., Kadota, A., Tanigawa, S., Koya, Y., Masutani, M. & Horie, T. (1996) [Clinical evaluation of fiberoptic bronchoscopy for the diagnosis of solitary pulmonary nodules 2 cm or less in diameter of chest roentgenogram]. [Japanese]. *Nihon Kyobu Shikkan Gakkai Zasshi. Japanese Journal of Thoracic Diseases*, 34: 266-269.
Not in PICO
- Cho, I., Miller, D., Scherzinger, A. & Garg, K. (2012) Inter-and intra-observer variation in measuring part-solid lung nodules using conventional and semi-automated methods. *Journal of Investigative Medicine*, 60: 216.
Not in PICO
- Chopra, A., Ford, A., De, N. R. & Matthews, S. (2012) Incidental findings on positron emission tomography/CT scans performed in the investigation of lung cancer. *British Journal of Radiology*, 85: e229-e237.
Not in PICO
- Colice, G. L., Chappel, G. J., Frenchman, S. M. & Solomon, D. A. (1985) Comparison of computerized tomography with fiberoptic bronchoscopy in identifying endobronchial abnormalities in patients with known or suspected lung cancer. *American Review of Respiratory Disease*, 131: 397-400.
Not in PICO
- Colice, G. L. (1997) Detecting lung cancer as a cause of hemoptysis in patients with a normal chest radiograph: bronchoscopy vs CT. *Chest*, 111: 877-884.
Not in PICO
- Colt, H. G. & Murgu, S. D. (2010) Interventional Bronchoscopy from Bench to Bedside: New Techniques for Early Lung Cancer Detection. *Clinics in Chest Medicine*, 31: 29-37.
Narrative review
- Colt, H. G., Davoudi, M. & Murgu, S. (2011) Scientific evidence and principles for the use of endobronchial ultrasound and transbronchial needle aspiration. *Expert Review of Medical Devices*, 8: 493-513.
Narrative review
- Connolly, E. & Burt, P. A. (2011) Are we achieving lung cancer waiting time guidelines? *Lung Cancer*, 71: S22.
Not in PICO
- Connolly, G. C., Menapace, L., Safadjou, S., Francis, C. W. & Khorana, A. A. (2013) Prevalence and clinical significance of incidental and clinically suspected venous thromboembolism in lung cancer patients. *Clinical Lung Cancer*, 14: 713-718.
Not in PICO
- Cooley, M. E., Lobach, D. F., Johns, E., Halpenny, B., Saunders, T. A., Del, F. G., Rabin, M. S., Calarese, P., Berenbaum, I. L., Zaner, K., Finn, K., Berry, D. L. & Abrahm, J. L. (2013) Creating computable algorithms for symptom management in an outpatient thoracic oncology setting. *Journal of Pain & Symptom Management*, 46: 911-924.
Not in PICO
- Cortes, S. R., Cossio San, J. P., Minambres, A. E., Rodriguez Pascual, J. M. & Puyo, G. M. (2003) Diagnostic and therapeutic attitude in patient with hemoptysis. [Spanish]. *MEDIFAM - Revista de*

- Medicina Familiar y Comunitaria*, 13: 258-264.
Narrative review
- Crotty, E. & Patz, E. F., Jr. (2001) FDG-PET imaging in patients with paraneoplastic syndromes and suspected small cell lung cancer. *Journal of Thoracic Imaging*, 16: 89-93.
Narrative review
- D'Urso, V., Doneddu, V., Marchesi, I., Collodoro, A., Pirina, P., Giordano, A. & Bagella, L. (2013) Sputum analysis: Non-invasive early lung cancer detection. *Journal of Cellular Physiology*, 228: 945-951.
Narrative review
- Dai, Z., Kelly, J. C., Meloni-Ehrig, A., Slovak, M. L., Boles, D., Christacos, N. C., Bryke, C. R., Schonberg, S. A., Otani-Rosa, J., Pan, Q., Ho, A. K., Sanders, H. R., Zhang, Z. J., Jones, D. & Mowrey, P. N. (2012) Incidence and patterns of ALK FISH abnormalities seen in a large unselected series of lung carcinomas. *Molecular Cytogenetics*, 5: 44.
Not in PICO
- Dang, Y. P., Liu, G., Wang, H. & Li, M. (2004) Clinical value of PET/CT for the diagnosis and management of lung nodules. [Chinese]. *Zhonghua zhong liu za zhi [Chinese journal of oncology]*, 26: 685-687.
Not in PICO
- Daniels, M. G., Leong, S., Bowman, R. V., Yang, I. A., Masel, P., Fiene, A., Robinson, P., Burke, A., McKeon, J., Ayres, J., Duhig, E., Clarke, B., Tran, K., Godbolt, D., Dettrick, A. & Fong, K. M. (2012) Bronchoscopy and transthoracic-needle aspiration yield for histomorphomolecular diagnosis. *Journal of Thoracic Oncology*, 7: S162-S163.
Not in PICO
- Darwiche, K., Zarogoulidis, P., Krauss, L., Oezkan, F., Walter, R. F., Werner, R., Theegarten, D., Sakkas, L., Sakkas, A., Hohenforst-Schmidt, W., Zarogoulidis, K. & Freitag, L. (2013) "One-stop shop" spectral imaging for rapid on-site diagnosis of lung cancer: a future concept in nano-oncology. *International Journal of Nanomedicine*, 8: 4533-4542.
Not in PICO
- De, F. D., Turner, R. D. & Rogers, T. K. (2013) Evaluation of an expedited referral pathway for suspected lung cancer. *Lung Cancer*, 79: S18-S19.
Not in PICO
- De, G. L., Giannoccaro, V., Lopriore, V., Caldarola, P., Lentini, S., Di, B. M. & Brunetti, N. D. (2014) - New onset right ventricular enlargement in recent dyspnea: Is echocardiography enough for a diagnosis of pulmonary thrombo-embolism? - *Heart & Lung*, 43: 328-330.
Not in PICO
- Deininger, H. K. & Schmidt, C. (1986) [Puncture biopsy of the lung. A retrospective evaluation of 127 observations]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 144: 656-661.
Not in PICO
- Demian, J. & Majer, I. (2006) Our experiences with autofluorescence bronchoscopy. [Slovak]. *Lekarsky Obzor*, 55: 11-14.
Not in PICO
- Deppen, S., Putnam, J. B., Jr., Andrade, G., Speroff, T., Nesbitt, J. C., Lambright, E. S., Massion, P. P., Walker, R. & Grogan, E. L. (1993) Accuracy of FDG-PET to diagnose lung cancer in a region of endemic granulomatous disease. *Annals of Thoracic Surgery*, 92: 428-432.
Not in PICO
- Devbhandari, M. P., Quennell, P., Krysiak, P., Shah, R. & Jones, M. T. (2008) Implications of a negative bronchoscopy on waiting times to treatment for lung cancer patients: results of a prospective tracking study. *European Journal of Cardio-Thoracic Surgery*, 34: 479-483.
Not in PICO

- Dewan, N. A., Reeb, S. D., Gupta, N. C., Gobar, L. S. & Scott, W. J. (1995) PET-FDG imaging and transthoracic needle lung aspiration biopsy in evaluation of pulmonary lesions. A comparative risk-benefit analysis. *Chest*, 108: 441-446.
Not in PICO
- Dhital, K., Saunders, C. A. B., Seed, P. T., O'Doherty, M. J. & Dussek, J. (2000) [F-18]fluorodeoxyglucose positron emission tomography and its prognostic value in lung cancer. *European Journal of Cardio-Thoracic Surgery*, 18: 425-428.
Not in PICO
- Diaz-Jimenez, J. P. (2000) Bronchoscopic early detection of lung cancer. *Monaldi Archives for Chest Disease*, 55: 33-35.
Narrative review
- Divisi, D., Di, T. S., De, V. A. & Crisci, R. (2010) Early diagnosis of lung cancer using a SAFE-3000 autofluorescence bronchoscopy. *Interactive Cardiovascular & Thoracic Surgery*, 11: 740-744.
Not in PICO
- Dong, X., Qiu, X., Liu, Q. & Jia, J. (2013) Endobronchial ultrasound-guided transbronchial needle aspiration in the mediastinal staging of non-small cell lung cancer: a meta-analysis. *Annals of Thoracic Surgery*, 96: 1502-1507.
Not in PICO
- Doseeva, V., Woodcock, J., Freedy, J., James, W. & Knezevic, V. (2014) A blood test for early detection of lung cancer using a mixed panel of tumor proteins and autoantibodies. *Clinical Cancer Research*, 20.
Not in PICO
- Dragomir, A., Moldoveanu, E. & Mihaltan, F. (2011) [Update regarding the role of biomarkers in early diagnosis of non-small cell bronchopulmonary cancer]. [Romanian]. *Pneumologia (Bucharest, Romania)*, 60: 7, 9-7,13.
Narrative review
- Dregan, A., Moller, H., Charlton, J. & Gulliford, M. C. (2013) Are alarm symptoms predictive of cancer survival? Population-based cohort study. *British Journal of General Practice*, 63: e807-e812.
Not in PICO
- Dull, W. L. (1980) Needle aspiration biopsy in suspected pulmonary carcinoma. *Respiration*, 39: 291-294.
Not in PICO
- Dwarakanath, A. & Callister, M. E. J. (2011) Rate of chest X-rays (CXR) twelve months prior diagnosis of lung cancer. *Thorax*, 66: A132.
Not in PICO
- Eberhardt, R., Morgan, R. K., Ernst, A., Beyer, T. & Herth, F. J. (2010) Comparison of suction catheter versus forceps biopsy for sampling of solitary pulmonary nodules guided by electromagnetic navigational bronchoscopy. *Respiration*, 79: 54-60.
Not in PICO
- Ebert, W., Hug, G., Stabrey, A., Bulzebruck, H. & Drings, P. (1989) Evaluation of tumor markers NSE and CEA for the diagnosis and follow-up of small cell lung cancer. [German]. *Arztliche Laboratorium*, 35: 1-10.
Not in PICO
- Ebert, W., Muley, T. & Drings, P. (1996) Does the assessment of serum markers in patients with lung cancer aid in the clinical decision making process? *Anticancer Research*, 16: 2161-2168.
Not in PICO
- Edell, E., Lam, S., Pass, H., Miller, Y. E., Sutedja, T., Kennedy, T., Loewen, G., Keith, R. L. & Gazdar, A. (2009) Detection and localization of intraepithelial neoplasia and invasive carcinoma using fluorescence-reflectance bronchoscopy: an international, multicenter clinical trial.[Erratum appears in J Thorac Oncol. 2009 Apr;4(4):558 Note: Gazdar, Adi [added]]. *Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer*, 4: 49-

54.

Not in PICO

Edoute, Y., Malberger, E., Kuten, A., Moscovitz, M. & Ben-Haim, S. A. (1990) Symptomatic pericardial effusion in lung cancer patients: the role of fluid cytology. *Journal of Surgical Oncology*, 45: 121-123.

Not in PICO

Englmeier, K.-H. & Seemann, M. D. (2008) Multimodal virtual bronchoscopy using PET/CT images. *Computer Aided Surgery*, 13: 106-113.

Not in PICO

Eremeishvili, K., Nagendran, R., Constantinescu, G., Gulati, M. & Stokes, T. C. (2011) Timeliness of referral of patients with abnormal chest X-ray suggestive of lung cancer. *European Journal of Cancer*, 47: S611.

Not in PICO

Erozan, Y. S. (1986) Cytopathologic diagnosis of pulmonary neoplasms in sputum and bronchoscopic specimens. *Seminars in Diagnostic Pathology*, 3: 188-195.

Narrative review

Escarguel, B., D'Amore, D., Chapel, F., Bec, J., Audigier-Valette, C., Lahlah, H., Milhe, F. & Marqueste, L. (2009) [Early diagnosis of lung cancer: impact of autofluorescence bronchoscopy]. [French]. *Revue de Pneumologie Clinique*, 65: 287-291.

Duplicate

Escarguel, B., D'Amore, D., Chapel, F., Bec, J., Audigier-Valette, C., Lahlah, H., Milhe, F. & Marqueste, L. (2009) Early diagnosis of lung cancer: Impact of autofluorescence bronchoscopy. [French]. *Revue de Pneumologie Clinique*, 65: 287-291.

Not in PICO

Evison, M., Crosbie, P., Martin, J., Barber, P. & Booton, R. (2013) EBUS-TBNA in the diagnosis of non-primary lung cancers. *Lung Cancer*, 79: S24.

Not in PICO

Fan, Y.-B., Wang, Q.-S., Ye, L., Wang, T.-Y. & Wu, G.-P. (2010) Clinical application of the SurePath liquid-based Pap test in cytological screening of bronchial brushing for the diagnosis of lung cancer. *Cytotechnology*, 62: 53-59.

Not in PICO

Fassina, A., Corradin, M., Zardo, D., Cappellesso, R., Corbetti, F. & Fassan, M. (2011) Role and accuracy of rapid on-site evaluation of CT-guided fine needle aspiration cytology of lung nodules. *Cytopathology*, 22: 306-312.

Not in PICO

Felten, M. K., Knoll, L., Schikowsky, C., Das, M., Feldhaus, C., Hering, K. G., Bocking, A. & Kraus, T. (2014) Is it useful to combine sputum cytology and low-dose spiral computed tomography for early detection of lung cancer in formerly asbestos-exposed power industry workers? *Journal of Occupational Medicine and Toxicology*, 9.

Not in PICO (screening)

Fenton, J. J. & Deyo, R. A. (2003) Patient self-referral for radiologic screening tests: Clinical and ethical concerns. *Journal of the American Board of Family Practice*, 16: 494-501.

Not in PICO

Field, J. K., Dietrich, D., Kneip, C., Raji, O., Liloglou, T., Seegebarth, A., Schlegel, T., Flemming, N., Rausch, S., Distler, J., Fleischhacker, M., Liebenberg, V., Giles, T., Walshaw, M., Wabbourton, C. & Schmidt, B. (2010) SHOX2 DNA methylation-a validated bio marker for detecting lung cancer in bronchial aspirates. *Tumor Biology*, 31: S47.

Not in PICO

Fielding, P., Turnbull, L., Prime, W., Walshaw, M. & Field, J. K. (1999) Heterogeneous nuclear ribonucleoprotein A2/B1 up-regulation in bronchial lavage specimens: a clinical marker of early

- lung cancer detection. *Clinical Cancer Research*, 5: 4048-4052.
Not in PICO
- Filderman, A. E., Shaw, C. & Matthay, R. A. (1986) Lung cancer. Part I: Etiology, pathology, natural history, manifestations, and diagnostic techniques. [Review] [117 refs]. *Investigative Radiology*, 21: 80-90.
Narrative review
- Filippetti, M., Visca, P., Bordignon, V., Sergi, D., Marolla, P., Ferretti, G., Tonachella, R., Corzani, F., Fattoruso, S. I. & Di, L. L. (2009) [Fiberoptic bronchoscopy as diagnostic tool in primitive lung cancer]. [Italian]. *Clinica Terapeutica*, 160: 43-46.
Not in PICO
- Fischer, B. M., Mortensen, J. & Hojgaard, L. (2001) Positron emission tomography in the diagnosis and staging of lung cancer: a systematic, quantitative review (DARE structured abstract). *Lancet Oncology*, 2: 659-666.
Not in PICO
- Fishman, J. E., Schwartz, D. S., Sais, G. J., Flores, M. R. & Sridhar, K. S. (1995) Bronchogenic carcinoma in HIV-positive patients: findings on chest radiographs and CT scans. *AJR.American Journal of Roentgenology*, 164: 57-61.
Not in PICO
- Flenaugh, E. L. (2003) Early diagnosis and treatment in lung cancer: Can the primary care provider make a difference? *Ethnicity and Disease*, 13: S3.
Narrative review
- Fontana, R. S., Sanderson, D. R. & Woolner, L. B. (1986) Lung cancer screening: The Mayo Program. *Journal of Occupational Medicine*, 28: 746-750.
Not in PICO
- Fowles, H., Brown, D., Morley, A. & Jones, M. (2014) The utility of chest X-rays in the diagnosis of lung cancer. *Lung Cancer*, 83: S18.
Not in PICO
- Franceschi, M., Roncevic, S., Sokcevic, M., Halec, T. & Kusic, Z. (2009) [The role of ultrasonography in detection of metastases in patients with lung carcinoma]. [Croatian]. *Acta Medica Croatica*, 63: Suppl-4.
Not in PICO
- Fuchs, F. S., Zirlik, S., Hildner, K., Schubert, J., Vieth, M. & Neurath, M. F. (2013) Confocal laser endomicroscopy for diagnosing lung cancer in vivo. *European Respiratory Journal*, 41: 1401-1408.
Not in PICO
- Fultz, P. J., Feins, R. H., Strang, J. G., Wandtke, J. C., Johnstone, D. W., Watson, T. J., Gottlieb, R. H., Voci, S. L. & Rubens, D. J. (2002) Detection and diagnosis of nonpalpable supraclavicular lymph nodes in lung cancer at CT and US. *Radiology*, 222: 245-251.
Not in PICO
- Furukawa, K., Ikeda, N., Miura, T., Kakihana, M., Saito, M. & Kato, H. (2003) Is autofluorescence bronchoscopy needed to diagnose early bronchogenic carcinoma? Pro: Autofluorescence bronchoscopy. *Journal of Bronchology*, 10: 64-69.
Narrative review
- Gaber, K. A., Goldman, J. M. & Farrell, D. J. (2002) Cytological examination of the whole endobronchial brush in bronchoscopic diagnosis of lung cancer. *Respiratory Medicine*, 96: 259-261.
Not in PICO
- Gao, L., Wang, Z., Li, F., Hammoudi, A. A., Thrall, M. J., Cagle, P. T. & Wong, S. T. (2012) Differential diagnosis of lung carcinoma with coherent anti-Stokes Raman scattering imaging. [Review]. *Archives of Pathology & Laboratory Medicine*, 136: 1502-1510.
Not in PICO

George, P. J. (1999) Fluorescence bronchoscopy for the early detection of lung cancer. [Review] [34 refs]. *Thorax*, 54: 180-183.
Narrative review

Ghosal, R., Lewis, K. E., Kloer, P. J., Davies, C. & Lewis, P. D. (2009) Assessing a panel of five biomarkers in the sputum of patients with and without lung cancer. *Thorax*, 64: A80-A81.
Not in PICO

Giarelli, E. (2002) To screen or not to screen: using spiral computerized tomography in the early detection of lung cancer. [Review] [12 refs]. *Clinical Journal of Oncology Nursing*, 6: 223-224.
Not in PICO

Gilbert, C., Akulian, J., Ortiz, R., Lee, H. & Yarmus, L. (2014) Novel bronchoscopic strategies for the diagnosis of peripheral lung lesions: Present techniques and future directions. *Respirology*, 19: 636-644.
Duplicate

Gilbert, C., Akulian, J., Ortiz, R., Lee, H. & Yarmus, L. (2014) - Novel bronchoscopic strategies for the diagnosis of peripheral lung lesions: present techniques and future directions. - *Respirology*, 19: 636-644.
Narrative review

Jimenez, A., Franquet, T., Prats, R., Estrada, P., Villalba, J. & Bague, S. (2002) Unusual primary lung tumors: a radiologic-pathologic overview. *Radiographics : a review publication of the Radiological Society of North America, Inc*, 22: 601-619.
Narrative review

Gjurchinov, D., Stojanovska-Nojkova, J., Grunevski, M., Nikolov, V. & Spasovski, G. (2007) Radiological and "imaging" methods in TNM classification of non-small-cell lung cancer. *Prilozi / Makedonska akademija na naukite i umetnostite, Oddelenie za biologski i medicinski nauki = Contributions / Macedonian Academy of Sciences and Arts, Section of Biological and Medical Sciences*, 28: 155-167.
Not in PICO

Glennon, C. & Seskevich, J. Relaxation technique to ease dyspnea: A tool for oncology nurses. [References]. *Clinical Journal of Oncology Nursing* 12[2], 369-371. 2008.
Ref Type: Generic
Ref ID: 548
Reprint: Not in File
Abstract: Presents the case of a 68-year-old man with lung cancer in remission, who was admitted to the oncology unit with increasing dyspnea. He reported symptoms that included shortness of breath, difficulty sleeping, and a lack of appetite. The patient's physician ordered supplemental oxygen and scheduled diagnostic imaging examinations, laboratory tests, and a possible bronchoscopy. The morning after admission, the patient experienced significantly increased dyspnea. The stress-management nurse realized that the sensation of breathlessness was creating panic, which increased anxiety and the need for oxygen, worsening the dyspnea. The stress-management nurse coached the patient in a structured relaxation technique as a tool to help him learn to control and regulate his breathing. Over time the response was positive, as reported by the patient and validated by the oncology nurse. Although dyspnea is a complex symptom that varies among patients, nonpharmacologic interventions to promote relaxation and provide instruction in breathing control may reduce stress and increase the ease and effectiveness of respiration and gas exchange. Nurses should be familiar with simple stress management approaches, such as relaxation breathing, to assist an anxious patient with ineffective breathing. (PsycINFO Database Record (c) 2012 APA, all rights reserved)
Notes: DB - PsycINFO
AN - Peer Reviewed Journal: 2008-04562-008
MA - Glennon, Cathy: cglennon@kumc.edu
SO - *Clinical Journal of Oncology Nursing*. Vol.12(2), Apr 2008, pp. 369-371

n

- Goldberg, M. & Unger, M. (2000) Lung cancer. Diagnostic tools. [Review] [73 refs]. *Chest Surgery Clinics of North America*, 10: 763-779.
Narrative review
- Gorbacheva, L. M., Shabarov, V. L., Kareva, L. P. & Nikitskaia, T. I. (1990) [The potentials of fiber bronchoscopy with immediate cytological study in the diagnosis of lung cancer under outpatient conditions]. [Russian]. *Voprosy Onkologii*, 36: 579-582.
Not in PICO
- Greene, R., Szyfelbein, W. M., Isler, R. J., Stark, P. & Janstsch, H. (1985) Supplementary tissue-core histology from fine-needle transthoracic aspiration biopsy. *AJR.American Journal of Roentgenology*, 144: 787-792.
Not in PICO
- Griffin, J. P., Zaman, M. K., Niell, H. B., Tolley, E. A., Cole, F. H., Jr. & Weiman, D. S. (2012) Diagnosis of lung cancer: a bronchoscopist's perspective. *Journal of Bronchology & Interventional Pulmonology*, 19: 12-18.
Not in PICO
- Grodzki, T., Alchimowicz, J., Wojcik, J., Kubisa, B., Pierog, J., Janowski, H., Kochanowski, L. & Wojcik, N. (2012) Early lung cancer detection programme: Its impact on activity of the local thoracic surgery department. *Interactive Cardiovascular and Thoracic Surgery*, 15: S32.
Not in PICO
- Gruning, W., Ammenwerth, W., Wurps, H., Kollmeier, J., Blum, T., Schonfeld, N., Griff, S. & Bauer, T. T. (2013) [Diagnostic yield and safety of bronchoscopic cryotechnique in routine diagnostics for suspected lung cancer]. [German]. *Pneumologie*, 67: 676-682.
Not in PICO
- Gu, T., Wang, X., Wang, X., Wang, W., Liu, Y., Zhang, B., Shi, Y., Zhang, Z., Sun, Q., Xue, T., Zhang, X., Liu, Z., Zhu, S. & Mao, X. (2001) [The value of detecting telomerase activity on early diagnosis of lung cancer]. [Chinese]. *Chinese Journal of Lung Cancer*, 4: 37-40.
Not in PICO
- Guan, X., Yang, X. & Zhang, Z. (2010) Role of fiberoptic bronchoscopy in the early diagnosis of 238 female lung cancer patients. [Chinese]. *Chinese Journal of Clinical Oncology*, 37: 223-225.
Not in PICO
- Guo, X.-J., Ni, P.-H., Li, L., Deng, W.-W., Wan, H.-Y. & Shi, G.-C. (2000) Detection of p53 gene mutation of bronchoscopic samples in the patients suspected to lung cancer. *Chinese Journal of Cancer Research*, 12: 282-285.
Not in PICO
- Gurney, J. W. (1994) Early detection of lung cancer by chest radiography. *AJR.American Journal of Roentgenology*, 163: 741.
Narrative review
- Hall, W. B., Truitt, S. G., Scheunemann, L. P., Shah, S. A., Rivera, M. P., Parker, L. A. & Carson, S. S. (2009) The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism. *Archives of Internal Medicine*, 169: 1961-1965.
Not in PICO
- Halling, K. C., Rickman, O. B., Kipp, B. R., Harwood, A. R., Doerr, C. H. & Jett, J. R. (2006) A comparison of cytology and fluorescence in situ hybridization for the detection of lung cancer in bronchoscopic specimens. *Chest*, 130: 694-701.
Not in PICO
- Hamilton, W. & Sharp, D. (2004) Diagnosis of lung cancer in primary care: a structured review. [Review] [83 refs]. *Family Practice*, 21: 605-611.
Narrative review

- Hamilton, W. & Roobottom, C. (2012) Early diagnosis of cancer by imaging: The primary care perspective. *Radiography*, 18: 5-8.
Narrative review
- Hamilton, W., Green, T., Martins, T., Elliott, K., Rubin, G. & Macleod, U. (2013) Evaluation of risk assessment tools for suspected cancer in general practice: a cohort study. *British Journal of General Practice*, 63: 30-36.
Not in PICO
- Hamilton, W. T., Round, A. P., Sharp, D. J. & Peters, T. J. (2004) High incidence of mesothelioma in an English city without heavy industrial use of asbestos. *Journal of Public Health*, 26: 77-78.
Not in PICO
- Hamm, J. (1981) Clinical and endoscopic diagnosis of bronchogenic cancer. [German]. *Langenbecks Archiv fur Chirurgie*, 355: 104-106.
Narrative review
- Hammerschmidt, S., Gessner, C., Kuhn, H. & Wirtz, H. (2006) Early diagnosis of lung cancer: Where do we stand?. [German]. *MMW-Fortschritte der Medizin*, 148: 28-31.
Narrative review
- Han, Y. M., Fang, L. Z., Zhang, X. H., Yuan, S. H., Chen, J. H. & Li, Y. M. (2012) Polyarthritis as a prewarning sign of occult lung cancer. *Kaohsiung Journal of Medical Sciences*, 28: 54-56.
Not in PICO
- Hanibuchi, M., Yano, S., Nishioka, Y., Miyoshi, T., Kondo, K., Uehara, H. & Sone, S. (2007) Autofluorescence bronchoscopy, a novel modality for the early detection of bronchial premalignant and malignant lesions. *The journal of medical investigation : JMI*, 54: 261-266.
Not in PICO
- Hanley, K. S. & Rubins, J. B. (2003) Classifying solitary pulmonary nodules - New imaging methods to distinguish malignant, benign lesions. *Postgraduate Medicine*, 114: 29-35.
Narrative review
- Harders, S. W., Madsen, H. H., Hjorthaug, K., Arveschoug, A. K., Rasmussen, T. R., Meldgaard, P., Andersen, J. B., Pilegaard, H. K., Hager, H., Rehling, M. & Rasmussen, F. (2012) Characterization of pulmonary lesions in patients with suspected lung cancer: computed tomography versus [18F] fluorodeoxyglucose-positron emission tomography/computed tomography. *Cancer Imaging*, 12: 437-446.
Not in PICO
- Harders, S. W., Madsen, H. H., Hjorthaug, K., Rehling, M., Rasmussen, T. R., Pedersen, U., Pilegaard, H. K., Meldgaard, P., Baandrup, U. T. & Rasmussen, F. (2012) Limited value of 99mTc depreotide single photon emission CT compared with CT for the evaluation of pulmonary lesions. *British Journal of Radiology*, 85: e307-e313.
Not in PICO
- Harders, S. W. (2012) LUCIS: lung cancer imaging studies. *Danish Medical Journal*, 59: B4542.
Not in PICO
- Harders, S. W., Madsen, H. H., Hjorthaug, K., Arveschoug, A. K., Rasmussen, T. R., Meldgaard, P., Andersen, J. B., Pilegaard, H. K., Hager, H., Rehling, M. & Rasmussen, F. (2012) Characterization of pulmonary lesions in patients with suspected lung cancer: Computed tomography versus [18F]fluorodeoxyglucose-positron emission tomography/computed tomography. *Cancer Imaging*, 12: 437-446.
Duplicate
- Harders, S. W., Madsen, H. H., Hjorthaug, K., Rehling, M., Rasmussen, T. R., Pedersen, U., Pilegaard, H. K., Meldgaard, P., Baandrup, U. T. & Rasmussen, F. (2012) Limited value of 99mTc depreotide single photon emission CT compared with CT for the evaluation of pulmonary lesions. *British Journal of Radiology*, 85: e307-e313.
Duplicate

- Harewood, G. C., Pascual, J., Raimondo, M., Woodward, T., Johnson, M., McComb, B., Odell, J., Jamil, L. H., Gill, K. R. & Wallace, M. B. (2010) Economic analysis of combined endoscopic and endobronchial ultrasound in the evaluation of patients with suspected non-small cell lung cancer. *Lung Cancer*, 67: 366-371.
Not in PICO
- Hariri, L. P., Applegate, M. B., Mino-Kenudson, M., Mark, E. J., Bouma, B. E., Tearney, G. J. & Suter, M. J. (2013) Optical Frequency Domain Imaging of Ex vivo Pulmonary Resection Specimens: Obtaining One to One Image to Histopathology Correlation. *Journal of Visualized Experiments*.(71), 2013..
Narrative review
- Harkness, H., Warke, T., Magee, N. & Ranaghan, E. (2012) Downgrading red flag referrals for lung cancer. *Lung Cancer*, 75: S24-S25.
Not in PICO
- Haro, E. M., Rubio, G. M., Vizcaya, S. M., Baldo, P., X, Casamitja Sot, M. T. & Sebastian, Q. F. (2004) [Bronchoscopic lung biopsy with fluoroscopy to study 164 localized pulmonary lesions]. [Spanish]. *Archivos de Bronconeumologia*, 40: 483-488.
Not in PICO
- Haro, M., Jimenez, J., Tornero, A., Vizcaya, M., Tirado, R. & Cros, T. (2002) [Usefulness of computerized tomography and bronchoscopy in patients with hemoptysis. Analysis of 482 cases]. [Spanish]. *Anales de Medicina Interna*, 19: 59-65.
Not in PICO
- Harris, J., Howard, W., Gulati, A. & Cooper, S. (2012) The Colchester fast-track chest X-ray referral pathway. *Lung Cancer*, 75: S25.
Not in PICO
- Hashimoto, M., Miyauchi, T., Heianna, J., Sugawara, M., Ishiyama, K., Watarai, J. & Nanjo, H. (2009) Accurate diagnosis of peripheral small cell lung cancer with computed tomography. *Tohoku Journal of Experimental Medicine*, 217: 217-221.
Not in PICO
- Haussinger, K., Stanzel, F., Markus, A., Bolliger, C. T. & Pichler, J. (1999) Early detection of lung cancer. [German]. *Pneumologie*, 53: 77-82.
Narrative review
- Hayata, Y., Kato, H., Ono, J., Matsushima, Y., Hayashi, N., Saito, T. & Kawate, N. (1982) Fluorescence fiberoptic bronchoscopy in the diagnosis of early stage lung cancer. *Recent Results in Cancer Research*, Fortschritte: 121-130.
Not in PICO
- Heeringa, A., de, V. N., Snow, G. B. & Stam, J. (1988) Laryngeal cancer and lung cancer in the same patient: a retrospective study. *European Journal of Surgical Oncology*, 14: 209-211.
Not in PICO
- Henderson, S., DeGroff, A., Richards, T. B., Kish-Doto, J., Soloe, C., Heminger, C. & Rohan, E. (2011) A Qualitative Analysis of Lung Cancer Screening Practices by Primary Care Physicians. *Journal of Community Health*, 36: 949-956.
Not in PICO
- Herth, F. J. F. (2010) Endoscopy and imaging: Their contributions in LC diagnosis. *Tumor Biology*, 31: S15-S16.
Narrative review
- Hetzel, J., Eberhardt, R., Herth, F. J., Petermann, C., Reichle, G., Freitag, L., Dobbertin, I., Franke, K. J., Stanzel, F., Beyer, T., Moller, P., Fritz, P., Ott, G., Schnabel, P. A., Kastendieck, H., Lang, W., Morresi-Hauf, A. T., Szyrach, M. N., Mucic, R., Shah, P. L., Babiak, A. & Hetzel, M. (2012) Cryobiopsy increases the diagnostic yield of endobronchial biopsy: a multicentre trial. *European Respiratory Journal*, 39: 685-690.
Not in PICO

- Heye, T., Ley, S., Heussel, C. P., Dienemann, H., Kauczor, H. U., Hosch, W. & Libicher, M. (2012) Detection and size of pulmonary lesions: how accurate is MRI? A prospective comparison of CT and MRI. *Acta Radiologica*, 53: 153-160.
Not in PICO
- Hillner, B. E., Tunuguntla, R. & Fratkin, M. (2004) Clinical decisions associated with positron emission tomography in a prospective cohort of patients with suspected or known cancer at one United States center. *Journal of Clinical Oncology*, 22: 4147-4156.
Not in PICO
- Hirsch, F. R. & Hansen, H. H. (2001) New techniques for early diagnosis of lung cancer. [Danish]. *Ugeskrift for Laeger*, 163: 4321-4323.
Narrative review
- Hirsch, F. R., Franklin, W. A., Gazdar, A. F. & Bunn, P. A., Jr. (2001) Early detection of lung cancer: Clinical perspectives of recent advances in biology and radiology. *Clinical Cancer Research*, 7: 5-22.
Narrative review
- Hirsch, F. R., Bunn, P. A., Jr., Dmitrovsky, E., Field, J. K., Franklin, W. A., Greenberg, R. E., Hansen, H. H., Henschke, C. I., Rigas, J. R., Smith, R. A., Toennesen, P. & Mulshine, J. L. (2002) IV international conference on prevention and early detection of lung cancer, Reykjavik, Iceland, August 9-12, 2001. *Lung Cancer*, 37: 325-344.
Narrative review
- Hirshberg, B., Biran, I., Glazer, M. & Kramer, M. R. (1997) Hemoptysis: etiology, evaluation, and outcome in a tertiary referral hospital. *Chest*, 112: 440-444.
Not in PICO
- Hobbins, S., Russell, C., Phillips, S., Walker, C. & Woolhouse, I. (2012) Lung cancer mimics and significant incidental findings in patients undergoing fast track pre-clinic computed tomography. *Lung Cancer*, 75: S13-S14.
Not in PICO
- Holmes, R. L. & Fadden, C. T. (2004) Evaluation of the Patient with Chronic Cough. *American Family Physician*, 69: 2159-2166+2169.
Narrative review
- Horai, T. (2008) Effectiveness of clinical cytology in the diagnosis and treatment of lung cancer. [Japanese]. *Japanese Journal of Lung Cancer*, 48: 5-10.
Narrative review
- Huang, Y., Xu, D., Jirapatnakul, A., Reeves, A. P., Farooqi, A., Zhang, L., Giunta, S., Zulueta, J., Aye, R., Miller, A., Mendelson, D. S., Aylesworth, C., Sheppard, B., Klingler, K., Yankelevitz, D. F. & Henschke, C. I. (2011) CT- and computer-based features of small hamartomas. *Clinical Imaging*, 35: 116-122.
Not in PICO
- Huber, R. M., Gamarra, F., Lebrig, A., Stepp, H., Rick, K., Haussinger, K. & Baumgartner, R. (1995) Value of photodynamic diagnosis in bronchology: Early detection of lung cancer possible?. [German]. *Atemwegs- und Lungenkrankheiten*, 21: 558-561.
Narrative review
- Huber, R. M. (2010) Screening and early detection for lung cancer-hope and reality. *Tumor Biology*, 31: S15.
Narrative review
- Hunt, I., Siva, M., Southon, R. & Treasure, T. (2006) Does lung cancer screening with chest X-ray improve disease-free survival? *Interactive Cardiovascular and Thoracic Surgery*, 5: 483-487.
Not in PICO
- Huq, S., Gautam, M., Haris, M., Ashish, A., Ledson, M. & Walshaw, M. (2010) Inappropriate referrals to the rapid access lung clinic (RALC). *Thorax*, 65: A173-A174.
Not in PICO

- Huq, S., Bin, S. J., Yu, H., Haris, M., Gautam, M., Ledson, M. & Walshaw, M. (2011) Accuracy of coded chest X-rays and grade of reporter in diagnosis of lung cancer - A 9 year comparative study. *American Journal of Respiratory and Critical Care Medicine*, 183.
Not in PICO
- Hur, J., Lee, H. J., Byun, M. K., Nam, J. E., Moon, J. W., Kim, H. S., Kim, Y. J., Choe, K. O. & Choi, B. W. (2010) Computed tomographic fluoroscopy-guided needle aspiration biopsy as a second biopsy technique after indeterminate transbronchial biopsy results for pulmonary lesions: comparison with second transbronchial biopsy. *Journal of Computer Assisted Tomography*, 34: 290-295.
Not in PICO
- Hurt, C. N., Roberts, K., Rogers, T. K., Griffiths, G. O., Hood, K., Prout, H., Nelson, A., Fitzgibbon, J., Barham, A., Thomas-Jones, E., Edwards, R. T., Yeo, S. T., Hamilton, W., Tod, A. & Neal, R. D. (2013) A feasibility study examining the effect on lung cancer diagnosis of offering a chest X-ray to higher-risk patients with chest symptoms: protocol for a randomized controlled trial. *Trials*, 14. Protocol
- Hurzeler, D. (1980) [When should a general practitioner order a bronchoscopy? (author's transl)]. [German]. *Schweizerische Rundschau fur Medizin Praxis*, 69: 1649-1652.
Narrative review
- Ikeda, N. (2012) Comprehensive diagnostic and therapeutic bronchoscopy for central type lung cancer. *Journal of Thoracic Oncology*, 7: S434-S435.
Narrative review
- Ishida, T., Inoue, T., Sugio, K., Inoue, K., Inuzuka, S., Tateishi, M. & Sugimachi, K. (1993) Early squamous lung cancer and longer survival rates. *Respiration*, 60: 359-365.
Not in PICO
- Iyen-Omofoman, B., Tata, L. J., Baldwin, D. R., Smith, C. J. & Hubbard, R. B. (2013) Using socio-demographic and early clinical features in general practice to identify people with lung cancer earlier. *Thorax*, 68: 451-459.
Already included
- Iyer, S., Roughley, A., Rider, A. & Taylor-Stokes, G. (2014) The symptom burden of non-small cell lung cancer in the USA: a real-world cross-sectional study. *Supportive Care in Cancer*, 22: 181-187.
Not in PICO
- Jack, C. I., Sheard, J. D., Lippitt, B., Fromholtz, A., Evans, C. C. & Hind, C. R. (1993) Lung cancer in elderly patients: the role of induced sputum production to obtain a cytological diagnosis. *Age & Ageing*, 22: 227-229.
Not in PICO
- Jantus-Lewintre, E., Uso, M., Sanmartin, E. & Camps, C. (2012) Update on biomarkers for the detection of lung cancer. *Lung Cancer: Targets and Therapy*, 3: 21-29.
Narrative review
- Jany, B., Fischbach, W. & Chowanetz, W. (1988) Usefulness of the tumor markers NSE, CEA and SCC as a diagnostic tool in suspected bronchial carcinoma?. [German]. *Medizinische Klinik*, 83: 121-124.
Not in PICO
- Jerse, M. & Tercelj, M. (2006) Contributions of cytology examination and methods in lung cancer diagnostic. *Radiology and Oncology*, 40: S77-S85.
Not in PICO
- Jeyabalan, A., Maskell, G., Hyslop, J. & Iles, S. (2010) Do radiologists and clinicians agree on the need for CT scanning in patients with suspected lung cancer? *American Journal of Respiratory and Critical Care Medicine*, 181.
Not in PICO
- Jiang, F., Todd, N. W., Li, R., Zhang, H., Fang, H. & Stass, S. A. (2010) A panel of sputum-based genomic marker for early detection of lung cancer. *Cancer Prevention Research*, 3: 1571-1578.
Not in PICO

- Jin, G. Y., Kim, Y. S., Han, Y. M., Lee, Y. C. & Kim, S. R. (2013) Combined pulmonary fibrosis and emphysema: Comparison of CT findings in symptomatic vs. Asymptomatic subjects. *Journal of Thoracic Imaging*, 28: W113.
Not in PICO
- Jones, A. M., Hanson, I. M., Armstrong, G. R. & O'Driscoll, B. R. (2001) Value and accuracy of cytology in addition to histology in the diagnosis of lung cancer at flexible bronchoscopy. *Respiratory Medicine*, 95: 374-378.
Not in PICO
- Joos, L., Patuto, N., Chhajed, P. N. & Tamm, M. (2006) Diagnostic yield of flexible bronchoscopy in current clinical practice. *Swiss Medical Weekly*, 136: 155-159.
Not in PICO
- Jordan, K. P., Hayward, R. A., Blagojevic-Bucknall, M. & Croft, P. (2013) Incidence of prostate, breast, lung and colorectal cancer following new consultation for musculoskeletal pain: a cohort study among UK primary care patients. *International Journal of Cancer*, 133: 713-720.
Cannot extract outcome in PICO (PPVs) as cancer data only reported in total for 10-year follow up
- Kadara, H., Kabbout, M. & Wistuba, I. I. (2012) Pulmonary adenocarcinoma: a renewed entity in 2011. [Review]. *Respirology*, 17: 50-65.
Narrative review
- Kaparianos, A., Argyropoulou, E., Sampsonas, F., Zania, A., Efremidis, G., Tsiamita, M. & Spiropoulos, K. (2008) Indications, results and complications of flexible fiberoptic bronchoscopy: a 5-year experience in a referral population in Greece. *European Review for Medical & Pharmacological Sciences*, 12: 355-363.
Not in PICO
- Kara, K. & Ozturk, E. (2012) Diagnostic imaging of lung cancer. *TAF Preventive Medicine Bulletin*, 11: 749-756.
Narrative review
- Kato, F., Hamasaki, M., Miyake, Y., Iwasaki, A., Iwasaki, H. & Nabeshima, K. (2012) Clinicopathological characteristics of subcentimeter adenocarcinomas of the lung. *Lung Cancer*, 77: 495-500.
Not in PICO
- Kato, H. & Cortese, D. A. (1985) Early detection of lung cancer by means of hematoporphyrin derivative fluorescence and laser photoradiation. *Clinics in Chest Medicine*, 6: 237-253.
Narrative review
- Katsimpoula, S., Patrinoou-Georgoula, M., Makrilia, N., Dimakou, K., Guialis, A., Orfanidou, D. & Syrigos, K. N. (2009) Overexpression of hnRNPA2/B1 in bronchoscopic specimens: a potential early detection marker in lung cancer. *Anticancer Research*, 29: 1373-1382.
Not in PICO
- Katz, R. L., Zaidi, T. M., Fernandez, R. L., Zhang, J., He, W., Acosta, C., Daniely, M., Madi, L., Vargas, M. A., Dong, Q., Jiang, X. G. F., Caraway, N. P., Vaporciyan, A. A., Roth, J. A. & Spitz, M. R. (2008) Automated detection of genetic abnormalities combined with cytology in sputum is a sensitive predictor of lung cancer. *Modern Pathology*, 21: 950-960.
Not in PICO
- Kawachi, H. & Shimokata, K. (1985) Factors affecting the rate of positivity of sputum cytology in lung cancer. *Japanese Journal of Clinical Oncology*, 15: 451-456.
Not in PICO
- Kawamura, T., Mochizuki, Y., Nakahara, Y., Kawanami, R., Tsuyuguchi, K. & Katsura, Y. (1996) Clinical study of patients with bloody sputum. [Japanese]. *Japanese Journal of Lung Cancer*, 36: 753-757.
Not in PICO
- Kawate, N., Tsuchida, T., Kakihana, M., Tsuboi, M., Furukawa, K., Okunaka, T., Konaka, C. & Kato, H. (2000) Bronchofiberscopy. [Japanese]. *Nippon rinsho*, Japanese: 1057-1064.
Narrative review

- Kennedy, T. C., Franklin, W. A., Prindiville, S. A., Cook, R., Dempsey, E. C., Keith, R. L., Hirsch, F. R., Merrick, T. A., Shroyer, K. R., Petty, T. L., Byers, T., Bunn, P. A., Jr. & Miller, Y. E. (2005) High prevalence of occult endobronchial malignancy in high risk patients with moderate sputum atypia. *Lung Cancer*, 49: 187-191.
Not in PICO
- Khajotia, R. R., Mohn, A., Pokieser, L., Schalleschak, J. & Vetter, N. (1991) Induced sputum and cytological diagnosis of lung cancer. *Lancet*, 338: 976-977.
Not in PICO
- Khanavkar, B., Gnudi, F., Muller, K.-M., Atay, Z., Topalidis, T., Muti, A. & Nakhosteen, J. A. (1997) Autofluorescence bronchoscopy with the LIFE system. A method for early diagnosis of lung cancer. [German]. *Atemwegs- und Lungenkrankheiten*, 23: 406-407.
Not in PICO
- Khanavkar, B., Gnudi, F., Muti, A., Marek, W., Muller, K. M., Atay, Z., Topalidis, T. & Nakhosteen, J. A. (1998) [Basic principles of LIFE--autofluorescence bronchoscopy. Results of 194 examinations in comparison with standard procedures for early detection of bronchial carcinoma--overview]. [Review] [28 refs] [German]. *Pneumologie*, 52: 71-76.
Not in PICO
- Khanavkar, B., Gnudi, F., Muti, A., Marek, W., Muller, K.-M., Atay, Z., Topalidis, T. & Nakhosteen, J. A. (1998) Principles and results of autofluorescence-(LIFE System) bronchoscopy compared to conventional bronchoscopy in the detection of early lung cancer. [German]. *Pneumologie*, 52: 71-76.
Duplicate
- Khani, F., Bidoki, S. K., Rahbarizadeh, F., Jabari, H., Kiani, A., Hamedani, M., Sajadi, M. & Sheikhnejad, R. (2012) An eleven-gene signature of lung biopsy specimens for cancer diagnostic. *European Journal of Cancer*, 48: S285.
Not in PICO
- Kim, E. B., Park, Y., Park, S. J., Kim, D. S., Kim, J. W., Seo, H. Y., Sung, H. J., Choi, I. K., Park, K. H., Oh, S. C., Choi, C. W., Kim, B. S., Kim, Y. H., Kim, J. S., Shin, S. W., Kim, C. Y. & Jung, K. Y. (2008) Clinical factors related to suspected second primary lung cancer development in patients with head and neck cancer. *Cancer Research & Treatment*, 40: 178-183.
Not in PICO
- Kim, H., Kim, S. J., Lee, S.-H., Seong, H. S., Lee, K.-O., Jeon, C.-H., Hong, Y. J., Lee, S. M. & Kim, T. H. (2010) Usefulness of melanoma antigen (MAGE) gene analysis in tissue samples from percutaneous needle aspiration biopsy of suspected lung cancer lesions. *Lung Cancer*, 69: 284-288.
Not in PICO
- Kim, H. C., Lee, G. D., Cho, Y.-J., Jeong, Y.-Y., Lee, J.-D. & Hwang, Y.-S. (2010) Significance of bronchial washing cytology in endoscopically visible lung cancer. *Journal of Thoracic Oncology*, 5: S388-S389.
Not in PICO
- Kim, S.-H., Eun, K. K., Shi, K.-D., Kim, J.-H., Yoo, J.-H., Kyung, S. K., Kim, J.-Y., Kim, G.-I., An, H.-J. & Lee, J.-H. (2007) A comparison of conventional cytology and ThinPrep cytology of bronchial washing fluid in the diagnosis of lung cancer. [Korean]. *Tuberculosis and Respiratory Diseases*, 62: 523-530.
Not in PICO
- King, E. G., Man, G. & Le, R. J. (1982) Fluorescence bronchoscopy in the localization of bronchogenic carcinoma. *Cancer*, 49: 777-782.
Not in PICO
- Kirmi, O., Woo, E., Meagher, T., Prasad, A. & Taylor, D. (2009) Improving the lung cancer pathway: A 1-year audit of CT evaluation of equivocal CXRs. *Thorax*, 64: A148.
Not in PICO

- Klabunde, C. N., Marcus, P. M., Silvestri, G. A., Han, P. K. J., Richards, T. B., Yuan, G., Marcus, S. E. & Vernon, S. W. (2010) U.S. primary care physicians' lung cancer screening beliefs and recommendations. *American Journal of Preventive Medicine*, 39: 411-420.
Not in PICO
- Klabunde, C. N., Marcus, P. M., Han, P. K., Richards, T. B., Vernon, S. W., Yuan, G. & Silvestri, G. A. (2012) Lung cancer screening practices of primary care physicians: results from a national survey. *Annals of family medicine*, 10: 102-110.
Not in PICO
- Kleemann, W. (1984) [Importance of sputum cytology for the diagnosis of bronchial cancer]. [German]. *Archiv fur Geschwulstforschung*, 54: 505-509.
Not in PICO (test positives only)
- Kobashi, Y., Mouri, K., Fukuda, M., Yoshida, K., Miyashita, N., Niki, Y., Nakata, M. & Oka, M. (2005) Clinical analysis of primary lung cancer with cavities. [Japanese]. *Japanese Journal of Chest Diseases*, 64: 653-661.
Not in PICO
- Kobayashi, T. (2003) Bronchoscopic Diagnosis of Lung Cancer. [Japanese]. *Japanese Journal of Lung Cancer*, 43: 807-810.
Narrative review
- Kono, M., Morita, M. & Adachi, S. (1988) [Conventional X-ray and CT diagnosis of lung cancer]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1349-1367.
Not in PICO
- Kono, M., Adachi, S., Yamasaki, K., Itouji, E., Kusumoto, M., Sakai, E. & Endo, M. (1993) Radiology of lung cancer. [Review] [16 refs]. *Radiation Medicine*, 11: 110-121.
Narrative review
- Konsuwan, N. (1985) Early diagnosis of cancer of the lung. *Southeast Asian Journal of Tropical Medicine & Public Health*, 16: 638-640.
Narrative review
- Kovach, A. E., Morales-Oyarvide, V., Shvets, D. E., Tammireddy, S., Klepeis, V., Mark, E. J., Dias, S. D., Iafrate, A. J. & Mino-Kenudson, M. (2013) Pathway interplay: Activation of EGFR, ERK, and AKT in early-stage lung adenocarcinomas. *Laboratory Investigation*, 93: 457A.
Not in PICO
- Kovacs, G. (2008) Risk group chest X-ray for the early detection of lung cancer. [Hungarian]. *Orvosi Hetilap*, 149: 975-982.
Not in PICO
- Kreuzer, M., Kreienbrock, L., Muller, K. M., Gerken, M. & Wichmann, E. (1999) Histologic types of lung carcinoma and age at onset. *Cancer*, 85: 1958-1965.
Not in PICO
- Kruger, S., Buck, A. K., Blumstein, N. M., Pauls, S., Schelzig, H., Kropf, C., Schumann, C., Mottaghy, F. M., Hombach, V. & Reske, S. N. (2006) Use of integrated FDG PET/CT imaging in pulmonary carcinoid tumours. *Journal of Internal Medicine*, 260: 545-550.
Not in PICO
- Kumarasinghe, P. & Jayasundera, C. I. (1992) Cytological diagnosis of bronchial malignancies using the fiberoptic bronchoscope. *Ceylon Medical Journal*, 37: 41-43.
Not in PICO
- Kuriyama, T. (1993) [Recent progress on diagnostic imaging of lung cancer]. [Review] [5 refs] [Japanese]. *Nippon Naika Gakkai Zasshi - Journal of Japanese Society of Internal Medicine*, 82: 356-359.
Narrative review
- Kusunoki, Y. & Nakayama, T. (2002) [CT diagnosis of lung cancer--current topics]. [Review] [15 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 60: Suppl-3.

- In Japanese with no English abstract, but 7/15 references about screening, so probably not in PICO
- Lal, A., Phillips, S., Russell, C. & Woolhouse, I. (2011) The novel use of fast track CT to select patients for lung cancer clinics: effect on clinic efficiency, waiting times, and patient satisfaction. *Postgraduate Medical Journal*, 87: 264-268.
Not in PICO
- Lam, B., Lam, S. Y., Wong, M. P., Ooi, C. G. C., Fong, D. Y. T., Lam, D. C. L., Lai, A. Y. K., Tam, C., Pang, C. B. Y., Ip, M. S. M. & Lam, W. (2009) Sputum cytology examination followed by autofluorescence bronchoscopy: A practical way of identifying early stage lung cancer in central airway. *Lung Cancer*, 64: 289-294.
Not in PICO (screening)
- Lam, S., MacAulay, C. & Palcic, B. (1992) Detection and localization of early lung cancer by imaging techniques. *Chest*, 103: 12S-14S.
Narrative review
- Lam, S. & Shibuya, H. (1999) Early diagnosis of lung cancer. [Review] [110 refs]. *Clinics in Chest Medicine*, 20: 53-61.
Narrative review
- Lam, S., MacAulay, C., LeRiche, J. C. & Palcic, B. (2000) Detection and localization of early lung cancer by fluorescence bronchoscopy. *Cancer*, 89: 2468-2473.
Not in PICO
- Lam, S., Lam, B. & Petty, T. L. (2001) Early detection for lung cancer. New tools for casefinding. *Canadian family physician Medecin de famille canadien*, 47: 537-544.
Not in PICO
- Laroche, C., Fairbairn, I., Moss, H., Pepke-Zaba, J., Sharples, L., Flower, C. & Coulden, R. (2000) Role of computed tomographic scanning of the thorax prior to bronchoscopy in the investigation of suspected lung cancer. *Thorax*, 55: 359-363.
Not in PICO
- Law, G. T., Wong, C. Y., Chan, Y. C., Shum, T. T., Lok, P. S. & Wong, K. Y. (2002) Cost-effectiveness of CT thorax and bronchoscopy in haemoptysis with normal CXR for exclusion of lung cancer. *Australasian Radiology*, 46: 381-383.
Not in PICO
- Leahy, A., Curtis, K., Masani, V. & Suntharalingam, J. (2012) The value of fibre-optic bronchoscopy in patients with haemoptysis and non-diagnostic CT scans. *Lung Cancer*, 75: S14.
Not in PICO
- Lee, E. W. (2010) Is sputum cytology using Thinprep instead of autofluorescence bronchoscopy for evaluation of abnormal lesion in central airway in a high-risk group useful? *Chest*, 138.
Not in PICO
- Lee, G., Lee, J. M., Gardner, B. K., Walser, T. C., Krysan, K., Pak, P. S., Mao, J., Hazra, S. & Dubinett, S. M. (2010) Blood-based biomarker profiles for detecting lung cancer. *Journal of Thoracic Oncology*, 5: S220-S221.
Not in PICO
- Lee, G. D., Ma, J. E., Youn, E. Y., Cho, Y. J., Jeong, Y. Y., Kim, H. C., Lee, J. D. & Hwang, Y. S. (2009) Significance of bronchial washing cytology in endoscopically visible lung cancer. *Respirology*, 14: A201.
Not in PICO
- Lee, J. E., Kim, H. Y., Lim, K. Y., Lee, S. H., Lee, G. K., Lee, H. S. & Hwangbo, B. (2010) Endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of lung cancer. *Lung Cancer*, 70: 51-56.
Not in PICO
- Lee, M. & Tariq, A. (2014) How many doctors does it take . . .? *HIV Medicine*, 15: 109.
Not in PICO

- Leidinger, P., Keller, A., Heisel, S., Ludwig, N., Rheinheimer, S., Klein, V., Andres, C., Staratschek-Jox, A., Wolf, J., Stoelben, E., Stephan, B., Stehle, I., Hamacher, J., Huwer, H., Lenhof, H. P. & Meese, E. (2010) Identification of lung cancer with high sensitivity and specificity by blood testing. *Respiratory research*, 11: 18.
Not in PICO
- Leong, S. C., Marshall, H. M., Bowman, R. V., Yang, I. A., Ree, A. M., Hong, J., Hewson, K. & Fong, K. M. (2012) First 24 cases from a health technology assessment field evaluation of electromagnetic navigation bronchoscopy. *Journal of Thoracic Oncology*, 7: S176.
Not in PICO
- Lewis, N. R., Le, J., I & Baldwin, D. R. (2005) Under utilisation of the 2-week wait initiative for lung cancer by primary care and its effect on the urgent referral pathway. *British Journal of Cancer*, 93: 905-908.
Not in PICO
- Leyakath Ali, K. S., Anwar, N., Nuttal, E., Clarke, S. & Zaman, F. (2014) Lung cancer from symptoms to referral across the Lancashire and South Cumbria Network. *Lung Cancer*, 83: S50.
Not in PICO
- Li, J., Chen, P., Li, X.-Q., Bao, Q.-L., Dai, C.-H. & Ge, L.-P. (2013) Elevated levels of survivin and livin mRNA in bronchial aspirates as markers to support the diagnosis of lung cancer. *International Journal of Cancer*, 132: 1098-1104.
Not in PICO
- Li, M., Peng, Z., Liu, Q., Sun, J., Yao, S. & Liu, Q. (2013) Value of 11C-choline PET/CT for lung cancer diagnosis and the relation between choline metabolism and proliferation of cancer cells. *Oncology Reports*, 29: 205-211.
Not in PICO
- Liang, S. T. (1983) [Cytologically positive but plain X-ray negative lung cancer: an analysis of 34 cases]. [Chinese]. *Chung-Hua Chieh Ho Ho Hu Hsi Hsi Chi Ping Tsa Chih Chinese Journal of Tuberculosis & Respiratory Diseases*, 6: 10-11.
Not in PICO
- Liang, X. M. (1989) Accuracy of cytologic diagnosis and cytotyping of sputum in primary lung cancer: analysis of 161 cases. *Journal of Surgical Oncology*, 40: 107-111.
Not in PICO
- Liao, M. L. (189) High risk factors of lung cancer and its early detection. [Chinese]. *Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases*, 13: 141-190.
Not in PICO
- Liddicoat, H., Duke, S. L., Ma, L. J. & Mier, A. (2010) The effect of bronchoscopic sampling techniques on patient comfort and their impact on diagnostic yield in suspected lung cancer. *American Journal of Respiratory and Critical Care Medicine*, 181.
Not in PICO
- Lim, W. S., Macfarlane, J. T., Deegan, P. C., Manhire, A., Holmes, W. F. & Baldwin, D. R. (1999) How do general practitioners respond to reports of abnormal chest X-rays? *Journal of the Royal Society of Medicine*, 92: 446-449.
Not in PICO
- Liu, C., Wen, Z., Li, Y. & Peng, L. (2014) - Application of ThinPrep bronchial brushing cytology in the early diagnosis of lung cancer: a retrospective study. - *PLoS ONE [Electronic Resource]*, 9: e90163.
Not in PICO
- Liu, Y. & Wang, M. (2011) Advances in early diagnosis of lung cancer. *Chinese Journal of Lung Cancer*, 14: 429-434.
Narrative review

- Loke, J., Matthay, R. A. & Ikeda, S. (1982) Techniques for diagnosing lung cancer. A critical review. [Review] [61 refs]. *Clinics in Chest Medicine*, 3: 321-329.
Narrative review
- Lopez Gonzalez, J. L., Navarro, E. F., Lamarca, L. A. & Alvarez-Mon, S. M. (2013) Protocol for early diagnosis of lung cancer in the clinical practice. [Spanish]. *Medicine (Spain)*, 11: 1484-1486.
Narrative review
- Lowry, B., Hughes, D. & Corless, J. A. (2009) Experiences of direct access CT scanning for general practitioners and implications for investigation of possible lung cancer. *Thorax*, 64: A92.
Not in PICO
- Lyll, J. R. W., Summers, G. D. & O'Brien, I. M. (1980) Sequential brush biopsy and conventional biopsy: Direct comparison of diagnostic sensitivity in lung malignancy. *Thorax*, 35: 929-931.
Not in PICO
- Ma, F. C. (125) [An analysis of 23 cases of early primary lung cancer]. [Chinese]. *Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih Chinese Journal of Tuberculosis & Respiratory Diseases*, 12: 79-81.
Not in PICO
- Mabeza, G. F. & Macfarlane, J. (2003) Pulmonary actinomycosis. *European Respiratory Journal*, 21: 545-551.
Narrative review
- MacDougall, B. & Weinerman, B. (1992) The value of sputum cytology. *Journal of General Internal Medicine*, 7: 11-13.
Not in PICO
- MacPherson, R., Benamore, R., Panakis, N., Sayeed, R., Breen, D., Bradley, K., Carter, R., Baldwin, D., Craig, J. & Gleeson, F. (2012) A proposed new imaging pathway for patients with suspected lung cancer. *Clinical Radiology*, 67: 564-573.
Not in PICO
- Maeda, J., Hamanaka, W., Sakata, Y., Yoshida, K., Honda, H., Kakihana, M., Kajiwara, N., Ohira, T. & Ikeda, N. (2013) Effectiveness of cytological diagnosis of small-cell lung carcinoma by bronchoscopic examination. *Acta Cytologica*, 57: 116.
Not in PICO
- Maji, A., Maikap, M. K., Jash, D., Saha, K., Kundu, A., Saha, D., Banerjee, S. & Patra, A. (2013) Role of common investigations in aetiological evaluation of exudative pleural effusions. *Journal of Clinical and Diagnostic Research*, 7: 2223-2226.
Not in PICO
- Makitaro, R., Paakko, P., Huhti, E., Bloigu, R. & Kinnula, V. L. (1999) An epidemiological study of lung cancer: History and histological types in a general population in northern Finland. *European Respiratory Journal*, 13: 436-440.
Not in PICO
- Manaker, S. & Vachani, A. (2013) The Changing Face of Outpatient Bronchoscopy in 2013. *Chest*, 143: 1214-1218.
Narrative review
- Mansson, J., Marklund, B. & Hultborn, R. (2001) The diagnosis of cancer in the "roar" of potential cancer symptoms of patients in primary health care. Research by means of the computerised journal. *Scandinavian Journal of Primary Health Care*, 19: 83-89.
Not in PICO
- Mantri, S. & Vigg, A. (2003) Pattern of lung cancer in elderly. *The Journal of the Association of Physicians of India*, 51: 963-966.
Not in PICO
- Marek, W., Krampe, S., Dickgreber, N. J., Nielsen, L., Muti, A., Khanavkar, B., Muller, K.-M., Atay, Z., Topalidis, T. & Nakhosteen, J. A. (1998) Automated quantitative image cytometry of bronchial washings in suspected lung cancer: Comparison with cytology, histology and final diagnosis.

- [German]. *Atemwegs- und Lungenkrankheiten*, 24: 316-319.
Not in PICO
- Matsubara, K., Takata, T., Koshida, K., Noto, K., Shimono, T., Horii, J., Yamamoto, T. & Matsui, O. (2009) Chest CT performed with 3D and z-axis automatic tube current modulation technique: breast and effective doses. *Academic Radiology*, 16: 450-455.
Not in PICO
- Mauri, D., Kamposioras, K., Proiskos, A., Xilomenos, A., Peponi, C., Dambrosio, M., Zacharias, G., Koukourakis, G., Pentheroudakis, G. & Pavlidis, N. (2006) Old habits die hard: Chest radiography for screening purposes in primary care. *American Journal of Managed Care*, 12: 650-656.
Not in PICO
- McCahon, E. (2006) Lung tumours in children. *Paediatric Respiratory Reviews*, 7: 191-196.
Not in PICO
- McCann, J. (1997) New techniques catch lung cancers earlier. *Journal of the National Cancer Institute*, 89: 1838-1839.
Narrative review
- McLennan, G. & Roder, D. M. (1989) Lung cancer in Australia. *Medical Journal of Australia*, 150: 206-213.
Narrative review
- Medford, A. R., Agrawal, S., Free, C. M. & Bennett, J. A. (2010) A prospective study of conventional transbronchial needle aspiration: performance and cost utility. *Respiration; international review of thoracic diseases*, 79: 482-489.
Not in PICO
- Medici, T. C., Wehrli, R. & Zullig, A. (1987) Early diagnosis of bronchial carcinoma using thoracic roentgen imaging and sputum cytology. [German]. *Schweizerische medizinische Wochenschrift*, 117: 1448-1457.
Not in PICO
- Medici, T. C., Wehrli, R. & Zullig, A. (1987) Early detection of bronchial carcinoma with chest roentgenography and sputum cytology. [German]. *Schweizerische medizinische Wochenschrift*, 117: 1448-1457.
Not in PICO
- Mehta, A. C., Marty, J. J. & Lee, F. Y. W. (1993) Sputum cytology. *Clinics in Chest Medicine*, 14: 69-85.
Narrative review
- Mehta, A. C. & Gildea, T. R. (2003) Is autofluorescence bronchoscopy needed to diagnose early bronchogenic carcinoma? Con: Autofluorescence bronchoscopy. *Journal of Bronchology*, 10: 70-74.
Narrative review
- Melamed, M. R. & Flehinger, B. J. (1987) Detection of lung cancer: Highlights of the Memorial Sloan-Kettering Study in New York City. *Schweizerische medizinische Wochenschrift*, 117: 1457-1463.
Not in PICO
- Melling, P. P., Hatfield, A. C., Muers, M. F., Peake, M. D., Storer, C. J., Round, C. E., Haward, R. A. & Crawford, S. M. (2002) Lung cancer referral patterns in the former Yorkshire region of the UK. *British Journal of Cancer*, 86: 36-42.
Not in PICO
- Mendez-Gonzalez, J., Gallegos-Marmolejo, M., Martinez-Figueroa, S., Antonijuan-Pares, A., Martinez-Couselo, S. & Mora-Brugues, J. (2009) Application of a methylation panel for the diagnosis of lung cancer in bronchoaspirates. Preliminary results. [Spanish]. *Revista del Laboratorio Clinico*, 2: 107-114.
Not in PICO
- Metzgeroth, G., Mantz, C., Kuhn, C., Schultheis, B., Hehlmann, R. & Hastka, J. (2007) Reliable identification of small cell lung cancer in cytological specimens by immunocytology. *Onkologie*,

- 30: 311-315.
Not in PICO
- Mi, B., Wan, W., Yu, C., You, X., Jiang, F. & You, Q. (2012) [The value of extra-lung lesions on 18F-FDG PET/CT in improving diagnosis of lung cancer]. [Chinese]. *Chinese Journal of Lung Cancer*, 15: 78-83.
Not in PICO
- Michaelides, S., Goulas, G., Kourtelessi, E., Vartzioti, O., Lekkakou, A. & Emmanouelidou, A. (2011) Cytological interspecimen diagnostic variability among different samples for histologic identification of lung cancer. *Chest*, 140.
Not in PICO
- Midthun, D. E. & Jett, J. R. (1998) Early detection of lung cancer: Today's approach. *Journal of Respiratory Diseases*, 19: 59-70.
Narrative review
- Milleron, B. (1999) Management of non-small cell lung cancer. What initial assessment for non-small cell lung cancer?. [French]. *Revue des Maladies Respiratoires*, 16: 3S120-3S121.
Narrative review
- Min, R., Li, M. M. & Yin, K. S. (2003) [Autofluorescence bronchoscopy for early localization of lung cancer]. [Review] [26 refs] [Chinese]. *Aizheng*, 22: 1110-1113.
Narrative review
- Minami, Y., Ishikawa, S., Saida, Y., Kajitani, M., Noguchi, M., Yamamoto, T., Sato, Y., Onizuka, M. & Sakakibara, Y. (2002) High resolution CT for localization of early hilar lung carcinoma. [Japanese]. *Japanese Journal of Lung Cancer*, 42: 1-6.
Not in PICO
- Mitchell, E. D., Rubin, G. & Macleod, U. (2013) Understanding diagnosis of lung cancer in primary care: qualitative synthesis of significant event audit reports. *British Journal of General Practice*, 63: 37-46.
Not in PICO
- Mitchell, G. & Mitchell, C. (2004) Lung cancer. [Review] [14 refs]. *Australian Family Physician*, 33: 321-325.
Narrative review
- Moguillansky, N. I., Raj, M., Keenan, R. & Singh, A. (2009) A case of a 19 year old woman with squamous cell carcinoma of the lung. *Chest*, 136.
Not in PICO
- Mohammad, T., Garratt, J., Torlakovic, E., Gilks, B. & Churg, A. (2012) Utility of a CEA, CD15, calretinin, and CK5/6 panel for distinguishing between mesotheliomas and pulmonary adenocarcinomas in clinical practice. *American Journal of Surgical Pathology*, 36: 1503-1508.
Not in PICO
- Moilanen, A., Antila, P., Kokko, M. L., Lahdensuo, T. & Veneskoski, T. (1984) Bronchography in patients with suspected lung malignancy. *Rontgen-Blatter*, 37: 273-275.
Not in PICO
- Molina, R., Leon, A., Trape, J., Garrido, A., Auge, J. M., Filella, X., De La Torre, P., Escudero, J. M., Blavia, R. & Perich, D. (2010) Lunch symposium: Abbott GMBH & co. kg improved lung cancer diagnosis by the combination of tumor markers. *Tumor Biology*, 31: S123.
Not in PICO
- Molina, R., Leon, A., Trape, J., Garrido, A., Auge, J. M., Filella, X., De La Torre, P., Escudero, J. M., Blavia, R. & Perich, D. (2011) Improved lung cancer diagnosis by the combination of tumor markers. *Tumor Biology*, 32: S32-S33.
Not in PICO
- Montuenga, L. M. & Pio, R. (2009) Current challenges in lung cancer early detection biomarkers. *European Journal of Cancer*, 45: Suppl-8.
Narrative review

- Motamed-Khorasani, A. & Etemadi, H. (2012) Further validation of DR-70 blood biomarker in the early detection of non-small cell lung cancer. *Journal of Thoracic Oncology*, 7: S27.
Not in PICO
- Motohiro, A., Hara, N., Ichinose, Y., Kuda, T., Aso, H., Chikama, H., Kawasaki, M., Kubota, I. & Ohta, M. (1990) Evaluation of prognostic factors in early lung cancer. [Japanese]. *Japanese Journal of Cancer and Chemotherapy*, 17: 31-36.
Not in PICO
- Mukherjee, S., Bandyopadhyay, G., Bhattacharya, A., Ghosh, R., Barui, G. & Karmakar, R. (2010) Computed tomography-guided fine needle aspiration cytology of solitary pulmonary nodules suspected to be bronchogenic carcinoma: Experience of a general hospital. *Journal of Cytology*, 27: 8-11.
Not in PICO
- Muller, K. M., Nakhosteen, J. A., Khanavkar, B. & Fisseler-Eckhoff, A. (1998) [Bronchopulmonary preneoplasia. Diagnosis using LIFE system and pathology panel of the European Early Lung Cancer Study Group (EELCSG)]. [German]. *Pathologe*, 19: 388-394.
Narrative review
- Murray, K. L., Duvall, E., Salter, D. M. & Monaghan, H. (2002) Efficacy and pattern of use of sputum cytology as a diagnostic test. *Cytopathology*, 13: 350-354.
Not in PICO
- Mzabi-Regaya, S., Makni, M. K., Khattech, A. & Chadli, A. (1988) [Bronchial cytology in the diagnosis of broncho-pulmonary cancer in Tunisia]. [French]. *Archives de l'Institut Pasteur de Tunis*, 65: 81-86.
Very little patient information, but seems to be Not in PICO
- Naalsund, A. & Maublant, J. (2006) The solitary pulmonary nodule--is it malignant or benign? Diagnostic performance of Tc-depreotide SPECT. *Respiration*, 73: 634-641.
Not in PICO
- Nakajima, T. & Yasufuku, K. (2013) Early Lung Cancer. Methods for Detection. *Clinics in Chest Medicine*, 34: 373-383.
Narrative review
- Nakhosteen, J. A., Khanavkar, B., Muti, A. & Marek, W. (1997) Early diagnosis of lung cancer with autofluorescent (LIFE) bronchoscopy and automated sputum cytometry: The next generation. [German]. *Atemwegs- und Lungenerkrankheiten*, 23: 211-217.
Narrative review
- Nasiell, M., Kinnman, J., Haglund, S., Roger, V. & Nasiell, K. (1982) Detection of early and roentgenologically occult bronchogenic carcinoma: preliminary report of the Sabbatsberg hospital sputum cytologic screening study. *Recent Results in Cancer Research*, Fortschritt: 159-162.
Not in PICO
- Navio Martin, M. P. & Dominguez, R. S. (2001) [Indications for repeating a bronchoscopy. Relevance of a second bronchoscopy suspecting a malignant condition]. [Spanish]. *Revista Clinica Espanola*, 201: 195-197.
Not in PICO (cancer casxes only)
- Neal, R. D., Hurt, C., Roberts, K., Rogers, T., Hamilton, W., Tudor, E. R., Tod, A. M., Parker, D., Thomas, J. E., Nelson, A., Prout, H., Hood, K. & Griffiths, G. (2014) A feasibility randomised controlled trial looking at the effect on lung cancer diagnosis of giving a chest X-ray to smokers aged over 60 with new chest symptoms the ELCID trial. *Lung Cancer*, 83: S81-S82.
Ongoing study
- Nechaeva, O. B. (1990) [The experience of detecting lung cancer in an industrial district]. [Russian]. *Voprosy Onkologii*, 36: 575-579.
Not in PICO

- Neel III, H. B., Sanderson, D. R. & Fontana, R. S. (1981) Sputum cytologic diagnosis of upper respiratory tract cancer. Second report. *Annals of Otolaryngology, Rhinology and Laryngology*, 90: 312-315.
Not in PICO
- Neumann, G. (1990) [Early diagnosis of bronchial carcinoma]. [Review] [201 refs] [German]. *Pneumologie*, 44: 925-942.
Narrative review
- Nieburgs, H. E. (1982) The cytologic basis for classification of lung tumors. *Cancer Detection & Prevention*, 5: 407-425.
Narrative review
- Ninane, V. (2005) [Bronchoscopic early detection of lung cancer]. [Review] [27 refs] [French]. *Revue des Maladies Respiratoires*, 22: t-42.
Narrative review
- Noel-Savina, E., Paleiron, N., Le, G. G. & Descourt, R. (2012) EGFR activating mutation in lung adenocarcinoma: Risk factor of thromboembolic event?. [French]. *Revue des Maladies Respiratoires*, 29: 1137-1140.
Not in PICO
- Nou, E. (1981) Bronchial adenocarcinoma: the value of attempts to exclude other primary tumors for randomized studies in an epidemiologic material. *Cancer*, 48: 2121-2125.
Not in PICO
- O'Dowd, E., McKeever, T., Powell, H. A., Anwar, S., Baldwin, D. & Hubbard, R. (2014) Predictors of early death from lung cancer in primary care. *Lung Cancer*, 83: S34-S35.
Not in PICO
- Oak, C. H., Wilson, D., Lee, H. J., Lim, H. J. & Park, E. K. (2012) Potential molecular approaches for the early diagnosis of lung cancer (review). *Molecular Medicine Reports*, 6: 931-936.
Narrative review
- Okamoto, S., Hatakeyama, Y., Hazeki, N., Ishikawa, Y., Kobayashi, K., Funada, Y., Kotani, Y., Yoshida, M. & Nishimura, Y. (2010) To develop the biomarker of lung cancer by the detection of metabolites expression pattern. *American Journal of Respiratory and Critical Care Medicine*, 181.
Not in PICO
- Okamura, K., Takayama, K., Izumi, M., Harada, T., Furuyama, K. & Nakanishi, Y. (2013) Diagnostic value of CEA and CYFRA 21-1 tumor markers in primary lung cancer. *Lung Cancer*, 80: 45-49.
Not in PICO
- Okereke, I. C., Gangadharan, S. P., Kent, M. S., Nicotera, S. P. & DeCamp, M. M. (2011) [(18)F]Fluorodeoxyglucose positron emission tomography-computerized tomography and lung cancer: a significant referral bias exists. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*, 39: 560-564.
Not in PICO
- Oki, M., Saka, H., Kitagawa, C., Kogure, Y., Murata, N., Adachi, T. & Ando, M. (2013) Rapid on-site cytologic evaluation during endobronchial ultrasound-guided transbronchial needle aspiration for diagnosing lung cancer: a randomized study. *Respiration*, 85: 486-492.
Not in PICO
- Ooi, H. E. A. N., Liu, C. & Chang, S. (2011) A new modified autofluorescence pleuroscopy in the undiagnosed lung cancer with pleural effusion. *European Journal of Cancer*, 47: S215.
Not in PICO
- Oshiro, Y., Gibo, M. & Murayama, S. (2007) Advance of diagnostic imaging in lung cancer. [Japanese]. *Gan to Kagaku Ryoho*, Cancer: 1347-1351.
Narrative review
- Ost, D., Shah, R., Anasco, E., Lusardi, L., Doyle, J., Austin, C. & Fein, A. (2008) A randomized trial of CT fluoroscopic-guided bronchoscopy vs conventional bronchoscopy in patients with suspected lung

- cancer. *Chest*, 134: 507-513.
Not in PICO
- Ost, D. E., Yeung, S. C., Tanoue, L. T. & Gould, M. K. (2013) Clinical and organizational factors in the initial evaluation of patients with lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*, 143: Suppl-41S.
Guideline/not in PICO
- Ost, D. E., Niu, J., Elting, L. S., Buchholz, T. A. & Giordano, S. H. (2014) - Determinants of practice patterns and quality gaps in lung cancer staging and diagnosis. - *Chest*, 145: 1097-1113.
Not in PICO
- Ostendorf, U., Scherff, A., Khanavkar, B., Ewig, S. & Hecker, E. (2011) Diagnosis of peripheral lung lesions by EBUS-guided TBB in routine practice. *Pneumologie*, 65: 730-735.
Not in PICO
- Ott, S. & Geiser, T. (2012) [Epidemiology of lung tumors]. [Review] [German]. *Therapeutische Umschau*, 69: 381-388.
Narrative review
- Oviatt, P. L., Stather, D. R., Michaud, G., Maceachern, P. & Tremblay, A. (2011) Exercise capacity, lung function, and quality of life after interventional bronchoscopy. *Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer*, 6: 38-42.
Not in PICO
- Pache, J.-C. (2003) Role of the surgical pathologist-cytologist in the management of the solitary pulmonary nodule. [French]. *Medecine et Hygiene*, 61: 2342-2345.
Narrative review
- Paciorek, M., DomagalaKulawik, J., Droszcz, P., Byskiniewicz, K., Krenke, R., Karwat, K. & Chazan, R. (2002) Correlation between bronchoscopically visible aspects and histopathologic results in patients with suspected lung cancer. [Polish]. *Polskie Archiwum Medycyny Wewnetrznej*, 108: 1193-1197.
Not in PICO
- Palcic, B., Lam, S., Hung, J. & MacAulay, C. (1991) Detection and localization of early lung cancer by imaging techniques. *Chest*, 99: 742-743.
Not in PICO
- Palcic, B., Garner, D. M., Beveridge, J., Sun, X. R., Doudkine, A., MacAulay, C., Lam, S. & Payne, P. W. (2002) Increase of sensitivity of sputum cytology using high-resolution image cytometry: field study results. *Cytometry*, 50: 168-176.
Not in PICO
- Paleiron, N., Pegorie, A., Quere, G., Andre, M., Natali, F. & Grassin, F. (2010) [Practical approach to an excavated pulmonary lesion]. [French]. *Revue de Pneumologie Clinique*, 66: 145-153.
Narrative review
- Pandya, C. M., Gadgeel, S. & Dogra, S. (2010) A 67-year-old woman with right lung mass: A rare diagnosis. *Chest*, 138.
Not in PICO
- Pang, B., Matthias, D., Ong, C. W., Dhewar, A. N., Gupta, S., Lim, G. L., Nga, M. E., Seet, J. E., Qasim, A., Chin, T. M., Soo, R., Soong, R. & Salto-Tellez, M. (2012) The positive impact of cytological specimens for EGFR mutation testing in non-small cell lung cancer: a single South East Asian laboratory's analysis of 670 cases. *Cytopathology*, 23: 229-236.
Not in PICO
- Pantzar, P., Meurala, H., Koivuniemi, A. & Laustela, E. (1983) Peroperative fine needle aspiration biopsy of lung tumors. *Scandinavian Journal of Thoracic & Cardiovascular Surgery*, 17: 51-53.
Not in PICO

- Patel, A. M. & Peters, S. G. (1993) Clinical manifestations of lung cancer. [Review] [51 refs]. *Mayo Clinic Proceedings*, 68: 273-277.
Narrative review
- Patel, H. & Sisson, S. (2010) Wegeners granulomatosis in a patient with fever of unknown origin. *Journal of General Internal Medicine*, 25: S564.
Not in PICO
- Patz, J., Caporaso, N. E., Dubinett, S. M., Massion, P. P., Hirsch, F. R., Minna, J. D., Gatsonis, C., Duan, F., Adams, A., Apgar, C., Medina, R. M. & Aberle, D. R. (2010) National lung cancer screening trial American college of radiology imaging network specimen biorepository originating from the contemporary screening for the detection of lung cancer trial (NLST, ACRIN 6654): Design, intent, and availability of specimens for validation of lung cancer biomarkers. *Journal of Thoracic Oncology*, 5: 1502-1506.
Not in PICO
- Peavie, S., Weisfelder, P. & Schuermann, M. (2012) A patient's presentation of persistent sweet taste in her mouth leads to a diagnosis of small cell lung cancer. *Journal of Hospital Medicine*, 7: S296.
Not in PICO
- Pedersen, U., Balle, V. H. & Greisen, O. (1981) Diagnostic value of brush biopsy in suspected bronchial carcinoma with the use of the flexible fibre bronchoscope. *Clinical Otolaryngology & Allied Sciences*, 6: 329-333.
Not in PICO
- Pepe, G., Rossetti, C., Sironi, S., Landoni, C., Gianolli, L., Pastorino, U., Zannini, P., Mezzetti, M., Grimaldi, A., Galli, L., Messa, C. & Fazio, F. (2005) Patients with known or suspected lung cancer: evaluation of clinical management changes due to 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET) study. *Nuclear Medicine Communications*, 26: 831-837.
Not in PICO
- Petty, T. L. (133) The predictive value of spirometry. Identifying patients at risk for lung cancer in the primary care setting. [Review] [14 refs]. *Postgraduate Medicine*, 101: 128-130.
Narrative review
- Petty, T. L. (2001) The early diagnosis of lung cancer. *Disease-a-Month*, 47: 204-264.
Narrative review
- Petty, T. L., Tockman, M. S. & Palcic, B. (2002) Diagnosis of roentgenographically occult lung cancer by sputum cytology. [Review] [53 refs]. *Clinics in Chest Medicine*, 23: 59-64.
Narrative review
- Petty, T. L. (2003) Sputum cytology for the detection of early lung cancer. [Review] [23 refs]. *Current Opinion in Pulmonary Medicine*, 9: 309-312.
Narrative review
- Pilotti, S., Rilke, F., Gribaudo, G. & Damascelli, B. (1982) Fine needle aspiration biopsy cytology of primary and metastatic pulmonary tumors. *Acta Cytologica*, 26: 661-666.
Not in PICO
- Plebani, M., Basso, D., Navaglia, F., De, P. M., Tommasini, A. & Cipriani, A. (1995) Clinical evaluation of seven tumour markers in lung cancer diagnosis: Can any combination improve the results? *British Journal of Cancer*, 72: 170-173.
Not in PICO
- Podbielski, F. J., Rodriguez, H. E., Brown, A. M., Blecha, M. J., Salazar, M. R. & Connolly, M. M. (2004) Percutaneous biopsy in evaluation of lung nodules. *Journal of the Society of Laparoendoscopic Surgeons*, 8: 213-216.
Not in PICO
- Pokieser, W., Hubner, M., Birgitta, P., Sabine, P., Ulrike, S., Meinhard, K. & Andreas, C. (2011) Rapid on-site evaluation of bronchoscopy specimens for EGFR mutation analysis: A retrospective study of 354 consecutive patients. *Cytopathology*, 22: 44.
Not in PICO

- Polverosi, R., Vigo, M., Baron, S. & Rossi, G. (2001) [Evaluation of tracheobronchial lesions with spiral CT: comparison between virtual endoscopy and bronchoscopy]. [Italian]. *Radiologia Medica*, 102: 313-319.
Not in PICO
- Porter, J. C. & Spiro, S. G. (2000) Detection of early lung cancer. [Review] [52 refs]. *Thorax*, 55: Suppl-62.
Narrative review
- Povoski, S. P., Hall, N. C., Murrey Jr, D. A., Chow, A. Z., Gaglani, J. R., Bahnson, E. E., Mojzisek, C. M., Kuhrt, M. P., Hitchcock, C. L., Knopp, M. V. & Martin Jr, E. W. (2011) Multimodal imaging and detection approach to 18F-FDG-directed surgery for patients with known or suspected malignancies: A comprehensive description of the specific methodology utilized in a single-institution cumulative retrospective experience. *World Journal of Surgical Oncology*, 9.
Not in PICO
- Price, D. B., Yawn, B. P. & Jones, R. C. M. (2010) Improving the differential diagnosis of chronic obstructive pulmonary disease in primary care. *Mayo Clinic Proceedings*, 85: 1122-1129.
Not in PICO
- Primack, S. L., Lee, K. S., Logan, P. M., Miller, R. R. & Muller, N. L. (1994) Bronchogenic carcinoma: Utility of CT in the evaluation of patients with suspected lesions. *Radiology*, 193: 795-800.
Not in PICO
- Raab, S. S., Hornberger, J. & Raffin, T. (1997) The importance of sputum cytology in the diagnosis of lung cancer: a cost-effectiveness analysis. *Chest*, 112: 937-945.
Not in PICO
- Rafanan, A. L. & Mehta, A. C. (2000) Role of bronchoscopy in lung cancer. *Seminars in Respiratory & Critical Care Medicine*, 21: 405-420.
Narrative review
- Rajasekaran, A. B., Silvey, D., Leung, B., Honeybourne, D., Cayton, R. M., Reynolds, J., Trotter, S. & Roland, M. A. (2006) Effect of a multidisciplinary lung investigation day on a rapid access lung cancer service. *Postgraduate Medical Journal*, 82: 414-416.
Not in PICO
- Read, C., Janes, S., George, J. & Spiro, S. (2006) Early Lung Cancer: screening and detection. *Primary Care Respiratory Journal*, 15: 332-336.
Narrative review
- Reddy, P. & Baker, L. (2002) The solitary lung nodule: What chest films can - and can't - tell you. *Consultant*, 42: 1150-1156.
Narrative review
- Reimann, B. (1985) Possibilities of bronchoscopy in general practice. [German]. *Praxis und Klinik der Pneumologie*, 39: 488-489.
Not in PICO
- Revannasiddaiah, S., Madabhavi, I., Thakur, P. & Seam, R. K. (2011) Undue delay in the diagnosis of lung cancer due to the clinician's preoccupation with pre-existing tuberculosis. *BMJ Case Reports*, 2011, 2011.
Not in PICO
- Ringrow, S. M., Ranaghan, E., Warke, T. J. & Magee, N. (2011) Red flag lung cancer clinic expedites patient pathway in lung cancer. *Lung Cancer*, 71: S22-S23.
Not in PICO
- Rivera, M. P. & Mehta, A. C. (2007) Initial diagnosis of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest*, 132: 131S-148S.
Not in PICO
- Rivera, M. P., Mehta, A. C. & Wahidi, M. M. (2013) Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians

- evidence-based clinical practice guidelines. *Chest*, 143: Suppl-65S.
Not in PICO
- Rogers, T. K., Athey, V., Tod, A., Walters, S. J. & Suckling, R. (2009) Early detection of lung cancer: A social marketing evaluation. *Thorax*, 64: A21.
Not in PICO
- Rogers, T. K. (2010) Primary care radiography in the early diagnosis of lung cancer. *Cancer Imaging*, 10: 73-76.
Narrative review
- Rosso, S., Battista, R. N., Segnan, N., Williams, J. I., Suissa, S. & Ponti, A. (1992) Determinants of preventive practices of general practitioners in Torino, Italy. *American Journal of Preventive Medicine*, 8: 339-344.
Not in PICO
- Ruan, Z., Zheng, J., Huang, H., Zhang, W. & Zhao, J. (2005) [Clinical evaluation of 18F-FDG-SPECT/CT imaging in diagnosis and staging of patients with suspected lung cancer]. [Chinese]. *Chinese Journal of Lung Cancer*, 8: 120-123.
Not in PICO
- Ruiz, M., Clark, R. & Besch, L. (2010) Early lung cancer detection in HIV-infected patients: The role of yearly chest CT scans in high-risk HIV-positive patients. *Journal of the International Association of Physicians in AIDS Care*, 9: 59.
Not in PICO
- Saa-Gandi, F. W. & Mearns, A. J. (1991) Fine needle aspiration biopsy of pulmonary lesions: a 2-year experience in a district general hospital with a literature review. *Journal of the Royal College of Surgeons of Edinburgh*, 36: 309-311.
Not in PICO
- Saba, L., Caddeo, G. & Mallarini, G. (2007) Computer-aided detection of pulmonary nodules in computed tomography: analysis and review of the literature (DARE structured abstract). *Journal of Computer Assisted Tomography*, 31: 611-619.
Does not appear to be in PICO, but very little reporting on patients or methods.
- Saenghirunvattana, S., Saenghirunvattana, K. & Masakul, P. (2012) Early detection of endobronchial carcinoma using autofluorescence bronchoscopy. *Journal of Thoracic Oncology*, 7: S27-S28.
Not in PICO
- Safa, A., Berry, A., Ali, H., Car, J. & Bowen, E. F. (2011) Naedi lung cancer awareness campaign in London. *Thorax*, 66: A131.
Not in PICO
- Saha, A., Ghosh, S., Saha, K. & Biswas, A. (1111) Relationship between chest X-ray and pathological cell types of lung cancer. *Lung India*, 30: S34-December.
Not in PICO
- Saida, Y., Kujiraoka, Y., Akaogi, E., Ogata, T., Kurosaki, Y. & Itai, Y. (1996) Early squamous cell carcinoma of the lung: CT and pathologic correlation. *Radiology*, 201: 61-65.
Not in PICO
- Sait, Y., Imai, T., Nagamoto, N., Sato, M., Ota, S., Kanma, K., Takahashi, S., Usuda, K., Sagawa, M., Suda, H., Sato, H., Hashimoto, K., Nakada, T. & Higashiiwai, H. (1988) A quantitative cytologic study of sputum in early squamous cell bronchogenic carcinoma. *Analytical and Quantitative Cytology and Histology*, 10: 365-370.
Not in PICO
- Saito, H., Yamada, K., Hamanaka, N., Oshita, F., Ito, H., Nakayama, H., Yokose, T., Kameda, Y. & Noda, K. (2009) Initial findings and progression of lung adenocarcinoma on serial computed tomography scans. *Journal of Computer Assisted Tomography*, 33: 42-48.
Not in PICO
- Saji, J., Kurimoto, N., Morita, K., Nakamura, M., Inoue, T., Nakamura, H. & Miyazawa, T. (2011) Comparison of 21-gauge and 22-gauge Needles for Endobronchial Ultrasound-Guided

Transbronchial Needle Aspiration of Mediastinal and Hilar Lymph Nodes. *Journal of Bronchology and Interventional Pulmonology*, 18: 239-246.

Not in PICO

Sakurada, A., Endo, C., Sato, M. & Kondo, T. (2004) Management of central-type early lung cancer: an evidence-based clinical guideline. [Japanese]. *Nippon Geka Gakkai zasshi*, 105: 388-391. Guideline

Sang, H. L., Jae, J. S., So, R. L., Sang, Y. L., Jung, K. S., Jae, Y. C., Han, G. K., Kwang, H., I, Young, H. C., Hark, J. K., Se, H. Y. & Kyung, H. K. (1997) Usefulness of LIFE in diagnosis of bronchogenic carcinoma. [Korean]. *Tuberculosis and Respiratory Diseases*, 44: 69-84.

Not in PICO

Saraceno, J. & Spivack, S. D. (1999) Strategies for early detection of lung cancer. *Clinical Pulmonary Medicine*, 6: 66-72.

Narrative review

Sasano, S., Torii, Y. & Onuki, T. (2007) Comparison of clinical characteristics of lung cancer cases according to the detection method. [Japanese]. *Japanese Journal of Lung Cancer*, 47: 21-25.

Not in PICO

Sato, M., Saito, Y., Nagamoto, N., Sagawa, M., Kanma, K., Takahashi, S., Usuda, K., Endo, C. & Fujimura, S. (1993) Diagnostic value of differential brushing of all branches of the bronchi in patients with sputum positive or suspected positive for lung cancer. *Acta Cytologica*, 37: 879-883.

Not in PICO

Sato, M., Saito, Y., Shibuya, K., Nakayama, T., Hirano, T., Kondo, T., Baba, M., Ikeda, N., Sagawa, M., Iyoda, A., Horai, T., Nakashima, R., Hirata, T., Miyake, S., Kusunoki, Y., Tada, H., Furukawa, K. & Watanabe, Y. (2011) Early hilar type lung cancer in Japan: A Survey from January 2006 to December 2007. [Japanese]. *Japanese Journal of Lung Cancer*, 51: 777-786.

Not in PICO

Satoh, Y. & Horai, T. (2002) [Diagnostic cytology for lung cancer]. [Review] [7 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 60: Suppl-5.

Not sure if narrative review as it is entirely in Japanese with no English abstract.

Schildge, J., Cegla, M., Ortlieb, H. & Schulte-Monting, J. (1989) The value of mass radiographic screening for the early detection of carcinoma of the lung. [German]. *Pneumologie*, 43: 500-506.

Not in PICO

Schmidt, B., Liebenberg, V., Dietrich, D., Schlegel, T., Kneip, C., Seegebarth, A., Flemming, N., Seemann, S., Distler, J., Lewin, J., Tetzner, R., Weickmann, S., Wille, U., Liloglou, T., Raji, O., Walshaw, M., Fleischhacker, M., Witt, C. & Field, J. K. (2010) SHOX2 DNA methylation is a biomarker for the diagnosis of lung cancer based on bronchial aspirates. *BMC Cancer*, 10: 600.

Not in PICO

Schmidt, B., Liebenberg, V., Dietrich, D., Walshaw, M. J., Schlegel, T., Kneip, C., Liloglou, T., Fleischhacker, M., Witt, C. & Field, J. K. (2010) Methylated SHOX2 DNA in bronchial lavage - A highly specific molecular tumor marker for lung carcinoma. *Journal of Thoracic Oncology*, 5: S40.

Not in PICO

Schneider, J. (2010) Early detection of lung cancers - Comparison of computed tomography, cytology and fuzzy-based tumor markers panels. [Review]. *Cancer Biomarkers: Section A of Disease Markers*, 6: 149-162.

Narrative review

Schramm, M., Wrobel, C., Born, I., Kazimirek, M., Pomjanski, N., William, M., Kappes, R., Gerharz, C. D., Biesterfeld, S. & Bocking, A. (2011) Equivocal cytology in lung cancer diagnosis: improvement of diagnostic accuracy using adjuvant multicolor FISH, DNA-image cytometry, and quantitative promoter hypermethylation analysis. *Cancer Cytopathology*, 119: 177-192.

Not in PICO

Schramm, N., Rominger, A., Schmidt, C., Morelli, J. N., Schmid-Tannwald, C., Meinel, F. G., Reiser, M. F. & Rist, C. (2013) Detection of underlying malignancy in patients with paraneoplastic

neurological syndromes: Comparison of 18F-FDG PET/CT and contrast-enhanced CT. *European Journal of Nuclear Medicine and Molecular Imaging*, 40: 1014-1024.

Not in PICO

Schreiber, G. & McCrory, D. C. (2003) Performance characteristics of different modalities for diagnosis of suspected lung cancer: summary of published evidence. [Review] [147 refs]. *Chest*, 123: Suppl-128S.

Systematic review, but any relevant individual studies will be included separately

Seaman, J. C., Benzaquen, S. & Hagaman, J. T. (2011) Navigational bronchoscopic biopsy, ir guided biopsy, or primary vats resection for the management of the solitary pulmonary nodule, a markov model. *American Journal of Respiratory and Critical Care Medicine*, 183.

Not in PICO

Seki, N., Eguchi, K., Kaneko, M., Ohmatsu, H., Kakinuma, R., Matsui, E., Kusumoto, M., Tsuchida, T., Nishiyama, H. & Moriyama, N. (2010) What size tumors should we detect as early-stage lung cancers in CT screening? Stage-size relationship in long-term repeated screening over 15 years. *Journal of Clinical Oncology*, 28.

Not in PICO

Sen, R. P. & Walsh, T. E. (1989) Bronchoscopy. Enough or too much? *Chest*, 96: 710-712.

Narrative review

Sen, S., Reddy, V. G., Khanna, N., Guleria, R., Kapila, K. & Singh, N. (2001) A comparative study of telomerase activity in sputum, bronchial washing and biopsy specimens of lung cancer. *Lung Cancer*, 33: 41-49.

Not in PICO

Sengul, B., Uzun, O., Findik, S., Atici, A. G. & Erkan, L. (2009) The evaluation of 92 interstitial lung disease patients. [Turkish]. *Tuberkuloz ve Toraks*, 57: 314-326.

Not in PICO

Shah, P. L. (2008) Flexible bronchoscopy. *Medicine*, 36: 151-154.

Narrative review

Sharma, S. K., Pande, J. N., Dey, A. B. & Verma, K. (1992) The use of diagnostic bronchoscopy in lung cancer. *The National medical journal of India*, 5: 162-166.

Not in PICO

Sheldon, R. L. (1985) Flexible fiberoptic bronchoscopy. *Primary Care; Clinics in Office Practice*, 12: 299-315.

Narrative review

Sheski, F. D. & Mathur, P. N. (2004) Diagnosis and treatment of early lung cancer: as it stands today. *Seminars in Respiratory & Critical Care Medicine*, 25: 387-397.

Narrative review

Shin, K. C., Choi, E. Y., Chung, J. H., Jeon, C. & Lee, K. H. (2012) Clinical Application of MAGE A1-6 RT-Nested PCR for Diagnosis of Lung Cancer Invisible by Bronchoscopy. *Anticancer Research*, 32: 163-167.

Not in PICO

Shure, D. (1991) Radiographically occult endobronchial obstruction in bronchogenic carcinoma. *American Journal of Medicine*, 91: 19-22.

Not in PICO

Siemon, G. & von, B. F. (1981) [Progress in pneumologic diagnosis in clinical medicine and general practice with special reference to serologico-immunologic, endoscopic and radiologic methods]. [German]. *Medizinische Welt*, 32: 1330-1333.

Narrative review

Silva, P. P., Pereira, J. R., Ikari, F. K. & Minamoto, H. (1992) [Lung cancer and the delay in the diagnosis: analysis of 300 cases]. [Portuguese]. *Revista da Associacao Medica Brasileira*, 38: 145-149.

Not in PICO

- Singh, M. P., Sivakumaran, S., Williams, D. & Rhodes, C. (2010) Impact of dedicated lung cancer clinic on the outcome of lung cancer management: Waiting time targets, are they achievable? Results of prospective tracking study. *Respirology*, 15: A70.
Not in PICO
- Skaansar, K. (2003) [Flexible bronchoscopy]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 123: 1529-1530.
Not in PICO
- Slade, M. G., Rahman, N. M., Stanton, A. E., Curry, L., Slade, G. C., Clelland, C. A. & Gleeson, F. V. (2011) Improving standards in flexible bronchoscopy for lung cancer. *European Respiratory Journal*, 37: 895-901.
Not in PICO
- Slade, M. G., Rahman, N. M., Stanton, A. E., Curry, L., Slade, G. C., Clelland, C. A. & Gleesone, F. V. (2011) Improving standards in flexible bronchoscopy for lung cancer. *European Respiratory Journal*, 37: 895-901.
Not in PICO
- Slomski, A. (2014) - Lung cancers overdiagnosed with low-dose CT. - *JAMA*, 311: 349-29.
Letter
- Smellie, W. S. A., Hampton, K. K., Bowlees, R., Martin, S. C., Shaw, N., Hoffman, J., Ng, J. P., Mackenzie, S. M. & Van, H. C. (2007) Best practice in primary care pathology: Review 8. *Journal of Clinical Pathology*, 60: 740-748.
Narrative review
- Smith, R. A. & Glynn, T. J. (2000) Early lung cancer detection: current and ongoing challenges. *Cancer*, 89: Suppl-8.
Narrative review
- Smith, R. A., von Eschenbach, A. C., Wender, R., Levin, B., Byers, T., Rothenberger, D., Brooks, D., Creasman, W., Cohen, C., Runowicz, C., Saslow, D., Cokkinides, V. & Eyre, H. (2001) American Cancer Society guidelines for the early detection of cancer: Update of early detection guidelines for prostate, colorectal, and endometrial cancers. *Ca-A Cancer Journal for Clinicians*, 51: 38-75.
Guideline
- Soeroso, N., Kasuma, D. & Hasibuan, P. (2011) Visualization assessment of fiber optic bronchoscopy with confirmation cytology of bronchus in establishing diagnosis lung cancer. *Respirology*, 16: 277.
Not in PICO
- Song, S. W., Jun, B. C., Cho, K. J., Lee, S., Kim, Y. J. & Park, S. H. (2011) CT evaluation of vocal cord paralysis due to thoracic diseases: a 10-year retrospective study. *Yonsei Medical Journal*, 52: 831-837.
Not in PICO
- Song, W. A., Liu, X., Tian, X. D., Wang, W., Liang, C. Y., Zhang, T., Guo, J. T., Peng, Y. H. & Zhou, N. K. (2011) Utility of squamous cell carcinoma antigen, carcinoembryonic antigen, Cyfra 21-1 and neuron specific enolase in lung cancer diagnosis: a prospective study from China. *Chinese Medical Journal*, 124: 3244-3248.
Not in PICO
- Sood, J. D., Wong, C., Bevan, R., Veale, A. & Sivakumaran, P. (2009) Delays in the assessment and management of primary lung cancers in South Auckland. *The New Zealand medical journal*, 122: 42-50.
Not in PICO
- Stamatelopoulos, A. & Kadjianis, F. (2008) Patient management with a solitary pulmonary nodule. [Review] [33 refs]. *Journal of B.U.On.*, 13: 479-485.
Narrative review

- Stapley, S., Sharp, D. & Hamilton, W. (2006) Negative chest X-rays in primary care patients with lung cancer. *British Journal of General Practice*, 56: 570-573.
Not in PICO
- Stevens, W., Lewis, C. A., Stevens, G., Garrett, J. E. & Kolbe, J. (2012) Lung cancer pathway from initial presentation to diagnosis in two centres in New Zealand. *Respirology*, 17: 69.
Not in PICO
- Stewart, C. J. & Stewart, I. S. (1996) Immediate assessment of fine needle aspiration cytology of lung. *Journal of Clinical Pathology*, 49: 839-843.
Not in PICO
- Stigt, J. A., Uil, S. M., Oostdijk, A. H., Boers, J. E., van den Berg, J. W. & Groen, H. J. (2012) A diagnostic program for patients suspected of having lung cancer. *Clinical Lung Cancer*, 13: 475-481.
Not in PICO
- Subortseva, I. N., Poddubnaya, I., Kovrigina, A. M., Kokosadze, N. V. & Osmanov, D. S. (2010) Difficulties in differential diagnosis of primary pulmonary lymphoma. *Journal of Thoracic Oncology*, 5: S115.
Not in PICO
- Suda, Y., Tanaka, A., Hayashi, K., Shindoh, Y. & Iijima, H. (2008) A novel needle-type sampling device for flexible ultrathin bronchoscopy. *Tohoku Journal of Experimental Medicine*, 216: 81-93.
Narrative review
- Sugihara, R., Kitajima, K., Maeda, T., Yoshikawa, T., Konishi, M., Kanata, N., Kanda, T., Koyama, H., Takenaka, D., Ohno, Y. & Sugimura, K. (2011) Comparison of capability of abdominal 320-detector row CT and of 16-detector row CT for small vasculature assessment. *Kobe Journal of Medical Sciences*, 56: E154-E161.
Not in PICO
- Sugiyamada, T., Tuchiya, K., Ishiyama, K., Takechi, A. & Harashima, S. (2003) Quality Control of Sputum Cytology. [Japanese]. *Japanese Journal of Lung Cancer*, 43: 998-1000.
Not in PICO
- Sun, Y. K., Hae, J. C., Geun, H. K., Dong, S. K., Jae, C. S., Kyoung, S. S., Seong, S. J. & Ju, O. K. (1998) Delayed diagnosis of primary lung cancer. [Japanese]. *Tuberculosis and Respiratory Diseases*, 45: 754-759.
Not in PICO
- Sutedja, G., Golding, R. P. & Postmus, P. E. (1996) High resolution computed tomography in patients referred for intraluminal bronchoscopic therapy with curative intent. *European Respiratory Journal*, 9: 1020-1023.
Not in PICO
- Sutedja, G. (2003) New techniques for early detection of lung cancer. *The European respiratory journal*, Supplement.: 57s-66s.
Narrative review
- Sutedja, T. G. (2012) Perspective for the t domain: Bronchoscopy. *Journal of Thoracic Oncology*, 7: S434.
Narrative review
- Szabo, E., Birrer, M. J. & Mulshine, J. L. (1993) Early detection of lung cancer. *Seminars in Oncology*, 20: 374-382.
Narrative review
- Szalus, N., Chcialowski, A., From, S., Zagrodzka, M., Pietrzykowski, J. & Dziuk, E. (2008) [Fusion of pulmonary scintigraphy with Tc99m-depreotide imaging with CT scan in recognizing solitary pulmonary nodule]. [Polish]. *Polski Merkurusz Lekarski*, 25: 330-334.
Not in PICO
- Tada, S., Miura, S., Miznuma, K., Kurisu, Y. & Yasuda, M. (1988) [Differential diagnosis of the early cancer: imaging diagnosis "CT"]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*,

34: 1223-1226.

Narrative review

Taira, N., Kawabata, T., Gabe, A., Ichi, T., Kushi, K., Yohena, T., Kawasaki, H., Yamashiro, T. & Ishikawa, K. (2014) - Lung cancer mimicking lung abscess formation on CT images. - *The American Journal of Case Reports*, 15: 243-245.

Not in PICO

Taiwo, E. O., Yorio, J. T., Yan, J. & Gerber, D. E. (2012) How have we diagnosed early-stage lung cancer without radiographic screening? A contemporary single-center experience. *PLoS ONE [Electronic Resource]*, 7: e52313.

Not in PICO

Takahama, M., Yamamoto, R., Tsukioka, T. & Tada, H. (2011) Usefulness of emergency coring out of airway neoplastic tumors obstructing the central airway with a rigid bronchoscope prior to radical surgery. [Japanese]. *Japanese Journal of Lung Cancer*, 51: 233-236.

Not in PICO

Tan, B. B., Flaherty, K. R., Kazerooni, E. A. & Iannettoni, M. D. (2003) The solitary pulmonary nodule. *Chest*, 123: 89S-96S.

Narrative review

Tan, X. J. (1962) [The diagnostic value of ribonuclease in bronchoalveolar lavage fluid to bronchogenic carcinoma]. [Chinese]. *Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih Chinese Journal of Tuberculosis & Respiratory Diseases*, 14: 25-26.

Not in PICO

Taniguchi, N., Ohsawa, N., Fukuda, Y., Akutagawa, S., Gotou, I., Min, K.-Y. & Hanafusa, T. (2003) The role of general practitioners in stepwise notification - From anxiety test results of the chest x-rays abnormality patients. [Japanese]. *Japanese Journal of Lung Cancer*, 43: 85-89.

Not in PICO

Tanner, K., Roden, K., Hancock, J. & Morgan, A. (2014) Haemoptysis referrals with a normal CT scan can be seen safely in a monthly haemoptysis clinic results of a retrospective audit. *Lung Cancer*, 83: S33.

Not in PICO

Tejerina, G. E., Lopez, G. A., Martin, L. J. & Perez, A. R. (2013) Intramuscular metastases as the initial presentation of non-small cell pulmonary carcinoma: Report of three cases diagnosed by fine needle aspiration cytology. *Virchows Archiv*, 463: 273.

Not in PICO

Terada, Y., Matsunobe, S., Nemoto, T., Tsuda, T. & Shimizu, Y. (1990) Feasibility of intraoperative cytodiagnosis of lung cancer. *Chest*, 98: 1156-1158.

Not in PICO

Thiberville, L., Salun, M., Corne, F. & Bota, S. (2006) Diagnosis of lung cancer: Fluorescence bronchoscopy. [French]. *Revue des Maladies Respiratoires*, 23: 16S17-16S22.

Narrative review

Thiberville, L. & Salaun, M. (2010) Bronchoscopic advances: on the way to the cells. *Respiration; international review of thoracic diseases*, 79: 441-449.

Narrative review

Thiberville, L. & Salaun, M. (2010) Early diagnosis of lung cancer, from autofluorescence bronchoscopy to in vivo confocal microimaging. [French]. *Revue des Maladies Respiratoires Actualites*, 2: 154-160.

Narrative review

Thiberville, L., Salaun, M., Lachkar, S., Morisse-Pradier, H. & Bota, S. (2014) The role of bronchoscopy in the screening and the early diagnosis of lung cancer. [French]. *Revue des Maladies Respiratoires Actualites*, 5: 591-597.

Narrative review

Thunnissen, F. B. J. M. (2003) Sputum examination for early detection of lung cancer. *Journal of Clinical Pathology*, 56: 805-810.

Narrative review

Tilve, G. A., Leiro, F. V., Botana, R. M., Gil, G. J. C., Pallares, S. A., Rodriguez, P. C., Garcia-Tejedor, J. L. & Fernandez, V. A. (2011) Effectiveness of a radiologic warning system when a thoracic neoplasm is suspected. *Journal of Thoracic Imaging*, 26: W124.

Not in PICO

Tockman, M. S., Gupta, P. K., Myers, J. D., Frost, J. K., Baylin, S. B., Gold, E. B., Chase, A. M., Wilkinson, P. H. & Mulshine, J. L. (1988) Sensitive and specific monoclonal antibody recognition of human lung cancer antigen on preserved sputum cells: A new approach to early lung cancer detection. *Journal of Clinical Oncology*, 6: 1685-1693.

Not in PICO

Tod, A. M. & Joanne, R. (2010) Overcoming delay in the diagnosis of lung cancer: a qualitative study. *Nursing Standard*, 24: 35-43.

Not in PICO

Tournoy, K. G., Rintoul, R. C., van Meerbeeck, J. P., Carroll, N. R., Praet, M., Buttery, R. C., van Kralingen, K. W., Rabe, K. F. & Annema, J. T. (2009) EBUS-TBNA for the diagnosis of central parenchymal lung lesions not visible at routine bronchoscopy. *Lung Cancer*, 63: 45-49.

Not in PICO

Uchida, J., Imamura, F., Takenaka, A., Yoshimura, M., Ueno, K., Oda, K., Nakayama, T., Tsukamoto, Y., Higashiyama, M. & Kusunoki, Y. (2006) Improved diagnostic efficacy by rapid cytology test in fluoroscopy-guided bronchoscopy. *Journal of Thoracic Oncology*, 1: 314-318.

Not in PICO

Unger, M. A Pause, Progress, and Reassessment in Lung Cancer Screening. [References]. *The New England Journal of Medicine* 355[17], 1822-1824. 2006.

Ref Type: Generic

Ref ID: 549

Reprint: Not in File

Abstract: Screening is not a test but a process. This distinction matters. Findings on radiographic screening lead to a diagnostic workup. Once a diagnosis is made, the process dictates the choice of treatment. Each of the steps in a screening algorithm is a medical decision in which the physician, acting as the patient's advocate, weighs benefits and risks. Physicians caring for people who are susceptible to lung cancer face four conflicting factors: the demand from the public to act, the need to consider cost-effectiveness and social responsibility, the need for scientific knowledge, and the lack of definitive evidence. One of the inherent weaknesses of any single radiographic or biomarker test for lung cancer is the inability to provide unequivocal information about the biology of a tumor - that is, its growth pattern and how it will respond to therapy. We are making solid progress in combining CT scanning with sputum analysis, fluorescence bronchoscopy, and analysis of pulmonary fluids, exhaled gases, and blood by genomic, proteomic, and immunologic methods. Routine clinical applications of these methods, however, are not available. These technological wonders require extensive validation and proof that markers alone or in combination are sufficiently specific for the detection and diagnosis of lung cancer. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Notes: DB - PsycINFO

AN - Peer Reviewed Journal: 2006-20691-005

SO - The New England Journal of Medicine. Vol.355(17), Oct 2006, pp. 1822-1824

n

Unsal, E., Koksall, D., Cimen, F., Taci, H. N. & Sipit, T. (2006) Analysis of patients with hemoptysis in a reference hospital for chest diseases. *Tuberkuloz ve Toraks*, 54: 34-42.

Not in PICO (referred population)

- Vakil, A., Abubaker, A., Upadhyay, H., Patel, V., Cervellione, K. & Shalanov, A. (2013) Soft tissue mass above the knee as the initial presentation of metastatic NSCLC in an asymptomatic patient. *Chest*, 144.
Not in PICO
- Valdes, D. S., Garcia, S. E., Perez, C. H. & Hernandez, H. M. (2010) Length of diagnostic delay in patients with non-small-cell lung cancer. *MEDICC Review*, 12: 29-32.
Not in PICO
- Van't Westeinde, S. C. & Van Klaveren, R. J. (2011) Screening and early detection of lung cancer. *Cancer Journal*, 17: 3-10.
Narrative review
- Van Den Bergh, H. (2003) Early detection of lung cancer and the role of endoscopic fluorescence imaging. *Medical Laser Application*, 18: 20-26.
Narrative review
- van der Drift, M. A., Van Der Wilt, G.-J., Thunnissen, F. B. J. M. & Janssen, J. P. (2005) A prospective study of the timing and cost-effectiveness of bronchial washing during bronchoscopy for pulmonary malignant tumors. *Chest*, 128: 394-400.
Not in PICO
- van der Drift, M. A., Prinsen, C. F., Knuiman, G. J., Janssen, J. P., Dekhuijzen, P. N. & Thunnissen, F. B. (2012) Diagnosing peripheral lung cancer: the additional value of the Ras-association domain family 1A gene methylation and Kirsten rat sarcoma 2 viral oncogene homolog mutation analyses in washings in nondiagnostic bronchoscopy. *Chest*, 141: 169-175.
Not in PICO
- Van Der Schee, M. P., Fens, N., Sterk, P. J. & Kunst, P. W. A. (2010) Bronchoscopic air-sampling by electronic nose for molecular assessment of lung cancer. *American Journal of Respiratory and Critical Care Medicine*, 181.
Not in PICO
- Van, R. A., Neethling, G. S., Schubert, P. T., Koegelenberg, C. F., Wright, C. A., Bolliger, C. T., Bernasconi, M. & Diacon, A. H. (2014) - Impact of routine sputum cytology in a population at high risk for bronchial carcinoma. - *International Journal of Tuberculosis & Lung Disease*, 18: 607-612.
Not in PICO
- Varella-Garcia, M., Schulte, A. P., Wolf, H. J., Feser, W. J., Zeng, C., Braudrick, S., Yin, X., Hirsch, F. R., Kennedy, T. C., Keith, R. L., Baron, A. E., Belinsky, S. A., Miller, Y. E., Byers, T. & Franklin, W. A. (2010) The detection of chromosomal aneusomy by fluorescence in situ hybridization in sputum predicts lung cancer incidence. *Cancer Prevention Research*, 3: 447-453.
Not in PICO
- Vathesatogkit, P., Charoenpan, P., Kiatboonsri, S., Samerkai, V. & Tansuphaswadikul, S. (1984) The use of fiberoptic bronchoscopy in the diagnosis of suspected pulmonary malignancy: Ramathibodi Hospital's experience with 542 patients. *Journal of the Medical Association of Thailand*, 67: 176-181.
Not in PICO
- Verger, P., Cabut, S., Viau, A., Souville, M., Pardon, C., Charrier, D., De, L. B., Lehucher-Michel, M. P. & Arnaud, S. (2011) Use of imaging in the follow-up of workers exposed to lung carcinogens: practices in occupational medicine and its determinants. *International Journal of Occupational & Environmental Health*, 17: 71-79.
Not in PICO
- Vergnenegre, A., Cruciani, G., Thomas, M., Guallar, E., Medina, E. & Carrato, A. (2010) Resource utilization and diagnostic approaches in non-small-cell lung cancer (NSCLC) across europe: Epiclin-lung study. *Value in Health*, 13: A272.
Not in PICO

- Vergnon, J.-M. (2014) The bronchoscopy in the diagnosis of lung cancer. [French]. *Revue des Maladies Respiratoires Actualites*, 5: 339-345.
Narrative review
- Vergnon, J.-M. (2014) The bronchoscopy in the diagnosis of lung cancer. [French]. *Revue des Maladies Respiratoires Actualites*, 5: 339-345.
Narrative review
- Vermylen, P., Pierard, P., Roufousse, C., Bosschaerts, T., Verhest, A., Sculier, J. P. & Ninane, V. (1999) Detection of bronchial preneoplastic lesions and early lung cancer with fluorescence bronchoscopy: a study about its ambulatory feasibility under local anaesthesia. *Lung Cancer*, 25: 161-168.
Not in PICO
- Vigg, A., Mantri, S., Vigg, A. & Vigg, A. (2003) Pattern of lung cancer in elderly. *Journal of the Association of Physicians of India*, 51: 963-966.
Not in PICO
- Villar, T. G., Nogueira, M. T. & Villar, M. (1980) Lung cancer in Portugal over the past 35 years (1940-1975). *Medicina Toracica*, 3: 261-278.
Not in PICO
- von Bartheld, M. B., Rabe, K. F. & Annema, J. T. (2009) Transaortic EUS-guided FNA in the diagnosis of lung tumors and lymph nodes. *Gastrointestinal Endoscopy*, 69: 345-349.
Not in PICO
- Von, E. M. (2004) Lung cancer screening. [German]. *Atemwegs- und Lungenkrankheiten*, 30: 191-197.
Not in PICO
- Votruba, J. & St'astny, B. (2000) Autofluorescent bronchoscopy and early diagnosis of lung cancer. [Czech]. *Endoskopie*, 9: 47-51.
Narrative review
- Vourlekis, J. S. & Szabo, E. (2004) Use of markers for the detection and treatment of lung cancer. *Disease Markers*, 20: 71-85.
Narrative review
- Vyas, J. J., Desai, P. B. & Rao, N. D. (1982) Relative accuracy of diagnostic method in bronchogenic carcinoma. *Journal of Surgical Oncology*, 21: 45-48.
Not in PICO
- Wagnetz, U., Menezes, R. J., Boerner, S., Paul, N. S., Wagnetz, D., Keshavjee, S. & Roberts, H. C. (2012) CT screening for lung cancer: Implication of lung biopsy recommendations. *American Journal of Roentgenology*, 198: 351-358.
Not in PICO
- Waller, R., Parris, B., Savarimuthu, S., Hollis, C., Vandeleur, A., Robinson, P. J., Yang, I. A., Bowman, R. V. & Fong, K. M. (2010) Discarded FOB samples for DNA PCR analyses. *Respirology*, 15: A71.
Not in PICO
- Walter, H. S., Plant, R., Law, A., Esler, C., Sridhar, T., Fennell, D. A. & Ahmed, S. I. (2014) Impact of an acute oncology service in patients with a suspected new diagnosis of lung cancer at University Hospitals of Leicester. *Lung Cancer*, 83: S36.
Not in PICO
- Wang, F., Zhang, Y., Feng, Y.-C. & Huang, Y.-C. (2013) Comparison between FISH and cytology of sputum samples in detection of lung cancer. [Chinese]. *Journal of Practical Oncology*, 28: 197-199.
Not in PICO
- Wang, X., Cao, A., Peng, M., Hu, C., Liu, D., Gu, T. & Liu, H. (2004) The value of chest CT scan and tumor markers detection in sputum for early diagnosis of peripheral lung cancer. *Chinese Journal of Lung Cancer*, 7: 58-63.
Not in PICO

- Wardwell, J. & Massion, P. P. (2005) Novel strategies for the early detection and prevention of lung cancer. *Seminars in Oncology*, 32: 259-268.
Narrative review
- Warner, K. A., Crawford, E. L., Zaher, A., Coombs, R. J., Elsamaloty, H., Roshong-Denk, S. L., Sharief, I., Amurao, G. V., Yoon, Y., Al-Astal, A. Y., Assaly, R. A., Hernandez, D. A., Graves, T. G., Knight, C. R., Harr, M. W., Sheridan, T. B., DeMuth, J. P., Zahorchak, R. J., Hammersley, J. R., Olson, D. E., Durham, S. J. & Willey, J. C. (2003) The c-myc x E2F-1/p21 interactive gene expression index augments cytomorphologic diagnosis of lung cancer in fine-needle aspirate specimens. *Journal of Molecular Diagnostics*, 5: 176-183.
Not in PICO
- Wassermann, K., Gassanov, N., Atay, Z., Topalidis, T., Dienes, H. P. & Mathen, F. (2004) The impact of cytology on the bronchoscopic diagnosis of lung cancer. *Journal of Bronchology*, 11: 154-159.
Not in PICO
- Watanabe, Y., Shimizu, J., Oda, M., Iwa, T., Takashima, T., Kamimura, R., Kitagawa, M., Nonomura, A., Nakamura, S., Tanimoto, K., Matsubara, F., Ikegaki, S. & Yamada, K. (1991) Early hilar lung cancer: Its clinical aspect. *Journal of Surgical Oncology*, 48: 75-80.
Not in PICO
- Webb, S., Thomas, M., Metcalf, C., Segal, A., Nowak, A. K., Bentel, J. & Millward, M. (2009) EGFR mutation testing in NSCLC: Patterns of care and outcomes in Western Australia. *Asia-Pacific Journal of Clinical Oncology*, 5: 66-71.
Not in PICO
- Wei, B., Wang, T. Y., Gong, M., Lu, K. J., Li, C. L. & Zou, L. F. (2005) [The role of 18F fluorodeoxyglucose triple-head coincidence imaging in the diagnosis of suspected lung cancer]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]*, 43: 80-82.
Not in PICO
- Werynski, W., Radziszewski, A. B., Paluchowski, A. & Radziszewski, A. S. (2006) Central located lung tumor in patients hospitalized in years 2004 in Pulmonology Department of the Internal Ward in Dabrowa Tarnowska. [Polish]. *Przegląd Lekarski*, 63: 62-64.
Not in PICO
- Wilde, J. (1981) Early detection of lung cancer. Possibilities--limits--organization. [German]. *Archiv für Geschwulstforschung*, 51: 721-726.
Narrative review
- Williams, S. M., Gray, W. & Gleeson, F. V. (2002) Macroscopic assessment of pulmonary fine needle aspiration biopsies: correlation with cytological diagnostic yield. *British Journal of Radiology*, 75: 28-30.
Not in PICO
- Williams, T. & Bowie, P. E. S. (2000) The bronchoscopic diagnosis of lung cancer: A prospective correlation between the bronchoscopic appearances and cytology and biopsy results. *Journal of Bronchology*, 7: 295-300.
Not in PICO
- Winter, H., Harrington, J., Batten, L. & Hardie, C. (2012) Lung cancer referrals in new zealand-the experience of one regional cancer service. *Journal of Thoracic Oncology*, 7: S188.
Not in PICO
- Wongsurakiat, P., Wongbunnate, S., Dejsomritrutai, W., Charoenratanakul, S., Tscheikuna, J., Youngchaiyud, P., Pushpakom, R., Maranetra, N., Nana, A., Chierakul, N., Sakiyalak, U. & Ruengjam, C. (1998) Diagnostic value of bronchoalveolar lavage and postbronchoscopic sputum cytology in peripheral lung cancer. *Respirology*, 3: 131-137.
Not in PICO
- Wu, G., Wang, E., Li, J., Fu, Z., Han, S. & Fan, Y. (2006) [Clinical value of liquid-based cytologic test in sputum examination of patients with lung cancer]. [Chinese]. *Chinese Journal of Lung Cancer*, 9:

192-195.

Not in PICO

Wu, R., Fang, W. & Lin, L. (2003) [The clinical analysis of lung cancer with paraneoplastic syndrome as initial symptom]. [Chinese]. *Chinese Journal of Lung Cancer*, 6: 204-205.

Not in PICO

Xu, J. Y. (1991) [Sputum drainage by ultrasonic nebulization and the diagnosis of pulmonary carcinoma]. [Chinese]. *Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih Chinese Journal of Tuberculosis & Respiratory Diseases*, 14: 285-286.

In Chinese, with no English abstract.

Yamada, K., Isobe, T., Katou, Y., Oshita, F., Nomura, I., Noda, K., Ishii, H., Tajiri, M., Kameda, Y. & Kaneko, M. (1996) Computed tomography imaging analysis of resected lung cancers detected by computed tomography. *Japanese Journal of Lung Cancer*, 36: 261-270.

Not in PICO

Yamazaki, Y., Hashimoto, R. & Shiozaki, K. (1980) Follow-up study of surgically excised early and relatively-early lung cancer. [Japanese]. *Journal of the Japanese Association for Thoracic Surgery*, 28: 210-215.

Not in PICO

Yang, S.-Y. (2011) The status quo, confusion and prospect of early diagnosis for lung cancer. [Chinese]. *Journal of Xi'an Jiaotong University (Medical Sciences)*, 32: 1-5.

Narrative review

Yasuda, H., Soejima, K., Nakayama, S., Kawada, I., Nakachi, I., Yoda, S., Satomi, R., Ikemura, S., Terai, H., Sato, T., Watanabe, H., Naoki, K., Hayashi, Y. & Ishizaka, A. (2011) Bronchoscopic microsampling is a useful complementary diagnostic tool for detecting lung cancer. *Lung Cancer*, 72: 32-38.

Not in PICO

Yasufuku, K. (2010) Early Diagnosis of Lung Cancer. *Clinics in Chest Medicine*, 31: 39-47.

Narrative review

Ye, T., Hu, H., Luo, X. & Chen, H. (2011) The role of endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) for qualitative diagnosis of mediastinal and hilar lymphadenopathy: a prospective analysis. *BMC Cancer*, 11: 100.

Not in PICO

Yoneda, R. (1985) Background factors of lung cancer patients in the Tokyo area. [Japanese]. *Japanese Journal of Lung Cancer*, 25: 129-141.

Not in PICO

Yoshida, S., Maeda, T., Morita, M., Nishioka, M., Sawada, A., Kamiike, O., Yamamoto, Y., Hamada, F., Inomata, T. & Ohara, S. (1988) [Table incremental slow injection CE-CT in lung cancer--usefulness of early and delayed images]. [Japanese]. *Nippon Igaku Hoshasen Gakkai Zasshi - Nippon Acta Radiologica*, 48: 173-180.

Not in PICO

Yoshimoto, A., Tsuji, H., Takazakura, E., Watanabe, T., Haratake, J., Kasahara, K., Fuiimura, M. & Nakao, S. (2002) Reasons for the delays in the definitive diagnosis of lung cancer for more than one year from the recognition of abnormal chest shadows. *Internal Medicine*, 41: 95-102.

Not in PICO

Zaric, B., Perin, B., Stojic, V., Carapic V, Matijasevic, J., Andrijevic, I. & Eri, Z. (2013) Detection of premalignant bronchial lesions can be significantly improved by combination of advanced bronchoscopic imaging techniques. *Annals of Thoracic Medicine*, 8: 93-98.

Not in PICO

Zaric, B., Perin, B., Becker, H. D., Felix, F. H., Eberhardt, R., Jovanovic, S., Orlic, T., Panjkovic, M., Zvezdin, B., Jovelic, A., Bijelovic, M., Jurisic, V. & Antonic, M. (2012) Combination of narrow band imaging (NBI) and autofluorescence imaging (AFI) videobronchoscopy in endoscopic assessment

- of lung cancer extension. *Medical Oncology*, 29: 1638-1642.
Not in PICO
- Zaric, B., Perin, B., Jovanovic, S., Lalic, N., Stojanovic, G. & Antonic, M. (2012) Detection of premalignant bronchial lesions can be improved by combination of autofluorescence imaging (AFI) and narrow band imaging (NBI) videobronchoscopy. *Journal of Thoracic Oncology*, 7: S51.
Not in PICO
- Zaric, B., Perin, B., Stojsic, V., Carapic, V., Matijasevic, J., Andrijevic, I. & Eri, Z. (2013) Detection of premalignant bronchial lesions can be significantly improved by combination of advanced bronchoscopic imaging techniques. *Annals of Thoracic Medicine*, 8: 93-98.
Not in PICO
- Zaric, B., Perin, B., Carapic, V., Stojsic, V., Matijasevic, J., Andrijevic, I. & Kopitovic, I. (2013) Diagnostic value of autofluorescence bronchoscopy in lung cancer. *Thoracic Cancer*, 4: 1-8.
Narrative review
- Zeng, H., Petek, M., Zorman, M. T., McWilliams, A., Palcic, B. & Lam, S. (2004) Integrated endoscopy system for simultaneous imaging and spectroscopy for early lung cancer detection. *Optics Letters*, 29: 587-589.
Narrative review
- Zeng, H., McWilliams, A. & Lam, S. (2004) Optical spectroscopy and imaging for early lung cancer detection: A review. *Photodiagnosis and Photodynamic Therapy*, 1: 111-122.
Narrative review
- Zhai, J. (2009) A comparison of cytology and fluorescence in situ hybridization for the detection of malignant bronchial brushing and washing specimens. *Laboratory Investigation*, 89: 99A.
Not in PICO
- Zhang, H., Zhao, J., Hua, F., Zuo, C. & Guan, Y. (2010) The application of 18F-FDG PET/CT in multiple primary cancer including lung cancer. *European Journal of Nuclear Medicine and Molecular Imaging*, 37: S350.
Not in PICO
- Zhang, L., Wang, M., Wang, Y. & Li, L. (2002) Clinico-pathological study of 98 patients with pulmonary solitary nodule. [Chinese]. *Zhonghua zhong liu za zhi [Chinese journal of oncology]*, 24: 491-493.
Not in PICO
- Zhang, W., Yang, W.-L., Yang, S.-Y., Huo, S.-F., Shang, W.-L., Du, J., Lin, X.-L. & Bu, L.-N. (2011) Diagnostic value of white light bronchoscopy combined with autofluorescence bronchoscopy for early diagnosis of lung cancer: A systematic review. [Chinese]. *Journal of Xi'an Jiaotong University (Medical Sciences)*, 32: 733-738.
Not in PICO
- Zhao, H., Xie, Z., Zhou, Z. L., Sui, X. Z. & Wang, J. (2013) Diagnostic value of endobronchial ultrasound-guided transbronchial needle aspiration in intrapulmonary lesions. *Chinese Medical Journal*, 126: 4312-4315.
Not in PICO
- Zhu, L. Y., Xu, Y. J., Liang, D. & Chen, P. (2012) [The clinical value of autofluorescence bronchoscopy for the diagnosis of lung cancer]. [Chinese]. *Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih Chinese Journal of Tuberculosis & Respiratory Diseases*, 35: 419-422.
Not in PICO

MESOTHELIOMA

Review question:

What is the risk of mesothelioma in patients presenting in primary care with symptom(s)?

Results

Literature search

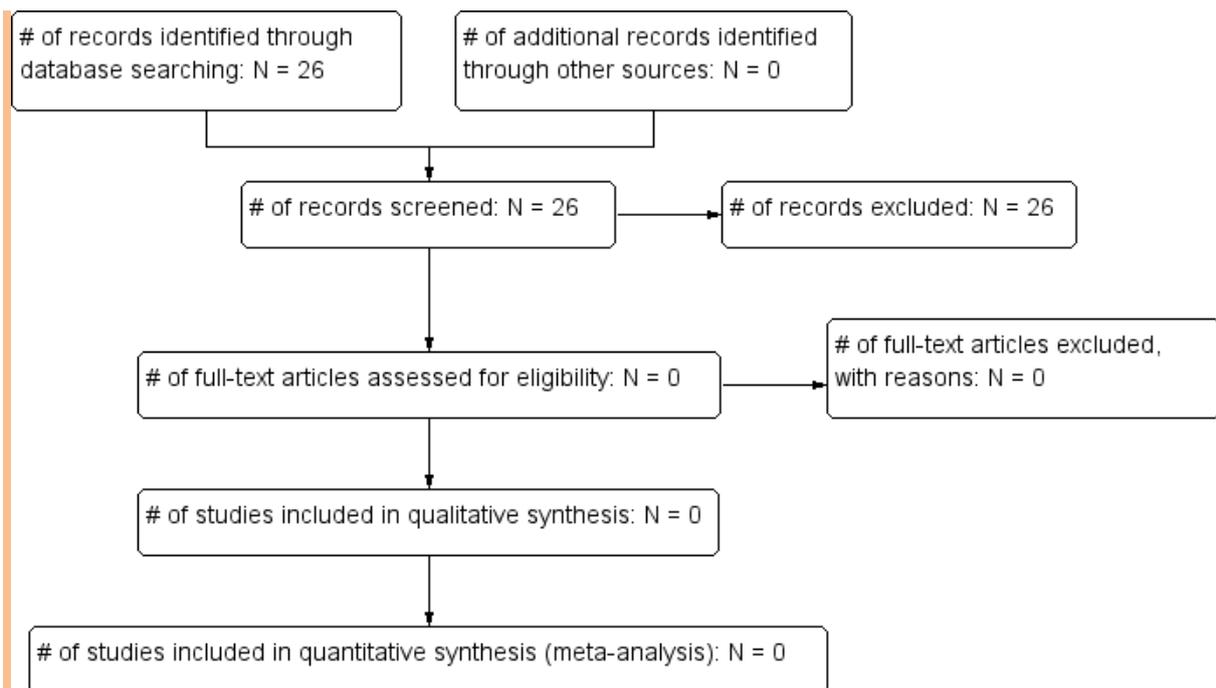
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	185	6	22/04/2013
<i>Premedline</i>	1980-2013	4	0	22/04/2013
<i>Embase</i>	1980-2013	301	15	22/04/2013
<i>Cochrane Library</i>	1980-2013	17	0	22/04/2013
<i>Psychinfo</i>	1980-2013	2	0	22/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	81	3	22/04/2013

Total References retrieved (after de-duplication): 21

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-20/08/2014	120	0	20/08/2014
<i>Premedline</i>	4/2013-20/08/2014	22	2	20/08/2014
<i>Embase</i>	4/2013-20/08/2014	37	2	20/08/2014
<i>Cochrane Library</i>	4/2013-20/08/2014	4	0	20/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	4/2013-20/08/2014	27	3	20/08/2014

Total References retrieved (after de-duplication): 5



Study results

No evidence was identified.

References

Included studies

None

Excluded studies (with excl reason)

Bass, L. & Hegeman, T. W. (2011) Multiple primary cancers including mesothelioma of the tunica vaginalis: case report and literature review with primary care focus. *Journal of the American Osteopathic Association*, 111: 483-486.

Not in PICO

Campbell, A. M., Mclean, E. & Pilling, J. E. (2013) Is cytological examination of pleural fluid obtained at VATS for suspected malignant pleural effusion useful? *Lung Cancer*, 79: S68-S69.

Not in PICO

Datta, A. K. (2013) Fast Track Referral of Patients with Malignant Mesothelioma Is Not Associated with Better Survival. *Thorax*, 68: A100-A101.

Not in PICO

de Pangher Manzini, V. (2005) Malignant peritoneal mesothelioma. *Tumori*, 91: 1-5.

Not in PICO

Dixon, D. L., Griggs, K. M., Ely, M., Henderson, D. W. & Klebe, S. (2013) The usefulness of expert opinion in medicolegal referrals of malignant mesothelioma. *Pathology*, 45: 523-525.

Not in PICO

Eswaran, M. & Ansar, M. (2013) Peritoneal mesothelioma with presentation of dermatomyositis. *Journal of General Internal Medicine*, 28: S370-S371.

Not in PICO

Falkenstern-Ge, R. F., Kimmich, M., Bode-Erdmann, S., Friedel, G., Ott, G. & Kohlhauf, M. (2013) Pleural mesothelioma presenting as periumbilical metastasis: the first clinical documentation. *Case Reports in Oncological Medicine*, 2013: 198729.

Not in PICO

- Friedberg, J. S. C. (2010) Pleural malignancies. *Seminars in Radiation Oncology*, 20: 208-214.
Narrative review
- Garrido, M.-J. (2006) Recurrent pericardial effusion as initial manifestation of primary diffuse pericardial malignant mesothelioma. *Clinical and Translational Oncology*, 8: 694-696.
Not in PICO
- Guha, K. (2008) Recurrent hydropneumothorax as a presenting feature of malignant mesothelioma. *European Journal of Internal Medicine*, 19: 63-64.
Not in PICO
- Haber, S. E. (2010) Synchronous malignant pleural mesothelioma and pulmonary carcinoma in a woman without evidence of asbestos exposure. *Respiratory Medicine CME*, 3: 160-161.
Not in PICO
- Hannaford-Turner, K. (2010) Surveillance of Australian workplace Based Respiratory Events (SABRE) in New South Wales. *Occupational Medicine*, 60: 376-382.
Not in PICO
- Huncharek, M. (2004) Presentation of malignant pleural mesothelioma with symptomatic brain metastasis: Report of a case. *Tumori*, 90: 424-427.
Not in PICO
- Katsuya, Y., Fukusumi, M., Morita, S., Ibe, T., Wakuda, K., Mouri, A., Hamamoto, Y., Yamada, K. & Kamimura, M. (2014) - Pseudomesotheliomatous carcinoma due to pleural metastasis from renal pelvic cancer. - *Internal Medicine*, 53: 871-874.
Not in PICO
- Khalid, U. (2007) Symptoms and weight loss in patients with gastrointestinal and lung cancer at presentation. *Supportive Care in Cancer*, 15: 39-46.
Not in PICO
- Makimoto, G., Fujiwara, K., Fujimoto, N., Yamadori, I., Sato, T. & Kishimoto, T. (2014) - Phrenic nerve paralysis as the initial presentation in pleural sarcomatoid mesothelioma. - *Case Reports Oncology*, 7: 389-392.
Not in PICO
- Manzini, V. D. P. (2005) Malignant peritoneal mesothelioma. *Tumori*, 91: 1-5.
Not in PICO
- Marta, M. J. S. (2003) Malignant mesothelioma - A diagnostic challenge. *Revista Portuguesa de Pneumologia*, 9: 411-425.
Not in PICO
- Mouawad, N. J., Daniel, V. C. & Starr, J. E. (2014) Advanced malignant mesothelioma mimicking acute contained thoracic aortic rupture. *Interactive Cardiovascular and Thoracic Surgery*, 18: 242-244.
Not in PICO
- Murray, L. J., Higham, J., Suvarna, S. K., Craig, G. T., Bridgewater, C. H., Fisher, P. M. & Thornhill, M. H. (2011) Oral presentation of malignant mesothelioma. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology*, 111: E21-E26.
Not in PICO
- Neumann, V., Loseke, S., Nowak, D., Herth, F. J. F. & Tannapfel, A. (2013) Malignant pleural mesothelioma: Incidence, etiology, diagnosis, treatment, and occupational health. [German, English]. *Deutsches Arzteblatt International*, 110: 319-326.
Narrative review
- O'Reilly, K. M. A. (2007) Asbestos-related lung disease. *American Family Physician*, 75: 683-688+690.
Narrative review
- Ohno, Y. (2014) New applications of magnetic resonance imaging for thoracic oncology. *Seminars in Respiratory and Critical Care Medicine*, 35: 27-40.
Narrative review

Pavia, R. (2005) Malignant pleural mesothelioma: early diagnosis and multimodality management. // *Giornale di chirurgia*, 26: 257-260.
Narrative review

Roberts, H. C. P. (2009) Screening for malignant pleural mesothelioma and lung cancer in individuals with a history of asbestos exposure. *Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer*, 4: 620-628.
Not in PICO

Robinson, L. A., Reilly, R. B., Robinson, L. A. & Reilly, R. B. (1994) Localized pleural mesothelioma. The clinical spectrum. [Review] [15 refs]. *Chest*, 106: 1611-1615.
Narrative review

Rosell-Murphy, M., Abos-Herrandiz, R., Tarres, J., Martinez-Artes, X., Garcia-Allas, I., Krier, I., Cantarell, G., Gallego, M., Orriols, R. & Alberti, C. (2010) Prospective study of asbestos-related diseases incidence cases in primary health care in an area of Barcelona province. *Bmc Public Health*, 10.
Not in PICO

Ruffie, P., Lehmann, M., Galateau-Salle, F., Lagrange, J. L. & Paireon, J. C. (1998) Standards, Options and Recommendations (SOR) for clinical care of malignant pleural mesothelioma. *Bulletin du Cancer*, 85: 545-561.
Guideline

Saguil, A., Wyrick, K. & Hallgren, J. (2014) Diagnostic approach to pleural effusion. *American Family Physician*, 90: 99-104.
Narrative review

Saraya, T., Yokoyama, T., Ishii, H., Tanaka, Y., Tsujimoto, N., Ogawa, Y., Sohara, E., Nakajima, A., Inui, T., Sayuki, H., Fujiwara, M., Oka, T., Kawachi, R., Goya, T., Takizawa, H. & Goto, H. (2013) A case of malignant peritoneal mesothelioma revealed with limitation of PET-CT in the diagnosis of thoracic metastasis. *Journal of Thoracic Disease*, 5: E11-E16.
Not in PICO

Sidorenko, B. A. D. (2009) Diagnosis of malignant pericardial mesothelioma. *Kardiologija*, 49: 84-89.
Not in PICO

Svorcan, P. (2003) Primary malignant mesothelioma of the peritoneum. *Romanian Journal of Gastroenterology*, 12: 135-137.
Not in PICO

Tomasetti, M. (2010) Biomarkers for early detection of malignant mesothelioma: Diagnostic and therapeutic application. *Cancers*, 2: 523-548.
Narrative review

Review question:

Which investigations of symptoms of suspected mesothelioma should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	118	27	14/05/2013
Premedline	1980-2013	13	4	14/05/2013
Embase	1980-2013	169	53	14/05/2013
Cochrane Library	1980-2013	12	0	14/05/2013

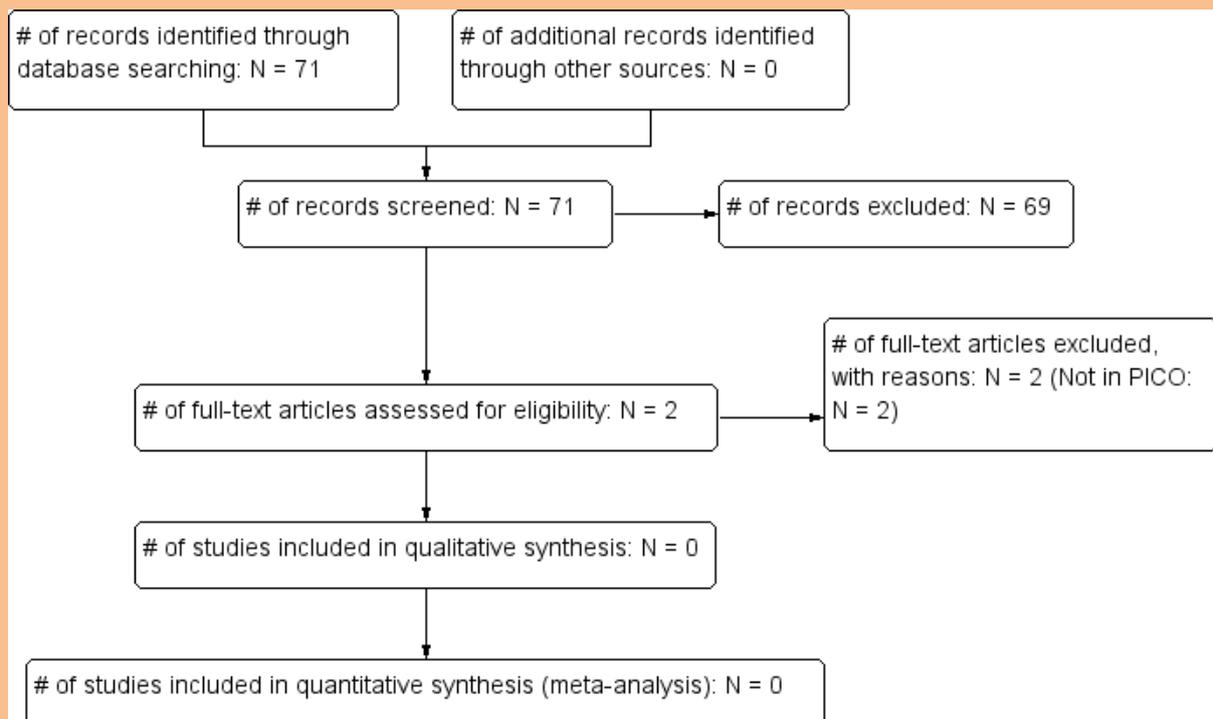
Psychinfo	1980-2013	1	0	14/05/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	24	0	14/05/2013

Total References retrieved (after de-duplication): 63

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-20/08/2014	7	0	20/08/2014
<i>Premedline</i>	5/2013-20/08/2014	17	3	20/08/2014
<i>Embase</i>	5/2013-20/08/2014	37	4	20/08/2014
<i>Cochrane Library</i>	5/2013-20/08/2014	4	0	20/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	5/2013-20/08/2014	6	1	20/08/2014

Total References retrieved (after de-duplication): 8



Study results

No evidence was identified pertaining to the diagnostic accuracy of chest x-ray, CT, abdominal x-ray, or ultrasound in patients with suspected mesothelioma where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

- Agarwal, P., Singer, J. & Russell, P. (2011) Defying the odds: An unusually long survival period following diagnosis of pleural mesothelioma and the use of a tunnelled indwelling pleural catheter for management of recurrent effusions. *American Journal of Respiratory and Critical Care Medicine*, 183.
Not in PICO
- Allen, R. K. A., Cramond, T., Lennon, D. & Waterhouse, M. (2011) A Retrospective Study of Chest Pain in Benign Asbestos Pleural Disease. *Pain Medicine*, 12: 1303-1308.
Not in PICO
- Basu, S., Saboury, B., Torigian, D. A. & Alavi, A. (2011) Current evidence base of FDG-PET/CT imaging in the clinical management of malignant pleural mesothelioma: Emerging significance of image segmentation and global disease assessment. *Molecular Imaging and Biology*, 13: 801-811.
Not in PICO
- Bayanati, H., Roberts, H., Dong, Z., Pereira, A., Sitartchouk, I., Kale, A., Paul, N. & Johnston, M. (2008) Low-dose computed tomography in prior asbestos-exposed workers: Assessment of pleural plaques and screening for lung cancer and malignant mesothelioma. *Journal of Thoracic Imaging*, 23: 66.
Not in PICO
- Bedrossian, C. W. M. (2012) Malignant mesothelioma in small cytohistological samples: Diagnosis, pitfalls and rare variants. *Cytopathology*, 23: 23.
Narrative review
- Benamore, R. E., O'Doherty, M. J. & Entwisle, J. J. (2005) Use of imaging in the management of malignant pleural mesothelioma. [Review] [58 refs]. *Clinical Radiology*, 60: 1237-1247.
Narrative review
- Benard, F., Sterman, D., Smith, R. J., Kaiser, L. R., Albelda, S. M. & Alavi, A. (1998) Metabolic imaging of malignant pleural mesothelioma with fluorodeoxyglucose positron emission tomography. *Chest*, 114: 713-722.
Not in PICO
- Bergonzini, R., Olivetti, L., Tassi, G. F. & Chiodera, P. L. (1996) [Malignant mesothelioma of the pleura: correlations between thoracoscopy and radiology]. [Italian]. *Radiologia Medica*, 92: 52-57.
Not in PICO
- Borghesi, M., Passaretti, G., Franceschelli, A., Gentile, G. & Colombo, F. (2012) Malignant mesothelioma of the tunica vaginalis of the testis. *Anticancer Research*, 32: 1907.
Not in PICO
- Brauer, C., Baandrup, U., Jacobsen, P., Krasnik, M., Olsen, J. H., Pedersen, J. H., Rasmussen, T. R., Schlunssen, V., Sherson, D., Svolgaard, B., Sorensen, J. B. & Omland, O. (2009) Screening for asbestos-related conditions. [Danish]. *Ugeskrift for Laeger*, 171: 433-436.
Not in PICO
- British Thoracic Society Standards of Care Committee (2001) Statement on malignant mesothelioma in the United Kingdom. [Review] [62 refs][Erratum appears in Thorax 2001 Oct;56(10):820]. *Thorax*, 56: 250-265.
Narrative review
- British Thoracic Society Standards of Care Committee (2007) BTS statement on malignant mesothelioma in the UK, 2007. [138 refs]. *Thorax*, 62: Suppl-ii19.
Narrative review
- Campbell, A. M., Mclean, E. & Pilling, J. E. (2013) Is cytological examination of pleural fluid obtained at VATS for suspected malignant pleural effusion useful? *Lung Cancer*, 79: S68-S69.
Not in PICO

- Chaisaowong, K., Jager, P., Vogel, S., Knepper, A., Kraus, T. & Aach, T. (2007) Computer-assisted diagnosis for early stage pleural mesothelioma: Towards automated detection and quantitative assessment of pleural thickenings from thoracic CT images. *Methods of Information in Medicine*, 46: 324-331.
Not in PICO
- Cicenas, S. & Vencevicius, V. (2008) [Malignant pleural diseases: diagnosis and treatment]. [Lithuanian]. *Medicina (Kaunas, Lithuania)*, 44: 929-935.
Not in PICO
- Clin, B., Luc, A., Morlais, F., Paris, C., Ameille, J., Brochard, P., De, G. J., Gislard, A., Laurent, F., Letourneux, M., Schorle, E., Launoy, G., Pairon, J. C. & National Network of Asbestos Post-Exposure Survey (APEXS) (2011) Pulmonary nodules detected by thoracic computed tomography scan after exposure to asbestos: diagnostic significance. *International Journal of Tuberculosis & Lung Disease*, 15: 1707-1714.
Not in PICO
- De, V. P. (1998) [Asbestos: current knowledge and perspectives]. [Review] [10 refs] [French]. *Revue Medicale de Bruxelles*, 19: A351-A354.
Narrative review
- Dubaniewicz, A. & Sieminska, A. (1992) Diagnostic difficulties in pleural mesothelioma. [Polish]. *Wiadomosci lekarskie (Warsaw, Poland : 1960)*, 45: 248-250.
Not in PICO
- Elboga, U., Yilmaz, M., Uyar, M., Zeki, C. Y., Bakir, K. & Dikensoy, O. (2012) The role of FDG PET-CT in differential diagnosis of pleural pathologies. *Revista Espanola de Medicina Nuclear e Imagen Molecular*, 31: 187-191.
Not in PICO
- Entwisle, J. (2004) The use of magnetic resonance imaging in malignant mesothelioma. [Review] [8 refs]. *Lung Cancer*, 45: Suppl-71.
Not in PICO
- Eswaran, M. & Ansar, M. (2013) Peritoneal mesothelioma with persentation of dermatomyositis. *Journal of General Internal Medicine*, 28: S370-S371.
Not in PICO
- Falkenstern-Ge, R. F., Kimmich, M., Bode-Erdmann, S., Friedel, G., Ott, G. & Kohlhaufel, M. (2013) Pleural mesothelioma presenting as periumbilical metastasis: the first clinical documentation. *Case Reports in Oncological Medicine*, 2013: 198729.
Not in PICO
- Fasola, G., Belvedere, O., Aita, M., Zanin, T., Follador, A., Cassetti, P., Meduri, S., De, P., V, Pignata, G., Rosolen, V., Barbone, F. & Grossi, F. (2007) Low-dose computed tomography screening for lung cancer and pleural mesothelioma in an asbestos-exposed population: baseline results of a prospective, nonrandomized feasibility trial--an Alpe-adria Thoracic Oncology Multidisciplinary Group Study (ATOM 002). *The Oncologist*, 12: 1215-1224.
Not in PICO
- Ferretti, G. (2011) [What are the tools for post-occupational follow-up, how should they be performed and what are their performance, limits and benefit/risk ratio? Chest X-Ray and CT scan]. [Review] [French]. *Revue des Maladies Respiratoires*, 28: 761-772.
Narrative review
- Flores, R. M., Akhurst, T., Gonen, M., Larson, S. M. & Rusch, V. W. (2003) Positron emission tomography defines metastatic disease but not locoregional disease in patients with malignant pleural mesothelioma. *Journal of Thoracic & Cardiovascular Surgery*, 126: 11-16.
Not in PICO
- Gerbaudo, V. H., Sugarbaker, D. J., Britz-Cunningham, S., Di Carli, M. F., Mauceri, C. & Treves, S. T. (2002) Assessment of malignant pleural mesothelioma with (18)F-FDG dual-head gamma-camera coincidence imaging: comparison with histopathology. *Journal of Nuclear Medicine*, 43: 1144-

1149.

Not in PICO

Hassman, P., Hassmanova, V. & Heger, L. (1990) Evaluating pulmonary findings in persons working with asbestos by repeated examination with computer tomography in the interval of three years. [Czech]. *Pracovni Lekarstvi*, 42: 208-210.

Not in PICO

Heelan, R. (2004) Staging and response to therapy of malignant pleural mesothelioma. [Review] [14 refs]. *Lung Cancer*, 45: Suppl-61.

Narrative review

Jimborean, G., Gabor, M. & Szilaj, D. (2001) [Considerations upon diagnosis and treatment of lung and pleural tumors in Mures county]. [Romanian]. *Pneumologia (Bucharest, Romania)*, 50: 148-153.

Not in PICO

Kao, S. C., Clarke, S., Vardy, J., Corte, P., Clarke, C. & van, Z. N. (2013) Patterns of care for malignant pleural mesothelioma patients compensated by the Dust Diseases Board in New South Wales, Australia. *Internal Medicine Journal*, 43: 402-410.

Not in PICO

Kent, M., Rice, D. & Flores, R. (2008) Diagnosis, staging, and surgical treatment of malignant pleural mesothelioma. *Current Treatment Options in Oncology*, 9: 158-170.

Narrative review

Knuuttila, A., Kivisaari, L., Kivisaari, A., Palomaki, M., Tervahartiala, P. & Mattson, K. (2001) Evaluation of pleural disease using MR and CT. With special reference to malignant pleural mesothelioma. *Acta Radiologica*, 42: 502-507.

Not in PICO

Kreel, L. (1981) Computed tomography in mesothelioma. *Seminars in Oncology*, 8: 302-312.

Narrative review

Laurent, F. & Tunon de, L. M. (1999) [Exposure to asbestos. Role of thoracic imagery in screening and follow-up]. [Review] [61 refs] [French]. *Revue des Maladies Respiratoires*, 16: t-202.

Narrative review

Laurent, F. & Tunon de, L. M. (1999) Asbestos exposure. Thoracic imagery as tool for early detection and follow-up. [French]. *Archives des Maladies Professionnelles et de Medecine du Travail*, 60: 192-201.

Narrative review

Letourneux, M., Galateau, F., Legendre, C., Leclerc, A., Beck, A., Launoy, G., Raffaelli, C. & Bazin, B. (1993) Malignant mesotheliomas diagnosed in Lower Normandy between 1980 and 1990. *European Respiratory Review*, 3: 87-88.

Not in PICO

Lone, N. I. & Antunes, G. (2007) Managing pleural disease in acute medicine (I): Pleural effusion. *Acute Medicine*, 6: 114-120.

Narrative review

Low, R. N. (2007) MR imaging of the peritoneal spread of malignancy. *Abdominal Imaging*, 32: 267-283.

Not in PICO

Makimoto, G., Fujiwara, K., Fujimoto, N., Yamadori, I., Sato, T. & Kishimoto, T. (2014) - Phrenic nerve paralysis as the initial presentation in pleural sarcomatoid mesothelioma. - *Case Reports Oncology*, 7: 389-392.

Not in PICO

Marciniak, S. J. (2008) Malignant mesothelioma in older people. *CME Journal Geriatric Medicine*, 10: 47-50.

Narrative review

- Massardier-Pilonchery, A. & Bergeret, A. (2011) [Follow-up after occupational asbestos exposure: terms and devices in foreign]. [Review] [French]. *Revue des Maladies Respiratoires*, 28: 556-564.
Not in PICO
- Meyer, M. & Krause, U. (1999) [Solitary fibrous tumors of the pleura]. [German]. *Chirurg*, 70: 949-952.
Not in PICO
- Minami, M., Kawauchi, N., Yoshikawa, K., Itai, Y., Kokubo, T., Iguchi, M., Masuyama, S., Takeuchi, K. & Iio, M. (1991) Malignancy associated with chronic empyema: Radiologic assessment. *Radiology*, 178: 417-423.
Not in PICO
- Moriyama, S., Tanahashi, M., Suzuki, E., Haneda, H., Yoshii, N., Yamada, T., Sasaki, H., Yano, M., Fujii, Y. & Niwa, H. (2012) Identification of pleural effusion with low levels of adenosine deaminase but without signs of acute inflammation or pleural thickening to diagnose early malignant pleural mesothelioma. [Japanese]. *Japanese Journal of Lung Cancer*, 52: 10-16.
Not in PICO
- Neumann, V., Loseke, S., Nowak, D., Herth, F. J. F. & Tannapfel, A. (2013) Malignant pleural mesothelioma: Incidence, etiology, diagnosis, treatment, and occupational health. [German, English]. *Deutsches Arzteblatt International*, 110: 319-326.
Narrative review
- O'Reilly, K. M. A., Mclaughlin, A. M., Beckett, W. S. & Sime, P. J. (2007) Asbestos-related lung disease. *American Family Physician*, 75: 683-688+690.
Narrative review
- Okonogi, N., Ebara, T., Ishikawa, H., Yoshida, D., Ueno, M., Maeno, T., Suga, T. & Nakano, T. (2012) A seven-year disease-free survivor of malignant pleural mesothelioma treated with hyperthermia and chemotherapy: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 6: 427.
Not in PICO
- Pass, H. I. & Carbone, M. (2009) Current status of screening for malignant pleural mesothelioma. [Review] [70 refs]. *Seminars in Thoracic & Cardiovascular Surgery*, 21: 97-104.
Not in PICO
- Patel, C. M., Sahdev, A. & Reznick, R. H. (2011) CT, MRI and PET imaging in peritoneal malignancy. *Cancer Imaging*, 11: 123-139.
Narrative review
- Patsios, D., Dong, G., Paul, N., Chung, T. B., Herman, S., Weisbrod, G., De, P. M. & Roberts, H. (2009) Screening for lung cancer and mesothelioma in workers with prior exposure to asbestos using low dose computed tomography (LDCT): The toronto experience so far. *Journal of Thoracic Imaging*, 24: w42.
Not in PICO
- Pickhardt, P. J. & Bhalla, S. (2005) Primary neoplasms of peritoneal and sub-peritoneal origin: CT findings. [Review] [20 refs]. *Radiographics*, 25: 983-995.
Narrative review
- Roach, H. D., Davies, G. J., Attanoos, R., Crane, M., Adams, H. & Phillips, S. (2002) Asbestos: when the dust settles an imaging review of asbestos-related disease. [Review] [60 refs]. *Radiographics*, 22: Spec-84.
Narrative review
- Roberts, H. C., Patsios, D. A., Paul, N. S., DePerrot, M., Teel, W., Bayanati, H., Shepherd, F. & Johnston, M. R. (2009) Screening for malignant pleural mesothelioma and lung cancer in individuals with a history of asbestos exposure. *Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer*, 4: 620-628.
Not in PICO

- Saguil, A., Wyrick, K. & Hallgren, J. (2014) Diagnostic approach to pleural effusion. *American Family Physician*, 90: 99-104.
Narrative review
- Saraya, T., Yokoyama, T., Ishii, H., Tanaka, Y., Tsujimoto, N., Ogawa, Y., Sohara, E., Nakajima, A., Inui, T., Sayuki, H., Fujiwara, M., Oka, T., Kawachi, R., Goya, T., Takizawa, H. & Goto, H. (2013) A case of malignant peritoneal mesothelioma revealed with limitation of PET-CT in the diagnosis of thoracic metastasis. *Journal of Thoracic Disease*, 5: E11-E16.
Not in PICO
- Saraya, T., Yokoyama, T., Ishii, H., Tanaka, Y., Tsujimoto, N., Ogawa, Y., Sohara, E., Nakajima, A., Inui, T., Sayuki, H., Fujiwara, M., Oka, T., Kawachi, R., Goya, T., Takizawa, H. & Goto, H. (2013) A case of malignant peritoneal mesothelioma revealed with limitation of PET-CT in the diagnosis of thoracic metastasis. *Journal of Thoracic Disease*, 5: E11-E16.
Not in PICO
- Shinkai, T., Imai, T., Sasaki, Y., Nishimoto, Y., Tsushima, J., Otsuji, H., Ohishi, H., Uchida, H., Tokuyama, T. & Narita, N. (1998) Clinical evaluation of malignant mesotheliomas with 67Ga (Ga), 201Tl (Tl) scintigraphy. [Japanese]. *Japanese Journal of Clinical Radiology*, 43: 55-63.
Not in PICO
- Spaggiari, L., Marulli, G., Bovolato, P., Alloisio, M., Pagan, V., Oliaro, A., Ratto, G. B., Facciolo, F., Sacco, R., Brambilla, D., Maisonneuve, P., Mucilli, F., Alessandrini, G., Leoncini, G., Ruffini, E., Fontana, P., Infante, M., Pariscenti, G. L., Casiraghi, M. & Rea, F. (2014) Extrapleural Pneumonectomy for Malignant Mesothelioma: An Italian Multicenter Retrospective Study. *Annals of Thoracic Surgery*, 97: 1859-1866.
Not in PICO
- Stigt, J. A., Oostdijk, A. H., Boers, J. E., Van Den Berg, J. W. K. & Groen, H. J. M. (2012) Percutaneous ultrasound-guided biopsies in the evaluation of thoracic tumours after PET-CT: A prospective diagnostic study. *Respiration*, 83: 45-52.
Not in PICO
- Sugarbaker, P. H. (2001) Review of a personal experience in the management of carcinomatosis and sarcomatosis. [Review] [24 refs]. *Japanese Journal of Clinical Oncology*, 31: 573-583.
Narrative review
- Suzuki, K. (2009) Diagnosis of malignant pleural mesothelioma--thoroscopic biopsy and tumor marker. [Japanese]. *Nippon Geka Gakkai zasshi*, 110: 333-337.
Narrative review
- Szubert, Z., Stankiewicz-Choroszuca, B., Wronska-Sobolewska, M., Siewierska, H., Kosinska, M., Borys, W., Jakubowski, J., Wrobel, R., Gazda, U., Kedzierska, B., Andrzejewski, M., Sova, M., Pawlowska-Koziell, H., Komorowska, E., Ksiązkiewicz, B., Sobala, W. & Szeszenia-Dabrowska, N. (2006) [Prophylactic examinations of workers formerly employed in asbestos processing plants: outcome of the Amiantus project in 2000-2004]. [Polish]. *Medycyna Pracy*, 57: 101-108.
Not in PICO
- Thomson, D., Hoyle, J. & Quennell, P. (2011) Malignant mesothelioma in the North West - Are diagnostic delays affecting survival? *Lung Cancer*, 71: S17-S18.
Not in PICO
- Tiitola, M., Kivisaari, L., Huuskonen, M. S., Mattson, K., Koskinen, H., Lehtola, H., Zitting, A. & Vehmas, T. (2002) Computed tomography screening for lung cancer in asbestos-exposed workers. *Lung Cancer*, 35: 17-22.
Not in PICO
- Tossavainen, A. (2000) International expert meeting on new advances in the radiology and screening of asbestos-related diseases. [Review] [15 refs]. *Scandinavian Journal of Work, Environment & Health*, 26: 449-454.
Not in PICO

Turlakow, A., Yeung, H. W., Salmon, A. S., Macapinlac, H. A. & Larson, S. M. (2003) Peritoneal carcinomatosis: role of (18)F-FDG PET. *Journal of Nuclear Medicine*, 44: 1407-1412.

Not in PICO

Ustun, H., Astarci, H. M., Sungu, N., Ozdemir, A. & Ekinci, C. (2011) Primary malignant deciduoid peritoneal mesothelioma: A report of the cytohistological and immunohistochemical appearances. *Diagnostic Cytopathology*, 39: 402-408.

Not in PICO

Vallerie, A. M., Lerner, J. P., Wright, J. D. & Baxi, L. V. (2009) Peritoneal inclusion cysts. *Obstetrical and Gynecological Survey*, 64: 321-334.

Not in PICO

Wentz, K. U., Irgartinger, G., Georgi, P., van, K. G., Kleckow, M. & Vollhaber, H. H. (1986) Malignant pleural mesothelioma. Value of 67Ga scintigraphy compared to computerized tomography. [German]. *RoFo : Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 145: 61-66.

Not in PICO

Wiggins, J. (2001) Statement on malignant mesothelioma in the United Kingdom. *Thorax*, 56: 250-265.

Not in PICO

Zhou, H., Tamura, T., Kusaka, Y., Suganuma, N., Subhannachart, P., Vijitsanguan, C., Noisiri, W., Hering, K. G., Akira, M., Itoh, H., Arakawa, H., Ishikawa, Y., Kumagai, S. & Kurumatani, N. (2012) Development of a guideline on reading CT images of malignant pleural mesothelioma and selection of the reference CT films. *European Journal of Radiology*, 81: 4203-4210.

Not in PICO

UPPER GASTRO-INTESTINAL TRACT CANCERS

OESOPHAGEAL

Review question:

What is the risk of oesophageal cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

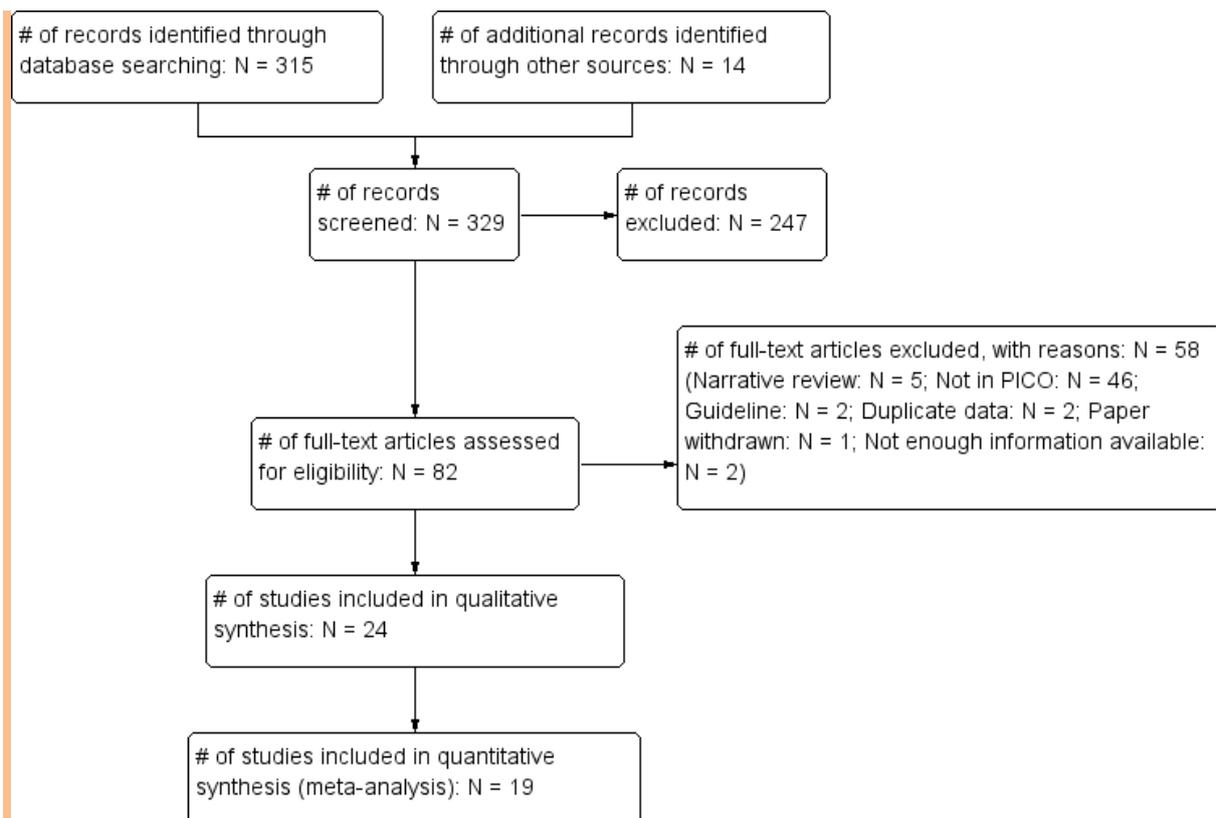
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	1593	122	08/05/2013
<i>Premedline</i>	All-2012	72	17	08/05/2013
<i>Embase</i>	All-2012	1831	182	09/05/2013
<i>Cochrane Library</i>	All-2012	483	5	10/05/2013
<i>Psychinfo</i>	All-2012	6	2	08/05/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	480	56	10/05/2013

Total References retrieved (after de-duplication): 294

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-20/08/2014	429	8	20/08/2014
<i>Premedline</i>	5/2013-20/08/2014	76	1	20/08/2014
<i>Embase</i>	5/2013-20/08/2014	458	11	20/08/2014
<i>Cochrane Library</i>	5/2013-20/08/2014	31	0	20/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	5/2013-20/08/2014	112	8	20/08/2014

Total References retrieved (after de-duplication): 21



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main bias and validity issues to note relates to patient selection and applicability with some studies employing non-consecutive patient sampling, e.g., case-control designs (which has been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection), and others being conducted in setting that may not directly translate to UK-based primary care. The other main issues of concern relates to missing data (and the concern that this may not be missing at random) and under specification of symptoms and reference standards, which makes it difficult to ascertain their applicability and/or validity. The evidence base is also limited by the fact that some of the positive predictive value estimates are based on low numbers of patients and a number of the studies do not provide different estimates for stomach nad oesophageal cancer, but only provide one estimate for these cancers combined.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Brignoli (1997)	?	+	-	+	?	+	+
Collins (2012)	+	+	+	+	+	+	+
Droogendijk (2011)	+	+	+	?	?	+	+
Duggan (2008)	?	+	+	+	+	+	+
Edenholm (1985)	?	+	+	-	?	+	+
Esfandyari (2002)	+	+	+	+	-	+	+
Farrus Palou (2000)	+	+	?	-	?	+	?
Hallissey (1990)	+	+	+	+	?	+	+
Hansen (1998)	+	+	+	?	?	+	+
Heikkinen (1995)	+	+	+	+	?	+	+
Hippisley-Cox (2011)	+	+	+	?	+	+	+
Jaskiewicz (1991)	?	+	+	+	?	?	+
Jones (2007)	+	+	+	+	+	+	+
Kagevi (1989)	+	+	+	+	?	+	+
Mahadeva (1998)	?	+	+	+	-	+	+
Meineche-Schmidt (2002)	+	+	+	+	?	+	+
Muris (1993)	+	+	+	+	?	?	+
Møllmann (1981)	+	+	?	-	?	+	+
Stapley (2013)	-	+	+	+	+	+	+
Stellon (1997)	+	+	+	+	+	+	+
Thomson (2003)	?	+	+	+	?	+	+
Tosetti (2010)	-	+	?	+	-	-	+
Vakil (2009)	?	+	+	+	+	+	+
Yates (2004)	+	+	+	+	?	+	+

High	Unclear	Low
------	---------	-----

Study results

Table 1: Oesophageal cancer: Meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)

Collins (2012) Hippisley-Cox (2011) Møllmann (1981)	Abdominal pain	All patients N = 3389979	0.23 (0.14-0.36)
Collins (2012) Droogendijk (2011) Farrus Palou (2000) Hippisley-Cox (2011) Stellon (1997) Yates (2004)	Anaemia	All patients N = 3375342	0.94 (0.54-1.64)
Brignoli (1997) Duggan (2008) Edenholm (1985) Hallissey (1990) Hansen (1998) Heikkinen (1995) Jaskiewicz (1991) Kagevi (1989) Meineche-Schmidt (2002) Thomson (2003) Vakil (2009)	Dyspepsia	All patients N = 11403	0.25 (0.13-0.5)
Collins (2012) Esfandyari (2002) Hippisley-Cox (2011) Jones (2007) at 6 months	Dysphagia	All patients N = 4136936	4.96 (3.49-7.01)
Collins (2012) Esfandyari (2002) Hippisley-Cox (2011) Jones (2007) at 3 years	Dysphagia	All patients N = 4136936	5.11 (3.7-7.01)

Please note that the data from Stapley (2013) are not included in these meta-analyses due to the case-control design of the study, and the data from Mahadeva (1998) is not included due to the limited and different age range of the population. These data are instead reported in the table below entitled "Additional results reported by the individual papers: Single symptoms". When the number of studies was < 3, the data were not meta-analysed, but presented for the individual studies instead.

Table 2: Oesophageal cancer: Individual positive predictive values from the meta-analyses

Study	Symptom(s)	Patient group	PPVs % (95% CI); prevalence
Collins (2012)	Abdominal pain	All patients	0.2 (0.2-0.2) 437/246998
Hippisley-Cox (2011)	Abdominal pain	All patients	0.3 (0.3-0.4) 309/91627
Møllmann (1981)	Upper abdominal pain > 2 weeks	All patients	0 (0-0.8) 0/577
Collins (2012)	Anaemia	All patients	0.6 (0.5-0.8) 116/18355
Droogendijk (2011)	Anaemia	All patients	0.35 (0.02-2.2) 1/287

Farrus Palou (2000)	Anaemia	All patients	0 (0-7.7) 0/58
Hippisley-Cox (2011)	Anaemia	All patients	1.1 (1-1.4) 119/10349
Stellon (1997)	Anaemia	All patients (N = 26)	0 (0-16) 0/26
Yates (2004)	Anaemia	All patients	2.55 (1.35-4.66) 11/431 has UGI cancer: No distinction made between the different kinds
Brignoli (1997)	Dyspepsia	All patients	0 (0-0.58) 0/828
Duggan (2008)	Dyspepsia	All patients	0.27 (0.05-1.1) 2/753
Edenholm (1985)	Persisten epigastric pain/ulcer-like dyspepsia	All patients who received an UGI endoscopy	0.61 (0.03-3.8) 1/165
Hallissey (1990)	Dyspepsia	All patients	0.58 (0.33-0.98) 15/2585
Hansen (1998)	Dyspepsia	All patients	1 (0.4-2.2) 6/612
Heikkinen (1995)	Dyspepsia	All patients	0.5 (0.09-2) 2/400
Jaskiewicz (1991)	Dyspepsia	All included patients	0 (0-0.8) 0/585
Kagevi (1989)	Dyspepsia	All included patients	0 (0-2.7) 0/172
Meineche-Schmidt (2002)	Dyspepsia	All patients	0.54 (0.25-1.1) 8/1491
Thomson (2003)	Dyspepsia	All patients	0.1 (0.01-0.6) 1/1040
Vakil (2009)	Dyspepsia without alarm symptoms	All included patients	0.1 (0.03-0.35) 3/2741
Collins (2012)	Dysphagia	All patients	4.2 (3.9-4.5) 810/19237
Esfandyari (2002)	Dysphagia	All patients	6 (2.5-13.1) 6/100
Hippisley-Cox (2011)	Dysphagia	All patients	7.8 (7.1-8.5) 434/5590
Jones (2007)	Dysphagia	All patients at 6 months	3.47 (3-4) 208/5999
Jones (2007)	Dysphagia	All patients at 3 years	3.85 (3.38-4.38) 231/5999

Table 3: Oesophageal cancer: Additional results reported by the individual papers: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Tosetti (2010)	Upper gastro-intestinal symptoms without	All patients	0.36 (0.02-2.3) 1/275

	alarming features		
Muris (1993)	Non-acute abdominal complaints	All patients	0 (0-0.8) 0/578
Collins (2012)	Abdominal pain	Women	0.1 (0.1-0.1) 139/144266
		Men	0.3 (0.3-0.3) 298/102732
Stapley (2013)	Abdominal pain	Patients ≥ 55 years	0.3 (0.2-0.3)
Stapley (2013)	Epigastric pain	Patients ≥ 55 years	0.9 (0.8-1)
Collins (2012)	Anaemia	Women	0.4 (0.3-0.5) 49/13792
		Men	1.5 (1.1-1.9) 67/4563
Møllmann (1981)	Anaemia	Males	0 (0-44) 0/7
Stapley (2013)	Low haemoglobin	Patients ≥ 55 years	0.2 (0.2-109)
Stapley (2013)	Dyspepsia	Patients ≥ 55 years	0.7 (0.6-0.7)
Stapley (2013)	Dyspepsia (reported ≥ twice)	Patients ≥ 55 years	1.2 (1-1.5)
Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 45 years old	0.18 (0.03-0.71) 2/1127
		Patients ≥ 50 years old	0.24 (0.04-1) 2/829
		Patients ≥ 55 years old	0.18 (0.01-1.16) 1/554
		Patients ≥ 60 years old	0.3 (0.02-2) 1/323
Hansen (1998)	Ulcer-like dyspepsia	All patients	0.6 (0.03-3.9) 1/161
Hansen (1998)	Dysmotility-like dyspepsia	All patients	0 (0-2.9) 0/163
Hansen (1998)	Reflux-like dyspepsia	All patients	1.16 (0.2-4.6) 2/173
Hansen (1998)	Unclassifiable dyspepsia	All patients	0.9 (0.05-5.8) 1/107
Mahadeva (2008)	Dyspepsia	All patients (they were aged 18-45 years)	0 (0-1.1) 0/432
Collins (2012)	Dysphagia	Women	2.5 (2.2-2.8) 262/10391
		Men	6.2 (5.7-6.7) 548/8846
Jones	Dysphagia	Men (all ages) at 6 months	5.3 (4.4-6.2) 138/2628
		Men (all ages) at 3 years	5.7 (4.9-6.7) 150/2628
		Men < 45 years at 3 years	0.21 (0-1.15) 1/482
		Men 45-54 years at 3 years	4.03 (2.36-6.37) 17/422
		Men 55-64 years at 3	5.98 (4.1-8.39)

		years	31/518
		Men 65-74 years at 3 years	9.03 (6.82-11.7) 52/576
		Men 75-84 years at 3 years	7.14 (5-9.84) 34/476
		Men ≥ 85 years at 3 years	9.74 (5.55-15.6) 15/154
Jones	Dysphagia	Women (all ages) at 6 months	2.1 (1.6-2.6) 70/3371
		Women (all ages) at 3 years	2.4 (1.9-3) 81/3371
		Women < 45 years at 3 years	0.16 (0-0.86) 1/642
		Women 45-54 years at 3 years	0.58 (0.12-1.68) 3/520
		Women 55-64 years at 3 years	1.92 (0.92-3.49) 10/522
		Women 65-74 years at 3 years	3.79 (2.47-5.55) 25/659
		Women 75-84 years at 3 years	4.03 (2.65-5.85) 26/645
		Women ≥ 85 years at 3 years	4.18 (2.41-6.7) 16/383
Stapley (2013)	Dysphagia	Patients ≥ 55 years	4.8 (4.3-5.9)
Stapley (2013)	Dysphagia (reported ≥ twice)	Patients ≥ 55 years	5.5 (4.2-7.9)
Collins (2012)	Appetite loss	All patients	0.6 (0.5-0.9) 37/5838
		Women	0.4 (0.2-0.7) 12/3317
		Men	1 (0.7-1.5) 25/2521
Hippisley-Cox (2011)	Appetite loss	All patients	1.1 (0.8-1.5) 35/3391
Møllmann (1981)	Weight loss and/or anorexia	All patients	0 (0-8.9) 0/50
Collins (2012)	Weight loss	All patients	0.8 (0.7-0.9) 218/28403
		Women	0.6 (0.4-0.7) 86/15465
		Men	1 (0.9-1.2) 132/12938
Hippisley-Cox (2011)	Weight loss	All patients	1.2 (1-1.4) 107/9170
Stapley (2013)	Weight loss	Patients ≥ 55 years	0.9 (0.7-1)
Collins (2012)	Haematemesis	All patients	1 (0.8-1.2) 110/10792
		Women	0.5 (0.3-0.7) 22/4630
		Men	1.4 (1.2-1.8)

			88/6162
Hippisley-Cox (2011)	Haematemesis	All patients	2.3 (1.9-2.7) 101/4477
Stapley (2013)	Constipation	Patients ≥ 55 years	0.2 (0.2-0.2)
Stapley (2013)	Chest pain	Patients ≥ 55 years	0.2 (0.2-0.2)
Stapley (2013)	Reflux	Patients ≥ 55 years	0.6 (0.6-0.7)
Møllmann (1981)	Nausea and/or vomiting > 2 weeks	All patients	0 (0-12.3) 0/35
Stapley (2013)	Nausea/vomiting	Patients ≥ 55 years	0.6 (0.5-0.7)
Stapley (2013)	Nausea/vomiting reported ≥ twice	Patients ≥ 55 years	1 (0.8-1.2)
Stapley (2013)	Raised platelets	Patients ≥ 55 years	0.5 (0.4-0.5)
Stapley (2013) reported that all PPVs for symptom combinations in patients < 55 years were < 1%, and that the highest PPV in this age group was for dysphagia, 0.8 (0.4-1.5)%			
Møllmann (1981)	Gastrointestinal bleeding	All patients	0 (0-32) 0/11

Please note:

- The calculations of the positive predictive values differ between all the other included studies using (TP)/(TP+FP) and Stapley (2013) using other statistics due to the case-control design of these studies. NR = Not reported.

Table 4: Oesophageal cancer: Additional results reported by the individual papers: Symptom combinations

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Meineche-Schmidt (2002)	Dyspepsia and jaundice	All patients	0 (0-48.32) 0/6
Meineche-Schmidt (2002)	Dyspepsia and black stools	All patients	0.91 (0.05-5.69) 1/110
Meineche-Schmidt (2002)	Dyspepsia and bloody stools	All patients	0.76 (0.04-4.81) 1/131
Stapley (2013)	Dysphagia and chest pain	Patients ≥ 55 years	5.8 (3.5-10.8)
Stapley (2013)	Dysphagia and loss of weight	Patients ≥ 55 years	9.2 (4.4-22.7)
Stapley (2013)	Dysphagia and abdominal pain	Patients ≥ 55 years	6.5 (3.5-13.5)
Stapley (2013)	Dysphagia and epigastric pain	Patients ≥ 55 years	9.3 (NR)
Stapley (2013)	Dysphagia and reflux	Patients ≥ 55 years	5 (3.3-8.4)
Stapley (2013)	Dysphagia and low haemoglobin	Patients ≥ 55 years	4.6 (3.4-6.6)
Stapley (2013)	Dysphagia and nausea/vomiting	Patients ≥ 55 years	7.3 (4.4-13.9)
Meineche-Schmidt (2002)	Dyspepsia and dysphagia	All patients	1.4 (0.04-4.36) 3/215
Stapley (2013)	Dysphagia and dyspepsia	Patients ≥ 55 years	9.8 (5.7-20.2)

Stapley (2013)	Dysphagia and raised platelets	Patients ≥ 55 years	6.1 (3.2-13.2)
Stapley (2013)	Dyspepsia and chest pain	Patients ≥ 55 years	0.7 (0.5-0.9)
Stapley (2013)	Dyspepsia and abdominal pain	Patients ≥ 55 years	1 (0.7-1.3)
Stapley (2013)	Dyspepsia and epigastric pain	Patients ≥ 55 years	1.4 (1-2)
Stapley (2013)	Dyspepsia and nausea/vomiting	Patients ≥ 55 years	1.3 (0.9-1.8)
Stapley (2013)	Dyspepsia and reflux	Patients ≥ 55 years	0.9 (0.7-1.2)
Meineche-Schmidt (2002)	Dyspepsia and weight loss	All patients	1.37 (0.35-4.28) 3/219
Stapley (2013)	Dyspepsia and loss of weight	Patients ≥ 55 years	2.1 (1.3-3.5)
Stapley (2013)	Dyspepsia and raised platelets	Patients ≥ 55 years	1.4 (0.9-2.2)
Meineche-Schmidt (2002)	Dyspepsia and anaemia	All patients	0 (0-11.71) 0/37
Stapley (2013)	Dyspepsia and low haemoglobin	Patients ≥ 55 years	1 (0.8-1.3)
Stapley (2013)	Constipation and chest pain	Patients ≥ 55 years	0.4 (0.3-0.5)
Stapley (2013)	Constipation and loss of weight	Patients ≥ 55 years	1.1 (0.8-1.7)
Stapley (2013)	Constipation and abdominal pain	Patients ≥ 55 years	0.4 (0.3-0.5)
Stapley (2013)	Constipation and epigastric pain	Patients ≥ 55 years	1.4 (0.8-2.3)
Stapley (2013)	Constipation and reflux	Patients ≥ 55 years	0.7 (0.5-1.1)
Stapley (2013)	Constipation and low haemoglobin	Patients ≥ 55 years	0.4 (0.4-0.5)
Stapley (2013)	Constipation and nausea/vomiting	Patients ≥ 55 years	0.6 (0.4-0.7)
Stapley (2013)	Constipation and dyspepsia	Patients ≥ 55 years	0.8 (0.6-1.1)
Stapley (2013)	Constipation and dysphagia	Patients ≥ 55 years	4.2 (2.7-7.2)
Stapley (2013)	Constipation and raised platelets	Patients ≥ 55 years	0.9 (0.6-1.4)
Stapley (2013)	Abdominal pain and chest pain	Patients ≥ 55 years	0.3 (0.3-0.4)
Stapley (2013)	Abdominal pain and epigastric pain	Patients ≥ 55 years	0.9 (0.7-1.2)
Stapley (2013)	Abdominal pain and reflux	Patients ≥ 55 years	0.6 (0.5-0.9)
Stapley (2013)	Abdominal pain and weight loss	Patients ≥ 55 years	1.4 (0.9-2.2)
Møllmann (1981)	Upper abdominal pain > 2 weeks and nausea	All patients	0 (0-1.6) 0/293

	and/or vomiting > 2 weeks		
Stapley (2013)	Abdominal pain and nausea/vomiting	Patients ≥ 55 years	0.7 (0.5-0.9)
Stapley (2013)	Abdominal pain and low haemoglobin	Patients ≥ 55 years	0.5 (0.4-0.6)
Stapley (2013)	Abdominal pain and raised platelets	Patients ≥ 55 years	0.8 (0.6-1.1)
Møllmann (1981)	Upper abdominal pain > 2 weeks and gastrointestinal bleeding	All patients	0 (0-21) 0/19
Møllmann (1981)	Upper abdominal pain > 2 weeks and nausea/vomiting > 2 weeks and gastrointestinal bleeding	All patients	0 (0-44) 0/7
Møllmann (1981)	Upper abdominal pain > 2 weeks and nausea/vomiting > 2 weeks and weight loss/anorexia	All patients	0 (0-4) 0/116
Møllmann (1981)	Upper abdominal pain > 2 weeks and weight loss/anorexia and gastrointestinal bleeding	All patients	0 (0-20) 0/5
Møllmann (1981)	Upper abdominal pain > 2 weeks and weight loss/anorexia	All patients	0 (0-4.7) 0/98
Stapley (2013)	Chest pain and epigastric pain	Patients ≥ 55 years	0.9 (0.6-1.4)
Stapley (2013)	Chest pain and reflux	Patients ≥ 55 years	0.6 (0.5-0.9)
Stapley (2013)	Chest pain and weight loss	Patients ≥ 55 years	1.1 (0.7-1.8)
Stapley (2013)	Chest pain and nausea/vomiting	Patients ≥ 55 years	0.6 (0.4-0.8)
Stapley (2013)	Chest pain and low haemoglobin	Patients ≥ 55 years	0.3 (0.3-0.4)
Stapley (2013)	Chest pain and raised platelets	Patients ≥ 55 years	0.8 (0.6-1.2)
Stapley (2013)	Epigastric pain and reflux	Patients ≥ 55 years	1.5 (1-2.4)
Stapley (2013)	Epigastric pain and weight loss	Patients ≥ 55 years	4.2 (1.8-11)
Stapley (2013)	Epigastric pain and low haemoglobin	Patients ≥ 55 years	1.6 (1.1-2.2)
Stapley (2013)	Reflux and loss of weight	Patients ≥ 55 years	3.1 (1.5-6.7)
Stapley (2013)	Reflux and low haemoglobin	Patients ≥ 55 years	0.9 (0.7-1.2)
Stapley (2013)	Weight loss and low haemoglobin	Patients ≥ 55 years	1 (0.8-1.3)
Møllmann (1981)	Weight loss/anorexia	All patients	0 (0-80)

	and gastrointestinal bleeding		0/2
Møllmann (1981)	Weight loss/anorexia and gastrointestinal bleeding and nausea/vomiting > 2 week	All patients	0 (0-80) 0/2
Møllmann (1981)	Weight loss/anorexia and nausea/vomiting > 2 week	All patients	0 (0-16.6) 0/25
Stapley (2013)	Nausea/vomiting and weight loss	Patients ≥ 55 years	2.8 (1.7-4.8)
Stapley (2013)	Nausea/vomiting and epigastric pain	Patients ≥ 55 years	1.3 (0.9-2)
Stapley (2013)	Nausea/vomiting and reflux	Patients ≥ 55 years	2.3 (1.5-3.5)
Stapley (2013)	Nausea/vomiting and low haemoglobin	Patients ≥ 55 years	0.9 (0.7-1.1)
Stapley (2013)	Reflux and raised platelets	Patients ≥ 55 years	1.6 (0.9-2.9)
Stapley (2013)	Weight loss and raised platelets	Patients ≥ 55 years	1.8 (1.1-3)
Stapley (2013)	Nausea/vomiting and raised platelets	Patients ≥ 55 years	1.4 (1-2.1)
Stapley (2013)	Epigastric pain and raised platelets	Patients ≥ 55 years	1.9 (1-3.8)
Stapley (2013)	Low haemoglobin and raised platelets	Patients ≥ 55 years	0.6 (0.6-0.7)
Møllmann (1981)	Any of the inclusion symptoms + previous dyspepsia	All patients	0 (0-0.62) 0/773
Møllmann (1981)	Any of the inclusion symptoms + no previous dyspepsia	All patients	0 (0-0.91) 0/524
Møllmann (1981)	Any of the inclusion symptoms + unchanged previous dyspepsia	All patients	0 (0-1.2) 0/407
Møllmann (1981)	Any of the inclusion symptoms + no previous or changed dyspepsia	All patients	0 (0-0.54) 0/890
Møllmann (1981)	Any of the inclusion symptoms + pain provoked by meals	All patients	0 (0-1.8) 0/257
Møllmann (1981)	Any of the inclusion symptoms + no pain provoked by meals	All patients	0 (0-0.52) 0/924
Møllmann (1981)	Any of the inclusion symptoms + relief of pain by meals	All patients	0 (0-0.7) 0/488
Møllmann (1981)	Any of the inclusion symptoms + no pain	All patients	0 (0-2.8) 0/687

	relief by meals		
Møllmann (1981)	Any of the inclusion symptoms + irritable bowel syndrome	All patients	0 (0-2.8) 0/167
Møllmann (1981)	Any of the inclusion symptoms + no irritable bowel syndrome	All patients	0 (0-0.42) 0/1129

Please note:

- The calculations of the positive predictive values differ between the all the other included studies using (TP)/(TP+FP) and Stapley (2013) using other statistics due to the case-control design of these studies. NR = not reported.

Evidence statement(s):

Abdominal pain (4 studies, N = 3416339) presenting in a primary care setting is associated with an overall positive predictive value of up to 0.3% for oesophageal cancer. The studies were associated with 0-3 bias or applicability concerns (see also Tables 1-3).

Anaemia (8 studies, N = 3417170) presenting in a primary care setting is associated with an overall positive predictive value of up to 0.94% for oesophageal cancer. The studies were associated with 0-4 bias or applicability concern (see also Tables 1-3).

Dyspepsia (13 studies, N = 52183) presenting in a primary care setting is associated with an overall positive predictive value of up to 1.2% for oesophageal cancer. The studies were associated with 1-3 bias or applicability concerns (see also Tables 1-3).

Dysphagia (5 studies, N = 4177284) presenting in a primary care setting is associated with an overall positive predictive value of up to 5.5% for oesophageal cancer. All the studies were associated with 0-1 bias or applicability concerns (see also Tables 1-3).

Other single symptoms (6 studies, N = 3417192) presenting in a primary care setting are associated with an overall positive predictive values for oesophageal cancer up to 2.3% (for haematemesis). The studies were associated with 0-4 bias or applicability concerns (see also Table 3).

Two or more symptom presenting in combination (3 studies, N = 43319) in a primary care setting are associated with overall positive predictive values for oesophageal cancer up to to 9.8% (for dysphagia and dyspepsia). The studies were associated with 1-3 bias or applicability concerns (see also Table 4).

Evidence tables

Brignoli (1997)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from Switzerland.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	

Patient characteristics and setting	N = 828; 329 men, 499 women; mean (SD) age = 41-42 (15-16) years. <u>Inclusion criteria</u> : "Adult patients with epigastric complaints were admitted to the multicentre [omega]-project if their symptoms persisted for over 1 month and their clinical history and appearance did not suggest an organic disorder (i.e. absence of alarm features, such as gastrointestinal blood loss, palpable tumour mass, massive weight loss, etc.). The studies were conducted by general practitioners acting as primary care physicians." <u>Exclusion criteria</u> : None listed <u>Clinical setting</u> : Primary care, Switzerland	
Are there concerns that the included patients and setting do not match the review question?		Unclear concern
INDEX TEST		
A. Risk of bias		
Index test	Epigastric complaints (dyspepsia)	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Endoscopy and 84-day follow up.	
Is the reference standard likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients are accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	3 patients had gastric cancer, 0 patients had oesophageal cancer, and 2 patients had cancer outside the digestive tract.	

Collins (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2135540 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Dysphagia (N = 19237; 8846 men, 10391 women), abdominal pain (N = 246998; 102732 men, 144266 women), appetite loss (N = 5838; 2521 men, 3317 women), weight loss (N = 28403; 12938 men, 15465 women), haematemesis (N = 10792; 6162 men, 4630 women), anaemia (N = 18355; 4563 men, 13792 women).</p> <p><u>Incident cases of gastro-oesophageal cancer during the 2-year follow up period:</u> N = 1766 (1184 men, 582 women; 32% gastric cancer, 68% oesophageal cancer).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of gastro-oesophageal cancer, registration with the general practice < 12 months, or with invalid dates.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Haematemesis, dysphagia, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	The study did not distinguish between gastric and oesophageal cancer

Droogendijk (2011)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective peripheral hospital laboratory database study serving 265 GPs in Dordrecht (Holland).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 287; 129 men, 158 women; median (range) age = 70 (19-87) years. <u>Inclusion criteria:</u> All women aged > 50 years and all men aged ≥ 18 years who between January 2004 and December 2005 were diagnosed with iron-deficiency anaemia (haemoglobin < 13.7 g/dl in men and < 12.1 g/dl in women, and a serum ferritin level < 25 µg/l for men and < 20 µg/l for women). <u>Exclusion criteria:</u> Patients with a known history of iron-deficiency anaemia in the previous 2 years, a history of gastrointestinal malignancy or congenital haemoglobinopathy. <u>Clinical setting:</u> GPs in Holland
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	New onset iron-deficiency anaemia (haemoglobin < 13.7 g/dl in men and < 12.1 g/dl in women, and a serum ferritin level < 25 µg/l for men and < 20 µg/l for women).
Were the index test results interpreted without knowledge	Yes

of the results of the reference standard?	
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy and 12-month follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	It is unclear if all patients are accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Unclear
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk
NOTES	In addition to the 24 patients with colorectal cancer, 3 patients had gastric cancer, 1 patient had oesophageal cancer and 1 patient had locally invasive endometrial cancer.

Duggan (2008)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 43 GP practices in the UK.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 762; 411 men, 351 women; mean (range) age = 42 (18-73) years. <u>Inclusion criteria:</u> Patients aged 18-70 with dyspepsia thought by the GP to arise from the upper GI tract and of sufficient severity to justify empirical treatment with an H ₂ antagonist or PPI. <u>Exclusion criteria:</u> Patients thought to be unfit for investigation, with alarm

	<p>symptoms suggestive of malignancy (dysphagia, weight loss > 5 g, anaemia, haematemesis, melaena or jaundice), previous radiological or endoscopic diagnosis of peptic ulcer disease or reflux oesophagitis, investigation for dyspepsia in the previous 5 years with either procedure or symptom onset within 6 months of commencement of NSAID therapy, previous H. pylori eradication therapy or more than 3 prescriptions for acid suppression therapy in the previous 6 months.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy and 1-2-year follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	At 12-month follow up GP data were available for 753/762.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	2 patients had gastric cancer, 2 patients had oesophageal cancer (the authors report that these patients should not have been included as they had a history of dysphagia).
Edenholm (1985)	
PATIENT SELECTION	

A. risk of bias	
Patient sampling	Prospective patient series from the Distric General Clinic in Huskvarna, Sweden.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 187; 96 men, 91 women; mean/median (range) age = 44 (17-80) years. <u>Inclusion criteria:</u> Patients who between November 1982 and June 1984 called on the clinic because of abdominal pain and who were diagnosed by the general practitioner as having ulcer-like dyspepsia. The criterion used was persistent epigastric pain. Most patients also had additional symptoms such as acid regurgitation, nausea, belching or vomiting. <u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> GPs in Sweden
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Ulcer-like dyspepsia. The criterion used was persistent epigastric pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	UGI endoscopy
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	20/187 patients declined endoscopy and it was unsuccessful in a further 2 patients. Thus the PPV is likely to be an over-estimate, calculated as 2/165.
Was there an appropriate interval between index test and	Yes probably

reference standard?	
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	There were a total of 3 cancers confirmed in the 165 patients who received UGI endoscopy: 1 oesophageal cancer, 1 stomach cancer, and 1 cancer of the duodenum, the latter of which was included with the stomach cancer
Esfandiyari (2002)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective/retrospective? patient series from USA
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 100; 49 men, 51 women; mean (SE) age = 64 (2) years. <u>Inclusion criteria:</u> Patients with new onset dysphagia without a prior work up who were evaluated at the Cleveland Clinic Foundation outpatient clinic by their primary care physician. <u>Exclusion criteria:</u> Neurological disease, oropharyngeal dysphagia or previous gastric or oesophageal surgery, and patients without a final diagnosis explaining their dysphagia. <u>Clinical setting:</u> Primary care outpatient clinic, USA.
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	New onset dysphagia
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Completed clinical and diagnostic testing after an initial barium swallow/upper GI endoscopy.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its	Low risk

interpretation have introduced bias?	
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	6 patients had malignancy, but the type of malignancy was not further specified

Farrus Palou (2000)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective consecutive patient series from urban general practice covering a population of 24000.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 87 of whom the data from 29 were unavailable as no etiological diagnosis was found (due to patient refusal of further investigation [?; 8], lost to follow up [7], patient deterioration rendering them unsuitable for further investigation [14]); of the remaining 58 patients there were 14 males, 44 females; mean? (SD?) age = 54.26 (19.95) years.</p> <p><u>Inclusion criteria:</u> Patients aged > 14 years who attended the health centre between 1 October 1995 and 31 September 1996 who were found to have new onset (previously unknown) anaemia (haemoglobin < 13 g/dl for men and 12 g/dl for women).</p> <p><u>Exclusion criteria:</u> Pregnant women.</p> <p><u>Clinical setting:</u> Spanish GP</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Anaemia (haemoglobin < 13 g/dl for men and 12 g/dl for women)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up I think	
Is the reference standard likely to correctly classify the target condition?		Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?		No
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Unclear concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	No diagnosis available for 29/87 patients	
Was there an appropriate interval between index test and reference standard?		Unclear
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		No
Could the patient flow have introduced bias?		High risk
NOTES	This paper is published in Spanish. One patient had gastric cancer, 2 patients had colon cancer.	
Hallissey (1990)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Propective consecutive patient series from a group of 10 general practices in England.	
Was a consecutive or random sample of patients enrolled?		Yes
Was a case-control design avoided?		Yes
Did the study avoid inappropriate exclusions?		Yes
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia.</p> <p><u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia</p> <p><u>Exclusion criteria:</u> None listed.</p> <p><u>Clinical setting:</u> Primary care, England.</p>	
Are there concerns that the included patients and setting		Unclear concern

do not match the review question?		
INDEX TEST		
A. Risk of bias		
Index test	Dyspepsia of any degree	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	2659 patients were seen and 2585 attended for investigation	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), carcinomatosis of unknown primary (7).	
Hansen (1998)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series from general an open-access endoscopy clinic in Denmark.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	

Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 612 from 66 GPs; 288 males / 324 females; mean age (SD) = 47 (16.8) years. <u>Inclusion criteria:</u> "All general practitioners (n = 108) in the city of Odense (population, 170,000) were invited to participate in the study. GPs were asked to refer all patients who consulted them with dyspepsia, regardless of the severity of the symptoms. To obtain compliance with this request the participating GPs were sent numerous reminders. Because of a limited endoscopy capacity not all GPs took part in the study at the same time." Study period was 11 March 1991-27 March 1992. <u>Exclusion criteria:</u> Aged < 18 years, signs of UGI bleeding, abdominal emergency, jaundice, previous surgery in the UGI tract except for closure of an ulcer, supposed acute bacterial or viral infection, pregnancy, or endoscopy contraindicated. <u>Clinical setting:</u> GPs in Denmark
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Epigastric or retrosternal pain or discomfort, with or without heartburn, nausea, vomiting, and any other symptom considered to be referable to the proximal alimentary tract.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy within 1 week of referral and follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	56 eligible patients declined participation. These patients were older than

	the study group (mean age = 52 years versus 47 years) and they were characterised by a shorter dyspepsia history (median duration = 1 month, range = 4 days to 35 years versus 2 months, range = 4 days to 14 years). Fewer of the non-participating patients had had a previous endoscopy or UGI radiography (22% versus 43%, but identical proportions of the patients had an ulcer history (11% versus 14%).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	There were a total of 4 cancers histologically confirmed in the study. No subclassification of the cancers reported. Follow up of the 364 patients with normal endoscopy revealed missing date in 5% of the cases and 1 lymphoma and 1 rectal carcinoma. These 6 cancers (NOS) are included in the overall PPV for dyspepsia.

Heikkinen (1995)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Consecutive patient series from 11 GPs (from 3 rural health centres) and from the catchment area of 6 physicians in the health centre of an urban area (population [individuals > 14 years old] of study area = 24600) in Finland.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 400; 152 males, 248 females; 77% were > 44 years. <u>Inclusion criteria:</u> Consecutive patients who consulted their GP from January 11th 1993 to January 12 th 1994 for dyspepsia (defined as upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptoms considered to be referable to the proximal alimentary tract). <u>Exclusion criteria:</u> Patients with symptoms of an acute condition within the abdomen or who had had an upper intestinal endoscopy performed within the last 3 months or aged < 15 years <u>Clinical setting:</u> Primary care, Finland.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia (defined as upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptoms considered to be referable to the proximal alimentary tract).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes

Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy, upper abdominal ultrasound, more detailed interview, blood count, serum screening (creatinine, alkaline phosphatase, alanine aminotransferase, amylase, and C-reactive protein), lactose intolerance test, and follow up of ≥ 1 month.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 9 had cancer: 0 colorectal, 2 oesophageal and 7 stomach (of which 3 were lymphomas of the MALT type (Mucosa-associated lymphoid tissue)).
Hippisley-Cox (2011)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	A total of 1238971 patients were identified from 189 practices (621478 males, 617493 females), mean (SD) age = 50.1 (15) years, mean (SD) Townsend score = -0.2 (3.6). Symptoms: Current dysphagia (N = 8165), current haematemesis (N = 7119), current

	<p>abdominal pain (N = 126161), current appetite loss (N = 6133), current weight loss (N = 5377), tiredness in the last year (N = 14119), haemoglobin recorded in the last year (N = 12638, haemoglobin < 11 g/dl in the last year (N = 218862).</p> <p><u>Incident cases of gastro-oesophageal cancer during the 2-year follow up period:</u> N = 1343 (776 oesophageal and 567 gastric).</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000); 12 months after the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of gastro-oesophageal cancer at baseline, and patients with a recorded ‘red-flag’ symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	‘Red-flag’ symptoms: Incident dysphagia, haematemesis, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	A total of 1342329 patients were initially identified of whom 103358 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of gastro-oesophageal cancer (N = 538), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 31973), leaving 1238971 patients. However, data is presented for 963040/1238971 patients for all symptoms. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Could the patient flow have introduced bias?	Unclear risk	
NOTES	Results not presented separately for gastric and oesophageal cancer	
Jaskiewicz (1991)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Patient series from a program aimed at screening patients with chronic gastric complaints for gastric carcinoma in the South and North-Western Cape Province of South Africa.	
Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?	Unclear risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 585, 355 males, 230 females; mean (range) age males = 45.1 (19-87) years, mean (range) age females = 47.2 (19-87) years.</p> <p><u>Inclusion criteria</u>: "participants who were treated for dyspeptic complaints such as epigastric pain, heartburn, post-prandial pain and bloating, vomiting or nausea with a duration of at least 3 months. Patients represented various areas in the south-and north-western Cape province including Namaqualand, and formed part of a programme aimed at screening patients with chronic gastric complaints for gastric carcinoma."</p> <p><u>Exclusion criteria</u>: None listed</p> <p><u>Clinical setting</u>: Unclear, South Africa.</p>	
Are there concerns that the included patients and setting do not match the review question?	Unclear concern	
INDEX TEST		
A. Risk of bias		
Index test	Unspecified dyspepsia (dyspeptic complaints such as epigastric pain, heartburn, post-prandial pain and bloating, vomiting or nausea with a duration of at least 3 months).	

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 16 had gastric cancer. No oesophageal cancers reported
Jones (2007)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective consecutive patient series using patients in the UK's General Practice Research Database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	A total of 923605 patients were identified, of whom 762325 were aged ≥ 15 years. Number of first occurrences in patients with no previous diagnosis of cancer: Haematuria: N = 11138, mean (SD) age at first symptom = 58.5 (18.9) years. Patients excluded due to incomplete dates for their first symptom: N = 30. Sex (of final sample): 6385 males, 4723 females.

	<p><u>Haemoptysis</u>: N = 4822, mean (SD) age at first symptom = 61.6 (18) years. Patients excluded due to incomplete dates for their first symptom: N = 10. Sex (of final sample): 2930 males, 1882 females.</p> <p><u>Dysphagia</u>: N = 6003, mean (SD) age at first symptom = 54.5 (19.4) years. Patients excluded due to incomplete dates for their first symptom: N = 4. Sex (of final sample): 2628 males, 3371 females.</p> <p><u>Rectal bleeding</u>: N = 15314, mean (SD) age at first symptom = 52.5 (18.8) years. Patients excluded due to incomplete dates for their first symptom: N = 25. Sex (of final sample): 7523 males, 7766 females.</p> <p><u>Inclusion criteria</u>: All patients from 128 general practices that provided data of a sufficient standard from 1 January 1994 to 31 December 2000 and which provided exclusively Read coded data, who were aged between 15 and 100 years, whose first ever recorded occurrence of each alarm symptom (haematuria, haemoptysis, dysphagia, or rectal bleeding) was after 31 December 1994 and who had not previously been diagnosed as having any cancer.</p> <p><u>Exclusion criteria</u>: Patients whose date of first symptom or first relevant diagnosis of cancer was before 1 January 1995 and patients with a diagnosis of any other cancer than the ones of interest before the date of the first recorded symptom or before the index cancer diagnosis date if the related symptom was not recorded.</p> <p><u>Clinical setting</u>: Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Identification of all patients who ever had symptoms recorded for haematuria, haemoptysis, dysphagia, or rectal bleeding.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	<p>Cancer code in the UK's General Practice Research Database:</p> <p><u>Haematuria</u>: Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs.</p> <p><u>Haemoptysis</u>: Respiratory tract neoplasms.</p> <p><u>Dysphagia</u>: Oesophageal neoplasms.</p> <p><u>Rectal bleeding</u>: Colorectal neoplasms.</p>
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)

Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	<p>Diagnoses of cancer were most often made in the first three months after the onset of alarm symptoms; very few diagnoses of cancer were made later than three years after symptom onset. In the 4th and 5th years of study, the small number of observed occurrences of cancer was similar to the number expected from background incidence rates.</p> <p>Secondary analyses evaluating whether the incidence of neoplasms other than those prespecified was increased after the occurrence of alarm symptoms showed for:</p> <p><u>Haematuria</u>: Inclusion of cancers of the reproductive organs yielded 21 additional cancers in women and 158 cancers in men, mostly cancers of the prostate. Inclusion of these cancers in the analysis would give a positive predictive value of 3.9% in women and 9.9% in men.</p> <p><u>Dysphagia</u>: Inclusion of gastric cancers yielded 17 additional cancer diagnoses in women and 30 in men. Inclusion of these cancers gave positive predictive values of 5.2% in women [reported in the paper, however, the numbers reported do not match up and I think the PPV is instead 2.91%; 98/3371] and 6.9% in men.</p> <p><i>Estimates based on the pre-specified cancers may be thus conservative for these symptoms.</i></p> <p><u>Haemoptysis</u>: Extension of the diagnostic criteria yielded 6 additional cancers.</p> <p><u>Rectal bleeding</u>: Extension of the diagnostic criteria yielded 2 additional cancers.</p>

Kagevi (1989)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Propective consecutive patient series from a primary care centre in Sweden.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	

Patient characteristics and setting	N = 172; 88 men, 84 women; mean (SD) age = 43 (16) years. <u>Inclusion criteria:</u> "All patients visiting the medical center with complaints referable to the digestive tract were considered for inclusion. Even when the patient consulted the primary care center because of another complaint and coincidentally mentioned gastrointestinal problem, the patient was considered for inclusion. The patient's gastrointestinal problem could have been reported in connection with an earlier visit at the primary care center." <u>Exclusion criteria:</u> Patients with jaundice, gastrointestinal bleeding or acute abdominal pain were excluded and so were patients judged to have a non-gastro-enterologic cause of their symptoms (gynaecologic problems, spondylosis deformans, etc), patients aged < 16 years and patients unwilling to participate. <u>Clinical setting:</u> Primary care Center, Sweden.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia defined as any pain, discomfort, or other symptoms referable to the digestive tract \geq 2 weeks. Symptoms could be intermittent or continuous.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Esophagogastroduodenoscopy within 1 week and 6 month follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	13/185 patients were excluded as they did not want to have an endoscopy
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

NOTES	2 patients had gastric cancer, 0 patients had oesophageal cancer.	
Mahadeva (2008)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series from the Primary Care Clinics of the University of Malaya in Malaysia	
Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?	Unclear risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 432; 198 males/234 females; mean ages (SDs) = 30-31 (8) years.</p> <p><u>Inclusion criteria:</u> "All patients were recruited from the Primary Care Clinics of the University of Malaya, which provide a regular service to the local community. Patients aged ≤ 45 years presenting with uninvestigated dyspepsia were invited to participate in the study", which ran from January 2004 until October 2005.</p> <p><u>Exclusion criteria:</u> Age > 45 or < 18 years; symptoms of weight loss, progressive dysphagia or those suggestive of anaemia; pregnancy; previous H pylori testing; any contra-indication to to endoscopy or sedation; failure to turn up for initial test ; and on regular doses of non-steroidal anti-inflammatory drugs.</p> <p><u>Clinical setting:</u> Primary care clinic, Malaysia</p>	
Are there concerns that the included patients and setting do not match the review question?	High concern	
INDEX TEST		
A. Risk of bias		
Index test	Uninvestigated dyspepsia. Dyspepsia defined as predominant upper abdominal discomfort for > 4 weeks, with any associated symptoms, including heart burn and regurgitation.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up ± upper endoscopy (oesophagogastroduodenoscopy)	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its	Low risk	

interpretation have introduced bias?		
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	39/471 eligible patients were excluded from the study for the following reasons: 34/39 patients declined to participate, 3/39 became pregnant before the test, 1/39 emigrated from the country and 1/39 had missing data.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	One patient was found to have cancer, which was metastatic pancreatic cancer. No oesophageal or gastric cancers were reported.	

Meineche-Schmidt (2002)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Consecutive patient series from 82 GPs in Denmark.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 1491; 688 males, 803 females; age groups: 18-37 years: N = 377; 38-50 years: N = 369; 51-64 years: N = 338; 65- years: N = 402.</p> <p><u>Inclusion criteria:</u> Consecutive patients who consulted their GP between June 1991 and May 1993 for dyspepsia (defined as pain or discomfort in the abdomen judged by the GP to be related to the gastrointestinal tract).</p> <p><u>Exclusion criteria:</u> None listed.</p> <p><u>Clinical setting:</u> Primary care, Denmark.</p>	
Are there concerns that the included patients and setting do not match the review question?	Unclear concern	
INDEX TEST		
A. Risk of bias		
Index test	Dyspepsia (defined as pain or discomfort in the abdomen judged by the GP to be related to the gastrointestinal tract).	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or	Low concern	

interpretation differ from the review question?		
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	18 months-3 years and 10 months follow up.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	In total N = 31 had cancer: 17 colorectal, 8 gastro-oesophageal (no subgroup analyses presented for these patients) and 6 other.	

Muris (1993)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective consecutive patient series from 11 general practitioners in Maastricht (Holland)	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 578; 212 males, 342 females; age groups: 18-39 years: N = 295; 40-49 years: N = 80; 50-59 years: N = 91; 60-75 years: N = 88.</p> <p><u>Inclusion criteria:</u> Patients who during a 3-month period consulted one of the participating GPs for abdominal complaints.</p> <p><u>Exclusion criteria:</u> Patients aged < 18 years and patients with a condition necessitating immediate referral or admission to hospital.</p> <p><u>Clinical setting:</u> GPs in Holland</p>	
Are there concerns that the included patients and setting do not match the review question?	Unclear concern	
INDEX TEST		

A. Risk of bias	
Index test	Abdominal complaints. Not further specified, but the authors do report that the duration of pain before the patient presented for the first time for the evaluation of abdominal pain varied from some days to more than 1 year.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up for 15 months.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Although not explicitly stated by the authors it is implied that the patients included were those presenting with the abdominal complaint for the first time.
Møllmann (1981)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from an open-access gastroscopy clinic in Denmark.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	

Patient characteristics and setting	N = 1480; gender not reported; 40-44 years: N = 144; 45-49 years: N = 186; 50-69 years: N = 882; 70-74 years: N = 130; 75-79 years: N = 83; 80-89 years N = 47; 90- years: N = 8. <u>Inclusion criteria:</u> All patients who, for a 2-year period, presented to their GP with (any of) the following symptoms were referred to the open access gastroscopy clinic: Upper abdominal pain > 2 weeks, nausea and/or vomiting > 2 weeks, weight loss and/or anorexia, gastrointestinal bleeding, and anaemia (i.e., Hb < 80%). <u>Exclusion criteria:</u> Patients who had been examined for any of the above symptoms within the last 6 months. <u>Clinical setting:</u> GPs in Denmark
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Upper abdominal pain > 2 weeks, nausea and/or vomiting > 2 weeks, weight loss and/or anorexia, gastrointestinal bleeding, and anaemia (i.e., Hb < 80%).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-stage process: Gastroscopy with photography, using a gastroscope, performed with only local anaesthesia of the pharynx. If this investigation disclosed abnormal conditions, the next stage was gastroscopy, possibly with biopsy, using diazepam sedation.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	177/1480 patients declined endoscopy, 2/1480 did not show up for endoscopy, and it was unsuccessful in a further 24 patients, leaving 1277 patients. However, the paper reports that only 1273 had primary endoscopy, and then reports the results for between 1181 and 1297 patients.
Was there an appropriate interval between index test and reference standard?	Yes probably

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	There were a total of 18 gastric cancers confirmed in the study. No oesophageal cancers were reported. This research was published in 2 papers.

Stapley (2013)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Matched case-control study using patients in the UK's General Practice Research Database (GPRD).
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> <u>Oesophageal cancer cases:</u> N = 4854, 3174 males / 1680 females; aged 40-54 years: N = 387; 55-69 years: N = 1712; 70-84 years: N = 2230; ≥ 85 years: N = 532. <u>Gastric cancer cases:</u> N = 2617, 1625 males / 992 females; aged 40-54 years: N = 130; 55-69 years: N = 671; 70-84 years: N = 1437; ≥ 85 years: N = 382. Median number of consultations (all cases) = 26 (IQR = 15-42) <u>Controls:</u> <u>Oesophageal cancer controls:</u> N = 21506, gender not reported; aged 40-54 years: N = 1539; 55-69 years: N = 7473; 70-84 years: N = 10296; ≥ 85 years: N = 2198. <u>Gastric cancer controls:</u> N = 11371, gender not reported; aged 40-54 years: N = 497; 55-69 years: N = 2887; 70-84 years: N = 6431; ≥ 85 years: N = 1556. Median number of consultations (all controls) = 15 (IQR = 7-28)</p> <p><u>Inclusion criteria:</u> Cases: Patients with a record of one of 42 (18 oesophageal, 24 gastric) GPRD tumour diagnostic codes between January 2000 and December 2009 inclusive, aged ≥ 40 years, with min. 1 year of data before diagnosis. The first instance of a oesophago-gastric cancer code was assigned the data of diagnosis/index date. Controls: Up to 5 controls were matched to cases on sex, general practice, and to 1 year of age of the case. The index date was the index date of the matched case.</p>

	<p><u>Exclusion criteria:</u> Oesophago-gastric cancer (controls), no consultations in the year before diagnosis.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	<p>All symptoms, physical signs or abnormal investigations compiled from the oesophago-gastric cancer literature were studied, and supplemented by literature from relevant cancer websites. The GPRD's code list has many synonyms for for similar symptoms, often including additional description such as severity or duration. These synonyms were identified and merged. The dyspepsia variable merged codes with either the word 'dyspepsia' or 'indigestion'; the reflux variable included 'regurgitation' as well as 'reflux'; the variable 'epigastric pain' required a precise anatomical description, whereas the variable 'abdominal pain' incorporated all other abdominal pain variables without a precise anatomical description. Occurrences of these features in the year before the index date were identified. Features were only retained for further study if they occurred in $\geq 5\%$ of cases or controls. For laboratory tests, the local laboratory range was used to identify abnormal results. Patients without a test were considered to be the same status as those with a normal result. All hepatic enzyme results were merged into a composite variable, deemed abnormal if any enzyme was raised; similarly, abnormal erythrocyte sedimentation rate, plasma viscosity and C-reactive protein were collated into a single variable called raised inflammatory markers. All codes for fractures were also identified, as a test for any recording bias between cases and controls (making the assumption that the fracture rate would be approximately equal).</p>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Oesophago-gastric cancer code in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	A total of 45356 patients were identified, 37699 controls and 7657 cases. Of the controls the following exclusions were applied: Already used as a case (N = 252), case excluded (N = 808), duplicate control (N = 427) and no data in year pre-index date (N = 3335). Of the cases the following exclusions were applied: No controls (N = 17), OG cancer diagnosis before 2000 (N = 28), case already used as case (for other O/G cancer: N = 131) and case with metastatic cancer (N = 10).	
Was there an appropriate interval between index test and reference standard?		Yes
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		Yes
Could the patient flow have introduced bias?		Low risk
NOTES	Results are not split for oesophageal cancer and gastric cancer.	

Stellon (1997)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective? consecutive patient series from semi-rural UK general practice with a patient list between 2400-3400 during the study period.	
Was a consecutive or random sample of patients enrolled?		Yes
Was a case-control design avoided?		Yes
Did the study avoid inappropriate exclusions?		Yes
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and setting	N = 26; 5 males, 21 females; age range = 51-87 years. <u>Inclusion criteria:</u> All patients aged > 50 years found to have iron deficiency anaemia between January 1989 and March 1994. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> UK GP	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	Iron deficiency anaemia (< 12 g/dl haemoglobin and/or mean corpuscular volume < 80 fl with ferritin ≤ 16 ng/l)	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern

REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up during 5 year study period.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Thomson (2003)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Propective patient series from a group of 49 family physician practices in Canada.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1040, 520 males / 520 females; mean (range) age =45.6 (18-84) years. <u>Inclusion criteria:</u> Patients ≥ 18 years with a primary complaint of ≥ 3 months intermittent or continuous dyspepsia. Patients could not have used proton pump inhibitors within 30 days or prokinetics or prescription H ₂ -receptor antagonists (H ₂ RAS) within 14 days of enrolment. <u>Exclusion criteria:</u> Heartburn or acid regurgitation as their sole symptom; documented history of upper GI pathology/surgery; clinical investigation of dyspepsia by endoscopy or radiology in the previous 6 months or more than twice in the past 10 years; H. pylori eradication treatment in the previous 6 months; irritable bowel syndrome as assessed by the presence of ≥ manning criteria; or severe concurrent disease. <u>Clinical setting:</u> Family physician practice, Canada.

Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia defined as symptom complex of epigastric pain/discomfort in association with other upper GI symptoms, including heartburn and acid regurgitation.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 10 days and 6-months follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for. 1100/1171 enrolled patients consented to endoscopy, but 60/1100 did not received endoscopy (eligibility criteria not fulfilled [27], lost to follow up [3], withdrew consent [9], non-compliant with the protocol [1], endoscopy-intolerable [2], other [18]).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 2 patients: Gastric (MALToma; 1), oesophageal cancer (1).
Tosetti (2010)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 63 general practitioners in Italy
Was a consecutive or random sample of patients enrolled?	Unclear

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk
<u>B. Concerns regarding applicability</u>	
Patient characteristics and setting	N = 275; 124 males, 151 females; median age (range) = 46 (18-92) years. Symptoms: Epigastric pain (72%), prolonged digestion (51.6%), heartburn (49.1%), epigastric postprandial fullness (45.5%), epigastric distension (41.5%), nausea (38.5%), acid regurgitation (34.5%), belching (28.7%), early satiety (20.7%). <u>Inclusion criteria:</u> "Each GP enrolled in the survey patients who, over a three-month period, presented with UGI [upper gastro-intestinal] symptoms at the first onset without alarming features." <u>Exclusion criteria:</u> "Patients with either previous or recurrent complaints or previously investigated for UGI symptoms were not included". <u>Clinical setting:</u> GPs in Italy
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
<u>A. Risk of bias</u>	
Index test	New onset UGI symptoms without alarming features. Not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High concern
REFERENCE STANDARD	
<u>A. risk of bias</u>	
Reference standard(s)	1-year follow up.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
<u>A. risk of bias</u>	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes

Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Cancers diagnosed in these patients were: Pancreas (1/275), and oesophageal (1/275).
Vakil (2009)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 2741, mean (range) age = not reported (not reported) years, numbers of females/males: Not reported.</p> <p><u>Inclusion criteria:</u> Patients aged 18-70 years who met Rome II criteria for dyspepsia (intermittent or continuous pain or burning centered in the upper abdomen for ≥ 3 months).</p> <p><u>Exclusion criteria:</u> Past diagnosis of gastro-oesophageal reflux disease, predominant symptom of heartburn or regurgitation, history of heartburn or regurgitation > 2 days/week, treatment > 2 days/week with non-steroidal anti-inflammatory drugs or cyclooxygenase-2 selective inhibitors or aspirin (except for cardiovascular prophylaxis at doses ≤ 325 mg/day), concurrent alarm features (e.g., dysphagia, recurrent vomiting, unexplained anaemia, gastro-intestinal bleeding), H pylori eradication treatment within 12 months, maintenance therapy with either a proton pump or an H2-receptor antagonist within 6 months.</p> <p><u>Clinical setting:</u> The study was conducted in 190 primary care health centers in 17 countries (Argentina, Belgium, Brazil, Canada, Denmark, France, Germany, Greece, Iceland, Italy, Norway, Romania, Singapore, South Africa, Spain, Sweden, Switzerland). Patients were recruited from primary care clinics where flyers publicising the study were placed and the primary care physicians recruited patients presenting to their offices with dyspepsia [random or consecutive sampling unlikely].</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia/ intermittent or continuous pain or burning centered in the upper abdomen for ≥ 3 months. Symptoms were evaluated using a scale validated in a number of languages
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	All patients received outpatient endoscopy	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All the patients are accounted for in the results.	
Was there an appropriate interval between index test and reference standard?	Yes (probably)	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	Supported by AstraZeneca R&D Sweden. The authors state that "The sponsor did not play any role in the calculations or in the writing of the manuscript". Six patients had cancer: 3 oesophagus and 3 stomach.	

Yates (2004)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective database study using the laboratory databases of two district general hospitals including all the general practices using these laboratories.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 431; 154 males, 277 females; median age (inter-quartile range) = 75 (65-81) years.</p> <p><u>Inclusion criteria:</u> All female patients aged > 50 years and male patients aged > 20, with haemoglobin concentrations ≤ 110 g/l (women) or ≤ 120 g/l (men), and mean cell volume < 82 fl (district 1) or 78 fl (district 2), and red cell count ≤ 5.5 x 10¹²/l between June 1997 and May 1998.</p> <p><u>Exclusion criteria:</u> History of anaemia within previous 12 months, known</p>	

	haematological abnormalities (e.g., haemoglobinopathy), unavailable notes at follow up. <i>That is, patients with a history of cancer were not excluded.</i> Clinical setting: UK GP
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Iron deficiency anaemia (haemoglobin concentrations ≤ 110 g/l (women) or ≤ 120 g/l (men), and mean cell volume < 82 fl (district 1) or 78 fl (district 2), and red cell count $\leq 5.5 \times 10^{12}/l$)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Minimum 3 years follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 48 had gastrointestinal cancer (11 upper, 2 small bowel and 35 lower, including recurrent tumours) and N = 23 had non-gastrointestinal cancers, but the study only reports the type of some of these cancers (3 lung + 1 lung tumour secondary to a previous breast tumour, 1 ovary, 2 bladder, 1 Hodgkin's, 1 Non-Hodgkin's, 1 endometrial sarcoma, 1 lymphoma, 1 endometrial) and has therefore not been added to the evidence reviews for the non-gastrointestinal cancers. The paper considers both the lower gastrointestinal cancers and the small bowel cancers as colorectal cancer and in order to present subgroup analyses by gender I have maintained this grouping and not added this paper to the evidence review for small intestine.

References

Included studies

- Brignoli, R., Watkins, P., Halter, F. The Omega-Project – a comparison of two diagnostic strategies for risk- and cost-oriented management of dyspepsia. *European Journal of Gastroenterology and Hepatology* 9, 337-343. 1997.
- Collins, G.S., Altman, D.G. Identifying patients with undetected gastro-oesophageal cancer in primary care: External validation of QCancer (Gastro-Oesophageal). *European Journal of Cancer*, <http://dx.doi.org/10.1016/j.ejca.2012.10.023>. 2012.
- Droogendijk, J., Beukers, R., Berendes, P. B., Tax, M. G. H. M., Sonneveld, P., and Levin, M. D. Screening for gastrointestinal malignancy in patients with iron deficiency anemia by general practitioners: An observational study. *Scandinavian Journal of Gastroenterology* 46[9], 1105-1110. 2011.
- Duggan, A.F., Elliott, C.A., Miller, P., Hawkey, C.J., Logan, R.F.A. Clinical trial: A randomized trial or early endoscopy, *Helicobacter pylori* testing and empirical therapy for the management of dyspepsia in primary care. *Alimentary Pharmacology and Therapeutics* 29, 55-68. 2008.
- Edenholm, M., Gustavsson, R., Jansson, O., et al. Endoscopic findings in patients with ulcer-like dyspepsia. *Scandinavian Journal of Gastroenterology* 20(suppl 109), 163-167. 1985.
- Esfandyari, T., Potter, J.W., Vaezi, M.F. Dysphagia: A cost analysis of the diagnostic approach. *American Journal of Gastroenterology*, 97, 2733-2737. 2002.
- Farrus, Palou M., Perez, Ocana A., Mayer Pujadas, M. A., Piquer, Gibert M., Mundet, Tuduri, X, and Iglesias, Rodal M. [Anemia in primary care: etiology and morphological characteristics]. [Spanish]. *Atencion Primaria* 25[4], 230-235. 15-3-2000.
- Hallissey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.
- Hansen, J.M., Bytzer, P., Schaffalitzky de Muckadell, O.B. Management of dyspeptic patients in primary care: Value of the unaided clinical diagnosis and of dyspepsia subgrouping. *Scandinavian Journal of Gastroenterology* 33, 799-805. 1998.
- Heikkinen, M., Pikkarainen, P., Takala, J., and Rasanen, H. Julkunen R. Etiology of dyspepsia: Four hundred unselected consecutive patients in general practice. *Scandinavian Journal of Gastroenterology* 30[6], 519-523. 1995.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected gastro-oesophageal cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice*; DOI: 10.3399/bjgp11X606609. 2011.
- Jaskiewicz, K., Iouwrens, H.D. Chronic atrophic gastritis in a population at risk for gastric carcinoma. *Anticancer Research* 11, 835-840. 1991.
- Jones, R., Latinovic, R., Charlton, J., and Gulliford, M. C. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *BMJ* 334[7602], 1040. 19-5-2007.
- Kagevi, I., Löfstedt, S., Persson, L.-G. Endoscopic findings and diagnoses in unselected dyspeptic patients at a primary health care center. *Scandinavian Journal of Gastroenterology* 24, 145-150. 1989.
- Mahadeva, S., Chia, Y.-C., Vinothini, A., et al. Cost-effectiveness of and satisfaction with a *Helicobacter pylori* "test and treat" strategy compared with prompt endoscopy in young Asians with dyspepsia. *Gut* 57, 1214-1220. 2008.
- Meineche-Schmidt, V. and Jorgensen, T. 'Alarm symptoms' in patients with dyspepsia: a three-year prospective study from general practice. *Scandinavian Journal of Gastroenterology* 37[9], 999-1007. 2002.
- Muris, J.W.M., Starmans, R., Fijten, G.H., Crebolder, F.J.M., Krebber, T.F.W.A., and Knottnerus, J.A., Abdominal pain in general practice. *Family Practice* 10[4], 387-390. 1993.

- Møllmann, K.-M. Early diagnosis of gastric cancer: The possibility of delimiting high risk groups. *Danish Medical Bulletin* 28, 89-92. 1981.
- Møllmann, K.-M. Endoscopic service for general practice. *Danish Medical Bulletin* 28, 96-99. 1981.
- Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M. & Hamilton, W. (2013) The risk of oesophago-gastric cancer in symptomatic patients in primary care: a large case-control study using electronic records. *British Journal of Cancer*, 108: 25-31.
- Stellon, A. J. and Kenwright, S. E. Iron deficiency anaemia in general practice: Presentations and investigations. *British Journal of Clinical Practice* 51[2], 78-80. 1997.
- Thomson, A.B.R., Barkun, A.N., Armstrong, D., Chiba, N., White, R.J., Daniels, S., Escobedo, S., Chakraborty, B., Sinclair, S. The prevalence of clinically significant endoscopic findings in primary care patients with uninvestigated dyspepsia: The Canadian Adult Dyspepsia Empiric Treatment-Prompt Endoscopy (CADET-PE) study. *Alimentary Pharmacology and Therapeutics* 17, 1481-1491. 2003.
- Tosetti, C.; Bellentani, S.; Benedetto, E.; Ubaldi, E.; Cardin, F.; Bozzani, A. (2010). The management of patients with new onset of upper gastro-intestinal symptoms in primary care. *Digestive and Liver Disease*, 42: 860-864.
- Vakil, N., Talley, N., van Zanten, S. V., Flook, N., Persson, T., Bjorck, E., Lind, T., and Bolling-Sternevald, E. Cost of Detecting Malignant Lesions by Endoscopy in 2741 Primary Care Dyspeptic Patients Without Alarm Symptoms. *Clinical Gastroenterology and Hepatology* 7[7], 756-761. 2009.
- Yates, J. M., Logan, E. C., and Stewart, R. M. Iron deficiency anaemia in general practice: clinical outcomes over three years and factors influencing diagnostic investigations. *Postgraduate Medical Journal* 80[945], 405-410. 2004.

Excluded studies (with excl reason)

- (2003) Information from your family doctor. Dyspepsia. *American Family Physician*, 68: 2040-2041.
Narrative Review
- (2010) Information from your family doctor. Dyspepsia: what it is and what to do about it. *American Family Physician*, 82: 1459-1460.
Narrative Review
- Adachi, Y., Kitamura, K., Tsutsui, S., Ikeda, Y., Matsuda, H. & Sugimachi, K. (1993) How to detect early carcinoma of the esophagus. *Hepato-Gastroenterology*, 40: 207-211.
Not in PICO
- Adang, R. P., Ambergen, A. W., Talmon, J. L., Hasman, A., Vismans, J. F. J. & Stockbrugger, R. W. (1996) The discriminative value of patient characteristics and dyspeptic symptoms for upper gastrointestinal endoscopic findings: A study on the clinical presentation of 1,147 patients. *Digestion*, 57: March/April.
Not in PICO
- Ahlgren, J. D. (2001) Gastrointestinal malignancies. *Primary Care - Clinics in Office Practice*, 28.
Narrative Review
- Akhtar, A. J. & Shaheen, M. A. (2004) Dyspepsia in African-American and Hispanic patients. *Journal of the National Medical Association*, 96: 635-640.
Not in PICO
- Amin, I., Steer, P. & Madhotra, R. (2009) Appropriateness of the "Straight to Test" gastroscopy request for patients with suspected gastrointestinal cancers. *Gut.Conference: British Society of Gastroenterology Annual General Meeting Glasgow United Kingdom.Conference Start: 20090323 Conference End: 20090325.Conference Publication: (var.pagings)*, 58.
Not in PICO
- Anderson, W. D., III & Strayer, S. M. (2013) Evaluation of nausea and vomiting: a case-based approach. *American Family Physician*, 88: 371-379.
Narrative review

- Ansari, S. & Ford, A. C. (2013) Initial management of dyspepsia in primary care: An evidence-based approach. *British Journal of General Practice*, 63: 498-499.
Narrative review
- Armstrong, D., Marshall, J. K., Chiba, N., Enns, R., Fallone, C. A., Fass, R., Hollingworth, R., Hunt, R. H., Kahrilas, P. J., Mayrand, S., Moayyedi, P., Paterson, W. G., Sadowski, D., van Zanten, S. J. & Canadian Association of Gastroenterology GERD Consensus Group (2005) Canadian Consensus Conference on the management of gastroesophageal reflux disease in adults - update 2004. [Review] [308 refs]. *Canadian Journal of Gastroenterology*, 19: 15-35.
Guideline
- Ashktorab, H., Nouri, Z., Nourai, M., Razjouyan, H., Lee, E. E., Dowlati, E., El-Sayed, E. W., Laiyemo, A., Brim, H. & Smoot, D. T. (2011) Esophageal Carcinoma in African Americans: A Five-Decade Experience. *Digestive Diseases and Sciences*, 56: 3577-3582.
Not in PICO
- Axon, A. T. R. (1997) Chronic dyspepsia: Who needs endoscopy? *Gastroenterology*, 112.
Narrative Review
- Bai, Y., Li, Z. S., Zou, D. W., Wu, R. P., Yao, Y. Z., Jin, Z. D., Ye, P., Li, S. D., Zhang, W. J., Du, Y. Q., Zhan, X. B., Liu, F., Gao, J. & Xu, G. M. (2010) Alarm features and age for predicting upper gastrointestinal malignancy in Chinese patients with dyspepsia with high background prevalence of *Helicobacter pylori* infection and upper gastrointestinal malignancy: an endoscopic database review of 102 665 patients from 1996 to 2006. *Gut*, 59: 722-728.
Not in PICO
- Barenys, M., Rota, R., Moreno, V., Villafafila, R., Garcia-Bayo, I., Abad, A., Pons, J. M. V. & Pique, J. M. (2003) Prospective validation of a clinical scoring system for the diagnosis of organic dyspepsia. *Medicina Clinica*, 121: 766-771.
Not in PICO
- Barge, J., Molas, G., Maillard, J. N., Fekete, F., Bogomoletz, W. V. & Potet, F. (1981) Superficial oesophageal carcinoma: an oesophageal counterpart of early gastric cancer. *Histopathology*, 5: 499-510.
Not in PICO
- Barloon, T. J., Bergus, G. R. & Lu, C. C. (1996) Diagnostic imaging in the evaluation of dysphagia. [Review] [22 refs]. *American Family Physician*, 53: 535-546.
Narrative Review
- Barra, S., Mattotti, M., Bertos, G. & Barzan, L. (1992) [The program for early diagnosis of the upper respiratory tract and digestive system neoplasms offered to alcoholics in the region of Friuli-Venice Giulia]. [Italian]. *Acta Otorhinolaryngologica Italica*, 12: 337-344.
Not in PICO
- Bazaldua, O. V. & Schneider, F. D. (1787) Evaluation and management of dyspepsia. [Review] [44 refs]. *American Family Physician*, 60: 1773-1784.
Narrative Review
- Behm, B. W. & Peura, D. A. (2011) Gastroesophageal reflux disease: Clinical features and management for the primary care physician. *Journal of Clinical Outcomes Management*, 18: January.
Narrative Review
- Belloc, C. J., Porta, S. M., Malats, R. N., Gallen, C. M. & Phanas, D. J. (1994) The initial symptom attributable to cancer in digestive tube tumors. A study of agreement between the patient and the physician. [Spanish]. *Medicina Clinica*, 103: 8.
Not in PICO
- Benaglia, T., Sharples, L. D., Fitzgerald, R. C. & Lyratzopoulos, G. (2013) Health benefits and cost effectiveness of endoscopic and nonendoscopic cytosponge screening for Barrett's esophagus (Structured abstract). *Gastroenterology*, 144: 62-73.
Not in PICO

- Bennouna, J., Bardet, E., Deguiral, P. & Douillard, J. Y. (2000) Small cell carcinoma of the esophagus - Analysis of 10 cases and review of the published data. *American Journal of Clinical Oncology-Cancer Clinical Trials*, 23: 455-459.
Not in PICO
- Berrill, J. W., Turner, J. K., Hurley, J. J., Swift, G., Dolwani, S. & Green, J. T. (2012) Upper gastrointestinal cancer in its early stages is predominantly asymptomatic. *Frontline Gastroenterology*, 3: January.
Not in PICO
- Bird-Lieberman, E. L. & Fitzgerald, R. C. (2009) Early diagnosis of oesophageal cancer. *British Journal of Cancer*, 101: 07.
Narrative Review
- Biyyani, R. S. S., Salah, W., Dumot, J. & Chak, A. (1111) Treatment of barrett's related adenocarcinoma in a roux-en-y-gastric bypass surgery patient: Is endoscopic therapy possible? *American Journal of Gastroenterology.Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States.Conference Start: 20131011 Conference End: 20131016.Conference Publication: (var.pagings)*, 108: October.
Not in PICO
- Bleyer, A. (2009) CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology*, 36: June.
Narrative Review
- Bonino, J. A. & Sharma, P. (2004) Barrett esophagus. *Current Opinion in Gastroenterology*, 20: 375-380.
Narrative Review
- Bonino, J. A. & Sharma, P. (2005) Barrett's esophagus. [Review] [25 refs]. *Current Opinion in Gastroenterology*, 21: 461-465.
Narrative Review
- Bowrey, D. J., Griffin, S. M., Wayman, J., Karat, D., Hayes, N. & Raimes, S. A. (2006) Use of alarm symptoms to select dyspeptics for endoscopy causes patients with curable esophagogastric cancer to be overlooked. *Surgical Endoscopy*, 20: 1725-1728.
Not in PICO
- Brahmania, M., Lam, E., Telford, J. & Enns, R. (2010) Endoscopic mucosal resection: early experience in British Columbia. *Canadian Journal of Gastroenterology*, 24: 239-244.
Not in PICO
- Bresalier, R. S. (2009) Barrett's esophagus and esophageal adenocarcinoma. *Annual Review of Medicine*, 60.
Narrative Review
- Breslin, N. P., Thomson, A. B. R., Bailey, R. J., Blustein, P. K., Meddings, J., Lalor, E., VanRosendaal, G. M. A., Verhoef, M. J. & Sutherland, L. R. (2000) Gastric cancer and other endoscopic diagnoses in patients with benign dyspepsia. *Gut*, 46: 93-97.
Not in PICO
- Brignoli, R., Merki, H., Miazza, B. & Beglinger, C. (1994) Endoscopic Findings in Volunteers and in Patients with Dyspepsia. *Schweizerische Medizinische Wochenschrift*, 124: 1240-1247.
Not in PICO
- Brock, M. V., Are, C., Wu, T. T., Canto, M., Yang, S. C. & Heitmiller, R. F. (2002) Polypoid esophageal adenocarcinoma--a clinicopathological variant of esophageal cancer? *Current Surgery*, 59: 336-341.
Not in PICO
- Buecher, B. & Galmiche, J. P. (2003) Early diagnosis of esophageal adenocarcinoma. [Review] [63 refs]. *Seminars in Gastrointestinal Disease*, 14: 136-145.
Narrative Review

- Buset, M. & Deviere, J. (1990) [Barrett's esophagus. Characterization and monitoring policy]. [Review] [30 refs] [French]. *Acta Gastroenterologica Belgica*, 53: 561-567.
Narrative Review
- Buset, M. & Demanet, E. (2008) [Heartburn: gastro-oesophageal reflux in 9 pictures]. [French]. *Revue Medicale de Bruxelles*, 29: 197-205.
Narrative review
- Bytzer, P. (2003) Goals of therapy and guidelines for treatment success in symptomatic gastroesophageal reflux disease patients. *American Journal of Gastroenterology*, 98: S31-S39.
Narrative Review
- Cann, P. A., Gleeson, M. H., Robinson, T. J. & Wicks, A. C. B. (1994) Assessing dyspepsia in general practice. *British Journal of Clinical Practice*, 48.
Narrative review
- Cappell, M. S. (2005) Clinical presentation, diagnosis, and management of gastroesophageal reflux disease. *Medical Clinics of North America*, 89: March.
Narrative Review
- Chan, D., Leggett, C., Gorospe, E., Chandra, S., Sharma, A., Chowdhury, S., Lutzke, L., Buttar, N., Iyer, P. & Wang, K. (1111) Low dose aspirin does not affect outcomes from radiofrequency ablation for barrett's esophagus. *American Journal of Gastroenterology.Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States.Conference Start: 20131011 Conference End: 20131016.Conference Publication: (var.pagings)*, 108: October.
Not in PICO
- Chawla, S., Seth, D., Mahajan, P. & Kamat, D. (2006) Gastroesophageal reflux disorder: A review for primary care providers. *Clinical Pediatrics*, 45: January/February.
Narrative Review
- Cheung, D., Menon, S. & Trudgill, N. (2013) How commonly is oesophageal cancer missed at endoscopy (a UK primary care based study)? *Gut*, 62: A5.
Not in PICO
- Cheung, D. & Trudgill, N. (2013) How Common Are Delays in Referral of Patients with Oesophageal Cancer from Primary Care? *Gut*, 62: A105.
Not in PICO
- Chun, S., Hui, L. & Jing, S. (2013) Application study of NBI and lugol staining in the diagnosis of early esophageal cancer. *Journal of Gastroenterology and Hepatology*, 28: 42.
Abstract only, not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Chung, J. W., Lee, G. H., Jung, H. Y., Choi, K. D., Song, H. J., Choi, K. S., Oh, H. C., Jung, K. W., Choe, J. W., Kim, J. W., Yu, E. & Kim, J. H. (2008) Clinicopathologic Characteristics of Barrett's Cancer in Korea. *Gut & Liver*, 2: 193-198.
Not in PICO
- Classen, M. & Phillip, J. (1981) [Endoscopy of esophageal cancer (author's transl)]. [German]. *Langenbecks Archiv fur Chirurgie*, 355: 59-61.
Narrative review
- Collins, B. J., Abbott, M., Thomas, R. J., Morstyn, G. & St John, D. J. (1991) Clinical profile in Barrett's esophagus: who should be screened for cancer? *Hepato-Gastroenterology*, 38: 341-344.
Not in PICO
- Conteduca, V., Sansonno, D., Ingravallo, G., Marangi, S., Russi, S., Lauletta, G. & Dammacco, F. (2012) Barrett's esophagus and esophageal cancer: an overview. [Review]. *International Journal of Oncology*, 41: 414-424.
Narrative Review
- Cooper, S. C., Prew, S., Podmore, L. K., Nightingale, P. & Trudgill, N. J. (2009) Gastro-oesophageal reflux symptoms and the development of oesophageal adenocarcinoma: Results from MOSES (midlands oesophageal adenocarcinoma epidemiology study). *Gastroenterology.Conference:*

- Digestive Disease Week, DDW 2009 Chicago, IL United States. Conference Start: 20090530 Conference End: 20090604. Conference Publication: (var.pagings), 136: May.*
Not in PICO
- Cooper, S. C., Prew, S., Podmore, L., Nightingale, P. & Trudgill, N. J. (2009) The influence of symptoms of gastro-oesophageal reflux in the development of oesophageal adenocarcinoma: Results from moses (Midlands oesophageal adenocarcinoma epidemiology study). *Gut. Conference: British Society of Gastroenterology Annual General Meeting Glasgow United Kingdom. Conference Start: 20090323 Conference End: 20090325. Conference Publication: (var.pagings), 58: 2009.*
Not in PICO
- Corder, A. P., Jones, R. H., Sadler, G. H., Daniels, P. & Johnson, C. D. (1996) Heartburn, oesophagitis and Barrett's oesophagus in self-medicating patients in general practice. *British Journal of Clinical Practice, 50: 245-248.*
Not in PICO
- da Silva, J. B., Mauricio, S. F., Bering, T. & Correia, M. I. (2013) The relationship between nutritional status and the Glasgow prognostic score in patients with cancer of the esophagus and stomach. *Nutrition & Cancer, 65: 25-33.*
Not in PICO
- Dabrowski, A., Misiuna, P. & Wallner, G. (1997) Cancer of the esophagus - The rules of diagnosis and staging. [Polish]. *Gastroenterologia Polska, 4: 1997.*
Narrative review
- Davis, A. J. M., Bowman, D. & Shepherd, H. A. (2004) Patients referred from primary care with iron-deficiency anaemia: Analysis of a nurse-led service. An improvement for both doctor and patient? *Quality in Primary Care, 12.*
Not in PICO
- Delaney, B., Ford, A. C., Forman, D., Moayyedi, P. & Qume, M. (2009) Initial management strategies for dyspepsia. *Cochrane Database of Systematic Reviews.*
Withdrawn from publication
- Delmotte, J. S., Pommelet, P., Houcke, M. & Paris, J. (1981) Early cancers of oesophagus. [French]. *Acta Endoscopica, 11.*
Not in PICO
- Dent, J., Armstrong, D., Delaney, B., Moayyedi, P., Talley, N. J. & Vakil, N. (2004) Symptom evaluation in reflux disease: Workshop background, processes, terminology, recommendations, and discussion outputs. *Gut, 53: May.*
Narrative review/workshop
- DeVault, K. R. (2000) Epidemiology and significance of Barrett's esophagus. *Digestive Diseases, 18: May.*
Narrative Review
- DeWitt, J., Alsatie, M., LeBlanc, J., McHenry, L. & Sherman, S. (2007) Endoscopic ultrasound-guided fine-needle aspiration of left adrenal gland masses. *Endoscopy, 39: 65-71.*
Not in PICO
- Dickman, R., Kim, J. L., Camargo, L., Green, S. B., Sampliner, R. E., Garewal, H. S. & Fass, R. (2006) Correlation of gastroesophageal reflux disease symptoms characteristics with long-segment Barrett's esophagus. *Diseases of the Esophagus, 19: October.*
Not in PICO
- Dregan, A., Moller, H., Charlton, J. & Gulliford, M. C. (2013) Are alarm symptoms predictive of cancer survival? Population-based cohort study. *British Journal of General Practice, 63: E807-E812.*
Not in PICO
- El-Serag, H., Hill, C. & Jones, R. (2009) Systematic review: The epidemiology of gastro-oesophageal reflux disease in primary care, using the UK general practice research database. *Alimentary Pharmacology and Therapeutics, 29: March.*

Not in PICO

Ellis, K. K., Oehlke, M., Helfand, M. & Lieberman, D. (1997) Management of symptoms of gastroesophageal reflux disease: does endoscopy influence medical management? *American Journal of Gastroenterology*, 92: 1472-1474.

Not in PICO

Enomoto, S., Nakazawa, K., Ueda, K., Mori, Y., Maeda, Y., Shingaki, N., Maekita, T., Ota, U., Oka, M. & Ichinose, M. (2011) Steakhouse syndrome causing large esophageal ulcer and stenosis. *World Journal of Gastrointestinal Endoscopy*, 3: 101-104.

Not in PICO

Erstad, B. L. (2002) Dyspepsia: initial evaluation and treatment. *Journal of the American Pharmaceutical Association*, 42: 460-468.

Narrative review

Estores, D. & Velanovich, V. (2013) Barrett esophagus: epidemiology, pathogenesis, diagnosis, and management. [Review]. *Current Problems in Surgery*, 50: 192-226.

Narrative review

Fashner, J. & Gitu, A. C. (2013) Common Gastrointestinal Symptoms: dyspepsia and Helicobacter pylori. [Review]. *Fp Essentials*, 413: 24-28.

Narrative review

Fennerty, M. B., Finke, K. B., Kushner, P. R., Peura, D. A., Record, L., Riley, L., Ruoff, G. E., Simonson, W. & Wright, W. L. (2009) Short- and long-term management of heartburn and other acid-related disorders: Development of an algorithm for primary care providers. *Journal of Family Practice*, 58: July.

Not in PICO

Fernandez Salazar, L. I., Alvarez, G. T., Sanz, R. A., Velayos, J. B., Aller, d. I. F. & Gonzalez Hernandez, J. M. (2007) Gastrointestinal stromal tumors (GISTs): clinical aspects. [Spanish]. *Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva*, 99: Jan.

Not in PICO

Fernandez, E., Porta, M., Malats, N., Belloc, J. & Gallen, M. (2002) Symptom-to-diagnosis interval and survival in cancers of the digestive tract. *Digestive Diseases and Sciences*, 47: 01.

Not in PICO

Fiorenza, J. & Chan, W. (2012) The management and endoscopic outcomes of dyspepsia in low-risk patients. *American Journal of Gastroenterology.Conference: 77th Annual Scientific Meeting of the American College of Gastroenterology Las Vegas, NV United States.Conference Start: 20121019 Conference End: 20121024.Conference Publication: (var.pagings)*, 107: October.

Not in PICO

Flameling, R. D., Numans, M. E., ter, L. J., de Wit, N. J. & Siersema, P. D. (2010) Different characteristics of patients with gastro-oesophageal reflux disease on their path through healthcare: a population follow-up study. *European Journal of Gastroenterology & Hepatology*, 22: 578-582.

Not in PICO

Flynn, C. A. (2001) The evaluation and treatment of adults with gastroesophageal reflux disease. *Journal of Family Practice*, 50.

Narrative review

Fock, K. M. (2009) GERD, NERD and Barrett's esophagus. *Digestion.Conference: 2nd International Gastrointestinal Consensus Symposium, IGICS: GERD Including NERD Tokyo Japan.Conference Start: 20090213 Conference End: 20090213.Conference Publication: (var.pagings)*, 79: January.

Narrative Review

Ford, A. C. & Moayyedi, P. (2009) Should we step-up or step-down in the treatment of new-onset dyspepsia in primary care?. [Review] [41 refs]. *Polskie Archiwum Medycyny Wewnetrznej*, 119:

391-396.

Narrative review

Ford, A. C. & Moayyedi, P. (2013) Dyspepsia. *BMJ (Online)*, 347.

Narrative review

Fransen, G. A., Janssen, M. J., Muris, J. W., Laheij, R. J. & Jansen, J. B. (2004) Meta-analysis: the diagnostic value of alarm symptoms for upper gastrointestinal malignancy (Structured abstract). *Alimentary Pharmacology and Therapeutics*, 20: 1045-1052.

Not in PICO

Fuessl, H. S. (2003) [Heartburn without esophagitis. Symptoms more important than the finding?]. [German]. *MMW Fortschritte der Medizin*, 145: 4-6.

Narrative review

Fujiwara, Y., Takahashi, S., Arakawa, T., Sollano, J. D., Zhu, Q., Kachintorn, U., Rani, A. A., Hahm, K. B., Joh, T., Kinoshita, Y., Matsumoto, T., Naito, Y., Takeuchi, K., Furuta, K., Terano, A. & IGICS Study Group (2009) A 2008 questionnaire-based survey of gastroesophageal reflux disease and related diseases by physicians in East Asian countries. *Digestion*, 80: 119-128.

Not in PICO

Galmiche, J.-P. & Tygat (1999) Treat or investigate? *European Journal of Gastroenterology and Hepatology, Supplement*, 11.

Narrative Review

Garcia Rodriguez, L. A., Lagergren, J. & Lindblad, M. (2006) Gastric acid suppression and risk of oesophageal and gastric adenocarcinoma: a nested case control study in the UK. *Gut*, 55: 1538-1544.

Not in PICO

Gillen, D. & Mccoll, K. E. L. (1999) Does concern about missing malignancy justify endoscopy in uncomplicated dyspepsia in patients aged less than 55? *American Journal of Gastroenterology*, 94: 75-79.

Not in PICO

Gisbert, J. P., Calvet, X., Ferrandiz, J., Mascort, J., Alonso-Coello, P. & Marzo, M. (2012) [Clinical practice guideline on the management of patients with dyspepsia. Update 2012]. [Spanish]. *Gastroenterologia y Hepatologia*, 35: 725-738.

Guideline

Gisbert, J. P., Calvet, X., Ferrandiz, J., Mascort, J., Alonso-Coello, P. & Marzo, M. (2012) [Clinical practice guideline on the management of patients with dyspepsia. Update 2012]. [Spanish]. *Atencion Primaria*, 44: 727.

Guideline

Gockel, I., Muller, M. & Schumacher, J. Achalasia-A disease of known cause that is often diagnosed too late. [References]. *Deutsches Arzteblatt International* 109[12], 209-214. 2012.

Narrative review

Goh, K.-L. (2012) The role of gastroesophageal reflux disease in functional dyspepsia: Does it matter? *Journal of Gastroenterology and Hepatology. Conference: Asian Pacific Digestive Week 2012 Bangkok Thailand. Conference Start: 20121205 Conference End: 20121208. Conference Publication: (var.pagings)*, 27: December.

Narrative review

Gordon, V. M., Madhotra, R. & Steer, P. (2011) A single centre experience of straight to test suspected ugi cancer service. *Gut. Conference: Annual General Meeting of the British Society of Gastroenterology Birmingham United Kingdom. Conference Start: 20110314 Conference End: 20110317. Conference Publication: (var.pagings)*, 60: April.

Not in PICO

Grannell, M. S., Kelly, S., Shannon, S., Chong, A. L. & Walsh, T. N. (2001) The sinister significance of dysphagia. *Irish Journal of Medical Science*, 170: 244-245.

Not in PICO

- Greenslade, J. & Wyman, A. (2006) Investigation of dysphagia. *Surgery*, 24: 89-92.
Narrative Review
- Guitron Cantu, J. A., Adalid, M. R., Sanchez, V. A. & Sanchez, M. T. (1991) [Carcinoma of the esophagus: clinical, radiologic, endoscopic, and histologic evaluation. Experience in Torreon City, Coahuila]. [Spanish]. *Revista de Gastroenterologia de Mexico*, 56: 17-21.
Not in PICO
- Haggitt, R. C. (1994) Barrett's esophagus, dysplasia, and adenocarcinoma. [Review] [113 refs]. *Human Pathology*, 25: 982-993.
Narrative Review
- Harle, I. A., Finley, R. J. & Belsheim, M. (1985) Management of adenocarcinoma in a columnar-lined esophagus. *Annals of Thoracic Surgery*, 40.
Not in PICO
- Harmon, R. C. & Peura, D. A. (2010) Review: Evaluation and management of dyspepsia. *Therapeutic Advances in Gastroenterology*, 3: March.
Narrative Review
- Harvey, J. C., Kagan, A. R., Hause, D., Sachs, T. & Frankl, H. (1990) Adenocarcinoma arising in Barrett's esophagus. *Journal of Surgical Oncology*, 45.
Not in PICO
- Hashemi, N., Loren, D., DiMarino, A. J. & Cohen, S. (2009) Presentation and Prognosis of Esophageal Adenocarcinoma in Patients Below Age 50. *Digestive Diseases and Sciences*, 54: 1708-1712.
Not in PICO
- Heikkinen, M., Pikkarainen, P., Eskelinen, M. & Julkunen, R. (2000) GPs' ability to diagnose dyspepsia based only on physical examination and patient history. *Scandinavian Journal of Primary Health Care*, 18: 99-104.
Same data as Heikkinen (1995), which is included.
- Henteleff, H. J., Darling, G. & CAGS Evidence Based Reviews in Surgery Group (2003) Canadian Association of General Surgeons Evidence Based Reviews in Surgery. 6. "GERD" as a risk factor for esophageal cancer. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *Canadian Journal of Surgery*, 46: 208-210.
Not in PICO
- Ho, C. H., Chau, W. K., Hsu, H. C., Gau, J. P., You, J. Y. & Chen, C. C. (2005) Predictive risk factors and prevalence of malignancy in patients with iron deficiency anemia in Taiwan. *American Journal of Hematology*, 78: 108-112.
Not in PICO
- Hollenz, M., Stolte, M. & Labenz, J. (2002) Prevalence of gastro-oesophageal reflux disease in general practice. [German]. *Deutsche Medizinische Wochenschrift*, 127: 10.
Not in PICO
- Holtmann, G., Maldonado-Lopez, E. & Haag, S. (2004) Heartburn in primary care: problems below the surface. [Review] [44 refs]. *Journal of Gastroenterology*, 39: 1027-1034.
Narrative Review
- Hosokawa, A., Shimada, Y., Matsumura, Y., Yamada, Y., Muro, K., Hamaguchi, T., Igaki, H., Tachimori, Y., Kato, H. & Shirao, K. (2005) Small cell carcinoma of the esophagus. Analysis of 14 cases and literature review. *Hepato-Gastroenterology*, 52: 1738-1741.
Not in PICO
- Howell, S. & Talley, N. J. (1999) Does fear of serious disease predict consulting behaviour amongst patients with dyspepsia in general practice? *European Journal of Gastroenterology and Hepatology*, 11.
Not in PICO
- Hsu, Y. C., Yang, T. H., Liou, J. M., Hsu, W. L., Lin, H. J., Wu, H. T., Lin, J. T., Wang, H. P. & Wu, M. S. (2012) Can clinical features stratify use of endoscopy for dyspeptic patients with high background prevalence of upper gastrointestinal cancer? *Digestive and Liver Disease*, 44: 218-223.

- Not in PICO
- Huffman, G. B. (2002) Evaluating and treating unintentional weight loss in the elderly. *American Family Physician*, 65: 640-650.
Narrative Review
- Hungin, A. P. S., Rubin, G. P., Russell, A. J. & Convery, B. (1997) Guidelines for dyspepsia management in general practice using focus groups. *British Journal of General Practice*, 47: 275-279.
Not in PICO
- Hussan, H., Bhatia, R., Hilton, R., Ringwala, J. & Hachem, C. (1111) Prevalence, natural history, and management of suspected barrett's esophagus in patients with cirrhosis. *American Journal of Gastroenterology.Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States.Conference Start: 20131011 Conference End: 20131016.Conference Publication: (var.pagings)*, 108: October.
Not in PICO
- Ioannou, G. N., Rockey, D. C., Bryson, C. L. & Weiss, N. S. (2002) Iron deficiency and gastrointestinal malignancy: a population-based cohort study. *American Journal of Medicine*, 113: 276-280.
Not in PICO
- Irving, M. J., Lamb, P. J., Irving, R. J. & Raimes, S. A. (2002) Speeding up the diagnosis of oesophago-gastric cancer. *Nursing Times*, 98: 35-37.
Not in PICO
- Irwin, R. S., Boulet, L. P., Cloutier, M. M., Fuller, R., Gold, P. M., Hoffstein, V., Ing, A. J., Mccool, F. D., O'Byrne, P., Poe, R. H., Prakash, U. B. S., Pratter, M. R. & Rubin, B. K. (1998) Managing cough as a defense mechanism and as a symptom - A consensus panel report of the American College of Chest Physicians. *Chest*, 114: 133S-181S.
Guideline
- Jamil, A. & Beejay, N. (2010) What direct costs are associated with evaluation of upper gastrointestinal cancers? results of a 32 month audit. *Annals of Oncology.Conference: 35th ESMO Congress Milan Italy.Conference Start: 20101008 Conference End: 20101012.Conference Publication: (var.pagings)*, 21: October.
Not in PICO
- Jankowski, J., Jones, R., Delaney, B. & Dent, J. (2002) 10-minute consultation: Gastro-oesophageal reflux disease. *BMJ*, 325: 945.
Narrative Review
- Jiang, W., Rice, T. W. & Goldblum, J. R. (2013) Esophageal leiomyoma: experience from a single institution. *Diseases of the Esophagus*, 26: 167-174.
Not in PICO
- Jimenez, F., Demaria, J. L. & Ahumada, C. A. (1999) Cancer of the esophagus and stomach: 3-year evaluation. [Spanish]. *Acta Gastroenterologica Latinoamericana*, 29.
Not in PICO
- Johansson, J., Johnsson, F., Walther, B., Willen, R., vonHolstein, C. S. & Zilling, T. (1996) Adenocarcinoma in the distal esophagus with and without Barrett esophagus - Differences in symptoms and survival rates. *Archives of Surgery*, 131: 708-713.
Not in PICO
- Jones, M. P. (2003) Evaluation and treatment of dyspepsia. *Postgraduate Medical Journal*, 79: 25-29.
Narrative Review
- Kanda, T., Sato, Y., Yajima, K., Kosugi, S., Matsuki, A., Ishikawa, T., Bamba, T., Umezu, H., Suzuki, T. & Hatakeyama, K. (2011) Pedunculated gastric tube interposition in an esophageal cancer patient with prepyloric adenocarcinoma. *World Journal of Gastrointestinal Oncology*, 3: 75-78.
Not in PICO

- Kapoor, N., Bassi, A., Sturges, R. & Bodger, K. (2005) Predictive value of alarm features in a rapid access upper gastrointestinal cancer service. *Gut*, 54: 40-45.
Not in PICO
- Katz, P. (1993) Esophageal carcinoma and achalasia: another call for screening? *American Journal of Gastroenterology*, 88: 783-784.
Not in PICO
- Kenya, P. R. & Asal, N. R. (1991) Epidemiologic and Clinical Aspects of Esophageal-Carcinoma in the Usa. *East African Medical Journal*, 68: 283-298.
Not in PICO
- Keren, D., Rainis, T., Stermer, E. & Lavy, A. (2011) A nine-year audit of open-access upper gastrointestinal endoscopic procedures: Results and experience of a single centre. *Canadian Journal of Gastroenterology*, 25: 83-88.
Not in PICO
- Khademi, H., Radmard, A.-R., Malekzadeh, F., Kamangar, F., Nasser-Moghaddam, S., Johansson, M., Byrnes, G., Brennan, P. & Malekzadeh, R. (2012) Diagnostic accuracy of age and alarm symptoms for upper GI malignancy in patients with dyspepsia in a GI clinic: A 7-year cross-sectional study. *PLoS ONE*, 7: e39173.
Not in PICO
- Kim, J. H. & Rhee, P. L. (2012) Recent Advances in Noncardiac Chest Pain in Korea. *Gut and Liver*, 6: 1-9.
Narrative Review
- Kostovski, A. (2006) Gastro-oesophageal reflux disease. [Croatian]. *Paediatrica Croatica, Supplement*, 50.
Narrative review
- Krishnamurthy, C., Hilden, K., Peterson, K. A., Mattek, N., Adler, D. G. & Fang, J. C. (2012) Endoscopic findings in patients presenting with dysphagia: analysis of a national endoscopy database. *Dysphagia*, 27: 101-105.
Not in PICO
- Krugmann, J., Neumann, H., Vieth, M. & Armstrong, D. (2013) What is the role of endoscopy and oesophageal biopsies in the management of GERD? *Best Practice and Research: Clinical Gastroenterology*, 27: 373-385.
Narrative review
- Kucera, S., Sharma, N. R. & Klapman, J. (2011) Endoscopic resection of a symptomatic esophageal granular cell tumor. *Gastrointestinal Endoscopy. Conference: Digestive Disease Week, DDW 2011 Chicago, IL United States. Conference Start: 20110507 Conference End: 20110510. Conference Publication: (var.pagings)*, 73: April.
Not in PICO
- Kuster, G. G. & Foroozan, P. (1989) Early diagnosis of adenocarcinoma developing in Barrett's esophagus. *Archives of Surgery*, 124: 925-927.
Not in PICO
- Lagergren, J. & Lagergren, P. (2010) Oesophageal cancer. *BMJ (Online)*, 341: 04.
Narrative Review
- Lambert, R. & Jacob, P. (1999) [Diagnosis and evaluation of the extent of cancer of the esophagus]. [French]. *Revue du Praticien*, 49: 1166-1171.
Narrative Review
- Lambert, R. & Jacob, P. (1999) Diagnosis and evaluation of oesophageal cancers. [French]. *Revue du Praticien*, 49: 01.
Narrative Review
- Leary, A., Assersohn, L., Cunningham, D., Norman, A. R., Chong, G., Brown, G., Ross, P. J., Costello, C., Higgins, L. & Oates, J. (2009) A phase II trial evaluating capecitabine and irinotecan as second line treatment in patients with oesophago-gastric cancer who have progressed on, or within 3 months

- of platinum-based chemotherapy. *Cancer Chemotherapy & Pharmacology*, 64: 455-462.
Not in PICO
- Lee, F. I. (1990) Complications of reflux disease. *Round Table Series - Royal Society of Medicine*.(22) (pp 119-128), 1990.Date of Publication: 1990., 1990.
Narrative Review
- Lee, J. I., Park, H., Jung, H.-Y., Rhee, P.-L., Song, C. W. & Choi, M. G. (2003) Prevalence of Barrett's esophagus in an urban Korean population: A multicenter study. *Journal of Gastroenterology*, 38: 23-27.
Not in PICO
- Lee, S.-W., Chang, C.-S., Yeh, H.-J., Lien, H.-C., Lee, T.-Y. & Chou, M.-C. (2012) The diagnostic value of alarm features for identifying types and stages of upper gastrointestinal malignancies: One medical center's experience. *Journal of Gastroenterology and Hepatology.Conference: Asian Pacific Digestive Week 2012 Bangkok Thailand.Conference Start: 20121205 Conference End: 20121208.Conference Publication: (var.pagings)*, 27: December.
Not in PICO
- Lenglinger, J., Riegler, M., Cosentini, E., Asari, R., Mesteri, I., Wrba, F. & Schoppmann, S. F. (2012) Review on the annual cancer risk of Barrett's esophagus in persons with symptoms of gastroesophageal reflux disease. *Anticancer Research*, 32: 5465-5473.
Not in PICO
- Levine, M. S., Dillon, E. C., Saul, S. H. & Laufer, I. (1986) Early esophageal cancer. *AJR.American Journal of Roentgenology*, 146: 507-512.
Not in PICO
- Lewin, K. J. (1992) Malignant and premalignant lesions of the esophagus. [Review] [51 refs]. *Keio Journal of Medicine*, 41: 177-183.
Narrative Review
- Li, J. R., Guo, H. G. & Sun, J. J. (2011) [Electronic laryngoscope for transnasal esophageal examination]. [Chinese]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi = Chinese Journal of Otorhinolaryngology Head & Neck Surgery*, 46: 936-938.
Not in PICO
- Li, Z. G. (2012) [Treatment of gastroesophageal reflux disease: comments from thoracic surgeon]. [Chinese]. *Zhonghua Weichang Waike Zazhi*, 15: 889-892.
Narrative Review
- Lieberman, D., Fennerty, M. B., Morris, C. D., Holub, J., Eisen, G. & Sonnenberg, A. (2004) Endoscopic evaluation of patients with dyspepsia: results from the national endoscopic data repository. *Gastroenterology*, 127: 1067-1075.
Not in PICO
- Liker, H., Hungin, P. & Wiklund, I. (2005) Managing gastroesophageal reflux disease in primary care: the patient perspective. [Review] [40 refs]. *Journal of the American Board of Family Practice*, 18: 393-400.
Not in PICO
- Liu, J., Wang, Q., Li, B., Meng, X., Zhang, Y., Du, X., Yan, J., Ping, Y. & Li, W. (1995) Superficial carcinomas of the esophagus and gastric cardia. A clinicopathological analysis of 141 cases. *Chinese Medical Journal*, 108: Oct.
Not in PICO
- Liu, X. X., Wong, A., Kadri, S. R., Corovic, A., O'Donovan, M., Lao-Sirieix, P., Lovat, L. B., Burnham, R. W. & Fitzgerald, R. C. (2014) Gastro-Esophageal Reflux Disease Symptoms and Demographic Factors as a Pre-Screening Tool for Barrett's Esophagus. *Plos One*, 9.
Not in PICO
- Lloyd, M. (1992) Early diagnosis of gastrointestinal cancer. *Practitioner*, 236: 980-983.
Narrative Review

- Loffeld, R. J., Liberov, B. & Dekkers, P. E. (2012) The changing prevalence of upper gastrointestinal endoscopic diagnoses: a single-centre study. *Netherlands Journal of Medicine*, 70: 222-226.
Not in PICO
- Lorenzo, P. Q., Rivas, A. D., Gonzalez, M. F., Fernandez, J. C., Sanchez, L. L., Garcia, M. J. G. & Seara, J. F. (2011) Referrals to a gastroenterology outpatient clinic from primary care: evaluation of two programs. *Gaceta Sanitaria*, 25: 468-473.
Not in PICO
- Loviscek, L. F., Cenoz, M. C., Badaloni, A. E. & Agarinakazato, O. (1998) Early cancer in achalasia. *Diseases of the Esophagus*, 11.
Not in PICO
- Loyd, R. A. & McClellan, D. A. (2011) Update on the Evaluation and Management of Functional Dyspepsia. *American Family Physician*, 83: 547-552.
Narrative Review
- Lozoya-Gonzalez, D., Farca-Belsaguy, A., Pelaez-Luna, M., Vazquez-Ballesteros, E., Gonzalez-Galeote, E. & Salceda-Otero, J. (2009) [Endoscopic mucosal resection due to adenocarcinoma of the esophagus caused by Barrett's esophagus.]. [Spanish]. *Revista de Gastroenterologia de Mexico*, 74: 383-386.
Not in PICO
- Luft, A. & Pons, Y. (2011) Signs of upper airways digestive tract cancers and the general practitioner. Study of the practices by a Script Test Concordance. [French]. *Revue de Laryngologie Otologie Rhinologie*, 132.
Not in PICO
- Luman, W. & Ng, K. L. (2003) Audit of Investigations in Patients with Iron Deficiency Anaemia. *Singapore Medical Journal*, 44: October.
Not in PICO
- Macdonald, C. E., Wicks, A. C. & Playford, R. J. (1997) Ten years' experience of screening patients with Barrett's oesophagus in a university teaching hospital. *Gut*, 41: 303-307.
Not in PICO
- Macdonald, S., Macleod, U., Campbell, N. C., Weller, D. & Mitchell, E. (2006) Systematic review of factors influencing patient and practitioner delay in diagnosis of upper gastrointestinal cancer. *British Journal of Cancer*, 94: 1272-1280.
Not in PICO
- Madani, A., Sowerby, L., Gregor, J. C., Wong, E. & Fung, K. (2010) Detecting the other reflux disease. *Journal of Family Practice*, 59: February.
Narrative review
- Madsen, L. G. & Bytzer, P. (2000) The value of alarm features in identifying organic causes of dyspepsia. [Review] [106 refs]. *Canadian Journal of Gastroenterology*, 14: 713-720.
Narrative Review
- Malats, N., Belloc, J., Gallen, M. & Porta, M. (1995) Disagreement between hospital medical records and a structured patient interview on the type and date of the first symptom in cancers of the digestive tract. *Revue d'Epidemiologie et de Sante Publique*, 43: 533-540.
Not in PICO
- Mankodi, S., Hayee, B. H., O'Donohue, J. & Reffitt, D. (2010) Anaemia investigation in practice: inappropriate, cost inefficient with a risk of missing gastrointestinal cancer. Can we improve? *Clinical Medicine*, 10: 115-118.
Not in PICO
- Mardosiene, S. & Qvist, P. (2002) Selection of patients referred for endoscopy from general practice. [Danish]. *Ugeskrift for Laeger*, 164: 11.
Not in PICO
- Mariscal, M., Llorca, J., Prieto, D. & Delgado-Rodriguez, M. (2001) Determinants of the interval between the onset of symptoms and diagnosis in patients with digestive tract cancers. *Cancer*

- Detection and Prevention*, 25: 2001.
Not in PICO
- Mariscal, M., Llorca, J., Prieto-Salceda, D., Palma, S. & Delgado-Rodriguez, M. (2003) Determinants of the interval between diagnosis and treatment in patients with digestive tract cancer. *Oncology Reports*, 10: -2Apr.
Not in PICO
- Marmo, R., Rotondano, G., Piscopo, R., Bianco, M. A., Russo, P., Capobianco, P. & Cipolletta, L. (2005) Combination of age and sex improves the ability to predict upper gastrointestinal malignancy in patients with uncomplicated dyspepsia: A prospective multicentre database study. *American Journal of Gastroenterology*, 100: 784-791.
Not in PICO
- Martin, R. & Leventhal, H. Symptom perception and health care-seeking behavior. [References]. 299-328. 2004.
Narrative review
- Martinez, S. D., Malagon, I. B., Garewal, H. S., Cui, H. & Fass, R. (2003) Non-erosive reflux disease (NERD)--acid reflux and symptom patterns. *Alimentary Pharmacology & Therapeutics*, 17: 537-545.
Not in PICO
- Mason, J. M., Delaney, B., Moayyedi, P., Thomas, M. & Walt, R. (2005) Managing dyspepsia without alarm signs in primary care: New national guidance for England and Wales. *Alimentary Pharmacology and Therapeutics*, 21: 01.
Paper on NICE Dyspepsia guideline
- Matsha, T., Stepien, A., Blanco-Blanco, E., Brink, L. T., Lombard, C. J., Van, R. S. & Erasmus, R. T. (2006) Self-induced vomiting -- risk for oesophageal cancer? *South African Medical Journal.Suid-Afrikaanse Tydskrif Vir Geneeskunde*, 96: 209-212.
Not in PICO
- Matsueda, K. (1998) Guidelines for dyspepsia treatment in Japan. *Clinical Therapeutics*, 20.
Guideline
- McCulloch, P., Brown, P., Martin, B. & Williams, E. (2003) The effects of an awareness-raising program for patients and primary care physicians on the early detection of gastro-oesophageal cancer. *Surgery*, 133: 154-161.
Not in PICO
- McIntyre, A. S. & Long, R. G. (1993) Prospective survey of investigations in outpatients referred with iron deficiency anaemia. *Gut*, 34: 1102-1107.
Not in PICO
- McLeman, L., McKinlay, A. W. & El-Omar, E. M. (2006) GP management of dyspepsia. [Review] [24 refs]. *Practitioner*, 250: 134.
Narrative Review
- Meineche-Schmidt, V. & Jorgensen, T. (2003) "Alarm symptoms" in dyspepsia: How does the general practitioner investigate? *Scandinavian Journal of Primary Health Care*, 21: December.
Same data as Meineche-Schmidt (2002)
- Melleney, E. M., Subhani, J. M. & Willoughby, C. P. (2004) Dysphagia referrals to a district general hospital gastroenterology unit: hard to swallow. *Dysphagia*, 19: 78-82.
Not in PICO
- Melleney, E. M. A. & Willoughby, C. P. (2002) Audit of a nurse endoscopist based one stop dyspepsia clinic. *Postgraduate Medical Journal*, 78.
Not in PICO
- Messmann, H. (2001) Squamous cell cancer of the oesophagus. *Best Practice and Research: Clinical Gastroenterology*, 15.
Narrative Review

- Minoo, A. & Nader, R. (2013) Acquired factor V inhibitor developing in a patient with esophageal squamous cell carcinoma. *Blood Coagulation & Fibrinolysis*, 24: 97-99.
Not in PICO
- Morris, D. L. & Deacon, J. (2009) The one stop swallowing shop: A better choice for suspected cancer. *Gut.Conference: Annual Meeting of the British Society of Gastroenterology Glasgow United Kingdom.Conference Start: 20090323 Conference End: 20090326.Conference Publication: (var.pagings)*, 58: April.
Not in PICO
- Mudawi, H. M. Y., Mahmoud, A. O. A., El Tahir, M. A., Suliman, S. H. & Ibrahim, S. Z. (2010) Use of endoscopy in diagnosis and management of patients with dysphagia in an African setting. *Diseases of the Esophagus*, 23: April.
Not in PICO
- Murakami, T., Tiwari, P., Musuku, S., Cunningham, J., Pugh, J. & Bhattacharyya, A. (1111) Dig deep to find the answer: The utility of endoscopic ultrasound with fine needle aspiration for a difficult diagnosis of esophageal cancer in chronic mucosal candidiasis. *American Journal of Gastroenterology.Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States.Conference Start: 20131011 Conference End: 20131016.Conference Publication: (var.pagings)*, 108: October.
Not in PICO
- Muris, J. W. M., Starmans, R., Pop, P., Crebolder, H. F. J. M. & Knottnerus, J. A. (1994) Discriminant value of symptoms in patients with dyspepsia. *Journal of Family Practice*, 38.
Not in PICO
- Murray, I. A., Palmer, J., Waters, C. & Dalton, H. R. (2012) Predictive value of symptoms and demographics in diagnosing malignancy or peptic stricture. *World Journal of Gastroenterology*, 18: 4357-4362.
Not in PICO
- Musana, A. K., Yale, S. H. & Lang, K. A. (2006) Managing dyspepsia in a primary care setting. *Clinical Medicine and Research*, 4: December.
Narrative Review
- Mutrie, C. J., Donahue, D. M., Wain, J. C., Wright, C. D., Gaissert, H. A., Grillo, H. C., Mathisen, D. J. & Allan, J. S. (2005) Esophageal leiomyoma: A 40-year experience. *Annals of Thoracic Surgery*, 79: April.
Not in PICO
- Nekhlyudov, L. & Latosinsky, S. (2010) The interface of primary and oncology specialty care: From symptoms to diagnosis. *Journal of the National Cancer Institute - Monographs.(40) (pp 11-17), 2010.Date of Publication: 2010..*
Narrative Review
- Netzer, P., Lazarevic, V. & Hammer, B. (1996) Value of abdominal ultrasonography in deep venous thrombosis. Retrospective study of 104 patients. [German]. *Schweizerische Medizinische Wochenschrift.Supplementum*, 79.
Not in PICO
- Neumann, H., Monkemuller, K., Kandulski, A. & Malfertheiner, P. (2008) Dyspepsia and IBS symptoms in patients with NERD, ERD and Barrett's esophagus. *Digestive Diseases*, 26: May.
Not in PICO
- Nord, H. J. (2004) Extraesophageal symptoms: what role for the proton pump inhibitors?. [Review] [42 refs]. *American Journal of Medicine*, 117: Suppl-62S.
Narrative Review
- Ntoumazios, S. K., Voulgari, P. V., Potsis, K., Koutis, E., Tsifetaki, N. & Assimakopoulos, D. A. (2006) Esophageal Involvement in Scleroderma: Gastroesophageal Reflux, the Common Problem. *Seminars in Arthritis and Rheumatism*, 36: December.
Not in PICO

- Numans, M. E., van der Graaf, Y., de Wit, N. J. & de Melker, R. A. (2001) How useful is selection based on alarm symptoms in requesting gastroscopy? An evaluation of diagnostic determinants for gastro-oesophageal malignancy. *Scandinavian Journal of Gastroenterology*, 36: 437-443.
Not in PICO
- Ogawa, F., Genevay, M., Lisovsky, M., Mino-Kenudson, M., Deshpande, V., Odze, R. D. & Lauwers, G. Y. (2009) Natural history of sporadic gastric dysplasia in the U.S.A: Follow up study of 54 patients. *Laboratory Investigation.Conference: 98th Annual Meeting of the United States and Canadian Academy of Pathology Boston, MA United States.Conference Start: 20090307 Conference End: 20090313.Conference Publication: (var.pagings)*, 89: January.
Not in PICO
- Olihtselvan, A. & Muller, A. F. (2003) Ageing and the gastrointestinal tract. *CME Journal Gastroenterology, Hepatology and Nutrition*, 5.
Narrative Review
- Oudega, R., Moons, K. G. M., Nieuwenhuis, H. K., van Nierop, F. L. & Hoes, A. W. (2006) Deep vein thrombosis in primary care: Possible malignancy? *British Journal of General Practice*, 56: September.
Not in PICO (no OG cancers and included in other reviews)
- Ozcelik, C., Onat, S., Dursun, M. & Arslan, A. (2004) Fibrovascular polyp of the esophagus: diagnostic dilemma. *Interactive Cardiovascular & Thoracic Surgery*, 3: 260-262.
Not in PICO
- Padula, D., Lenti, M. V., Di, S. M., Miceli, E. & Corazza, G. R. (2013) A youngwoman with dysphagia. *Digestive and Liver Disease*, 45: S155-S156.
Not in PICO
- Panter, S. J., Bramble, M. G., O'Flanagan, H. & Hungin, A. P. (2004) Urgent cancer referral guidelines: a retrospective cohort study of referrals for upper gastrointestinal adenocarcinoma. *British Journal of General Practice*, 54: 611-613.
Not in PICO
- Park, J. S., Park, D. I., Park, S. K., Choi, J. S., Kim, Y. H., Chang, D. K., Son, H. J., Kim, J. E., Kim, J. O., Lee, S. H., Kim, H. S., Sin, J. E., Lee, S. G., Lee, S.-Y., Park, S. J., Park, C. H., Baek, I. H., Jang, B. I., Jeon, Y. T. & Huh, K. C. (2009) Endoscopic evaluation of significant gastrointestinal lesions in patients with iron deficiency with and without anaemia: A Korean Association for the Study of Intestinal Disease Study. *Internal Medicine Journal*, 39: July.
Not in PICO
- Parvin, S. & Firouz, S. (2003) A Study of 415 Cases of Esophageal Carcinoma in Northwest of Iran. *Medical Journal of Malaysia*, 58: August.
Not in PICO
- Peck, J., Martin, J., Li, F., Latchana, N., Bekaii-Saab, T., El-Dika, S. & Walker, J. (1111) Endoscopic ultrasound is of limited benefit in the management of obstructing esophageal cancers. *American Journal of Gastroenterology.Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States.Conference Start: 20131011 Conference End: 20131016.Conference Publication: (var.pagings)*, 108: October.
Not in PICO
- Pengelly, S., Fabricius, M., McMenamin, D., Wu, E., Metzner, M., Lewis, S. J. & Hosie, K. B. (2013) Attendance at iron deficiency anaemia clinic: audit of outcomes 5 years on. *Colorectal Disease*, 15: 423-427.
Not in PICO
- Pera, M., Trastek, V. F., Carpenter, H. A., Allen, M. S., Deschamps, C. & Pairolero, P. C. (1992) Barrett's esophagus with high-grade dysplasia: an indication for esophagectomy? *Annals of Thoracic Surgery*, 54: 199-204.
Not in PICO

- Peracchia, A., Bonavina, L., Pavanello, M., Montorsi, M., Ruol, A. & Segalin, A. (1994) Adenocarcinoma in Barrett's esophagus: long-term results of curative resection. [Italian]. *Chirurgia Italiana*, 46.
Not in PICO
- Peters, F. T. & Kleibeuker, J. H. (1993) Barrett's oesophagus and carcinoma. Recent insights into its development and possible prevention. [Review] [86 refs]. *Scandinavian Journal of Gastroenterology - Supplement*, 200: 59-64.
Narrative Review
- Phull, P. S., Salmon, C. A., Park, K. G., Rapson, T., Thompson, A. M. & Gilbert, F. J. (2006) Age threshold for endoscopy and risk of missing upper gastrointestinal malignancy--data from the Scottish audit of gastric and oesophageal cancer. *Alimentary Pharmacology & Therapeutics*, 23: 229-233.
Not in PICO
- Phung, N., Kalantar, J. & Talley, N. J. (1998) Management of dyspepsia in general practice. *Modern Medicine of Australia*, 41.
Narrative Review
- Pierzchajlo, R. P. J., Ackermann, R. J. & Vogel, R. L. (1998) Esophagogastroduodenoscopy performed by a family physician: A case series of 793 procedures. *Journal of Family Practice*, 46: January.
Not in PICO
- Polkowski, W., Polkowska, G. & Melko, J. (2001) Barrett oesophagus and adenocarcinoma of the oesophagus: Progress in the diagnosis and treatment at the end of XX century. [Polish]. *Gastroenterologia Polska*, 8.
Narrative Review
- Pons, Y., Luft, A. & Conessa, C. (2011) Alarm and detection signs of upper digestive and respiratory tract cancers. [French]. *Revue du Praticien*, 61: November.
Narrative Review
- Qureshi, N. A., Hallissey, M. T. & Fielding, J. W. (2007) Outcome of index upper gastrointestinal endoscopy in patients presenting with dysphagia in a tertiary care hospital - A 10 years review. *Bmc Gastroenterology*, 7.
Not in PICO
- Rasul, I. & Kandel, G. P. (2001) An approach to iron-deficiency anemia. *Canadian Journal of Gastroenterology*, 15.
Narrative Review
- Razorenov, L. V. (1980) [Diagnostic errors in esophageal cancer]. [Russian]. *Voprosy Onkologii*, 26: 35-38.
Not in PICO
- Read, L., Pass, T. M. & Komaroff, A. L. (1982) Diagnosis and treatment of dyspepsia: a cost-effectiveness analysis (Structured abstract). *Medical Decision Making*, 2: 415-438.
Not in PICO
- Reid, B. J. (1991) Barrett's esophagus and esophageal adenocarcinoma. [Review] [124 refs]. *Gastroenterology Clinics of North America*, 20: 817-834.
Narrative Review
- Reid, B. J., Kostadinov, R. & Maley, C. C. (2011) New strategies in Barrett's esophagus: Integrating clonal evolutionary theory with clinical management. *Clinical Cancer Research*, 17: 3512-3519.
Narrative Review
- Reyes, C. V. & Wang, T. (1981) Primary adenocarcinoma of the esophagus: A review of 12 cases. *Journal of Surgical Oncology*, 18.
Not in PICO
- Ribet, M. E. & Mensier, E. A. (1992) Reflux esophagitis and carcinoma. *Surgery, Gynecology & Obstetrics*, 175: 121-125.
Not in PICO

- Richert, Z. & Robaszekiewicz, M. (2008) [Gastroesophageal reflux disease and malignancy]. [French]. *Revue du Praticien*, 58: 1414-1415.
Narrative Review
- Rivera, C. F., Serra, C. M., Carretero, S. A., Uribes, F. R., Bonias Perez-Fuster, M. D. & Barrera, R., I (2002) Characteristics of diagnoses of malignant neoplasms in primary care. [Spanish]. *Atencion primaria / Sociedad Espanola de Medicina de Familia y Comunitaria*, 29: 30.
Not in PICO
- Robinson, M. (2001) Dyspepsia: Challenges in diagnosis and selection of treatment. *Clinical Therapeutics*, 23: 1130-1144.
Narrative Review
- Roorda, A. K., Marcus, S. N. & Triadafilopoulos, G. (2011) Algorithmic approach to patients presenting with heartburn and epigastric pain refractory to empiric proton pump inhibitor therapy. *Digestive Diseases & Sciences*, 56: 2871-2878.
Not in PICO
- Rothwell, J. F., Feehan, E., Reid, I., Walsh, T. N. & Hennessy, T. P. (1997) Delay in treatment for oesophageal cancer. *British Journal of Surgery*, 84: 690-693.
Not in PICO
- Rueth, N. M., Shaw, D., D'Cunha, J., Cho, C., Maddaus, M. A. & Andrade, R. (2012) A multimodality approach for palliation of symptomatic malignant dysphagia. *Annals of Surgical Oncology. Conference: 65th Annual Cancer Symposium of the Society of Surgical Oncology Orlando, FL United States. Conference Start: 20120321 Conference End: 20120324. Conference Publication: (var.pagings)*, 19: February.
Not in PICO
- Ryan, J. & Murkies, A. (2006) Diagnosis of upper gastrointestinal malignancy. [Review] [3 refs]. *Australian Family Physician*, 35: 200-201.
Narrative Review
- Sadler, G. J., Jothimani, D., Zanetto, U. & Anderson, M. R. (2009) The effect of ethnicity on the presentation and management of oesophageal and gastric cancers: a UK perspective. *European Journal of Gastroenterology & Hepatology*, 21: 996-1000.
Not in PICO
- Salo, M., Collin, P., Kyronpalo, S., Rasmussen, M., Huhtala, H. & Kaukinen, K. (2008) Age, symptoms and upper gastrointestinal malignancy in primary care endoscopy. *Scandinavian Journal of Gastroenterology*, 43: 122-127.
Not in PICO
- Saxena, P. & Canto, M. I. (2013) Red flag imaging techniques in Barrett's Esophagus. *Gastrointestinal Endoscopy Clinics of North America*, 23: 535-547.
Not in PICO
- Schmidt, L. W., Dean, P. J. & Wilson, R. T. (1986) Superficially invasive squamous cell carcinoma of the esophagus. A study of seven cases in Memphis, Tennessee. *Gastroenterology*, 91: 1456-1461.
Not in PICO
- Schumacher, B. & Neuhaus, H. (2001) Precancerous lesions and early cancer in the upper gastrointestinal tract. [German]. *Deutsche Medizinische Wochenschrift*, 126: 08.
Not in PICO
- Schumpelick, V., Dreuw, B., Ophoff, K. & Fass, J. (1979) [Adenocarcinoma of the esophagogastric junction: association with Barrett esophagus and gastroesophageal reflux--surgical results in 122 patients]. [German]. *Leber, Magen, Darm*, 26: 75-76.
Not in PICO
- Schweigert, M., Dubecz, A. & Stein, H. J. (2013) Oesophageal cancer--an overview. [Review]. *Nature Reviews Gastroenterology & Hepatology*, 10: 230-244.
Narrative review

- Seifert, B., Vojtiskova, J., Charvatova, E. & Koudelka, T. (2006) Management of gastroesophageal reflux disease (GERD) in primary care. [Czech]. *Ceska a Slovenska Gastroenterologie a Hepatologie*, 60.
Not in PICO (only 3593/9759 registered patients followed up > 12 months, and only 1724 had endoscopy; outcome unclear)
- Seitz, J. F., Monges, G., Navarro, P., Giovannini, M. & Gauthier, A. (1990) [Endoscopic detection of dysplasia and subclinical cancer of the esophagus. Results of a prospective study using toluidine blue vital staining in 100 patients with alcoholism and smoking]. [French]. *Gastroenterologie Clinique et Biologique*, 14: 15-21.
Not in PICO
- Selgrad, M., Kandulski, A. & Malfertheiner, P. (2008) Dyspepsia and Helicobacter pylori. [Review] [45 refs]. *Digestive Diseases*, 26: 210-214.
Narrative Review
- Shaheen, N. & Ransohoff, D. F. (2002) Gastroesophageal reflux, Barrett esophagus, and esophageal cancer - Clinical applications. *Jama-Journal of the American Medical Association*, 287: 1982-1986.
Narrative Review
- Sharma, P., Chey, W., Hunt, R., Laine, L., Malfertheiner, P. & Wani, S. (2009) Endoscopy of the esophagus in gastroesophageal reflux disease: are we losing sight of symptoms? Another perspective. *Diseases of the Esophagus*, 22: 461-466.
Narrative Review
- Sherman, P. (2009) A global, evidence-based consensus on the definition of gastroesophageal reflux disease (GERD) in the pediatric population. *Canadian Journal of Gastroenterology.Conference: Canadian Digestive Diseases Week 2009 Banff, AB Canada.Conference Start: 20090227 Conference End: 20090302.Conference Publication: (var.pagings)*, 23.
Not in PICO
- Shimizu, M., Zaninotto, G., Nagata, K., Graham, D. Y. & Lauwers, G. Y. (2013) Esophageal squamous cell carcinoma with special reference to its early stage. [Review]. *Best Practice & Research in Clinical Gastroenterology*, 27: 171-186.
Narrative review
- Siersema, P. D. (2008) Esophageal cancer. [Review] [60 refs]. *Gastroenterology Clinics of North America*, 37: 943-964.
Narrative Review
- Siewert, J. R. & Stein, H. J. (1997) Barrett's cancer: indications, extent, and results of surgical resection. [Review] [54 refs]. *Seminars in Surgical Oncology*, 13: 245-252.
Narrative Review
- Singh, A., Siddiqui, U., Konda, V., Xiao, S.-Y. & Waxman, I. (1111) Use of high-definition narrow band imaging with magnification to successfully identify early esophageal squamous cancer, predict depth of invasion, and guide endoscopic therapy. *American Journal of Gastroenterology.Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States.Conference Start: 20131011 Conference End: 20131016.Conference Publication: (var.pagings)*, 108: October.
Not in PICO
- Small, M., Vidyarthi, G., Boyd, W. & Haley, J. A. (2010) Amyloidosis in a patient with maltoma of stomach. *American Journal of Gastroenterology.Conference: 75th Annual Scientific Meeting of the American College of Gastroenterology San Antonio, TX United States.Conference Start: 20101015 Conference End: 20101020.Conference Publication: (var.pagings)*, 105: October.
Not in PICO
- Smith, G. (1936) Red flags are key to managing dyspepsia. [Review] [8 refs]. *Practitioner*, 251: 31-34.
Narrative review
- Smithers, B. M., Fahey, P. P., Corish, T., Gotley, D. C., Falk, G. L., Smith, G. S., Kiroff, G. K., Clouston, A. D., Watson, D. I. & Whiteman, D. C. (2010) Symptoms, investigations and management of

patients with cancer of the oesophagus and gastro-oesophageal junction in Australia. *Medical Journal of Australia*, 193: 572-577.

Not in PICO

Solaymani-Dodaran, M., Logan, R. F., West, J., Card, T. & Coupland, C. (2004) Risk of oesophageal cancer in Barrett's oesophagus and gastro-oesophageal reflux. *Gut*, 53: 1070-1074.

Not in PICO

Soll, A. H. & Fass, R. (2003) Gastroesophageal reflux disease: presentation and assessment of a common, challenging disorder. [Review] [39 refs]. *Clinical Cornerstone*, 5: 2-14.

Narrative Review

Sorbi, D. & Fleischer, D. E. (2003) Nonsurgical approaches to esophageal malignancy. [Review] [49 refs]. *Current Gastroenterology Reports*, 5: 213-220.

Narrative Review

Soumekh, A., Schnoll-Sussman, F. H. & Katz, P. O. (2014) Reflux and Acid Peptic Diseases in the Elderly. *Clinics in Geriatric Medicine*, 30: 29-41.

Narrative review

Soumekh, A., Schnoll-Sussman, F. H. & Katz, P. O. (2014) - Reflux and acid peptic diseases in the elderly. [Review]. - *Clinics in Geriatric Medicine*, 30: 29-41.

Narrative review
Schlansky, B., DiMarino, A. J., Loren, D., Infantolino, A., Kowalski, T. & Cohen, S. (2006) A survey of oesophageal cancer: pathology, stage and clinical presentation. *Alimentary Pharmacology & Therapeutics*, 23: 587-593.

Not in PICO

Spechler, S. J. (1949) Esophageal complications of gastroesophageal reflux disease: presentation, diagnosis, management, and outcomes. [Review] [46 refs]. *Clinical Cornerstone*, 5: 41-48.

Narrative Review

Spechler, S. J., Jain, S. K., Tendler, D. A. & Parker, R. A. (2002) Racial differences in the frequency of symptoms and complications of gastro-oesophageal reflux disease. *Alimentary Pharmacology & Therapeutics*, 16: 1795-1800.

Not in PICO

Spelsberg, F. W., Hoffmann, R. T., Lang, R. A., Winter, H., Weidenhagen, R., Reiser, M., Jauch, K. W. & Trumm, C. (2013) CT fluoroscopy guided percutaneous gastrostomy or jejunostomy without (CT-PG/PJ) or with simultaneous endoscopy (CT-PEG/PEJ) in otherwise untreatable patients. *Surgical Endoscopy*, 27: 1186-1195.

Not in PICO

Spiegel, B. M. R., Farid, M., Van Oijen, M. G. H., Laine, L., Howden, C. W. & Esrailian, E. (2009) Adherence to best practice guidelines in dyspepsia: A survey comparing dyspepsia experts, community gastroenterologists and primary-care providers. *Alimentary Pharmacology and Therapeutics*, 29: April.

Not in PICO

Stanghellini, V., Tosetti, C., Barbara, G., De, G. R., Salvioli, B. & Corinaldesi, R. (2000) Review article: The continuing dilemma of dyspepsia. *Alimentary Pharmacology and Therapeutics, Supplement*, 14.

Narrative Review

Starkov, I. G., Solodinina, E. N., Konstantinova, M. M., Shishin, K. V., Kurushkina, N. A. & Gordienko, E. N. (2013) [Synchronous esophageal lesions: early cancer and gastrointestinal tumor]. [Russian]. *Khirurgiia*, 58-60.

In Russian. Not enough information can be extracted to ascertain relevance.

Steele, G. H. (1996) Cost-effective management of dyspepsia and gastroesophageal reflux disease. *Primary Care - Clinics in Office Practice*, 23.

Narrative review

Stein, E. & Katz, P. O. (2009) Reflux monitoring. *Reviews in gastroenterological disorders*, 9.

Narrative Review

- Stein, H. J. & Siewert, J. R. (1993) Barrett's esophagus: pathogenesis, epidemiology, functional abnormalities, malignant degeneration, and surgical management. [Review] [133 refs]. *Dysphagia*, 8: 276-288.
Narrative Review
- Stein, H. J., Feith, M. & Siewert, J. R. (2000) Malignant degeneration of Barrett's esophagus: clinical point of view. [Review] [42 refs]. *Recent Results in Cancer Research*, 155: 42-53.
Narrative Review
- Streitz, J. M., Jr., Ellis, F. H., Jr., Gibb, S. P., Balogh, K. & Watkins E Jr (1991) Adenocarcinoma in Barrett's esophagus. A clinicopathologic study of 65 cases. *Annals of Surgery*, 213: 122-125.
Not in PICO
- Streitz, J., Ellis, J., Gibb, S. P. & Heatley, G. M. (1995) Achalasia and squamous cell carcinoma of the esophagus: Analysis of 241 patients. *Annals of Thoracic Surgery*, 59.
Not in PICO
- Subramaniam, S., Goodchild, G. & Besherdas, K. (2014) Odynophagia - A symptom worth asking about? *Gut*, 63: A60-A61.
Not in PICO
- Sugimachi, K., Ohno, S., Matsuda, H., Mori, M., Matsuoka, H. & Kuwano, H. (1989) Clinicopathologic study of early stage esophageal carcinoma. *British Journal of Surgery*, 76: 759-763.
Not in PICO
- Sugimachi, K., Ohno, S., Matsuda, H., Mori, M., Matsuoka, H. & Kuwano, H. (1989) Clinicopathologic study of early stage esophageal carcinoma. *Surgery*, 105: 706-710.
Not in PICO
- Sun, X., Wang, J. & Yang, G. (2012) Surgical treatment of esophageal leiomyoma larger than 5 cm in diameter: A case report and review of the literature. *Journal of Thoracic Disease*, 4: 323-326.
Not in PICO
- Sundar, N., Muraleedharan, V., Pandit, J., Green, J. T., Crimmins, R. & Swift, G. L. (2006) Does endoscopy diagnose early gastrointestinal cancer in patients with uncomplicated dyspepsia? *Postgraduate Medical Journal*, 82: 52-54.
Not in PICO
- Swisher, S. G., Roth, J. A. & Putnam, J. (1995) Diagnosis and management of benign esophageal tumors. *Cancer Bulletin*, 47.
Narrative Review
- Talley, N. J. (1996) Modern management of dyspepsia. *Australian Family Physician*, 25: Jan.
Narrative Review
- Talley, N. J., Axon, A., Bytzer, P., Holtmann, G., Lam, S. K. & van Zanten, S. V. (1999) Management of uninvestigated and functional dyspepsia: a working party report for the World Congresses of Gastroenterology 1998. *Alimentary Pharmacology & Therapeutics*, 13: 1135-1148.
Guideline
- Talley, N. J. (2004) What the physician needs to know for correct management of gastro-oesophageal reflux disease and dyspepsia. *Alimentary Pharmacology & Therapeutics*, 20: 23-30.
Narrative Review
- Taylor, A., Stapley, S. & Hamilton, W. (2012) Jaundice in primary care: a cohort study of adults aged >45 years using electronic medical records. *Family Practice*, 29: 416-420.
Not in PICO
- Tentzeris, V., Lake, B., Cherian, T., Milligan, J. & Sigurdsson, A. (2011) Poor awareness of symptoms of oesophageal cancer. *Interactive Cardiovascular & Thoracic Surgery*, 12: 32-34.
Not in PICO
- Thrift, A. P., Kramer, J. R., Qureshi, Z., Richardson, P. A. & El-Serag, H. B. (2013) Age at onset of GERD symptoms predicts risk of Barrett's esophagus. *American Journal of Gastroenterology*, 108: 915-922.
Not in PICO

- Thuler, F. P., Forones, N. M. & Ferrari, A. P. (2006) [Advanced esophageal cancer: still a delayed diagnosis]. [Portuguese]. *Arquivos de Gastroenterologia*, 43: 206-211.
Not in PICO
- Tosetti, C. (1998) Management of dyspepsia in general practice: A critical assessment. *Pharmacoeconomics*, 14: 1998.
Narrative review
- Towpik, E. (1982) [Early symptoms of cancer of the esophagus and cardia]. [Polish]. *Wiadomosci Lekarskie*, 35: 1209-1212.
Not in PICO
- Tutuian, R. (2006) Update in the diagnosis of gastroesophageal reflux disease. [Review] [20 refs]. *Journal of Gastrointestinal & Liver Diseases*, 15: 243-247.
Narrative Review
- Uno, K., Iijima, K., Koike, T., Ara, N., Hatta, W., Kusaka, G. & Shimosegawa, T. (2011) The direct measurement of non-acid reflux episodes in patients with or without squamous cell carcinoma by 24 hours pH-impedance monitoring. *Gastroenterology.Conference: Digestive Disease Week, DDW 2011 Chicago, IL United States.Conference Start: 20110507 Conference End: 20110510.Conference Publication: (var.pagings)*, 140: May.
Not in PICO
- Urquhart, J., Eisen, G., Faigel, D. O., Mattek, N., Holub, J. & Lieberman, D. A. (2009) A closer look at same-day bidirectional endoscopy. *Gastrointestinal Endoscopy*, 69: 271-277.
Not in PICO
- Urquhart, P., DaCosta, R. & Marcon, N. (1111) Endoscopic mucosal imaging of gastrointestinal neoplasia in 2013. *Current gastroenterology reports*, 15: Jul.
Narrative review
- Vaira, D. (1996) How to manage the dyspeptic patient. *Helicobacter*, 1: 261-262.
Narrative Review
- Vakil, N. (2003) Review article: test and treat or treat and test in reflux disease?. [Review] [17 refs]. *Alimentary Pharmacology & Therapeutics*, 17: Suppl-9.
Narrative Review
- Vakil, N., Moayyedi, P., Fennerty, M. B. & Talley, N. J. (2006) Limited value of alarm features in the diagnosis of upper gastrointestinal malignancy: Systematic review and meta-analysis. *Gastroenterology*, 131: 390-401.
Most populations of included studies not in PICO, have checked for relevant papers which will be included separately.
- Vakil, N., Malfertheiner, P., Salis, G., Flook, N. & Hongo, M. (2008) An international primary care survey of GERD terminology and guidelines. *Digestive Diseases*, 26: 231-236.
Not in PICO
- Vakil, N. B., Halling, K., Wernersson, B. & Ohlsson, L. (2011) Silent unrecognized GERD in an unselected population of primary care patients with upper GI symptoms. *Gastroenterology.Conference: Digestive Disease Week, DDW 2011 Chicago, IL United States.Conference Start: 20110507 Conference End: 20110510.Conference Publication: (var.pagings)*, 140: May.
Not in PICO
- Van Oijen, M. G. H., Josemanders, D. F. G. M., Laheij, R. J. F., van Rossum, L. G. M., Tan, A. C. I. T. & Jansen, J. B. M. J. (2006) Gastrointestinal disorders and symptoms: Does body mass index matter? *Netherlands Journal of Medicine*, 64: February.
Not in PICO
- Vasavi, M., Kiran, V., Ravishankar, B., Prabhakar, B., Ahuja, Y. R. & Hasan, Q. (2010) Microsatellite instability analysis and its correlation with hMLH1 repair gene hypermethylation status in esophageal pathologies including cancers. *Cancer Biomarkers: Section A of Disease Markers*, 7: 1-

10.

Not in PICO

Veldhuyzen Van Zanten, S. J. O., Thomson, A. B. R., Barkun, A. N., Armstrong, D., Chiba, N., White, R. J., Escobedo, S. & Sinclair, P. (2006) The prevalence of Barrett's oesophagus in a cohort of 1040 Canadian primary care patients with uninvestigated dyspepsia undergoing prompt endoscopy. *Alimentary Pharmacology and Therapeutics*, 23: March.

Not in PICO

Voltaggio, L., Montgomery, E. A. & Lam-Himlin, D. (2011) A clinical and histopathologic focus on Barrett esophagus and Barrett-related dysplasia. [Review]. *Archives of Pathology & Laboratory Medicine*, 135: 1249-1260.

Narrative Review

von Rahden, B. H., Stein, H. J. & Siewert, J. R. (2003) Barrett's esophagus and Barrett's carcinoma. [Review] [66 refs]. *Current Oncology Reports*, 5: 203-209.

Narrative Review

Vos, B., Rozema, T., Miller, R. C., Hendlisz, A., Van Laethem, J. L., Khanfir, K., Weber, D. C., El Nakadi, I. & Van Houtte, P. (2011) Small cell carcinoma of the esophagus: a multicentre Rare Cancer Network study. *Diseases of the Esophagus*, 24: 258-264.

Not in PICO

Voutilainen, M., Mantynen, T., Mauranen, K., Kunnamo, I. & Juhola, M. (2005) Is it possible to reduce endoscopy workload using age, alarm symptoms and H. pylori as predictors of peptic ulcer and oesophagogastric cancers? *Digestive & Liver Disease*, 37: 526-532.

Not in PICO

Wang, J., Liu, F., Gao, H., Wei, W., Zhang, X., Liang, Y. & Cheng, Y. (2008) The symptom-to-treatment delay and stage at the time of treatment in cancer of esophagus. *Japanese Journal of Clinical Oncology*, 38: February.

Not in PICO

Wang, L. D., Zheng, S., Zheng, Z. Y. & Casson, A. G. (2003) Primary adenocarcinomas of lower esophagus, esophagogastric junction and gastric cardia: in special reference to China. [Review] [151 refs]. *World Journal of Gastroenterology*, 9: 1156-1164.

Narrative Review

Watson, A. & Galloway, J. (2014) Heartburn, Barrett's oesophagus and cancer: implications for primary care. *British Journal of General Practice*, 64: 120.

Editorial material

Weiser, H. F., Lange, R. & Feussner, H. (1986) How can we diagnose the early stage of esophageal cancer? Diagnosis of early esophageal cancer. *Endoscopy*, 18: 1986.

Not in PICO

Weiser, M. A., Cabanillas, M., Vu, K., Tamm, E. P., Wallace, M. J., Escalante, C. P. & Bresalier, R. S. (2005) Diagnostic evaluation of patients with a high suspicion of malignancy: Comorbidities and clinical predictors of cancer. *American Journal of the Medical Sciences*, 330: July.

Not in PICO

West, R. L., Hirsch, D. P., Bartelsman, J. F., de, B. J., Ferwerda, G., Tytgat, G. N. & Boeckxstaens, G. E. (2002) Long term results of pneumatic dilation in achalasia followed for more than 5 years. *American Journal of Gastroenterology*, 97: 1346-1351.

Not in PICO

Westbrook, J. I., McIntosh, J. H. & Duggan, J. M. (2001) Accuracy of provisional diagnoses of dyspepsia in patients undergoing first endoscopy. *Gastrointestinal Endoscopy*, 53: 283-288.

Not in PICO

Westhoff, B., Brotze, S., Weston, A., McElhinney, C., Cherian, R., Mayo, M. S., Smith, H. J. & Sharma, P. (2005) The frequency of Barrett's esophagus in high-risk patients with chronic GERD. *Gastrointestinal Endoscopy*, 61: February.

Not in PICO

- Wild, C. P. & Hardie, L. J. (2003) Reflux, Barrett's oesophagus and adenocarcinoma: burning questions. [Review] [112 refs]. *Nature Reviews.Cancer*, 3: 676-684.
Narrative Review
- Wilkins, W. E., Walker, J. & McNulty, M. R. (1984) The organisation and evaluation of an open-access dysphagia clinic. *Annals of the Royal College of Surgeons of England*, 66.
Not in PICO
- Williams, B., Luckas, M., Ellingham, J. H., Dain, A. & Wicks, A. C. (1988) Do young patients with dyspepsia need investigation? *Lancet*, 2: 1349-1351.
Not in PICO
- Williams, J. F., Sontag, S. J., Schnell, T. & Leya, J. (2009) Non-cardiac chest pain: the long-term natural history and comparison with gastroesophageal reflux disease. *American Journal of Gastroenterology*, 104: 2145-2152.
Not in PICO
- Witt, T. R., Bains, M. S., Zaman, M. B. & Martini, N. (1983) Adenocarcinoma in Barrett's esophagus. *Journal of Thoracic & Cardiovascular Surgery*, 85: 337-345.
Not in PICO
- Wo, J. M., Mendez, C., Harrell, S., Joubran, R., Bressoud, P. F. & McKinney, W. P. (2004) Clinical impact of upper endoscopy in the management of patients with gastroesophageal reflux disease. *American Journal of Gastroenterology*, 99: 2311-2316.
Included in the Oesophageal tests papers to order
- Wojtkowiak, M., Wojtun, S., Blaszk, A., Gil, J., Dyrła, P. & Jalocho, L. (2009) [The importance of functional tests in gastroesophageal reflux disease diagnosing, monitoring and treatment]. [Review] [20 refs] [Polish]. *Polski Merkurusz Lekarski*, 26: 517-520.
Narrative Review
- Wolf, L. L., Ibrahim, R., Miao, C., Muyco, A., Hosseinipour, M. C. & Shores, C. (2012) Esophagogastroduodenoscopy in a public referral hospital in Lilongwe, Malawi: spectrum of disease and associated risk factors. *World Journal of Surgery*, 36: 1074-1082.
Not in PICO
- Wu, J., Pan, Y.-M., Wang, T.-T., Gao, D.-J. & Hu, B. (1111) Endotherapy versus surgery for early neoplasia in Barrett's esophagus: A meta-analysis. *Gastrointestinal Endoscopy*, 79: February.
Not in PICO
- Wu, J., Huang, C., Xiao, H., Tang, Q. & Cai, W. (2013) Weight loss and resting energy expenditure in male patients with newly diagnosed esophageal cancer. *Nutrition*, 29: 1310-1314.
Not in PICO
- Yantiss, R. K. (2010) Diagnostic challenges in the pathologic evaluation of Barrett esophagus. [Review]. *Archives of Pathology & Laboratory Medicine*, 134: 1589-1600.
Narrative Review
- Yekeler, E., Koca, T. & Vural, S. (2012) A rare cause of the cough: primary small cell carcinoma of esophagus-case report. *Case Reports in Medicine*, 2012: 870783.
Not in PICO
- Yentz, S. & Wang, T. D. (2011) Molecular imaging for guiding oncologic prognosis and therapy in esophageal adenocarcinoma. [Review]. *Hospital practice (1995) Hospital practice*, 39: 97-106.
Narrative Review
- Younes, Z. & Johnson, D. A. (1999) Diagnostic evaluation in gastroesophageal reflux disease. *Gastroenterology Clinics of North America*, 28.
Narrative Review
- Yun, G. W., Yang, Y. J., Song, I. C., Park, K. U., Baek, S. W., Yun, H. J., Kim, S., Jo, D. Y. & Lee, H. J. (2011) A prospective evaluation of adult men with iron-deficiency anemia in Korea. *Internal Medicine*, 50: 1371-1375.
Not in PICO

Zanca, A., Crucitti, P., Pandolfi, M., Montesano, M., Gabbrielli, A. & Coppola, R. (2006) Sems (self expanding metal stents) in palliation of esophageal cancer dysphagia. [Review] [21 refs]. *Rays*, 31: 67-71.

Narrative Review

Zimmerman, T. G. (2014) Common questions about Barrett esophagus. *American Family Physician*, 89: 92-98.

Narrative review

Zuccaro, G., Jr., Rice, T. W., Vargo, J. J., Goldblum, J. R., Rybicki, L. A., Dumot, J. A., Adelstein, D. J., Trolli, P. A. & Blackstone, E. H. (2005) Endoscopic ultrasound errors in esophageal cancer.[Erratum appears in Am J Gastroenterol. 2005 May;100(5):1216 Note: Zuccaro, Gregory [added]; Rybicki, Lisa [added]]. *American Journal of Gastroenterology*, 100: 601-606.

Not in PICO

Review question:

Which investigations of symptoms of suspected oesophageal cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

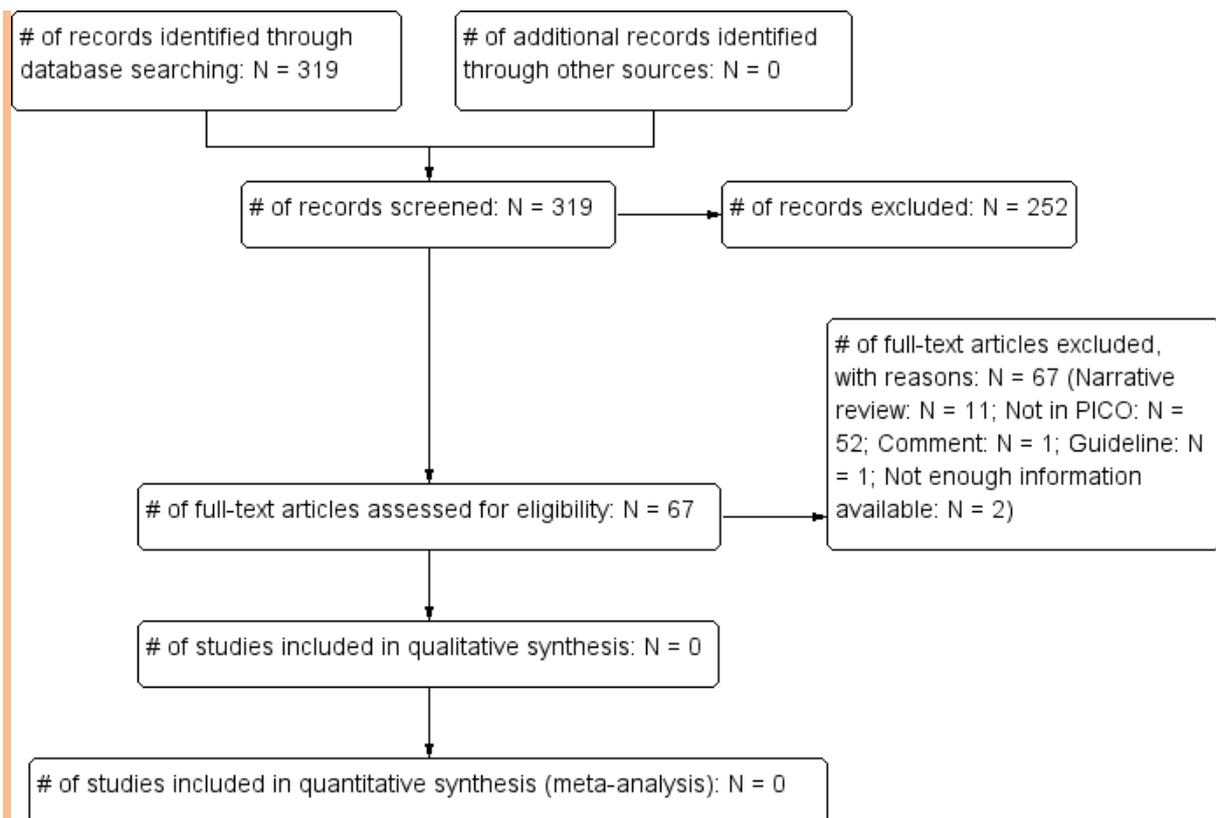
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	339	136	04/06/2013
<i>Premedline</i>	1980-2013	46	16	04/06/2013
<i>Embase</i>	1980-2013	675	142	05/06/2013
<i>Cochrane Library</i>	1980-2013	29	7	05/06/2013
<i>Psychinfo</i>	1980-2013	1	0	05/06/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	176	45	05/06/2013

Total References retrieved (after de-duplication): 294

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-20/08/2014	9	0	20/08/2014
<i>Premedline</i>	5/2013-20/08/2014	73	19	20/08/2014
<i>Embase</i>	5/2013-20/08/2014	34	10	20/08/2014
<i>Cochrane Library</i>	5/2013-20/08/2014	4	1	20/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	5/2013-20/08/2014	28	4	20/08/2014

Total References retrieved (after de-duplication): 25



Study results

No evidence was identified pertaining to the diagnostic accuracy of upper gastrointestinal endoscopy, barium swallow or chest x-ray in patients with suspected oesophageal cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

(2006) Dilemmas in managing Barrett's oesophagus. [Review] [72 refs]. *Drug & Therapeutics Bulletin*, 44: 69-72.

Narrative Review

(2007) PET for head and neck and oesophageal gastric (Project record). *Health Technology Assessment.Database*.

Not in PICO

Abou-Nader, L., Wilson, J. A. & Paleri, V. (2014) Transnasal oesophagoscopy: Diagnostic and management outcomes in a prospective cohort of 257 consecutive cases and practice implications. *Clinical Otolaryngology*, 39: 108-113.

Not in PICO

Ackermann, R. J. (1997) Performance of gastrointestinal tract endoscopy by primary care physicians - Lessons from the US Medicare database. *Archives of Family Medicine*, 6: 52-58.

Not in PICO

Aedo, M. R., Zavala-Gonzalez, M. A., Meixueiro-Daza, A. & Remes-Troche, J. M. (2014) - Accuracy of transnasal endoscopy with a disposable esophagoscope compared to conventional endoscopy. -

World Journal of Gastrointestinal Endoscopy, 6: 128-136.

Not in PICO

Ahlgren, J. D. (2001) Gastrointestinal malignancies. *Primary Care - Clinics in Office Practice*, 28: 647-660.

Narrative Review

Ajumobi, A., Bahjri, K., Jackson, C. & Griffin, R. (2010) Surveillance in Barrett's esophagus: an audit of practice. *Digestive Diseases & Sciences*, 55: 1615-1621.

Not in PICO

Alikhan, M., Rex, D., Khan, A., Rahmani, E., Cummings, O. & Ulbright, T. M. (1999) Variable pathologic interpretation of columnar lined esophagus by general pathologists in community practice. *Gastrointestinal Endoscopy*, 50: 23-26.

Not in PICO

Allum, W. H., Blazeby, J. M., Griffin, S. M., Cunningham, D., Jankowski, J. A. & Wong, R. (2011) Guidelines for the management of oesophageal and gastric cancer. *Gut*, 60: 1449-1472.

Not in PICO

Anderson, W. D., III & Strayer, S. M. (2013) Evaluation of nausea and vomiting: a case-based approach. *American Family Physician*, 88: 371-379.

Narrative review

Ansari, S. & Ford, A. C. (2013) Initial management of dyspepsia in primary care: An evidence-based approach. *British Journal of General Practice*, 63: 498-499.

Narrative review

Antonovich, V. B. & Pukhkaya, V. K. (1980) Diagnosis of minor (early) tumor of the esophagus. [Russian]. *Vestnik Rentgenologii i Radiologii*, 55: 5-8.

Not in PICO

Arantes, V., Forero Pineros, E. A., Yoshimura, K. & Toyonaga, T. (2012) Advances in the management of early esophageal carcinoma. *Revista do Colegio Brasileiro de Cirurgioes*, 39: 534-543.

Narrative Review

Arantes, V., Albuquerque, W., Salles, J. M., Freitas Dias, C. A., Alberti, L. R., Kahaleh, M., Ferrari, T. C. & Coelho, L. G. (2013) Effectiveness of unsedated transnasal endoscopy with white-light, flexible spectral imaging color enhancement, and lugol staining for esophageal cancer screening in high-risk patients. *Journal of Clinical Gastroenterology*, 47: 314-321.

Not in PICO

Arima, M., Tasaki, K., Tobita, K., Watanabe, Y., Kaiho, T., Nakajima, Y., Okazumi, S., Kouzu, T. & Ochiai, T. (2000) X-ray and endoscopic diagnosis of esophageal achalasia. [Japanese]. *Nippon Geka Gakkai zasshi*, 101: 327-332.

Not in PICO

Arima, M. (2011) [Early detection of esophageal neoplasms by magnifying endoscopy]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 38: 1417-1420.

In Japanese. Not enough information can be extracted to ascertain relevance.

Axon, A. & Marshall, J. B. (1998) Open access endoscopy in Britain: A service in evolution. *Gastrointestinal Endoscopy*, 48: 653-658.

Narrative review

Axon, A. T. R. (1997) Chronic dyspepsia: Who needs endoscopy? *Gastroenterology*, 112: 1376-1380.

Narrative Review

Bai, Y., Li, Z. S., Zou, D. W., Wu, R. P., Yao, Y. Z., Jin, Z. D., Ye, P., Li, S. D., Zhang, W. J., Du, Y. Q., Zhan, X. B., Liu, F., Gao, J. & Xu, G. M. (2010) Alarm features and age for predicting upper gastrointestinal malignancy in Chinese patients with dyspepsia with high background prevalence of *Helicobacter pylori* infection and upper gastrointestinal malignancy: an endoscopic database review of 102 665 patients from 1996 to 2006. *Gut*, 59: 722-728.

Not in PICO

- Baldi, F., Crotta, S. & Penagini, R. (1998) Guidelines for the diagnostic and therapeutic management of patients with gastro-oesophageal reflux disease. [Italian]. *Giornale Italiano di Endoscopia Digestiva*, 21: 53-60.
Not in PICO
- Barenys De, L. M., Rota, R., Moreno, V., Villafafila, R., Garcia-Bayo, I., Abad, A., Pons, J. M. V. & Pique, J. M. (2003) Prospective validation of a clinical scoring system for the diagnosis of organic dyspepsia. [Spanish]. *Medicina Clinica*, 121: 766-771.
Not in PICO
- Barenys, M., Abad, A., Pons, J. M. V., Moreno, V., Rota, R., Granados, A., Admetlla, M. & Pique, J. M. (2000) Scoring system has better discriminative value than Helicobacter pylori testing in patients with dyspepsia in a setting with high prevalence of infection. *European Journal of Gastroenterology & Hepatology*, 12: 1275-1282.
Not in PICO
- Barge, J., Molas, G., Maillard, J. N., Fekete, F., Bogomoletz, W. V. & Potet, F. (1981) Superficial oesophageal carcinoma: an oesophageal counterpart of early gastric cancer. *Histopathology*, 5: 499-510.
Not in PICO
- Barloon, T. J., Bergus, G. R. & Lu, C. C. (1996) Diagnostic imaging in the evaluation of dysphagia. *American Family Physician*, 53: 535-546.
Narrative Review
- Barroso, A. O. (2011) Advanced endoscopy procedures in private practice: Is the juice worth the squeeze? *Gastrointestinal Endoscopy*, 74: 913-915.
Narrative Review
- Batra, M., Handa, U., Mohan, H. & Sachdev, A. (2008) Comparison of cytohistologic techniques in diagnosis of gastroesophageal malignancy. *Acta Cytologica*, 52: 77-82.
Not in PICO
- Beck, C. & Steinbach, G. (1966) [Critical observations on ambulatory esophagoscopy]. [German]. *HNO*, 14: 223-224.
Outsode of date range
- Behm, B. W. & Peura, D. A. (2011) Gastroesophageal reflux disease: Clinical features and management for the primary care physician. *Journal of Clinical Outcomes Management*, 18: 45-56.
Narrative Review
- Benaglia, T., Sharples, L. D., Fitzgerald, R. C. & Lyratzopoulos, G. (2013) Health benefits and cost effectiveness of endoscopic and nonendoscopic cytosponge screening for Barrett's esophagus (Structured abstract). *Gastroenterology*, 144: 62-73.
Not in PICO
- Bergholt, M. S., Zheng, W., Lin, K., Ho, K. Y., Teh, M., Yeoh, K. G., So, J. B. & Huang, Z. (2011) Characterizing variability in in vivo Raman spectra of different anatomical locations in the upper gastrointestinal tract toward cancer detection. *Journal of biomedical optics*, 16: 037003.
Not in PICO
- Bergman, J. (2004) New endoscopic imaging techniques for improved detection of early neoplasia in patients with Barrett's esophagus. *Current Gastroenterology Reports*, 6: 343-345.
Not in PICO
- Bergman, J. J. & Tytgat, G. N. (2005) New developments in the endoscopic surveillance of Barrett's oesophagus. [Review] [27 refs]. *Gut*, 54: Suppl-42.
Narrative Review
- Bhasin, D. K., Kochhar, R., Rajwanshi, A., Gupta, S. K. & Mehta, S. K. (1988) Endoscopic suction cytology in upper gastrointestinal tract malignancy. *Acta Cytologica*, 32: 452-454.
Not in PICO

- Bhutta, H. Y., Alexandre, L., Clark, A., Holt, S., Lewis, M. & Hart, A. (2012) Do Statins Prevent the Histological Subtypes of Oesophageal Cancer? Prospective Data from the Uk General Practice Research Database (Gprd). *Gut*, 61: A299-A300.
Not in PICO
- Biyyani, R. S. S., Salah, W., Dumot, J. & Chak, A. (1111) Treatment of barrett's related adenocarcinoma in a roux-en-y-gastric bypass surgery patient: Is endoscopic therapy possible? *American Journal of Gastroenterology*. Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States. Conference Start: 20131011 Conference End: 20131016. Conference Publication: (var.pagings), 108: October.
Not in PICO
- Blanchi, S., Picasso, M., Bastardini, R., Filiberti, R., Di, M. M. & Conio, M. (2005) Diagnosis and therapy of high-grade dysplasia and early cancer in Barrett's esophagus. [Italian]. *Giornale Italiano di Endoscopia Digestiva*, 28: 187-194.
Not in PICO
- Boeriu, A. M., Dobru, D. E. & Mocan, S. (2009) Magnifying endoscopy and chromoendoscopy of the upper gastrointestinal tract. *Journal of Gastrointestinal & Liver Diseases*, 18: 109-113.
Narrative Review
- Boerwinkel, D. F., Shariff, M. K., di, P. M., Holz, J. A., Aalders, M. C., Curvers, W. L., Fitzgerald, R. C. & Bergman, J. J. (2014) - Fluorescence imaging for the detection of early neoplasia in Barrett's esophagus: old looks or new vision? - *European Journal of Gastroenterology & Hepatology*, 26: 691-698.
Narrative review
- Boerwinkel, D. F., Holz, J. A., Kara, M. A., Meijer, S. L., Wallace, M. B., Wong Kee Song, L. M., Ragnath, K., Wolfsen, H. C., Iyer, P. G., Wang, K. K., Weusten, B. L., Aalders, M. C., Curvers, W. L. & Bergman, J. J. (2014) - Effects of autofluorescence imaging on detection and treatment of early neoplasia in patients with Barrett's esophagus. - *Clinical Gastroenterology & Hepatology*, 12: 774-781.
Not in PICO
- Boerwinkel, D. F., Holz, J. A., Aalders, M. C., Visser, M., Meijer, S. L., Van Berge Henegouwen, M. I., Weusten, B. L. & Bergman, J. J. (2014) - Third-generation autofluorescence endoscopy for the detection of early neoplasia in Barrett's esophagus: a pilot study. - *Diseases of the Esophagus*, 27: 276-284.
Not in PICO
- Bonino, J. A. & Sharma, P. (2004) Barrett esophagus. *Current Opinion in Gastroenterology*, 20: 375-380.
Narrative Review
- Boolchand, V., Faulx, A., Das, A., Zyzanski, S., Isenberg, G., Cooper, G., Sivak, M. V. & Chak, A. (2006) Primary care physician attitudes toward endoscopic screening for GERD symptoms and unsedated esophagoscopy. *Gastrointestinal Endoscopy*, 63: 228-233.
Not in PICO
- Boulton-Jones, J. R., Follows, M. C. & Mahmoud, A. A. (2003) Open-access endoscopy: Are age-based guidelines justified? An audit of experience of 1000 open-access endoscopies at a district general hospital. *Endoscopy*, 35: 68-73.
Not in PICO
- Bourg-Heckly, G., Blais, J., Padilla, J. J., Bourdon, O., Etienne, J., Guillemin, F. & Lafay, L. (2000) Endoscopic ultraviolet-induced autofluorescence spectroscopy of the esophagus: tissue characterization and potential for early cancer diagnosis. *Endoscopy*, 32: 756-765.
Not in PICO
- Boyer, J., Laugier, R., Chemali, M., Arpurt, J. P., Boustiere, C., Canard, J. M., Dalbies, P. A., Gay, G., Escourrou, J., Napoleon, B., Palazzo, L., Ponchon, T., Richard-Mollard, B., Sautereau, D., Tucac, G., Vedrenne, B. & French Society of Digestive Endoscopy SFED (2007) French Society of Digestive

- Endoscopy SFED guideline: monitoring of patients with Barrett's esophagus. *Endoscopy*, 39: 840-842.
Not in PICO
- Bramble, M. G., Suvakovic, Z. & Hungin, A. P. (2000) Detection of upper gastrointestinal cancer in patients taking antisecretory therapy prior to gastroscopy. *Gut*, 46: 464-467.
Not in PICO
- Budzynski, J., Manerowski, M. & Swiatkowski, M. (2007) The neoplasms of digestive tract in patients referred with abdominal tumor suspicion by family doctors to gastroenterology department in 2006. [Polish]. *Family Medicine and Primary Care Review*, 9: 378-380.
Not in PICO
- Buset, M. & Deviere, J. (1990) [Barrett's esophagus. Characterization and monitoring policy]. [Review] [30 refs] [French]. *Acta Gastroenterologica Belgica*, 53: 561-567.
Narrative Review
- Bytzer, P., Hansen, J. M., Havelund, T., MalchowMoller, A. & deMuckadell, O. B. S. (1996) Predicting endoscopic diagnosis in the dyspeptic patient: The value of clinical judgement. *European Journal of Gastroenterology & Hepatology*, 8: 359-363.
Not in PICO
- Calvo, A., Pruyas, M., Nilsen, E. & Verdugo, P. (2001) Frequency of gastric cancer in endoscopies performed in symptomatic patients at a secondary care health center. *Revista Medica de Chile*, 129: 749-755.
Not in PICO
- Canto, M., I, Setrakian, S., Willis, J., Chak, A., Petras, R., Powe, N. R. & Sivak, M., V (2000) Methylene blue-directed biopsies improve detection of intestinal metaplasia and dysplasia in Barrett's esophagus (Structured abstract). *Gastrointestinal.Endoscopy*, 51: 560-568.
Not in PICO
- Cappell, M. S. & Friedel, D. (2002) The role of esophagogastroduodenoscopy in the diagnosis and management of upper gastrointestinal disorders. *Medical Clinics of North America*, 86: 1165-+.
Narrative Review
- Cayir, K., Bilici, M., Tekin, S. B., Kara, F., Turkyilmaz, A. & Yildirim, A. (2010) Serum paraoxonase and arylesterase activities in esophageal cancer: A controlled study. [Turkish]. *European Journal of General Medicine*, 7: 398-403.
Not in PICO
- Chadwick, G., Groene, O., Hoare, J., Hardwick, R. H., Riley, S., Crosby, T. D., Hanna, G. B. & Cromwell, D. A. (2014) A population-based, retrospective, cohort study of esophageal cancer missed at endoscopy. *Endoscopy*, 46: 553-559.
Not in PICO
- Chan, D., Leggett, C., Gorospe, E., Chandra, S., Sharma, A., Chowdhury, S., Lutzke, L., Buttar, N., Iyer, P. & Wang, K. (1111) Low dose aspirin does not affect outcomes from radiofrequency ablation for barrett's esophagus. *American Journal of Gastroenterology.Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States.Conference Start: 20131011 Conference End: 20131016.Conference Publication: (var.pagings)*, 108: October.
Not in PICO
- Chennat, J., Konda, V. J. & Waxman, I. (2011) Endotherapy for Barrett's esophagus: Which, how, when, and who?. [Review]. *Gastrointestinal Endoscopy Clinics of North America*, 21: 119-133.
Narrative Review
- Cheung, D., Menon, S. & Trudgill, N. (2013) How Commonly Is Oesophageal Cancer Missed at Endoscopy (A Uk Primary Care Based Study)? *Gut*, 62: A5.
Duplicate
- Cheung, D., Menon, S. & Trudgill, N. (2013) How commonly is oesophageal cancer missed at endoscopy (a UK primary care based study)? *Gut*, 62: A5.
Not in PICO

- Chun, S., Hui, L. & Jing, S. (2013) Application study of NBI and lugol staining in the diagnosis of early esophageal cancer. *Journal of Gastroenterology and Hepatology*, 28: 42.
Abstract only, not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Classen, M. & Phillip, J. (1981) [Endoscopy of esophageal cancer (author's transl)]. [German]. *Langenbecks Archiv fur Chirurgie*, 355: 59-61.
Narrative review
- Cooper, S. C., El-agib, A., Dar, S., Mohammed, I., Nightingale, P., Murray, I. A., Cooper, B. T. & Trudgill, N. J. (2009) Endoscopic surveillance for Barrett's oesophagus: the patients' perspective. *European Journal of Gastroenterology & Hepatology*, 21: 850-854.
Not in PICO
- Corder, A. P., Jones, R. H., Sadler, G. H. M., Daniels, P. & Johnson, C. D. (1996) Heartburn, oesophagitis and Barrett's oesophagus in self-medicating patients in general practice. *British Journal of Clinical Practice*, 50: 245-248.
Not in PICO
- Craanen, M. E., Blok, P., Meijer, G. A. & Meuwissen, S. G. (2002) Surveillance in Barrett's oesophagus: a critical reappraisal. [Review] [25 refs]. *Scandinavian Journal of Gastroenterology - Supplement.(236):4-8, 2002.*, 4-8.
Not in PICO
- Cross, S. (2011) Barrett esophagus: a practical challenge for primary care. *Nurse Practitioner*, 36: 18-21.
Narrative review
- Cukovic-Cavka, S. (2003) [Barrett esophagus--a premalignant disorder requiring a program of endoscopic follow-up?]. [Croatian]. *Medicinski Arhiv*, 57: Suppl-8.
Narrative review
- Curvers, W. L., Kiesslich, R. & Bergman, J. J. (2008) Novel imaging modalities in the detection of oesophageal neoplasia. [Review] [123 refs]. *Best Practice & Research in Clinical Gastroenterology*, 22: 687-720.
Narrative Review
- Curvers, W. L., Singh, R., Song, L. M., Wolfsen, H. C., Ragnath, K., Wang, K., Wallace, M. B., Fockens, P. & Bergman, J. J. (2008) Endoscopic tri-modal imaging for detection of early neoplasia in Barrett's oesophagus: a multi-centre feasibility study using high-resolution endoscopy, autofluorescence imaging and narrow band imaging incorporated in one endoscopy system. *Gut*, 57: 167-172.
Not in PICO
- Curvers, W. L., Kiesslich, R. & Bergman, J. J. G. H. (2008) Novel imaging modalities in the detection of oesophageal neoplasia. *Best Practice and Research: Clinical Gastroenterology*, 22: 687-720.
Narrative Review
- Curvers, W. L., Singh, R., Wallace, M. B., Song, L. M., Ragnath, K., Wolfsen, H. C., ten Kate, F. J., Fockens, P. & Bergman, J. J. (2009) Identification of predictive factors for early neoplasia in Barrett's esophagus after autofluorescence imaging: a stepwise multicenter structured assessment. *Gastrointestinal Endoscopy*, 70: 9-17.
Not in PICO
- Curvers, W. L., ten Kate, F. J., Krishnadath, K. K., Visser, M., Elzer, B., Baak, L. C., Bohmer, C., Mallant-Hent, R. C., van, O. A., Naber, A. H., Scholten, P., Busch, O. R., Blaauwgeers, H. G., Meijer, G. A. & Bergman, J. J. (2010) Low-grade dysplasia in Barrett's esophagus: overdiagnosed and underestimated. *American Journal of Gastroenterology*, 105: 1523-1530.
Not in PICO
- Curvers, W. L., van Vilsteren, F. G., Baak, L. C., Bohmer, C., Mallant-Hent, R. C., Naber, A. H., van, O. A., Ponsioen, C. Y., Scholten, P., Schenk, E., Schoon, E., Seldenrijk, C. A., Meijer, G. A., ten Kate, F. J. & Bergman, J. J. (2011) Endoscopic trimodal imaging versus standard video endoscopy for

- detection of early Barrett's neoplasia: a multicenter, randomized, crossover study in general practice. *Gastrointestinal Endoscopy*, 73: 195-203.
Not in PICO
- Davila, R. E. (2009) Chromoendoscopy. *Gastrointestinal Endoscopy Clinics of North America*, 19: 193-208.
Narrative Review
- Dawsey, S. M., Wang, G. Q., Weinstein, W. M., Lewin, K. J., Liu, F. S., Wiggett, S., Nieberg, R. K., Li, J. Y. & Taylor, P. R. (1993) Squamous dysplasia and early esophageal cancer in the Linxian region of China: distinctive endoscopic lesions. *Gastroenterology*, 105: 1333-1340.
Not in PICO
- da Silva, J. B., Mauricio, S. F., Bering, T. & Correia, M. I. (2013) The relationship between nutritional status and the Glasgow prognostic score in patients with cancer of the esophagus and stomach. *Nutrition & Cancer*, 65: 25-33.
Not in PICO
- De Moura, E. G. H., Domingos, T. A., Neto, M. G., Fylyk, S. N., Sakai, P., Sallum, R. A. & Cecconello, I. (2011) Comparative evaluation of the epithelium of Barrett's esophagus through the esophageal capsule endoscopy and methylene blue chromoendoscopy. *Gastrointestinal Endoscopy*, 73: AB285.
Not in PICO
- De, H. G. (2011) Barrett's oesophagus: Pathology for the clinician. [Dutch]. *Tijdschrift voor Geneeskunde*, 67: 911-917.
Narrative Review
- Delmotte, J. S., Pommelet, P., Houcke, M. & Paris, J. (1981) Early cancers of oesophagus. [French]. *Acta Endoscopica*, 11: 327-337.
Not in PICO
- DeVault, K. R. (2000) Epidemiology and significance of Barrett's esophagus. *Digestive Diseases*, 18: 195-202.
Narrative Review
- Di, G. E., Hassan, C., Pickhardt, P. J., Zullo, A., Laghi, A., Kim, D. H. & Iafrate, F. (2009) Cost-effectiveness of upper gastrointestinal endoscopy according to the appropriateness of the indication. *Scandinavian Journal of Gastroenterology*, 44: 491-498.
Not in PICO
- Di, G. E., Hassan, C., Marmo, R., Zullo, A. & Annibale, B. (2010) Appropriateness of the indication for upper endoscopy: A meta-analysis. *Digestive and Liver Disease*, 42: 122-126.
Not in PICO
- Duggan, A. E., Elliott, C. A., Miller, P., Hawkey, C. J. & Logan, R. F. A. (2009) Clinical trial: A randomized trial of early endoscopy, Helicobacter pylori testing and empirical therapy for the management of dyspepsia in primary care. *Alimentary Pharmacology and Therapeutics*, 29: 55-68.
Not in PICO
- Eckardt, V. F. (1993) Early detection of gastrointestinal malignancies: what is new?. [German]. *Bildgebung = Imaging*, 60: 13-15.
Narrative Review
- Eckardt, V. F. (1997) [Barrett syndrome and risk of carcinoma. To screen or not to screen--that is the question]. [German]. *Zeitschrift fur Gastroenterologie*, 35: 597-599.
Not in PICO
- El-Serag, H. B., Duan, Z., Hinojosa-Lindsey, M., Hou, J., Shakhathreh, M., Naik, A. D., Chen, G. J., Street, J. & Kramer, J. R. (2012) Practice patterns of surveillance endoscopy in a Veterans Affairs database of 29,504 patients with Barrett's esophagus. *Gastrointestinal Endoscopy*, 76: 743-755.
Not in PICO

- Ell, C. (2002) [Early esophageal carcinoma: diagnosis and endoscopic therapy]. [German]. *Zeitschrift fur Gastroenterologie*, 40: Suppl-4.
Narrative review
- Ellis, F. H., Jr. & Loda, M. (1997) Role of surveillance endoscopy, biopsy and biomarkers in early detection of Barrett's adenocarcinoma. [Review] [85 refs]. *Diseases of the Esophagus*, 10: 165-171.
Narrative Review
- Endlicher, E., Knuechel, R., Hauser, T., Szeimies, R. M., Scholmerich, J. & Messmann, H. (2001) Endoscopic fluorescence detection of low and high grade dysplasia in Barrett's oesophagus using systemic or local 5-aminolaevulinic acid sensitisation. *Gut*, 48: 314-319.
Not in PICO
- Endo, M., Takeshita, K. & Yoshida, M. (1986) How can we diagnose the early stage of esophageal cancer? Endoscopic diagnosis. *Endoscopy*, 18: Suppl-8.
Narrative review
- Endo, T., Yamashita, K. & Shinomura, Y. (2005) [Diagnosis of Barrett's esophagus and Barrett's carcinoma using magnifying endoscopy]. [Review] [19 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 63: 1399-1404.
Narrative Review
- Esfandyari, T., Potter, J. W. & Vaezi, M. F. (2002) Dysphagia: a cost analysis of the diagnostic approach. *American Journal of Gastroenterology*, 97: 2733-2737.
Not in PICO
- Espino, A., Cirocco, M., Dacosta, R. & Marcon, N. (2014) - Advanced imaging technologies for the detection of dysplasia and early cancer in barrett esophagus. [Review]. - *Clinical Endoscopy*, 47: 47-54.
Narrative review
- Estores, D. & Velanovich, V. (2013) Barrett esophagus: epidemiology, pathogenesis, diagnosis, and management. [Review]. *Current Problems in Surgery*, 50: 192-226.
Narrative review
- Faintuch, J. J., Silva, F. M., Navarro-Rodriguez, T., Barbuti, R. C., Hashimoto, C. L., Rossini, A. R. A. L., Diniz, M. A. & Eisig, J. N. (2014) Endoscopic findings in uninvestigated dyspepsia. *Bmc Gastroenterology*, 14.
Not in PICO
- Falk, G. W., Ours, T. M. & Richter, J. E. (2000) Practice patterns for surveillance of Barrett's esophagus in the united states. *Gastrointestinal Endoscopy*, 52: 197-203.
Not in PICO
- Fashner, J. & Gitu, A. C. (2013) Common Gastrointestinal Symptoms: dyspepsia and Helicobacter pylori. [Review]. *Fp Essentials*, 413: 24-28.
Narrative review
- Fennerty, M. B. (2001) Chromoscopy in the diagnosis and management of Barrett's esophagus. *Acta Endoscopica*, 31: 151-159.
Narrative Review
- Flameling, R. D., Numans, M. E., ter, L. J., de Wit, N. J. & Siersema, P. D. (2010) Different characteristics of patients with gastro-oesophageal reflux disease on their path through healthcare: a population follow-up study. *European Journal of Gastroenterology & Hepatology*, 22: 578-582.
Not in PICO
- Flynn, C. A. (2001) The evaluation and treatment of adults with gastroesophageal reflux disease. *Journal of Family Practice*, 50: 57-63.
Narrative review

- Ford, A. C. & Moayyedi, P. (2009) Should we step-up or step-down in the treatment of new-onset dyspepsia in primary care?. [Review] [41 refs]. *Polskie Archiwum Medycyny Wewnętrznej*, 119: 391-396.
Narrative review
- Ford, A. C. & Moayyedi, P. (2013) Dyspepsia. *BMJ (Online)*, 347.
Narrative review
- Fornari, F. & Wagner, R. (2012) Update on endoscopic diagnosis, management and surveillance strategies of esophageal diseases. *World Journal of Gastrointestinal Endoscopy*, 4: 117-122.
Narrative Review
- Fortun, P. J., Anagnostopoulos, G. K., Kaye, P., James, M., Foley, S., Samuel, S., Shonde, A., Badreldin, R., Campbell, E., Hawkey, C. J. & Ragnath, K. (2006) Acetic acid-enhanced magnification endoscopy in the diagnosis of specialized intestinal metaplasia, dysplasia and early cancer in Barrett's esophagus. *Alimentary Pharmacology & Therapeutics*, 23: 735-742.
Not in PICO
- Fraser, A. G., Ali, M. R., McCullough, S., Yeates, N. J. & Haystead, A. (1996) Diagnostic tests for Helicobacter pylori - Can they help select patients for endoscopy. *New Zealand Medical Journal*, 109: 95-98.
Not in PICO
- Freitag, C. P. F., Barros, S. G. S., Krueh, C. D. P., Putten, A. C. K., Dietz, J., Gruber, A. C., Diehl, A. S., Meurer, L., Breyer, H. P., Wolff, F., Vidal, R., Arruda, C. A., Luz, L. P., Fagundes, R. B. & Prolla, J. C. (1999) Esophageal dysplasias are detected by endoscopy with Lugol in patients at risk for squamous cell carcinoma in southern Brazil. *Diseases of the Esophagus*, 12: 191-195.
Not in PICO
- Galloway, J. M., Gibson, J. & Dalrymple, J. (2002) Endoscopy in primary care - a survey of current practice. *British Journal of General Practice*, 52: 536-538.
Not in PICO
- Giacchino, M., Bansal, A., Kim, R. E., Singh, V., Hall, S. B., Singh, M., Rastogi, A., Moloney, B., Wani, S. B., Gaddam, S., Mathur, S. C., Wallace, M. B., Kanakadandi, V., Balasubramanian, G., Gupta, N. & Sharma, P. (2013) Clinical utility and interobserver agreement of autofluorescence imaging and magnification narrow-band imaging for the evaluation of Barrett's esophagus: A prospective tandem study. *Gastrointestinal Endoscopy*, 77: 711-718.
Not in PICO
- Giangreco, E., D'agate, C., Barbera, C., Puzzo, L., Aprile, G., Naso, P., Bonanno, G., Russo, F. P., Nicoletti, A., Incarbone, S., Trama, G. & Russo, A. (2008) Prevalence of celiac disease in adult patients with refractory functional dyspepsia: value of routine duodenal biopsy. *World Journal of Gastroenterology*, 14: 6948-6953.
Not in PICO
- Gill, R. S. & Singh, R. (2012) Endoscopic imaging in Barrett's esophagus: Current practice and future applications. *Annals of Gastroenterology*, 25: 89-95.
Narrative Review
- Gillen, D. & Mccoll, K. E. L. (1999) Does concern about missing malignancy justify endoscopy in uncomplicated dyspepsia in patients aged less than 55? *American Journal of Gastroenterology*, 94: 75-79.
Not in PICO
- Gisbert, J. P., Calvet, X., Ferrandiz, J., Mascort, J., Alonso-Coello, P. & Marzo, M. (2012) [Clinical practice guideline on the management of patients with dyspepsia. Update 2012]. [Spanish]. *Gastroenterologia y Hepatologia*, 35: 725-738.
Not in PICO
- Giulio, E., Hassan, C., Pickhardt, P. J., Zullo, A., Laghi, A., Kim, D. H. & Iafate, F. (2009) Cost-effectiveness of upper gastrointestinal endoscopy according to the appropriateness of the

- indication (Provisional abstract). *Scandinavian Journal of Gastroenterology*, 44: 491-498.
Duplicate
- Giulio, E., Hassan, C., Marmo, R., Zullo, A. & Annibale, B. (2010) Appropriateness of the indication for upper endoscopy: a meta-analysis (DARE structured abstract). *Digestive and Liver Disease.*, 42: 122-126.
Duplicate
- Gladman, L., Chapman, W., Iqbal, T. H., Gearty, J. C. & Cooper, B. T. (2006) Barrett's oesophagus: an audit of surveillance over a 17-year period. *European Journal of Gastroenterology & Hepatology*, 18: 271-276.
Not in PICO
- Goda, K., Kato, T. & Tajiri, H. (2014) Endoscopic diagnosis of early Barrett's neoplasia: Perspectives for advanced endoscopic technology. *Digestive Endoscopy*, 26: 311-321.
Narrative review
- Gono, K., Obi, T., Yamaguchi, M., Ohyama, N., Machida, H., Sano, Y., Yoshida, S., Hamamoto, Y. & Endo, T. (2004) Appearance of enhanced tissue features in narrow-band endoscopic imaging. *Journal of biomedical optics*, 9: 568-577.
Not in PICO
- Goto, O., Kambe, H., Niimi, K., Mochizuki, S., Asada-Hirayama, I., Minatsuki, C., Ono, S., Kodashima, S., Yamamichi, N., Yamaji, Y., Fujishiro, M. & Koike, K. (2012) Discrepancy in diagnosis of gastric submucosal tumor among esophagogastroduodenoscopy, CT, and endoscopic ultrasonography: a retrospective analysis of 93 consecutive cases. *Abdominal Imaging*, 37: 1074-1078.
Not in PICO
- Greenslade, J. & Wyman, A. (2006) Investigation of dysphagia. *Surgery*, 24: 89-92.
Narrative Review
- Gruber, A. C., de Barros, S. G., Putten, A. C., Gigante, L., Coelho, N., Sekine, S. & Prolla, J. C. (1998) Esophageal dysplasia and chronic esophagitis: detection at upper gastrointestinal tract endoscopy. *Arquivos de Gastroenterologia*, 35: 258-263.
Not in PICO
- Grunewald, M., Vieth, M., Kreibich, H., Bethke, B. & Stolte, M. (1997) [The status of diagnosis of Barrett esophagus. An analysis of 1000 histologically diagnosed cases]. [German]. *Deutsche Medizinische Wochenschrift*, 122: 427-431.
Not in PICO
- Guanrei, Y., He, H., Sungliang, Q. & Yuming, C. (1982) Endoscopic diagnosis of 115 cases of early esophageal carcinoma. *Endoscopy*, 14: 157-161.
Not in PICO
- Guelrud, M. & Ehrlich, E. E. (2004) Enhanced magnification endoscopy in the upper gastrointestinal tract. *Gastrointestinal Endoscopy Clinics of North America*, 14: 461-473.
Narrative Review
- Guitron Cantu, J. A., Adalid, M. R., Sanchez, V. A. & Sanchez, M. T. (1991) [Carcinoma of the esophagus: clinical, radiologic, endoscopic, and histologic evaluation. Experience in Torreon City, Coahuila]. [Spanish]. *Revista de Gastroenterologia de Mexico*, 56: 17-21.
Not in PICO
- Guo, H., Zhu, H., Xi, Y., Zhang, B., Li, L., Huang, Y., Zhang, J., Fu, Z., Yang, G., Yuan, S. & Yu, J. (2007) Diagnostic and prognostic value of 18F-FDG PET/CT for patients with suspected recurrence from squamous cell carcinoma of the esophagus. *Journal of Nuclear Medicine*, 48: 1251-1258.
Not in PICO
- Guo, X. Q., Wang, S. J., Zhang, L. W., Wu, M. L., Liu, Y. F., Gao, Y., Wang, S. P., Li, Y. S., Er, L. M. & Cong, Q. W. (2005) [Clinical value of esophageal mucosal iodine stain during esophagoscopy for patients without swallowing symptoms]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 27: 238-240.
Not in PICO

- Habibollahi, P., Figueiredo, J. L., Heidari, P., Dulak, A. M., Imamura, Y., Bass, A. J., Ogino, S., Chan, A. T. & Mahmood, U. (2012) Optical Imaging with a Cathepsin B Activated Probe for the Enhanced Detection of Esophageal Adenocarcinoma by Dual Channel Fluorescent Upper GI Endoscopy. *Theranostics*, 2: 227-234.
Not in PICO
- Heikkinen, M., Pikkarainen, P., Takala, J., Rasanen, H. & Julkunen, R. (1995) Etiology of Dyspepsia - 400 Unselected Consecutive Patients in General-Practice. *Scandinavian Journal of Gastroenterology*, 30: 519-523.
Not in PICO
- Heresbach, D. (2008) Endoscopic diagnosis of early neoplasm in oesophagus. [French, English]. *Acta Endoscopica*, 38: 135-147.
Narrative Review
- Heresbach, D., Leray, E., d'Halluin, P. N., Cholet, F., Lapalus, M. G., Gaudric, M., Ben, S. E., Gaudin, J. L., Vahedi, K., Quentin, V., Filoche, B., Saurin, J. C., Chaussade, S. & Ponchon, T. (2010) Diagnostic accuracy of esophageal capsule endoscopy versus conventional upper digestive endoscopy for suspected esophageal squamous cell carcinoma. *Endoscopy*, 42: 93-97.
Not in PICO
- Herrero, L. A., Weusten, B. L. & Bergman, J. J. (2010) Autofluorescence and narrow band imaging in Barrett's esophagus. [Review]. *Gastroenterology Clinics of North America*, 39: 747-758.
Not in PICO
- Herszenyi, L., Pregun, I. & Tulassay, Z. (2009) Diagnosis and recognition of early esophageal neoplasia. [Review] [60 refs]. *Digestive Diseases*, 27: 24-30.
Narrative Review
- Hirota, W. K., Zuckerman, M. J., Adler, D. G., Davila, R. E., Egan, J., Leighton, J. A., Qureshi, W. A., Rajan, E., Fanelli, R., Wheeler-Harbaugh, J., Baron, T. H., Faigel, D. O. & Standards of Practice Committee, A. S. f. G. E. (2006) ASGE guideline: the role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. *Gastrointestinal Endoscopy*, 63: 570-580.
Guideline
- Hirst, N. G., Gordon, L. G., Whiteman, D. C., Watson, D. I. & Barendregt, J. J. (2011) Is endoscopic surveillance for non-dysplastic Barrett's esophagus cost-effective? Review of economic evaluations. [Review]. *Journal of Gastroenterology & Hepatology*, 26: 247-254.
Not in PICO
- Hollenz, M., Stolte, M. & Labenz, J. (2002) Prevalence of gastro-oesophageal reflux disease in general practice. [German]. *Deutsche Medizinische Wochenschrift*, 127: 1007-1012.
Not in PICO
- Hu, X.-R., Cui, X.-N. & Qiu, N.-N. (2009) Use of pasty iohexol as an oral contrast agent in spiral computed tomography for diagnosis of esophageal cancer: An analysis of 113 cases. [Chinese]. *World Chinese Journal of Digestology*, 17: 2940-2943.
Not in PICO
- Huang, L.-Y., Cui, J., Wu, C.-R., Liu, Y.-X. & Xu, N. (2009) Narrow-band imaging in the diagnosis of early esophageal cancer and precancerous lesions. *Chinese Medical Journal*, 122: 776-780.
Not in PICO
- Huppertz-Hauss, G., Chengarov, L., Dahler, S., Jorgensen, A., Moritz, V., Paulsen, J. & Hoff, G. (2012) "Drop in" gastroscopy outpatient clinic--experience after 9 months. *BMC gastroenterology*, 12: 12.
Not in PICO
- Hussan, H., Bhatia, R., Hilton, R., Ringwala, J. & Hachem, C. (1111) Prevalence, natural history, and management of suspected barrett's esophagus in patients with cirrhosis. *American Journal of Gastroenterology.Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States.Conference Start: 20131011 Conference End:*

20131016. Conference Publication: (var. pagings), 108: October.
Not in PICO
- Ide, E., Maluf-Filho, F., Chaves, D. M., Matuguma, S. E. & Sakai, P. (2011) Narrow-band imaging without magnification for detecting early esophageal squamous cell carcinoma. *World Journal of Gastroenterology*, 17: 4408-4413.
Not in PICO
- Ide, H. (1985) Clinical diagnosis of early esophageal cancer with submucosal involvement. [Japanese]. *Stomach and Intestine*, 20: 1339-1349.
Not in PICO
- Inshakov, L. N., Suleimenov, A. A. & Dzhumashev, E. Z. (1980) [Clinical endoscopic criteria of the early forms of esophageal cancer]. [Russian]. *Voprosy Onkologii*, 26: 38-41.
Not in PICO
- Inshakov, L. N. & Karimova, F. R. (1981) [Limits and potentials of fiber esophagoscopy in detecting background diseases and early forms of esophageal cancer]. [Russian]. *Voprosy Onkologii*, 27: 86-87.
In Russian. Not enough information can be extracted to ascertain relevance.
- Ishihara, R., Inoue, T., Uedo, N., Yamamoto, S., Kawada, N., Tsujii, Y., Kanzaki, H., Hanafusa, M., Hanaoka, N., Takeuchi, Y., Higashino, K., Iishi, H., Tatsuta, M., Tomita, Y. & Ishiguro, S. (2010) Significance of each narrow-band imaging finding in diagnosing squamous mucosal high-grade neoplasia of the esophagus. *Journal of Gastroenterology & Hepatology*, 25: 1410-1415.
Not in PICO
- Jagadesham, V. P. & Kelty, C. J. (2014) - Low grade dysplasia in Barrett's esophagus: Should we worry?. [Review]. - *World Journal of Gastrointestinal Pathophysiology*, 5: 91-99.
Narrative review
- Jonasson, C., Moum, B., Bang, C., Andersen, K. R. & Hatlebakk, J. G. (2012) Randomised clinical trial: a comparison between a GerdQ-based algorithm and an endoscopy-based approach for the diagnosis and initial treatment of GERD. *Alimentary Pharmacology & Therapeutics*, 35: 1290-1300.
Not in PICO
- Jones, M. P. (2003) Evaluation and treatment of dyspepsia. *Postgraduate Medical Journal*, 79: 25-29.
Narrative Review
- Jones, R. (1995) Gastroesophageal Reflux Disease in General-Practice. *Scandinavian Journal of Gastroenterology*, 30: 35-38.
Narrative Review
- Jones, R. (2008) Primary care research and clinical practice: gastroenterology. *Postgraduate Medical Journal*, 84: 454-458.
Narrative Review
- Jores-Nguyen-Xuan, T. H., Lanyi, B., Kruis, W. & Leifeld, L. (2010) Chromoendoscopy and virtual chromoendoscopy - Is there a practical value for the patient and gastroenterologist?. [German]. *Verdauungskrankheiten*, 28: 253-265.
Narrative review
- Jung, M. & Kiesslich, R. (1999) Chromoendoscopy and intravital staining techniques. *Bailliere's Clinical Gastroenterology*, 13: 11-19.
Narrative Review
- Jung, M., Hoffman, A. & Kiesslich, R. (2003) Early neoplasias in the gastrointestinal tract - How accurate is endoscopic diagnosis?. [German]. *Deutsche Medizinische Wochenschrift*, 128: S124-S126.
Narrative Review
- Kadri, S. R., Lao-Sirieix, P., O'Donovan, M., Debiram, I., Das, M., Blazeby, J. M., Emery, J., Boussioutas, A., Morris, H., Walter, F. M., Pharoah, P., Hardwick, R. H. & Fitzgerald, R. C. (2010) Acceptability

- and accuracy of a non-endoscopic screening test for Barrett's oesophagus in primary care: cohort study. *British Medical Journal*, 341.
Not in PICO
- Kanthan, R., Torkian, B. & Kanthan, S. C. (2004) Pathological validity of esophageal endoscopy. How real is what we see? Myth or reality? *Diseases of the Esophagus*, 17: 304-306.
Not in PICO
- Kara, M., DaCosta, R. S., Wilson, B. C., Marcon, N. E. & Bergman, J. (2004) Autofluorescence-based detection of early neoplasia in patients with Barrett's esophagus. *Digestive Diseases*, 22: 134-141.
Not in PICO
- Kara, M. A., Peters, F. P., Fockens, P., ten Kate, F. J. & Bergman, J. J. (2006) Endoscopic video-autofluorescence imaging followed by narrow band imaging for detecting early neoplasia in Barrett's esophagus. *Gastrointestinal Endoscopy*, 64: 176-185.
Not in PICO
- Kara, M. A. & Bergman, J. J. (2006) Autofluorescence imaging and narrow-band imaging for the detection of early neoplasia in patients with Barrett's esophagus. [Review] [20 refs]. *Endoscopy*, 38: 627-631.
Narrative Review
- Kastelein, F. & Kuipers, E. J. (2012) [Surveillance for Barrett's oesophagus: worthwhile?]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 156: A5497.
Narrative Review
- Katona, B. W. & Falk, G. W. (2011) Barrett's esophagus surveillance: When, how often, does it work? [Review]. *Gastrointestinal Endoscopy Clinics of North America*, 21: 9-24.
Narrative Review
- Kawano, T. & Endo, M. (1989) [Diagnosis and treatment of early esophageal carcinoma]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 47: 1102-1106.
In Japanese. Not enough information can be extracted to ascertain relevance.
- Kochhar, R., Rajwanshi, A., Malik, A. K., Gupta, S. K. & Mehta, S. K. (1988) Endoscopic fine needle aspiration biopsy of gastroesophageal malignancies. *Gastrointestinal Endoscopy*, 34: 321-323.
Not in PICO
- Kominek, P., Vitek, P., Urban, O., Zelenik, K., Halamka, M., Feltl, D., Cvek, J. & Matousek, P. (2013) Chromoendoscopy to detect early synchronous second primary esophageal carcinoma in patients with squamous cell carcinomas of the head and neck? *Gastroenterology Research and Practice*, 2013.
Not in PICO
- Kondo, N., Tsukuda, M. & Nishimura, G. (2012) Diagnostic sensitivity of 18fluorodeoxyglucose positron emission tomography for detecting synchronous multiple primary cancers in head and neck cancer patients. *European Archives of Oto-Rhino-Laryngology*, 269: 1503-1507.
Not in PICO
- Kostovski, A. (2006) Gastro-oesophageal reflux disease. [Croatian]. *Paediatrica Croatica, Supplement*, 50: 93-102.
Not in PICO
- Krauss, E., Agaimy, A., Douplik, A., Albrecht, H., Neumann, H., Hartmann, A., Hohenstein, R., Raithe, M., Hahn, E. G., Neurath, M. F. & Mudter, J. (2012) Normalized autofluorescence imaging diagnostics in upper GI tract: a new method to improve specificity in neoplasia detection. *International Journal of Clinical & Experimental Pathology*, 5: 956-964.
Not in PICO
- Krugmann, J., Neumann, H., Vieth, M. & Armstrong, D. (2013) What is the role of endoscopy and oesophageal biopsies in the management of GERD? *Best Practice and Research: Clinical Gastroenterology*, 27: 373-385.
Narrative review

- Kula, Z. & Welshof, A. (2007) The prevalence of Barrett's oesophagus in own material of 6326 endoscopies. *Gastroenterologia Polska*, 14: 85-89.
Not in PICO
- Kumagai, Y., Toi, M., Kawada, K. & Kawano, T. (2010) Angiogenesis in superficial esophageal squamous cell carcinoma: magnifying endoscopic observation and molecular analysis. [Review]. *Digestive Endoscopy*, 22: 259-267.
Narrative Review
- Kuzela, L., Vavrecka, A., Oltman, M. & Novotna, T. (1999) Treatment and surveillance of patients with Barrett's esophagus. [Slovak]. *Endoskopie*, 8: 9-11.
Narrative Review
- Kwon, K. A., Choi, I. J., Kim, Y. T., Dong, S. H. & Hahm, K. B. (2012) International digestive endoscopy network 2012: a patchwork of networks for the future.[Erratum appears in Clin Endosc. 2012 Nov;45(4):454 Note: Kim, Eun Young [corrected to Kim, Young-Tae]]. *Clinical Endoscopy*, 45: 209-210.
Not in PICO
- Ladabaum, U. & Dinh, V. (2010) Rate and yield of repeat upper endoscopy in patients with dyspepsia. *World Journal of Gastroenterology*, 16: 2520-2525.
Not in PICO
- Lambert, R. & Jacob, P. (1999) Diagnosis and evaluation of oesophageal cancers. [French]. *Revue du Praticien*, 49: 1166-1171.
Narrative Review
- Leclaire, S., Antonietti, M., Iwanicki-Caron, I., Duclos, A., Lemoine, F., Pessot, F. L., Michel, P., Ducrotté, P. & Fiore, F. (2011) Lugol chromo-endoscopy versus narrow band imaging for endoscopic screening of esophageal squamous-cell carcinoma in patients with a history of cured esophageal cancer: a feasibility study. *Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus / I.S.D.E.*, 24: 418-422.
Not in PICO
- Lee, M. H., Buterbaugh, K., Richards-Kortum, R. & Anandasabapathy, S. (2012) Advanced endoscopic imaging for Barrett's Esophagus: current options and future directions. [Review]. *Current Gastroenterology Reports*, 14: 216-225.
Narrative Review
- LeLorier, J., Page, V., Castilloux, A. M. & LeLorier, Y. (1997) Management of new symptoms of dyspepsia in the elderly in Quebec. *Canadian Journal of Gastroenterology*, 11: 669-672.
Not in PICO
- Lenglinger, J., Riegler, M., Cosentini, E., Asari, R., Mesteri, I., Wrba, F. & Schoppmann, S. F. (2012) Review on the annual cancer risk of Barrett's esophagus in persons with symptoms of gastroesophageal reflux disease. *Anticancer Research*, 32: 5465-5474.
Not in PICO
- Levy, M. J., Clain, J. E., Clayton, A., Halling, K. C., Kipp, B. R., Rajan, E., Roberts, L. R., Root, R. M., Sebo, T. J., Topazian, M. D., Wang, K. K., Wiersema, M. J. & Gores, G. J. (2007) Preliminary experience comparing routine cytology results with the composite results of digital image analysis and fluorescence in situ hybridization in patients undergoing EUS-guided FNA. *Gastrointestinal Endoscopy*, 66: 483-490.
Not in PICO
- Lieberman, D., Fennerty, M. B., Morris, C. D., Holub, J., Eisen, G. & Sonnenberg, A. (2004) Endoscopic evaluation of patients with dyspepsia: results from the national endoscopic data repository. *Gastroenterology*, 127: 1067-1075.
Not in PICO
- Liker, H., Hungin, P. & Wiklund, I. (2005) Managing gastroesophageal reflux disease in primary care: the patient perspective. [Review] [40 refs]. *Journal of the American Board of Family Practice*, 18:

- 393-400.
Not in PICO
- Loffeld, R. J. L. F. & van der Putten, A. B. M. M. (2003) The yield of UGIE: A study of a ten-year period in the 'Zaanstreek'. *Netherlands Journal of Medicine*, 61: 14-18.
Not in PICO
- Loffeld, R. J. L. F., Liberov, B. & Dekkers, P. E. P. (2012) The changing prevalence of upper gastrointestinal endoscopic diagnoses: a single-centre study. *Netherlands Journal of Medicine*, 70: 222-226.
Not in PICO
- Longcroft-Wheaton, G., Duku, M., Mead, R., Poller, D. & Bhandari, P. (2010) Acetic acid spray is an effective tool for the endoscopic detection of neoplasia in patients with Barrett's esophagus. *Clinical Gastroenterology & Hepatology*, 8: 843-847.
Not in PICO
- Lopes, A. B. & Fagundes, R. B. (2012) Esophageal squamous cell carcinoma - precursor lesions and early diagnosis. *World Journal of Gastrointestinal Endoscopy*, 4: 9-16.
Narrative Review
- Lu, X.-J., Chen, Z.-F., Guo, C.-L., Li, S.-S., Bai, W.-L., Jin, G.-L., Wang, Y.-X., Meng, F.-S., Gao, F. & Hou, J. (2004) Endoscopic survey of esophageal cancer in a high-risk area of China. *World Journal of Gastroenterology*, 10: 2931-2935.
Not in PICO
- Lunedei, V., Bazzoli, F., Pozzato, P., De, L. L., Zagari, R. M., Fossi, S., Ricciardiello, L., Maltoni, S. & Roda, E. (2002) Endoscopic surveillance in Barrett's esophagus. *Minerva Gastroenterologica e Dietologica*, 48: 63-71.
Not in PICO
- Mahadeva, S. & Goh, K. L. (2012) Clinically Significant Endoscopic Findings in a Multi-Ethnic Population With Uninvestigated Dyspepsia. *Digestive Diseases and Sciences*, 57: 3205-3212.
Not in PICO
- Makuuchi, H., Sugihara, T. & Nakasaki, H. (1981) Diagnosis of early esophageal carcinoma. 17 Cases and endoscopical examination. [Japanese]. *Journal of the Japan Broncho-Esophagological Society*, 32: 406-412.
Not in PICO
- Manes, G., Balzano, A., Marone, P., Lioniello, M. & Mosca, S. (2002) Appropriateness and diagnostic yield of upper gastrointestinal endoscopy in an open-access endoscopy system: a prospective observational study based on the Maastricht guidelines. *Alimentary Pharmacology & Therapeutics*, 16: 105-110.
Not in PICO
- Martinez De Haro, L. F., Munitiz, V., Ortiz, A., De Angulo, D. R., Navarro, M. D. & Parrilla, P. (2008) Outpatient monitoring of oesophageal pH with a catheter-free pH-meter (Bravo system). A study of tolerance, safety and efficacy. [Spanish]. *Cirugia Espanola*, 84: 201-209.
Not in PICO
- Masclée, G., Coloma, P. M., De, W. M., Kuipers, E. J. & Sturkenboom, M. C. (2014) Incidence of barrett's esophagus and esophageal adenocarcinoma in the United Kingdom and the Netherlands: Have we reached a plateau? *Gastroenterology*, 146: S147-S148.
Not in PICO
- Mason, J. M., Delaney, B., Moayyedi, P., Thomas, M. & Walt, R. (2005) Managing dyspepsia without alarm signs in primary care: new national guidance for England and Wales. *Alimentary Pharmacology & Therapeutics*, 21: 1135-1143.
NICE guideline on dyspepsia
- Mayinger, B., Neidhardt, S., Reh, H., Martus, P. & Hahn, E. G. (2001) Fluorescence induced with 5-aminolevulinic acid for the endoscopic detection and follow-up of esophageal lesions.

- Gastrointestinal Endoscopy*, 54: 572-578.
Not in PICO
- Mayinger, B., Horner, P., Jordan, M., Gerlach, C., Horbach, T., Hohenberger, W. & Hahn, E. G. (2001) Endoscopic fluorescence spectroscopy in the upper GI tract for the detection of GI cancer: initial experience. *American Journal of Gastroenterology*, 96: 2616-2621.
Not in PICO
- Mayinger, B. (2004) Endoscopic fluorescence spectroscopic imaging in the gastrointestinal tract. *Gastrointestinal Endoscopy Clinics of North America*, 14: 487-505.
Narrative Review
- Melleney, E. M. & Willoughby, C. P. (2002) Audit of a nurse endoscopist based one stop dyspepsia clinic. *Postgraduate Medical Journal*, 78: 161-164.
Not in PICO
- Meng, X. & Zhang, S. (2007) Endoscopic diagnosis of early upper gastrointestinal tumors. [Chinese]. *Chinese Journal of Gastroenterology*, 12: 259-262.
Narrative Review
- Meyer, V., Burtin, P., Bour, B., Blanchi, A., Cales, P., Oberti, F., Person, B., Croue, A., Dohn, S., Benoit, R., Fabiani, B. & Boyer, J. (1997) Endoscopic detection of early esophageal cancer in a high-risk population: Does Lugol staining improve videoendoscopy? *Gastrointestinal Endoscopy*, 45: 480-484.
Not in PICO
- Minami, H., Isomoto, H., Inoue, H., Akazawa, Y., Yamaguchi, N., Ohnita, K., Takeshima, F., Hayashi, T., Nakayama, T. & Nakao, K. (2014) Significance of Background Coloration in Endoscopic Detection of Early Esophageal Squamous Cell Carcinoma. *Digestion*, 89: 6-11.
Narrative review
- Modiano, N. & Gerson, L. B. (2007) Barrett's esophagus: Incidence, etiology, pathophysiology, prevention and treatment. *Therapeutics & Clinical Risk Management*, 3: 1035-1145.
Narrative Review
- Monma, K. (2003) Trends in widening application of endoscopic therapy for early-stage esophageal neoplasms. [Japanese]. *Nihon Naika Gakkai zasshi*, The: 10-20.
Not in PICO
- Monnier, P. & Savary, M. (1991) Early squamous cell carcinoma of the esophagus. Endoscopic morphology. [German]. *Verdauungskrankheiten*, 9: 88-93.
Not in PICO
- Morita, Y., Tanaka, S., Toyonaga, T. & Azuma, T. (2013) Barrett's adenocarcinoma in long-segment Barrett's esophagus successfully detected by narrow-band imaging with magnifying endoscopy. *Digestive Endoscopy*, 25: Suppl-5.
Not in PICO
- Mudawi, H. M. Y., Mahmoud, A. O. A., El Tahir, M. A., Suliman, S. H. & Ibrahim, S. Z. (2010) Use of endoscopy in diagnosis and management of patients with dysphagia in an African setting. *Diseases of the Esophagus*, 23: 196-200.
Not in PICO
- Muller-Gerbes, D., Aymaz, S. & Dormann, A. (2011) [Diagnostic and therapeutic management of Barrett's esophagus]. [German]. *Deutsche Medizinische Wochenschrift*, 136: 1796-1800.
Not in PICO
- Murakami, T., Tiwari, P., Musuku, S., Cunningham, J., Pugh, J. & Bhattacharyya, A. (1111) Dig deep to find the answer: The utility of endoscopic ultrasound with fine needle aspiration for a difficult diagnosis of esophageal cancer in chronic mucosal candidiasis. *American Journal of Gastroenterology. Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States. Conference Start: 20131011 Conference End: 20131016. Conference Publication: (var.pagings)*, 108: October.
Not in PICO

- Murphy, S. J., Dickey, W., Hughes, D. & O'Connor, F. A. (2005) Surveillance for Barrett's oesophagus: results from a programme in Northern Ireland. *European Journal of Gastroenterology & Hepatology*, 17: 1029-1035.
Not in PICO
- Muto, M., Minashi, K., Yano, T., Saito, Y., Oda, I., Nonaka, S., Omori, T., Sugiura, H., Goda, K., Kaise, M., Inoue, H., Ishikawa, H., Ochiai, A., Shimoda, T., Watanabe, H., Tajiri, H. & Saito, D. (2010) Early detection of superficial squamous cell carcinoma in the head and neck region and esophagus by narrow band imaging: a multicenter randomized controlled trial. *Journal of Clinical Oncology*, 28: 1566-1572.
Not in PICO
- Nabeya, K., Irimura, T. & Date, Y. (1981) [Early esophageal cancer]. [Japanese]. *Rinsho Kyobu Geka*, 1: 579-588.
Not in PICO
- Nagorni, A. & Brzacki, V. (2008) Staining in endoscopy of the upper segment of the gastrointestinal tract. *Archives of Gastroenterohepatology*, 27: 59-66.
Narrative Review
- Nakayama, K. & Yazawa, T. (1969) [Early diagnosis and treatment of esophageal tumor]. [Japanese]. *Naika - Internal Medicine*, 23: 1019-1025.
Outside date range.
- Ngamruengphong, S., Sharma, V. K. & Das, A. (2009) Diagnostic yield of methylene blue chromoendoscopy for detecting specialized intestinal metaplasia and dysplasia in Barrett's esophagus: a meta-analysis. *Gastrointestinal Endoscopy*, 69: 1021-1028.
Not in PICO
- Nguyen, V. X., Li Nguyen, V. T. & Nguyen, C. C. (2010) Appropriate use of endoscopy in the diagnosis and treatment of gastrointestinal diseases: Up-to-date indications for primary care providers. *International Journal of General Medicine*, 3: 345-357.
Narrative Review
- Nishizawa, M., Yamaki, G., Nomoto, K., Hosoi, T., Okada, T., Makino, T., Yamada, K., Shiga, T., Etoh, K. & Furusawa, H. (1984) Early detection of esophageal cancers, with special reference to the intraepithelial stage. [Japanese]. *Gan no rinsho*, Japan: 226-229.
In Japanese. Not enough information can be extracted to ascertain relevance.
- Nishizawa, M. (1988) [Differential diagnosis of early esophagus cancer: endoscopy]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1311-1315.
Narrative Review
- Norris, T. E. (1997) Esophagogastroduodenoscopy. *Primary Care - Clinics in Office Practice*, 24: 327-340.
Narrative Review
- Numans, M. E., van der Graaf, Y., de Wit, N. J. & de Melker, R. A. (2001) How useful is selection based on alarm symptoms in requesting gastroscopy? An evaluation of diagnostic determinants for gastro-oesophageal malignancy. *Scandinavian Journal of Gastroenterology*, 36: 437-443.
Not in PICO
- Nyren, O. (1991) Therapeutic Trial in Dyspepsia - Its Role in the Primary Care Setting. *Scandinavian Journal of Gastroenterology*, 26: 61-69.
Narrative review
- Oikonomidou, E., Anastasiou, F., Pilpilidis, I., Kouroumalis, E. & Lionis, C. (2011) Upper gastrointestinal endoscopy for dyspepsia: Exploratory study of factors influencing patient compliance in Greece. *BMC gastroenterology*, 11.
Not in PICO
- Op den Orth, J. O. (1989) Use of barium in evaluation of disorders of the upper gastrointestinal tract: current status. [Review] [76 refs][Erratum appears in Radiology 1990 May;175(2):586]. *Radiology*,

173: 601-608.

Narrative Review

Ormeçi, N., Savas, B., Coban, S., Palabiyikoglu, M., Ensari, A., Kuzu, I. & Kursun, N. (2008) The usefulness of chromoendoscopy with methylene blue in Barrett's metaplasia and early esophageal carcinoma. *Surgical Endoscopy*, 22: 693-700.

Not in PICO

Ortner, M. (2000) [Barrett esophagus. Regular referral for endoscopy]. [German]. *MMW Fortschritte der Medizin*, 142: 33-34.

Not in PICO

Ott, D. J., Gelfand, D. W., Wu, W. C. & Kerr, R. M. (1979) Secondary achalasia in esophagogastric carcinoma: re-emphasis of a difficult differential problem. *Revista Interamericana de Radiologia*, 4: 135-139.

Outside date range

Ottenjann, R. (1970) [Early diagnosis of gastrointestinal carcinoma]. [German]. *Medizinische Klinik*, 65: 2127-2131.

Outside date range

Overholt, B. F. & Panjehpour, M. (1995) Photodynamic therapy in Barrett's esophagus: reduction of specialized mucosa, ablation of dysplasia, and treatment of superficial esophageal cancer. *Seminars in Surgical Oncology*, 11: 372-376.

Not in PICO

Oyama, T. (2013) Diagnostic strategies of superficial Barrett's esophageal cancer for endoscopic submucosal dissection. *Digestive Endoscopy*, 25: Suppl-12.

Narrative Review

Pace, F. & Bianchi, P. G. (2004) Gastroesophageal reflux disease: a typical spectrum disease (a new conceptual framework is not needed). *The American journal of gastroenterology*, 99: 946-949.

Narrative Review

Padula, D., Lenti, M. V., Di, S. M., Miceli, E. & Corazza, G. R. (2013) A youngwoman with dysphagia. *Digestive and Liver Disease*, 45: S155-S156.

Not in PICO

Parente, F., Bargiggia, S. & Bianchi, P. G. (2002) Prospective audit of gastroscopy under the 'three-day rule': A regional initiative in Italy to reduce waiting time for suspected malignancy. *Alimentary Pharmacology and Therapeutics*, 16: 1011-1014.

Not in PICO

Paterson, H. M., McCole, D. & Auld, C. D. (2006) Impact of open-access endoscopy on detection of early oesophageal and gastric cancer 1994 - 2003: population-based study. *Endoscopy*, 38: 503-507.

Not in PICO

Patterson, R. N. & Johnston, S. D. (2003) Iron deficiency anaemia: Are the British Society of Gastroenterology guidelines being adhered to? *Postgraduate Medical Journal*, 79: 226-228.

Not in PICO

Pech, O., Rabenstein, T., Manner, H., Petrone, M. C., Pohl, J., Vieth, M., Stolte, M. & Ell, C. (2008) Confocal laser endomicroscopy for in vivo diagnosis of early squamous cell carcinoma in the esophagus. *Clinical Gastroenterology & Hepatology*, 6: 89-94.

Not in PICO

Peck, J., Martin, J., Li, F., Latchana, N., Bekaii-Saab, T., El-Dika, S. & Walker, J. (1111) Endoscopic ultrasound is of limited benefit in the management of obstructing esophageal cancers. *American Journal of Gastroenterology. Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States. Conference Start: 20131011 Conference End: 20131016. Conference Publication: (var.pagings)*, 108: October.

Not in PICO

- Peng, G.-Y., Wu, Y.-W., Long, Q.-L., Chen, L., Zhao, J.-J. & Li, X.-H. (2011) A new endoscopic classification system of early-stage esophageal carcinoma and its usefulness in assessing the infiltration depth of esophageal carcinoma. *Cancer Investigation*, 29: 167-172.
Narrative Review
- Peng, G., Long, Q., Wu, Y., Zhao, J., Chen, L. & Li, X. (2011) Evaluation of double vital staining with lugol's iodine and methylene blue in diagnosing superficial esophageal lesions. *Scandinavian Journal of Gastroenterology*, 46: 406-413.
Not in PICO
- Peters, F. P., Curvers, W. L., Rosmolen, W. D., de Vries, C. E., ten Kate, F. J., Krishnadath, K. K., Fockens, P. & Bergman, J. J. (2008) Surveillance history of endoscopically treated patients with early Barrett's neoplasia: nonadherence to the Seattle biopsy protocol leads to sampling error. *Diseases of the Esophagus*, 21: 475-479.
Not in PICO
- Pierzchajlo, R. P. J., Ackermann, R. J. & Vogel, R. L. (1998) Esophagogastroduodenoscopy performed by a family physician - A case series of 793 procedures. *Journal of Family Practice*, 46: 41-46.
Not in PICO
- Pohl, H., Koch, M., Khalifa, A., Papanikolaou, I. S., Scheiner, K., Wiedenmann, B. & Rosch, T. (2007) Evaluation of endocytoscopy in the surveillance of patients with Barrett's esophagus. *Endoscopy*, 39: 492-496.
Not in PICO
- Pohl, H., Aschenbeck, J., Drossel, R., Schroder, A., Mayr, M., Koch, M., Rothe, K., Anders, M., Voderholzer, W., Hoffmann, J., Schulz, H. J., Liehr, R. M., Gottschalk, U., Wiedenmann, B. & Rosch, T. (2008) Endoscopy in Barrett's oesophagus: adherence to standards and neoplasia detection in the community practice versus hospital setting. *Journal of Internal Medicine*, 264: 370-378.
Not in PICO
- Pohl, H., Rosch, T., Vieth, M., Koch, M., Becker, V., Anders, M., Khalifa, A. C. & Meining, A. (2008) Miniprobe confocal laser microscopy for the detection of invisible neoplasia in patients with Barrett's oesophagus. *Gut*, 57: 1648-1653.
Not in PICO
- Polkowski, W., Polkowska, G. & Melko, J. (2001) Barrett oesophagus and adenocarcinoma of the oesophagus: Progress in the diagnosis and treatment at the end of XX century. [Polish]. *Gastroenterologia Polska*, 8: 341-353.
Narrative Review
- Pomakov, P., Lyutzkanova, E., Baburov, S. & Batanova, S. (2000) Double contrast radiography of the esophagus. [Bulgarian]. *Rentgenologiya i Radiologiya*, 39: 269-271.
Narrative Review
- Ponchon, T., Makuuchi, H., Morita, Y., Fukuda, M., Mitani, T., Shirasaka, D., Aoyama, N., Amano, Y., Moriyama, I., Oose, T. & Kinoshita, Y. (2004) Images of early cancer: esophageal squamous-cell carcinoma. *Endoscopy*, 36: 811-820.
Not in PICO
- Provenzale, D., Schmitt, C. & Wong, J. B. (1999) Barrett's esophagus: a new look at surveillance based on emerging estimates of cancer risk (Structured abstract). *American Journal of Gastroenterology*, 94: 2043-2053.
Not in PICO
- Qizilbash, A. H., Castelli, M., Kowalski, M. A. & Churly, A. (1980) Endoscopic brush cytology and biopsy in the diagnosis of cancer of the upper gastrointestinal tract. *Acta Cytologica*, 24: 313-318.
Not in PICO
- Quera, R., O'Sullivan, K. & Quigley, E. M. (2006) Surveillance in Barrett's oesophagus: will a strategy focused on a high-risk group reduce mortality from oesophageal adenocarcinoma? *Endoscopy*, 38: 162-169.
Not in PICO

- Raman, A., Sternbach, J., Babajide, A., Sheth, K. & Schwaitzberg, S. D. (2010) When does testing for GERD become cost effective in an integrated health network? *Surgical Endoscopy and Other Interventional Techniques*, 24: 1245-1249.
Not in PICO
- Ramus, J. R., Caygill, C. P., Gatenby, P. A. & Watson, A. (2008) Current United Kingdom practice in the diagnosis and management of columnar-lined oesophagus: results of the United Kingdom National Barrett's Oesophagus Registry endoscopist questionnaire. *European Journal of Cancer Prevention*, 17: 422-425.
Not in PICO
- Razorenov, L. V. (1980) [Diagnostic errors in esophageal cancer]. [Russian]. *Voprosy Onkologii*, 26: 35-38.
Not in PICO
- Reid, B. J. (1991) Barrett's esophagus and esophageal adenocarcinoma. [Review] [124 refs]. *Gastroenterology Clinics of North America*, 20: 817-834.
Narrative Review
- Reid, B. J., Kostadinov, R. & Maley, C. C. (2011) New strategies in Barrett's esophagus: Integrating clonal evolutionary theory with clinical management. *Clinical Cancer Research*, 17: 3512-3519.
Narrative Review
- Rey, J. W., Labenz, J., Hansen, T. & Kiesslich, R. (2011) Gastroesophageal reflux disease and its complications - Endoscopic approaches. [German]. *Viszeralmedizin: Gastrointestinal Medicine and Surgery*, 27: 133-140.
Narrative Review
- Robertson, C. S., Mayberry, J. F., Nicholson, D. A., James, P. D. & Atkinson, M. (1988) Value of endoscopic surveillance in the detection of neoplastic change in Barrett's oesophagus. *British Journal of Surgery*, 75: 760-763.
Not in PICO
- Roedl, J. B., Colen, R. R., King, K., Fischman, A. J., Mueller, P. R. & Blake, M. A. (2008) Visual PET/CT scoring for nonspecific 18F-FDG uptake in the differentiation of early malignant and benign esophageal lesions. *AJR.American Journal of Roentgenology*, 191: 515-521.
Not in PICO
- Roth, A., Lang, S. & Kolaric, K. (1981) Esophageal tumors--the role of esophagoscopy. *Cancer Detection & Prevention*, 4: 351-359.
Not in PICO
- Ruigomez, A., Rodriguez, L. A. G., Wallander, M.-A., Johansson, S. & Dent, J. (2008) Endoscopic findings in a cohort of newly diagnosed gastroesophageal reflux disease patients registered in a UK primary care database. *Diseases of the Esophagus*, 21: 251-256.
Not in PICO
- Salo, M., Collin, P., Kyronpalo, S., Rasmussen, M., Huhtala, H. & Kaukinen, K. (2008) Age, symptoms and upper gastrointestinal malignancy in primary care endoscopy. *Scandinavian Journal of Gastroenterology*, 43: 122-127.
Not in PICO
- Sampliner, R. E. (2010) Surveillance of Barrett's esophagus. *Techniques in Gastrointestinal Endoscopy*, 12: 67-68.
Narrative Review
- Sanchez-del, R. A., Quintero, E. & Alarcon, O. (2004) [Appropriateness of indications for upper gastrointestinal endoscopy in open-access endoscopy units]. [Spanish]. *Gastroenterologia y Hepatologia*, 27: 119-124.
- Savage, N. (2011) Early detection: Spotting the first signs. *Nature*, 471: S14-S15.
Narrative Review

- Savary, M. (1985) [Cancer of the esophagus: early endoscopic diagnosis]. [French]. *Gastroenterologie Clinique et Biologique*, 9: 7-9.
Narrative review
- Saxena, P. & Canto, M. I. (2013) Red flag imaging techniques in Barrett's Esophagus. *Gastrointestinal Endoscopy Clinics of North America*, 23: 535-547.
Not in PICO
- Schmid, E., Blaich, E., Schwarzkopf, H. & Kovarik, P. (1978) [Diagnostic accuracy of fiber endoscopy in esophageal and gastric carcinoma. Attempt at error analysis]. [German]. *Zeitschrift fur Gastroenterologie*, 16: 229-234.
Outside date range
- Schweigert, M., Dubecz, A. & Stein, H. J. (2013) Oesophageal cancer--an overview. [Review]. *Nature Reviews Gastroenterology & Hepatology*, 10: 230-244.
Narrative review
- Seifert, B., Vojtiskova, J., Charvatova, E. & Koudelka, T. (2006) Management of gastroesophageal reflux disease (GERD) in primary care. [Czech]. *Ceska a Slovenska Gastroenterologie a Hepatologie*, 60: 157-162.
Not in PICO
- Seitz, J. F., Monges, G., Navarro, P., Giovannini, M. & Gauthier, A. (1990) Endoscopic detection of dysplasia and subclinical cancer of the esophagus. Results of a prospective study using toluidine blue vital staining in 100 patients with alcoholism and smoking. [French]. *Gastroenterologie Clinique et Biologique*, 14: 15-21.
Not in PICO
- Shaheen, N. & Ransohoff, D. F. (2002) Gastroesophageal reflux, Barrett esophagus, and esophageal cancer: Clinical applications. *Journal of the American Medical Association*, 287: 1982-1986.
Narrative Review
- Shaheen, N. J., Green, B., Medapalli, R. K., Mitchell, K. L., Wei, J. T., Schmitz, S. M., West, L. M., Brown, A., Noble, M., Sultan, S. & Provenzale, D. (2005) The perception of cancer risk in patients with prevalent Barrett's esophagus enrolled in an endoscopic surveillance program. *Gastroenterology*, 129: 429-436.
Not in PICO
- Sharma, P. & Sidorenko, E. I. (2005) Are screening and surveillance for Barrett's oesophagus really worthwhile? *Gut*, 54: 127-132.
Narrative Review
- Sharma, P., Chey, W., Hunt, R., Laine, L., Malfertheiner, P. & Wani, S. (2009) Endoscopy of the esophagus in gastroesophageal reflux disease: are we losing sight of symptoms? Another perspective. *Diseases of the Esophagus*, 22: 461-466.
Narrative Review
- Sharma, P. (2009) Barrett's esophagus and cancer. Preface. *Surgical Oncology Clinics of North America*, 18: xv-xvi.
Narrative Review
- Sharma, V. K. (2014) - Role of endoscopy in GERD. - *Gastroenterology Clinics of North America*, 43: 39-46.
Narrative review
- Sharpe, D., Williams, R. N., Ubhi, S. S., Sutton, C. D. & Bowrey, D. J. (2010) The "two-week wait" referral pathway allows prompt treatment but does not improve outcome for patients with oesophago-gastric cancer. *European Journal of Surgical Oncology*, 36: 977-981.
Not in PICO
- Shawihdi, M., Thompson, E., Kapoor, N., Powell, G., Sturgess, R. P., Stern, N., Roughton, M., Pearson, M. G. & Bodger, K. (2014) Variation in gastroscopy rate in English general practice and outcome for oesophagogastric cancer: retrospective analysis of Hospital Episode Statistics. *Gut*, 63: 250-

261.

Not in PICO

Shimizu, Y., Omori, T., Yokoyama, A., Yoshida, T., Hirota, J., Ono, Y., Yamamoto, J., Kato, M. & Asaka, M. (2008) Endoscopic diagnosis of early squamous neoplasia of the esophagus with iodine staining: high-grade intra-epithelial neoplasia turns pink within a few minutes. *Journal of Gastroenterology & Hepatology*, 23: 546-550.

Not in PICO

Shimizu, M., Zaninotto, G., Nagata, K., Graham, D. Y. & Lauwers, G. Y. (2013) Esophageal squamous cell carcinoma with special reference to its early stage. [Review]. *Best Practice & Research in Clinical Gastroenterology*, 27: 171-186.

Narrative review

Shukla, R., Abidi, W. M., Richards-Kortum, R. & Anandasabapathy, S. (2011) Endoscopic imaging: How far are we from real-time histology? *World Journal of Gastrointestinal Endoscopy*, 3: 183-194.

Narrative Review

Siewert, J. R. & Fink, U. (1997) Delays in the diagnosis of oesophagogastric cancer: a consecutive case series. Commentary: Britain does better than Germany before patients reach hospital. *BMJ*, 314: 471.

Comment

Singh, A., Siddiqui, U., Konda, V., Xiao, S.-Y. & Waxman, I. (1111) Use of high-definition narrow band imaging with magnification to successfully identify early esophageal squamous cancer, predict depth of invasion, and guide endoscopic therapy. *American Journal of Gastroenterology. Conference: 78th Annual Scientific Meeting of the American College of Gastroenterology San Diego, CA United States. Conference Start: 20131011 Conference End: 20131016. Conference Publication: (var.pagings)*, 108: October.

Not in PICO

Slehria, S. & Sharma, P. (2003) Barrett esophagus. *Current Opinion in Gastroenterology*, 19: 387-393.

Narrative Review

Smithers, B. M., Fahey, P. P., Corish, T., Gotley, D. C., Falk, G. L., Smith, G. S., Kiroff, G. K., Clouston, A. D., Watson, D. I. & Whiteman, D. C. (2010) Symptoms, investigations and management of patients with cancer of the oesophagus and gastro-oesophageal junction in Australia. *Medical Journal of Australia*, 193: 572-577.

Not in PICO

Song, S. W., Jun, B. C., Cho, K. J., Lee, S., Kim, Y. J. & Park, S. H. (2011) CT evaluation of vocal cord paralysis due to thoracic diseases: a 10-year retrospective study. *Yonsei Medical Journal*, 52: 831-837.

Not in PICO

Soumekh, A., Schnoll-Sussman, F. H. & Katz, P. O. (2014) Reflux and Acid Peptic Diseases in the Elderly. *Clinics in Geriatric Medicine*, 30: 29-41.

Narrative review

Spechler, S. J. (1949) Esophageal complications of gastroesophageal reflux disease: presentation, diagnosis, management, and outcomes. [Review] [46 refs]. *Clinical Cornerstone*, 5: 41-48.

Narrative Review

Stanghellini, V., Tosetti, C., Barbara, G., De Giorgio, R., Salvioli, B. & Corinaldesi, R. (2000) Review article: the continuing dilemma of dyspepsia. *Alimentary Pharmacology & Therapeutics*, 14: 23-30.

Narrative Review

Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M. & Hamilton, W. (2013) The risk of oesophago-gastric cancer in symptomatic patients in primary care: a large case-control study using electronic records. *British Journal of Cancer*, 108: 25-31.

Not in PICO

- Starkov, I. G., Solodinina, E. N., Konstantinova, M. M., Shishin, K. V., Kurushkina, N. A. & Gordienko, E. N. (2013) [Synchronous esophageal lesions: early cancer and gastrointestinal tumor]. [Russian]. *Khirurgiia*, 58-60.
In Russian. Not enough information can be extracted to ascertain relevance.
- Steele, G. H. (1996) Cost-effective management of dyspepsia and gastroesophageal reflux disease. *Primary Care - Clinics in Office Practice*, 23: 561-576.
Narrative review
- Stellon, A. J. & Kenwright, S. E. (1997) Iron deficiency anaemia in general practice: Presentations and investigations. *British Journal of Clinical Practice*, 51: 78-80.
- Suzuki, H., Kobayashi, S., Endo, M. & Nakayama, K. (1972) Diagnosis of early esophageal cancer. *Surgery*, 71: 99-103.
Outside date range
- Takahashi, A. & Oyama, T. (2013) Barrett's esophageal adenocarcinoma diagnosed by narrow-band imaging magnifying endoscopy. *Digestive Endoscopy*, 25: Suppl-9.
Not in PICO
- Takeshita, K., Kawano, T., Saito, N., Nagai, K., Tani, M., Honda, T., Inoue, H., Yano, K., Hayashi, S., Saeki, I. & Iwai, T. (1998) [Endoscopic diagnosis of early cancer in the esophagogastric junctional region]. [Japanese]. *Nippon Geka Gakkai Zasshi. Journal of Japan Surgical Society*, 99: 558-563.
Not in PICO
- Talley, N. J., Lam, S. K., Goh, K. L. & Fock, K. M. (1998) Management guidelines for uninvestigated and functional dyspepsia in the Asia-Pacific region: First Asian Pacific working party on functional dyspepsia. *Journal of Gastroenterology and Hepatology*, 13: 335-353.
Narrative review
- Talley, N. J. (2004) What the physician needs to know for correct management of gastro-oesophageal reflux disease and dyspepsia. *Alimentary Pharmacology & Therapeutics*, 20: 23-30.
Narrative Review
- Taylor, J. B. & Rubenstein, J. H. (2010) Meta-Analyses of the Effect of Symptoms of Gastroesophageal Reflux on the Risk of Barrett's Esophagus. *American Journal of Gastroenterology*, 105: 1730-1737.
Not in PICO
- Thomson, A. B., Barkun, A. N., Armstrong, D., Chiba, N., White, R. J., Daniels, S., Escobedo, S., Chakraborty, B., Sinclair, P. & Van Zanten, S. J. (2003) The prevalence of clinically significant endoscopic findings in primary care patients with uninvestigated dyspepsia: the Canadian Adult Dyspepsia Empiric Treatment - Prompt Endoscopy (CADET-PE) study.[Erratum appears in Aliment Pharmacol Ther. 2004 Sep 15;20(6):702]. *Alimentary Pharmacology & Therapeutics*, 17: 1481-1491.
Not in PICO
- Thrift, A. P., Kramer, J. R., Qureshi, Z., Richardson, P. A. & El-Serag, H. B. (2013) Age at onset of GERD symptoms predicts risk of Barrett's esophagus. *American Journal of Gastroenterology*, 108: 915-922.
Not in PICO
- Tomizawa, Y. & Waxman, I. (2014) - Enhanced mucosal imaging and the esophagus--ready for prime time? - *Current Gastroenterology Reports*, 16: 389.
Narrative review
- Trillo, S. E., Lopez Fananas, M. S., Villaverde Royo, M. V. & Isanta, P. C. (2005) Study of the gastroscopies requested at a health centre. [Spanish]. *Atencion Primaria*, 35: 375-377.
Not in PICO
- Tu, C.-H., Muto, M., Horimatsu, T., Taku, K., Yano, T., Minashi, K., Onozawa, M., Nihei, K., Ishikura, S., Ohtsu, A. & Yoshida, S. (2011) Submucosal tumor appearance is a useful endoscopic predictor of early primary-site recurrence after definitive chemoradiotherapy for esophageal squamous cell carcinoma. *Diseases of the Esophagus*, 24: 274-278.
Not in PICO

- Tutuian, R. (2006) Update in the diagnosis of gastroesophageal reflux disease. *Journal of Gastrointestinal and Liver Diseases*, 15: 243-247.
Narrative Review
- Tytgat, G. N. (1999) Barrett's esophagus: is it all that bad?. [Review] [54 refs]. *Canadian Journal of Gastroenterology*, 13: 385-388.
Narrative Review
- Tytgat, G. N., Van Sandick, J. W., Lanschot, J. J. & Obertop, H. (2003) Role of surveillance in intestinal metaplasia of the esophagus and gastroesophageal junction. [Review] [59 refs]. *World Journal of Surgery*, 27: 1021-1025.
Narrative Review
- Urquhart, P., Dacosta, R. & Marcon, N. (1111) Endoscopic mucosal imaging of gastrointestinal neoplasia in 2013. *Current Gastroenterology Reports*, 15: Jul.
Narrative review
- Vakil, N. (2003) Review article: test and treat or treat and test in reflux disease? *Alimentary Pharmacology & Therapeutics*, 17: 57-59.
Narrative Review
- Vakil, N. (2008) Endoscopy in GERD: Boondoggle, diagnostic test, or risk management tool? *American Journal of Gastroenterology*, 103: 276-278.
Narrative Review
- Vakil, N., Talley, N., van Zanten, S. V., Flook, N., Persson, T., Bjorck, E., Lind, T. & Bolling-Sternevald, E. (2009) Cost of Detecting Malignant Lesions by Endoscopy in 2741 Primary Care Dyspeptic Patients Without Alarm Symptoms. *Clinical Gastroenterology and Hepatology*, 7: 756-761.
Not in PICO
- van Kerkhoven, L. A. S., van Rijswijk, S. J., van Rossum, L. G. M., Laheij, R. J. F., Witteman, E. M., Tan, A. C. I. T. & Jansen, J. B. M. J. (2007) Is there any association between referral indications for open-access upper gastrointestinal endoscopy and endoscopic findings? *Endoscopy*, 39: 502-506.
Not in PICO
- Van Sandick, J. W., Bartelsman, J. F., van Lanschot, J. J., Tytgat, G. N. & Obertop, H. (2000) Surveillance of Barrett's oesophagus: physicians' practices and review of current guidelines. *European Journal of Gastroenterology & Hepatology*, 12: 111-117.
Not in PICO
- Van Soest, E. M., Dieleman, J. P., Siersema, P. D., Sturkenboom, M. C. & Kuipers, E. J. (2005) Increasing incidence of Barrett's oesophagus in the general population. *Gut*, 54: 1062-1066.
Not in PICO
- Van Soest, E. M., Dieleman, J. P., Sturkenboom, M. C., Siersema, P. D. & Kuipers, E. J. (2008) Gastro-oesophageal reflux, medical resource utilization and upper gastrointestinal endoscopy in patients at risk of oesophageal adenocarcinoma. *Alimentary Pharmacology & Therapeutics*, 28: 137-143.
Not in PICO
- van Zanten, S. J. O. V., Thomson, A. B. R., Barkun, A. N., Armstrong, D., Chiba, N., White, R. J., Escobedo, S. & Sinclair, P. (2006) The prevalence of Barrett's oesophagus in a cohort of 1040 Canadian primary care patients with uninvestigated dyspepsia undergoing prompt endoscopy. *Alimentary Pharmacology & Therapeutics*, 23: 595-599.
Not in PICO
- Veldhuyzen van Zanten, S. J., Bradette, M., Chiba, N., Armstrong, D., Barkun, A., Flook, N., Thomson, A., Bursey, F. & Canadian Dyspepsia Working Group (2005) Evidence-based recommendations for short- and long-term management of uninvestigated dyspepsia in primary care: an update of the Canadian Dyspepsia Working Group (CanDys) clinical management tool. [Review] [233 refs]. *Canadian Journal of Gastroenterology*, 19: 285-303.
Guideline
- Voutilainen, M., Mantynen, T., Mauranen, K., Kunnamo, I. & Juhola, M. (2005) Is it possible to reduce endoscopy workload using age, alarm symptoms and H-pylori as predictors of peptic ulcer and

- oesophagogastric cancers? *Digestive and Liver Disease*, 37: 526-532.
Not in PICO
- Wang, G. Q. (1981) Endoscopic diagnosis of early oesophageal carcinoma. *Journal of the Royal Society of Medicine*, 74: 502-503.
Not in PICO
- Wang, K. K. (2010) Endoscopic treatment for Barrett's esophagus and early esophageal cancer. *Journal of Gastrointestinal Surgery*, 14: 946-947.
Not in PICO
- Wang, R. H. (2010) [New developments for endoscopic management of Barrett's esophagus with high grade dysplasia]. [Review] [Chinese]. *Zhejiang da Xue Xue Bao.Yi Xue Ban/Journal of Zhejiang University.Medical Sciences*, 39: 534-541.
Narrative Review
- Wang, Z. Y. (1988) Diagnosis of early esophageal carcinoma: correlational study of radiologic fiber-esophagoscopy and pathologic findings. [Chinese]. *Zhonghua yi xue za zhi*, 68: 693-695.
In Chinese. Not enough information can be extracted to ascertain relevance.
- Warich-Eitel, S., Fischbach, W. & Eck, M. (2010) Endoscopic-biopic diagnostics, surveillance of and therapy for gastrointestinal diseases according to guidelines. [German]. *Zeitschrift fur Gastroenterologie*, 48: 414-419.
Not in PICO
- Weiser, H. F., Lange, R. & Feussner, H. (1986) How can we diagnose the early stage of esophageal cancer? Diagnosis of early esophageal cancer. *Endoscopy*, 18: Suppl-10.
Narrative review
- Westhoff, B., Brotze, S., Weston, A., McElhinney, C., Cherian, R., Mayo, M. S., Smith, H. J. & Sharma, P. (2005) The frequency of Barrett's esophagus in high-risk patients with chronic GERD. *Gastrointestinal Endoscopy*, 61: 226-231.
Not in PICO
- Wickramasinghe, K. S., Chandrasoma, P. T. & Chandraratna, P. A. (2002) Detection of Barrett's epithelium by acoustic microscopy. *Ultrasound in Medicine & Biology*, 28: 203-207.
Not in PICO
- Wilkins, T. & Gillies, R. A. (2005) Office-based unsedated ultrathin esophagoscopy in a primary care setting. *Annals of Family Medicine*, 3: 126-130.
Not in PICO
- Williams, J. F., Sontag, S. J., Schnell, T. & Leya, J. (2009) Non-Cardiac Chest Pain: The Long-Term Natural History and Comparison With Gastroesophageal Reflux Disease. *American Journal of Gastroenterology*, 104: 2145-2152.
Not in PICO
- Wilson, J. A. & Vela, M. F. (2008) New esophageal function testing (impedance, Bravo pH monitoring, and high-resolution manometry): Clinical relevance. *Current Gastroenterology Reports*, 10: 222-230.
Narrative Review
- Wlodarczyk, J. (2007) Application of Lugol solution in the gastroesophageal reflux disease. [Polish]. *Przegląd Lekarski*, 64: 549-551.
Not in PICO
- Wo, J. M., Mendez, C., Harrell, S., Joubran, R., Bressoud, P. F. & McKinney, W. P. (2004) Clinical impact of upper endoscopy in the management of patients with gastroesophageal reflux disease. *American Journal of Gastroenterology*, 99: 2311-2316.
Not in PICO
- Wong Kee Song, L. M. (2005) Optical spectroscopy for the detection of dysplasia in Barrett's esophagus. [Review] [23 refs]. *Clinical Gastroenterology & Hepatology*, 3: Suppl-7.
Narrative Review

- Wong, T., Tian, J. & Nagar, A. B. (2010) Barrett's surveillance identifies patients with early esophageal adenocarcinoma. *American Journal of Medicine*, 123: 462-467.
Not in PICO
- Wu, J. C. Y. (2008) Gastroesophageal reflux disease: An Asian perspective. *Journal of Gastroenterology and Hepatology*, 23: 1785-1793.
Narrative Review
- Wu, J., Pan, Y.-M., Wang, T.-T., Gao, D.-J. & Hu, B. (1111) Endotherapy versus surgery for early neoplasia in Barrett's esophagus: A meta-analysis. *Gastrointestinal Endoscopy*, 79: February.
Not in PICO
- Wu, J., Huang, C., Xiao, H., Tang, Q. & Cai, W. (2013) Weight loss and resting energy expenditure in male patients with newly diagnosed esophageal cancer. *Nutrition*, 29: 1310-1314.
Not in PICO
- Xiong, C.-L. & Huang, Y. (2008) Diagnostic value of magnifying endoscopy in early-stage gastrointestinal tumors and their precancerous lesions. [Chinese]. *World Chinese Journal of Digestology*, 16: 3086-3090.
Narrative Review
- Yamamoto, I., Yamaki, G., Kobayashi, S., Maruyama, T. & Shirakabe, H. (1983) Radiological diagnosis of early esophageal carcinoma. *Journal Belge de Radiologie*, 66: 1-8.
Narrative review
- Yamamuro, E. M., Cecconello, I., Iriya, K., Tomishigue, T., Oliveira, M. A. & Pinotti, H. W. (1999) Lugol dye endoscopy for analysis of esophageal mucosa in achalasia. *Hepato-Gastroenterology*, 46: 1687-1691.
Not in PICO
- Yamashina, T., Uedo, N., Matsui, F., Ishihara, R. & Tomita, Y. (2013) Usefulness of chromoendoscopy and magnifying narrow band imaging endoscopy for diagnosis of demarcation of adenocarcinoma in Barrett's esophagus. *Digestive Endoscopy*, 25: Suppl-6.
Narrative Review
- Yao, K., Takaki, Y., Matsui, T., Iwashita, A., Anagnostopoulos, G. K., Kaye, P. & Ragunath, K. (2008) Clinical Application of Magnification Endoscopy and Narrow-Band Imaging in the Upper Gastrointestinal Tract: New Imaging Techniques for Detecting and Characterizing Gastrointestinal Neoplasia. *Gastrointestinal Endoscopy Clinics of North America*, 18: 415-433.
Not in PICO
- Young, J. A., Hughes, H. E. & Lee, F. D. (1980) Evaluation of endoscopic brush and biopsy touch smear cytology and biopsy histology in the diagnosis of carcinoma of the lower oesophagus and cardia. *Journal of Clinical Pathology*, 33: 811-814.
Not in PICO
- Zaninotto, G., Avellini, C., Barbazza, R., Baruchello, G., Battaglia, G., Benedetti, E., Bernardi, A., Boccu, C., Bonoldi, E., Bottona, E., Bozzola, L., Canizzaro, R., Canzonieri, V., Caroli, A., Carta, A., Colonna, A., Costa-Biedo, F., Dal, B. N., De, B. R., De, B. M., De, B. F., De, P. G., Di, M. F., Doglioni, C., Donisi, P. M., Franceschi, M., Furlanetto, A., Germana, B., Grassi, S. A., Macor, V., Marcon, V., Marin, R., Meggiato, T., Melina, V., Menghi, A., Milan, R., Militello, C., Molena, D., Monica, F., Murer, B., Nisi, E., Olivieri, P., Orzes, N., Parenti, A., Paternello, E., Penelli, N., Pilotto, A., Pisciole, F., Pozzato, F., Ronzani, G., Rugge, M., Saggiaro, A., Stracca-Pansa, V., Togni, R., Valiante, F. & Vianello, F. (2001) Prevalence of intestinal metaplasia in the distal oesophagus, oesophagogastric junction and gastric cardia in symptomatic patients in north-east Italy: a prospective, descriptive survey. The Italian Ulcer Study Group "GISU". *Digestive & Liver Disease*, 33: 316-321.
Not in PICO
- Zhu, L. Y. & Li, X. B. (2014) - Narrow band imaging: application for early-stage gastrointestinal neoplasia. - *Journal of Digestive Diseases*, 15: 217-223.
Narrative review

PANCREATIC CANCER

Review question:

What is the risk of pancreatic cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

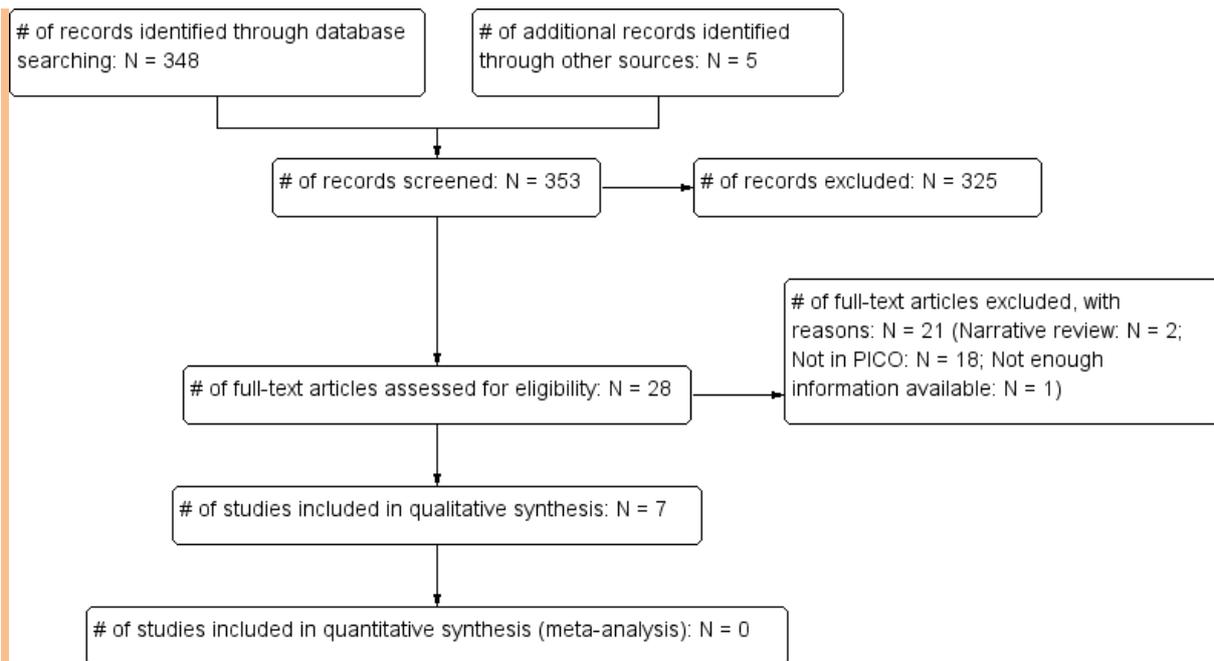
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	973	152	31/05/2013
<i>Premedline</i>	All-2012	130	19	31/05/2013
<i>Embase</i>	All-2012	1396	245	07/06/2013
<i>Cochrane Library</i>	All-2012	191	0	07/06/2013
<i>Psychinfo</i>	All-2012	29	6	31/05/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	368	35	10/06/2013

Total References retrieved (after de-duplication): 331

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-20/08/2014	48	2	20/08/2014
<i>Premedline</i>	5/2013-20/08/2014	90	4	20/08/2014
<i>Embase</i>	5/2013-20/08/2014	151	11	20/08/2014
<i>Cochrane Library</i>	5/2013-20/08/2014	60	0	20/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	5/2013-20/08/2014	55	2	20/08/2014

Total References retrieved (after de-duplication): 17



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main bias and applicability concerns to note in terms of patient selection were that this was not clearly consecutive or random in four of the studies, with three of these studies conducted in a setting that is not clearly directly representative of UK-based primary care. The other bias and applicability concerns to note include missing data, population with restricted age range, short follow up and underspecified presenting symptoms. These issues should all be born in mind when evaluating the evidence.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Collins (2013)	+	+	+	+	+	+	+
Hallissey (1990)	+	+	+	+	?	+	+
Hippisley-Cox (2012)	+	+	+	-	+	+	+
Mahadeva (2008)	?	+	+	+	-	+	+
Muris (1995)	-	+	+	+	-	-	+
Stapley (2012)	-	+	+	+	+	+	+
Tosetti (2010)	-	+	?	+	-	-	+

- High
 ? Unclear
 + Low

Study results

Table 1: Pancreatic cancer: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI)
Collins (2013)	Abdominal pain	All patients	0.14 (0.12-0.15) 354/254704
		Women	0.1 (0.09-0.12) 154/148290
		Men	0.19 (0.16-0.22) 200/106768
Hippisley-Cox (2012)	Abdominal pain	All patients	0.3 (0.3-0.4) 311/94103
Stapley (2012)	Abdominal pain	All patients	0.2 (0.19-0.22) Cases: 1540/3635 Controls: 1004/16459
Stapley (2012)	Abdominal pain	Patients ≥ 60 years	0.3 (0.3-0.4)
Stapley (2012)	Abdominal pain (attended ≥ twice)	Patients ≥ 60 years	1 (0.8-1.2)
Hallissey (1990)	Dyspepsia	All patients	0.23 (0.09-0.53) 6/2585
Mahadeva (2008)	Dyspepsia	All patients (they were aged 18-45 years)	0.23 (0.01-1.49) 1/432
Hippisley-Cox (2012)	Abdominal distension	All patients	0.3 (0.1-0.5) 9/3456
Collins (2013)	Abdominal distension	Women	0.16 (0.07-0.34) 7/4457
Muris (1995)	Non-acute abdominal complaints	All patients	0.21 (0.04-0.86) 2/933
Hippisley-Cox (2012)	Dysphagia	All patients	0.2 (0.1-0.4) 11/5442
Collins (2013)	Dysphagia	Men	0.1 (0.05-0.19) 9/9326
Collins (2013)	Appetite loss	All patients	0.39 (0.26-0.59) 24/6078
		Women	0.32 (0.17-0.59) 11/3433
		Men	0.49 (0.27-0.86) 13/2645
Hippisley-Cox (2012)	Appetite loss	All patients	0.8 (0.5-1.2) 27/3382
Collins (2013)	Weight loss	All patients	0.28 (0.22-0.35) 82/29382
		Women	0.16 (0.11-0.24) 26/15954
		Men	0.42 (0.32-0.54) 56/13428
Hippisley-Cox (2012)	Weight loss	All patients	0.6 (0.5-0.8) 61/9415

Stapley (2012)	Weight loss	All patients	0.44 (0.36-0.55) Cases: 353/3635 Controls: 105/16459
Stapley (2012)	Weight loss	Patients ≥ 60 years	0.8 (0.7-1)
Stapley (2012)	Nausea/vomiting	All patients	0.19 (0.17-0.21) Cases: 590/3635 Controls: 408/16459
Stapley (2012)	Nausea/vomiting	Patients ≥ 60 years	0.3 (0.3-0.4)
Stapley (2012)	Back pain	All patients	0.06 (0.05-0.07) Cases: 452/3635 Controls: 1007/16459
Stapley (2012)	Back pain	Patients ≥ 60 years	0.1 (0.1-0.1)
Stapley (2012)	Back pain (attended ≥ twice)	Patients ≥ 60 years	0.2 (0.1-0.2)
Stapley (2012)	Constipation	All patients	0.1 (0.09-0.11) Cases: 427/3635 Controls: 555/16459
Stapley (2012)	Constipation	Patients ≥ 60 years	0.2 (0.2-0.2)
Collins (2013)	Constipation	Males	0.21 (0.11-0.38) 11/5315
Stapley (2012)	Diarrhoea	All patients	0.09 (0.08-0.11) Cases: 385/3635 Controls: 539/16459
Stapley (2012)	Diarrhoea	Patients ≥ 60 years	0.2 (0.2-0.2)
Stapley (2012)	Malaise	All patients	0.12 (0.1-0.15) Cases: 187/3635 Controls: 197/16459
Stapley (2012)	Malaise	Patients ≥ 60 years	0.2 (0.2-0.3)
Stapley (2012)	Jaundice	All patients	12.9 (7.89-27.1) Cases: 1110/3635 Controls: 10/16459
Stapley (2012)	Jaundice	Patients ≥ 60 years	21.6 (14-52)
Stapley (2012)	Jaundice (attended ≥ twice)	Patients ≥ 60 years	31.6 (NR)
Stapley (2012)	New-onset diabetes	All patients	0.09 (0.08-0.1) Cases: 804/3635 Controls: 1201/16459
Stapley (2012)	New-onset diabetes	Patients ≥ 60 years	0.2 (0.2-0.2)
Tosetti (2010)	Upper gastro-intestinal symptoms without alarming features	All patients	0.36 (0.02-2.33) 1/275
Stapley (2012)	Abnormal liver function	All patients	0.16 (0.15-0.17) Cases: 1834/3635 Controls: 1506/16459
Stapley (2012)	Low haemoglobin	All patients	0.1 (0.09-0.11) Cases: 728/3635 Controls: 978/16459
Stapley (2012)	Raised inflammatory	All patients	0.16 (0.15-0.17)

	markers		Cases: 892/3635 Controls: 734/16459
Stapley (2012)	The authors report that in patients ≥ 70 years the PPVs for most symptoms were 1.5-4.5 times higher than in patients < 70 years.		

Stapley (2012) calculated the positive predictive values using Bayesian statistics. Meta-analyses are not undertaken as the Stapley data cannot be included due to the case-control design of the study. NR = not reported.

Table 2: Pancreatic cancer: Symptom combinations

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI)
Stapley (2012)	Abdominal pain and back pain	Patients ≥ 60 years	0.4 (0.3-0.5)
Stapley (2012)	Abdominal pain and constipation	Patients ≥ 60 years	0.5 (0.4-0.7)
Stapley (2012)	Abdominal pain and malaise	Patients ≥ 60 years	0.6 (0.4-0.8)
Stapley (2012)	Abdominal pain and diarrhoea	Patients ≥ 60 years	0.4 (0.3-0.5)
Stapley (2012)	Abdominal pain and nausea/vomiting	Patients ≥ 60 years	0.9 (0.7-1.2)
Stapley (2012)	Abdominal pain and loss of weight	Patients ≥ 60 years	2.5 (1.5-4.4)
Stapley (2012)	Abdominal pain and new onset diabetes	Patients ≥ 60 years	0.9 (0.7-1.1)
Stapley (2012)	Abdominal pain and jaundice	Patients ≥ 60 years	15 (NR)
Stapley (2012)	Back pain and constipation	Patients ≥ 60 years	0.3 (0.2-0.4)
Stapley (2012)	Back pain and malaise	Patients ≥ 60 years	0.3 (0.2-0.6)
Stapley (2012)	Back pain and diarrhoea	Patients ≥ 60 years	0.2 (0.1-0.3)
Stapley (2012)	Back pain and nausea/vomiting	Patients ≥ 60 years	0.3 (0.2-0.5)
Stapley (2012)	Back pain and loss of weight	Patients ≥ 60 years	2 (1-4.3)
Stapley (2012)	Back pain and new onset diabetes	Patients ≥ 60 years	0.3 (0.2-0.4)
Stapley (2012)	Back pain and jaundice	Patients ≥ 60 years	8.9 (NR)
Stapley (2012)	Diarrhoea and constipation	Patients ≥ 60 years	0.2 (0.1-0.3)
Stapley (2012)	Diarrhoea and malaise	Patients ≥ 60 years	0.3 (0.1-0.5)
Stapley (2012)	Diarrhoea and nausea/vomiting	Patients ≥ 60 years	0.2 (0.2-0.3)
Stapley (2012)	Diarrhoea and loss of weight	Patients ≥ 60 years	2.7 (NR)
Stapley (2012)	Diarrhoea and new onset diabetes	Patients ≥ 60 years	0.4 (0.3-0.5)
Stapley (2012)	Diarrhoea and jaundice	Patients ≥ 60 years	$> 10^*$
Stapley (2012)	Constipation and malaise	Patients ≥ 60 years	0.3 (0.2-0.5)

Stapley (2012)	Nausea/vomiting and malaise	Patients ≥ 60 years	0.5 (0.3-0.8)
Stapley (2012)	Constipation and weight loss	Patients ≥ 60 years	1.5 (0.8-3)
Stapley (2012)	Constipation and nausea/vomiting	Patients ≥ 60 years	0.6 (0.4-0.8)
Stapley (2012)	Nausea/vomiting and weight loss	Patients ≥ 60 years	2.2 (1.1-4.6)
Stapley (2012)	Weight loss and new onset diabetes	Patients ≥ 60 years	1.6 (1-2.9)
Stapley (2012)	New onset diabetes and jaundice	Patients ≥ 60 years	22.3 (NR)
Stapley (2012)	Constipation and new onset diabetes	Patients ≥ 60 years	0.4 (0.3-0.6)
Stapley (2012)	Malaise and new onset diabetes	Patients ≥ 60 years	0.5 (0.3-0.9)
Stapley (2012)	Nausea/vomiting and new onset diabetes	Patients ≥ 60 years	0.7 (0.5-1)
Stapley (2012)	Weight loss and malaise	Patients ≥ 60 years	0.9 (0.4-2.1)
Stapley (2012)	Jaundice and nausea/vomiting	Patients ≥ 60 years	14.6 (NR)
Stapley (2012)	Jaundice and constipation	Patients ≥ 60 years	>10*
Stapley (2012)	Jaundice and malaise	Patients ≥ 60 years	>10*
Stapley (2012)	Jaundice and weight loss	Patients ≥ 60 years	>10*

Stapley (2012) calculated the positive predictive values using Bayesian statistics. NR = not reported.
* > 40 cases and 0 controls had these symptoms.

Evidence statement(s):

For pancreatic cancer the positive predictive values of single symptoms (7 studies, N = 3146347) presenting in primary care ranged from 0.06% (for back pain) to 21.6% (for jaundice). The included studies were associated with 0-4 bias/applicability concerns (see also Table 1).

For pancreatic cancer the positive predictive values of symptom combinations (1 study, N = 20094) presenting in primary care ranged from 0.2% (for diarrhoea in combination with either constipation, nausea/vomiting or back pain) to 22.3% (for new onset diabetes combined with jaundice). The included study was associated with 1 bias concern (see also Table 2).

Evidence tables

Collins (2013)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2150322 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Dysphagia (men only: N = 9326), abdominal pain (N = 255058; 106768 men, 148290 women), appetite loss (N = 6102; 2658 men, 3444 women), weight loss (N = 29464; 13484 men, 15980 women), abdominal distension (women only: N = 4457), constipation (men only, N = 5326).</p> <p><u>Incident cases of pancreatic cancer during the 2-year follow up period:</u> N = 618 (331 men, 287 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of pancreatic cancer, registration < 12 months with the general practice, or invalid dates.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Dysphagia (men only), loss of appetite, weight loss, abdominal pain, abdominal distension (women only), and constipation (men only).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Hallissey (1990)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive patient series from a group of 10 general practices in England.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia. <u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, England.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia of any degree
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	2659 patients were seen and 2585 attended for investigation
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), carcinomatosis of unknown primary (7).

Hippisley-Cox (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1243740 patients were identified from 189 practices (624352 males, 619388 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Current symptoms and symptoms in the preceding year:</u> Current dysphagia (N = 8507), current abdominal pain (N = 129924), current abdominal distension (N = 4929), current appetite loss (N = 5567), current weight loss (N = 14686), constipation in the last year (N = 8476), diarrhoea in the last year (N = 12233), tiredness in the last year (N = 12688), itching in the last year (N = 1454), haemoglobin recoded in the last year (N = 214497), haemoglobin < 11 g/dl in the last year (N = 16172).</p> <p><u>Incident cases of pancreatic cancer during the 2-year follow up period:</u> N = 781.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from</p>

	<p>patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months' registration prior to study entry. For patients with incident haematuria, appetite loss, weight loss, or abdominal pain, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of pancreatic cancer at baseline, and patients with a recorded 'red-flag' (see "Definition of symptom" below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of pancreatic cancer; that is, symptoms of dysphagia, loss of appetite, weight loss, abdominal distension or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Pancreatic cancer, which was defined as incident diagnosis of pancreatic cancer during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 code (157) or ICD-10 diagnostic codes (C25).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 98589 patients

	<p>were excluded for the following reasons: No recorded Townsend score (N = 70847), history of pancreatic cancer (N = 96), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 27646), leaving 1243740 patients. However, data is presented for 971706 / 1243740 patients. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.</p>
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	
Mahadeva (2008)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from the Primary Care Clinics of the University of Malaya in Malaysia
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 432; 198 males/234 females; mean ages (SDs) = 30-31 (8) years.</p> <p><u>Inclusion criteria</u>: "All patients were recruited from the Primary Care Clinics of the University of Malaya, which provide a regular service to the local community. Patients aged \leq 45 years presenting with uninvestigated dyspepsia were invited to participate in the study", which ran from January 2004 until October 2005.</p> <p><u>Exclusion criteria</u>: Age > 45 or < 18 years; symptoms of weight loss, progressive dysphagia or those suggestive of anaemia; pregnancy; previous H pylori testing; any contra-indication to endoscopy or sedation; failure to turn up for initial test ; and on regular doses of non-steroidal anti-inflammatory drugs.</p> <p><u>Clinical setting</u>: Primary care clinic, Malaysia</p>
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	Uninvestigated dyspepsia. Dyspepsia defined as predominant upper abdominal discomfort for > 4 weeks, with any associated symptoms, including heart burn and regurgitation.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up ± upper endoscopy (oesophagogastroduodenoscopy)	
Is the reference standard likely to correctly classify the target condition?		Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?		No
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	39/471 eligible patients were excluded from the study for the following reasons: 34/39 patients declined to participate, 3/39 became pregnant before the test, 1/39 emigrated from the country and 1/39 had missing data.	
Was there an appropriate interval between index test and reference standard?		Yes
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		Yes
Could the patient flow have introduced bias?		Low risk
NOTES	One patient was found to have cancer, which was metastatic pancreatic cancer. No oesophageal or gastric cancers were reported.	
Muris (1995)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series from 80/460 general practitioners in Limburg (Holland)	
Was a consecutive or random sample of patients enrolled?		No
Was a case-control design avoided?		Yes
Did the study avoid inappropriate exclusions?		Unclear
Could the selection of patients have introduced bias?		High risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 933; 335 males, 598 females; age range = 18-75, aged > 30 years: N = 712, aged > 40 years: N = 517, aged > 60 years: N = 171.</p> <p><u>Inclusion criteria:</u> Patients who in 1989 consulted one of the participating GPs for new abdominal complaints lasting ≥ 2 weeks and with whom the GPs had a diagnostic problem.</p> <p><u>Exclusion criteria:</u> None listed.</p>	

	Clinical setting: GPs in Holland	
Are there concerns that the included patients and setting do not match the review question?		High concern
INDEX TEST		
A. Risk of bias		
Index test	New abdominal complaints lasting ≥ 2 weeks. Not further specified.	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		High concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up for ≥ 12 months (mean = 18 months).	
Is the reference standard likely to correctly classify the target condition?		Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?		No
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?		Unclear
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		Yes
Could the patient flow have introduced bias?		Low risk
NOTES	Cancers diagnosed in these patients were: Stomach (2/933), pancreas (2/933), trachea/bronchus/lung (2/933), kidney (1/933), colorectal (4/933), cervix (1/933), other cancer of the female genital system (2/933), and other and unspecified sites (2/933).	
Stapley (2012)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Matched case-control study using patients in the UK's General Practice Research Database (GPRD).	
Was a consecutive or random sample of patients enrolled?		No
Was a case-control design avoided?		No

Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
<u>B. Concerns regarding applicability</u>	
Patient characteristics and setting	<p><u>Cases:</u> N = 3635, 1743 males / 1892 females; median number of consultations = 18 (IQR = 11-27); aged 40-49 years: N = 107; 50-59 years: N = 529; 60-69 years: N = 829; 70-79 years: N = 1212; ≥ 80 years: N = 958; UK.</p> <p><u>Controls:</u> N = 16459, gender not reported; median number of consultations = 9 (IQR = 4-15); aged 40-49 years: N = 422; 50-59 years: N = 2239; 60-69 years: N = 3755; 70-79 years: N = 5702; ≥ 80 years: N = 4341; UK.</p> <p><u>Inclusion criteria:</u> Cases: Patients with a record of one of 25 GPRD pancreatic cancer codes between January 2000 and December 2009 inclusive, aged ≥ 40 years, with min. 1 year of data before diagnosis. The first instance of a pancreatic cancer code was assigned the data of diagnosis/index date. Controls: Up to 5 controls were matched to cases on sex, general practice, and to 1 year of age of the case. The index date was the index date of the matched case.</p> <p><u>Exclusion criteria:</u> Pancreatic cancer (controls), no consultations in the year before diagnosis.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
<u>A. Risk of bias</u>	
Index test	All symptoms, physical signs or abnormal investigations compiled from the pancreatic cancer literature were studied, and supplemented by discussion with two pancreatic cancer charities. Libraries of codes relating to these were collated. All codes for fractures were also identified, as a test for any recording bias between cases and controls (making the assumption that the fracture rate would be approximately equal). Occurrences of these features in the year before the index date were identified. Features were only retained for further study if they occurred in ≥5% of cases or controls. Repeat attendances with the same symptom were also retained if the subsequent consultation also occurred in ≥5% of cases or controls. New-onset diabetes was defined as a code for diabetes, or a random blood glucose above the local laboratory's normal range, without similar codes more than 1 year before the index date. For laboratory tests, patients without a test were considered to be the same status as those with a normal result, making our binary variable abnormal result/ no abnormal result. Abnormal liver function was defined as any liver enzyme above the normal range, and raised inflammatory markers as either abnormal erythrocyte sedimentation rate or

	C-reactive protein, as there were too few plasma viscosity results.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Pancreatic cancer code in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 21624 patients were identified, 17977 controls and 3647 cases. Of the controls the following exclusions were applied: pancreatic cancer (N = 64), case excluded (N = 40), and no data in year pre-index date (N = 1414). Of the cases the following exclusions were applied: No controls (N = 2), and cancer not of pancreatic origin (N = 10).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Tosetti (2010)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 63 general practitioners in Italy
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability	
Patient characteristics and setting	N = 275; 124 males, 151 females; median age (range) = 46 (18-92) years. Symptoms: Epigastric pain (72%), prolonged digestion (51.6%), heartburn (49.1%), epigastric postprandial fullness (45.5%), epigastric distension (41.5%), nausea (38.5%), acid regurgitation (34.5%), belching (28.7%), early satiety (20.7%). <u>Inclusion criteria</u> : "Each GP enrolled in the survey patients who, over a three-month period, presented with UGI [upper gastro-intestinal] symptoms at the first onset without alarming features." <u>Exclusion criteria</u> : "Patients with either previous or recurrent complaints or previously investigated for UGI symptoms were not included". <u>Clinical setting</u> : GPs in Italy
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	New onset UGI symptoms without alarming features. Not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	1-year follow up.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Cancers diagnosed in these patients were: Pancreas (1/275), and

References

Included studies

- Collins, G.S.; Altman, D.G. (2013). Identifying patients with undetected pancreatic cancer in primary care: an independent and external validation of Q Cancer[®] (Pancreas). *British Journal of General Practice*, 63: 636-642.
- Hallissey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.
- Hippisley-Cox, J. & Coupland, C. (2012) Identifying patients with suspected pancreatic cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice*, 62: e38-e45.
- Mahadeva, S., Chia, Y.-C., Vinothini, A., et al. Cost-effectiveness of and satisfaction with a *Helicobacter pylori* "test and treat" strategy compared with prompt endoscopy in young Asians with dyspepsia. *Gut* 57, 1214-1220. 2008.
- Muris, J. W., Starmans, R., Fijten, G. H., Crebolder, H. F., Schouten, H. J., and Knottnerus, J. A. (1995). Non-acute abdominal complaints in general practice: diagnostic value of signs and symptoms. *British Journal of General Practice* 45[395], 313-316.
- Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M. & Hamilton, W. (2012) The risk of pancreatic cancer in symptomatic patients in primary care: a large case-control study using electronic records. *British Journal of Cancer*, 106: 1940-1944.
- Tosetti, C.; Bellentani, S.; Benedetto, E.; Ubaldi, E.; Cardin, F.; Bozzani, A. (2010). The management of patients with new onset of upper gastro-intestinal symptoms in primary care. *Digestive and Liver Disease*, 42: 860-864.

Excluded studies (with reason)

- (1994) Draft of recommendations from the NCI-sponsored workshop on detection and treatment of early pancreatic carcinoma. *International Journal of Pancreatology*, 16: 310.
Not in PICO
- (2010) Abstracts of Papers Submitted to the 41st Annual Meeting of the American Pancreatic Association. *Pancreas*, 39.
Not in PICO
- Adelow, C., Ahlbom, A., Feychting, M., Johnsson, F., Schwartzbaum, J. & Tomson, T. (2006) Epilepsy as a risk factor for cancer. *Journal of Neurology Neurosurgery and Psychiatry*, 77: 784-786.
Not in PICO
- Aggarwal, G., Petersen, G. M. & Chari, S. T. (2010) New-onset diabetes in pancreatic cancer: A study in the primary care setting. *Pancreas*, 39: 1306.
Not in PICO
- Aggarwal, G., Rabe, K. G., Petersen, G. M. & Chari, S. T. (2012) New-onset diabetes in pancreatic cancer: a study in the primary care setting. *Pancreatology*, 12: 156-161.
Not in PICO
- Ahn, J. & Lee, J. K. (2013) [New-onset diabetes as an early sign of pancreatic cancer]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 62: 263-266.
Narrative review
- Aikens, G. B., Rivey, M. P. & Hansen, C. J. (2013) Primary venous thromboembolism prophylaxis in ambulatory cancer patients. *Annals of Pharmacotherapy*, 47: 198-209.
Not in PICO
- Aimoto, T., Uchida, E., Nakamura, Y., Katsuno, A., Chou, K., Kawamoto, M., Tajiri, T. & Naito, Z. (2006) Clinicopathologic study on pancreatic groove carcinoma. *Pancreas*, 33: 255-259.
Not in PICO

- Akisik, M. F., Jennings, S. G., Aisen, A. M., Sherman, S., Cote, G. A., Sandrasegaran, K. & Tirkes, T. (2013) MRCP in patient care: a prospective survey of gastroenterologists. *AJR.American Journal of Roentgenology*, 201: 573-577.
Not in PICO
- Al-Haddad, M., DeWitt, J., Sherman, S., Schmidt, C. M., LeBlanc, J. K., McHenry, L., Cote, G., El Chafic, A. H., Luz, L., Stuart, J. S., Johnson, C. S., Klochan, C. & Imperiale, T. F. (2014) Performance characteristics of molecular (DNA) analysis for the diagnosis of mucinous pancreatic cysts. *Gastrointestinal Endoscopy*, 79: 79-87.
Not in PICO
- Al-Haddad, M. A., Waters, J. A., DeWitt, J. M., Sherman, S., El Chafic, A. H., Stuart, J. S., El-Jawad, K. A. & Schmidt, C. M. (2011) Prevalence of malignancy in symptomatic and asymptomatic patients with pure main duct intraductal papillary mucinous neoplasms (MD-IPMNS). *Gastroenterology*, 140: S710.
Not in PICO
- Al-Mashat, F. & Sibiany, A. M. (2010) Sister Mary Joseph's nodule of the umbilicus: Is it always of gastric origin A review of eight cases at different sites of origin. *Indian Journal of Cancer*, 47: 65-69.
Not in PICO
- Alcindor, T., Trutschnigg, B., Chaudhury, P., Hassanain, M., Metrakos, P. & Vigano, A. (2008) Is the platelet count a prognostic factor in pancreas cancer and cholangiocarcinoma? *Annals of Oncology*, 19: viii185.
Not in PICO
- Amikura, K., Kobari, M. & Matsuno, S. (1996) [The role of screening for carcinoma of the pancreas]. [Review] [21 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 54: 1431-1434.
Not in PICO
- Amin, S., Dimaio, C. J. & Kim, M. K. (2013) Advanced EUS imaging for early detection of pancreatic cancer. *Gastrointestinal Endoscopy Clinics of North America*, 23: 607-623.
Narrative review
- Ansorge, C., Skarin, A., Segersvard, R., Sandblom, G. & Andren-Sandberg, A. (2010) Are pancreatic incidentalomas worthy of consideration? *Pancreatology*, 10: 363.
Not in PICO
- Ares, D. M., Aguirre, P. A. A., Barrenechea, I. M. G., Gomez, L. C. & Peral, A. P. (2008) Usefulness of ultrasonography in diagnosing patients suspect for digestive tract neoplasms. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 100: 545-551.
Not in PICO
- Argiles, J. M. (2005) Cancer-associated malnutrition. [Review] [112 refs]. *European Journal of Oncology Nursing*, 9: Suppl-50.
Not in PICO
- Ariyama, J., Sumida, M., Shirota, K., Shimaguchi, H. & Suyama, M. (1983) [Problems of early diagnosis of pancreatic cancer and evaluation of various morphological studies]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 29: 511-516.
Not in PICO
- Arya, V., Goyal, H. & Iqbal, F. (2012) Cutaneous metastasis as the first clinical manifestation of pancreatic adenocarcinoma. *American Journal of Gastroenterology*, 107: S336.
Not in PICO
- Atef, E., El, N. A., El, H. E., El, H. M., Hamdy, E. & El-Geidie, A. (2013) Pancreatic cystic neoplasms: predictors of malignant behavior and management. *Saudi Journal of Gastroenterology*, 19: 45-53.
Not in PICO

- Atef, E., El, N. A., El, H. E., El, H. M., Hamdy, E. & El-Geidie, A. (2013) Pancreatic cystic neoplasms: predictors of malignant behavior and management. *Saudi Journal of Gastroenterology*, 19: 45-53.
Not in PICO
- Azar, C., Van De Stadt, J., Rickaert, F., Deviere, J., Delhay, M., Baize, M., Kloppel, G., Gelin, M. & Cremer, M. (1996) Intraductal papillary mucinous tumours of the pancreas. Clinical and therapeutic issues in 32 patients. *Gut*, 39: 457-464.
Not in PICO
- Bach, P., Mohring, C., Krawzak, H. W. & Goepel, M. (2007) [Retroperitoneal extravasation as the primary symptom of a pancreatic carcinoma]. [German]. *Urologe (Ausg.A)*, 46: 1548-1550.
Not in PICO
- Barkin, J. S. (1980) Update: Pancreatic carcinoma. *Comprehensive Therapy*, 6: 51-57.
Narrative review
- Bartosch-Harlid, A. & Andersson, R. (2010) Diabetes mellitus in pancreatic cancer and the need for diagnosis of asymptomatic disease. [Review]. *Pancreatology*, 10: 423-428.
Narrative review
- Bazaldua, O. V. & Schneider, F. D. (1787) Evaluation and management of dyspepsia. [Review] [44 refs]. *American Family Physician*, 60: 1773-1784.
Narrative review
- Belarbi, N., Benelbarhdadi, I., Zahzah, M., Afifi, R., Benazzouz, M., Essaid, A., Mohsine, R. & Balafrej, S. (2006) Development of pancreatic adenocarcinoma in chronic calcifying pancreatitis. *Acta Endoscopica*, 36: 173-177.
Not in PICO
- Ben, Q., Cai, Q., Li, Z., Yuan, Y., Ning, X., Deng, S. & Wang, K. (2011) The relationship between new-onset diabetes mellitus and pancreatic cancer risk: a case-control study. *European Journal of Cancer*, 47: 248-254.
Not in PICO
- Bernades, P. (1990) [Conclusions concerning the symptomatic treatment of cancer of the pancreas]. [French]. *Bulletin du Cancer*, 77: 295-298.
Narrative review
- Bozzetti, F. & SCRINIO Working Group (2009) Screening the nutritional status in oncology: a preliminary report on 1,000 outpatients. *Supportive Care in Cancer*, 17: 279-284.
Not in PICO
- Bracci, P. M., Wang, F., Hassan, M. M., Gupta, S., Li, D. & Holly, E. A. (2009) Pancreatitis and pancreatic cancer in two large pooled case-control studies. *Cancer Causes and Control*, 20: 1723-1731.
Not in PICO
- Brodovicz, K. G., Kou, T. D., Alexander, C. M., Engel, S. & Girman, C. J. (2011) Synergistic effect of type 2 diabetes (T2D) and history of pancreatitis on pancreatic cancer risk: A retrospective cohort study from the general practice research database (GPRD). *Pharmacoepidemiology and Drug Safety*, 20: S283.
Same as Brodovicz 2011 and 2012
- Brodovicz, K. G., Kou, T. D., Alexander, C. M., O'Neill, E. A., Engel, S. & Girman, C. J. (2011) Synergistic effect of type 2 diabetes and history of chronic pancreatitis on pancreatic cancer risk: A retrospective cohort study from the General Practice Research Database (GPRD). *Diabetologia*, 54: S312.
Not in PICO. Same as Brodovicz 2011 and 2012
- Brodovicz, K. G., Kou, T. D., Alexander, C. M., O'Neill, E. A., Engel, S. S., Girman, C. J. & Goldstein, B. J. (2012) Impact of diabetes duration and chronic pancreatitis on the association between type 2 diabetes and pancreatic cancer risk. *Diabetes, Obesity and Metabolism*, 14: 1123-1128.
Not in PICO as not symptomatic patients presenting to primary care. same as Brodovicz 2011 and 2012

- Buechter, M., Klein, C. G., Kloeters, C., Gerken, G., Canbay, A. & Kahraman, A. (2012) Diagnostic Dilemma in a Patient with Jaundice: How to Differentiate between Autoimmune Pancreatitis, Primary Sclerosing Cholangitis and Pancreas Carcinoma. *Case Reports Gastroenterology*, 6: 211-216.
Not in PICO
- Buscaglia, J. M., Giday, S. A., Kantsevov, S. V., Jagannath, S. B., Magno, P., Wolfgang, C. L., Daniels, J. A., Canto, M. I. & Okolo III, P. I. (2009) Patient- and cyst-related factors for improved prediction of malignancy within cystic lesions of the pancreas. *Pancreatology*, 9: 631-638.
Not in PICO
- Buscail, L. & Bournet, B. (2007) [Risk factors of pancreatic carcinoma]. [Review] [21 refs] [French]. *Presse Medicale*, 36: t-8.
Narrative review
- Caglar, E., Senturk, H., Atasoy, D., Sisman, G., Canbakan, B. I. & Tuncer, M. (2013) The role of EUS and EUS-FNA in the management of pancreatic masses: five-year experience. *Hepato-Gastroenterology*, 60: 896-899.
Not in PICO
- Calle, E. E., Murphy, T. K., Rodriguez, C., Thun, M. J. & Heath, C. W., Jr. (1998) Diabetes mellitus and pancreatic cancer mortality in a prospective cohort of United States adults. *Cancer Causes & Control*, 9: 403-410.
Not in PICO
- Camacho-Aguilera, J. F., Romero-Mejia, C. & Valenzuela-Espinoza, A. (2010) Solid pseudopapillary tumor of the pancreas: case report and literature review. *Cirugia y Cirujanos*, 78: 67-72.
Not in PICO
- Cappelli, G., Paladini, S. & D'Agata, A. (1999) [Tumor markers in the diagnosis of pancreatic cancer]. [Review] [9 refs] [Italian]. *Tumori*, 85: Suppl-21.
Narrative review
- Capurso, G., Larghi, A., Boccia, S., Salvia, R., Del, C. M., Piciocchi, M., Carnuccio, A., Carrara, S., Manta, R., Fabbri, C., De, F. E., Leonardi, G., Arcidiacono, P. G., Boggi, U., Costamagna, G., Delle, F. G. & Bassi, C. (2011) Risk factors for intraductal papillary mucinous neoplasm (IPMN) of the pancreas: Preliminary results of a prospective Italian multicentre case-control study. *Digestive and Liver Disease*, 43: S142-S143.
Not in PICO
- Catanzaro, R. & Dimartino, A. (2012) [Autoimmune pancreatitis today: clinical features and diagnostic strategies]. [Review] [Italian]. *Minerva Gastroenterologica e Dietologica*, 58: 151-166.
Narrative review
- Chari, S. T., Klee, G. G., Miller, L. J., Raimondo, M. & DiMugno, E. P. (2001) Islet amyloid polypeptide is not a satisfactory marker for detecting pancreatic cancer. *Gastroenterology*, 121: 640-645.
Not in PICO
- Chari, S. T., Leibson, C. L., Rabe, K. G., Ransom, J., de, A. M. & Petersen, G. M. (2005) Probability of pancreatic cancer following diabetes: a population-based study. *Gastroenterology*, 129: 504-511.
Not in PICO
- Cheema, A., Weber, J., Kvols, L. & Strosberg, J. (2011) Incidental diagnosis of pancreatic neuroendocrine tumors. *Pancreas*, 40: 326.
Not in PICO
- Choi, J. H., Kim, M.-H., Seo, D. W., Lee, S. S., Park, D. H. & Lee, S. K. (1111) Clinical features and risk factors of pancreatic cancer in chronic pancreatitis. *Pancreatology*, 13: S38-August.
Not in PICO
- Clement Chia, L. K., Shelat, V. G., Junnarkar, S. P., Winston Woon, W. L. & Low, J. K. (2013) Diabetes mellitus in pancreatic cancer. *HPB*, 15: 113-114.
Not in PICO

- Collins, G. S. & Altman, D. G. (2013) Identifying patients with undetected pancreatic cancer in primary care: an independent and external validation of Qcancer (R) (Pancreas). *British Journal of General Practice*, 63: E636-E642.
Duplicate
- Colonna, J., Plaza, J. A., Frankel, W. L., Yearsley, M., Bloomston, M. & Marsh, W. L. (2008) Serous cystadenoma of the pancreas: Clinical and pathological features in 33 patients. *Pancreatology*, 8: 135-141.
Not in PICO
- Conrath, S. M. (1986) The use of epidemiology, scientific data, and regulatory authority to determine risk factors in cancers of some organs of the digestive system. 6. Pancreatic cancer. *Regulatory Toxicology & Pharmacology*, 6: 193-210.
Narrative review
- Costamagna, G., Cotroneo, A. R., Mutignani, M., Di, S. C. & Perri, V. (1995) Carcinoma of the pancreatic head area. Therapy: nonoperative biliary drainage for palliation. [Review] [11 refs]. *Rays*, 20: 326-337.
Narrative review
- da Silva, J. A., Machado Igreja, A. C. S., Freitas, A. F., Carvalho Costa, I. M., Mesquita, K. C., Naves Lucas, I. C. R., de Oliveira, S. M. & Campbell, I. T. (2013) Paraneoplastic cutaneous manifestations: Concepts and updates. *Anais Brasileiros de Dermatologia*, 88: 9-22.
Narrative review
- Damiano, J., Bordier, L., Le Berre, J., Margery, J., Dupuy, O., Mayaudon, H. & Bauduceau, B. (2004) Should pancreas imaging be recommended in patients over 50 years when diabetes is discovered because of acute symptoms? *Diabetes & Metabolism*, 30: 203-207.
Not in PICO
- Das, K. K., Marchegiani, G., Geng, X., Xiao, H., Fernandez-del, C. C., Forcione, D. G., Casey, B., Brugge, W. R., Pitman, M. B., Das, K. M. & Mino-Kenudson, M. (2014) Comparison of the international consensus guidelines for management of intraductal papillary mucinous neoplasm (IPMN) with analysis of pancreatic cyst fluid aspirates for MAB-DAS-1 reactivity in identifying high-risk and malignant IPMN. *Gastroenterology*, 146: S-25.
Not in PICO
- De La Cruz, M. S., Young, A. P. & Ruffin, M. T. (2014) - Diagnosis and management of pancreatic cancer. - *American Family Physician*, 89: 626-632.
Narrative review
- De, B. F., Cascinu, S. & Gatta, G. (2004) Cancer of pancreas. *Critical Reviews in Oncology/Hematology*, 50: 147-155.
Narrative review
- De, L. H., Allende, H., Merino, X., Balsells, J., Guarner, L. & Molero, X. (11111) Autoimmune pancreatitis in Barcelona as assessed by the Honolulu diagnostic criteria. Review of a series of 16 patients. *Pancreatology*, 12: 565-December.
Not in PICO
- Defachelles, A. S., Rocourt, N., Branchereau, S. & Peuchmaur, M. (2012) [Pancreatoblastoma in children: diagnosis and therapeutic management]. [French]. *Bulletin du Cancer*, 99: 793-799.
Narrative review
- Del, C. M., Verbeke, C., Salvia, R., Kloppel, G., Werner, J., McKay, C., Friess, H., Manfredi, R., Van, C. E., Lohr, M., Segersvard, R. & European Study Group on Cystic Tumours of the Pancreas (2013) European experts consensus statement on cystic tumours of the pancreas. *Digestive & Liver Disease*, 45: 703-711.
Guideline/narrative review
- Deng, R. X., Lu, X. H., Wang, L., Li, H., Qian, J. M., Yang, A. M., Zhong, S. X., Guo, X. Z., Zhou, L., Wu, X., Yang, X. O. & Jiang, W. J. (2005) [Developing a hospital-based high risk scoring model and screening strategy for pancreatic cancer]. [Chinese]. *Chung-Hua i Hsueh Tsa Chih [Chinese*

- Medical Journal*], 85: 2038-2042.
Not in PICO (population)
- DeWitt, J., Alsatie, M., LeBlanc, J., McHenry, L. & Sherman, S. (2007) Endoscopic ultrasound-guided fine-needle aspiration of left adrenal gland masses. *Endoscopy*, 39: 65-71.
Not in PICO
- Dhamija, M., Rosemurgy, A. & Kulkarni, P. (2010) Solid pseudo-papillary tumor of pancreas: Lessons learned from two cases. *American Journal of Gastroenterology*, 105: S202.
Not in PICO
- Dill-Muller, D. & Tilgen, W. (2002) [Skin manifestations with internal diseases. Finding the origin]. [German]. *MMW Fortschritte der Medizin*, 144: 26-30.
Narrative review
- DiMagno, E. P. (1999) Pancreatic cancer: clinical presentation, pitfalls and early clues. [Review] [44 refs]. *Annals of Oncology*, 10: Suppl-2.
Narrative review
- Dina, R., Tran-Dang, M. A., Mauri, F., Gudi, M., Cohen, P., Ahmad, R., Batav, L., Vlavianos, P. & Spalding, D. (2013) Pancreatobiliary cytology in the multidisciplinary setting. [Review]. *Cytopathology*, 24: 150-158.
Narrative review
- Dite, P., Novotny, I., Precechtelova, M., Ruzicka, M., Zakova, A., Hermanova, M., Trna, J. & Sevcikova, A. (2009) Pancreatic carcinoma during the course of chronic pancreatitis. [Czech]. *Ceska a Slovenska Gastroenterologie a Hepatologie*, 63: 216-220.
Not in PICO
- Dite, P., Novotny, I., Precechtelova, M., Ruzicka, M., Zakova, A., Trna, J., Hermannova, M. & Sevcikova, A. (2009) Incidence of pancreatic carcinoma in persons with chronic pancreatitis. [Czech]. *Vnitřní Lekarství*, 55: 18-21.
Not in PICO
- Dite, P., Hermanova, M., Trna, J., Novotny, I., Ruzicka, M., Liberda, M. & Bartkova, A. (2012) The role of chronic inflammation: Chronic pancreatitis as a risk factor of pancreatic cancer. *Digestive Diseases*, 30: 277-283.
Not in PICO
- Dumitra, S., Abou-Khalil, J., Jamal, M., Zogopoulos, G., Chaudhury, P., Metrakos, P., Tchervenkov, J. & Barkun, J. (2012) Pancreatic cancer and predictors of survival: Comparing the ca 19-9/bilirubin ratio with the mcgill brisbane scoring system. *HPB*, 14: 68.
Not in PICO
- Dumitrascu, D. L., Suci, O., Grad, C. & Gheban, D. (2010) Thrombotic complications of pancreatic cancer: classical knowledge revisited. [Review]. *Digestive Diseases*, 28: 350-354.
Narrative review
- Efevbokhan, N., Makol, A., Cuisson, R. V., Minter, R. M., Kotaru, V. P., Conley, B. A. & Chandana, S. R. (2011) An unusual case of autoimmune pancreatitis presenting as pancreatic mass and obstructive jaundice: a case report and review of the literature. *Journal of Medical Case Reports [Electronic Resource]*, 5: 253.
Not in PICO
- Egawa, S., Takeda, K., Fukuyama, S., Motoi, F., Sunamura, M. & Matsuno, S. (2004) Clinicopathological aspects of small pancreatic cancer. *Pancreas*, 28: 235-240.
Not in PICO
- Egawa, S., Toma, H., Ohigashi, H., Okusaka, T., Nakao, A., Hatori, T., Maguchi, H., Yanagisawa, A., Matsuno, S. & Tanaka, M. (2009) Diagnosis and treatment of early pancreatic cancer. From Nation-Wide pancreatic registry. *Gastroenterology*, 136: A897.
Not in PICO
- Egorov, V., Vishnevsky, V., Karmazanovsky, G., Schegolev, A., Yashina, N., Vinokurova, L. & Dubova, H. (2009) Pancreatic cancer or local form of autoimmune pancreatitis: is it possible to

differentiate them preoperatively? *Pancreatology*, 9: 512.

Not in PICO

Ekbom, A., McLaughlin, J. K., Karlsson, B. M., Nyren, O., Gridley, G., Adami, H. O. & Fraumeni, J. F. (1994) Pancreatitis and Pancreatic-Cancer - A Population-Based Study. *Journal of the National Cancer Institute*, 86: 625-627.

Not in PICO

Elena, J. W., Steplowski, E., Yu, K., Hartge, P., Tobias, G. S., Brotzman, M. J., Chanock, S. J., Stolzenberg-Solomon, R. Z., Arslan, A. A., Bueno-de-Mesquita, H. B., Helzlsouer, K., Jacobs, E. J., Lacroix, A., Petersen, G., Zheng, W., Albanes, D., Allen, N. E., Amundadottir, L., Bao, Y., Boeing, H., Boutron-Ruault, M.-C., Buring, J. E., Gaziano, J. M., Giovannucci, E. L., Duell, E. J., Hallmans, G., Howard, B. V., Hunter, D. J., Hutchinson, A., Jacobs, K. B., Kooperberg, C., Kraft, P., Mendelsohn, J. B., Michaud, D. S., Palli, D., Phillips, L. S., Overvad, K., Patel, A. V., Sansbury, L., Shu, X.-O., Simon, M. S., Slimani, N., Trichopoulos, D., Visvanathan, K., Virtamo, J., Wolpin, B. M., Zeleniuch-Jacquotte, A., Fuchs, C. S., Hoover, R. N. & Gross, M. (2013) Diabetes and risk of pancreatic cancer: A pooled analysis from the pancreatic cancer cohort consortium. *Cancer Causes and Control*, 24: 13-25.

Not in PICO

Elli, M., Piazza, E., Franzone, P. C., Isabella, L., Poliziani, D. & Taschieri, A. M. (2003) Considerations on early diagnosis of carcinoma of the pancreas. *Hepato-Gastroenterology*, 50: 2205-2207.

Not in PICO

Eloubeidi, M. A., Varadarajulu, S., Desai, S., Shirley, R., Heslin, M. J., Mehra, M., Arnoletti, J. P., Eltoun, I., Wilcox, C. M. & Vickers, S. M. (2007) A prospective evaluation of an algorithm incorporating routine preoperative endoscopic ultrasound-guided fine needle aspiration in suspected pancreatic cancer. *Journal of Gastrointestinal Surgery*, 11: 813-819.

Not in PICO

Elshafie, O., Grant, C., Al-Hamdani, A., Jain, R. & Woodhouse, N. (2011) VIPoma Crisis: Immediate and life saving reduction of massive stool volumes on starting treatment with octreotide. *Sultan Qaboos University Medical Journal*, 11: 104-107.

Not in PICO

Evans, J., Chapple, A., Salisbury, H., Corrie, P. & Ziebland, S. (2014) "It can't be very important because it comes and goes"-patients' accounts of intermittent symptoms preceding a pancreatic cancer diagnosis: a qualitative study. *Bmj Open*, 4.

Not in PICO

Ewald, N. & Bretzel, R. G. (2013) Diabetes mellitus secondary to pancreatic diseases (Type 3c)--are we neglecting an important disease? *European Journal of Internal Medicine*, 24: 203-206.

Narrative review

Fabris, C., Del, F. G., Basso, D., Piccoli, A., Meggiato, T., Angonese, C., Plebani, M., Leandro, G., Burlina, A. & Naccarato, R. (1988) Serum markers and clinical data in diagnosing pancreatic cancer: a contrastive approach. *American Journal of Gastroenterology*, 83: 549-553.

Not in PICO

Fathy, O., Abdel-Wahab, M., Elghwalby, N., Sultan, A., El-Ebidy, G., Abu-Zeid, M., Abd-Allah, T., El-Shobary, M., Fouad, A., Kandeel, T., Abo-Elenien, A., El-Hah, N. G., Abdel-Raouf, A., Sultan, A. M. & Ezzat, F. (2008) Surgical management of peri-ampullary tumors: a retrospective study. *Hepato-Gastroenterology*, 55: 1463-1469.

Not in PICO

Foley, W. D. & Quiroz, F. A. (2007) The role of sonography in imaging of the biliary tract. [Review] [45 refs]. *Ultrasound Quarterly*, 23: 123-135.

Narrative review

Freelove, R. & Walling, A. D. (2006) Pancreatic cancer: Diagnosis and management. *American Family Physician*, 73: 485-492.

Narrative review

- Fric, P. & Zavoral, M. (2012) Early diagnosis of pancreatic adenocarcinoma: role of stroma, surface proteases, and glucose-homeostatic agents. [Review]. *Pancreas*, 41: 663-670.
Narrative review
- Furuhashi, S., Takamori, H., Abe, S., Nakahara, O., Tanaka, H., Horino, K., Beppu, T., Iyama, K. & Baba, H. (2011) Solid-pseudopapillary pancreatic tumor, mimicking submucosal tumor of the stomach: A case report. *World Journal of Gastrointestinal Surgery*, 3: 201-203.
Not in PICO
- Furukawa, H., Okada, S., Saisho, H., Ariyama, J., Karasawa, E., Nakaizumi, A., Nakazawa, S., Murakami, K. & Kakizoe, T. (1996) Clinicopathologic features of small pancreatic adenocarcinoma. A collective study. *Cancer*, 78: 986-990.
Not in PICO
- Furukawa, M., Lee, L., Funakoshi, A., Nishiyama, K. & Itaba, S. (2009) Giardia lamblia infection accompanied with pancreatic cancer diagnosed by endoscopic ultrasound-guided fine-needle aspiration. *Pancreas*, 38: 997.
Not in PICO
- Gagnon, B., Rodriguez, A. M. & MacDonald, N. (2011) From expert opinion to patients: Classifying people with cancer cachexia. *Journal of Cachexia, Sarcopenia and Muscle*, 2: 224.
Not in PICO
- Gall, F. P. & Kessler, H. (1987) [Early cancer of the exocrine pancreas: diagnosis and prognosis]. [German]. *Chirurg*, 58: 78-83.
Not in PICO
- Gandhi, S., Patel, N., Patel, K. & Patel, L. (2012) A betaHCG secreting pancreatic tumor. *American Journal of Gastroenterology*, 107: S334.
Not in PICO
- Garcia-Roca, R., Samame, J., Sendino, O., Ferna, n. G., Gines, A., Bombi, J., Ayuso, J. R., Ferrer, J., Garcia-Valdecasas, J. C. & Ferna, n. (2010) Groove pancreatitis: Review of 23 consecutive cases at a single institution. *HPB*, 12: 330.
Not in PICO
- Gasiorowka, A. & Malecka-Panas, E. (2007) Impaired glucose tolerance in patients with pancreatic cancer. [Polish]. *Przegląd Gastroenterologiczny*, 2: 130-134.
Narrative review
- Geraldine, N., Marc, A., Carla, T., Chantal, M., Stefaan, B., Welcome, W. & Frank, B. (2012) Relation between diabetes, metformin treatment and the occurrence of malignancies in a Belgian primary care setting. *Diabetes Research and Clinical Practice*, 97: 331-336.
Not in PICO
- Gerritsen, A., Molenaar, I. Q., Bollen, T. L., Nio, C. Y., Dijkgraaf, M. G., Van Santvoort, H. C., Offerhaus, G. J., Sieders, E., De Jong, K. P., Van Dam, R. M., Van Der Harst, E., Van, G. H., Van, R. B., Bonsing, B. A., De Hingh, I. H., Gerhards, M. F., Van Eijck, C. H., Gouma, D. J., Borel Rinkes, I. H. M., Busch, O. R. & Besselink, M. G. H. (1111) Preoperative characteristics of patients with presumed pancreatic cancer but ultimately benign disease: A multicenter series of 344 pancreatoduodenectomies. *Pancreatology*, 13: S11-June.
Not in PICO
- Ghadimi, B. M., Horstmann, O., Jacobsen, K., Feth, J. & Becker, H. (2002) Delay of diagnosis in pancreatic cancer due to suspected symptomatic cholelithiasis. *Scandinavian Journal of Gastroenterology*, 37: 1437-1439.
Not in PICO
- Ghadir, M. R., Sheikhesmaili, F., Attari, F., Safdari, R., Ghanooni, A. & Vaez-Javadi, M. (2012) Autoimmune pancreatitis mimicking carcinoma of the head of the pancreas: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 6: 11.
Not in PICO

- Giger, U., Stanga, Z. & DeLegge, M. H. (2004) Management of chronic pancreatitis. *Nutrition in Clinical Practice*, 19: 37-49.
Narrative review
- Girelli, C. M., Reguzzoni, G., Limido, E., Savastano, A. & Rocca, F. (1995) Pancreatic carcinoma: differences between patients with or without diabetes mellitus. *Recenti Progressi in Medicina*, 86: 143-146.
Not in PICO
- Girelli, C. M. & Rocca, F. (2001) [Early diagnosis of pancreatic carcinoma]. [Review] [15 refs] [Italian]. *Recenti Progressi in Medicina*, 92: 400-401.
Narrative review
- Goh, B. K., Tan, D. M., Thng, C. H., Lee, S. Y., Low, A. S., Chan, C. Y., Wong, J. S., Lee, V. T., Cheow, P. C., Chow, P. K., Chung, A. Y., Wong, W. K. & Ooi, L. L. (2014) - Are the Sendai and Fukuoka consensus guidelines for cystic mucinous neoplasms of the pancreas useful in the initial triage of all suspected pancreatic cystic neoplasms? A single-institution experience with 317 surgically-treated patients. - *Annals of Surgical Oncology*, 21: 1919-1926.
Duplicate
- Goh, B. K. P., Tan, D. M. Y., Thng, C.-H., Lee, S.-Y., Low, A. S. C., Chan, C.-Y., Wong, J.-S., Lee, V. T. W., Cheow, P.-C., Chow, P. K. H., Chung, A. Y. F., Wong, W.-K. & Ooi, L. L. P. J. (2014) Are the sendai and fukuoka consensus guidelines for cystic mucinous neoplasms of the pancreas useful in the initial triage of all suspected pancreatic cystic neoplasms? A single-institution experience with 317 surgically-treated patients. *Annals of Surgical Oncology*, 21: 1919-1926.
Not in PICO
- Goujon, G., Couvelard, A., Vullierme, M.-P., Gaujoux, S., Cros, J., Sauvanet, A., Rebours, V., Maire, F., Hentic, O., Levy, P., Ruszniewski, P. & Hammel, P. (11111) Solid and pseudopapillary tumours of the pancreas: Are the epidemiology and imaging features changing? *Pancreatology*, 12: 575-December.
Not in PICO
- Green, A. I. & Austin, C. P. (1993) Psychopathology of pancreatic cancer. A psychobiologic probe. *Psychosomatics*, 34: 208-221.
Narrative review
- Greenberger, N. J. (1964) Diagnostic approach to the patient with chronic pancreatic disease and suspected pancreatic carcinoma. *The Journal of the Kansas Medical Society*, 85: 53-55, 64.
Not in PICO
- Greenhalf, W., Malats, N., Nilsson, M., Bartsch, D. & Neoptolemos, J. (2008) International registries of families at high risk of pancreatic cancer. *Pancreatology*, 8: 558-565.
Narrative review
- Greenwald, H. P., Bonica, J. J. & Bergner, M. (1987) The prevalence of pain in four cancers. *Cancer*, 60: 2563-2569.
Not in PICO
- Gullo, L., Tomassetti, P., Migliori, M., Casadei, R. & Marrano, D. (2001) Do early symptoms of pancreatic cancer exist that can allow an earlier diagnosis? *Pancreas*, 22: 210-213.
Not in PICO
- Gullo, L., Migliori, M., Falconi, M., Pederzoli, P., Bettini, R., Casadei, R., Delle Fave, G., Corleto, V. D., Ceccarelli, C., Santini, D. & Tomassetti, P. (2003) Nonfunctioning pancreatic endocrine tumors: A multicenter clinical study. *American Journal of Gastroenterology*, 98: 2435-2439.
Not in PICO
- Gyokeres, T. (2011) [Symptoms and diagnosis of neuroendocrine tumors of the digestive system]. [Review] [Hungarian]. *Orvosi Hetilap*, 152: 371-378.
Narrative review
- Halfdanarson, T. R., Bamlet, W. R., Hobday, T. J., McWilliams, R. R. & Petersen, G. M. (2010) Risk factors for sporadic pancreatic neuroendocrine tumors (PNETs): a single-center case control

study. *Pancreas*, 39: 273.
Not in PICO

Halls, B. S. & Ward-Smith, P. (2007) Identifying early symptoms of pancreatic cancer. [Review] [24 refs]. *Clinical Journal of Oncology Nursing*, 11: 245-248.
Narrative review

Haut, E., Abbas, A. & Schuricht, A. (1999) Pancreatic cancer: The role of the primary care physician. *Consultant*, 39: 3329-3335.
Narrative review

Hayakawa, T., Kondo, T., Shibata, T., Kitagawa, M., Katada, N., Kato, K. & Takeichi, M. (1990) Prospective trial for early detection of pancreatic cancer by elevated serum immunoreactive elastase. *Gastroenterologia Japonica*, 25: 727-731.
Not in PICO

Heikkinen, M., Pikkarainen, P., Takala, J., Rasanen, H. & Julkunen, R. (1995) Etiology of Dyspepsia - 400 Unselected Consecutive Patients in General-Practice. *Scandinavian Journal of Gastroenterology*, 30: 519-523.
Not in PICO

Helm, F. (1983) Cutaneous signs of internal malignancies. *Journal of Surgical Oncology*, 23: 1-4.
Narrative review

Helmstaedter, L. & Riemann, J. F. (2008) Pancreatic cancer--EUS and early diagnosis. [Review] [24 refs]. *Langenbecks Archives of Surgery*, 393: 923-927.
Narrative review

Hennig, R., Kis, A., Hinz, U., Kleeff, J., Schmidt, J., Friess, H. & Buchler, M. W. (2010) Diabetes is associated to malignant pancreatic tumors and serves as prognostic factor for ductal adenocarcinoma. *Pancreas*, 39: 1323.
Not in PICO

Hippisley-Cox, J. & Coupland, C. (2012) Predictive effect of heartburn and indigestion and risk of upper gastro-intestinal malignancy. *British Journal of General Practice*, March: 124-126.
Not in PICO (does not present PPVs)

Hippisley-Cox, J. & Coupland, C. (2013) Symptoms and risk factors to identify women with suspected cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice*, 63: e11-e21.
Data in Hippisley-Cox 2012 on pancreatic cancer

Hiramatsu, K., Hasuoka, H., Watanabe, M. & Ochi, K. (2009) Three cases of minute pancreatic cancer (less than 10 mm) in our institutes. *Pancreas*, 38: 1003.
Not in PICO

Hoem, D., Jensen, D., Steine, S., Thorsen, T. E., Viste, A. & Molven, A. (2008) Clinicopathological characteristics and non-adhesive organ culture of insulinomas. *Scandinavian Journal of Surgery*, 97: 42-49.
Not in PICO

Homma, T. & Tsuchiya, R. (1991) The study of the mass screening of persons without symptoms and of the screening of outpatients with gastrointestinal complaints or icterus for pancreatic cancer in Japan, using CA19-9 and elastase-1 or ultrasonography. *International Journal of Pancreatology*, 9: 119-124.
Not in PICO

Homma, T. (1991) [Tumor marker--personal experience. Mass survey and outpatients screening of pancreatic cancer]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 18: 497-501.
Same as Homma 1991

Horiuchi, A., Kawa, S., Hamano, H., Hayama, M., Ota, H. & Kiyosawa, K. (2002) ERCP features in 27 patients with autoimmune pancreatitis. *Gastrointestinal Endoscopy*, 55: 494-499.
Not in PICO

- Horsted, F., Grainge, M. & West, J. (2010) What is the risk of venous thromboembolism in patients with cancer? - A systematic review and meta-analysis. *European Journal of Cancer, Supplement*, 8: 16-17.
Not in PICO
- Huang, J. Q., Bao, X. J. & Lu, X. H. (1993) [The common causes and differential diagnosis of malignant jaundice]. [Chinese]. *Chung-Hua Nei Ko Tsa Chih Chinese Journal of Internal Medicine*, 32: 400-404.
Not in PICO
- Hucl, T., Saglova, A., Honsova, E., Oliverius, M. & Spicak, J. (11111) High incidence of pancreatic cancer in patients with autoimmune pancreatitis undergoing surgery. *Pancreatology*, 12: 532-December.
Not in PICO
- Huggett, M. T. & Pereira, S. P. (2011) Diagnosing and managing pancreatic cancer. *Practitioner*, 255: 21-25.
Narrative review
- Hunaid, H., Rajinder, S., Devbrata, A., Saurabh, J. & Rajeev, J. (2011) Cystic lesions of the pancreas: Therapeutic and diagnostic dilemmas. *HPB*, 13: 155.
Not in PICO
- Hwang, T. L., Hsu, J. T. & Shan, Y. S. (2012) Clinical manifestations of patients with pancreatic beta cells hyperplasia. *Neuroendocrinology*, 96: 37.
Not in PICO
- Idilbi, N. M., Barchana, M., Milman, U. & Carel, R. S. (2013) Incidence of cancer among diabetic and nondiabetic adult Israeli arabs. *Journal of Diabetes*, 5: 116.
Not in PICO
- Iglesias-Garcia, J. & Dominguez-Munoz, J. E. (2014) Early detection of pancreatic cancer in patients with intraductal papillary mucinous neoplasms: the pivotal role of endoscopic ultrasound. *Endoscopy*, 46: 30-31.
Not in PICO
- Imai, K., Matsubayashi, H., Ono, H., Uesaka, K. & Sasaki, K. (2009) Three cases of solid papillary tumor - Typical and atypical cases. *Pancreas*, 38: 1006.
Not in PICO
- Iordache, S., Saftoiu, A., Cazacu, S., Gheonea, D. I., Dumitrescu, D., Popescu, C. & Ciurea, T. (2008) Endoscopic ultrasound approach of pancreatic cancer in chronic pancreatitis patients in a tertiary referral centre. *Journal of Gastrointestinal & Liver Diseases*, 17: 279-284.
Not in PICO
- Iqbal, S., Quddus, u. R., Latif, U., Mujeebullah & Elahi, A. (2012) Etiology and diagnosis of obstructive jaundice, our experience. *Medical Forum Monthly*, 23: 39-43.
Not in PICO
- Isozaki, H., Okajima, K., Morita, S., Takeda, Y., Ishibashi, T., Tanimura, M., Hara, H., Niki, M., Akimoto, H. & Kobayashi, M. (1990) Review of pancreatic cancer. *Bulletin of the Osaka Medical College*, 36: 1-11.
Not in PICO
- Iusco, D. R., Navarra, G., Bonomi, S., Grassi, A., Vicari, S. & Virzi, S. (2012) Pancreatic large mucinous cystoadenoma with invasive ductal carcinoma in pregnancy. Case report. *Giornale di Chirurgia*, 33: 163-167.
Not in PICO
- Izikson, L., English, J. C., III & Zirwas, M. J. (2006) The flushing patient: differential diagnosis, workup, and treatment. [Review] [101 refs]. *Journal of the American Academy of Dermatology*, 55: 193-208.
Narrative review

- Janes, R. H., Jr., Niederhuber, J. E., Chmiel, J. S., Winchester, D. P., Ocwieja, K. C., Karnell, J. H., Clive, R. E. & Menck, H. R. (1996) National patterns of care for pancreatic cancer. Results of a survey by the Commission on Cancer. *Annals of Surgery*, 223: 261-272.
Not in PICO
- Johnson, J. A., Bowker, S. L., Richardson, K. & Marra, C. (2011) Time-varying incidence of cancer after the onset of type 2 diabetes: Evidence of potential surveillance bias. *Diabetes*, 60: A69.
Not in PICO
- Kamata, K., Kitano, M., Kudo, M., Sakamoto, H., Kadosaka, K., Miyata, T., Imai, H., Maekawa, K., Chikugo, T., Kumano, M., Hyodo, T., Murakami, T., Chiba, Y. & Takeyama, Y. (2014) Value of EUS in early detection of pancreatic ductal adenocarcinomas in patients with intraductal papillary mucinous neoplasms. *Endoscopy*, 46: 22-29.
Not in PICO
- Kamisawa, T., Egawa, N., Nakajima, H., Tsuruta, K., Okamoto, A. & Kamata, N. (2003) Clinical difficulties in the differentiation of autoimmune pancreatitis and pancreatic carcinoma. *American Journal of Gastroenterology*, 98: 2694-2699.
Not in PICO
- Kang, C. M., Kim, K. S., Choi, J. S., Lee, W. J. & Kim, B. R. (2005) Experiences with nonfunctioning neuroendocrine neoplasms of the pancreas. *Digestive Surgery*, 22: 453-458.
Not in PICO
- Kang, S. P. & Saif, M. W. (2010) Clinical outcome of pancreatic cancer patients with diabetes mellitus: is diabetes a poor prognostic factor? Highlights from the "2010 ASCO Annual Meeting". Chicago, IL, USA. June 4-8, 2010. [Review] [10 refs]. *Jop: Journal of the Pancreas [Electronic Resource]*, 11: 334-335.
Narrative review
- Katsinelos, P., Paroutoglou, G., Kountouras, J., Beltsis, A., Papaziogas, B., Mimidis, K., Zavos, C. & Dimiropoulos, S. (2006) Safety and long-term follow-up of endoscopic snare excision of ampullary adenomas. *Surgical Endoscopy and Other Interventional Techniques*, 20: 608-613.
Not in PICO
- Katz, P., Ripellino, C., Heiman, F. & Chatenoud, L. (2011) The use of large GPS longitudinal database in the reasearch of causal associations among pathologies: The case of diabetes and cancer incidence. *Value in Health*, 14: A470.
Not in PICO
- Kavanagh, D. O., O'Riain, C., Ridgway, P. F., Neary, P., Crotty, T. C., Geoghegan, J. G. & Traynor, O. (2008) Radical pancreaticoduodenectomy for benign disease. *TheScientificWorldJournal*, 8: 1156-1167.
Not in PICO
- Keane, M. G., Horsfall, L., Hait, G. & Pereira, S. P. (1111) Socio-demographic trends and frequency of early symptoms and frequency of early symptoms in pancreatic cancer. *Pancreatology*, 13: e14-February.
Abstract only, not enough information is available to ascertain relevance or potentially extract results
- Kei, K., Shinichi, E., Naoaki, S., Takaho, O., Fuyuhiko, M., Shoji, F., Toshiki, R., Yu, K. & Michiaki, U. (2008) An experience of the successful treatment for repeated hemorrhage from arterial stump after pancreaticoduodenectomy. *Pancreas*, 36: 220-221.
Not in PICO
- Keil, R., Pipkova, R. & Belsan, T. (1999) Diagnosis of tumors of the subhepatic region. [Czech]. *Endoskopie*, 8: S9-S11.
Narrative review
- Keswani, R. N., Noffsinger, A. & Waxman, I. (2006) A family history of pancreatic cancer. *Nature Clinical Practice Gastroenterology & Hepatology*, 3: 586-591.
Not in PICO

- Khan, S., Sclabas, G. & Reid-Lombardo, K. M. (2010) Population-based epidemiology, risk factors and screening of intraductal papillary mucinous neoplasm patients. *World Journal of Gastrointestinal Surgery*, 2: 314-318.
Narrative review
- Khorana, A. A., Ahrendt, S. A., Ryan, C. K., Francis, C. W., Hruban, R. H., Hu, Y. C., Hostetter, G., Harvey, J. & Taubman, M. B. (2007) Tissue factor expression, angiogenesis, and thrombosis in pancreatic cancer. *Clinical Cancer Research*, 13: 2870-2875.
Not in PICO
- Kim, J. D., Han, Y. S. & Choi, D. L. (2011) Characteristic clinical and pathologic features for preoperative diagnosed groove pancreatitis. *Journal of The Korean Surgical Society*, 80: 342-347.
Not in PICO
- Kim, K. W., Park, S. H., Pyo, J., Yoon, S. H., Byun, J. H., Lee, M. G., Krajewski, K. M. & Ramaiya, N. H. (2013) Imaging features to distinguish malignant and benign branch-duct type intraductal papillary mucinous neoplasms of the pancreas: a meta-analysis (Provisional abstract). *Database of Abstracts of Reviews of Effects.*, epub.
Not in PICO
- Kim, T. D., Oh, H. J., Kim, K. H., Kim, S. M., Kim, J. H., Jang, B. I., Kim, T. N. & Chung, M. K. (2004) [Clinical characteristics of pancreatic cancer according to the presence of diabetes mellitus]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 43: 35-40.
Not in PICO
- Kim, Y. H., Jang, S. I., Rhee, K. & Lee, D. K. (2014) - Endoscopic treatment of pancreatic calculi. [Review]. - *Clinical Endoscopy*, 47: 227-235.
Narrative review
- Kimura, H., Furukawa, Y., Kuwada, Y., Hananoki, M., Matumoto, N., Yamamoto, M. & Fujiwara, M. (2009) A patient with pancreatic cancer associated with brain and skin metastases. *Pancreas*, 38: 486.
Not in PICO
- Klapman, J. B., Chang, K. J., Lee, J. G. & Nguyen, P. (2005) Negative predictive value of endoscopic ultrasound in a large series of patients with a clinical suspicion of pancreatic cancer. *American Journal of Gastroenterology*, 100: 2658-2661.
Not in PICO
- Knight, K., Wade, S. & Balducci, L. (2004) Prevalence and outcomes of anemia in cancer: A systematic review of the literature. *American Journal of Medicine*, 116: 11-26.
Not in PICO
- Koch, T. R., Michener, S. R. & Go, V. L. (1991) Plasma vasoactive intestinal polypeptide concentration determination in patients with diarrhea. *Gastroenterology*, 100: 99-106.
Not in PICO
- Kochar, R., Tamhane, A., Christein, J. D. & Varadarajulu, S. (2009) Racial disparity in communication between physicians and patients with suspected pancreatic cancer referred for EUS. *Gastrointestinal Endoscopy*, 69: AB329.
Not in PICO
- Kodama, T. & Mori, W. (1983) Morphological lesions of the pancreatic ducts. Significance of pyloric gland metaplasia in carcinogenesis of exocrine and endocrine pancreas. *Acta Pathologica Japonica*, 33: 645-660.
Not in PICO
- Konda, V. J. A., Meining, A., Jamil, L. H., Giovannini, M., Hwang, J. H., Wallace, M. B., Chang, K. J., Siddiqui, U. D., Hart, J., Lo, S. K., Saunders, M. D., Aslanian, H. R., Wroblewski, K. & Waxman, I. (2013) A pilot study of in vivo identification of pancreatic cystic neoplasms with needle-based confocal laser endomicroscopy under endosonographic guidance. *Endoscopy*, 45: 1006-1013.
Not in PICO

- Kongkam, P., Ang, T. L., Vu, C. K., Dy, F. T., Yasuda, K., Rerknimitr, R., Varadarajulu, S., Dhir, V., Chong, V. H., Zhen, D. J., Wong, J. Y., Ho, K. Y. & Asian Consortium of EUS (2013) Current status on the diagnosis and evaluation of pancreatic tumor in Asia with particular emphasis on the role of endoscopic ultrasound. [Review]. *Journal of Gastroenterology & Hepatology*, 28: 924-930.
Narrative review
- Kornreich, D. A. & Saif, M. W. (2012) Pancreatic cancer and thromboembolism in the ambulatory community. [Review]. *Jop: Journal of the Pancreas [Electronic Resource]*, 13: 185-186.
Narrative review
- Krech, R. L. & Walsh, D. (1991) Symptoms of pancreatic cancer. *Journal of Pain & Symptom Management*, 6: 360-367.
Not in PICO
- Krechler, T., Novotny, J., Zeman, M., Krska, Z., Svestka, T., Svab, J., Lukas, M., Filipova, R. & Zak, A. (2004) [Pancreatic carcinoma and diabetes mellitus]. [Czech]. *Casopis Lekarů Ceskych*, 143: 97-100.
Not in PICO
- Kuang, T. T., Jin, d. Y., Wang, D. S., Xu, X. F., Ni, X. L., Wu, W. C. & Lou, W. H. (2009) Clinical epidemiological analysis of the relationship between pancreatic cancer and diabetes mellitus: data from a single institution in China. *Journal of Digestive Diseases*, 10: 26-29.
Not in PICO
- Lachter, J. (2009) Prevention and/or early detection of pancreatic cancer: From forming a registry through risk factor intervention and eus screening tests: From concept to cure. *Gastrointestinal Endoscopy*, 69: AB252.
Not in PICO
- Lahat, G., Lubezky, N., Haim, M. B., Nachmany, I., Blachar, A., Santo, I., Nakache, R. & Klausner, J. M. (2011) Cystic tumors of the pancreas: high malignant potential. *Israel Medical Association Journal: Imaj*, 13: 284-289.
Not in PICO
- Lakatos, G. & Tulassay, Z. (2010) The epidemiology of pancreatic cancer. [Hungarian]. *Orvosi Hetilap*, 151: 1816-1822.
Narrative review
- Lankisch, P. G. (1997) Case history, symptoms, laboratory and function tests in chronic pancreatitis. [German]. *Verdauungskrankheiten*, 15: 110-117.
Narrative review
- Larijani, B., Aghakhani, S., Lor, S. S. M., Zahedi, F., Pajouhi, M. & Bastanagh, M. H. (2005) Insulinoma in Iran: a 20-year review. *Annals of Saudi Medicine*, 25: 477-480.
Not in PICO
- Larsen, A. C., Dabrowski, T., Fisker, R. V., Kristensen, S. R., Moller, B. K. & Thorlacius-Ussing, O. (2012) Venous thromboembolism and haemostatic disturbances in patients with upper gastrointestinal cancer. *Thrombosis Research*, 129: S165.
Not in PICO
- Lebedeva, A. N., Demidova, V. S., Shevchenko, T. V. & Kriger, A. G. (2010) [Carbohydrate metabolism disturbances after pancreatoduodenal resection in patients with cancer of the head of pancreas]. [Russian]. *Khirurgiia.(5):21-4, 2010.*, 21-24.
Not in PICO
- Lee, A. Y. Y. (2003) Epidemiology and management of venous thromboembolism in patients with cancer. *Thrombosis Research*, 110: 167-172.
Narrative review
- Lee, C. J., Scheiman, J., Anderson, M. A., Hines, O. J., Reber, H. A., Farrell, J., Kochman, M. L., Foley, P. J., Drebin, J., Oh, Y. S., Ginsberg, G., Ahmad, N., Merchant, N. B., Isbell, J., Parikh, A. A., Stokes, J. B., Bauer, T., Adams, R. B. & Simeone, D. M. (2008) Risk of malignancy in resected cystic tumors of the pancreas < or =3 cm in size: is it safe to observe asymptomatic patients? A multi-

- institutional report. *Journal of Gastrointestinal Surgery*, 12: 234-242.
Not in PICO
- Lee, H., Lee, J. K., Kang, S. S., Choi, D., Jang, K. T., Kim, J. H., Lee, K. T., Paik, S. W., Yoo, B. C. & Rhee, J. C. (2007) Is there any clinical or radiologic feature as a preoperative marker for differentiating mass-forming pancreatitis from early-stage pancreatic adenocarcinoma? *Hepato-Gastroenterology*, 54: 2134-2140.
Not in PICO
- Lee, S. J., Waters, J. A., Schmidt, C. M., Pitt, H. A. & Zyromski, N. J. (2012) Does acute pancreatitis change the natural history of intraductal papillary mucinous neoplasm (IPMN)? *Pancreas*, 41: 1379.
Not in PICO
- Lee, W. J., Park, Y. T., Choi, J. S., Chi, H. S. & Kim, B. R. (1996) Solid and papillary neoplasms of the pancreas. *Yonsei Medical Journal*, 37: 131-141.
Not in PICO
- Lee, Y. T. & Williams, M. D. (1984) Clinical and laboratory findings of carcinoma of the pancreas and periampullary structures. *Journal of Surgical Oncology*, 25: 1-7.
Not in PICO
- Leivonen, M. K., Halttunen, J. A. & Kivilaakso, E. O. (1996) Duodenal diverticulum at endoscopic retrograde cholangiopancreatography, analysis of 123 patients. *Hepato-Gastroenterology*, 43: 961-966.
Not in PICO
- Lennon, A. M., Wolfgang, C. L., Canto, M. I., Klein, A. P., Herman, J. M., Goggins, M., Fishman, E. K., Kamel, I., Weiss, M. J., Diaz, L. A., Papadopoulos, N., Kinzler, K. W., Vogelstein, B. & Hruban, R. H. (2014) The early detection of pancreatic cancer: What will it take to diagnose and treat curable pancreatic neoplasia? *Cancer Research*, 74: 3381-3389.
Narrative review
- Leung, J. & Silverman, W. (2009) Diagnostic and therapeutic approach to pancreatic cancer-associated gastroparesis: literature review and our experience. [Review] [21 refs]. *Digestive Diseases & Sciences*, 54: 401-405.
Not in PICO
- Lewandowska, A., Suslo, A., Paradowski, L. & Drobnik, J. (2009) Problems in establishing pancreas tumors diagnosis - Family doctor role. [Polish]. *Family Medicine and Primary Care Review*, 11: 385-388.
Not in PICO
- Li, D. (2012) Diabetes and pancreatic cancer. *Molecular Carcinogenesis*, 51: 64-74.
Narrative review
- Li, J., Li, Y., Cao, G., Guo, K., Zhang, L. & Ma, Q. (2013) Early manifestations of pancreatic cancer: The effect of cancer-nerve interaction. *Medical Hypotheses*, 81: 180-182.
Narrative review
- Li, J.-S., Zhang, Z.-D., Tang, Y. & Jiang, R. (2007) Retrospective analysis of 88 patients with pancreatic duct stone. *Hepatobiliary and Pancreatic Diseases International*, 6: 208-212.
Not in PICO
- Liao, K. F., Lai, S. W., Li, C. I. & Chen, W. C. (2012) Diabetes mellitus correlates with increased risk of pancreatic cancer: a population-based cohort study in Taiwan. *Journal of Gastroenterology & Hepatology*, 27: 709-713.
Not in PICO
- Liu, T. & Wang, L. (2012) Advances in study on correlation between diabetes mellitus and development and progression of pancreatic cancer. [Chinese]. *Chinese Journal of Gastroenterology*, 17: 496-498.
Narrative review

- Lomberk, G. (2009) Diabetes. *Pancreatology*, 9: 200-202.
Narrative review
- Lopez, S. A. (2010) Risk factors and early diagnosis of pancreatic cancer. [Spanish]. *Gastroenterologia y Hepatologia*, 33: 382-390.
Narrative review
- Lovecek, M., Skalicky, P., Klos, D., Tozzi, D. A., I, Kliment, M., Kremer, M. & Havlik, R. (1111) The significance of endo-ultrasonography in the preoperative management of patients with (early) pancreatic cancer. *Pancreatology*, 12: 526-December.
Not in PICO
- Lowenfels, A. B., Maisonneuve, P., DiMagno, E. P., Elitsur, Y., Gates, L. K., Perrault, J., Whitcomb, D. C., Aranha, G., Banks, P., Burton, F. R., CarrLocke, D., Dyck, W. P., Gish, R. G., Goodale, R. L., Lehman, G., Martin, S. P., Potts, J., Sherman, S., Ulrich, C. D., Yakshe, P., Yeaton, P., Hamanaka, Y., Koizumi, M., Tomioka, T., Tsunoda, T., Yamadera, K., Delmont, J. P., Beger, H. G., Holstege, A., Keim, V., Layer, P., Triantafillidis, J., Boyle, P., Cavallini, G., Gullo, L., Pedrazzoli, S., Uomo, G., Castano, D. G. L., Ihse, I., Buchler, M. & Elias, E. (1997) Hereditary pancreatitis and the risk of pancreatic cancer. *Journal of the National Cancer Institute*, 89: 442-446.
Not in PICO
- Lowenfels, A. B., Maisonneuve, P. & Lankisch, P. G. (1999) Chronic pancreatitis and other risk factors for pancreatic cancer. *Gastroenterology Clinics of North America*, 28: 673-685.
Narrative review
- Lutz, M. P. & Pourebrahim, S. (1087) [Pancreatic carcinoma]. [Review] [14 refs] [German]. *Internist*, 49: 1079-1086.
Narrative review
- Lyon, C. & Clark, D. C. (2006) Diagnosis of acute abdominal pain in older patients. *American Family Physician*, 74: 1537-1544.
Narrative review
- Lyratzopoulos, G., Neal, R. D., Barbiere, J. M., Rubin, G. P. & Abel, G. A. (2012) Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. *Lancet Oncology*, 13: 353-365.
Not in PICO
- Maisonneuve, P., Lowenfels, A. B., Bueno-de-Mesquita, H. B., Ghadirian, P., Baghurst, P. A., Zatonski, W. A., Miller, A. B., Duell, E. J., Boffetta, P. & Boyle, P. (2010) Past medical history and pancreatic cancer risk: Results from a multicenter case-control study. *Annals of Epidemiology*, 20: 92-98.
Not in PICO
- Maluf-Filho, F., Sakai, P., Cunha, J. E., Garrido, T., Rocha, M., Machado, M. C. & Ishioka, S. (2004) Radial endoscopic ultrasound and spiral computed tomography in the diagnosis and staging of periampullary tumors. *Pancreatology*, 4: 122-128.
Not in PICO
- Manji, G., Manji, S. K. & Mehdi, S. (2010) Metastatic pancreatic cancer or two primaries: An oncologist's dilemma. *American Journal of Gastroenterology*, 105: S213.
Not in PICO
- Mansfield, A., Tafur, A., Smithedajkul, P., Corsini, M., Quevedo, F. & Miller, R. (2010) Mayo clinic experience with very rare exocrine pancreatic neoplasms. *Pancreas*, 39: 972-975.
Not in PICO
- Manta, R., Messerotti, A., Bertani, H., Dabizzi, E., Barbera, C., Manno, M., Mirante, V. & Conigliaro, R. (2010) Linear ultrasonography clinical impact in patients suspected of neuroendocrine pancreatic tumor. *Digestive and Liver Disease*, 42: S172.
Not in PICO
- Manta, R., Bertani, H., Barbera, C., Marini, F., Germani, U., Messerotti, A., Dabizzi, E., Lorenzini, I. & Conigliaro, R. (2011) Linear ultrasonography clinical impact in patients suspected of

- neuroendocrine pancreatic tumor. *Gastrointestinal Endoscopy*, 73: AB254.
Not in PICO
- Manta, R., Nardi, E., Bertani, H., Castellani, D., Messerotti, A., Germani, U., Lorenzini, I., Marini, F., Sabatino, G., Bassotti, G. & Conigliaro, R. L. (2012) Preoperative diagnosis of small or non functional pancreatic neuroendocrine tumors using endoscopic ultrasonography. *Digestive and Liver Disease*, 44: S144-S145.
Not in PICO
- Marangoni, G., Dickinson, K., Bokhari, S., Hakeem, A., Hamady, Z., Storey, R., Morris-Stiff, G. & Smith, A. (2012) Single center experience of groove pancreatitis. *HPB*, 14: 642.
Not in PICO
- Martinez, A. D., Alonso Aguirre, P. A., Martin-Granizo, B., I, Cid, G. L. & Pallares, P. A. (2008) [Usefulness of ultrasonography in diagnosing patients suspect for digestive tract neoplasms]. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 100: 545-551.
Not in PICO
- Matsumoto, I., Shirakawa, S., Shinzeki, M., Asari, S., Goto, T., Ajiki, T., Fukumoto, T., Kitajima, K. & Ku, Y. (2013) 18-Fluorodeoxyglucose positron emission tomography does not aid in diagnosis of pancreatic ductal adenocarcinoma. *Clinical Gastroenterology & Hepatology*, 11: 712-718.
Not in PICO
- Matteo, P., Roberto, V., Serena, S., Livia, A., Giulia, Z., Marianna, S., Alberto, L., Guido, C., Gianfranco, D. F. & Gabriele, C. (2013) Cachexia is an Insidious Symptom of Pancreatic Ductal Adenocarcinoma Associated with Delayed Diagnosis and Advanced Stage of Disease. *Journal of the Pancreas*, 14: 589.
Not in PICO
- McLaughlin, S. (1994) Pancreatic cancer and diabetes. [Review] [15 refs]. *Diabetes Educator*, 20: 20-Feb.
Narrative review
- Meggiato, T., Basso, D., Piccoli, A., Del, F. G., Fogar, P., Panozzo, M. P., Scalon, P., Fabris, C., Angonese, C. & Faggian, D. (1989) [Role of serum markers and or various clinical parameters in the diagnosis of pancreatic carcinoma]. [Italian]. *Annali Italiani di Medicina Interna*, 4: 367-372.
Not in PICO
- Meisterfeld, R., Eehalt, F., Saeger, H. D. & Solimena, M. (2008) Pancreatic disorders and diabetes mellitus. [Review] [75 refs]. *Experimental & Clinical Endocrinology & Diabetes*, 116: Suppl-S12.
Narrative review
- Menapace, L. A. & Khorana, A. A. (2010) The role of thromboprophylaxis in cancer patients: emerging data. [Review]. *Current Opinion in Hematology*, 17: 450-456.
Narrative review
- Menapace, L. A., Peterson, D. R., Berry, A., Sousou, T. & Khorana, A. A. (2011) Symptomatic and incidental thromboembolism are both associated with mortality in pancreatic cancer. *Thrombosis & Haemostasis*, 106: 371-378.
Not in PICO
- Mendieta, Z. H., Garcia Flores, J. R. & Romero Prieto, M. L. (2009) Limitations in improving detection of pancreatic adenocarcinoma. *Future oncology (London, England)*, 5: 657-668.
Not in PICO
- Miki, A., Sata, N., Sakuma, Y., Taguchi, M., Kasahara, N., Morishima, K., Kaneda, Y., Endo, K., Koizumi, M., Sasanuma, H., Shimizu, A., Hyodo, M., Lefor, A. T. & Yasuda, Y. (2012) Clinicopathological study of stage ia pancreas cancer: Single center experience. *Pancreas*, 41: 1386.
Not in PICO
- Miura, F., Takada, T., Amano, H., Yoshida, M., Furui, S. & Takeshita, K. (2006) Diagnosis of pancreatic cancer. *HPB*, 8: 337-342.
Narrative review

- Mizuno, S., Nakai, Y., Isayama, H., Yanai, A., Takahara, N., Miyabayashi, K., Yamamoto, K., Kawakubo, K., Mohri, D., Kogure, H., Sasaki, T., Yamamoto, N., Sasahira, N., Hirano, K., Tsujino, T., Ijichi, H., Tateishi, K., Akanuma, M., Tada, M. & Koike, K. (2013) Risk factors and early signs of pancreatic cancer in diabetes: screening strategy based on diabetes onset age. *Journal of Gastroenterology*, 48: 238-246.
Not in PICO
- Modolell, I., Guarner, L. & Malagelada, J. R. (1999) Vagaries of clinical presentation of pancreatic and biliary tract cancer. [Review] [34 refs]. *Annals of Oncology*, 10: Suppl-4.
Narrative review
- Monreal, M., Fernandez-Llamazares, J., Perandreu, J., Urrutia, A., Sahuquillo, J. C. & Contel, E. (1997) Occult cancer in patients with venous thromboembolism: which patients, which cancers. *Thrombosis & Haemostasis*, 78: 1316-1318.
Not in PICO
- Mori, E., Yuen, K., Medrano, H., Torres, J., Garcia, C. & Montes, J. (2012) [Management of pancreatic cystic tumors in the Alberto Sabogal Sologuren hospital]. [Spanish]. *Revista de Gastroenterologia del Peru*, 32: 169-177.
Not in PICO
- Morita, R., Yoshii, M., Nakajima, K., Kohsaka, T., Miki, M. & Torizuka, K. (1981) Clinical evaluation of serum ferritin to iron ratio in malignant diseases. *European Journal of Nuclear Medicine*, 6: 331-336.
Not in PICO
- Morris, D. V. & Nabarro, J. D. (1984) Pancreatic cancer and diabetes mellitus. *Diabetic Medicine*, 1: 119-121.
Not in PICO
- Munigala, S., Kanwal, F., Xian, H., Scherrer, J. F. & Agarwal, B. (2014) - Increased risk of pancreatic adenocarcinoma after acute pancreatitis. - *Clinical Gastroenterology & Hepatology*, 12: 1143-1150.
Not in PICO
- Munk, E. M., Drewes, A. M., Gorst-Rasmussen, A., Funch-Jensen, P., Gregersen, H. & Norgard, B. (2007) Risk of gastrointestinal cancer in patients with unexplained chest/epigastric pain and normal upper endoscopy: A Danish 10-year follow-up study. *Digestive Diseases and Sciences*, 52: 1730-1737.
Not in PICO
- Murray, I. A., Palmer, J., Waters, C. & Dalton, H. R. (2012) Predictive value of symptoms and demographics in diagnosing malignancy or peptic stricture. *World Journal of Gastroenterology*, 18: 4357-4362.
Not in PICO
- Mustak, M., Boltuch-Sherif, J., Frisch, M., Erlacher, L. & Atamaniuk, J. (2010) Autoimmune pancreatitis-an important differential diagnosis of pancreatic cancer: Report of three cases. *Zeitschrift fur Rheumatologie*, 69: 76-77.
Not in PICO
- Nagahama, H., Okada, S., Okusaka, T., Ishii, H., Ikeda, M., Nakasuka, H. & Yoshimori, M. (1999) Clinicopathological features in misdiagnosed pancreatic carcinoma. *Hepato-Gastroenterology*, 46: 2983-2985.
Not in PICO
- Nair, R. J., Lawler, L. & Miller, M. R. (2007) Chronic pancreatitis. *American Family Physician*, 76: 1679-1694.
Narrative review
- Nakazawa, S. (1983) [Early diagnosis of pancreatic cancer]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 29: 1124-1130.
Not in PICO

- Nicholson, J. A., Harrison, S., Sutton, R., Rousseau, A., Mountford, R., Hammel, P., Rebours, V., Mayerle, J., Charnley, R., Neoptolemos, J. P., Lerch, M. & Greenhal, W. (2011) Analysis of hereditary pancreatitis families in europe (EUROPAC): Incidence of prss1 associated pancreatic adenocarcinoma does not correlate to symptoms of pancreatitis. *Pancreas*, 40: 1344.
Not in PICO
- Niederle, M. B. & Niederle, B. (2011) Diagnosis and treatment of gastroenteropancreatic neuroendocrine tumors: current data on a prospectively collected, retrospectively analyzed clinical multicenter investigation. *The Oncologist*, 16: 602-613.
Not in PICO
- Nix, G. A., Schmitz, P. I., Wilson, J. H., Van, B. M., Groeneveld, C. F. & Hofwijk, R. (1984) Carcinoma of the head of the pancreas. Therapeutic implications of endoscopic retrograde cholangiopancreatography findings. *Gastroenterology*, 87: 37-43.
Not in PICO
- Nomura, N., Fujii, T., Kanazumi, N., Takeda, S., Nomoto, S., Kasuya, H., Sugimoto, H., Yamada, S. & Nakao, A. (2009) Nonfunctioning neuroendocrine pancreatic tumors: our experience and management. *Journal of Hepato-Biliary-Pancreatic Surgery*, 16: 639-647.
Not in PICO
- Noy, A. & Bilezikian, J. P. (1994) Clinical review 63: Diabetes and pancreatic cancer: clues to the early diagnosis of pancreatic malignancy. [Review] [56 refs]. *Journal of Clinical Endocrinology & Metabolism*, 79: 1223-1231.
Not in PICO
- O'Driscoll, D., O'Rorke, M., Fitzgerald, M., Conlon, K., Eatock, M., Murray, L. & Sharp, L. (2011) Inflammatory processes and risk of pancreatic cancer: Preliminary results from the all-Ireland PanCAM case-control study. *Pancreatology*, 11: 322.
Not in PICO
- O'Mara, B. A., Byers, T. & Schoenfeld, E. (1985) Diabetes mellitus and cancer risk: a multisite case-control study. *Journal of Chronic Diseases*, 38: 435-441.
Not in PICO
- Ogawa, Y., Tanaka, M., Inoue, K., Yamaguchi, K., Chijiwa, K., Mizumoto, K., Tsutsu, N. & Nakamura, Y. (2002) A prospective pancreatographic study of the prevalence of pancreatic carcinoma in patients with diabetes mellitus. *Cancer*, 94: 2344-2349.
Not in PICO
- Oi, I. (1986) Early detection of small pancreatic carcinoma. *Gann Monographs on Cancer Research*, VOL.: 147-149.
Not in PICO
- Ong, E. C., Medina, I. J. & Roffe, E. (2013) Is it itchy unfortunate Grandpa? *Journal of the American Geriatrics Society*, 61: S196.
Not in PICO
- Onitilo, A. A., Engel, J. M., Glurich, I., Stankowski, R. V., Williams, G. M. & Doi, S. A. (2012) Diabetes and cancer I: risk, survival, and implications for screening. [Review]. *Cancer Causes & Control*, 23: 967-981.
Narrative review
- Onyekwere, C. A. & Ojukwu, J. C. (2008) The epidemiologic profile of pancreatic cancer and management outcome in Lagos, Nigeria. *Pakistan Journal of Medical Sciences*, 24: 340-343.
Not in PICO
- Ooi, L. L., Ho, G. H., Chew, S. P., Low, C. H. & Soo, K. C. (1998) Cystic tumours of the pancreas: a diagnostic dilemma. *Australian & New Zealand Journal of Surgery*, 68: 844-846.
Not in PICO
- Ozaki, H. & Naito, S. (1980) Diagnosis of carcinoma of the pancreas in early stage. Review of 1210 cases collected from 63 major clinics in Japan. [Japanese]. *Japanese Journal of Gastroenterology*,

77: 1979-1983.

Not in PICO

Ozaki, H., Ishii, K., Sato, T., Karasawa, E., Kitamura, T., Tsuchiya, R., Kasugai, T., Abe, M., Ueda, M. & Takeuchi, T. (1985) Diagnosis of small pancreatic carcinoma. *Japanese Journal of Clinical Oncology*, 15: 115-120.

Not in PICO

Palsson, B., Masson, P. & Andren-Sandberg, A. (1997) Tumour marker CA 50 levels compared to signs and symptoms in the diagnosis of pancreatic cancer. *European Journal of Surgical Oncology*, 23: 151-156.

Not in PICO

Panagiotarakou, M., Gupta, A., Syrigos, K. & Saif, M. W. (2012) Use of supportive care for symptom management in pancreatic cancer: application of clinical research to patient care. *Jop: Journal of the Pancreas [Electronic Resource]*, 13: 342-344.

Not in PICO

Pandya, A., Xia, X. J., Blanton, S. H., Landa, B., Markello, T. & Nance, W. E. (1997) Implications of molecular diagnostic testing in families with hereditary pancreatitis. *Genetic Testing*, 1: 207-211.

Not in PICO

Paneesha, S., McManus, A., Arya, R., Scriven, N., Farren, T., Nokes, T., Bacon, S., Nieland, A., Cooper, D., Smith, H., O'Shaughnessy, D. & Rose, P. (2010) Frequency, demographics and risk (according to tumour type or site) of cancer-associated thrombosis among patients seen at outpatient DVT clinics. *Thrombosis and Haemostasis*, 103: 338-343.

Not in PICO

Pannala, R., Basu, A., Petersen, G. M. & Chari, S. T. (2009) New-onset diabetes: a potential clue to the early diagnosis of pancreatic cancer. [Review] [62 refs]. *Lancet Oncology*, 10: 88-95.

Narrative review

Parks, R. W. & Garden, O. J. (340) Ensuring early diagnosis in pancreatic cancer. [Review] [14 refs]. *Practitioner*, 244: 336-338.

Narrative review

Pasanen, P., Partanen, K., Pikkarainen, P., Alhava, E., Pirinen, A. & Janatuinen, E. (1992) Diagnostic accuracy of ultrasound, computed tomography and endoscopic retrograde cholangiopancreatography in the detection of pancreatic cancer in patients with jaundice or cholestasis. *In Vivo*, 6: 297-301.

Not in PICO

Peng, H. Q., Darwin, P., Papadimitriou, J. C. & Drachenberg, C. B. (2006) Liver metastases of pancreatic acinar cell carcinoma with marked nuclear atypia and pleomorphism diagnosed by EUS FNA cytology: a case report with emphasis on FNA cytological findings. *Cytojournal*, 3: 29.

Not in PICO

Persson, B. (1997) [Pancreatic cancer, difficult to diagnose. Few early symptoms, often normal laboratory values]. [Review] [29 refs] [Swedish]. *Lakartidningen*, 94: 1980-1982.

Narrative review

Pezzilli, R. (2004) Screening tests for pancreatic cancer: searching for the early symptoms or the population at risk. *Jop: Journal of the Pancreas [Electronic Resource]*, 5: 240-242.

Not in PICO

Pfeffer, F., Nauck, M. A., Benz, S. & Hopt, U. T. (1999) [Secondary diabetes in pancreatic carcinoma and after pancreatectomy: pathophysiology, therapeutic peculiarities and prognosis]. [Review] [36 refs] [German]. *Zeitschrift fur Gastroenterologie.Suppl 1:10-4, 1999 Jun.*, 10-14.

Narrative review

Phoe, O. B. & Huei, K. B. (2012) A rare cause of a pancreatic head mass. *Journal of Gastroenterology and Hepatology*, 27: 355.

Not in PICO

- Picard, C., Doat, M., Pilloy, W. J. & Als, C. (2011) Retrospective evaluation of the role of whole body 18F-FDG PET-CT in clinically suspected neoplasia but with negative initial diagnostic workup. *Medecine Nucleaire*, 35: 305-306.
Not in PICO
- Piciocchi, M., Capurso, G., Valente, R., Cavallini, M., Barrucca, V., Romiti, A., Marchetti, P., Ziparo, V. & Delle, F. G. (2010) Risk factors, clinical features and outcome of early onset pancreatic cancer patients compared to older patients. *Pancreatology*, 10: 368-369.
Not in PICO
- Piciocchi, M., Capurso, G., Valente, R., Barrucca, V., Carnuccio, A., Romiti, A., Pilozi, E., Cavallini, M., Larghi, A., Costamagna, G., Ziparo, V. & Delle, F. G. (2011) Risk factors, clinical features and outcome of early onset pancreatic cancer patients compared to older patients. *Gastroenterology*, 140: S710-S711.
Not in PICO
- Ping, Z. (2013) Diagnosis of early diabetes-related pancreatic cancer. *Journal of Gastroenterology and Hepatology*, 28: 675.
Not in PICO
- Popiela-Mizera, A. (1985) [The Marton model in the early detection of pancreatic cancer]. [Polish]. *Przegląd Lekarski*, 42: 662-667.
Not in PICO
- Porta, M., Fabregat, X., Malats, N., Guarner, L., Carrato, A., de, M. A., Ruiz, L., Jariod, M., Costafreda, S., Coll, S., Alguacil, J., Corominas, J. M., Sola, R., Salas, A. & Real, F. X. (2005) Exocrine pancreatic cancer: symptoms at presentation and their relation to tumour site and stage. *Clinical & Translational Oncology: Official Publication of the Federation of Spanish Oncology Societies & of the National Cancer Institute of Mexico*, 7: 189-197.
Not in PICO
- Postier, R. G. & Williams, G. R. (1993) Pancreatic adenocarcinoma: a review for primary care physicians. [Review] [27 refs]. *Journal - Oklahoma State Medical Association*, 86: 492-495.
Narrative review
- Price, S., Cole, D. & Alcolado, J. C. (2010) Diabetes due to exocrine pancreatic disease--a review of patients attending a hospital-based diabetes clinic. *QJM*, 103: 759-763.
Not in PICO
- Ragulin-Coyne, E., Smith, J. K., Ng, S., McDade, T. P., Shah, S. A. & Tseng, J. F. (2011) Potential predictors of pancreatic cancer: A population-based screen. *Journal of Clinical Oncology*, 29.
Not in PICO
- Rahman, S. H., Verbeke, C. S., Gomez, D., McMahan, M. J. & Menon, K. V. (2007) Pancreatico-duodenectomy for complicated groove pancreatitis. *HPB*, 9: 229-234.
Not in PICO
- Raimondi, S., Maisonneuve, P. & Lowenfels, A. B. (2009) Epidemiology of pancreatic cancer: An overview. *Nature Reviews Gastroenterology and Hepatology*, 6: 699-708.
Narrative review
- Raptis, D. A., Fessas, C., Belasyse-Smith, P., Skipworth, J., Graf, R. & Kurzawinski, T. R. (2009) Clinical presentation and waiting time targets do not affect prognosis in patients with pancreatic cancer. *Pancreatology*, 9: 527.
Not in PICO
- Raptis, D. A., Fessas, C., Belasyse-Smith, P. & Kurzawinski, T. R. (2010) Clinical presentation and waiting time targets do not affect prognosis in patients with pancreatic cancer. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 8: 239-246.
Not in PICO
- Reisman, Y., Gips, C. H., Lavelle, S. M. & Wilson, J. H. P. (1996) Clinical presentation of (subclinical) jaundice - The Euricterus project in The Netherlands. *Hepato-Gastroenterology*, 43: 1190-1195.
Not in PICO

- Reusch, J., Keck, A. M., Link, K. H. & Mohr, H. H. (1998) Coexistence of two different neuroendocrine tumours of the gastrointestinal tract and the pancreas. *Deutsche Medizinische Wochenschrift*, 123: 1472-1477.
Not in PICO
- Richter, J. M. & Barry, M. J. (1985) Decision analysis for the practicing gastroenterologist. 2. Insights into the efficacy of diagnostic strategies using decision analysis. *American Journal of Gastroenterology*, 80: 493-497.
Narrative review
- Richter, J. M., Christensen, M. R., Rustgi, A. K. & Silverstein, M. D. (1989) The clinical utility of the Ca19-9 radioimmunoassay for the diagnosis of pancreatic cancer presenting as pain or weight loss. A cost-effectiveness analysis. *Archives of Internal Medicine*, 149: 2292-2297.
Not in PICO
- Ridder, G. J. & Klempnauer, J. (1996) Presenting symptoms of cancer of the exocrine pancreas and the periampullary region: Established facts and new insights from an analysis of surgically treated patients. *Zentralblatt fur Chirurgie*, 121: 557-564.
Not in PICO
- Ridwelski, K., Meyer, F., Ebert, M., Malfertheiner, P. & Lippert, H. (2001) Prognostic parameters determining survival in pancreatic carcinoma and, in particular, after palliative treatment. *Digestive Diseases*, 19: 85-92.
Not in PICO
- Rigaux, J., Arvanitakis, M., Closset, J., Demetter, P., Matos, C., Delhay, M. & Deviere, J. M. (2009) Endoscopic management of paraduodenal pancreatitis. *Gastrointestinal Endoscopy*, 69: AB311.
Not in PICO
- Robison, L. S., Canon, C. L., Varadarajulu, S., Eloubeidi, M. A., Vickers, S. & Mel, W. C. (2011) Autoimmune pancreatitis mimicking pancreatic cancer. *Journal of Hepato-biliary-pancreatic Sciences*, 18: 162-169.
Not in PICO
- Roche, S. P. & Kobos, R. (2004) Jaundice in the Adult Patient. *American Family Physician*, 69: 299-304.
Narrative review
- Rong, Y., Lou, W. & Jin, D. (2008) Pancreatic tuberculosis with splenic tuberculosis mimicking advanced pancreatic cancer with splenic metastasizes: a case report. *Cases journal*, 1: 84.
Not in PICO
- Ronga, I., Gallucci, F., Riccardi, F. & Uomo, G. (2014) - Anorexia-cachexia syndrome in pancreatic cancer: recent advances and new pharmacological approach. - *Advances in Medical Sciences*, 59: 1-6.
Narrative review
- Rosch, T., Hofrichter, K., Frimberger, E., Meining, A., Born, P., Weigert, N., Allescher, H. D., Classen, M., Barbur, M., Schenck, U. & Werner, M. (2004) ERCP or EUS for tissue diagnosis of biliary strictures? A prospective comparative study. *Gastrointestinal Endoscopy*, 60: 390-396.
Not in PICO
- Rubio-Tapia, A., Hill, I. D., Kelly, C. P., Calderwood, A. H., Murray, J. A. & American College of Gastroenterology (677) ACG clinical guidelines: diagnosis and management of celiac disease. *American Journal of Gastroenterology*, 108: 656-676.
Not in PICO
- Ruf, J., Lopez, H. E., Oettle, H., Plotkin, M., Pelzer, U., Stroszczyński, C., Felix, R. & Amthauer, H. (2005) Detection of recurrent pancreatic cancer: comparison of FDG-PET with CT/MRI. *Pancreatology*, 5: 266-272.
Not in PICO

- Sah, R. P., Nagpal, S. J., Mukhopadhyay, D. & Chari, S. T. (2013) New insights into pancreatic cancer-induced paraneoplastic diabetes. *Nature Reviews Gastroenterology & Hepatology*, 10: 423-433.
Narrative review
- Sahin, I. H., Shama, M. A., Tanaka, M., Abbruzzese, J. L., Curley, S. A., Hassan, M. & Li, D. (2012) Association of diabetes and perineural invasion in pancreatic cancer. *Cancer Medicine*, 1: 357-362.
Not in PICO
- Saif, M. W. (2007) Pancreatoblastoma. *Jop: Journal of the Pancreas [Electronic Resource]*, 8: 55-63.
Narrative review
- Sakorafas, G. H. & Sarr, M. G. (2003) Pancreatic cancer after surgery for chronic pancreatitis. *Digestive & Liver Disease*, 35: 482-485.
Not in PICO
- Sanchez, M., Gomez, C., De Las, H. G. & Lopez-Hoyos, M. (2009) Anti-carbonic anhydrase II antibodies and IGG4 levels as serological parameters determinant for the diagnosis of autoimmune pancreatitis. *European Journal of Immunology*, 39: S669.
Not in PICO
- Santhosh, S., Mittal, B. R., Bhasin, D., Srinivasan, R., Rana, S., Das, A., Nada, R., Bhattacharya, A., Gupta, R. & Kapoor, R. (2013) Role of (18)F-fluorodeoxyglucose positron emission tomography/computed tomography in the characterization of pancreatic masses: experience from tropics. *Journal of Gastroenterology & Hepatology*, 28: 255-261.
Not in PICO
- Saruc, M. & Pour, P. M. (2003) Diabetes and its relationship to pancreatic carcinoma. [Review] [81 refs]. *Pancreas*, 26: 381-387.
Narrative review
- Saruc, M., Karaarslan, M., Rasa, K., Saygili, O., Ince, U., Baysal, C., Pour, P. M., Cakmakci, M. & Tozun, N. (2009) Pancreatic cancer and glucose metabolism. *Turkish Journal of Gastroenterology*, 20: 257-260.
Not in PICO
- Savopoulos, C. G., Tsesmeli, N. E., Kaiafa, G. D., Zantidis, A. T., Bobos, M. T., Hatzitolios, A. I., Papavramidis, S. T. & Kostopoulos, I. S. (2005) Primary pancreatic anaplastic large cell lymphoma, ALK negative: A case report. *World Journal of Gastroenterology*, 11: 6221-6224.
Not in PICO
- Schroder, J., Wesner, F. & Kremer, B. (2000) Diagnostic procedures in patients with the principal sign of weight loss. [German]. *Chirurgische Gastroenterologie Interdisziplinär*, 16: 61-64.
Narrative review
- Shah, I. A., Dolan, W. V., Ramirez, F. C. & Iqbal, J. (1997) Diagnosis of early peri-ampullary carcinoma. *Digestive Surgery*, 14: 323-326.
Narrative review
- Sharma, A., Alfa-Wali, M., Rodriguez-Justo, M. & Polychronis, A. (2013) Squamous cell carcinoma of pancreas: an unusual site of relapse from early-stage lung cancer: 12-month postsurgery. *BMJ Case Reports*, 2013, 2013.
Not in PICO
- Shiratori, K. (2006) [Early diagnosis and staging of pancreatic cancer]. [Review] [13 refs] [Japanese]. *Nippon Geka Gakkai Zasshi. Journal of Japan Surgical Society*, 107: 164-167.
Narrative review
- Silverstein, M. D., Richter, J. M., Podolsky, D. K. & Warshaw, A. L. (1984) Suspected pancreatic cancer presenting as pain or weight loss: Analysis of diagnostic strategies. *World Journal of Surgery*, 8: 839-845.
Not in PICO

- Skipworth, J. R., Shankar, A. & Pereira, S. P. (2002) Managing acute and chronic pancreatitis. [Review]. *Practitioner*, 254: 23-27.
Narrative review
- Smith, A., Miller, M., Groome, M. & Dillon, J. F. (2011) Predictors of neoplasia in patients presenting with obstructive jaundice. *Hepatology*, 54: 1423A-1424A.
Not in PICO
- Sohn, T. A., Yeo, C. J., Cameron, J. L., Iacobuzio-Donahue, C. A., Hruban, R. H. & Lillemoe, K. D. (2001) Intraductal papillary mucinous neoplasms of the pancreas: An increasingly recognized clinicopathologic entity. *Annals of Surgery*, 234: 313-321.
Not in PICO
- Spalding, D. & Williamson, R. C. N. (2007) Pancreatic cancer. *Medicine*, 35: 325-329.
Narrative review
- Spalding, D. & Williamson, R. C. N. (2011) Pancreatic cancer. *Medicine*, 39: 274-278.
Narrative review
- Speets, A. M., Kalmijn, S., Hoes, A. W., Van Der Graaf, Y. & Mali, W. P. T. (2006) Yield of abdominal ultrasound in patients with abdominal pain referred by general practitioners. *European Journal of General Practice*, 12: 135-137.
Not in PICO
- Stegmueller, K. W. & Fischer, R. (1980) Total duodenopancreatectomy in chronic relapsing pancreatitis. [German]. *Zeitschrift fur Gastroenterologie*, 18: 633-638.
Not in PICO
- Suda, K., Takase, M., Fukumura, Y. & Kashiwagi, S. (2007) Pathology of autoimmune pancreatitis and tumor-forming pancreatitis. *Journal of Gastroenterology*, 42: 22-27.
Narrative review
- Sueyoshi, R., Okazaki, T., Lane, G. J., Arakawa, A., Yao, T. & Yamataka, A. (2013) Multicystic adenomatoid pancreatic hamartoma in a child: Case report and literature review. *International Journal of Surgery Case Reports*, 4: 98-100.
Not in PICO
- Sultan, M., Jensen, M., Werlin, S. & Venkatasubramani, N. (2010) Chronic and recurrent acute pancreatitis in children. *Journal of Pediatric Gastroenterology and Nutrition*, 51: E105-E106.
Not in PICO
- Sultan, M., Werlin, S. & Venkatasubramani, N. (2012) Genetic prevalence and characteristics in children with recurrent pancreatitis. *Journal of Pediatric Gastroenterology and Nutrition*, 54: 645-650.
Not in PICO
- Szczeblowska, D. (2007) [Diagnostics and treatment of neuroendocrine tumors of the digestive tract in the light of the present standards]. [Review] [23 refs] [Polish]. *Polski Merkurusz Lekarski*, 22: 437-441.
Narrative review
- Tahrani, A. A., Sharma, S., Rangan, S. & Macleod, A. F. (2008) A patient with worsening mobility: A diagnostic challenge. *European Journal of Internal Medicine*, 19: 292-294.
Not in PICO
- Takagi, K., Takekoshi, T., Ohashi, K. & Maruyama, M. (1984) Early diagnosis of pancreatic carcinoma. *Asian Medical Journal*, 27: 100-122.
Narrative review
- Takayama, R., Naota, H., Imai, N., Fujiwara, M., Kaneko, M., Urade, S. & Kobayashi, K. (2009) An early stage anaplastic carcinoma of the pancreas with 5-year postoperative survival. *Pancreas*, 38: 1054.
Not in PICO
- Talamini, G., Bassi, C., Falconi, M., Sartori, N., Pasetto, M., Salvia, R., Di, F., V, Frulloni, L., Vaona, B., Bovo, P., Pederzoli, P. & Cavallini, G. (1999) Early detection of pancreatic cancer following the

- diagnosis of chronic pancreatitis. *Digestion*, 60: 554-561.
Not in PICO
- Talamini, G., Falconi, M., Bassi, C., Sartori, N., Salvia, R., Caldiron, E., Frulloni, L., Di, F., V, Vaona, B., Bovo, P., Vantini, I., Pederzoli, P. & Cavallini, G. (1999) Incidence of cancer in the course of chronic pancreatitis. *American Journal of Gastroenterology*, 94: 1253-1260.
Not in PICO
- Tamagno, G., De Carlo, E., Martini, C., Rubello, D., Fallo, F. & Sicolo, N. (2004) The early diagnosis of multiple endocrine neoplasia type 1 (MEN1): A case report. *Journal of Endocrinological Investigation*, 27: 878-882.
Not in PICO
- Tan, D. M. Y., Chuah, S. W., Lim, K. H., Low, S. C. A. & Ng, K. Y. (2009) Autoimmune pancreatitis in Singapore. Epidemiologic and clinical features. *Journal of Gastroenterology and Hepatology*, 24: A131.
Not in PICO
- Tanaka, K. & Kida, M. (2009) Role of endoscopy in screening of early pancreatic cancer and bile duct cancer. [Review] [7 refs]. *Digestive Endoscopy*, 21: Suppl-S100.
Narrative review
- Tanaka, M. (2005) Important clues to the diagnosis of pancreatic cancer. [Review] [30 refs]. *Roczniki Akademii Medycznej W Bialymstoku*, 50: 69-72.
Not in PICO
- Tanaka, M. (2008) Strategies for early diagnosis and treatment of pancreatic cancer. [Review] [33 refs]. *Nippon Shokakibyō Gakkai Zasshi - Japanese Journal of Gastroenterology*, 105: 26-30.
Narrative review
- Tapping, C. R., Byass, O. R. & Cast, J. E. (2012) Cytological sampling versus forceps biopsy during percutaneous transhepatic biliary drainage and analysis of factors predicting success. *Cardiovascular & Interventional Radiology*, 35: 883-889.
Not in PICO
- Tartaglia, A., Bianchini, S. & Vezzadini, P. (2003) Biochemical diagnosis of gastroenteropancreatic endocrine tumors. [Review] [22 refs]. *Minerva Medica*, 94: 1-7.
Narrative review
- Taylor, A., Stapley, S. & Hamilton, W. (2012) Jaundice in primary care: a cohort study of adults aged >45 years using electronic medical records. *Family Practice*, 29: 416-420.
Exclude: Not in PICO; patients with jaundice could have had a prior diagnosis of pancreatic cancer which could explain the jaundice; i.e., it didn't have to be jaundice first then diagnosis.
- Teixeira Da Silva, M. L. (1994) Carcinoma of the pancreas: Symptomatic treatment. [Portuguese]. *Arquivos de Gastroenterologia*, 31: 111-118.
Narrative review
- Tessler, D. A., Catanzaro, A., Velanovich, V., Havstad, S. & Goel, S. (2006) Predictors of cancer in patients with suspected pancreatic malignancy without a tissue diagnosis. *American Journal of Surgery*, 191: 191-197.
Not in PICO
- Thaler, J., Ay, C. & Pabinger, I. (2012) Venous thromboembolism in cancer patients - Risk scores and recent randomised controlled trials. *Thrombosis and Haemostasis*, 108: 1042-1048.
Narrative review
- Thompson, J. S., Murayama, K. M., Edney, J. A. & Rikkers, L. F. (573) Pancreaticoduodenectomy for suspected but unproven malignancy. *American Journal of Surgery*, 168: 571-573.
Not in PICO
- Tingstedt, B., Weitkamper, C. & Andersson, R. (2010) Early onset pancreatic cancer - Comparison against matched controls. *HPB*, 12: 227.
Not in PICO

- Toomey, D. P., Swan, N., Torreggiani, W. & Conlon, K. C. (2007) Autoimmune pancreatitis. [Review] [38 refs]. *British Journal of Surgery*, 94: 1067-1074.
Not in PICO
- Toosi, M. N. & Heathcote, J. (2004) Pancreatic Pseudotumor with Sclerosing Pancreato-Cholangitis: Is This a Systemic Disease? *American Journal of Gastroenterology*, 99: 377-382.
Not in PICO
- Torres Bermudez, J. R., Becerra Garcia, F. C., Abellan, R. B., Del Valle Ruiz, S. R., Riad, N., Martin, J. L. & Sanchez, D. I., V (2011) Laparoscopic resection of a solid - Pseudopapilar pancreatic tumor. *Surgical Endoscopy and Other Interventional Techniques*, 25: S181.
Not in PICO
- Trna, J., Dite, P., Hermanova, M. & Sevcikova, A. (2008) Diabetes mellitus in patients suffering from pancreatic cancer. [Czech]. *Ceska a Slovenska Gastroenterologie a Hepatologie*, 62: 69-73.
Not in PICO
- Truninger, K. (2000) Risk groups for pancreatic and bile duct carcinomas. [German]. *Schweizerische Rundschau fur Medizin Praxis = Revue suisse de medecine Praxis*, 89: 1299-1304.
Narrative review
- Tseng, J. F., Warshaw, A. L., Sahani, D. V., Lauwers, G. Y., Rattner, D. W. & Fernandez-del, C. C. (419) Serous cystadenoma of the pancreas: tumor growth rates and recommendations for treatment. *Annals of Surgery*, 242: 413-419.
Not in PICO
- Turna, H., Ozguroglu, M., Gursu, R. U., Karaaslan, S., Yildiz, O. & Yanmaz, M. T. (2008) Characteristics of thromboembolic complications in cancer patients. *Annals of Oncology*, 19: viii256-viii257.
Not in PICO
- Uchida, M., Shiga, N., Nakamura, T., Niina, Y., Fujimori, N., Yasuda, M., Oono, T., Igarashi, H., Aishima, S., Ishigami, K., Nakamura, M., Ito, T. & Takayanagi, R. (2010) A case of solid pseudopapillary neoplasm presenting with strong fluorodeoxyglucose uptake on positron emission tomography mimicking malignancy. *Pancreatology*, 10: 71.
Not in PICO
- Ulla Rocha, J. L., Alvarez Sanchez, M. V., Paz, E. J., Fernandez, S. E., Alvarez, A. C., Vazquez Sanluis, M. J., Ledo, B. L. & Vazquez, A. E. (2007) Evaluation of the bilio-pancreatic region using endoscopic ultrasonography in patients referred with and without abdominal pain and CA 19-9 serum level elevation. *Jop: Journal of the Pancreas [Electronic Resource]*, 8: 191-197.
Not in PICO for s&s or tests
- Urayama, S. & Madan, A. (2010) Pattern of pancreatic cancer patients among EUS-referral center: Glucose-impairment predating pancreatic cancer and staging characteristics. *Gastrointestinal Endoscopy*, 71: AB275.
Not in PICO
- Valsangkar, N. P., Thayer, S. P., Warshaw, A. L. & Fernandez-del, C. C. (2011) Serous cystadenoma of the pancreas: Experiences with 130 resected tumors at the MGH. *Pancreatology*, 11: 58.
Not in PICO
- van Leeuwen, D. J., Huibregtse, K., Reeders, J. A., Tytgat, G. N. & van der Heyde, M. N. (1989) [Guidelines in (suspected) pancreas head carcinoma]. [Review] [35 refs] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 133: 2499-2504.
Guideline
- Wagner, H. J. & Knyrim, K. (1993) Relief of malignant obstructive jaundice by endoscopic or percutaneous insertion of metal stents. *Bildgebung*, 60: 76-82.
Not in PICO
- Walker, A. J., Card, T. R., West, J., Crooks, C. & Grainge, M. J. (2013) Incidence of venous thromboembolism in patients with cancer-A cohort study using linked United Kingdom databases. *European Journal of Cancer*, 49: 1404-1413.
Not in PICO

- Walsh, R. M., Vogt, D. P., Henderson, J. M., Zuccaro, G., Vargo, J., Dumot, J., Herts, B., Biscotti, C. V. & Brown, N. (2005) Natural history of indeterminate pancreatic cysts. *Surgery*, 138: 665-671.
Not in PICO
- Wang, F., Gupta, S. & Holly, E. A. (2006) Diabetes mellitus and pancreatic cancer in a population-based case-control study in the San Francisco Bay Area, California. *Cancer Epidemiology, Biomarkers & Prevention*, 15: 1458-1463.
Not in PICO
- Weiser, M. A., Cabanillas, M., Vu, K., Tamm, E. P., Wallace, M. J., Escalante, C. P. & Bresalier, R. S. (2005) Diagnostic evaluation of patients with a high suspicion of malignancy: Comorbidities and clinical predictors of cancer. *American Journal of the Medical Sciences*, 330: 11-18.
Not in PICO
- Whitcomb, D. C. & Pogue-Geile, K. (2002) Pancreatitis as a risk for pancreatic cancer. *Gastroenterology Clinics of North America*, 31: 663-678.
Narrative review
- Whittemore, A. S., Paffenbarger, R. S., Jr., Anderson, K. & Halpern, J. (1983) Early precursors of pancreatic cancer in college men. *Journal of Chronic Diseases*, 36: 251-256.
Not in PICO
- Whittemore, A. S., Paffenbarger, R. S., Jr., Anderson, K. & Lee, J. E. (1985) Early precursors of site-specific cancers in college men and women. *Journal of the National Cancer Institute*, 74: 43-51.
Not in PICO
- Wu, G., Li, X. D., Shi, R., Liu, Y., Li, B. F. & Liu, Y. F. (2010) [Clinical analysis of autoimmune pancreatitis: a single center study of 14 consecutive cases]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]*, 48: 484-487.
Not in PICO
- Wu, J., Meng, X., Li, D. & Lu, H. (2002) Abnormal metabolism of glucose as clue for early diagnosing pancreatic cancer. [Chinese]. *Zhonghua yi xue za zhi*, 82: 312-314.
Not in PICO
- Yagi, A., Mizutani, S., Hoshino, A., Muraki, A., Aimoto, T., Suzuki, H. & Uchida, E. (1111) Clinicopathologic study on pancreatic groove carcinoma. *Pancreatology*, 12: 523-December.
Not in PICO
- Yalniz, M. & Pour, P. M. (2005) Diabetes mellitus: a risk factor for pancreatic cancer?. [Review] [79 refs]. *Langenbecks Archives of Surgery*, 390: 66-72.
Narrative review
- Yamaguchi, K. & Tanaka, M. (317) Groove pancreatitis masquerading as pancreatic carcinoma. *American Journal of Surgery*, 163: 312-316.
Not in PICO
- Yamaguchi, K., Ogawa, Y., Yokohata, K., Konomi, H., Nakamura, M., Nagata, S. & Tanaka, M. (2005) Recent advances in diagnosis of pancreatic cancer. [Japanese]. *Gan to Kagaku Ryoho, Cancer*: 612-616.
Narrative review
- Yamazaki, M., Suzuki, S., Kosugi, S., Okamoto, T., Uchino, S., Miya, A., Imai, T., Kaji, H., Komoto, I., Miura, D., Yamada, M., Uruno, T., Horiuchi, K., Sato, A., Miyauchi, A., Imamura, M. & Sakurai, A. (2012) Delay in the diagnosis of multiple endocrine neoplasia type 1: typical symptoms are frequently overlooked. *Endocrine Journal*, 59: 797-807.
Not in PICO
- Yu, Y. P., Jiang, H. T., Yao, Z., Xia, Q. R., Hong, F. M., Zeng, H. & Li, S. (2013) [Feasibility and safety of CT-guided percutaneous needle biopsy and subsequent iodine-125 seed interstitial implantation for pancreatic cancer]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 35: 608-612.
Not in PICO

Yuan, Y. & Li, W. (2010) Emphasis on the study of intrinsic relationship between diabetes mellitus and pancreatic cancer for lowering the incidence of pancreatic cancer. [Chinese]. *Chinese Journal of Gastroenterology*, 15: 65-67.

Narrative review

Zdanyte, E., Strupas, K., Bubnys, A. & Stratilatovas, E. (2004) [Difficulties of differential diagnosis of pancreatic pseudocysts and cystic neoplasms]. [Lithuanian]. *Medicina (Kaunas, Lithuania)*, 40: 1180-1188.

Not in PICO

Zhang, W.-X., Shi, H. & Xu, J.-M. (2011) Survival and prognosis of patients with pancreatic carcinoma: An analysis of 156 cases. *World Chinese Journal of Digestology*, 19: 3526-3531.

Not in PICO

Review question:

Which investigations of symptoms of suspected pancreatic cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

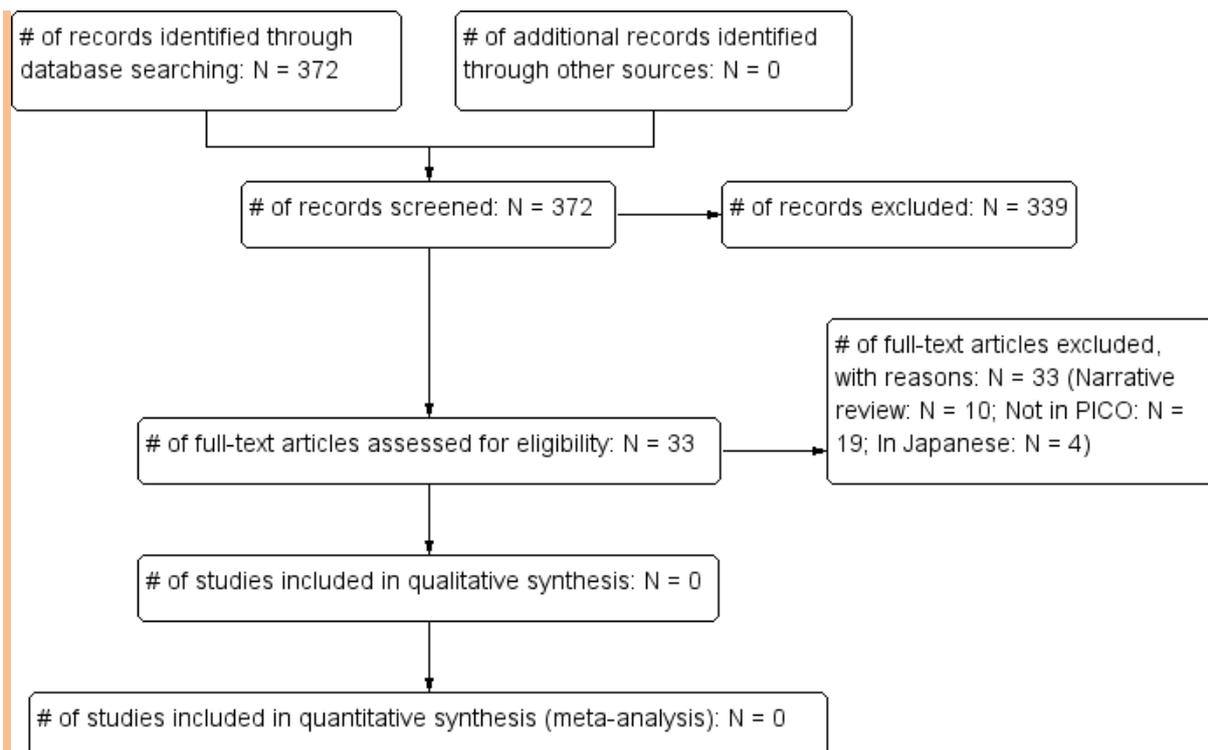
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	951	257	14/06/2013
<i>Premedline</i>	1980-2013	81	3	14/06/2013
<i>Embase</i>	1980-2013	1407	132	14/06/2013
<i>Cochrane Library</i>	1980-2013	67	12	14/06/2013
<i>Psychinfo</i>	1980-2013	1	0	14/06/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	42	10	14/06/2013

Total References retrieved (after de-duplication): 339

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	6/2013-20/08/2014	42	12	20/08/2014
<i>Premedline</i>	6/2013-20/08/2014	93	16	20/08/2014
<i>Embase</i>	6/2013-20/08/2014	24	6	20/08/2014
<i>Cochrane Library</i>	6/2013-20/08/2014	9	1	20/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	6/2013-20/08/2014	4	2	20/08/2014

Total References retrieved (after de-duplication): 33



Study results

No evidence was identified pertaining to the diagnostic accuracy of CT scan, ultrasound, MRI, CEA, Beta hCG or tumour markers CA19-9 and CA72-4 in patients with suspected pancreatic cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Abe, M. (1984) Early diagnosis of pancreatic cancer. [Japanese]. *Nihon Naika Gakkai zasshi*, The: 740-744.

In Japanese, not enough information can be extracted, but I think it is a narrative review

Adimoolam, V., Sanchez, M. J., Siddiqui, U. D., Yu, S., Dzuira, J. D., Padda, M. S. & Aslanian, H. R. (2011) Endoscopic ultrasound identifies synchronous pancreas cystic lesions not seen on initial cross-sectional imaging. *Pancreas*, 40: 1070-1072.

Not in PICO

Agarwal, B., Abu-Hamda, E., Molke, K. L., Correa, A. M. & Ho, L. (2004) Endoscopic ultrasound-guided fine needle aspiration and multidetector spiral CT in the diagnosis of pancreatic cancer. *American Journal of Gastroenterology*, 99: 844-850.

Not in PICO

Aggarwal, G., Rabe, K. G., Petersen, G. M. & Chari, S. T. (2012) New-onset diabetes in pancreatic cancer: A study in the primary care setting. *Pancreatology*, 12: 156-161.

Not in PICO

Ahn, J. & Lee, J. K. (2013) [New-onset diabetes as an early sign of pancreatic cancer]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwhagi Hakhoe Chi*, 62: 263-266.

Narrative review

- Ahn, S. S., Kim, M. J., Choi, J. Y., Hong, H. S., Chung, Y. E. & Lim, J. S. (2009) Indicative findings of pancreatic cancer in prediagnostic CT. *European Radiology*, 19: 2448-2455.
Not in PICO
- Akisik, M. F., Jennings, S. G., Aisen, A. M., Sherman, S., Cote, G. A., Sandrasegaran, K. & Tirkes, T. (2013) MRCP in patient care: a prospective survey of gastroenterologists. *AJR.American Journal of Roentgenology*, 201: 573-577.
Not in PICO
- Al-Haddad, M., DeWitt, J., Sherman, S., Schmidt, C. M., LeBlanc, J. K., McHenry, L., Cote, G., El Chafic, A. H., Luz, L., Stuart, J. S., Johnson, C. S., Klochan, C. & Imperiale, T. F. (2014) Performance characteristics of molecular (DNA) analysis for the diagnosis of mucinous pancreatic cysts. *Gastrointestinal Endoscopy*, 79: 79-87.
Not in PICO
- Amin, S., Dimaio, C. J. & Kim, M. K. (2013) Advanced EUS imaging for early detection of pancreatic cancer. *Gastrointestinal Endoscopy Clinics of North America*, 23: 607-623.
Narrative review
- Andersen, H. B., Effersoe, H., Tjalve, E. & Burcharth, F. (1993) CT for assessment of pancreatic and periampullary cancer. *Acta Radiologica*, 34: 569-572.
Not in PICO
- Anderson, M. A., Sheth, N. M., Scheiman, J., Plonka, C. M., Zhu, B., Elta, G. H., Kwon, R. S., Piraka, C. R., Wamsteker, E.-J. & Elmunzer, B. J. (2011) Elevated serum carcinoembryonic antigen 19-9 (CA 19-9) levels are highly specific for malignancy in patients referred for endoscopic ultrasound (EUS) with suspected pancreatic cancer but without a tissue diagnosis. *Gastroenterology*, 140: S714.
Not in PICO
- Andersson, M., Kostic, S., Johansson, M., Lundell, L., Asztely, M. & Hellstrom, M. (2005) MRI combined with MR cholangiopancreatography versus helical CT in the evaluation of patients with suspected periampullary tumors: a prospective comparative study. *Acta Radiologica*, 46: 16-27.
Not in PICO
- Arbul, M., Karakus, F., Alper, E., Kandemir, A., Celik, M., Karakus, V., Yucel, K. & Unsal, B. (2012) Comparison of multidetector CT and endoscopic ultrasonography in malignant pancreatic mass lesions. *Hepato-Gastroenterology*, 59: 1599-1603.
Not in PICO
- Ares, D. M., Aguirre, P. A. A., Barrenechea, I. M. G., Gomez, L. C. & Peral, A. P. (2008) Usefulness of ultrasonography in diagnosing patients suspect for digestive tract neoplasms. *Revista Espanola de Enfermedades Digestivas*, 100: 545-551.
Not in PICO
- Ariyama, J., Sumida, M., Shimaguchi, S. & Shirakabe, H. (1983) Integrated approach to the diagnosis of pancreatic carcinoma. *Radiation Medicine*, 1: 46-51.
Not in PICO
- Ariyama, J. (1992) Diagnosis of early-stage pancreatic neoplasms. [Japanese]. *Nihon Naika Gakkai zasshi*, The: 334-337.
In Japanese, not enough information can be extracted, but I think it is Narrative review
- Atef, E., El, N. A., El, H. E., El, H. M., Hamdy, E. & El-Geidie, A. (2013) Pancreatic cystic neoplasms: predictors of malignant behavior and management. *Saudi Journal of Gastroenterology*, 19: 45-53.
Not in PICO
- Audisio, R. A., Veronesi, P., Maisonneuve, P., Chiappa, A., Andreoni, B., Bombardieri, E. & Geraghty, J. G. (1996) Clinical relevance of serological markers in the detection and follow-up of pancreatic adenocarcinoma. [Review] [171 refs]. *Surgical Oncology*, 5: 49-63.
Narrative review

- Augustyn, M. & Serwin, D. (2007) [Credibility of diagnostic methods in pathology of pancreas]. [Polish]. *Polski Merkurusz Lekarski*, 22: 388-390.
Not in PICO
- Ba-Ssalamah, A. & Schima, W. (2003) [Imaging of endocrine tumours of the pancreas]. [Review] [38 refs] [German]. *Wiener Klinische Wochenschrift*, 115: Suppl-5.
Narrative review
- Baba, T., Yamaguchi, T., Ishihara, T., Kobayashi, A., Oshima, T., Sakaue, N., Kato, K., Ebara, M. & Saisho, H. (2004) Distinguishing benign from malignant intraductal papillary mucinous tumors of the pancreas by imaging techniques. *Pancreas*, 29: 212-217.
Not in PICO
- Barber, T. W., Kalf, V., Cherk, M. H., Yap, K. S. K., Evans, P. & Kelly, M. J. (2009) 18F-FDG PET/CT (PET/CT) influences management in patients with known or suspected pancreatic cancer. *Internal Medicine Journal*, 39: A114.
Not in PICO
- Baron, P. L., Kay, C. & Hoffman, B. (1999) Pancreatic imaging. [Review] [67 refs]. *Surgical Oncology Clinics of North America*, 8: 35-58.
Narrative review
- Benini, L., Cavallini, G., Zordan, D., Rizzotti, P., Rigo, L., Brocco, G., Perobelli, L., Zanchetta, M., Pederzoli, P. & Scuro, L. A. (1988) A clinical evaluation of monoclonal (CA19-9, CA50, CA12-5) and polyclonal (CEA, TPA) antibody-defined antigens for the diagnosis of pancreatic cancer. *Pancreas*, 3: 61-66.
Not in PICO
- Benzaken, T., Novellas, S., Baudin, G., Maillard, M., Iannessi, A., Gelsi, E. & Chevallerier, P. (2009) Imaging-guided core biopsy of pancreatic masses: Results and complications. *Cardiovascular and Interventional Radiology*, 32: 382-383.
Not in PICO
- Berberat, P., Friess, H., Kashiwagi, M., Beger, H. G. & Buchler, M. W. (1999) Diagnosis and staging of pancreatic cancer by positron emission tomography. [Review] [54 refs]. *World Journal of Surgery*, 23: 882-887.
Narrative review
- Bernardino, M. E. & Barnes, P. A. (1982) Imaging the pancreatic neoplasm. *Cancer*, 50: Suppl-8.
Narrative review
- Bersch, V. P., da Silva, V. D., Osvaldt, A. B., da Costa, M. S., Rohde, L. & Mossmann, D. (2003) Digital karyometry in pancreatic adenocarcinoma. *Analytical & Quantitative Cytology & Histology*, 25: 108-114.
Not in PICO
- Bipat, S., Phoa, S. S., van Delden, O. M., Bossuyt, P. M., Gouma, D. J., Lameris, J. S. & Stoker, J. (2005) Ultrasonography, computed tomography and magnetic resonance imaging for diagnosis and determining resectability of pancreatic adenocarcinoma: a meta-analysis. *Journal of Computer Assisted Tomography*, 29: 438-445.
Not in PICO
- Birchard, K. R., Semelka, R. C., Hyslop, W. B., Brown, A., Armao, D., Firat, Z. & Vaidean, G. (2005) Suspected pancreatic cancer: evaluation by dynamic gadolinium-enhanced 3D gradient-echo MRI. *AJR.American Journal of Roentgenology*, 185: 700-703.
Not in PICO
- Bohmig, M. & Rosewicz, S. (2004) [Pancreatic carcinoma]. [Review] [49 refs] [German]. *Zeitschrift fur Gastroenterologie*, 42: 261-268.
Narrative review
- Bohuslavizki, K. H., Mester, J., Brenner, W., Buchert, R., Klutmann, S., Clausen, M. & Henze, E. (1997) Value of scintigraphic imaging in the detection of pancreatic tumors - The role of FDG-PET.

- Radiology and Oncology*, 31: 21-26.
Narrative review
- Boll, D. T. & Merkle, E. M. (2003) Differentiating a chronic hyperplastic mass from pancreatic cancer: a challenge remaining in multidetector CT of the pancreas. [Review] [56 refs]. *European Radiology*, 13: Suppl-9.
Narrative review
- Bottger, T. C. & Junginger, T. (162) Treatment of tumors of the pancreatic head with suspected but unproved malignancy: is a nihilistic approach justified? *World Journal of Surgery*, 23: 158-162.
Not in PICO
- Brand, B., Pfaff, T., Binmoeller, K. F., Sriram, P. V., Fritscher-Ravens, A., Knofel, W. T., Jackle, S. & Soehendra, N. (2000) Endoscopic ultrasound for differential diagnosis of focal pancreatic lesions, confirmed by surgery. *Scandinavian Journal of Gastroenterology*, 35: 1221-1228.
Not in PICO
- Brand, R. (2001) The diagnosis of pancreatic cancer. [Review] [119 refs]. *Cancer Journal*, 7: 287-297.
Narrative review
- Brugge, W. R. (2001) Role of endoscopic ultrasound in the diagnosis of cystic lesions of the pancreas. [Review] [17 refs]. *Pancreatology*, 1: 637-640.
Narrative review
- Brugge, W. R. (2006) Advances in the endoscopic management of patients with pancreatic and biliary malignancies. [Review] [46 refs]. *Southern Medical Journal*, 99: 1358-1366.
Narrative review
- Bruno, M., Carucci, P., Repici, A., Pellicano, R., Mezzabotta, L., Goss, M., Fagoonee, S., Allegranza, P., Reggio, D., Rizzetto, M. & De, A. C. (2011) Negative predictive value of endoscopic ultrasound in patients referred for fine-needle aspiration. *Panminerva Medica*, 53: 179-183.
Not in PICO
- Buscaglia, J. M., Shin, E. J., Giday, S. A., Kapoor, S., Dunbar, K. B., Eloubeidi, M. A., Canto, M. I. & Jagannath, S. B. (820) Awareness of guidelines and trends in the management of suspected pancreatic cystic neoplasms: survey results among general gastroenterologists and EUS specialists. *Gastrointestinal Endoscopy*, 69: 813-820.
Not in PICO
- Buscail, L., Pages, P., Bouisson, M., Vaysse, N., Pradayrol, L. & Escourrou, J. (1999) Early markers in pancreatic cancer. [French]. *Hepato-Gastro*, 6: 85-91.
Narrative review
- Buscail, L. & Bournet, B. (2007) Risk factors of pancreatic carcinoma. [French]. *Presse Medicale*, 36: 1244-1248.
Narrative review
- Caglar, E., Senturk, H., Atasoy, D., Sisman, G., Canbakan, B. I. & Tuncer, M. (2013) The role of EUS and EUS-FNA in the management of pancreatic masses: five-year experience. *Hepato-Gastroenterology*, 60: 896-899.
Not in PICO
- Caletti, G. & Fusaroli, P. (2001) Endoscopic ultrasonography. [Review] [49 refs]. *Endoscopy*, 33: 158-166.
Narrative review
- Camera, L., Bresciani, M., Soscia, E., Percopo, V., Mainenti, P. P. & Salvatore, M. (2001) [Morphological imaging of gastroenteropancreatic neuroendocrine tumours]. [Review] [23 refs] [Italian]. *Minerva Endocrinologica*, 26: 123-128.
Narrative review
- Camus, M., Trouilloud, I., Villacis, A. L., Mangialavori, L., Duchmann, J. C., Gaudric, M., Roseau, G., Terris, B., Mitry, E., Chaussade, S. & Prat, F. (2012) Effectiveness of combined endoscopic ultrasound-guided fine-needle aspiration biopsy and stenting in patients with suspected

- pancreatic cancer. *European Journal of Gastroenterology & Hepatology*, 24: 1281-1287.
Not in PICO
- Canzonieri, V. (2007) [EUS-FNA cytology of pancreatic exocrine tumors. Comparison of experiences with pathological diagnosis]. [Review] [13 refs] [Italian]. *Minerva Medica*, 98: 367-372.
Narrative review
- Cappelli, G., Paladini, S. & D'Agata, A. (1999) [Tumor markers in the diagnosis of pancreatic cancer]. [Review] [9 refs] [Italian]. *Tumori*, 85: Suppl-21.
Narrative review
- Cardone, G., Di, G. M., Messina, A., Chichiarelli, A., Corsetti, A., Di, C. E., Lupattelli, L. & Passariello, R. (1995) [Carcinoma of the pancreas. Typical and atypical aspects using midfield-strength magnetic resonance]. [Italian]. *Radiologia Medica*, 90: 740-746.
Not in PICO
- Carlucci, M., Zerbi, A., Parolini, D., Sironi, S., Vanzulli, A., Staudacher, C., Faravelli, A., Garancini, P., Del, M. A. & Di, C., V (1989) CT-guided pancreatic percutaneous fine-needle biopsy in differential diagnosis between pancreatic cancer and chronic pancreatitis. *HPB Surgery*, 1: 309-317.
Not in PICO
- Cassol, M., Rotunno, S., Bianchi, A., La, S. F., Armiento, A. & Sagrafoli, C. (2012) A Kappa light chain deposition disease (LCDD). *Italian Journal of Medicine*, 6: 28.
Not in PICO
- Chan, C.-C., Tang, C.-K., Lai, L. S. W. & Cheung, C.-C. (2014) Is endoscopic ultrasound (EUS) a powerful tool in diagnosing patients with suspected pancreatic tumour. *HPB*, 16: 648.
Not in PICO
- Chari, S. T., Klee, G. G., Miller, L. J., Raimondo, M. & DiMagno, E. P. (2001) Islet amyloid polypeptide is not a satisfactory marker for detecting pancreatic cancer. *Gastroenterology*, 121: 640-645.
Not in PICO
- Chen, J., Yang, R., Lu, Y., Xia, Y. & Zhou, H. (2012) Diagnostic accuracy of endoscopic ultrasound-guided fine-needle aspiration for solid pancreatic lesion: a systematic review. [Review]. *Journal of Cancer Research & Clinical Oncology*, 138: 1433-1441.
Not in PICO
- Chen, V. K., Arguedas, M. R., Kilgore, M. L. & Eloubeidi, M. A. (2004) A cost-minimization analysis of alternative strategies in diagnosing pancreatic cancer. *American Journal of Gastroenterology*, 99: 2223-2234.
Not in PICO
- Chen, Y. K. (2007) Pancreatoscopy: present and future role. [Review] [67 refs]. *Current Gastroenterology Reports*, 9: 136-143.
Narrative review
- Chiou, Y. Y., Chiang, J. H., Hwang, J. I., Yen, C. H., Tsay, S. H. & Chang, C. Y. (2004) Acinar cell carcinoma of the pancreas: clinical and computed tomography manifestations. *Journal of Computer Assisted Tomography*, 28: 180-186.
Not in PICO
- Choi, E. R., Jang, T. H., Chung, Y. H., Jang, K.-T., Park, S.-M., Lee, J. K., Lee, K. T. & Lee, K. H. (2011) A prospective comparison of liquid-based cytology and traditional smear cytology in pancreatic endoscopic ultrasound-guided fine needle aspiration. *Acta Cytologica*, 55: 401-407.
Not in PICO
- Choi, J. H., Kim, M.-H., Seo, D. W., Lee, S. S., Park, D. H. & Lee, S. K. (1111) Clinical features and risk factors of pancreatic cancer in chronic pancreatitis. *Pancreatology*, 13: S38-August.
Not in PICO
- Chung, E. M., Travis, M. D. & Conran, R. M. (2006) Pancreatic tumors in children: radiologic-pathologic correlation. [Review] [115 refs]. *Radiographics*, 26: 1211-1238.
Narrative review

- Cieslak, K. P., van Santvoort, H. C., Vleggaar, F. P., van Leeuwen, M. S., ten Kate, F. J., Besselink, M. G. & Molenaar, I. Q. (2014) - The role of routine preoperative EUS when performed after contrast enhanced CT in the diagnostic work-up in patients suspected of pancreatic or periampullary cancer. - *Pancreatology*, 14: 125-130.
Not in PICO
- Cleveland, P., Gill, K. R. S., Coe, S. G., Woodward, T. A., Raimondo, M., Jamil, L., Gross, S. A., Heckman, M. G., Crook, J. E. & Wallace, M. B. (2010) An evaluation of risk factors for inadequate cytology in EUS-guided FNA of pancreatic tumors and lymph nodes. *Gastrointestinal Endoscopy*, 71: 1194-1199.
Not in PICO
- Clores, M. J., Thosani, A. & Buscaglia, J. M. (2014) - Multidisciplinary diagnostic and therapeutic approaches to pancreatic cystic lesions. [Review]. - *Journal of multidisciplinary healthcare*, 7: 81-91.
Narrative review
- Costamagna, G., Gabrielli, A., Mutignani, M., Perri, V., Buononato, M. & Crucitti, F. (1993) Endoscopic diagnosis and treatment of malignant biliary strictures: review of 505 patients. *Acta Gastroenterologica Belgica*, 56: 201-206.
Not in PICO
- Cotton, P. B., Denyer, M. E. & Kreel, L. (1980) Comparative clinical impact of endoscopic pancreatography, grey-scale ultrasonography, and computed tomography (EMI scanning) in pancreatic disease. A preliminary report. [French]. *Acta Endoscopica*, 10: 47.
Not in PICO
- Craanen, M. E., Van, W. J. H., Van Der Peet, D. L., Loffeld, R. J. L. F., Cuesta, M. A. & Mulder, C. J. J. (2006) Endoscopic ultrasound in patients with obstructive jaundice and inconclusive ultrasound and computer tomography findings. *European Journal of Gastroenterology and Hepatology*, 18: 1289-1292.
Not in PICO
- da Silva, J. A., Machado Igreja, A. C. S., Freitas, A. F., Carvalho Costa, I. M., Mesquita, K. C., Naves Lucas, I. C. R., de Oliveira, S. M. & Campbell, I. T. (2013) Paraneoplastic cutaneous manifestations: Concepts and updates. *Anais Brasileiros de Dermatologia*, 88: 9-22.
Narrative review
- Das, D. K., Bhambhani, S., Kumar, N., Chachra, K. L., Prakash, S., Gupta, R. K. & Tripathi, R. P. (1995) Ultrasound guided percutaneous fine needle aspiration cytology of pancreas: a review of 61 cases. *Tropical Gastroenterology*, 16: 101-109.
Not in PICO
- De Gaetano, A. M., Brizi, M. G., Barbaro, B. & De, F. A. (1995) Carcinoma of the pancreatic head area. Diagnostic imaging: ultrasound. [Review] [38 refs]. *Rays*, 20: 237-248.
Narrative review
- De La Cruz, M. S., Young, A. P. & Ruffin, M. T. (2014) - Diagnosis and management of pancreatic cancer. - *American Family Physician*, 89: 626-632.
Narrative review
- De, A. C., Repici, A., Carucci, P., Bruno, M., Goss, M., Mezzabotta, L., Pellicano, R., Saracco, G. & Rizzetto, M. (2007) Pancreatic cancer imaging: the new role of endoscopic ultrasound. *Jop: Journal of the Pancreas [Electronic Resource]*, 8: Suppl-97.
Narrative review
- Deerenberg, E. B., Poley, J. W., Hermans, J. J., Ganesh, S., Van Der Harst, E. & van Eijck, C. H. (2011) Role of endoscopic ultrasonography in patients suspected of pancreatic cancer with negative helical MDCT scan. *Digestive Surgery*, 28: 398-403.
Not in PICO
- Del, C. M., Verbeke, C., Salvia, R., Kloppel, G., Werner, J., McKay, C., Friess, H., Manfredi, R., Van, C. E., Lohr, M., Segersvard, R. & European Study Group on Cystic Tumours of the Pancreas (2013)

- European experts consensus statement on cystic tumours of the pancreas. *Digestive & Liver Disease*, 45: 703-711.
Guideline/narrative review
- Delbeke, D., Rose, D. M., Chapman, W. C., Pinson, C. W., Wright, J. K., Beauchamp, R. D., Shyr, Y. & Leach, S. D. (1999) Optimal interpretation of FDG PET in the diagnosis, staging and management of pancreatic carcinoma. *Journal of Nuclear Medicine*, 40: 1784-1791.
Not in PICO
- Delbeke, D. & Pinson, C. W. (2004) Pancreatic tumors: role of imaging in the diagnosis, staging, and treatment. [Review] [51 refs]. *Journal of Hepato-Biliary-Pancreatic Surgery*, 11: 4-10.
Narrative review
- DelMaschio, A., Vanzulli, A., Sironi, S., Castrucci, M., Mellone, R., Staudacher, C., Carlucci, M., Zerbi, A., Parolini, D. & Faravelli, A. (1991) Pancreatic cancer versus chronic pancreatitis: diagnosis with CA 19-9 assessment, US, CT, and CT-guided fine-needle biopsy. *Radiology*, 178: 95-99.
Not in PICO
- DeWitt, J., Alsatie, M., LeBlanc, J., McHenry, L. & Sherman, S. (2007) Endoscopic ultrasound-guided fine-needle aspiration of left adrenal gland masses. *Endoscopy*, 39: 65-71.
Not in PICO
- DeWitt, J. & Kahaleh, M. (2008) The role of endoscopy in the evaluation of suspected pancreatic malignancy. *ASGE Clinical Update*, 16: 1-4.
Narrative review
- Dim, D. C., Jiang, F., Qiu, Q., Li, T., Darwin, P., Rodgers, W. H. & Peng, H. Q. (2014) - The usefulness of S100P, mesothelin, fascin, prostate stem cell antigen, and 14-3-3 sigma in diagnosing pancreatic adenocarcinoma in cytological specimens obtained by endoscopic ultrasound guided fine-needle aspiration. - *Diagnostic Cytopathology*, 42: 193-199.
Not in PICO
- Dina, R., Tran-Dang, M. A., Mauri, F., Gudi, M., Cohen, P., Ahmad, R., Batav, L., Vlavianos, P. & Spalding, D. (2013) Pancreatobiliary cytology in the multidisciplinary setting. *Cytopathology*, 24: 150-158.
Not in PICO
- Dina, R., Tran-Dang, M. A., Mauri, F., Gudi, M., Cohen, P., Ahmad, R., Batav, L., Vlavianos, P. & Spalding, D. (2013) Pancreatobiliary cytology in the multidisciplinary setting. [Review]. *Cytopathology*, 24: 150-158.
Narrative review
- Draganov, P. V., Nicaud, M., Hou, W., Collins, D., Wagh, M. S. & Chauhan, S. (2010) The utility of repeat endoscopic ultrasound-guided fine needle aspiration for suspected pancreatic cancer. *Gastroenterology Research and Practice*.
Not in PICO
- Ducceschi, M., Pusceddu, S. & Platania, M. (2010) 7. False positives and false negatives in neuroendocrine tumors diagnosis: Clinical reports. *Tumori*, 96: 827-832.
Narrative review
- Duchmann, J. C. & Joly, J. P. (1996) Ambulatory ultrasound-guided puncture in abdominal tumoral pathology. Study of 131 cases. [French]. *Gastroenterologie Clinique et Biologique*, 20: 258-262.
Not in PICO
- Duda, S. H., Huppert, P. E. & Claussen, C. D. (1995) Radiological diagnostic and interventional therapy of neuroendocrine tumors in the pancreas and intestinal tract. [German]. *Chirurgische Gastroenterologie*, 11: 6-11.
Narrative review
- Early, D. S., Janec, E., Azar, R., Ristvedt, S., Gao, F. & Edmundowicz, S. A. (2006) Patient preference and recall of results of EUS-guided FNA. *Gastrointestinal Endoscopy*, 64: 735-739.
Not in PICO

- El-Mesallamy, H. O., Hamdy, N. M., Zaghloul, A. S. & Sallam, A. M. (2013) Clinical value of circulating lipocalins and insulin-like growth factor axis in pancreatic cancer diagnosis. *Pancreas*, 42: 149-154.
Not in PICO
- Ell, C. (1993) [Suspected pancreatic cancer--diagnostic procedure]. [German]. *Fortschritte der Medizin*, 111: 242-244.
Narrative review
- Elli, M., Piazza, E., Franzone, P. C., Isabella, L., Poliziani, D. & Taschieri, A. M. (2003) Considerations on early diagnosis of carcinoma of the pancreas. *Hepato-Gastroenterology*, 50: 2205-2207.
Not in PICO
- Eloubeidi, M. A., Chen, V. K., Eltoun, I. A., Jhala, D., Chhieng, D. C., Jhala, N., Vickers, S. M. & Wilcox, C. M. (2003) Endoscopic ultrasound-guided fine needle aspiration biopsy of patients with suspected pancreatic cancer: diagnostic accuracy and acute and 30-day complications. *American Journal of Gastroenterology*, 98: 2663-2668.
Not in PICO
- Eloubeidi, M. A., Jhala, D., Chhieng, D. C., Chen, V. K., Eltoun, I., Vickers, S., Mel, W. C. & Jhala, N. (2003) Yield of endoscopic ultrasound-guided fine-needle aspiration biopsy in patients with suspected pancreatic carcinoma. *Cancer*, 99: 285-292.
Not in PICO
- Eloubeidi, M. A., Tamhane, A., Varadarajulu, S. & Wilcox, C. M. (2006) Frequency of major complications after EUS-guided FNA of solid pancreatic masses: a prospective evaluation. *Gastrointestinal Endoscopy*, 63: 622-629.
Not in PICO
- Eloubeidi, M. A., Varadarajulu, S., Desai, S., Shirley, R., Heslin, M. J., Mehra, M., Arnoletti, J. P., Eltoun, I., Wilcox, C. M. & Vickers, S. M. (2007) A prospective evaluation of an algorithm incorporating routine preoperative endoscopic ultrasound-guided fine needle aspiration in suspected pancreatic cancer. *Journal of Gastrointestinal Surgery*, 11: 813-819.
Not in PICO
- Eloubeidi, M. A., Varadarajulu, S., Desai, S. & Wilcox, C. M. (2008) Value of repeat endoscopic ultrasound-guided fine needle aspiration for suspected pancreatic cancer. *Journal of Gastroenterology & Hepatology*, 23: 567-570.
Not in PICO
- Eloubeidi, M. A., Luz, L. P., Tamhane, A., Khan, M. & Buxbaum, J. L. (2013) Ratio of pancreatic duct caliber to width of pancreatic gland by endosonography is predictive of pancreatic cancer. *Pancreas*, 42: 670-679.
Not in PICO
- Ergul, N., Gundogan, C., Tozlu, M., Toprak, H., Kadioglu, H., Aydin, M. & Cermik, T. F. (2014) - Role of (18)F-fluorodeoxyglucose positron emission tomography/computed tomography in diagnosis and management of pancreatic cancer; comparison with multidetector row computed tomography, magnetic resonance imaging and endoscopic ultrasonography. - *Revista Espanola de Medicina Nuclear e Imagen Molecular*, 33: 159-164.
Not in PICO
- Fabris, C., Del, F. G., Basso, D., Piccoli, A., Meggiato, T., Angonese, C., Plebani, M., Leandro, G., Burlin, A. & Naccarato, R. (1988) Serum markers and clinical data in diagnosing pancreatic cancer: A contrastive approach. *American Journal of Gastroenterology*, 83: 549-553.
Not in PICO
- Faigel, D. O., Ginsberg, G. G., Bentz, J. S., Gupta, P. K., Smith, D. B. & Kochman, M. L. (1997) Endoscopic ultrasound-guided real-time fine-needle aspiration biopsy of the pancreas in cancer patients with pancreatic lesions. *Journal of Clinical Oncology*, 15: 1439-1443.
Not in PICO

- Farini, R., Nitti, D., Del, F. G., Rossi, C. R., Costantin, G., Rebuffi, A., Farini, A., Piccoli, A., Matarazzo, R., Lise, M. & Naccarato, R. (1980) CEA concentration and cytology in duodenal fluid collected during the Secretin-Pancreozymin test. Attempt at an early diagnosis of pancreatic carcinoma by means of simple procedure. *Hepato-Gastroenterology*, 27: 213-216.
Not in PICO
- Farrell, J. J. & Fernandez-del Castillo, C. (2013) Pancreatic Cystic Neoplasms: Management and Unanswered Questions. *Gastroenterology*, 144: 1303-1315.
Narrative review
- Ferrone, C. R., Correa-Gallego, C., Warshaw, A. L., Brugge, W. R., Forcione, D. G., Thayer, S. P. & Fernandez-del, C. C. (2009) Current trends in pancreatic cystic neoplasms. *Archives of Surgery*, 144: 448-454.
Not in PICO
- Fineberg, H. V. & Wittenberg, J. (1980) Evaluation of computed tomography in pancreatic cancer. *Bulletin du Cancer*, 67: 390-394.
Not in PICO
- Fischer, L., Mehrabi, A. & Buchler, M. W. (2011) [Neuroendocrine tumors of the duodenum and pancreas. Surgical strategy]. [Review] [German]. *Chirurg*, 82: 583-590.
Narrative review
- Fletcher, J. G., Wiersema, M. J., Farrell, M. A., Fidler, J. L., Burgart, L. J., Koyama, T., Johnson, C. D., Stephens, D. H., Ward, E. M. & Harmsen, W. S. (2003) Pancreatic malignancy: value of arterial, pancreatic, and hepatic phase imaging with multi-detector row CT. *Radiology*, 229: 81-90.
Not in PICO
- Foley, W. D., Stewart, E. T., Lawson, T. L., Geenan, J., Loguidice, J., Maher, L. & Unger, G. F. (1980) Computed tomography, ultrasonography, and endoscopic retrograde cholangiopancreatography in the diagnosis of pancreatic disease: a comparative study. *Gastrointestinal Radiology*, 5: 29-35.
Not in PICO
- Forsmark, C. E., Lambiase, L. & Vogel, S. B. (1994) Diagnosis of pancreatic cancer and prediction of unresectability using the tumor-associated antigen CA19-9. *Pancreas*, 9: 731-734.
Not in PICO
- Foutch, P. G. (1994) A diagnostic approach to pancreatic cancer. [Review] [41 refs]. *Digestive Diseases*, 12: 129-138.
Narrative review
- Franke, C., Klapdor, R., Meyerhoff, K. & Schauman, M. (1999) 18-FDG positron emission tomography of the pancreas: Diagnostic benefit in the follow-up of pancreatic carcinoma. *Anticancer Research*, 19: 2437-2442.
Not in PICO
- Frebourg, T., Bercoff, E., Manchon, N., Senant, J., Basuyau, J. P., Breton, P., Janvresse, A., Brunelle, P. & Bourreille, J. (1988) The evaluation of CA 19-9 antigen level in the early detection of pancreatic cancer. A prospective study of 866 patients. *Cancer*, 62: 2287-2290.
Not in PICO
- Fritscher-Ravens, A., Topalidis, T. & Burmester, E. (2011) High quality ultrasound allows incidental EUS findings of very small neuroendocrine tumors not seen on CT/MRI scanning. *Gastrointestinal Endoscopy*, 73: AB257-AB258.
Not in PICO
- Furukawa, Y. (1985) [Early diagnosis of pancreatic cancer by routine CT scanning; significance of the pancreatic bile duct scanning]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 12: 200-211.
Narrative review
- Fusaroli, P., Spada, A., Mancino, M. G. & Caletti, G. (2010) Contrast Harmonic Echo-Endoscopic Ultrasound Improves Accuracy in Diagnosis of Solid Pancreatic Masses. *Clinical Gastroenterology*

and *Hepatology*, 8: 629-634.

Not in PICO

Fusaroli, P., Kypraios, D., Caletti, G. & Eloubeidi, M. A. (2012) Pancreatico-biliary endoscopic ultrasound: a systematic review of the levels of evidence, performance and outcomes. [Review]. *World Journal of Gastroenterology*, 18: 4243-4256.

Not in PICO

Futakawa, N., Kimura, W., Yamagata, S., Zhao, B., Ilsoo, H., Inoue, T., Sata, N., Kawaguchi, Y., Kubota, Y. & Muto, T. (2000) Significance of K-ras mutation and CEA level in pancreatic juice in the diagnosis of pancreatic cancer. *Journal of Hepato-Biliary-Pancreatic Surgery*, 7: 63-71.

Not in PICO

Gagnon, P., Boustiere, C., Ponchon, T., Valette, P. J., Genin, G. & Labadie, M. (1991) Percutaneous fine-needle aspiration cytologic study of main pancreatic duct stenosis under pancreatographic guidance. *Cancer*, 67: 2395-2400.

Not in PICO

Gagovic, V., Spier, B. J., DeLee, R. J., Barancin, C., Lindstrom, M., Einstein, M., Byrne, S., Harter, J., Agni, R., Pfau, P. R., Frick, T. J., Soni, A. & Gopal, D. V. (2012) Endoscopic ultrasound fine-needle aspiration characteristics of primary adenocarcinoma versus other malignant neoplasms of the pancreas. *Canadian Journal of Gastroenterology*, 26: 691-696.

Not in PICO

Gall, F. P. & Kessler, H. (1987) Early carcinoma of the exocrine pancreas: Diagnosis and prognosis. [German]. *Chirurg*, 58: 78-83.

Not in PICO

Gallotta, A., Orzes, E. & Fassina, G. (2012) Biomarkers Quantification with Antibody Arrays in Cancer Early Detection. *Clinics in Laboratory Medicine*, 32: 33-45.

Not in PICO

Garcia-Carbonero, R., Capdevila, J., Crespo-Herrero, G., Diaz-Perez, J. A., Martinez del Prado, M. P., Alonso, O., V, Sevilla-Garcia, I., Villabona-Artero, C., Beguiristain-Gomez, A., Llanos-Munoz, M., Marazuela, M., Alvarez-Escola, C., Castellano, D., Vilar, E., Jimenez-Fonseca, P., Teule, A., Sastre-Valera, J., Benavent-Vinuelas, M., Monleon, A. & Salazar, R. (2010) Incidence, patterns of care and prognostic factors for outcome of gastroenteropancreatic neuroendocrine tumors (GEP-NETs): Results from the National Cancer Registry of Spain (RGETNE). *Annals of Oncology*, 21: 1794-1803.

Not in PICO

Gentile, M., Perri, F., Terracciano, F., Scimeca, D. & Andriulli, A. (2010) Looking deep into the pancreas: Endoscopic Ultrasound (EUS) as a useful diagnostic tool in asymptomatic subjects with chronic benign pancreatic hyperenzymemia. *Pancreatology*, 10: 297.

Not in PICO

Gerritsen, A., Molenaar, I. Q., Bollen, T. L., Nio, C. Y., Dijkgraaf, M. G., van Santvoort, H. C., Offerhaus, G. J., Sieders, E., De Jong, K. P., Van Dam, R. M., Van Der Harst, E., Van, G. H., Van, R. B., Bonsing, B. A., De Hingh, I. H., Gerhards, M. F., van Eijck, C. H., Gouma, D. J., Borel Rinkes, I. H. M., Busch, O. R. & Besselink, M. G. H. (1111) Preoperative characteristics of patients with presumed pancreatic cancer but ultimately benign disease: A multicenter series of 344 pancreatoduodenectomies. *Pancreatology*, 13: S11-June.

Not in PICO

Gines, A., Vazquez-Sequeiros, E., Soria, M. T., Clain, J. E. & Wiersema, M. J. (2002) Usefulness of EUS-guided fine needle aspiration (EUS-FNA) in the diagnosis of functioning neuroendocrine tumors. *Gastrointestinal Endoscopy*, 56: 291-296.

Not in PICO

Gines, A., Wiersema, M. J., Clain, J. E., Pochron, N. L., Rajan, E. & Levy, M. J. (2005) Prospective study of a Trucut needle for performing EUS-guided biopsy with EUS-guided FNA rescue.

- Gastrointestinal Endoscopy*, 62: 597-601.
Not in PICO
- Giuffra, F., Odicino, M., Comes, P. & Zanetti, P. P. (1984) [Evaluation of various instrumental studies in the differential diagnosis of early pancreatic carcinoma and chronic pancreatitis. Review of the literature]. [Italian]. *Minerva Dietologica e Gastroenterologica*, 30: 103-106.
Narrative review
- Glass, J. P., Parasher, G., Arias-Pulido, H., Donohue, R., Cerilli, L. A. & Prossnitz, E. R. (2011) Mesothelin and GPR30 staining among a spectrum of pancreatic epithelial neoplasms. *International Journal of Surgical Pathology*, 19: 588-596.
Not in PICO
- Gloor, B., Todd, K. E. & Reber, H. A. (1997) Diagnostic workup of patients with suspected pancreatic carcinoma: the University of California-Los Angeles approach. [Review] [32 refs]. *Cancer*, 79: 1780-1786.
Narrative review
- Glover, J. R., Shorvon, P. J. & Lees, W. R. (1992) Endoscopic ultrasound for localisation of islet cell tumours. *Gut*, 33: 108-110.
Not in PICO
- Goh, B. K., Tan, D. M., Thng, C. H., Lee, S. Y., Low, A. S., Chan, C. Y., Wong, J. S., Lee, V. T., Cheow, P. C., Chow, P. K., Chung, A. Y., Wong, W. K. & Ooi, L. L. (2014) - Are the Sendai and Fukuoka consensus guidelines for cystic mucinous neoplasms of the pancreas useful in the initial triage of all suspected pancreatic cystic neoplasms? A single-institution experience with 317 surgically-treated patients. - *Annals of Surgical Oncology*, 21: 1919-1926.
Not in PICO
- Goh, K. L. & Yoon, B. K. (2012) Early detection of pancreatic cancer: A possibility in some cases but not a reality in most. *Journal of Digestive Diseases*, 13: 389-392.
Narrative review
- Gold, D. V., Karanjawala, Z., Modrak, D. E., Goldenberg, D. M. & Hruban, R. H. (2007) PAM4-reactive MUC1 is a biomarker for early pancreatic adenocarcinoma. *Clinical Cancer Research*, 13: 7380-7387.
Not in PICO
- Goymer, P. (2008) Imaging: Early detection for pancreatic cancer. *Nature Reviews Cancer*, 8: 408+409.
Narrative review
- Graham, R. A., Bankoff, M., Hediger, R., Shaker, H. Z. & Reinhold, R. B. (1994) Fine-needle aspiration biopsy of pancreatic ductal adenocarcinoma: loss of diagnostic accuracy with small tumors. *Journal of Surgical Oncology*, 55: 92-94.
Not in PICO
- Gress, F., Gottlieb, K., Sherman, S. & Lehman, G. (2001) Endoscopic ultrasonography-guided fine-needle aspiration biopsy of suspected pancreatic cancer. *Annals of Internal Medicine*, 134: 459-464.
Not in PICO
- Grossjohann, H. S. (2012) Contrast-enhanced ultrasound for diagnosing, staging and assessment of operability of pancreatic cancer. *Danish Medical Journal*, 59: B4536.
Not in PICO
- Gualdi, G., Caterino, M., Di, B. C., Risi, D., Polettini, E., Pingi, A., Trasimeni, G., Ceroni, L., Melone, A. & Pirolli, F. M. (1989) [CT in the evaluation of carcinoma of the pancreas]. [Italian]. *Radiologia Medica*, 78: 200-203.
Not in PICO
- Gullo, L. (1994) CA19-9: the Italian experience. [Review] [20 refs]. *Pancreas*, 9: 717-719.
Narrative review

- Guo, Q., Kang, M., Zhang, B., Chen, Y., Dong, X. & Wu, Y. (2010) Elevated levels of CA 19-9 and CEA in pancreatic cancer-associated diabetes. *Journal of Cancer Research & Clinical Oncology*, 136: 1627-1631.
Not in PICO
- Gupta, R. K. (1995) Value of image guided fine-needle aspiration cytology in the diagnosis of pancreatic malignancies. *Diagnostic Cytopathology*, 13: 120-123.
Not in PICO
- Gyokeres, T. (2011) [Symptoms and diagnosis of neuroendocrine tumors of the digestive system]. [Review] [Hungarian]. *Orvosi Hetilap*, 152: 371-378.
Narrative review
- Hamori, J., Arkosy, P., Lenkey, A. & Sapy, P. (1997) The role of different tumor markers in the early diagnosis and prognosis of pancreatic carcinoma and chronic pancreatitis. *Acta Chirurgica Hungarica*, 36: 125-127.
Not in PICO
- Hanbidge, A. E. (2002) Cancer of the pancreas: the best image for early detection--CT, MRI, PET or US?. [Review] [30 refs]. *Canadian Journal of Gastroenterology*, 16: 101-105.
Narrative review
- Hancke, S., Holm, H. H. & Koch, F. (1984) Ultrasonically guided puncture of solid pancreatic mass lesions. *Ultrasound in Medicine & Biology*, 10: 613-615.
Not in PICO
- Harinck, F., Poley, J. W., Kluijft, I., Fockens, P. & Bruno, M. J. (2010) Is Early Diagnosis of Pancreatic Cancer Fiction? Surveillance of Individuals at High Risk for Pancreatic Cancer. *Digestive Diseases*, 28: 670-678.
Narrative review
- Hashimoto, L., Walsh, R. M., Vogt, D., Henderson, J. M., Mayes, J. & Hermann, R. (1998) Presentation and management of cystic neoplasms of the pancreas. *Journal of Gastrointestinal Surgery*, 2: 504-508.
Not in PICO
- Hayakawa, T., Naruse, S., Kitagawa, M., Ishiguro, H., Kondo, T., Kurimoto, K., Fukushima, M., Takayama, T., Horiguchi, Y., Kuno, N., Noda, A. & Furukawa, T. (1999) A prospective multicenter trial evaluating diagnostic validity of multivariate analysis and individual serum marker in differential diagnosis of pancreatic cancer from benign pancreatic diseases. *International Journal of Pancreatology*, 25: 23-29.
Not in PICO
- Hayashi, D., Tkacz, J. N., Hammond, S., Devenney-Cakir, B. C., Zaim, S., Bouzegaou, N., Ounadjela, S. & Guermazi, A. (2011) Gastroenteropancreatic neuroendocrine tumors: Multimodality imaging features with pathological correlation. *Japanese Journal of Radiology*, 29: 85-91.
Narrative review
- Hayashi, T., Ishiwatari, H., Yoshida, M., Ono, M., Sato, T., Miyanishi, K., Sato, Y., Kobune, M., Takimoto, R., Mitsuhashi, T., Asanuma, H., Ogino, J., Hasegawa, T., Sonoda, T. & Kato, J. (2013) Rapid on-site evaluation by endosonographer during endoscopic ultrasound-guided fine needle aspiration for pancreatic solid masses. *Journal of Gastroenterology and Hepatology*, 28: 656-663.
Not in PICO
- Hillner, B. E., Siegel, B. A., Liu, D., Shields, A. F., Gareen, I. F., Hanna, L., Stine, S. H. & Coleman, R. E. (2008) Impact of positron emission tomography/computed tomography and positron emission tomography (PET) alone on expected management of patients with cancer: initial results from the National Oncologic PET Registry.[Erratum appears in J Clin Oncol. 2008 Sep 1;26(25): 4229]. *Journal of Clinical Oncology*, 26: 2155-2161.
Not in PICO
- Hocke, M., Cui, X.-W., Domagk, D., Ignee, A. & Dietrich, C. F. (2014) Pancreatic cystic lesions: The value of contrast-enhanced endoscopic ultrasound to influence the clinical pathway. *Endoscopic*

- Ultrasound*, 3: 123-130.
Not in PICO
- Hollingsworth, M. A. (1994) Markers for detecting early pancreatic cancer: Summary. *International Journal of Pancreatology*, 16: 305-307.
Narrative review
- Honda, K., Hayashida, Y., Umaki, T., Okusaka, T., Kosuge, T., Kikuchi, S., Endo, M., Tsuchida, A., Aoki, T., Itoi, T., Moriyasu, F., Hirohashi, S. & Yamada, T. (2005) Possible detection of pancreatic cancer by plasma protein profiling. *Cancer Research*, 65: 10613-10622.
Not in PICO
- Honda, K., Ono, M., Shitashige, M. & Yamada, T. (2006) [Early detection of pancreatic cancer by novel proteomic technique]. [Review] [14 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 64: 1745-1755.
Not in PICO
- Horton, K. M., Hruban, R. H., Yeo, C. & Fishman, E. K. (2006) Multi-detector row CT of pancreatic islet cell tumors. [Review] [29 refs]. *Radiographics*, 26: 453-464.
Narrative review
- Huggett, M. T. & Pereira, S. P. (2011) Diagnosing and managing pancreatic cancer. *Practitioner*, 255: 21-25.
Narrative review
- Hyrdel, R., Reznak, I., Hyrdel, P., Polacek, H., Jr., Polacek, H., Hladka, M., Agouba, S. M., Janik, J. & Laca, L. (2011) [Neuroendocrine tumours of the upper gastrointestinal tract, characteristics and comparison of localization diagnostics]. [Review] [Slovak]. *Vnitrni Lekarstvi*, 57: 1017-1024.
Not in PICO
- Ichikawa, T. & Kumazaki, T. (1995) [Early diagnosis of pancreatic carcinoma and utility of helical CT]. [Review] [11 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 53: 2868-2873.
Narrative review
- Iglesias-Garcia, J. & Dominguez-Munoz, J. E. (2014) - Early detection of pancreatic cancer in patients with intraductal papillary mucinous neoplasms: the pivotal role of endoscopic ultrasound. - *Endoscopy*, 46: 30-31.
Not in PICO
- Iglesias-Garcia, J., Larino-Noia, J. & Dominguez-Munoz, J. E. (2014) When to puncture, when not to puncture: Pancreatic masses. *Endoscopic Ultrasound*, 3: 91-97.
Narrative review
- Iglesias-Garcia, J. & Dominguez-Munoz, J. E. (2014) Early detection of pancreatic cancer in patients with intraductal papillary mucinous neoplasms: the pivotal role of endoscopic ultrasound. *Endoscopy*, 46: 30-31.
Not in PICO
- Iboshi, T., Hanada, K., Fukuda, T., Yonehara, S., Sasaki, T. & Chayama, K. (2012) Value of cytodiagnosis using endoscopic nasopancreatic drainage for early diagnosis of pancreatic cancer: establishing a new method for the early detection of pancreatic carcinoma in situ. *Pancreas*, 41: 523-529.
Not in PICO
- Imai, H., Horiguchi, Y., Sekoguchi, B., Miura, S., Ogawa, H., Suzuki, T., Takeuchi, F., Nishii, M., Ban, M. & Itoh, M. (1994) [Recent advances in imaging diagnosis of pancreatic neoplasma with special reference to early diagnosis of the cancer]. [Japanese]. *Rinsho Byori - Japanese Journal of Clinical Pathology*, 42: 111-117.
Narrative review
- Innocenti, P., Falchini, M. & Stecco, A. (1999) [Ultrasonography of pancreatic neoplasms]. [Review] [11 refs] [Italian]. *Tumori*, 85: Suppl-3.
Narrative review

- Inokuma, T., Tamaki, N., Torizuka, T., Magata, Y., Fujii, M., Yonekura, Y., Kajiyama, T., Ohshio, G., Imamura, M. & Konishi, J. (1995) Evaluation of pancreatic tumors with positron emission tomography and F-18 fluorodeoxyglucose: comparison with CT and US. *Radiology*, 195: 345-352.
Not in PICO
- Inokuma, T., Tamaki, N., Torizuka, T., Fujita, T., Magata, Y., Yonekura, Y., Ohshio, G., Imamura, M. & Konishi, J. (1995) Value of fluorine-18-fluorodeoxyglucose and thallium-201 in the detection of pancreatic cancer. *Journal of Nuclear Medicine*, 36: 229-235.
Not in PICO
- Iordache, S., Saftoiu, A., Cazacu, S., Gheonea, D. I., Dumitrescu, D., Popescu, C. & Ciurea, T. (2008) Endoscopic ultrasound approach of pancreatic cancer in chronic pancreatitis patients in a tertiary referral centre. *Journal of Gastrointestinal & Liver Diseases*, 17: 279-284.
Not in PICO
- Ishida, T., Nakaizumi, A., Tanaka, S. & Tatsuta, M. (2006) [Early detection of pancreatic cancer]. [Review] [15 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 64: Suppl-9.
Narrative review
- Ishii, M. (1995) [Limitation of clinical usefulness of tumor marker]. [Review] [15 refs] [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 22: 1139-1145.
Narrative review
- Itani, K. M., Taylor, T. V. & Green, L. K. (1997) Needle biopsy for suspicious lesions of the head of the pancreas: pitfalls and implications for therapy. *Journal of Gastrointestinal Surgery*, 1: 337-341.
Not in PICO
- Itoh, A., Goto, H., Hirooka, Y., Hashimoto, S., Hirai, T., Niwa, K., Takeda, K. & Hayakawa, T. (2001) Endoscopic diagnosis of pancreatic cancer using intraductal ultrasonography. *Hepato-Gastroenterology*, 48: 928-932.
Not in PICO
- Iwasaki, Y., Arai, K., Katayanagi, S., Takahashi, K., Yamaguchi, T., Matsumoto, H. & Miyamoto, H. (2004) [Biomarkers for neoplasmas in digestive organs]. [Review] [53 refs] [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 31: 1015-1020.
Narrative review
- Jablonska, A. & Smoczynski, M. (2007) The diagnostics of pancreatic cancer with special consideration of pancreatic juice and brush cytology. [Polish]. *Gastroenterologia Polska*, 14: 209-212.
Narrative review
- Jadvar, H. & Fischman, A. J. (2001) Evaluation of pancreatic carcinoma with FDG PET. *Abdominal Imaging*, 26: 254-259.
Not in PICO
- Jani, N. & McGrath, K. (2006) What is the negative predictive value of endoscopic ultrasonography in patients with suspected pancreatic cancer? Commentary. *Nature Clinical Practice Gastroenterology and Hepatology*, 3: 308-309.
Not in PICO
- Jin, Z. D., Cai, Z. Z., Li, Z. S., Zou, D. W., Zhan, X. B., Chen, J. & Xu, G. M. (2007) The clinical value of endoscopic ultrasonography in early diagnosis of pancreatic tumor. [Chinese]. *Zhonghua nei ke za zhi [Chinese journal of internal medicine]*, 46: 984-987.
Not in PICO
- Jung, M. (1999) Early diagnosis of pancreatic cancer. Impossible mission. *Acta Endoscopica*, 29: 79-83.
Narrative review
- Kahl, S., Glasbrenner, B., Zimmermann, S. & Malfertheiner, P. (2002) Endoscopic ultrasound in pancreatic diseases. [Review] [71 refs]. *Digestive Diseases*, 20: 120-126.
Narrative review

- Kamata, K., Kitano, M., Kudo, M., Sakamoto, H., Kadosaka, K., Miyata, T., Imai, H., Maekawa, K., Chikugo, T., Kumano, M., Hyodo, T., Murakami, T., Chiba, Y. & Takeyama, Y. (2014) Value of EUS in early detection of pancreatic ductal adenocarcinomas in patients with intraductal papillary mucinous neoplasms. *Endoscopy*, 46: 22-29.
Not in PICO
- Kann, P. H. (2007) The value of endoscopic ultrasound in localizing gastrinoma. *Wiener Klinische Wochenschrift*, 119: 585-587.
Narrative review
- Karasawa, E. & Saisho, H. (1989) Early diagnosis of carcinoma of the pancreas with emphasis on utility of ultrasonography. [Japanese]. *Japanese Journal of Gastroenterology*, 86: 2794-2803.
Not in PICO
- Karlson, B. M., Ekblom, A., Lindgren, P. G., Kallskog, V. & Rastad, J. (1999) Abdominal US for diagnosis of pancreatic tumor: Prospective cohort analysis. *Radiology*, 213: 107-111.
Not in PICO
- Kaur, S., Baine, M. J., Jain, M., Sasson, A. R. & Batra, S. K. (2012) Early diagnosis of pancreatic cancer: Challenges and new developments. *Biomarkers in Medicine*, 6: 597-612.
Narrative review
- Kaushik, N., Khalid, A., Brody, D. & McGrath, K. (2006) EUS-guided paracentesis for the diagnosis of malignant ascites. *Gastrointestinal Endoscopy*, 64: 908-913.
Not in PICO
- Kausitz, J., Lesny, P. & Belan, V. (1993) Use of the CA 19-9 tumor marker in the diagnosis of pancreatic carcinoma. [Slovak]. *Bratislavske Lekarske Listy*, 94: 201-203.
Not in PICO
- Kaya, B., Bat, O. & Taskin, A. K. (2014) The diagnostic value of tumor markers in diagnosis of pancreas adenocarcinoma. [Turkish]. *Konuralp Tip Dergisi*, 6: 70-73.
Narrative review
- Kayhan, B., Kayhan, B. & Akdogan, M. (2004) Can IL-2R alpha be a valuable marker along with CA 19-9 in the diagnosis of chronic pancreatitis and pancreatic cancer? *International Journal of Biological Markers*, 19: 196-202.
Not in PICO
- Keane, M. G., Horsfall, L., Hait, G. & Pereira, S. P. (1111) Socio-demographic trends and frequency of early symptoms and frequency of early symptoms in pancreatic cancer. *Pancreatology*, 13: e14-February.
Abstract only, not enough information is available to ascertain relevance or potentially extract results
- Khan, A. H., Austin, G. L., Fukami, N., Sethi, A., Brauer, B. C. & Shah, R. J. (2013) Cholangiopancreatography and endoscopic ultrasound for indeterminate pancreaticobiliary pathology. *Digestive Diseases & Sciences*, 58: 1110-1115.
Not in PICO
- Kim, K. W., Park, S. H., Pyo, J., Yoon, S. H., Byun, J. H., Lee, M. G., Krajewski, K. M. & Ramaiya, N. H. (2013) Imaging features to distinguish malignant and benign branch-duct type intraductal papillary mucinous neoplasms of the pancreas: a meta-analysis (Provisional abstract). *Database of Abstracts of Reviews of Effects*, epub.
Not in PICO
- Kim, Y. S. (1994) Markers for detecting early pancreatic cancer. What do we need to know? *International Journal of Pancreatology*, 16: 252-254.
Narrative review
- Klapdor, R. (1989) [The status of early detection of pancreatic cancer]. [Review] [61 refs] [German]. *Internist*, 30: 752-758.
Narrative review

- Klapman, J. B., Chang, K. J., Lee, J. G. & Nguyen, P. (2005) Negative predictive value of endoscopic ultrasound in a large series of patients with a clinical suspicion of pancreatic cancer. *American Journal of Gastroenterology*, 100: 2658-2661.
Not in PICO
- Kliment, M., Urban, O., Cegan, M., Fojtik, P., Falt, P., Dvorackova, J., Lovecek, M., Straka, M. & Jaluvka, F. (2010) Endoscopic ultrasound-guided fine needle aspiration of pancreatic masses: the utility and impact on management of patients. *Scandinavian Journal of Gastroenterology*, 45: 1372-1379.
Not in PICO
- Kloppel, R., Neumann, T. & Schmidt, F. (1989) [Diagnostic imaging of pancreatic cancer]. [German]. *Zeitschrift für Die Gesamte Innere Medizin und Ihre Grenzgebiete*, 44: 580-583.
Not in PICO
- Knoflach, P., Judmaier, G., Reiner, A. & Mikuz, G. (1983) [Ultrasonically guided fine-needle biopsy]. [German]. *Wiener Medizinische Wochenschrift*, 133: 514-519.
Not in PICO
- Koide, K. & Sekiguchi, R. (2001) Contrast-enhanced helical CT of the pancreas; optimal timing of imaging for pancreatic tumor evaluation. [Japanese]. *Japanese Journal of Clinical Radiology*, 46: 228-234.
Not in PICO
- Kolmannskog, F., Kolbenstvedt, A. & Aakhus, T. (1980) Computed tomography of the pancreas. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 100: 1734-1738+1743.
Not in PICO
- Konda, V. J. A., Meining, A., Jamil, L. H., Giovannini, M., Hwang, J. H., Wallace, M. B., Chang, K. J., Siddiqui, U. D., Hart, J., Lo, S. K., Saunders, M. D., Aslanian, H. R., Wroblewski, K. & Waxman, I. (2013) A pilot study of in vivo identification of pancreatic cystic neoplasms with needle-based confocal laser endomicroscopy under endosonographic guidance. *Endoscopy*, 45: 1006-1013.
Not in PICO
- Kongkam, P., Ang, T. L., Vu, C. K., Dy, F. T., Yasuda, K., Rerknimitr, R., Varadarajulu, S., Dhir, V., Chong, V. H., Zhen, D. J., Wong, J. Y., Ho, K. Y. & Asian Consortium of EUS (2013) Current status on the diagnosis and evaluation of pancreatic tumor in Asia with particular emphasis on the role of endoscopic ultrasound. [Review]. *Journal of Gastroenterology & Hepatology*, 28: 924-930.
Narrative review
- Koopmann, J., Rosenzweig, C. N., Zhang, Z., Canto, M. I., Brown, D. A., Hunter, M., Yeo, C., Chan, D. W., Breit, S. N. & Goggins, M. (2006) Serum markers in patients with resectable pancreatic adenocarcinoma: macrophage inhibitory cytokine 1 versus CA19-9. *Clinical Cancer Research*, 12: 442-446.
Not in PICO
- Krishna, N., Tummala, P., Reddy, A. V., Mehra, M. & Agarwal, B. (2012) Dilation of both pancreatic duct and the common bile duct on computed tomography and magnetic resonance imaging scans in patients with or without obstructive jaundice. *Pancreas*, 41: 767-772.
Not in PICO
- Krishna, N. B., LaBundy, J. L., Saripalli, S., Safdar, R. & Agarwal, B. (2009) Diagnostic value of EUS-FNA in patients suspected of having pancreatic cancer with a focal lesion on CT scan/MRI but without obstructive jaundice. *Pancreas*, 38: 625-630.
Not in PICO
- Krishna, N. B., Mehra, M., Reddy, A. V. & Agarwal, B. (2009) EUS/EUS-FNA for suspected pancreatic cancer: influence of chronic pancreatitis and clinical presentation with or without obstructive jaundice on performance characteristics. *Gastrointestinal Endoscopy*, 70: 70-79.
Not in PICO
- Krudy, A. G., Doppman, J. L., Jensen, R. T., Norton, J. A., Collen, M. J., Shawker, T. H., Gardner, J. D., McArthur, K. & Gorden, P. (1984) Localization of islet cell tumors by dynamic CT: comparison with

- plain CT, arteriography, sonography, and venous sampling. *AJR.American Journal of Roentgenology*, 143: 585-589.
Not in PICO
- Kuckein, D. (1980) [Computed tomography in cases of pancreas neoplasms (author's transl)]. [German]. *Rontgen-Blatter*, 33: 520-524.
Narrative review
- Kumar, M. & Wilkinson, M. (2013) Diagnosis and management of pancreatic exocrine insufficiency. *Prescriber*, 24: 39-42.
Narrative review
- Kumar, Y., Gurusamy, K., Pamecha, V. & Davidson, B. R. (2007) Tumor M2-pyruvate kinase as tumor marker in exocrine pancreatic cancer a meta-analysis. *Pancreas*, 35: 114-119.
Not in PICO
- Kuno, N., Kurimoto, K., Fukushima, M., Hayakawa, T., Shibata, T., Suzuki, T., Sakakibara, A., Katada, N., Nakano, S. & Takayama, T. (1994) Effectiveness of multivariate analysis of tumor markers in diagnosis of pancreatic carcinoma: a prospective study in multiinstitutions. *Pancreas*, 9: 725-730.
Not in PICO
- Kurihara, N., Kawamoto, H., Kobayashi, Y., Okamoto, Y., Yamamoto, N., Tsutsumi, K., Fujii, M., Kato, H. & Yamamoto, K. (2012) Vascular patterns in nodules of intraductal papillary mucinous neoplasms depicted under contrast-enhanced ultrasonography are helpful for evaluating malignant potential. *European Journal of Radiology*, 81: 66-70.
Not in PICO
- La, S. F., Cottone, M., Marceno, M. P., Maringhini, A., Sciarrino, E. & Pagliaro, L. (1983) [Echography in patients with clinically suspected pancreatic carcinoma. Analysis of a prospective study]. [Italian]. *Radiologia Medica*, 69: 538-540.
Not in PICO
- Lahav, M., Maor, Y., Avidan, B., Novis, B. & Bar-Meir, S. (2007) Nonsurgical management of asymptomatic incidental pancreatic cysts. *Clinical Gastroenterology & Hepatology*, 5: 813-817.
Not in PICO
- Lai, R., Stanley, M. W., Bardales, R., Linzie, B. & Mallery, S. (2002) Endoscopic ultrasound-guided pancreatic duct aspiration: diagnostic yield and safety. *Endoscopy*, 34: 715-720.
Not in PICO
- LeBlanc, J. K., Emerson, R. E., DeWitt, J., Symms, M., Cramer, H. M., McHenry, L., Wade, C. L., Wang, X., Musto, P., Eichelberger, L., Al-Haddad, M., Johnson, C. & Sherman, S. (2010) A prospective study comparing rapid assessment of smears and ThinPrep for endoscopic ultrasound-guided fine-needle aspirates. *Endoscopy*, 42: 389-394.
Not in PICO
- Lee, E. S. & Lee, J. M. (2014) - Imaging diagnosis of pancreatic cancer: a state-of-the-art review. - *World Journal of Gastroenterology*, 20: 7864-7877.
Narrative review
- Lee, J. G. & Leung, J. (1998) Tissue sampling at ERCP in suspected pancreatic cancer. [Review] [53 refs]. *Gastrointestinal Endoscopy Clinics of North America*, 8: 221-235.
Narrative review
- Lee, J. K., Choi, E. R., Jang, T. H., Chung, Y. H., Jang, K. T., Park, S. M., Lee, J. K., Lee, K. T. & Lee, K. H. (2011) A prospective comparison of liquid-based cytology and traditional smear cytology in pancreatic endoscopic ultrasound-guided fine needle aspiration. *Acta Cytologica*, 55: 401-407.
Not in PICO
- Lemke, A.-J., Niehues, S. M., Hosten, N., Amthauer, H., Boehmig, M., Stroszczyński, C., Rohlfing, T., Rosewicz, S. & Felix, R. (2004) Retrospective digital image fusion of multidetector CT and 18F-FDG PET: Clinical value in pancreatic lesions - A prospective study with 104 patients. *Journal of Nuclear Medicine*, 45: 1279-1286.
Not in PICO

- Li, J., Li, Y., Cao, G., Guo, K., Zhang, L. & Ma, Q. (2013) Early manifestations of pancreatic cancer: The effect of cancer-nerve interaction. *Medical Hypotheses*, 81: 180-182.
Narrative review
- Lim, L. G., Itoi, T., Lim, W. C., Mesenas, S. J., Seo, D. W., Tan, J., Wang, H. P., Akaraviputh, T., Lakhtakia, S., Omar, S., Rantachu, T., Sachitanandan, S., Yasuda, K., Varadarajulu, S., Wong, J., Dhir, V., Ho, K. Y. & Asian Consortium of EUS (2011) Current status on the diagnosis and management of pancreatic cysts in the Asia-Pacific region: role of endoscopic ultrasound. [Review]. *Journal of Gastroenterology & Hepatology*, 26: 1702-1708.
Narrative review
- Liu, F.-J. & Cheng, Y.-S. (2010) Advances in imaging diagnosis of pancreatic cancer. [Chinese]. *World Chinese Journal of Digestology*, 18: 495-501.
Narrative review
- Lloyd, D., Al-Badri, A. & Gordon, H. (2014) Benefit of real time cytological examination in eus guided biopsy of suspected pancreatic malignancy. *Gut*, 63: A251-A252.
Not in PICO
- Lopez, H. E., Amthauer, H., Hosten, N., Ricke, J., Bohmig, M., Langrehr, J., Hintze, R., Neuhaus, P., Wiedenmann, B., Rosewicz, S. & Felix, R. (2002) Prospective evaluation of pancreatic tumors: accuracy of MR imaging with MR cholangiopancreatography and MR angiography. *Radiology*, 224: 34-41.
Not in PICO
- Lowenstein, E. B. & Lowenstein, E. J. (2010) Cutaneous manifestations of endocrine neoplasia. *Giornale Italiano di Dermatologia e Venereologia*, 145: 229-244.
Narrative review
- Lytras, D., Connor, S., Bosonnet, L., Jayan, R., Evans, J., Hughes, M., Garvey, C. J., Ghaneh, P., Sutton, R., Vinjamuri, S. & Neoptolemos, J. P. (1962) Positron emission tomography does not add to computed tomography for the diagnosis and staging of pancreatic cancer. *Digestive Surgery*, 22: 55-61.
Not in PICO
- Maguchi, H., Osanai, M., Katanuma, A., Takahashi, K., Kurita, A., Kin, T., Yane, K., Otsubo, M. & Hashigo, S. (2009) [Diagnostic imaging to detect early stages of pancreas cancer]. [Japanese]. *Gan to Kagaku Ryoho*, Cancer: 1634-1637.
In Japanese, not enough information can be extracted, but I think it's a narrative review
- Maire, F., Voitot, H., Aubert, A., Palazzo, L., O'Toole, D., Couvelard, A., Levy, P., Vidaud, M., Sauvanet, A., Ruszniewski, P. & Hammel, P. (2008) Intraductal papillary mucinous neoplasms of the pancreas: performance of pancreatic fluid analysis for positive diagnosis and the prediction of malignancy. *American Journal of Gastroenterology*, 103: 2871-2877.
Not in PICO
- Malesci, A., Montorsi, M., Mariani, A., Santambrogio, R., Bonato, C., Bissi, O., Tacconi, M., Wizemann, G. & Spina, G. (1992) Clinical utility of the serum CA 19-9 test for diagnosing pancreatic carcinoma in symptomatic patients: a prospective study. *Pancreas*, 7: 497-502.
Not in PICO
- Maluf-Filho, F., Sakai, P., Cunha, J. E., Garrido, T., Rocha, M., Machado, M. C. & Ishioka, S. (2004) Radial endoscopic ultrasound and spiral computed tomography in the diagnosis and staging of periampullary tumors. *Pancreatology*, 4: 122-128.
Not in PICO
- Matsubara, J., Honda, K., Ono, M., Tanaka, Y., Kobayashi, M., Jung, G., Yanagisawa, K., Sakuma, T., Nakamori, S., Sata, N., Nagai, H., Ioka, T., Okusaka, T., Kosuge, T., Tsuchida, A., Shimahara, M., Yasunami, Y., Chiba, T., Hirohashi, S. & Yamada, T. (2011) Reduced plasma level of CXCL chemokine ligand 7 in patients with pancreatic cancer. *Cancer Epidemiology, Biomarkers & Prevention*, 20: 160-171.
Not in PICO

- Matsugi, S., Hamada, T., Shioi, N., Tanaka, T., Kumada, T. & Satomura, S. (2007) Serum carboxypeptidase A activity as a biomarker for early-stage pancreatic carcinoma. *Clinica Chimica Acta*, 378: 147-153.
Not in PICO
- Matsumoto, I., Shirakawa, S., Shinzeki, M., Asari, S., Goto, T., Ajiki, T., Fukumoto, T., Kitajima, K. & Ku, Y. (2013) 18-Fluorodeoxyglucose positron emission tomography does not aid in diagnosis of pancreatic ductal adenocarcinoma. *Clinical Gastroenterology & Hepatology*, 11: 712-718.
Not in PICO
- Matsumoto, S., Harada, H., Tanaka, J., Ochi, K., Seno, T., Tsurumi, T. & Kunichika, K. (1994) Evaluation of cytology and tumor markers of pure pancreatic juice for the diagnosis of pancreatic cancer at early stages. *Pancreas*, 9: 741-747.
Not in PICO
- Matteo, P., Roberto, V., Serena, S., Livia, A., Giulia, Z., Marianna, S., Alberto, L., Guido, C., Gianfranco, D. F. & Gabriele, C. (2013) Cachexia is an Insidious Symptom of Pancreatic Ductal Adenocarcinoma Associated with Delayed Diagnosis and Advanced Stage of Disease. *Journal of the Pancreas*, 14: 589.
Not in PICO
- McGuire, D. E., Venu, R. P., Brown, R. D., Etkorn, K. P., Glaws, W. R. & Abu-Hammour, A. (1996) Brush cytology for pancreatic carcinoma: an analysis of factors influencing results. *Gastrointestinal Endoscopy*, 44: 300-304.
Not in PICO
- Megibow, A. J., Lombardo, F. P., Guarise, A., Carbognin, G., Scholes, J., Rofsky, N. M., Macari, M., Balthazar, E. J. & Procacci, C. (2001) Cystic pancreatic masses: cross-sectional imaging observations and serial follow-up. *Abdominal Imaging*, 26: 640-647.
Not in PICO
- Meijer, O. L., Weersma, R. K., van der Jagt, E. J. & van Dullemen, H. M. (2010) Endoscopic ultrasonography in suspected pancreatic malignancy and indecisive CT. *Netherlands Journal of Medicine*, 68: 360-364.
Not in PICO
- Mertz, H. R., Sechopoulos, P., Delbeke, D. & Leach, S. D. (2000) EUS, PET, and CT scanning for evaluation of pancreatic adenocarcinoma. *Gastrointestinal Endoscopy*, 52: 367-371.
Not in PICO
- Midwinter, M. J., Beveridge, C. J., Wilsdon, J. B., Bennett, M. K., Baudouin, C. J. & Charnley, R. M. (1999) Correlation between spiral computed tomography, endoscopic ultrasonography and findings at operation in pancreatic and ampullary tumours. *British Journal of Surgery*, 86: 189-193.
Not in PICO
- Miskiewicz, M. & Wardyn, K. A. (2011) Pancreatic cancer - the silent killer. *Family Medicine and Primary Care Review*, 13: 611-613.
Narrative review
- Miura, F., Takada, T., Amano, H., Yoshida, M., Furui, S. & Takeshita, K. (2006) Diagnosis of pancreatic cancer. *HPB*, 8: 337-342.
Narrative review
- Mizuno, N., Hara, K., Hijioka, S., Bhatia, V., Shimizu, Y., Yatabe, Y. & Yamao, K. (2011) Current concept of endoscopic ultrasound-guided fine needle aspiration for pancreatic cancer. [Review]. *Pancreatology*, 11: Suppl-6.
Narrative review
- Moehler, M., Voigt, J., Kastor, M., Heil, M., Sengespeick, C., Biesterfeld, S., Dippold, W., Kanzler, S. & Galle, P. R. (2011) Endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) as primary diagnostic tool for unclear lesions in the upper gastrointestinal tract. *Deutsche*

- Medizinische Wochenschrift*, 136: 303-308.
Not in PICO
- Moossa, A. R. (1982) Pancreatic cancer: approach to diagnosis, selection for surgery and choice of operation. *Cancer*, 50: Suppl-98.
Narrative review
- Moparty, B., Logrono, R., Nealon, W. H., Waxman, I., Raju, G. S., Pasricha, P. J. & Bhutani, M. S. (2007) The role of endoscopic ultrasound and endoscopic ultrasound-guided fine-needle aspiration in distinguishing pancreatic cystic lesions. *Diagnostic Cytopathology*, 35: 18-25.
Not in PICO
- Mu, D. Q., Wang, G. F. & Peng, S. Y. (2003) p53 protein expression and CA19.9 values in differential cytological diagnosis of pancreatic cancer complicated with chronic pancreatitis and chronic pancreatitis. *World Journal of Gastroenterology*, 9: 1815-1818.
Not in PICO
- Nagahama, H., Okada, S., Okusaka, T., Ishii, H., Ikeda, M., Nakasuka, H. & Yoshimori, M. (1999) Clinicopathological features in misdiagnosed pancreatic carcinoma. *Hepato-Gastroenterology*, 46: 2983-2985.
Not in PICO
- Nakae, Y., Naruse, S., Shibata, T., Kitagawa, M., Kondo, T., Hayakawa, T., Kuno, N. & Kurimoto, K. (1994) [Early detection of pancreatic cancer by serum markers]. [Japanese]. *Rinsho Byori - Japanese Journal of Clinical Pathology*, 42: 139-142.
Not in PICO
- Nakaizumi, A., Tatsuta, M., Uehara, H., Takenaka, A., Iishi, H., Kitamura, T., Ohigashi, H., Ishikawa, O., Okuda, S. & Wada, A. (1995) Effectiveness of the cytologic examination of pure pancreatic juice in the diagnosis of early neoplasia of the pancreas. *Cancer*, 76: 750-757.
Not in PICO
- Navarro, S., Vaquero, E., Maurel, J., Bombi, J. A., De, J. C., Feliu, J., Fernandez, C. L., Gines, A., Girela, E., Rodriguez, R., Sabater, L., Representacion del Grupo Espanol de Consenso en Cancer de Pancreas, Club Espanol Biliopancreatico, C., Grupo Espanol Multidisciplinar de Cancer Digestivo (GEMCAD), Sociedad Espanola de Diagnostico por Imagen del Abdomen (SEDIA), Sociedad Espanola de Endoscopia Digestiva (SEED) & Sociedad Espanola de Anatomia Patologica (SEAP) (2010) [Recommendations for diagnosis, staging and treatment of pancreatic cancer (Part I). Grupo Espanol de Consenso en Cancer de Pancreas]. [144 refs] [Spanish]. *Medicina Clinica*, 134: 643-655.
Guideline
- Nazli, O., Bozdog, A. D., Tansug, T., Kir, R. & Kaymak, E. (2000) The diagnostic importance of CEA and CA 19-9 for the early diagnosis of pancreatic carcinoma. *Hepato-Gastroenterology*, 47: 1750-1752.
Not in PICO
- Nesbigall, T., Koch, B. & Albert, F. W. (2003) Endosonographically guided fine-needle aspiration biopsy. Is this technique a meaningful contribution to the histological/cytological evaluation of suspected pancreatic carcinoma?. [German]. *Chirurgische Praxis*, 61: 585-589.
Narrative review
- Nicaud, M., Hou, W., Collins, D., Wagh, M. S., Chauhan, S. & Draganov, P. V. (2010) The utility of repeat endoscopic ultrasound-guided fine needle aspiration for suspected pancreatic cancer. *Gastroenterology research & practice*, 2010: 268290.
Not in PICO
- Niederau, C. & Grendell, J. H. (1992) Diagnosis of pancreatic carcinoma. Imaging techniques and tumor markers. [Review] [257 refs]. *Pancreas*, 7: 66-86.
Narrative review
- Nishiyama, Y., Yamamoto, Y., Monden, T., Sasakawa, Y., Tsutsui, K., Wakabayashi, H. & Ohkawa, M. (2005) Evaluation of delayed additional FDG PET imaging in patients with pancreatic tumour.

- Nuclear Medicine Communications*, 26: 895-901.
Not in PICO
- Nolen, B. M., Brand, R. E., Prosser, D., Velikokhatnaya, L., Allen, P. J., Zeh, H. J., Grizzle, W. E., Lomakin, A. & Lokshin, A. E. (2014) - Prediagnostic serum biomarkers as early detection tools for pancreatic cancer in a large prospective cohort study. - *PLoS ONE [Electronic Resource]*, 9: e94928.
Not in PICO
- O'Connell, A. M., Lyon, S. M., O'Sullivan, P., Given, M. F., Morrin, M. & Lee, M. J. (2008) Secretin-assisted CT of the pancreas: improved pancreatic enhancement and tumour conspicuity. *Clinical Radiology*, 63: 401-406.
Not in PICO
- O'Connell, M. J., Paulson, E. K., Jaffe, T. A. & Ho, L. M. (2004) Percutaneous biopsy of periarterial soft tissue cuffs in the diagnosis of pancreatic carcinoma. *Abdominal Imaging*, 29: 115-119.
Not in PICO
- Ochs, A., Allgaier, H. P., Schwacha, H., Siegerstetter, V., Sawatzki, M. & Blum, H. E. (2000) [Pancreatic and biliary tract tumors--diagnosis: ultrasonic diagnosis--endosonography]. [Review] [34 refs] [German]. *Praxis*, 89: 1553-1558.
Narrative review
- Okai, T., Watanabe, H., Yamaguchi, Y., Mouri, I., Motoo, Y. & Sawabu, N. (1999) EUS and K-ras analysis of pure pancreatic juice collected via a duodenoscope after secretin stimulation for diagnosis of pancreatic mass lesion: a prospective study. *Gastrointestinal Endoscopy*, 50: 797-803.
Not in PICO
- Ooi, L. L., Ho, G. H., Chew, S. P., Low, C. H. & Soo, K. C. (1998) Cystic tumours of the pancreas: a diagnostic dilemma. *Australian & New Zealand Journal of Surgery*, 68: 844-846.
Not in PICO
- Oppong, K., Raine, D., Nayar, M., Wadehra, V., Ramakrishnan, S. & Charnley, R. M. (2010) EUS-FNA versus biliary brushings and assessment of simultaneous performance in jaundiced patients with suspected malignant obstruction. *Jop: Journal of the Pancreas [Electronic Resource]*, 11: 560-567.
Not in PICO
- Paivansalo, M., Makarainen, H., Siniluoto, T., Stahlberg, M. & Jalovaara, P. (1989) Ultrasound compared with computed tomography and pancreatic arteriography in the detection of endocrine tumours of the pancreas. *European Journal of Radiology*, 9: 173-178.
Not in PICO
- Palazzo, L., Roseau, G., Chaussade, S., Salmeron, M., Gaudric, M. & Paolaggi, J. A. (1993) [Pancreatic endocrine tumors: contribution of ultrasound endoscopy in the diagnosis of localization]. [French]. *Annales de Chirurgie*, 47: 419-424.
Not in PICO
- Palazzo, L., Roseau, G., Gayet, B., Vilgrain, V., Belghiti, J., Fekete, F. & Paolaggi, J. A. (1993) Endoscopic ultrasonography in the diagnosis and staging of pancreatic adenocarcinoma. Results of a prospective study with comparison to ultrasonography and CT scan. *Endoscopy*, 25: 143-150.
Not in PICO
- Palsson, B., Masson, P. & Andren-Sandberg, A. (1997) Tumour marker CA 50 levels compared to signs and symptoms in the diagnosis of pancreatic cancer. *European Journal of Surgical Oncology*, 23: 151-156.
Not in PICO
- Pariente, E. A. (1984) [Is early diagnosis of pancreatic cancer possible?]. [French]. *Revue du Praticien*, 34: 1797-1802.
Narrative review
- Parikh, D. A., Durbin-Johnson, B. & Urayama, S. (2014) - Utility of serum CA19-9 levels in the diagnosis of pancreatic ductal adenocarcinoma in an endoscopic ultrasound referral population. -

Journal of Gastrointestinal Cancer, 45: 74-79.

Not in PICO

Pasanen, P., Partanen, K., Pikkarainen, P., Alhava, E., Pirinen, A. & Janatuinen, E. (1992) Diagnostic accuracy of ultrasound, computed tomography and endoscopic retrograde cholangiopancreatography in the detection of pancreatic cancer in patients with jaundice or cholestasis. *In Vivo*, 6: 297-301.

Not in PICO

Pasanen, P. A., Eskelinen, M., Partanen, K., Pikkarainen, P., Penttila, I. & Alhava, E. (1992) A prospective study of the value of imaging, serum markers and their combination in the diagnosis of pancreatic carcinoma in symptomatic patients. *Anticancer Research*, 12: 2309-2314.

Not in PICO

Pedrazzoli, S., Sperti, C., Pasquali, C., Bissoli, S. & Chierichetti, F. (2011) Comparison of International Consensus Guidelines versus 18-FDG PET in detecting malignancy of intraductal papillary mucinous neoplasms of the pancreas. *Annals of Surgery*, 254: 971-976.

Not in PICO

Pelsang, R. E. & Johlin, F. C. (1997) A percutaneous biopsy technique for patients with suspected biliary or pancreatic cancer without a radiographic mass. *Abdominal Imaging*, 22: 307-310.

Not in PICO

Pereira, P. L. & Wiskirchen, J. (2003) Morphological and functional investigations of neuroendocrine tumors of the pancreas. [Review] [88 refs]. *European Radiology*, 13: 2133-2146.

Narrative review

Pezzilli, R., Billi, P., Plate, L., Laudadio, M. & Sprovieri, G. (1995) Serum CA 242 in pancreatic cancer. Comparison with CA 19-9 and CEA. *Italian Journal of Gastroenterology*, 27: 296-299.

Not in PICO

Phillips, V. M., Knopf, D. R. & Bernardino, M. E. (1984) Percutaneous hepatic biopsy in suspected pancreatic carcinoma. *Journal of Computed Tomography*, 8: 307-310.

Not in PICO

Ping, Z. (2013) Diagnosis of early diabetes-related pancreatic cancer. *Journal of Gastroenterology and Hepatology*, 28: 675.

Not in PICO

Pleskow, D. K., Berger, H. J., Gyves, J., Allen, E., McLean, A. & Podolsky, D. K. (1989) Evaluation of a serologic marker, CA19-9, in the diagnosis of pancreatic cancer. *Annals of Internal Medicine*, 110: 704-709.

Not in PICO

Postier, R. G. & Williams, G. R. (1993) Pancreatic adenocarcinoma: a review for primary care physicians. [Review] [27 refs]. *Journal - Oklahoma State Medical Association*, 86: 492-495.

Narrative review

Prachayakul, V., Sriprayoon, T., Asawakul, P., Pongprasobchai, S., Pausawasdi, N. & Kachintorn, U. (2012) Repeated endoscopic ultrasound guided fine needle aspiration (EUS-FNA) improved diagnostic yield of inconclusive initial cytology for suspected pancreatic cancer and unknown intra-abdominal lymphadenopathy. *Journal of the Medical Association of Thailand*, 95: Suppl-74.

Not in PICO

Pruszynski, B. & Rajszyz, R. (1980) Advances in the diagnosis of pancreatic tumours. Diagnostic efficacy of the presently used examination methods. Optimal tactics of diagnostic management. [Polish]. *Polski Przegląd Radiologii i Medycyny Nuklearnej*, 44: 485-489.

Not in PICO

Queneau, P. E., Adessi, G. L., Thibault, P., Cleau, D., Heyd, B., Manton, G. & Carayon, P. (2001) Early detection of pancreatic cancer in patients with chronic pancreatitis: diagnostic utility of a K-ras point mutation in the pancreatic juice. *American Journal of Gastroenterology*, 96: 700-704.

Not in PICO

- Raedsch, R. & Sauerbruch, T. (1992) [Use of ERCP in suspected bile duct and pancreatic cancer]. [Review] [96 refs] [German]. *Zeitschrift fur Gastroenterologie*, 30: 765-769.
Narrative review
- Ramsay, D., Marshall, M., Song, S., Zimmerman, M., Edmunds, S., Yusoff, I., Cullingford, G., Fletcher, D. & Mendelson, R. (2004) Identification and staging of pancreatic tumours using computed tomography, endoscopic ultrasound and mangafodipir trisodium-enhanced magnetic resonance imaging. *Australasian Radiology*, 48: 154-161.
Not in PICO
- Raut, C. P., Grau, A. M., Staerkel, G. A., Kaw, M., Tamm, E. P., Wolff, R. A., Vauthey, J. N., Lee, J. E., Pisters, P. W. & Evans, D. B. (2007) Diagnostic accuracy of endoscopic ultrasound-guided fine-needle aspiration in patients with presumed pancreatic cancer. *Journal of Gastrointestinal Surgery*, 7: 118-126.
Not in PICO
- Redman, H. C. (1981) Standard radiologic diagnosis and CT scanning in pancreatic cancer. *Cancer*, 47: Suppl-61.
Narrative review
- Ribeiro, A., Peng, J., Casas, C. & Fan, Y. S. (2014) - Endoscopic ultrasound guided fine needle aspiration with fluorescence in situ hybridization analysis in 104 patients with pancreatic mass. - *Journal of Gastroenterology & Hepatology*, 29: 1654-1658.
Not in PICO
- Richter, J. M. & Barry, M. J. (1985) Decision analysis for the practicing gastroenterologist. 2. Insights into the efficacy of diagnostic strategies using decision analysis. *American Journal of Gastroenterology*, 80: 493-497.
Narrative review
- Rickes, S., Unkrodt, K., Ocran, K., Neye, H. & Wermke, W. (2003) Differentiation of neuroendocrine tumors from other pancreatic lesions by echo-enhanced power Doppler sonography and somatostatin receptor scintigraphy. *Pancreas*, 26: 76-81.
Not in PICO
- Rijkers, A. P., Valkema, R., Duivenvoorden, H. J. & van Eijck, C. H. (2014) - Usefulness of F-18-fluorodeoxyglucose positron emission tomography to confirm suspected pancreatic cancer: a meta-analysis. [Review]. - *European Journal of Surgical Oncology*, 40: 794-804.
Not in PICO
- Ringold, D. A. & Shah, R. J. (2009) Peroral Pancreatocopy in the Diagnosis and Management of Intraductal Papillary Mucinous Neoplasia and Indeterminate Pancreatic Duct Pathology. *Gastrointestinal Endoscopy Clinics of North America*, 19: 601-613.
Narrative review
- Ritts, R. E., Jr., Nagorney, D. M., Jacobsen, D. J., Talbot, R. W. & Zurawski, V. R., Jr. (1994) Comparison of preoperative serum CA19-9 levels with results of diagnostic imaging modalities in patients undergoing laparotomy for suspected pancreatic or gallbladder disease. *Pancreas*, 9: 707-716.
Not in PICO
- Rocca, R., Daperno, M., Crocella, L., Lavagna, A. & Salvetto, M. (2007) Endoscopic ultrasound-fine needle aspiration (EUS-FNA) for pancreatic lesions: Effectiveness in clinical practice. [Italian]. *Minerva Medica*, 98: 339-342.
Narrative review
- Rockall, A. G. & Reznick, R. H. (2007) Imaging of neuroendocrine tumours (CT/MR/US). [Review] [84 refs]. *Best Practice & Research Clinical Endocrinology & Metabolism*, 21: 43-68.
Narrative review
- Roder, J. D., Rosch, T., Bautz, W., Gerhardt, P. & Siewert, J. R. (1994) [Pancreatic carcinoma--preoperative diagnosis and indications for surgery]. [Review] [49 refs] [German]. *Chirurg*, 65: 225-231.
Narrative review

- Rodriguez, S. & Faigel, D. (2010) Absence of a dilated duct predicts benign disease in suspected pancreas cancer: a simple clinical rule. *Digestive Diseases & Sciences*, 55: 1161-1166.
Not in PICO
- Rolny, P. (1980) Diagnosis of pancreatic disease with special reference to the secretin-CCK test. *Scandinavian Journal of Gastroenterology, Supplement*, 15.
Narrative review
- Rosch, T., Lorenz, R., Braig, C., Feuerbach, S., Siewert, J. R. & Classen, M. (1990) [Endosonographic diagnosis of pancreatic tumors]. [German]. *Deutsche Medizinische Wochenschrift*, 115: 1339-1347.
Not in PICO
- Rosch, T., Lorenz, R., Braig, C., Feuerbach, S., Siewert, J. R., Schusdziarra, V. & Classen, M. (1991) Endoscopic ultrasound in pancreatic tumor diagnosis. *Gastrointestinal Endoscopy*, 37: 347-352.
Not in PICO
- Rosch, T., Braig, C. & Classen, M. (1992) [Early diagnosis of pancreatic cancer--is it senseless?]. [German]. *Bildgebung*, 59: Suppl-6.
Narrative review
- Rosty, C. & Goggins, M. (2002) Early detection of pancreatic carcinoma. [Review] [110 refs]. *Hematology - Oncology Clinics of North America*, 16: 37-52.
Narrative review
- Rubio-Tapia, A., Hill, I. D., Kelly, C. P., Calderwood, A. H., Murray, J. A. & American College of Gastroenterology (677) ACG clinical guidelines: diagnosis and management of celiac disease. *American Journal of Gastroenterology*, 108: 656-676.
Not in PICO
- Saftoiu, A. & Vilmann, P. (2009) Role of endoscopic ultrasound in the diagnosis and staging of pancreatic cancer. [Review] [186 refs]. *Journal of Clinical Ultrasound*, 37: 1-17.
Narrative review
- Sah, R. P., Nagpal, S. J., Mukhopadhyay, D. & Chari, S. T. (2013) New insights into pancreatic cancer-induced paraneoplastic diabetes. *Nature Reviews Gastroenterology & Hepatology*, 10: 423-433.
Narrative review
- Sahani, D. V., Kambadakone, A., Macari, M., Takahashi, N., Chari, S. & Fernandez-del, C. C. (2013) Diagnosis and management of cystic pancreatic lesions. [Review]. *AJR.American Journal of Roentgenology*, 200: 343-354.
Narrative review
- Sakamoto, H., Kitano, M., Suetomi, Y., Maekawa, K., Takeyama, Y. & Kudo, M. (2008) Utility of contrast-enhanced endoscopic ultrasonography for diagnosis of small pancreatic carcinomas. *Ultrasound in Medicine & Biology*, 34: 525-532.
Not in PICO
- Sakorafas, G. H. & Sarr, M. G. (2005) Cystic neoplasms of the pancreas; what a clinician should know. [Review] [169 refs]. *Cancer Treatment Reviews*, 31: 507-535.
Narrative review
- Sakuma, S. & Ishigaki, T. (1989) [Imaging diagnosis of early cancer: prospect and problems of present investigation]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 47: 983-989.
Not in PICO
- Sand, J., Uusimaki, J., Raty, S., Tyrvaenen, T. & Nordback, I. (2005) [Successful endoscopic examination of gallbladder and pancreatic ducts of outpatients]. [Finnish]. *Duodecim*, 121: 763-767.
Not in PICO
- Santander, C., Jimenez, I., Martin, E., Melon, A. & Pajares, J. M. (1994) [Is the carbohydrate antigen Ca 19.9 useful in the diagnosis of pancreatic carcinoma?]. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 86: 819-821.
Not in PICO

- Santhosh, S., Mittal, B. R., Bhasin, D., Srinivasan, R., Rana, S., Das, A., Nada, R., Bhattacharya, A., Gupta, R. & Kapoor, R. (2013) Role of (18)F-fluorodeoxyglucose positron emission tomography/computed tomography in the characterization of pancreatic masses: experience from tropics. *Journal of Gastroenterology & Hepatology*, 28: 255-261.
Not in PICO
- Schima, W., Ba-Ssalamah, A., Plank, C., Kulinna-Cosentini, C., Prokesch, R., Tribl, B., Sautner, T. & Niederle, B. (438) [Pancreas. Part II: Tumors]. [Review] [66 refs] [German]. *Radiologe*, 46: 421-437.
Narrative review
- Schima, W. & Ba-Ssalamah, A. (1999) [Radiologic staging of liver and pancreatic malignancies]. [Review] [53 refs] [German]. *Radiologe*, 39: 568-577.
Narrative review
- Schima, W. (2002) [Organ specific MRI contrast media in general practice]. [German]. *Wiener Medizinische Wochenschrift - Supplement*.(113):8-11, 2002., 8-11.
Narrative review
- Schmidt, C. (2012) Early detection tools for pancreatic cancer. *Journal of the National Cancer Institute*, 104: 1117-1118.
Narrative review
- Schorner, W., Claussen, C. & Peter, F. W. (1983) [Value of hypotonic duodenography in pancreatic diagnosis. Comparison with computer-tomographic findings]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 139: 15-20.
Not in PICO
- Schueller, G., Schima, W., Schueller-Weidekamm, C., Weber, M., Stift, A., Gnant, M. & Prokesch, R. (2006) Multidetector CT of pancreas: effects of contrast material flow rate and individualized scan delay on enhancement of pancreas and tumor contrast. *Radiology*, 241: 441-448.
Not in PICO
- Schultz, N. A., Dehlendorff, C., Jensen, B. V., Bjerregaard, J. K., Nielsen, K. R., Bojesen, S. E., Calatayud, D., Nielsen, S. E., Yilmaz, M., Hollander, N. H., Andersen, K. K. & Johansen, J. S. (2014) - MicroRNA biomarkers in whole blood for detection of pancreatic cancer. - *JAMA*, 311: 392-404.
Not in PICO
- Schwerk, W. B., Durr, H. K. & Schmitz, M. P. (1983) Ultrasound guided fine-needle biopsies in pancreatic and hepatic neoplasms. *Gastrointestinal Radiology*, 8: 219-225.
Not in PICO
- Segard, T., Robins, P. D., Yusoff, I. F., Ee, H., Morandau, L., Campbell, E. M. & Francis, R. J. (2013) Detection of hypoxia with 18F-fluoromisonidazole (18F-FMISO) PET/CT in suspected or proven pancreatic cancer. *Clinical Nuclear Medicine*, 38: 1-6.
Not in PICO
- Seligson, U. & Soderlund, C. (1986) ERCP and serum alkaline phosphatase in pancreatic carcinoma. *Acta Chirurgica Scandinavica*, 152: 309-312.
Not in PICO
- Seregini, E., Ferrari, L., Martinetti, A. & Bombardieri, E. (2001) Diagnostic and prognostic tumor markers in the gastrointestinal tract. *Seminars in Surgical Oncology*, 20: 147-166.
Narrative review
- Shiratori, K. (2006) [Early diagnosis and staging of pancreatic cancer]. [Review] [13 refs] [Japanese]. *Nippon Geka Gakkai Zasshi*.*Journal of Japan Surgical Society*, 107: 164-167.
Narrative review
- Shoup, M., Hodul, P., Aranha, G. V., Choe, D., Olson, M., Leya, J. & Losurdo, J. (2000) Defining a role for endoscopic ultrasound in staging periampullary tumors. *American Journal of Surgery*, 179: 453-456.
Not in PICO

- Shrikhande, S. V., Barreto, S. G., Goel, M. & Arya, S. (2012) Multimodality imaging of pancreatic ductal adenocarcinoma: a review of the literature. [Review]. *HPB*, 14: 658-668.
Not in PICO
- Siddiqui, A. A., Fein, M., Kowalski, T. E., Loren, D. E. & Eloubeidi, M. A. (2012) Comparison of the influence of plastic and fully covered metal biliary stents on the accuracy of EUS-FNA for the diagnosis of pancreatic cancer. *Digestive Diseases & Sciences*, 57: 2438-2445.
Not in PICO
- Siddiqui, U. D., Padda, M. S., Rossi, F., Rosenthal, L. S., Murali-Dharan, V. & Aslanian, H. R. (2009) Endoscopic ultrasound guided fine needle aspiration (EUS-FNA) of pancreatic masses: Patient preferences at a tertiary referral center. *Gastrointestinal Endoscopy*, 69: AB335.
Not in PICO
- Silverstein, M. D., Richter, J. M., Podolsky, D. K. & Warshaw, A. L. (1984) Suspected pancreatic cancer presenting as pain or weight loss: analysis of diagnostic strategies. *World Journal of Surgery*, 8: 839-845.
Not in PICO
- Simeone, D. M., Ji, B., Banerjee, M., Arumugam, T., Li, D., Anderson, M. A., Bamberger, A. M., Greenon, J., Brand, R. E., Ramachandran, V. & Logsdon, C. D. (2007) CEACAM1, a novel serum biomarker for pancreatic cancer. *Pancreas*, 34: 436-443.
Not in PICO
- Simon, C., Hoffmann, V., Richter, G. M., Seelos, R., Senninger, N. & Kauffmann, G. W. (1996) [Hydrosonography of the pancreas. Initial results of a pilot study]. [German]. *Radiologe*, 36: 389-396.
Not in PICO
- Skvortsov, S. V., Kalinin, A. V. & Lytsar', B. N. (1993) The use of the carbohydrate antigen CA-19-9, the carcinoembryonic antigen and alpha fetoprotein in the diagnosis of pancreatic cancer. [Russian]. *Vestnik Rossiiskoi akademii meditsinskikh nauk / Rossiiskaia akademiia meditsinskikh nauk*, 47-49.
Not in PICO
- Speets, A. M., Kalmijn, S., Hoes, A. W., Van Der Graaf, Y. & Mali, W. P. T. (2006) Yield of abdominal ultrasound in patients with abdominal pain referred by general practitioners. *European Journal of General Practice*, 12: 135-137.
Not in PICO
- Stark, D. D., Moss, A. A., Goldberg, H. I. & Deveney, C. W. (1984) CT of pancreatic islet cell tumors. *Radiology*, 150: 491-494.
Not in PICO
- Stephens, D. H. (1997) CT of pancreatic neoplasms. Part I: Adenocarcinoma. [Review] [45 refs]. *Current Problems in Diagnostic Radiology*, 26: 59-80.
Narrative review
- Strohm, W. D., Kurtz, W., Hagenmuller, F. & Classen, M. (1984) Diagnostic efficacy of endoscopic ultrasound tomography in pancreatic cancer and cholestasis. *Scandinavian Journal of Gastroenterology - Supplement*, 102: 18-23.
Not in PICO
- Szajda, S. D., Waszkiewicz, N., Chojnowska, S. & Zwierz, K. (2011) Carbohydrate markers of pancreatic cancer. *Biochemical Society Transactions*, 39: 340-343.
Narrative review
- Szczablowska, D. (2007) [Diagnostics and treatment of neuroendocrine tumors of the digestive tract in the light of the present standards]. [Review] [23 refs] [Polish]. *Polski Merkurusz Lekarski*, 22: 437-441.
Narrative review

- Takagi, K., Takekoshi, T., Ohashi, K. & Maruyama, M. (1984) Early diagnosis of pancreatic carcinoma. *Asian Medical Journal*, 27: 100-122.
Narrative review
- Takahashi, Y., Sai, J. K., Suyama, M., Kubokawa, Y., Tadokoro, H., Kamiya, T., Kato, K., Matsumura, Y., Inami, K., Chikamori, M. & Shigoka, H. (2006) [MRCP in the diagnosis of pancreatic carcinoma]. [Review] [6 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 64: Suppl-8.
Narrative review
- Takami, H., Hishinuma, S., Shintoku, J., Furuuchi, T., Ogata, Y. & Abe, O. (1985) [Tumor markers of pancreatic cancer]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 12: 212-219.
Not in PICO
- Takami, H., Hishinuma, S., Shintoku, J., Ogata, Y. & Abe, O. (1985) Diagnostic usefulness of serum levels of pancreatic oncofetal antigen (POA) and CA 19-9 in pancreatic cancers: monitoring of postoperative recurrences. [Japanese]. *Gan no rinsho*, Japan: 631-637.
Not in PICO
- Takami, H. & Kodaira, S. (1996) [Tumor markers: neoplasmas in digestive organs]. [Review] [5 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 54: 1616-1620.
Narrative review
- Tapping, C. R., Byass, O. R. & Cast, J. E. (2012) Cytological sampling versus forceps biopsy during percutaneous transhepatic biliary drainage and analysis of factors predicting success. *Cardiovascular & Interventional Radiology*, 35: 883-889.
Not in PICO
- Tatsumi, M., Isohashi, K., Onishi, H., Hori, M., Kim, T., Higuchi, I., Inoue, A., Shimosegawa, E., Takeda, Y. & Hatazawa, J. (2011) 18F-FDG PET/MRI fusion in characterizing pancreatic tumors: comparison to PET/CT. *International Journal of Clinical Oncology*, 16: 408-415.
Not in PICO
- Tessler, D. A., Catanzaro, A., Velanovich, V., Havstad, S. & Goel, S. (2006) Predictors of cancer in patients with suspected pancreatic malignancy without a tissue diagnosis. *American Journal of Surgery*, 191: 191-197.
Not in PICO
- Testoni, P. A. & Mangiavillano, B. (2008) Optical coherence tomography in detection of dysplasia and cancer of the gastrointestinal tract and bilio-pancreatic ductal system. *World journal of gastroenterology : WJG*, 14: 6444-6452.
Narrative review
- Theodor, L., Melzer, E., Sologov, M., Idelman, G., Friedman, E. & Bar-Meir, S. (1999) Detection of pancreatic carcinoma: diagnostic value of K-ras mutations in circulating DNA from serum. *Digestive Diseases & Sciences*, 44: 2014-2019.
Not in PICO
- Thoeni, R. F. & Blankenberg, F. (1993) Pancreatic imaging. Computed tomography and magnetic resonance imaging. [Review] [65 refs]. *Radiologic Clinics of North America*, 31: 1085-1113.
Narrative review
- Thorlacius, H., Kalaitzakis, E., Johansson, G. W., Ljungberg, O., Ekberg, O. & Toth, E. (2014) - Cystic neuroendocrine tumor in the pancreas detected by endoscopic ultrasound and fine-needle aspiration: a case report. - *BMC Research Notes*, 7: 510.
Not in PICO
- Tilleman, E. H., Phoa, S. S., van Delden, O. M., Rauws, E. A., van Gulik, T. M., Lameris, J. S. & Gouma, D. J. (2003) Reinterpretation of radiological imaging in patients referred to a tertiary referral centre with a suspected pancreatic or hepatobiliary malignancy: impact on treatment strategy. *European Radiology*, 13: 1095-1099.
Not in PICO

- Torre-Bravo, A., Dominguez-Perez, A. E., Bermudes-Ruiz, H., Torres-Vargas, S. & Alfaro-Fattel, L. G. (2001) [Endoscopic diagnosis of tumors of Vater's ampulla]. [Spanish]. *Gaceta Medica de Mexico*, 137: 9-14.
Not in PICO
- Touchefeu, Y., Le, R. M., Coron, E., Alamdari, A., Heymann, M. F., Mosnier, J. F., Matysiak, T. & Galmiche, J. P. (2009) Endoscopic ultrasound-guided fine-needle aspiration for the diagnosis of solid pancreatic masses: the impact on patient-management strategy. *Alimentary Pharmacology & Therapeutics*, 30: 1070-1077.
Not in PICO
- Trifunovic, J. (1999) [Sonographic imaging in the diagnosis of tumors of the pancreas]. [Croatian]. *Medicinski Pregled*, 52: 363-368.
Not in PICO
- Tseng, J. F., Warshaw, A. L., Sahani, D. V., Lauwers, G. Y., Rattner, D. W. & Fernandez-del, C. C. (419) Serous cystadenoma of the pancreas: tumor growth rates and recommendations for treatment. *Annals of Surgery*, 242: 413-419.
Not in PICO
- Tsugeno, H., Nunoue, T., Inokuchi, T., Seki, H., Kubota, J., Miyoshi, K., Takemoto, K., Takenaka, R., Taira, A. & Fujiki, S. (2010) A comparison of the diagnostic capability between Magnetic Resonance Imaging (MRI) with Diffusion Weighted Imaging (DWI) and 18-fluoro-2-dglucose positron emission tomography (FDG-PET/CT) for pancreaticobiliary malignancies. *Gastroenterology*, 138: S509-S510.
Not in PICO
- Turowska, A., Lebkowska, U., Kubas, B., Janica, J. R., Ladny, R. J. & Kordecki, K. (2007) The role of magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP) in the diagnosis and assessment of resectability of pancreatic tumors. *Medical Science Monitor*, 13: Suppl-7.
Not in PICO
- Uehara, H., Ikezawa, K., Kawada, N., Fukutake, N., Katayama, K., Takakura, R., Takano, Y., Ishikawa, O. & Takenaka, A. (2011) Diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration for suspected pancreatic malignancy in relation to the size of lesions. *Journal of Gastroenterology & Hepatology*, 26: 1256-1261.
Not in PICO
- Urgell, E., Puig, P., Boadas, J., Capella, G., Queralto, J. M., Boluda, R., Antonijuan, A., Farre, A., Lluís, F., Gonzalez-Sastre, F. & Mora, J. (2000) Prospective evaluation of the contribution of K-ras mutational analysis and CA 19.9 measurement to cytological diagnosis in patients with clinical suspicion of pancreatic cancer. *European Journal of Cancer*, 36: 2069-2075.
Not in PICO
- van Leeuwen, D. J., Huibregtse, K., Reeders, J. A., Tytgat, G. N. & van der Heyde, M. N. (1989) [Guidelines in (suspected) pancreas head carcinoma]. [Review] [35 refs] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 133: 2499-2504.
Guideline
- Vasen, H. F., Wasser, M., van, M. A., Tollenaar, R. A., Konstantinovski, M., Gruis, N. A., Bergman, W., Hes, F. J., Hommes, D. W., Offerhaus, G. J., Morreau, H., Bonsing, B. A. & de Vos tot Nederveen Cappel WH (2011) Magnetic resonance imaging surveillance detects early-stage pancreatic cancer in carriers of a p16-Leiden mutation. *Gastroenterology*, 140: 850-856.
Not in PICO
- Vignesh, S. & Brugge, W. R. (2008) Endoscopic diagnosis and treatment of pancreatic cysts. [Review] [124 refs]. *Journal of Clinical Gastroenterology*, 42: 493-506.
Narrative review
- Walker, A. J., Card, T. R., West, J., Crooks, C. & Grainge, M. J. (2013) Incidence of venous thromboembolism in patients with cancer-A cohort study using linked United Kingdom

- databases. *European Journal of Cancer*, 49: 1404-1413.
Not in PICO
- Walsh, R. M., Henderson, J. M., Vogt, D. P., Baker, M. E., O'malley, C. M., Jr., Herts, B., Zuccaro, G., Jr., Vargo, J. J., Dumot, J. A., Conwell, D. L., Biscotti, C. V. & Brown, N. (633) Prospective preoperative determination of mucinous pancreatic cystic neoplasms. *Surgery*, 132: 628-633.
Not in PICO
- Walsh, R. M., Connelly, M. & Baker, M. (2003) Imaging for the diagnosis and staging of perampullary carcinomas. [Review] [61 refs]. *Surgical Endoscopy*, 17: 1514-1520.
Narrative review
- Wang, G., Lipert, R. J., Jain, M., Kaur, S., Chakraborty, S., Torres, M. P., Batra, S. K., Brand, R. E. & Porter, M. D. (2011) Detection of the potential pancreatic cancer marker MUC4 in serum using surface-enhanced Raman scattering. *Analytical Chemistry*, 83: 2554-2561.
Narrative review
- Wang, J. Y., Chen, F. Z. & Yang, Y. Z. (1990) Evaluation of non-invasive diagnostic tests in detecting cancer of the pancreas. *Chinese Medical Journal*, 103: 817-820.
Not in PICO
- Wang, X.-H. & Cheng, Y.-S. (2012) Advances in magnetic resonance molecular and functional imaging to diagnose pancreatic cancer. *World Chinese Journal of Digestology*, 20: 2063-2069.
Narrative review
- Wang, Y. & Lin, L.-W. (2006) Medical imaging diagnostic methods of perampullary carcinoma. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 22: 471-474.
Narrative review
- Watanabe, T., Ito, T., Yoneda, S., Maruyama, M., Kodama, R., Muraki, T., Hamano, H., Arakura, N. & Tanaka, E. (2012) Yields of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) for pancreatic lesion, lymph node and gastrointestinal submucosal tumor. [Japanese]. *Endoscopic Forum for Digestive Disease*, 28: 8-15.
Not in PICO
- Wiersema, M. J. (2001) Accuracy of endoscopic ultrasound in diagnosing and staging pancreatic carcinoma. [Review] [35 refs]. *Pancreatology*, 1: 625-632.
Not in PICO
- Winkelmann, M., Schoppe, W. D., Volk, N., Burring, K. F., Jungblut, R. M. & Schneider, W. (1987) Correlation of abdominal CT imaging with autopsy findings in patients with malignant tumors. *Journal of Cancer Research & Clinical Oncology*, 113: 279-284.
Not in PICO
- Winternitz, T., Habib, H., Kiss, K. & Tihanyi, T. (2000) Pancreatic head mass: what can be done? Diagnosis: computed tomography scan. [Review] [8 refs]. *Jop: Journal of the Pancreas [Electronic Resource]*, 1: Suppl-9.
Narrative review
- Wu, W. M., Zhao, Y. P., Liao, Q., Dai, M. H., Cai, L. X. & Zhu, Y. (2005) [Diagnosis and treatment of pancreatic serous cystadenoma]. [Chinese]. *Chung-Kuo i Hsueh Ko Hsueh Yuan Hsueh Pao Acta Academiae Medicinae Sinicae*, 27: 749-752.
Not in PICO
- Wyatt, S. H. & Fishman, E. K. (1994) Spiral CT of the pancreas. *Seminars in Ultrasound CT and MRI*, 15: 122-132.
Narrative review
- Yamaguchi, T., Saisho, H., Ohto, M. & Karasawa, E. (1992) [The diagnostic process in carcinoma of the pancreas]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 19: 2319-2324.
Narrative review
- Yamamoto, R., Tatsuta, M., Noguchi, S., Kasugai, H., Okano, Y., Okuda, S., Wada, A. & Tamura, H. (1985) Histocytologic diagnosis of pancreatic cancer by percutaneous aspiration biopsy under

ultrasonic guidance. *American Journal of Clinical Pathology*, 83: 409-414.

Not in PICO

Yamao, K., Mizuno, N., Sawaki, A., Shimizu, Y. & Chang, K. J. (2008) Risk factors for pancreatic cancer and early diagnosis of pancreatic cancer. [Japanese]. *Japanese Journal of Gastroenterology*, 105: 8-16.

In Japanese. Not enough information can be extracted, but I think it is a narrative review

Yang, R., Tai, J.-H., Jin, Z.-J., Pan, L.-L. & Mu, W.-L. (2012) Application of combined test for serum tumor markers in diagnosis of pancreatic adenocarcinoma. [Chinese]. *Chinese Journal of Biologicals*, 25: 361-363.

Not in PICO

Ylagan, L. R., Edmundowicz, S., Kasal, K., Walsh, D. & Lu, D. W. (2002) Endoscopic ultrasound guided fine-needle aspiration cytology of pancreatic carcinoma: a 3-year experience and review of the literature. *Cancer*, 96: 362-369.

Not in PICO

Yoshida, K., Iwao, T., Tada, Y., Morimoto, S., Nomura, Y., Kawase, T., Nagata, Y., Nishina, S., Tomiyama, Y., Yoshioka, N., Ishino, A., Ushio, J., Hara, Y., Korenaga, K., Korenaga, M., Miyata, H., Sato, K. & Hino, K. (2009) Clinicopathological features of "early" pancreatic cancer. *Pancreas*, 38: 1065.

Not in PICO

Yu, Y. P., Jiang, H. T., Yao, Z., Xia, Q. R., Hong, F. M., Zeng, H. & Li, S. (2013) [Feasibility and safety of CT-guided percutaneous needle biopsy and subsequent iodine-125 seed interstitial implantation for pancreatic cancer]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 35: 608-612.

Not in PICO

Yue, T., Maupin, K. A., Fallon, B., Li, L., Partyka, K., Anderson, M. A., Brenner, D. E., Kaul, K., Zeh, H., Moser, A. J., Simeone, D. M., Feng, Z., Brand, R. E. & Haab, B. B. (2011) Enhanced discrimination of malignant from benign pancreatic disease by measuring the CA 19-9 antigen on specific protein carriers. *PLoS one*, 6: e29180.

Not in PICO

Zech, C. J., Helmberger, T., Wichmann, M. W., Holzknacht, N., Diebold, J. & Reiser, M. F. (2002) Large core biopsy of the pancreas under CT fluoroscopy control: results and complications. *Journal of Computer Assisted Tomography*, 26: 743-749.

Not in PICO

Zeh, H. J., Winikoff, S., Landsittel, D. P., Gorelik, E., Marrangoni, A. M., Velikokhatnaya, L., Winans, M. T., Lee, K., Moser, A., Bartlett, D., Lotze, M. T., Siegfried, J. M., Whitcomb, D., Papacristou, G., Slivka, A., Bigbee, W. L. & Lokshin, A. E. (2005) Multianalyte profiling of serum cytokines for detection of pancreatic cancer. [Erratum appears in *Cancer Biomarkers*. 2006;2(3-4):175 Note: Papacristou, G [added]]. *Cancer Biomarkers: Section A of Disease Markers*, 1: 259-269.

Not in PICO

Zhang, P., Zou, M., Wen, X., Gu, F., Li, J., Liu, G., Dong, J., Deng, X., Gao, J., Li, X., Jia, X., Dong, Z., Chen, L., Wang, Y. & Tian, Y. (2014) - Development of serum parameters panels for the early detection of pancreatic cancer. - *International Journal of Cancer*, 134: 2646-2655.

Not in PICO

Zhang, Y., Ji, S. R., Feng, D. X., Ji, J. & Han, T. Q. (2003) [Significance of detection of K-ras gene mutations and CA19-9 in serum for diagnosis of pancreatic carcinoma]. [Chinese]. *Aizheng*, 22: 295-297.

Not in PICO

Zhong, L., Li, L. & Yao, Q. Y. (2005) Preoperative evaluation of pancreaticobiliary tumor using MR multi-imaging techniques. *World Journal of Gastroenterology*, 11: 3756-3761.

Not in PICO

Zhou, J., Hu, L., Yu, Z., Zheng, J., Yang, D., Bouvet, M. & Hoffman, R. M. (2011) Marker expression in circulating cancer cells of pancreatic cancer patients. *Journal of Surgical Research*, 171: 631-636.
Not in PICO

Zimny, M. & Schumpelick, V. (2001) Fluorodeoxyglucose positron emission tomography (FDG-PET) in the differential diagnosis of pancreatic lesions. [German]. *Der Chirurg; Zeitschrift für alle Gebiete der operativen Medizen*, 72: 989-994.

Narrative review

Zisuh, A. V., Han, T.-Q. & Zhan, S.-D. (2012) Expression of telomerase & its significance in the diagnosis of pancreatic cancer. *Indian Journal of Medical Research*, 135: 26-30.

Narrative review

STOMACH CANCER

Review question:

What is the risk of stomach cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

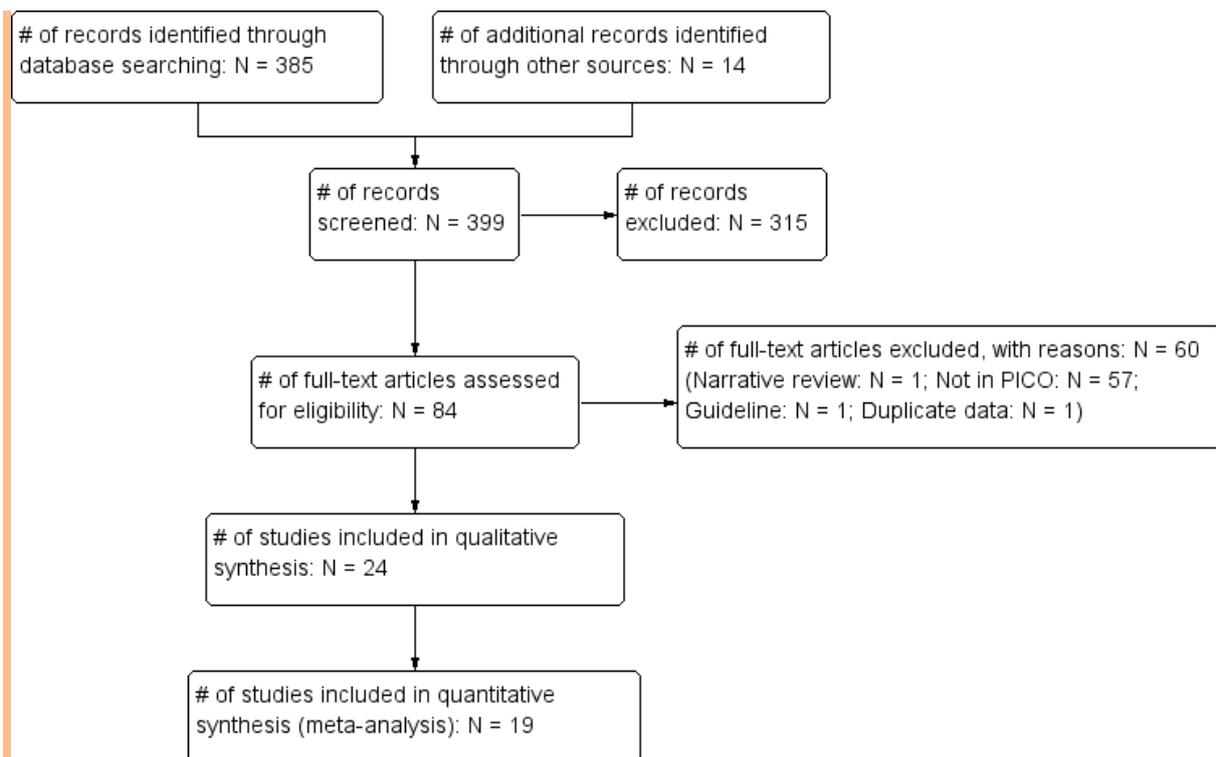
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	965	199	20/05/2013
Premedline	All-2012	108	33	21/05/2013
Embase	All-2012	1500	227	24/05/2013
Cochrane Library	All-2012	215	0	28/05/2013
Psychinfo	All-2012	13	2	21/05/2013
Web of Science (SCI & SSCI) and ISI Proceedings	All-2012	436	58	28/05/2013

Total References retrieved (after de-duplication): 369

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-26/08/2014	43	5	26/08/2014
<i>Premedline</i>	5/2013-26/08/2014	82	10	26/08/2014
<i>Embase</i>	5/2013-26/08/2014	109	5	26/08/2014
<i>Cochrane Library</i>	5/2013-26/08/2014	88	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	5/2013-26/08/2014	101	0	26/08/2014

Total References retrieved (after de-duplication): 16



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main bias and validity issues to note relates to patient selection and applicability with some studies employing non-consecutive patient sampling, e.g., case-control designs (which has been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection), and others being conducted in a setting that may not directly translate to UK-based primary care. The other main issues of concern relates to missing data (and the concern that this may not be missing at random) and under specification of symptoms and reference standards, which makes it difficult to ascertain their applicability and/or validity. The evidence base is also limited by the fact that some of the positive predictive value estimates are based on low numbers of patients and a number of the studies do not provide different estimates for stomach and oesophageal cancer, but only provide one estimate for these cancers combined.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Brignoli (1997)	?	+	-	+	?	+	+
Collins (2012)	+	+	+	+	+	+	+
Droogendijk (2011)	+	+	+	?	?	+	+
Duggan (2008)	?	+	+	+	+	+	+
Edenholm (1985)	?	+	+	-	?	+	+
Esfandyari (2002)	+	+	+	+	-	+	+
Farrus Palou (2000)	+	+	?	-	?	+	?
Hallissey (1990)	+	+	+	+	?	+	+
Hansen (1998)	+	+	+	?	?	+	+
Heikkinen (1995)	+	+	+	+	?	+	+
Hippisley-Cox (2011)	+	+	+	?	+	+	+
Jaskiewicz (1991)	?	+	+	+	?	?	+
Jones (2007)	+	+	+	+	+	+	+
Kagevi (1989)	+	+	+	+	?	+	+
Mahadeva (1998)	?	+	+	+	-	+	+
Meineche-Schmidt (2002)	+	+	+	+	?	+	+
Muris (1993)	+	+	+	+	?	?	+
Møllmann (1981)	+	+	?	-	?	+	+
Stapley (2013)	-	+	+	+	+	+	+
Stellon (1997)	+	+	+	+	+	+	+
Thomson (2003)	?	+	+	+	?	+	+
Tosetti (2010)	-	+	?	+	-	-	+
Vakil (2009)	?	+	+	+	+	+	+
Yates (2004)	+	+	+	+	?	+	+

- High
 ? Unclear
 + Low

Study results

Table 1: Stomach cancer: Meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)

Collins (2012) Hippisley-Cox (2011) Møllmann (1981)	Abdominal pain	All patients N = 3389979	0.34 (0.16-0.71)
Collins (2012) Droogendijk (2011) Farrus Palou (2000) Hippisley-Cox (2011) Stellon (1997) Yates (2004)	Anaemia	All patients N = 3375342	1.09 (0.67-1.77)
Brignoli (1997) Duggan (2008) Edenholm (1985) Hallissey (1990) Hansen (1998) Heikkinen (1995) Jaskiewicz (1991) Kagevi (1989) Meineche-Schmidt (2002) Thomson (2003) Vakil (2009)	Dyspepsia	All patients N = 11403	0.65 (0.33-1.3)
Collins (2012) Esfandyari (2002) Hippisley-Cox (2011) Jones (2007)	Dysphagia	All patients N = 4136936	3.6 (1.58-8.01)

Please note that the data from Stapley (2013) are not included in these meta-analyses due to the case-control design of the study, and the data from Mahadeva (1998) is not included due to the limited and different age range of the population. These data are instead reported in the table below entitled "Additional results reported by the individual papers: Single symptoms". When the number of studies was < 3, the data were not meta-analysed, but presented for the individual studies instead.

Table 2: Stomach cancer: Individual positive predictive values from the meta-analyses

Study	Symptom(s)	Patient group	PPVs % (95% CI); prevalence
Collins (2012)	Abdominal pain	All patients	0.2 (0.2-0.2) 437/246998
Hippisley-Cox (2011)	Abdominal pain	All patients	0.3 (0.3-0.4) 309/91627
Møllmann (1981)	Upper abdominal pain > 2 weeks	All patients	1 (0.4-2.4) 6/577
Collins (2012)	Anaemia	All patients	0.6 (0.5-0.8) 116/18355
Droogendijk (2011)	Anaemia	All patients	1.04 (0.27-3.28) 3/287
Farrus Palou (2000)	Anaemia	All patients	1.7 (0.09-10.5) 1/58
Hippisley-Cox (2011)	Anaemia	All patients	1.1 (1-1.4) 119/10349
Stellon (1997)	Anaemia	All patients (N = 26)	0 (0-16)

			0/26
Yates (2004)	Anaemia	All patients	2.55 (1.35-4.66) 11/431 has UGI cancer: No distinction made between the different kinds
Brignoli (1997)	Dyspepsia	All patients	0.4 (0.09-1.14) 3/828
Duggan (2008)	Dyspepsia	All patients	0.27 (0.05-1.1) 2/753
Edenholm (1985)	Persisten epigastric pain/ulcer-like dyspepsia	All patients who received an UGI endoscopy	1.2 (0.21-4.77) 2/165
Hallissey (1990)	Dyspepsia	All patients	2.28 (1.76-3) 59/2585
Hansen (1998)	Dyspepsia	All patients	1 (0.4-2.2) 6/612
Heikkinen (1995)	Dyspepsia	All patients	1.75 (0.8-3.7) 7/400
Jaskiewicz (1991)	Dyspepsia	All included patients	2.7 (1.6-4.5) 16/585
Kagevi (1989)	Dyspepsia	All included patients	1.16 (0.2-4.6) 2/172
Meineche-Schmidt (2002)	Dyspepsia	All patients	0.54 (0.25-1.1) 8/1491
Thomson (2003)	Dyspepsia	All patients	0.1 (0.01-0.6) 1/1040
Vakil (2009)	Dyspepsia without alarm symptoms	All included patients	0.1 (0.03-0.35) 3/2741
Collins (2012)	Dysphagia	All patients	4.2 (3.9-4.5) 810/19237
Esfandyari (2002)	Dysphagia	All patients	6 (2.5-13.1) 6/100
Hippisley-Cox (2011)	Dysphagia	All patients	7.8 (7.1-8.5) 434/5590
Jones (2007)	Dysphagia	All patients	0.78 (0.58-1.05) 47/5999

Table 3: Stomach cancer: Additional results reported by the individual papers: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Tosetti (2010)	Upper gastro-intestinal symptoms without alarming features	All patients	0 (0-1.7) 0/275
Muris (1993)	Non-acute abdominal complaints	All patients	0 (0-0.8) 0/578
Collins (2012)	Abdominal pain	Women	0.1 (0.1-0.1) 139/144266
		Men	0.3 (0.3-0.3) 298/102732

Stapley (2013)	Abdominal pain	Patients ≥ 55 years	0.3 (0.2-0.3)
Stapley (2013)	Epigastric pain	Patients ≥ 55 years	0.9 (0.8-1)
Collins (2012)	Anaemia	Women	0.4 (0.3-0.5) 49/13792
		Men	1.5 (1.1-1.9) 67/4563
Møllmann (1981)	Anaemia	Men	0 (0-44) 0/7
Stapley (2013)	Low haemoglobin	Patients ≥ 55 years	0.2 (0.2-109)
Jaskiewicz (1991)	Dyspepsia	Males	3.4 (1.8-6) 12/355
		Females	1.7 (0.6-4.7) 4/230
Stapley (2013)	Dyspepsia	Patients ≥ 55 years	0.7 (0.6-0.7)
Stapley (2013)	Dyspepsia (reported ≥ twice)	Patients ≥ 55 years	1.2 (1-1.5)
Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 45 years old	0.27 (0.07-0.84) 3/1127
		Patients ≥ 50 years old	0.36 (0.09-1.15) 3/829
		Patients ≥ 55 years old	0 (0-0.86) 0/554
		Patients ≥ 60 years old	0 (0-1.47) 0/323
Hansen (1998)	Ulcer-like dyspepsia	All patients	0.6 (0.03-3.9) 1/161
Hansen (1998)	Dysmotility-like dyspepsia	All patients	0 (0-2.9) 0/163
Hansen (1998)	Reflux-like dyspepsia	All patients	1.16 (0.2-4.6) 2/173
Hansen (1998)	Unclassifiable dyspepsia	All patients	0.9 (0.05-5.8) 1/107
Mahadeva (2008)	Dyspepsia	All patients (they were aged 18-45 years)	0 (0-1.1) 0/432
Collins (2012)	Dysphagia	Women	2.5 (2.2-2.8) 262/10391
		Men	6.2 (5.7-6.7) 548/8846
Jones (2007)	Dysphagia	Women	0.5 (0.3-0.8) 17/3371
		Men	1.14 (0.79-1.65) 30/2628
Stapley (2013)	Dysphagia	Patients ≥ 55 years	4.8 (4.3-5.9)
Stapley (2013)	Dysphagia (reported ≥ twice)	Patients ≥ 55 years	5.5 (4.2-7.9)
Collins (2012)	Appetite loss	All patients	0.6 (0.5-0.9) 37/5838
		Women	0.4 (0.2-0.7) 12/3317
		Men	1 (0.7-1.5)

			25/2521
Hippisley-Cox (2011)	Appetite loss	All patients	1.1 (0.8-1.5) 35/3391
Møllmann (1981)	Weight loss and/or anorexia	All patients	2 (0.1-12) 1/50
Collins (2012)	Weight loss	All patients	0.8 (0.7-0.9) 218/28403
		Women	0.6 (0.4-0.7) 86/15465
		Men	1 (0.9-1.2) 132/12938
Hippisley-Cox (2011)	Weight loss	All patients	1.2 (1-1.4) 107/9170
Stapley (2013)	Weight loss	Patients ≥ 55 years	0.9 (0.7-1)
Collins (2012)	Haematemesis	All patients	1 (0.8-1.2) 110/10792
		Women	0.5 (0.3-0.7) 22/4630
		Men	1.4 (1.2-1.8) 88/6162
Hippisley-Cox (2011)	Haematemesis	All patients	2.3 (1.9-2.7) 101/4477
Stapley (2013)	Constipation	Patients ≥ 55 years	0.2 (0.2-0.2)
Stapley (2013)	Chest pain	Patients ≥ 55 years	0.2 (0.2-0.2)
Stapley (2013)	Reflux	Patients ≥ 55 years	0.6 (0.6-0.7)
Møllmann (1981)	Nausea and/or vomiting > 2 weeks	All patients	0 (0-12.3) 0/35
Stapley (2013)	Nausea/vomiting	Patients ≥ 55 years	0.6 (0.5-0.7)
Stapley (2013)	Nausea/vomiting reported ≥ twice	Patients ≥ 55 years	1 (0.8-1.2)
Stapley (2013)	Raised platelets	Patients ≥ 55 years	0.5 (0.4-0.5)
Stapley (2013) reported that all PPVs for symptom combinations in patients < 55 years were < 1%, and that the highest PPV in this age group was for dysphagia, 0.8 (0.4-1.5)%			
Møllmann (1981)	Gastrointestinal bleeding	All patients	0 (0-32) 0/11

Please note:

- The calculations of the positive predictive values differ between all the other included studies using (TP)/(TP+FP) and Stapley (2013) using other statistics due to the case-control design of these studies. NR = Not reported.

Table 4: Stomach cancer: Additional results reported by the individual papers: Symptom combinations

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Meineche-Schmidt (2002)	Dyspepsia and jaundice	All patients	0 (0-48.32) 0/6
Meineche-Schmidt (2002)	Dyspepsia and black stools	All patients	0.91 (0.05-5.69) 1/110
Meineche-Schmidt	Dyspepsia and bloody	All patients	0.76 (0.04-4.81)

(2002)	stools		1/131
Stapley (2013)	Dysphagia and chest pain	Patients ≥ 55 years	5.8 (3.5-10.8)
Stapley (2013)	Dysphagia and loss of weight	Patients ≥ 55 years	9.2 (4.4-22.7)
Stapley (2013)	Dysphagia and abdominal pain	Patients ≥ 55 years	6.5 (3.5-13.5)
Stapley (2013)	Dysphagia and epigastric pain	Patients ≥ 55 years	9.3 (NR)
Stapley (2013)	Dysphagia and reflux	Patients ≥ 55 years	5 (3.3-8.4)
Stapley (2013)	Dysphagia and low haemoglobin	Patients ≥ 55 years	4.6 (3.4-6.6)
Stapley (2013)	Dysphagia and nausea/vomiting	Patients ≥ 55 years	7.3 (4.4-13.9)
Meineche-Schmidt (2002)	Dyspepsia and dysphagia	All patients	1.4 (0.04-4.36) 3/215
Stapley (2013)	Dysphagia and dyspepsia	Patients ≥ 55 years	9.8 (5.7-20.2)
Stapley (2013)	Dysphagia and raised platelets	Patients ≥ 55 years	6.1 (3.2-13.2)
Stapley (2013)	Dyspepsia and chest pain	Patients ≥ 55 years	0.7 (0.5-0.9)
Stapley (2013)	Dyspepsia and abdominal pain	Patients ≥ 55 years	1 (0.7-1.3)
Stapley (2013)	Dyspepsia and epigastric pain	Patients ≥ 55 years	1.4 (1-2)
Stapley (2013)	Dyspepsia and nausea/vomiting	Patients ≥ 55 years	1.3 (0.9-1.8)
Stapley (2013)	Dyspepsia and reflux	Patients ≥ 55 years	0.9 (0.7-1.2)
Meineche-Schmidt (2002)	Dyspepsia and weight loss	All patients	1.37 (0.35-4.28) 3/219
Stapley (2013)	Dyspepsia and loss of weight	Patients ≥ 55 years	2.1 (1.3-3.5)
Stapley (2013)	Dyspepsia and raised platelets	Patients ≥ 55 years	1.4 (0.9-2.2)
Meineche-Schmidt (2002)	Dyspepsia and anaemia	All patients	0 (0-11.71) 0/37
Stapley (2013)	Dyspepsia and low haemoglobin	Patients ≥ 55 years	1 (0.8-1.3)
Stapley (2013)	Constipation and chest pain	Patients ≥ 55 years	0.4 (0.3-0.5)
Stapley (2013)	Constipation and loss of weight	Patients ≥ 55 years	1.1 (0.8-1.7)
Stapley (2013)	Constipation and abdominal pain	Patients ≥ 55 years	0.4 (0.3-0.5)
Stapley (2013)	Constipation and epigastric pain	Patients ≥ 55 years	1.4 (0.8-2.3)
Stapley (2013)	Constipation and reflux	Patients ≥ 55 years	0.7 (0.5-1.1)

Stapley (2013)	Constipation and low haemoglobin	Patients ≥ 55 years	0.4 (0.4-0.5)
Stapley (2013)	Constipation and nausea/vomiting	Patients ≥ 55 years	0.6 (0.4-0.7)
Stapley (2013)	Constipation and dyspepsia	Patients ≥ 55 years	0.8 (0.6-1.1)
Stapley (2013)	Constipation and dysphagia	Patients ≥ 55 years	4.2 (2.7-7.2)
Stapley (2013)	Constipation and raised platelets	Patients ≥ 55 years	0.9 (0.6-1.4)
Stapley (2013)	Abdominal pain and chest pain	Patients ≥ 55 years	0.3 (0.3-0.4)
Stapley (2013)	Abdominal pain and epigastric pain	Patients ≥ 55 years	0.9 (0.7-1.2)
Stapley (2013)	Abdominal pain and reflux	Patients ≥ 55 years	0.6 (0.5-0.9)
Stapley (2013)	Abdominal pain and weight loss	Patients ≥ 55 years	1.4 (0.9-2.2)
Møllmann (1981)	Upper abdominal pain > 2 weeks and nausea and/or vomiting > 2 weeks	All patients	0.7 (0.12-2.7) 2/293
Stapley (2013)	Abdominal pain and nausea/vomiting	Patients ≥ 55 years	0.7 (0.5-0.9)
Stapley (2013)	Abdominal pain and low haemoglobin	Patients ≥ 55 years	0.5 (0.4-0.6)
Stapley (2013)	Abdominal pain and raised platelets	Patients ≥ 55 years	0.8 (0.6-1.1)
Møllmann (1981)	Upper abdominal pain > 2 weeks and gastrointestinal bleeding	All patients	0 (0-21) 0/19
Møllmann (1981)	Upper abdominal pain > 2 weeks and nausea/vomiting > 2 weeks and gastrointestinal bleeding	All patients	0 (0-44) 0/7
Møllmann (1981)	Upper abdominal pain > 2 weeks and nausea/vomiting > 2 weeks and weight loss/anorexia	All patients	5.2 (2.1-11.4) 6/116
Møllmann (1981)	Upper abdominal pain > 2 weeks and weight loss/anorexia and gastrointestinal bleeding	All patients	20 (1.1-70) 1/5
Møllmann (1981)	Upper abdominal pain > 2 weeks and weight loss/anorexia	All patients	2 (0.4-7.9) 2/98
Stapley (2013)	Chest pain and epigastric pain	Patients ≥ 55 years	0.9 (0.6-1.4)
Stapley (2013)	Chest pain and reflux	Patients ≥ 55 years	0.6 (0.5-0.9)

Stapley (2013)	Chest pain and weight loss	Patients ≥ 55 years	1.1 (0.7-1.8)
Stapley (2013)	Chest pain and nausea/vomiting	Patients ≥ 55 years	0.6 (0.4-0.8)
Stapley (2013)	Chest pain and low haemoglobin	Patients ≥ 55 years	0.3 (0.3-0.4)
Stapley (2013)	Chest pain and raised platelets	Patients ≥ 55 years	0.8 (0.6-1.2)
Stapley (2013)	Epigastric pain and reflux	Patients ≥ 55 years	1.5 (1-2.4)
Stapley (2013)	Epigastric pain and weight loss	Patients ≥ 55 years	4.2 (1.8-11)
Stapley (2013)	Epigastric pain and low haemoglobin	Patients ≥ 55 years	1.6 (1.1-2.2)
Stapley (2013)	Reflux and loss of weight	Patients ≥ 55 years	3.1 (1.5-6.7)
Stapley (2013)	Reflux and low haemoglobin	Patients ≥ 55 years	0.9 (0.7-1.2)
Stapley (2013)	Weight loss and low haemoglobin	Patients ≥ 55 years	1 (0.8-1.3)
Møllmann (1981)	Weight loss/anorexia and gastrointestinal bleeding	All patients	0 (0-80) 0/2
Møllmann (1981)	Weight loss/anorexia and gastrointestinal bleeding and nausea/vomiting > 2 week	All patients	0 (0-80) 0/2
Møllmann (1981)	Weight loss/anorexia and nausea/vomiting > 2 week	All patients	0 (0-16.6) 0/25
Stapley (2013)	Nausea/vomiting and weight loss	Patients ≥ 55 years	2.8 (1.7-4.8)
Stapley (2013)	Nausea/vomiting and epigastric pain	Patients ≥ 55 years	1.3 (0.9-2)
Stapley (2013)	Nausea/vomiting and reflux	Patients ≥ 55 years	2.3 (1.5-3.5)
Stapley (2013)	Nausea/vomiting and low haemoglobin	Patients ≥ 55 years	0.9 (0.7-1.1)
Stapley (2013)	Reflux and raised platelets	Patients ≥ 55 years	1.6 (0.9-2.9)
Stapley (2013)	Weight loss and raised platelets	Patients ≥ 55 years	1.8 (1.1-3)
Stapley (2013)	Nausea/vomiting and raised platelets	Patients ≥ 55 years	1.4 (1-2.1)
Stapley (2013)	Epigastric pain and raised platelets	Patients ≥ 55 years	1.9 (1-3.8)
Stapley (2013)	Low haemoglobin and raised platelets	Patients ≥ 55 years	0.6 (0.6-0.7)
Møllmann (1981)	Any of the inclusion symptoms + previous dyspepsia	All patients	0.9 (0.4-1.9) 7/773

Møllmann (1981)	Any of the inclusion symptoms + no previous dyspepsia	All patients	2.1 (1.1-3.8) 11/524
Møllmann (1981)	Any of the inclusion symptoms + unchanged previous dyspepsia	All patients	1.2 (0.5-3) 5/407
Møllmann (1981)	Any of the inclusion symptoms + no previous or changed dyspepsia	All patients	1.5 (0.8-2.6) 13/890
Møllmann (1981)	Any of the inclusion symptoms + pain provoked by meals	All patients	2.3 (1.5-3) 6/257
Møllmann (1981)	Any of the inclusion symptoms + no pain provoked by meals	All patients	1.1 (0.6-2.1) 10/924
Møllmann (1981)	Any of the inclusion symptoms + relief of pain by meals	All patients	1.2 (0.5-2.8) 6/488
Møllmann (1981)	Any of the inclusion symptoms + no pain relief by meals	All patients	1.5 (0.7-2.8) 10/687
Møllmann (1981)	Any of the inclusion symptoms + irritable bowel syndrome	All patients	1.2 (0.2-4.7) 2/167
Møllmann (1981)	Any of the inclusion symptoms + no irritable bowel syndrome	All patients	1.4 (0.8-2.3) 16/1129

Please note:

- The calculations of the positive predictive values differ between the all the other included studies using (TP)/(TP+FP) and Stapley (2013) using other statistics due to the case-control design of these studies. NR = not reported.

Evidence statement(s):

Abdominal pain (4 studies, N = 3416339) presenting in a primary care setting is associated with an overall positive predictive value of up to 0.34% for stomach cancer. The studies were associated with 0-3 bias or applicability concerns (see also Tables 1-3).

Anaemia (8 studies, N = 3417170) presenting in a primary care setting is associated with an overall positive predictive value of up to 1.09% for stomach cancer. The studies were associated with 0-4 bias or applicability concern (see also Tables 1-3).

Dyspepsia (13 studies, N = 52183) presenting in a primary care setting is associated with an overall positive predictive value of up to 1.2% for stomach cancer. The studies were associated with 1-3 bias or applicability concerns (see also Tables 1-3).

Dysphagia (5 studies, N = 4177284) presenting in a primary care setting is associated with an overall positive predictive value of up to 5.5% for stomach cancer. All the studies were associated with 0-1 bias or applicability concerns (see also Tables 1-3).

Other single symptoms (6 studies, N = 3417192) presenting in a primary care setting are associated with an overall positive predictive values for stomach cancer up to 2.3% (for haematemesis). The studies were associated with 0-4 bias or applicability concerns (see also Table 3).

Two or more symptom presenting in combination (3 studies, N = 43319) in a primary care setting are associated with overall positive predictive values for stomach cancer ranging from 0% (dyspepsia with jaundice or anaemia, for 'gastrointestinal bleeding and nausea/vomiting and upper abdominal pain', and for 'gastrointestinal bleeding and anorexia/weightloss' with or without nausea/vomiting) to 20% (for 'upper abdominal pain and weight loss/anorexia and gastrointestinal bleeding'), but some of these positive predictive values were based on bvery low numbers of patients. The studies were associated with 1-3 bias or applicability concerns (see also Table 4).

Evidence tables

Brignoli (1997)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from Switzerland.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 828; 329 men, 499 women; mean (SD) age = 41-42 (15-16) years. <u>Inclusion criteria:</u> "Adult patients with epigastric complaints were admitted to the multicentre [omega]-project if their symptoms persisted for over 1 month and their clinical history and appearance did not suggest an organic disorder (i.e. absence of alarm features, such as gastrointestinal blood loss, palpable tumour mass, massive weight loss, etc.). The studies were conducted by general practitioners acting as primary care physicians." <u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> Primary care, Switzerland
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Epigastric complaints (dyspepsia)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference	Endoscopy and 84-day follow up.

standard(s)	
Is the reference standard likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	3 patients had gastric cancer, 0 patients had oesophageal cancer, and 2 patients had cancer outside the digestive tract.

Collins (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2135540 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Dysphagia (N = 19237; 8846 men, 10391 women), abdominal pain (N = 246998; 102732 men, 144266 women), appetite loss (N = 5838; 2521 men, 3317 women), weight loss (N = 28403; 12938 men, 15465 women), haematemesis (N = 10792; 6162 men, 4630 women), anaemia (N = 18355; 4563 men, 13792 women).</p> <p><u>Incident cases of gastro-oesophageal cancer during the 2-year follow up period:</u> N = 1766 (1184 men, 582 women; 32% gastric cancer, 68% oesophageal cancer).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p>

	<p><u>Exclusion criteria:</u> Patients with a prior diagnosis of gastro-oesophageal cancer, registration with the general practice < 12 months, or with invalid dates.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Haematemesis, dysphagia, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Droogendijk (2011)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective peripheral hospital laboratory database study serving 265 GPs in Dordrecht (Holland).
Was a consecutive or random sample of patients enrolled?	Yes

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 287; 129 men, 158 women; median (range) age = 70 (19-87) years. <u>Inclusion criteria:</u> All women aged > 50 years and all men aged ≥ 18 years who between January 2004 and December 2005 were diagnosed with iron-deficiency anaemia (haemoglobin < 13.7 g/dl in men and < 12.1 g/dl in women, and a serum ferritin level < 25 µg/l for men and < 20 µg/l for women). <u>Exclusion criteria:</u> Patients with a known history of iron-deficiency anaemia in the previous 2 years, a history of gastrointestinal malignancy or congenital haemoglobinopathy. <u>Clinical setting:</u> GPs in Holland
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	New onset iron-deficiency anaemia (haemoglobin < 13.7 g/dl in men and < 12.1 g/dl in women, and a serum ferritin level < 25 µg/l for men and < 20 µg/l for women).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy and 12-month follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	It is unclear if all patients are accounted for
Was there an appropriate interval between index test and reference standard?	Unclear

Did all patients receive the same reference standard?	Unclear
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk
NOTES	In addition to the 24 patients with colorectal cancer, 3 patients had gastric cancer, 1 patient had oesophageal cancer and 1 patient had locally invasive endometrial cancer.
Duggan (2008)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 43 GP practices in the UK.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 762; 411 men, 351 women; mean (range) age = 42 (18-73) years. <u>Inclusion criteria:</u> Patients aged 18-70 with dyspepsia thought by the GP to arise from the upper GI tract and of sufficient severity to justify empirical treatment with an H ₂ antagonist or PPI. <u>Exclusion criteria:</u> Patients thought to be unfit for investigation, with alarm symptoms suggestive of malignancy (dysphagia, weight loss > 5 g, anaemia, haematemesis, melaena or jaundice), previous radiological or endoscopic diagnosis of peptic ulcer disease or reflux oesophagitis, investigation for dyspepsia in the previous 5 years with either procedure or symptom onset within 6 months of commencement of NSAID therapy, previous H. pylori eradication therapy or more than 3 prescriptions for acid suppression therapy in the previous 6 months. <u>Clinical setting:</u> Primary care, UK
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy and 1-2-year follow up.
Is the reference standard likely to correctly classify the	Yes

target condition?	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	At 12-month follow up GP data were available for 753/762.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	2 patients had gastric cancer, 2 patients had oesophageal cancer (the authors report that these patients should not have been included as they had a history of dysphagia).
Edenholm (1985)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from the Distric General Clinic in Huskvarna, Sweden.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 187; 96 men, 91 women; mean/median (range) age = 44 (17-80) years. <u>Inclusion criteria:</u> Patients who between November 1982 and June 1984 called on the clinic because of abdominal pain and who were diagnosed by the general practitioner as having ulcer-like dyspepsia. The criterion used was persistent epigastric pain. Most patients also had additional symptoms such as acid regurgitation, nausea, belching or vomiting. <u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> GPs in Sweden
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Ulcer-like dyspepsia. The criterion used was persistent epigastric pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes

Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	UGI endoscopy
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	20/187 patients declined endoscopy and it was unsuccessful in a further 2 patients. Thus the PPV is likely to be an over-estimate, calculated as 2/165.
Was there an appropriate interval between index test and reference standard?	Yes probably
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	There were a total of 3 cancers confirmed in the 165 patients who received UGI endoscopy: 1 oesophageal cancer, 1 stomach cancer, and 1 cancer of the duodenum, the latter of which was included with the stomach cancer

Esfandyari (2002)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective/retrospective? patient series from USA
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 100; 49 men, 51 women; mean (SE) age = 64 (2) years. Inclusion criteria: Patients with new onset dysphagia without a prior work up who were evaluated at the Cleveland Clinic Foundation outpatient clinic by their primary care physician. Exclusion criteria: Neurological disease, oropharyngeal dysphagia or previous

	gastric or oesophageal surgery, and patients without a final diagnosis explaining their dysphagia. Clinical setting: Primary care outpatient clinic, USA.	
Are there concerns that the included patients and setting do not match the review question?		High concern
INDEX TEST		
A. Risk of bias		
Index test	New onset dysphagia	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Completed clinical and diagnostic testing after an initial barium swallow/upper GI endoscopy.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients are accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	6 patients had malignancy, but the type of malignancy was not further specified	
Farrus Palou (2000)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective consecutive patient series from urban general practice covering a population of 24000.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	

Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 87 of whom the data from 29 were unavailable as no etiological diagnosis was found (due to patient refusal of further investigation [?; 8], lost to follow up [7], patient deterioration rendering them unsuitable for further investigation [14]); of the remaining 58 patients there were 14 males, 44 females; mean? (SD?) age = 54.26 (19.95) years.</p> <p><u>Inclusion criteria:</u> Patients aged > 14 years who attended the health centre between 1 October 1995 and 31 September 1996 who were found to have new onset (previously unknown) anaemia (haemoglobin < 13 g/dl for men and 12 g/dl for women).</p> <p><u>Exclusion criteria:</u> Pregnant women.</p> <p><u>Clinical setting:</u> Spanish GP</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Anaemia (haemoglobin < 13 g/dl for men and 12 g/dl for women)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up I think
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	No diagnosis available for 29/87 patients
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No

Could the patient flow have introduced bias?		High risk
NOTES	This paper is published in Spanish. One patient had gastric cancer, 2 patients had colon cancer.	
Hallissey (1990)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Propective consecutive patient series from a group of 10 general practices in England.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia.</p> <p><u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia</p> <p><u>Exclusion criteria:</u> None listed.</p> <p><u>Clinical setting:</u> Primary care, England.</p>	
Are there concerns that the included patients and setting do not match the review question?		Unclear concern
INDEX TEST		
A. Risk of bias		
Index test	Dyspepsia of any degree	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern

FLOW AND TIMING	
A. risk of bias	
Flow and timing	2659 patients were seen and 2585 attended for investigation
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), circinomatosis of unknown primary (7).
Hansen (1998)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from general an open-access endoscopy clinic in Denmark.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 612 from 66 GPs; 288 males / 324 females; mean age (SD) = 47 (16.8) years. <u>Inclusion criteria:</u> "All general practitioners (n = 108) in the city of Odense (population, 170,000) were invited to participate in the study. GPs were asked to refer all patients who consulted them with dyspepsia, regardless of the severity of the symptoms. To obtain compliance with this request the participating GPs were sent numerous reminders. Because of a limited endoscopy capacity not all GPs took part in the study at the same time." Study period was 11 March 1991-27 March 1992. <u>Exclusion criteria:</u> Aged < 18 years, signs of UGI bleeding, abdominal emergency, jaundice, previous surgery in the UGI tract except for closure of an ulcer, supposed acute bacterial or viral infection, pregnancy, or endoscopy contryraindicated. <u>Clinical setting:</u> GPs in Denmark
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Epigastric or retrosternal pain or discomfort, with or without heartburn, nausea, vomiting, and any other symptom considered to be referable to the proximal alimentary tract.
Were the index test results interpreted without knowledge	Yes

of the results of the reference standard?	
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy within 1 week of referral and follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	56 eligible patients declined participation. These patients were older than the study group (mean age = 52 years versus 47 years) and they were characterised by a shorter dyspepsia history (median duration = 1 month, range = 4 days to 35 years versus 2 months, range = 4 days to 14 years). Fewer of the non-participating patients had had a previous endoscopy or UGI radiography (22% versus 43%, but identical proportions of the patients had an ulcer history (11% versus 14%).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	There were a total of 4 cancers histologically confirmed in the study. No subclassification of the cancers reported. Follow up of the 364 patients with normal endoscopy revealed missing data in 5% of the cases and 1 lymphoma and 1 rectal carcinoma. These 6 cancers (NOS) are included in the overall PPV for dyspepsia.
Heikkinen (1995)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Consecutive patient series from 11 GPs (from 3 rural health centres) and from the catchment area of 6 physicians in the health centre of an urban area (population [individuals > 14 years old] of study area = 24600) in Finland.
Was a consecutive or random sample of patients enrolled?	Yes

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 400; 152 males, 248 females; 77% were > 44 years. <u>Inclusion criteria:</u> Consecutive patients who consulted their GP from January 11th 1993 to January 12 th 1994 for dyspepsia (defined as upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptoms considered to be referable to the proximal alimentary tract). <u>Exclusion criteria:</u> Patients with symptoms of an acute condition within the abdomen or who had had an upper intestinal endoscopy performed within the last 3 months or aged < 15 years <u>Clinical setting:</u> Primary care, Finland.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia (defined as upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptoms considered to be referable to the proximal alimentary tract).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy, upper abdominal ultrasound, more detailed interview, blood count, serum screening (creatinine, alkaline phosphatase, alanine aminotransferase, amylase, and C-reactive protein), lactose intolerance test, and follow up of ≥ 1 month.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and	Yes

reference standard?	
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 9 had cancer: 0 colorectal, 2 oesophageal and 7 stomach (of which 3 were lymphomas of the MALT type (Mucosa-associated lymphoid tissue)).
Hippisley-Cox (2011)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1238971 patients were identified from 189 practices (621478 males, 617493 females), mean (SD) age = 50.1 (15) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Symptoms:</u> Current dysphagia (N = 8165), current haematemesis (N = 7119), current abdominal pain (N = 126161), current appetite loss (N = 6133), current weight loss (N = 5377), tiredness in the last year (N = 14119), haemoglobin recorded in the last year (N = 12638, haemoglobin < 11 g/dl in the last year (N = 218862).</p> <p><u>Incident cases of colorectal cancer during the 2-year follow up period:</u> N = 1343 (776 oesophageal and 567 gastric).</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000); 12 months after the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of gastro-oesophageal cancer at baseline, and patients with a recorded 'red-flag' symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern

INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Incident dysphagia, haematemesis, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 103358 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of gastro-oesophageal cancer (N = 538), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 31973), leaving 1238971 patients. However, data is presented for 963040/1238971 patients for all symptoms. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	Results not presented separately for gastric and oesophageal cancer
Jaskiewicz (1991)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Patient series from a program aimed at screening patients with chronic gastric complaints for gastric carcinoma in the South and North-Western Cape Province of South Africa.

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 585, 355 males, 230 females; mean (range) age males = 45.1 (19-87) years, mean (range) age females = 47.2 (19-87) years. <u>Inclusion criteria:</u> "participants who were treated for dyspeptic complaints such as epigastric pain, heartburn, post-prandial pain and bloating, vomiting or nausea with a duration of at least 3 months. Patients represented various areas in the south-and north-western Cape province including Namaqualand, and formed part of a programme aimed at screening patients with chronic gastric complaints for gastric carcinoma." <u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> Unclear, South Africa.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Unspecified dyspepsia (dyspeptic complaints such as epigastric pain, heartburn, post-prandial pain and bloating, vomiting or nausea with a duration of at least 3 months).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and	Yes

reference standard?	
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 16 had gastric cancer. No oesophageal cancers reported
Jones (2007)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective consecutive patient series using patients in the UK's General Practice Research Database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 923605 patients were identified, of whom 762325 were aged ≥ 15 years.</p> <p><u>Number of first occurrences in patients with no previous diagnosis of cancer:</u></p> <p><u>Haematuria:</u> N = 11138, mean (SD) age at first symptom = 58.5 (18.9) years. Patients excluded due to incomplete dates for their first symptom: N = 30. Sex (of final sample): 6385 males, 4723 females.</p> <p><u>Haemoptysis:</u> N = 4822, mean (SD) age at first symptom = 61.6 (18) years. Patients excluded due to incomplete dates for their first symptom: N = 10. Sex (of final sample): 2930 males, 1882 females.</p> <p><u>Dysphagia:</u> N = 6003, mean (SD) age at first symptom = 54.5 (19.4) years. Patients excluded due to incomplete dates for their first symptom: N = 4. Sex (of final sample): 2628 males, 3371 females.</p> <p><u>Rectal bleeding:</u> N = 15314, mean (SD) age at first symptom = 52.5 (18.8) years. Patients excluded due to incomplete dates for their first symptom: N = 25. Sex (of final sample): 7523 males, 7766 females.</p> <p><u>Inclusion criteria:</u> All patients from 128 general practices that provided data of a sufficient standard from 1 January 1994 to 31 December 2000 and which provided exclusively Read coded data, who were aged between 15 and 100 years, whose first ever recorded occurrence of each alarm symptom (haematuria, haemoptysis, dysphagia, or rectal bleeding) was after 31 December 1994 and who had not previously been diagnosed as having any cancer.</p> <p><u>Exclusion criteria:</u> Patients whose date of first symptom or first relevant diagnosis of cancer was before 1 January 1995 and patients with a diagnosis of any other cancer than the ones of interest before the date of the first recorded symptom or before the index cancer diagnosis date if the related symptom was not recorded.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	

A. Risk of bias	
Index test	Identification of all patients who ever had symptoms recorded for haematuria, haemoptysis, dysphagia, or rectal bleeding.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Cancer code in the UK's General Practice Research Database: <u>Haematuria</u> : Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs. <u>Haemoptysis</u> : Respiratory tract neoplasms. <u>Dysphagia</u> : Oesophageal neoplasms. <u>Rectal bleeding</u> : Colorectal neoplasms.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Diagnoses of cancer were most often made in the first three months after the onset of alarm symptoms; very few diagnoses of cancer were made later than three years after symptom onset. In the 4th and 5th years of study, the small number of observed occurrences of cancer was similar to the number expected from background incidence rates. Secondary analyses evaluating whether the incidence of neoplasms other than those prespecified was increased after the occurrence of alarm symptoms showed for: <u>Haematuria</u> : Inclusion of cancers of the reproductive organs yielded 21 additional cancers in women and 158 cancers in men, mostly cancers of the prostate. Inclusion of these cancers in the analysis would give a positive predictive value of 3.9% in women and 9.9% in men.

	<p><u>Dysphagia</u>: Inclusion of gastric cancers yielded 17 additional cancer diagnoses in women and 30 in men. Inclusion of these cancers gave positive predictive values of 5.2% in women [reported in the paper, however, the numbers reported do not match up and I think the PPV is instead 2.91%; 98/3371] and 6.9% in men.</p> <p><i>Estimates based on the pre-specified cancers may be thus conservative for these symptoms.</i></p> <p><u>Haemoptysis</u>: Extension of the diagnostic criteria yielded 6 additional cancers.</p> <p><u>Rectal bleeding</u>: Extension of the diagnostic criteria yielded 2 additional cancers.</p>
--	--

Kagevi (1989)

PATIENT SELECTION

A. risk of bias

Patient sampling	Propective consecutive patient series from a primary care centre in Sweden.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability

Patient characteristics and setting	<p>N = 172; 88 men, 84 women; mean (SD) age = 43 (16) years.</p> <p><u>Inclusion criteria</u>: "All patients visiting the medical center with complaints referable to the digestive tract were considered for inclusion. Even when the patient consulted the primary care center because of another complaint and coincidentally mentioned gastrointestinal problem, the patient was considered for inclusion. The patient's gastrointestinal problem could have been reported in connection with an earlier visit at the primary care center."</p> <p><u>Exclusion criteria</u>: Patients with jaundice, gastrointestinal bleeding or acute abdominal pain were excluded and so were patients judged to have a non-gastro-enterologic cause of their symptoms (gynaecologic problems, spondylosis deformans, etc), patients aged < 16 years and patients unwilling to participate.</p> <p><u>Clinical setting</u>: Primary care Center, Sweden.</p>
-------------------------------------	---

Are there concerns that the included patients and setting do not match the review question?	Unclear concern
--	------------------------

INDEX TEST

A. Risk of bias

Index test	Dyspepsia defined as any pain, discomfort, or other symptoms referable to the digestive tract ≥ 2 weeks. Symptoms could be intermittent or continuous.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
--	--------------------

REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Esophagogastroduodenoscopy within 1 week and 6 month follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	13/185 patients were excluded as they did not want to have an endoscopy
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	2 patients had gastric cancer, 0 patients had oesophageal cancer.
Mahadeva (2008)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from the Primary Care Clinics of the University of Malaya in Malaysia
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 432; 198 males/234 females; mean ages (SDs) = 30-31 (8) years. <u>Inclusion criteria:</u> "All patients were recruited from the Primary Care Clinics of the University of Malaya, which provide a regular service to the local community. Patients aged ≤ 45 years presenting with uninvestigated dyspepsia were invited to participate in the study", which ran from January 2004 until October 2005. <u>Exclusion criteria:</u> Age > 45 or < 18 years; symptoms of weight loss, progressive dysphagia or those suggestive of anaemia; pregnancy; previous H pylori testing; any contra-indication to endoscopy or sedation; failure to turn up for initial test ; and on regular doses of non-steroidal anti-inflammatory drugs. <u>Clinical setting:</u> Primary care clinic, Malaysia

Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	Uninvestigated dyspepsia. Dyspepsia defined as predominant upper abdominal discomfort for > 4 weeks, with any associated symptoms, including heart burn and regurgitation.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up ± upper endoscopy (oesophagogastroduodenoscopy)
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	39/471 eligible patients were excluded from the study for the following reasons: 34/39 patients declined to participate, 3/39 became pregnant before the test, 1/39 emigrated from the country and 1/39 had missing data.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	One patient was found to have cancer, which was metastatic pancreatic cancer. No oesophageal or gastric cancers were reported.
Meineche-Schmidt (2002)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Consecutive patient series from 82 GPs in Denmark.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes

Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1491; 688 males, 803 females; age groups: 18-37 years: N = 377; 38-50 years: N = 369; 51-64 years: N = 338; 65- years: N = 402. <u>Inclusion criteria</u> : Consecutive patients who consulted their GP between June 1991 and May 1993 for dyspepsia (defined as pain or discomfort in the abdomen judged by the GP to be related to the gastrointestinal tract). <u>Exclusion criteria</u> : None listed. <u>Clinical setting</u> : Primary care, Denmark.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia (defined as pain or discomfort in the abdomen judged by the GP to be related to the gastrointestinal tract).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	18 months-3 years and 10 months follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 31 had cancer: 17 colorectal, 8 gastro-oesophageal (no subgroup analyses presented for these patients) and 6 other.

Muris (1993)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive patient series from 11 general practitioners in Maastricht (Holland)
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 578; 212 males, 342 females; age groups: 18-39 years: N = 295; 40-49 years: N = 80; 50-59 years: N = 91; 60-75 years: N = 88. <u>Inclusion criteria:</u> Patients who during a 3-month period consulted one of the participating GPs for abdominal complaints. <u>Exclusion criteria:</u> Patients aged < 18 years and patients with a condition necessitating immediate referral or admission to hospital. <u>Clinical setting:</u> GPs in Holland
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Abdominal complaints. Not further specified, but the authors do report that the duration of pain before the patient presented for the first time for the evaluation of abdominal pain varied from some days to more than 1 year.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up for 15 months.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	

A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Although not explicitly stated by the authors it is implied that the patients included were those presenting with the abdominal complaint for the first time.

Møllmann (1981)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from an open-access gastroscopy clinic in Denmark.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1480; gender not reported; 40-44 years: N = 144; 45-49 years: N = 186; 50-69 years: N = 882; 70-74 years: N = 130; 75-79 years: N = 83; 80-89 years N = 47; 90- years: N = 8. <u>Inclusion criteria:</u> All patients who, for a 2-year period, presented to their GP with (any of) the following symptoms were referred to the open access gastroscopy clinic: Upper abdominal pain > 2 weeks, nausea and/or vomiting > 2 weeks, weight loss and/or anorexia, gastrointestinal bleeding, and anaemia (i.e., Hb < 80%). <u>Exclusion criteria:</u> Patients who had been examined for any of the above symptoms within the last 6 months. <u>Clinical setting:</u> GPs in Denmark
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Upper abdominal pain > 2 weeks, nausea and/or vomiting > 2 weeks, weight loss and/or anorexia, gastrointestinal bleeding, and anaemia (i.e., Hb < 80%).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	

Reference standard(s)	2-stage process: Gastroscopy with photography, using a gastrocamera, performed with only local anaesthesia of the pharynx. If this investigation disclosed abnormal conditions, the next stage was gastroscopy, possibly with biopsy, using diazepam sedation.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	177/1480 patients declined endoscopy, 2/1480 did not show up for endoscopy, and it was unsuccessful in a further 24 patients, leaving 1277 patients. However, the paper reports that only 1273 had primary endoscopy, and then reports the results for between 1181 and 1297 patients.
Was there an appropriate interval between index test and reference standard?	Yes probably
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	There were a total of 18 gastric cancers confirmed in the study. No oesophageal cancers were reported. This research was published in 2 papers.

Stapley (2013)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Matched case-control study using patients in the UK's General Practice Research Database (GPRD).
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	Cases: Oesophageal cancer cases: N = 4854, 3174 males / 1680 females; aged 40-54 years: N = 387; 55-69

	<p>years: N = 1712; 70-84 years: N = 2230; ≥ 85 years: N = 532.</p> <p><u>Gastric cancer cases:</u> N = 2617, 1625 males / 992 females; aged 40-54 years: N = 130; 55-69 years: N = 671; 70-84 years: N = 1437; ≥ 85 years: N = 382. Median number of consultations (all cases) = 26 (IQR = 15-42)</p> <p><u>Controls:</u> <u>Oesophageal cancer controls:</u> N = 21506, gender not reported; aged 40-54 years: N = 1539; 55-69 years: N = 7473; 70-84 years: N = 10296; ≥ 85 years: N = 2198. <u>Gastric cancer controls:</u> N = 11371, gender not reported; aged 40-54 years: N = 497; 55-69 years: N = 2887; 70-84 years: N = 6431; ≥ 85 years: N = 1556. Median number of consultations (all controls) = 15 (IQR = 7-28)</p> <p><u>Inclusion criteria:</u> Cases: Patients with a record of one of 42 (18 oesophageal, 24 gastric) GPRD tumour diagnostic codes between January 2000 and December 2009 inclusive, aged ≥ 40 years, with min. 1 year of data before diagnosis. The first instance of a oesophago-gastric cancer code was assigned the data of diagnosis/index date. Controls: Up to 5 controls were matched to cases on sex, general practice, and to 1 year of age of the case. The index date was the index date of the matched case. <u>Exclusion criteria:</u> Oesophago-gastric cancer (controls), no consultations in the year before diagnosis. <u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	<p>All symptoms, physical signs or abnormal investigations compiled from the oesophago-gastric cancer literature were studied, and supplemented by literature from relevant cancer websites. The GPRD's code list has many synonyms for for similar symptoms, often including additional description such as severity or duration. These synonyms were identified and merged. The dyspepsia variable merged codes with either the word 'dyspepsia' or 'indigestion'; the reflux variable included 'regurgitation' as well as 'reflux'; the variable 'epigastric pain' required a precise anatomical description, whereas the variable 'abdominal pain' incorporated all other abdominal pain variables without a precise anatomical description. Occurrences of these features in the year before the index date were identified. Features were only retained for further study if they occurred in ≥5% of cases or controls. For laboratory tests, the local laboratory range was used to identify abnormal results. Patients without a test were considered to be the same status as those with a normal result. All hepatic enzyme results were merged into a composite variable, deemed abnormal if any enzyme was raised; similarly, abnormal erythrocyte sedimentation rate, plasma viscosity and C-reactive protein were collated into a single variable called raised inflammatory markers. All codes for fractures were also identified, as a test for any recording bias between cases and controls (making the assumption that the fracture rate would be approximately equal).</p>

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Oesophago-gastric cancer code in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 45356 patients were identified, 37699 controls and 7657 cases. Of the controls the following exclusions were applied: Already used as a case (N = 252), case excluded (N = 808), duplicate control (N = 427) and no data in year pre-index date (N = 3335). Of the cases the following exclusions were applied: No controls (N = 17), OG cancer diagnosis before 2000 (N = 28), case already used as case (for other O/G cancer: N = 131) and case with metastatic cancer (N = 10).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Results are not split for oesophageal cancer and gastric cancer.
Stellon (1997)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective? consecutive patient series from semi-rural UK general practice with a patient list between 2400-3400 during the study period.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes

Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 26; 5 males, 21 females; age range = 51-87 years. <u>Inclusion criteria:</u> All patients aged > 50 years found to have iron deficiency anaemia between January 1989 and March 1994. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> UK GP
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Iron deficiency anaemia (< 12 g/dl haemoglobin and/or mean corpuscular volume < 80 fl with ferritin ≤ 16 ng/l)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up during 5 year study period.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	

Thomson (2003)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Propective patient series from a group of 49 family physician practices in Canada.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1040, 520 males / 520 females; mean (range) age =45.6 (18-84) years. <u>Inclusion criteria:</u> Patients ≥ 18 years with a primary complaint of ≥ 3 months intermittent or continuous dyspepsia. Patients could not have used proton pump inhibitors within 30 days or prokinetics or prescription H ₂ -receptor antagonists (H ₂ RAS) within 14 days of enrolment. <u>Exclusion criteria:</u> Heartburn or acid regurgitation as their sole symptom; documented history of upper GI pathology/surgery; clinical investigation of dyspepsia by endoscopy or radiology in the previous 6 months or more than twice in the past 10 years; H. pylori eradication treatment in the previous 6 months; irritable bowel syndrome as assessed by the presence of ≥ manning criteria; or severe concurrent disease. <u>Clinical setting:</u> Family physician practice, Canada.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia defined as symptom complex of epigastric pain/discomfort in association with other upper GI symptoms, including heartburn and acid regurgitation.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 10 days and 6-months follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients are accounted for. 1100/1171 enrolled patients consented to endoscopy, but 60/1100 did not received endoscopy (eligibility criteria not fulfilled [27], lost to follow up [3], withdrew consent [9], non-compliant with the protocol [1], endoscopy-intolerable [2], other [18]).	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk
NOTES	Malignancy was detected in 2 patients: Gastric (MALToma; 1), oesophageal cancer (1).	

Tosetti (2010)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series from 63 general practitioners in Italy	
Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?		High risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 275; 124 males, 151 females; median age (range) = 46 (18-92) years. Symptoms: Epigastric pain (72%), prolonged digestion (51.6%), heartburn (49.1%), epigastric postprandial fullness (45.5%), epigastric distension (41.5%), nausea (38.5%), acid regurgitation (34.5%), belching (28.7%), early satiety (20.7%).</p> <p><u>Inclusion criteria</u>: "Each GP enrolled in the survey patients who, over a three-month period, presented with UGI [upper gastro-intestinal] symptoms at the first onset without alarming features."</p> <p><u>Exclusion criteria</u>: "Patients with either previous or recurrent complaints or previously investigated for UGI symptoms were not included".</p> <p><u>Clinical setting</u>: GPs in Italy</p>	
Are there concerns that the included patients and setting do not match the review question?		High concern
INDEX TEST		
A. Risk of bias		
Index test	New onset UGI symptoms without alarming features. Not further specified.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	1-year follow up.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Cancers diagnosed in these patients were: Pancreas (1/275), and oesophageal (1/275).

Vakil (2009)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 2741, mean (range) age = not reported (not reported) years, numbers of females/males: Not reported.</p> <p><u>Inclusion criteria:</u> Patients aged 18-70 years who met Rome II criteria for dyspepsia (intermittent or continuous pain or burning centered in the upper abdomen for ≥ 3 months).</p> <p><u>Exclusion criteria:</u> Past diagnosis of gastro-oesophageal reflux disease, predominant symptom of heartburn or regurgitation, history of heartburn or regurgitation > 2 days/week, treatment > 2 days/week with non-steroidal anti-inflammatory drugs or cyclooxygenase-2 selective inhibitors or aspirin (except for cardiovascular prophylaxis at doses ≤ 325 mg/day), concurrent alarm features (e.g., dysphagia, recurrent vomiting, unexplained anaemia,</p>

	gastro-intestinal bleeding), H pylori eradication treatment within 12 months, maintenance therapy with either a proton pump or an H2-receptor antagonist within 6 months. <u>Clinical setting</u> : The study was conducted in 190 primary care health centers in 17 countries (Argentina, Belgium, Brazil, Canada, Denmark, France, Germany, Greece, Iceland, Italy, Norway, Romania, Singapore, South Africa, Spain, Sweden, Switzerland). Patients were recruited from primary care clinics where flyers publicising the study were placed and the primary care physicians recruited patients presenting to their offices with dyspepsia [random or consecutive sampling unlikely].
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia/ intermittent or continuous pain or burning centered in the upper abdomen for ≥ 3 months. Symptoms were evaluated using a scale validated in a number of languages
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	All patients received outpatient endoscopy
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Supported by AstraZeneca R&D Sweden. The authors state that "The sponsor did not play any role in the calculations or in the writing of the manuscript".

	Six patients had cancer: 3 Oesophagus and 3 stomach.
Yates (2004)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective database study using the laboratory databases of two district general hospitals including all the general practices using these laboratories.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 431; 154 males, 277 females; median age (inter-quartile range) = 75 (65-81) years. <u>Inclusion criteria:</u> All female patients aged > 50 years and male patients aged > 20, with haemoglobin concentrations ≤ 110 g/l (women) or ≤ 120 g/l (men), and mean cell volume < 82 fl (district 1) or 78 fl (district 2), and red cell count ≤ 5.5 x 10 ¹² /l between June 1997 and May 1998. <u>Exclusion criteria:</u> History of anaemia within previous 12 months, known haematological abnormalities (e.g., haemoglobinopathy), unavailable notes at follow up. <i>That is, patients with a history of cancer were not excluded.</i> <u>Clinical setting:</u> UK GP
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Iron deficiency anaemia (haemoglobin concentrations ≤ 110 g/l (women) or ≤ 120 g/l (men), and mean cell volume < 82 fl (district 1) or 78 fl (district 2), and red cell count ≤ 5.5 x 10 ¹² /l)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Minimum 3 years follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 48 had gastrointestinal cancer (11 upper, 2 small bowel and 35 lower, including recurrent tumours) and N = 23 had non-gastrointestinal cancers, but the study only reports the type of some of these cancers (3 lung + 1 lung tumour secondary to a previous breast tumour, 1 ovary, 2 bladder, 1 Hodgkin's, 1 Non-Hodgkin's, 1 endometrial sarcoma, 1 lymphoma, 1 endometrial) and has therefore not been added to the evidence reviews for the non-gastrointestinal cancers. The paper considers both the lower gastrointestinal cancers and the small bowel cancers as colorectal cancer and in order to present subgroup analyses by gender I have maintained this grouping and not added this paper to the evidence review for small intestine.

References

Included studies

- Brignoli, R., Watkins, P., Halter, F. The Omega-Project – a comparison of two diagnostic strategies for risk- and cost-oriented management of dyspepsia. *European Journal of Gastroenterology and Hepatology* 9, 337-343. 1997.
- Collins, G.S., Altman, D.G. Identifying patients with undetected gastro-oesophageal cancer in primary care: External validation of QCancer (Gastro-Oesophageal). *European Journal of Cancer*, <http://dx.doi.org/10.1016/j.ejca.2012.10.023>. 2012.
- Drøogendijk, J., Beukers, R., Berendes, P. B., Tax, M. G. H. M., Sonneveld, P., and Levin, M. D. Screening for gastrointestinal malignancy in patients with iron deficiency anemia by general practitioners: An observational study. *Scandinavian Journal of Gastroenterology* 46[9], 1105-1110. 2011.
- Duggan, A.F., Elliott, C.A., Miller, P., Hawkey, C.J., Logan, R.F.A. Clinical trial: A randomized trial or early endoscopy, *Helicobacter pylori* testing and empirical therapy for the management of dyspepsia in primary care. *Alimentary Pharmacology and Therapeutics* 29, 55-68. 2008.
- Edenholm, M., Gustavsson, R., Jansson, O., et al. Endoscopic findings in patients with ulcer-like dyspepsia. *Scandinavian Journal of Gastroenterology* 20(suppl 109), 163-167. 1985.
- Esfandyari, T., Potter, J.W., Vaezi, M.F. Dysphagia: A cost analysis of the diagnostic approach. *American Journal of Gastroenterology*, 97, 2733-2737. 2002.
- Farrus, Palou M., Perez, Ocana A., Mayer Pujadas, M. A., Piquer, Gibert M., Mundet, Tuduri, X, and Iglesias, Rodal M. [Anemia in primary care: etiology and morphological characteristics]. [Spanish]. *Atencion Primaria* 25[4], 230-235. 15-3-2000.
- Hallisey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.

- Hansen, J.M., Bytzer, P., Schaffalitzky de Muckadell, O.B. Management of dyspeptic patients in primary care: Value of the unaided clinical diagnosis and of dyspepsia subgrouping. *Scandinavian Journal of Gastroenterology* 33, 799-805. 1998.
- Heikkinen, M., Pikkarainen, P., Takala, J., and Rasanen, H. Julkunen R. Etiology of dyspepsia: Four hundred unselected consecutive patients in general practice. *Scandinavian Journal of Gastroenterology* 30[6], 519-523. 1995.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected gastro-oesophageal cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice*; DOI: 10.3399/bjgp11X606609. 2011.
- Jaskiewicz, K., Louwrens, H.D. Chronic atrophic gastritis in a population at risk for gastric carcinoma. *Anmticancer Research* 11, 835-840. 1991.
- Jones, R., Latinovic, R., Charlton, J., and Gulliford, M. C. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *BMJ* 334[7602], 1040. 19-5-2007.
- Kagevi, I., Löfstedt, S., Persson, L.-G. Endoscopic findings and diagnoses in unselected dyspeptic patients at a primary health care center. *Scandinavian Journal of Gastroenterology* 24, 145-150. 1989.
- Mahadeva, S., Chia, Y.-C., Vinothini, A., et al. Cost-effectiveness of and satisfaction with a *Helicobacter pylori* "test and treat" strategy compared with prompt endoscopy in young Asians with dyspepsia. *Gut* 57, 1214-1220. 2008.
- Meineche-Schmidt, V. and Jorgensen, T. 'Alarm symptoms' in patients with dyspepsia: a three-year prospective study from general practice. *Scandinavian Journal of Gastroenterology* 37[9], 999-1007. 2002.
- Muris, J.W.M., Starmans, R., Fijten, G.H., Crebolder, F.J.M., Krebber, T.F.W.A., and Knottnerus, J.A., Abdominal pain in general practice. *Family Practice* 10[4], 387-390. 1993.
- Møllmann, K.-M. Early diagnosis of gastric cancer: The possibility of delimiting high risk groups. *Danish Medical Bulletin* 28, 89-92. 1981.
- Møllmann, K.-M. Endoscopic service for general practice. *Danish Medical Bulletin* 28, 96-99. 1981.
- Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M. & Hamilton, W. (2013) The risk of oesophago-gastric cancer in symptomatic patients in primary care: a large case-control study using electronic records. *British Journal of Cancer*, 108: 25-31.
- Stellon, A. J. and Kenwright, S. E. Iron deficiency anaemia in general practice: Presentations and investigations. *British Journal of Clinical Practice* 51[2], 78-80. 1997.
- Thomson, A.B.R., Barkun, A.N., Armstrong, D., Chiba, N., White, R.J., Daniels, S., Escobedo, S., Chakraborty, B., Sinclair, S. The prevalence of clinically significant endoscopic findings in primary care patients with uninvestigated dyspepsia: The Canadian Adult Dyspepsia Empiric Treatment-Prompt Endoscopy (CADET-PE) study. *Alimentary Pharmacology and Therapeutics* 17, 1481-1491. 2003.
- Tosetti, C.; Bellentani, S.; Benedetto, E.; Ubaldi, E.; Cardin, F.; Bozzani, A. (2010). The management of patients with new onset of upper gastro-intestinal symptoms in primary care. *Digestive and Liver Disease*, 42: 860-864.
- Vakil, N., Talley, N., van Zanten, S. V., Flook, N., Persson, T., Bjorck, E., Lind, T., and Bolling-Sternevald, E. Cost of Detecting Malignant Lesions by Endoscopy in 2741 Primary Care Dyspeptic Patients Without Alarm Symptoms. *Clinical Gastroenterology and Hepatology* 7[7], 756-761. 2009.
- Yates, J. M., Logan, E. C., and Stewart, R. M. Iron deficiency anaemia in general practice: clinical outcomes over three years and factors influencing diagnostic investigations. *Postgraduate Medical Journal* 80[945], 405-410. 2004.

Excluded studies (with excl reason)

- (2003) Information from your family doctor. Dyspepsia. *American Family Physician*, 68: 2040-2041.
Narrative review
- (2010) Information from your family doctor. Dyspepsia: what it is and what to do about it. *American Family Physician*, 82: 1459-1460.
Narrative review
- Abahussain, E. A., Hasan, F. A. & Nicholls, P. J. (1998) Dyspepsia and Helicobacter pylori infection: Analysis of 200 Kuwaiti patients referred for endoscopy. *Annals of Saudi Medicine*, 18: 502-505.
Not in PICO
- Abdel-Wahab, M., Attallah, A. M., Elshal, M. F., Eldousoky, I., Zalata, K. R., el-Ghawalby, N. A., Gad el-Hak, N., el-Ebidy, G. & Ezzat, F. (1996) Correlation between endoscopy, histopathology, and DNA flow cytometry in patients with gastric dyspepsia. *Hepato-Gastroenterology*, 43: 1313-1320.
Not in PICO
- Adler, A. C., Cestero, C., Lewis, E. H., III, Roberts, I. M. & Castillo, E. A. (2011) Composite adenocarcinoma and carcinoid gastric tumor in chronic atrophic gastritis and pernicious anemia. *Case Reports Gastroenterology*, 5: 232-238.
Not in PICO
- Afridi, S. P., Bano, F. & Shafiq, u. R. (2011) Pattern and presentation of carcinoma stomach. *Journal of the College of Physicians and Surgeons Pakistan*, 21: 161-163.
Not in PICO
- Ahlgren, J. D. (2001) Gastrointestinal malignancies. *Primary Care - Clinics in Office Practice*, 28: 647-660.
Narrative review
- Akasbi, Y., Bouyahia, N., Oualla, K., Benhammane, H., Daoudi, K., Benbrahim, Z., Brahmi, S., El, M. F., Arifi, S., Maazaz, K., Ibrahim, A., Tizniti, S., Amarti, A., Ait, T. K. & El, M. O. (2010) Primary signet ring cell carcinoma of stomach about 16 cases. *Annals of Oncology*, 21: vi113.
Not in PICO
- Akhtar, A. J. & Shaheen, M. A. (2004) Dyspepsia in African-American and Hispanic patients. *Journal of the National Medical Association*, 96: 635-640.
Not in PICO
- Alexandrino, P., Baptista, A. S. & Pinto, C. J. (1980) Early gastric cancer. Review of 42 cases. *Acta Medica Portuguesa*, 2: 3-11.
Not in PICO
- Allum, W. H., Hallissey, M. T., Dorrell, A., Low, J. & Fielding, J. W. (1986) Programme for early detection of gastric cancer. *British Medical Journal Clinical Research Ed.*, 293: 541.
Same data as Hallissey (included).
- Allum, W. H., Blazeby, J. M., Griffin, S. M., Cunningham, D., Jankowski, J. A. & Wong, R. (2011) Guidelines for the management of oesophageal and gastric cancer. *Gut*, 60: 1449-1472.
Guideline
- Almofleh, I. A. (1992) Gastric-Cancer in Upper Gastrointestinal Endoscopy Population - Prevalence and Clinicopathological Characteristics. *Annals of Saudi Medicine*, 12: 548-551.
Not in PICO
- Amin, I., Steer, P. & Madhotra, R. (2009) Appropriateness of the "straight to test" gastroscopy request for patients with suspected gastrointestinal cancers. *Gut*, 58: A150.
Not in PICO
- An, J. W., Cheung, D. Y., Seo, M. W., Lee, H. J., Lee, I. K., Kim, T. J., Kim, J. I. & Kim, J. K. (2013) [A case of spindle cell carcinoma of the stomach presenting with hematochezia and weight loss due to fistulous tract formation with colon]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 62: 126-130.
Not in PICO

- Anderson, W. D., III & Strayer, S. M. (2013) Evaluation of nausea and vomiting: a case-based approach. *American Family Physician*, 88: 371-379.
Narrative review
- Andrade, B., Alvarado, L., Zurita, M. & Andrade, S. (2013) Early and advanced gastric cancer: Clinical, endoscopy, histopathology and comparative study. *Journal of Gastroenterology and Hepatology*, 28: 652-653.
Not in PICO
- Ansari, S. & Ford, A. C. (2013) Initial management of dyspepsia in primary care: An evidence-based approach. *British Journal of General Practice*, 63: 498-499.
Narrative review
- Antic, V., Micev, M., Baskic, D. & Mladenovic, V. (2014) - Giant liver hemangioma in patient with ileal gastrointestinal stromal tumor. - *Medicinski Pregled*, 67: 55-59.
Not in PICO
- Ares, D. M., Aguirre, P. A. A., Barrenechea, I. M. G., Gomez, L. C. & Peral, A. P. (2008) Usefulness of ultrasonography in diagnosing patients suspect for digestive tract neoplasms. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 100: 545-551.
Not in PICO
- Armstrong, D., Marshall, J. K., Chiba, N., Enns, R., Fallone, C. A., Fass, R., Hollingworth, R., Hunt, R. H., Kahrilas, P. J., Mayrand, S., Moayyedi, P., Paterson, W. G., Sadowski, D. & Veldhuyzen van Zanten, S. J. O. (2005) Canadian Consensus Conference on the management of gastroesophageal reflux disease in adults - Update 2004. *Canadian Journal of Gastroenterology*, 19: 15-35.
Guideline
- Arruda, S. M. B., Juca, N. T., Oliveira, E. P., Macedo, F. M., Albuquerque, M. C. & Pereira, M. G. (1997) Profile of gastric cancer at the University Hospital of the Federal University of Pernambuco. [Portuguese]. *GED - Gastrenterologia Endoscopia Digestiva*, 16: 14-18.
Not in PICO
- Axon, A. (2002) Management of uninvestigated dyspepsia: review and commentary. *Gut*, 50: 51-55.
Narrative_review
- Axon, A. (2006) Symptoms and diagnosis of gastric cancer at early curable stage. [Review] [37 refs]. *Best Practice & Research in Clinical Gastroenterology*, 20: 697-708.
Narrative_review
- Axon, A. T. R. (1997) Chronic dyspepsia: Who needs endoscopy? *Gastroenterology*, 112: 1376-1380.
Narrative_review
- Baako, B. N. & Darko, R. (1996) Incidence of Helicobacter pylori infection in Ghanaian patients with dyspeptic symptoms referred for upper gastrointestinal endoscopy. *West African Journal of Medicine*, 15: 223-227.
Not in PICO
- Bai, Y., Li, Z. S., Zou, D. W., Wu, R. P., Yao, Y. Z., Jin, Z. D., Ye, P., Li, S. D., Zhang, W. J., Du, Y. Q., Zhan, X. B., Liu, F., Gao, J. & Xu, G. M. (2010) Alarm features and age for predicting upper gastrointestinal malignancy in Chinese patients with dyspepsia with high background prevalence of Helicobacter pylori infection and upper gastrointestinal malignancy: an endoscopic database review of 102 665 patients from 1996 to 2006. *Gut*, 59: 722-728.
Pat Not in PICO
- Bakari, A. A., Ibrahim, A. G., Gali, B. M., Dogo, D. & Nggada, H. A. (2010) Pattern of gastric cancer in north-eastern Nigeria: A clinicopathological study. *Journal of Chinese Clinical Medicine*, 5: 211-215.
Not in PICO
- Ballinger, A. (2007) Gastroenterology and anaemia. *Medicine*, 35: 142-146.
Narrative review
- Barenys De, L. M., Rota, R., Moreno, V., Villafafila, R., Garcia-Bayo, I., Abad, A., Pons, J. M. V. & Pique, J. M. (2003) Prospective validation of a clinical scoring system for the diagnosis of organic

- dyspepsia. [Spanish]. *Medicina Clinica*, 121: 766-771.
Not in PICO
- Bazaldúa, O. V. & Schneider, F. D. (1987) Evaluation and management of dyspepsia. [Review] [44 refs]. *American Family Physician*, 60: 1773-1784.
Narrative review
- Belcastro, G., Ferri, M., Chiavellati, L., Nicolanti, V. & Schillaci, A. (1988) Early gastric cancer. *Italian Journal of Surgical Sciences*, 18: 227-232.
Not in PICO
- Berrill, J. W., Turner, J., Hurley, J., Swift, J., Dolwani, S. & Green, J. T. (2011) Referral criteria for open access gastroscopy: Do they inevitably delay the diagnosis of cancer? *Gut*, 60: A101-A102.
Not in PICO
- Besherdas, K., Oben, J. A., Beck, E., Vicary, F. R. & Wong, V. S. (2000) What proportion of dyspeptic patients having H. pylori breath test subsequently undergo endoscopy? *Journal of the Royal College of Physicians of London*, 34: 552-554.
Not in PICO
- Bianchi, A., Sunol, J., Hidalgo, L. A., Diloy, R., Castellvi, J. M., Gorgas, F., Soler, T., Muns, R. & Gubern, J. M. (1998) Upper digestive tract dyspepsia and early gastric cancer. *Revista Espanola de Enfermedades Digestivas*, 90: 639-645.
Not in PICO
- Bleyer, A. (2009) CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology*, 36: 207-212.
Narrative review
- Boldys, H., Marek, T. A., Wanczura, P., Matusik, P. & Nowak, A. (2003) Even young patients with no alarm symptoms should undergo endoscopy for earlier diagnosis of gastric cancer. *Endoscopy*, 35: 61-67.
Not in PICO
- Borch, K. (1986) Epidemiologic, clinicopathologic, and economic aspects of gastroscopic screening of patients with pernicious anemia. *Scandinavian Journal of Gastroenterology*, 21: 21-30.
Not in PICO
- Boregowda, U. N. & Hammoud, I. O. (2012) A rare gastrointestinal tumor. *American Journal of Gastroenterology*, 107: S65.
Not in PICO
- Borsch, G., Coenen, C., Zumbobel, V. & Theus, T. (1986) Retrospective study of gastric carcinoma in 201 patients: Factors related to outcome. *Digestive Surgery*, 3: 7-14.
Not in PICO
- Bowrey, D. J., Clark, G. W. B., Rees, B. I., Williams, G. T. & Carey, P. D. (1999) Outcome of oesophagogastric carcinoma in young patients. *Postgraduate Medical Journal*, 75: 22-26.
Not in PICO
- Bovio, G., Fonte, M. L. & Baiardi, P. (2014) Prevalence of upper gastrointestinal symptoms and their influence on nutritional state and performance status in patients with different primary tumors receiving palliative care. *American Journal of Hospice & Palliative Medicine*, 31: 20-26.
Not in PICO
- Bowrey, D. J., Griffin, S. M., Wayman, J., Karat, D., Hayes, N. & Rames, S. A. (2006) Use of alarm symptoms to select dyspeptics for endoscopy causes patients with curable esophagogastric cancer to be overlooked. *Surgical Endoscopy*, 20: 1725-1728.
Not in PICO
- Bramble, M. G., Suvakovic, Z. & Hungin, A. P. (2000) Detection of upper gastrointestinal cancer in patients taking antisecretory therapy prior to gastroscopy. *Gut*, 46: 464-467.
Not in PICO

- Bresky, G., Mata, A., Llach, J., Ginis, M. A., Pellisi, M., Soria, M. T., Fernandez-Esparrach, G., Mondelo, F. & Bordas, J. M. (2003) Endoscopic findings in a biennial follow-up program in patients with pernicious anemia. *Hepato-Gastroenterology*, 50: 2264-2266.
Not in PICO
- Breslin, N. P., Thomson, A. B. R., Bailey, R. J., Blustein, P. K., Meddings, J., Lalor, E., VanRosendaal, G. M. A., Verhoef, M. J. & Sutherland, L. R. (2000) Gastric cancer and other endoscopic diagnoses in patients with benign dyspepsia. *Gut*, 46: 93-97.
Not in PICO
- Brignoli, R., Merki, H., Miazza, B. & Beglinger, C. (1994) Endoscopic Findings in Volunteers and in Patients with Dyspepsia. *Schweizerische medizinische Wochenschrift*, 124: 1240-1247.
Not in PICO
- Broe, M., Barry, M., Patchett, S. & Hill, A. D. (2013) Evaluating the clinical efficacy and cost effectiveness of direct access endoscopy. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 11: 304-308.
Not in PICO
- Bundhoo, K., Aravinthan, A., Lithgo, K., Price, T. & Johnson, M. (2014) Cost efficiency of faecal calprotectin in assessing new referrals with altered bowel habit. *Gut*, 63: A81.
Not in PICO
- Bytzer, P. & Schaffalitzky de Muckadell, O. B. (1992) Prediction of major pathologic conditions in dyspeptic patients referred for endoscopy. A prospective validation study of a scoring system. *Scandinavian Journal of Gastroenterology*, 27: 987-992.
Not in PICO
- Calvo, A., Galleguillos, B. J., Baez, S., Diaz, A., Pruyas, M., Nilsen, E. M., Aguayo, G., Villarroel, L., Dominguez, A. & Ferreccio, C. (2011) Results of a population-based gastric cancer screening program conducted in Chile 1996-2008. *Gastroenterology*, 140: S419.
Not in PICO
- Cann, P. A., Gleeson, M. H., Robinson, T. J. & Wicks, A. C. B. (1994) Assessing dyspepsia in general practice. *British Journal of Clinical Practice*, 48: 263-267.
Narrative review
- Cardin, F., Zorzi, M. & Terranova, O. (2007) Implementation of a guideline versus use of individual prognostic factors to prioritize waiting lists for upper gastrointestinal endoscopy. *European Journal of Gastroenterology & Hepatology*, 19: 549-553.
Not in PICO
- Carlsson, L., Hakansson, A. & Nordenskjold, B. (2001) Common cancer-related symptoms among GP patients: Opportunistic screening in primary health care. *Scandinavian Journal of Primary Health Care*, 19: 199-203.
Not in PICO
- Carmalt, H. L., Gillett, D. J. & Lin, B. P. (1990) Early gastric cancer. *Australian & New Zealand Journal of Surgery*, 60: 865-869.
Not in PICO
- Carter, K. J., Schaffer, H. A. & Ritchie, J. (1984) Early gastric cancer. *Annals of Surgery*, 199: 604-609.
Not in PICO
- Casburn-Jones, A. C., Murray, L. S., Gillen, D. & McColl, K. E. (2006) Endoscopy has minimal impact on mortality from upper gastrointestinal cancer in patients older than 55 years with uncomplicated dyspepsia. *European Journal of Gastroenterology & Hepatology*, 18: 645-648.
Not in PICO
- Chang, F.-Y., Lee, O. & Lee, S. D. (1994) Coexistent duodenal ulcer among patients with gastric carcinoma. *South African Medical Journal*, 84: 618-621.
Not in PICO
- Chaves, D. M., Iriya, K., Filho, F. M., Tomishige, T., Sakai, P. & Ishioka, S. (1997) Gastric adenoma: Endoscopic and histological aspects, and general considerations. [Portuguese]. *GED* -

- Gastroenterologia Endoscopia Digestiva*, 16: 119-123.
Not in PICO
- Chey, W. D., Wong, B. C. & Practice Parameters Committee of the American College of Gastroenterology (2007) American College of Gastroenterology guideline on the management of *Helicobacter pylori* infection. *American Journal of Gastroenterology*, 102: 1808-1825.
Guideline
- Chiang, I.-P., Wang, H.-H., Cheng, A.-L., Lin, J.-T. & Su, I.-J. (1996) Low-grade gastric B-cell lymphoma of mucosa-associated lymphoid tissue: Clinicopathologic analysis of 19 cases. *Journal of the Formosan Medical Association*, 95: 857-865.
Not in PICO
- Cho, A., Chaudhry, A., Minsky-Primus, L., Tso, A., Perez-Perez, G., Diehl, D., Marcus, S. G. & Gany, F. M. (2006) Acceptance of repeat esophagogastroduodenoscopy to detect gastric cancer in a Chinese immigrant cohort. *Journal of Clinical Gastroenterology*, 40: 606-611.
Not in PICO
- Christie, J., Shepherd, N. A., Codling, B. W. & Valori, R. M. (1997) Gastric cancer below the age of 55: implications for screening patients with uncomplicated dyspepsia. *Gut*, 41: 513-517.
- Chu, J.-S., Yang, K.-C., Hsu, T.-C., Kao, C.-R., Chou, S.-Y. & Shih, S.-C. (1993) Concomitant digestive malignancy in pregnancy. *Chinese Journal of Gastroenterology*, 10: 1-8.
Not in PICO
- Cift, T., Aydogan, B., Akbas, M., Aydin, B., Demirkiran, F., Bakkaloglu, D. V. & Ilvan, S. (2011) Case report: gastric carcinoma diagnosed at the second trimester of pregnancy. *Case Reports in Obstetrics and Gynecology*, 2011: 532854.
Not in PICO
- Colarossi, A., Inga, R., Prochazka, R., Reyes, U., Bussalleu, A. & Barua, R. L. (2011) [Pepsinogen and gastrin in the noninvasive diagnosis of gastric atrophy. A case-control study in Peruvian population]. [Spanish]. *Revista de Gastroenterologia del Peru*, 31: 110-115.
Not in PICO
- Craanen, M. E., Dekker, W., Blok, P., Ferwerda, J. & Tytgat, G. N. (1992) Time trends in gastric carcinoma: changing patterns of type and location. *American Journal of Gastroenterology*, 87: 572-579.
Not in PICO
- Craven, J. L. (1991) Gastric cancer. *Current Opinion in Gastroenterology*, 7: 933-938.
Narrative review
- Crean, G. P., Holden, R. J., Knill-Jones, R. P., Beattie, A. D., James, W. B., Marjoribanks, F. M. & Spiegelhalter, D. J. (1994) A database on dyspepsia. *Gut*, 35: 191-202.
Not in PICO
- Cristina, O. M. & Sundblad, A. S. (1993) [Gastric cancer. Clinico-pathological characteristics and expression of c-erbB-2 oncogene in 122 cases]. [Spanish]. *Medicina*, 53: 97-102.
Not in PICO
- Crosta, C., Gobbi, V., Crestani, B., Polizzi, P., Vasicuro, M. & Contessini, A. E. (1991) [Early gastric carcinoma: short and long term results of surgical treatment]. [Italian]. *Giornale di Chirurgia*, 12: 493-497.
Not in PICO
- Csendes, A., Braghetto, I., Smok, G., Nava, O. & Medina, E. (1992) [A cooperative study on early and intermediate gastric cancer: clinical, diagnostic and therapeutic aspects]. [Spanish]. *Revista Medica de Chile*, 120: 397-406.
Not in PICO
- da Silva, J. B., Mauricio, S. F., Bering, T. & Correia, M. I. (2013) The relationship between nutritional status and the Glasgow prognostic score in patients with cancer of the esophagus and stomach. *Nutrition & Cancer*, 65: 25-33.
Not in PICO

- Daker, C., Kalkan, C. G., Belman, D., Van Someren, N. M. & Besherdas, K. (2011) Straight to endoscopy triage saves significant time for cancer diagnosis. *Gastroenterology*, 140: S566.
Not in PICO
- Dakubo, J. C., Clegg-Lampsey, J. N. & Sowah, P. (2011) Appropriateness of referrals for upper gastrointestinal endoscopy. *West African Journal of Medicine*, 30: 342-347.
Not in PICO
- de Dombal, F. T., Price, A. B., Thompson, H., Williams, G. T., Morgan, A. G., Softley, A., Clamp, S. E. & Unwin, B. J. (1990) The British Society of Gastroenterology early gastric cancer/dysplasia survey: an interim report. *Gut*, 31: 115-120.
Not in PICO
- De, L. S., Covarelli, P., Borgognoni, F., Lepri, P., Carlini, G. F., Lagrutta, A. & Dominici, C. (1990) [Our experience with early gastric cancer]. [Italian]. *Minerva Chirurgica*, 45: 1133-1136.
Not in PICO
- Debrinas, J. M. P. L. (1993) Early Gastric-Cancer at A University Hospital in Barcelona During 1981-1990 - Clinical-Features. *Revista Espanola de Enfermedades Digestivas*, 84: 90-94.
Not in PICO
- Delaney, B. C. (1998) Why do dyspeptic patients over the age of 50 consult their general practitioner? A qualitative investigation of health beliefs relating to dyspepsia. *British Journal of General Practice*, 48: 1481-1485.
Not in PICO
- Della, B., V, Saroglia, G., Fontana, D., Leli, R., Polimeni, D., Carelli-Basile, A. & Seglie, E. (1996) Early gastric cancer at IA stage. Analysis of a recent series. [Italian]. *Chirurgia*, 9: 25-27.
Not in PICO
- Deltenre, M. (2000) [Dyspepsia in general medicine: current diagnostic approach]. [Review] [16 refs] [French]. *Revue Medicale de Bruxelles*, 21: A309-A313.
Narrative review
- Diaz-Zorrilla, C., Grube-Pagola, P., Remes-Troche, J. M. & Ramos-De la Medina, A. (2012) Glomus tumour of the stomach: an unusual cause of gastrointestinal bleeding. *BMJ Case Reports*, 2012, 2012.
Not in PICO
- Diaz, J., Plasencia, Yan, E., Quiroz, Burgos, O., Chavez, Balmaceda, T., Fraselle, Patron, G., Rios, Santillan, J. & Medina (2002) Clinic-pathologic pattern and survival range in resectable gastric carcinoma. [Spanish]. *Revista de gastroenterologia del Peru : organo oficial de la Sociedad de Gastroenterologia del Peru*, 22: 19-27.
Not in PICO
- Dickerson, L. M. & King, D. E. (2004) Evaluation and management of nonulcer dyspepsia. *American Family Physician*, 70: 107-114.
Narrative review
- Diez, D. V., I, Pe, R. D., V, Barrenetxea, A. J., Loureiro, G. C., Ruiz, C. S., Garcia, C. M., Del, H. A., I, Bilbao Axpe, J. E. & Mendez Martin, J. J. (2012) Gastric cancer in the remnant stomach after salmon-type gastric bypass. *Obesity Surgery*, 22: 1196.
Not in PICO
- Dobru, D., Pascu, O., Tantau, M., Gheorghe, C., Goldis, A., Balan, G., Coman, F., Fraticiu, A., Dumitru, E., Mutescu, E., Saftoiu, A. & Bacarea, V. (2004) An epidemiological study of gastric cancer in the adult population referred to gastroenterology medical services in Romania -- a multicentric study. *Romanian Journal of Gastroenterology*, 13: 275-279.
Not in PICO
- Du, X. (1982) Analysis of 37 operated cases misdiagnosed as carcinoma of esophagus or cardia. [Chinese]. *Chinese Journal of Oncology*, 4: 48-50.
Not in PICO

- Durrani, A. A., Yaqoob, N., Abbasi, S., Siddiq, M. & Moin, S. (2009) Pattern of upper gastro intestinal malignancies in northern Punjab. *Pakistan Journal of Medical Sciences*, 25: 302-307.
Not in PICO
- Edgren, G., Bagnardi, V., Bellocco, R., Hjalgrim, H., Rostgaard, K., Melbye, M., Reilly, M., Adami, H. O., Hall, P. & Nyren, O. (2010) Pattern of declining hemoglobin concentration before cancer diagnosis. *International Journal of Cancer*, 127: 1429-1436.
Not in PICO
- Eguchi, T., Takahashi, Y., Yamagata, M., Kasahara, M. & Fujii, M. (1999) Gastric cancer in young patients. *Journal of the American College of Surgeons*, 188: 22-26.
Not in PICO
- Eitner, K., Bosseckert, H., Koppe, P., Fritze, C., Kuhne-Heid, R. & Machnik, G. (1985) [Early stomach cancer in our clinical sample]. [German]. *Deutsche Zeitschrift fur Verdauungs- und Stoffwechselkrankheiten*, 45: 141-148.
Not in PICO
- Eo, W. K. (2008) Breast cancer metastasis to the stomach resembling early gastric cancer. *Cancer Research & Treatment*, 40: 207-210.
Not in PICO
- Erstad, B. L. (2002) Dyspepsia: initial evaluation and treatment. *Journal of the American Pharmaceutical Association*, 42: 460-468.
Not in PICO
- Espejo, R. H. & Navarrete, S. J. (2005) [Gastric Cancer in Early Stage: study of 371 lesions in 340 patients in the E. Rebagliati National, Lima-Peru]. [Review] [75 refs] [Spanish]. *Revista de Gastroenterologia del Peru*, 25: 48-75.
Not in PICO
- Falt, P., Hanousek, M., Kundratova, E. & Urban, O. (2013) [Precancerous conditions and lesions of the stomach]. [Czech]. *Klinicka Onkologie*, 26: Suppl-8.
Narrative review
- Fashner, J. & Gitu, A. C. (2013) Common Gastrointestinal Symptoms: dyspepsia and Helicobacter pylori. [Review]. *Fp Essentials*, 413: 24-28.
Narrative review
- Fernandez Salazar, L. I., Alvarez, G. T., Sanz, R. A., Velayos, J. B., Aller, d. I. F. & Gonzalez Hernandez, J. M. (2007) [Gastrointestinal stromal tumors (GISTs): clinical aspects]. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 99: 19-24.
Not in PICO
- Ferrara, F., Franceschet, I., Rigoli, R., Pascoli, S., Slongo, T., Dal, B. N., Caroli, A., Marcello, R., Scarpignato, C., Schiavinato, A. & Di, M. F. (2013) Gastropanel, a non-invasive, safe endoscopy method: A prospective 1000 patients study in primary care setting. *Digestive and Liver Disease*, 45: S157.
Not in PICO
- Ferrara, F., Dal, B. N., Furlanetto, A., Dei Tos, A. P., Slongo, T., Loperfido, S., Heras, S. H., Scarpignato, C. & Rugge, M. (2013) Gastropanel and olga: Two innovative tools for the detection of atrophic gastritis. A prospective study in primary care. *Digestive and Liver Disease*, 45: S156-S157.
Not in PICO
- Ferrarese, S. & Margari, A. (1980) Early diagnosis of the gastric cancer. A proposal for mass-screening. [Italian]. *Folia Oncologica*, 3: 10-15.
Narrative review
- Fielding, J. W., Ellis, D. J., Jones, B. G., Paterson, J., Powell, D. J., Waterhouse, J. A. & Brookes, V. S. (1980) Natural history of "early" gastric cancer: results of a 10-year regional survey. *British Medical Journal*, 281: 965-967.
Not in PICO

- Ford, A. C. & Moayyedi, P. (2009) Should we step-up or step-down in the treatment of new-onset dyspepsia in primary care? *Polskie Archiwum Medycyny Wewnetrznej-Polish Archives of Internal Medicine*, 119: 391-396.
Narrative review
- Frank-Stromborg, M. (1989) The epidemiology and primary prevention of gastric and esophageal cancer. A worldwide perspective. *Cancer Nursing*, 12: 53-64.
Narrative review
- Freitas, D., Gouveia, H., Sofia, C., Cabral, J. P. & Donato, A. (1995) Endoscopic Nd-YAG laser therapy as palliative treatment for esophageal and cardiac cancer. *Hepato-Gastroenterology*, 42: 633-637.
Not in PICO
- Fric, P., Ronsky, R. & Huslarova, A. (1986) [Early diagnosis of cancer of the stomach. Groups at risk for the disease]. [Czech]. *Sbornik Lekarsky*, 88: 289-298.
Narrative review/ Not in PICO
- Froehlich, F., Bochud, M., Gonvers, J. J., Dubois, R. W., Vader, J. P., Wietlisbach, V. & Burnand, B. (1999) 1. Appropriateness of gastroscopy: dyspepsia. [Review] [167 refs]. *Endoscopy*, 31: 579-595.
Narrative review
- Fujiwara, T., Hirose, S., Hamazaki, K., Iwagaki, H., Mano, K. & Orita, K. (1996) Clinicopathological features of gastric cancer in the remnant stomach. *Hepato-Gastroenterology*, 43: 416-419.
Patients_not_relevant_to_PICO
- Funk, L., Hartmann, D., Apel, D., Spiethoff, A., Schiele, R., Schilling, D., Adamek, H. E. & Riemann, J. F. (2003) Symptomatic pericardial effusion as initial manifestation of gastric signet ring carcinoma. *Deutsche Medizinische Wochenschrift*, 128: 870-873.
Not in PICO
- Furtado, W., Mello, D., Santos, V., Bringel, T., Oliveira, J. W. & Moura, H. (2013) [Gastric lipoma and pyloric obstruction in a 51-year-old woman]. [Spanish]. *Anales del Sistema Sanitario de Navarra*, 36: 145-148.
Not in PICO
- Furuhashi, S., Takamori, H., Abe, S., Nakahara, O., Tanaka, H., Horino, K., Beppu, T., Iyama, K. & Baba, H. (2011) Solid-pseudopapillary pancreatic tumor, mimicking submucosal tumor of the stomach: A case report. *World Journal of Gastrointestinal Surgery*, 3: 201-203.
Not in PICO
- Galvez-Munoz, E., Gallego-Plazas, J., Gonzalez-Orozco, V., Menarguez-Pina, F., Ruiz-Macia, J. A. & Morcillo, M. A. (2009) Hepatoid adenocarcinoma of the stomach - a different histology for not so different gastric adenocarcinoma: a case report. *International Seminars in Surgical Oncology*, 6: 13.
Not in PICO
- Garcia Marcilla, J. A., Parrilla, P. P., Sanchez, B. F., Martinez de Haro, L. F., Molina, M. J. & Bermejo, L. J. (1990) [Early cancer of the stomach. Review of 29 cases]. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 77: 317-321.
Not in PICO
- Garcia Rodriguez, L. A., Lagergren, J. & Lindblad, M. (2006) Gastric acid suppression and risk of oesophageal and gastric adenocarcinoma: a nested case control study in the UK. *Gut*, 55: 1538-1544.
Not in PICO
- Gavazzi, C., Colatruoglio, S., Sironi, A., Mazzaferro, V. & Miceli, R. (2011) Importance of early nutritional screening in patients with gastric cancer. *British Journal of Nutrition*, 106: 1773-1778.
Not in PICO
- Geboes, K., De, J. E., Rutgeerts, P. & Vantrappen, G. (1988) Symptomatic gastrointestinal metastases from malignant melanoma. A clinical study. *Journal of Clinical Gastroenterology*, 10: 64-70.
Not in PICO

- Gencer, D., Kastle-Larralde, N., Pilz, L. R., Weiss, A., Buchheidt, D., Hochhaus, A. & Hofheinz, R. D. (2009) Presentation, Treatment, and Analysis of Prognostic Factors of Terminally ill Patients with Gastrointestinal Tumors. *Onkologie*, 32: 380-386.
Not in PICO
- Genovese, F., Becchina, G., Nagar, C., Ottoveggio, G., Giacalone, B., Scaglione, G., Varriale, E. & Tralongo, V. (2014) - Primary diffuse large B-cell lymphoma developing within a rectal tubular adenoma with low-grade dysplasia: a case report. - *Journal of Medical Case Reports [Electronic Resource]*, 8: 103.
Not in PICO
- George, J., Johnson, D. K., Rajan, R. A., Kolassery, S. & Thazhath, R. M. (2013) An unusual presentation of carcinoma stomach. *The Pan African medical journal*, 14: 84.
Narrative review
- Gillen, D. & Mccoll, K. E. L. (1999) Does concern about missing malignancy justify endoscopy in uncomplicated dyspepsia in patients aged less than 55? *American Journal of Gastroenterology*, 94: 75-79.
Not in PICO
- Gisbert, J. P., Calvet, X., Ferrandiz, J., Mascort, J., Alonso-Coello, P. & Marzo, M. (2012) Clinical practice guideline on the management of patients with dyspepsia. Update 2012. [Spanish]. *Gastroenterologia y Hepatologia*, 35: 725.
Guideline
- Goh, K. L. (2011) Clinical and epidemiological perspectives of dyspepsia in a multiracial Malaysian population. *Journal of Gastroenterology & Hepatology*, 26: Suppl-8.
Narrative review
- Golabek-Dropiewska, K., Kardel-Reszkewicz, E., Hac, S., Pawlowska, A. & Sledzinski, Z. (2009) Double gastrointestinal stromal tumour (GIST) of the stomach. *BMJ Case Reports*, 2009, 2009.
Not in PICO
- Goldstein, F., Kline, T. S., Kline, I. K., Thornton, J. J., III, Abramson, J. & Bell, L. (1983) Early gastric cancer in a United States hospital. *American Journal of Gastroenterology*, 78: 715-719.
Not in PICO
- Gordon, V. M., Madhotra, R. & Steer, P. (2011) A single centre experience of straight to test suspected ugi cancer service. *Gut*, 60: A250-A251.
Not in PICO
- Graham, D. Y., Rakel, R. E., Fendrick, A. M., Go, M. F., Marshall, B. J., Peura, D. A. & Scherger, J. E. (121) Recognizing peptic ulcer disease. Keys to clinical and laboratory diagnosis. [Review] [31 refs]. *Postgraduate Medicine*, 105: 113-116.
Narrative review
- Guirguis, E. M. (1989) Gastric cancer in primary care: how hard should you look? *Canadian Family Physician*, 35: 243-248.
Narrative review
- Gurzu, S., Copotoiu, C., Azamfirei, L. & Jung, I. (2013) A Caliber Persistent Artery (Dieulafoy's Lesion) which is Associated with an Early-Stage Gastric Stump Cancer Following a Distal Gastrectomy. *Journal of Clinical and Diagnostic Research JCDR*, 7: 1717-1719.
Not in PICO
- Habibi, H., Majumder, S., Bagavathy, K. & Dasanu, C. (2012) Diffuse signet-ring cell gastric adenocarcinoma 'linitis plastica' and pernicious anemia: A rare association. *American Journal of Gastroenterology*, 107: S288-S289.
Not in PICO
- Hafeez, M., Salamat, A., Saeed, F., Zafar, H., Hassan, F. & Farooq, A. (2011) Endoscopic findings and treatment outcome in cases presenting with dysphagia. *Journal of Ayub Medical College, Abbottabad: JAMC*, 23: 46-48.
Not in PICO

- Hallissey, M. T., Dunn, J. A. & Fielding, J. W. (1994) Evaluation of pepsinogen A and gastrin-17 as markers of gastric cancer and high-risk pathologic conditions. *Scandinavian Journal of Gastroenterology*, 29: 1129-1134.
Not in PICO
- Harmon, R. C. & Peura, D. A. (2010) Evaluation and management of dyspepsia. *Therapeutic Advances in Gastroenterology*, 3: 87-98.
Narrative review
- Harrison, J. D., Morris, D. L. & Hardcastle, J. D. (1993) Screening for gastric carcinoma in coal miners. *Gut*, 34: 494-498.
Not in PICO
- Harrison, J. D., Steele, R. J. C., Morris, D. L. & Hardcastle, J. D. (2001) Screening for gastric cancer: Endoscopic investigation of dyspeptic subjects identified by postal questionnaire. *GI Cancer*, 3: 335-342.
Not in PICO
- Hartley, L., Evans, E., Dickey, D. & Van, D. A. (1985) Early gastric cancer. *Australian & New Zealand Journal of Surgery*, 55: 341-346.
Not in PICO
- Hataji, K., Ami, K., Nagahama, T., Ohara, T., Ganno, H., Kawasaki, N., Fukuda, A., Ando, M., Arai, K. & Tei, S. (2009) A case of unresectable cardiac gastric cancer patient who maintained a long-term QOL with chemotherapy and detention of metallic stent. [Japanese]. *Japanese Journal of Cancer and Chemotherapy*, 36: 2290-2293.
Not in PICO
- Hedenbro, J. L., Ekelund, M. & Wetterberg, P. (1991) Endoscopic diagnosis of submucosal gastric lesions. The results after routine endoscopy. *Surgical Endoscopy*, 5: 20-23.
Not in PICO
- Heughan, C., Kepkay, D., Cruz, A. M. & Idikio, H. (1982) Early gastric cancer. *Canadian Journal of Surgery*, 25: 83-85.
Not in PICO
- Hicks, S. (2001) Gastric cancer: diagnosis, risk factors, treatment and life issues. [Review] [36 refs]. *British Journal of Nursing*, 10: 529-536.
Narrative review
- Hirakawa, K., Adachi, K., Amano, K., Katsube, T., Ishihara, S., Fukuda, R., Yamashita, Y., Shiozawa, S., Watanabe, M. & Kinoshita, Y. (1999) Prevalence of non-ulcer dyspepsia in the Japanese population. *Journal of Gastroenterology and Hepatology*, 14: 1083-1087.
Not in PICO
- Ho, M. S., Chui, P. S., Teh, L. B., Low, C. H. & Hoe, S. (1989) Early gastric cancer in Singapore. *Annals of the Academy of Medicine, Singapore*, 18: 63-68.
Not in PICO
- Hosseini, S. N., Mousavinasab, S. N., Moghimi, M. H. & Fallah, R. (2007) Delay in diagnosis and treatment of gastric cancer: from the beginning of symptoms to surgery--an Iranian study. *Turkish Journal of Gastroenterology*, 18: 77-81.
Not in PICO
- Houghton, P. W., Mortensen, N. J., Allan, A., Williamson, R. C. & Davies, J. D. (1985) Early gastric cancer: the case for long term surveillance. *British Medical Journal Clinical Research Ed.*, 291: 305-308.
Not in PICO
- Hsu, Y. C., Yang, T. H., Liou, J. M., Hsu, W. L., Lin, H. J., Wu, H. T., Lin, J. T., Wang, H. P. & Wu, M. S. (2012) Can clinical features stratify use of endoscopy for dyspeptic patients with high background prevalence of upper gastrointestinal cancer? *Digestive and Liver Disease*, 44: 218-223.
Not in PICO

- Hu, J., Zhang, X., Li, B., Zhang, M., Wang, C. & Chen, G. (2013) The clinical value of 18F-FDG PET/CT in the evaluation of bone metastases undetermined origin. *Clinical Imaging*, 37: 922-924.
Not in PICO
- Huang, J. Y., Jiang, H. P., Chen, D. & Tang, H. L. (2011) Primary gastric signet ring cell carcinoma presenting as cardiac tamponade. *World Journal of Gastrointestinal Oncology*, 3: 67-70.
Not in PICO
- Humphreys, C., Kingston, R. D. & Robinson, C. A. (1995) Stomach cancer--is it a lost cause? *European Journal of Surgical Oncology*, 21: 159-161.
Not in PICO
- Hungin, A. P. S., Rubin, G. P., Russell, A. J. & Convery, B. (1997) Guidelines for dyspepsia management in general practice using focus groups. *British Journal of General Practice*, 47: 275-279.
Not in PICO
- Hussain, D., Zafar, H. & Raja, A. J. (2006) Gastric stromal tumors: clinical presentations, diagnosis and outcome. *Jcpsp, Journal of the College of Physicians & Surgeons - Pakistan*, 16: 696-699.
Not in PICO
- Hussain, T., Elahi, B., McManus, P., Mahapatra, T. & Kneeshaw, P. J. (2012) Gastric obstruction secondary to metastatic breast cancer: a case report and literature review. *Journal of Medical Case Reports [Electronic Resource]*, 6: 232.
Not in PICO
- Hwang, E. J., Jang, J. Y., Kim, Y. W., Dong, S. H., Kim, H. J., Kim, B. H. & Chang, Y. W. (2013) A case of early gastric cancer with solitary metastasis to the pleura. *Clinical Endoscopy*, 46: 666-670.
Not in PICO
- Ibingira, C. B. (2001) Management of cancer of the stomach in Mulago Hospital Kampala, Uganda. *East African Medical Journal*, 78: 233-237.
Not in PICO
- Ihara, E., Matsuzaka, H., Honda, K., Hata, Y., Sumida, Y., Akiho, H., Misawa, T., Toyoshima, S., Chijiwa, Y., Nakamura, K. & Takayanagi, R. (2013) Mucosal-incision assisted biopsy for suspected gastric gastrointestinal stromal tumors. *World Journal of Gastrointestinal Endoscopy*, 5: 191-196.
Not in PICO
- Imada, T., Rino, Y., Hatori, S., Shiozawa, M., Takahashi, M., Amano, T., Kondo, J., Kobayashi, O., Sairenji, M. & Motohashi, H. (2000) Clinicopathologic differences between early gastric remnant cancer and early primary gastric cancer in the upper third of the stomach. *Hepato-Gastroenterology*, 47: 1186-1188.
Not in PICO
- Inoue, K., Kamiyama, K., Nishimura, M., Fujita, H., Horiguchi, H., Tani, H., Inoue, H., Inoue, Y. & Fujita, Y. A case of end-stage cancer with pain of indeterminate cause. [References]. *International Medical Journal* 14[3], 191-193. 2007.
Not in PICO
- Irving, M. J., Lamb, P. J., Irving, R. J. & Raimes, S. A. (2002) Speeding up the diagnosis of oesophago-gastric cancer. *Nursing Times*, 98: 35-37.
Not in PICO
- James, M. W., Chen, C. M., Goddard, W. P., Scott, B. B. & Goddard, A. F. (2005) Risk factors for gastrointestinal malignancy in patients with iron-deficiency anaemia. *European Journal of Gastroenterology & Hepatology*, 17: 1197-1203.
Not in PICO
- Jatzko, G., Pertl, A. & Jagoditsch, M. (1999) Surgical therapy and results in patients with early gastric cancer. [German]. *Chirurgische Gastroenterologie mit Interdisziplinären Gesprächen*, 15: 223-226.
Narrative review
- Jones, M. P. (2003) Evaluation and treatment of dyspepsia. *Postgraduate Medical Journal*, 79: 25-29.
Narrative review

- Jung, E. S., Kwon, O., Lee, S. H., Lee, K. B., Kim, J. H., Yoon, S. H., Kim, G. M., Jeung, H. C. & Rha, S. Y. (2010) Wernicke's encephalopathy in advanced gastric cancer. *Cancer Research & Treatment*, 42: 77-81.
Not in PICO
- Kanda, T., Sato, Y., Yajima, K., Kosugi, S., Matsuki, A., Ishikawa, T., Bamba, T., Umezu, H., Suzuki, T. & Hatakeyama, K. (2011) Pedunculated gastric tube interposition in an esophageal cancer patient with prepyloric adenocarcinoma. *World Journal of Gastrointestinal Oncology*, 3: 75-78.
Not in PICO
- Kapoor, N., Bassi, A., Sturges, R. & Bodger, K. (2005) Predictive value of alarm features in a rapid access upper gastrointestinal cancer service. *Gut*, 54: 40-45.
Not in PICO
- Kapoor, S., Savlania, A., Kohli, M., Singh, T. & Kapoor, K. (2012) Prevalence of gastrointestinal cancer. *Journal of Gastroenterology and Hepatology*, 27: 334.
Not in PICO
- Karbasi, A., Karbasi-Afshar, R., Ahmadi, J. & Saburi, A. (2013) Retroperitoneal fibrosis as a result of signet ring cell gastric cancer: a case-based review. *Journal of Gastrointestinal Cancer*, 44: 94-97.
Not in PICO
- Khademi, H., Radmard, A.-R., Malekzadeh, F., Kamangar, F., Nasser-Moghaddam, S., Johansson, M., Byrnes, G., Brennan, P. & Malekzadeh, R. (2012) Diagnostic accuracy of age and alarm symptoms for upper GI malignancy in patients with dyspepsia in a GI clinic: A 7-year cross-sectional study. *PLoS ONE*, 7.
Not in PICO
- Khan, M. A., Luz, L. P. & Eloubeidi, M. A. (2009) Combined use of endoscopic ultrasonography (EUS) guided fine-needle aspiration (FNA) cytological analysis and immunohistochemistry for the diagnosis of gastrointestinal stromal tumors (GIST). *Gastrointestinal Endoscopy*, 69: AB338.
Not in PICO
- Kiguchi, G., Ito, T., Kamada, Y., Tanaka, T., Nishikawa, T., Sugano, M., Soma, T. & Hattori, Y. (2013) A case of laparoscopic total gastrectomy for a 12-cm-diameter giant malignant gastric gist. *Surgical Endoscopy and Other Interventional Techniques*, 27: S99.
Not in PICO
- Kim, E. M., Lee, B. S., Moon, H. S., Sung, J. K., Kim, S. H., Lee, H. Y. & Kang, D. Y. (2009) Distal cholangiocarcinoma with gastric metastasis mimicking early gastric cancer. *Gut & Liver*, 3: 222-225.
Not in PICO
- Kim, J. H. & Rhee, P. L. (2012) Recent advances in noncardiac chest pain in Korea. *Gut & Liver*, 6: 1-9.
Narrative review
- Kim, N., Kim, J. J., Choe, Y. H., Kim, H. S., Kim, J. I., Chung, I. S., Korean College of Helicobacter and Upper Gastrointestinal Research & Korean Association of Gastroenterology (2009) [Diagnosis and treatment guidelines for Helicobacter pylori infection in Korea]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 54: 269-278.
Guideline
- Kim, P. S., Lee, J. W., Pai, S. H., Kim, Y. B., Cho, J. K., Lee, J. W., Jeong, S., Lee, D. H., Kim, H. G., Kwon, K. S., Cho, H. G., Shin, Y. W. & Kim, Y. S. (2002) Detection of Helicobacter pylori antigen in stool by enzyme immunoassay. *Yonsei Medical Journal*, 43: 7-13.
Not in PICO
- Kim, S. J., Ha, S. Y., Choi, B. M., Lee, M. Y., Jin, J. Y., Yeom, S. J., Kim, T. W., Kim, Y. M. & Lee, K. (2013) The prevalence and clinical characteristics of cancer among anemia patients treated at an outpatient clinic. *Blood Research*, 48: 46-50.
Not in PICO
- Kim, T. O., Kang, D. H., Kim, G. H., Heo, J., Song, G. A., Cho, M., Kim, D. H. & Sim, M. S. (2007) Self-expandable metallic stents for palliation of patients with malignant gastric outlet obstruction

- caused by stomach cancer. *World Journal of Gastroenterology*, 13: 916-920.
Not in PICO
- Kokkola, A. & Sipponen, P. (2001) Gastric carcinoma in young adults. *Hepato-Gastroenterology*, 48: 1552-1555.
Narrative review
- Koneri, K., Hirano, Y., Fujimoto, D., Sawai, K., Morikawa, M., Murakami, M., Goi, T., Iida, A., Katayama, K. & Yamaguchi, A. (2013) Five-year survival of alpha-fetoprotein-producing gastric cancer with synchronous liver metastasis: a case report. *Journal of Gastric Cancer*, 13: 58-64.
Not in PICO
- Korstanje, A., den, H. G., Biemond, I. & Lamers, C. B. H. W. (2002) The serological gastric biopsy: A non-endoscopical diagnostic approach in management of the dyspeptic patient: Significance for primary care based on a survey of the literature. *Scandinavian Journal of Gastroenterology, Supplement*, 37: 22-26.
Narrative review
- Kroupa, R. & Jecmenova, M. (2013) Gastric disorders in general practice. [Czech]. *Interni Medicina pro Praxi*, 15: 60-63.
Narrative review
- Kurihara, Y., Oku, K., Suzuki, A., Ohson, Y. & Okano, Y. (2012) [A case of calcinomatous polyarthritis presenting rheumatoid arthritis-like polyarthritis as the initial symptom of gastric cancer]. [Japanese]. *Nihon Rinsho Meneki Gakkai Kaishi*, 35: 439-445.
Not in PICO
- Kusano, M. (2004) Review article: diagnosis and investigation of gastro-oesophageal reflux disease in Japanese patients. [Review] [26 refs]. *Alimentary Pharmacology & Therapeutics*, 20: Suppl-8.
Narrative review
- Lagergren, J. (2000) [Increased incidence of adenocarcinoma of the esophagus and cardia. Reflux and obesity are strong and independent risk factors according to the SECC study]. [Review] [24 refs] [Swedish]. *Lakartidningen*, 97: 1950-1953.
Narrative review
- Lai, I. R., Lee, W. J., Chen, C. N., Lee, P. H., Chang, K. J., Chang-Yu, S. & Chen, K. M. (1997) Gastric cancer in the young. *Hepato-Gastroenterology*, 44: 1641-1645.
Not in PICO
- Larsen, A. C., Dabrowski, T., Fisker, R. V., Kristensen, S. R., Moller, B. K. & Thorlacius-Ussing, O. (2012) Venous thromboembolism and haemostatic disturbances in patients with upper gastrointestinal cancer. *Thrombosis Research*, 129: S165.
Not in PICO
- Lawrence, M. & Shiu, M. H. (1991) Early gastric cancer. Twenty-eight-year experience. *Annals of Surgery*, 213: 327-334.
Not in PICO
- Layke, J. C. & Lopez, P. P. (2004) Gastric cancer: diagnosis and treatment options. [Review] [34 refs]. *American Family Physician*, 69: 1133-1140.
Narrative review
- Lee, H. J., Song, I. C., Yun, G. W., Yun, H. J., Kim, S. & Jo, D. Y. (2010) A prospective evaluation of adult men with iron deficiency anemia. *Blood*, 116.
Not in PICO
- Lee, M. G. (2004) Dyspepsia: review of management options. [Review] [21 refs]. *West Indian Medical Journal*, 53: 188-190.
Narrative review
- Lee, S.-W., Chang, C.-S., Yeh, H.-J., Lien, H.-C., Lee, T.-Y. & Chou, M.-C. (2012) The diagnostic value of alarm features for identifying types and stages of upper gastrointestinal malignancies: One medical center's experience. *Journal of Gastroenterology and Hepatology*, 27: 350.
Not in PICO

- LeLorier, J., Page, V., Castilloux, A. M. & LeLorier, Y. (1997) Management of new symptoms of dyspepsia in the elderly in Quebec. *Canadian Journal of Gastroenterology*, 11: 669-672.
Not in PICO
- Levine, M. S., Laufer, I. & Thompson, J. J. (1983) Carcinoma of the gastric cardia in young people. *AJR.American Journal of Roentgenology*, 140: 69-72.
Not in PICO
- Li, S. H. (1989) [Clinico-pathologic comparison between early gastric cancer and early cancriform progressive cancer]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 11: 44-46.
Not in PICO
- Li, W., Sun, X. W., Xu, D. Z., Guan, Y. X. & Zhan, Y. Q. (2007) [Comparative study on clinical characteristics of gastric carcinoma between young and elderly patients]. [Chinese]. *Zhonghua Weichang Waike Zazhi*, 10: 476-478.
Not in PICO
- Liberati, G., Lucchetta, M. C., Petraccia, L., Nocchi, S., Rosentzweig, R., De, M. A. & Grassi, M. (2003) [Meta-analytical study of gastrointestinal stromal tumors (GIST)]. [Italian]. *Clinica Terapeutica*, 154: 85-91.
Not in PICO
- Lieberman, D., Fennerty, M. B., Morris, C. D., Holub, J., Eisen, G. & Sonnenberg, A. (2004) Endoscopic evaluation of patients with dyspepsia: results from the national endoscopic data repository. *Gastroenterology*, 127: 1067-1075.
Not in PICO
- Lin, C. Y., Chien, R. N., Lin, P. Y., Chen, P. C. & Wu, C. S. (1995) Early gastric cancer--a clinicopathological study. *Changeng Yi Xue Za Zhi*, 18: 1-7.
Not in PICO
- Lin, J. T., Wu, M. S., Wang, J. T., Chen, K. M., Wei, T. C., Shun, C. T., Chen, C. J., Wang, H. P., Chan, T. M. & Wang, T. H. (1993) Secular changes in the clinical manifestation and pathologic pattern of early gastric cancer in Taiwan. *Journal of the Formosan Medical Association*, 92: 969-976.
Not in PICO
- Lin, J. T., Wu, M. S., Wang, J. T., Shun, C. T., Chen, C. J. & Wang, T. H. (1994) Clinicopathologic study of 208 patients with early gastric cancer in Taiwan: a comparison between Eastern and Western countries. *Journal of Gastroenterology & Hepatology*, 9: 344-349.
Not in PICO
- Liou, J. M., Lin, J. T., Wang, H. P., Huang, S. P., Lee, Y. C., Shun, C. T., Lin, M. T. & Wu, M. S. (2005) The optimal age threshold for screening upper endoscopy for uninvestigated dyspepsia in Taiwan, an area with a higher prevalence of gastric cancer in young adults. *Gastrointestinal Endoscopy*, 61: 819-825.
Not in PICO
- Liu, J., Wang, Q., Li, B., Meng, X., Zhang, Y., Du, X., Yan, J., Ping, Y. & Li, W. (1995) Superficial carcinomas of the esophagus and gastric cardia. A clinicopathological analysis of 141 cases. *Chinese Medical Journal*, 108: 754-759.
Not in PICO
- Locke III, G. R. (2005) Current medical management of gastroesophageal reflux disease. *Thoracic Surgery Clinics*, 15: 369-375.
Narrative review
- Look, M., Tan, Y. Y., Vijayan, A., Teh, C. H. & Low, C. H. (2003) Management delays for early gastric cancer in a country without mass screening. *Hepato-Gastroenterology*, 50: 873-876.
Not in PICO
- Lloyd, R. A. & McClellan, D. A. (2011) Update on the Evaluation and Management of Functional Dyspepsia. *American Family Physician*, 83: 547-552.
Narrative review

- Luckers, A. E. G., Thijs, J. C. & Westerveld, B. D. (1985) Is endoscopy of the proximal digestive tract at the GP's request useful?. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 129: 117-119.
Not in PICO
- Luman, W. & Ng, K. L. (2003) Audit of Investigations in Patients with Iron Deficiency Anaemia. *Singapore Medical Journal*, 44: 504-510.
Not in PICO
- Lyratzopoulos, G., Neal, R. D., Barbiere, J. M., Rubin, G. P. & Abel, G. A. (2012) Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. *Lancet Oncology*, 13: 353-365.
Not in PICO
- Ma, Q., Xin, J., Zhao, Z., Guo, Q., Yu, S., Xu, W., Liu, C. & Zhai, W. (2013) Value of 8F-FDG PET/CT in the diagnosis of primary gastric cancer via stomach distension. *European Journal of Radiology*, 82: e302-e306.
Not in PICO
- Macdonald, S., Macleod, U., Campbell, N. C., Weller, D. & Mitchell, E. (2006) Systematic review of factors influencing patient and practitioner delay in diagnosis of upper gastrointestinal cancer. *British Journal of Cancer*, 94: 1272-1280.
Not in PICO
- Maconi, G., Manes, G. & Porro, G. B. (2008) Role of symptoms in diagnosis and outcome of gastric cancer. *World Journal of Gastroenterology*, 14: 1149-1155.
Narrative review
- Madsen, L. G. & Bytzer, P. (2000) The value of alarm features in identifying organic causes of dyspepsia. [Review] [106 refs]. *Canadian Journal of Gastroenterology*, 14: 713-720.
Narrative review
- Maev, I. V., Mel'nikova, E. V., Kashin, S. V., Nadezhin, A. S. & Kriukova, T. V. (2008) [Serologic screening for preneoplastic pathology and early stomach cancer]. [Russian]. *Klinicheskaja Meditsina*, 86: 43-48.
Narrative review
- Mahachai, V., Ratanachu-Ek, T., Khuhaprema, T. & Vilaichone, R. (2009) Gastric cancer and H. pylori infection in Thailand: A 10-year review. *Helicobacter*, 14: 380.
Not in PICO
- Mahajan, V., Gupta, N., Gupta, S. & Sharma, R. (2014) - Hepatoid adenocarcinoma of stomach: case report of a rare histological variant. - *Indian Journal of Pathology & Microbiology*, 57: 116-119.
Not in PICO
- Malats, N., Belloc, J., Gallen, M. & Porta, M. (1995) Disagreement between hospital medical records and a structured patient interview on the type and date of the first symptom in cancers of the digestive tract. *Revue d'Epidemiologie et de Sante Publique*, 43: 533-540.
Not in PICO
- Malfertheiner, P., Megraud, F., O'Morain, C., Bazzoli, F., El-Omar, E., Graham, D., Hunt, R., Rokkas, T., Vakil, N. & Kuipers, E. J. (2007) Current concepts in the management of Helicobacter pylori infection: the Maastricht III Consensus Report. [99 refs]. *Gut*, 56: 772-781.
Guideline
- Manes, G., Balzano, A., Marone, P., Lioniello, M. & Mosca, S. (2002) Appropriateness and diagnostic yield of upper gastrointestinal endoscopy in an open-access endoscopy system: a prospective observational study based on the Maastricht guidelines. *Alimentary Pharmacology & Therapeutics*, 16: 105-110.
Not in PICO
- Mansour-Ghanaei, F., Joukar, F., Soati, F., Mansour-Ghanaei, A. & Naserani, S. B. (2012) Knowledge about gastric carcinoma in North of Iran, a high prevalent region for gastric carcinoma: a population-based telephone survey. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 13: 3361-

3366.

Not in PICO

Mantynen, T., Farkkila, M., Kunnamo, I., Mecklin, J. P., Juhola, M. & Voutilainen, M. (2002) The impact of upper GI endoscopy referral volume on the diagnosis of gastroesophageal reflux disease and its complications: a 1-year cross-sectional study in a referral area with 260,000 inhabitants. *American Journal of Gastroenterology*, 97: 2524-2529.

Not in PICO

Mardosiene, S. & Qvist, P. (2002) Selection of patients referred for endoscopy from general practice. [Danish]. *Ugeskrift for Laeger*, 164: 899-901.

Not in PICO

Mariette, C., De Botton, M. L. & Piessen, G. (2012) Surgery in esophageal and gastric cancer patients: what is the role for nutrition support in your daily practice? *Annals of Surgical Oncology*, 19: 2128-2134.

Narrative review

Mariscal, M., Llorca, J., Prieto, D. & Delgado-Rodriguez, M. (2001) Determinants of the interval between the onset of symptoms and diagnosis in patients with digestive tract cancers. *Cancer Detection and Prevention*, 25: 420-429.

Not in PICO

Mariscal, M., Llorca, J., Prieto-Salceda, D., Palma, S. & Delgado-Rodriguez, M. (2003) Determinants of the interval between diagnosis and treatment in patients with digestive tract cancer. *Oncology Reports*, 10: 463-467.

Not in PICO

Marmo, R., Rotondano, G., Piscopo, R., Bianco, M. A., Russo, P., Capobianco, P. & Cipolletta, L. (2005) Combination of age and sex improves the ability to predict upper gastrointestinal malignancy in patients with uncomplicated dyspepsia: A prospective multicentre database study. *American Journal of Gastroenterology*, 100: 784-791.

Not in PICO

Martin, I. G., Young, S., Sue-Ling, H. & Johnston, D. (1997) Delays in the diagnosis of oesophagogastric cancer: a consecutive case series. *BMJ*, 314: 467-470.

Not in PICO

Martinez-Ares, D., Alonso Aguirre, P. A., Yanez, L. J., Martin-Granizo, B., I, Martinez, C. J., Rodriguez, M. D. & Pallares, P. A. (2009) Sensitivity of ultrasonography for gastric cancer diagnosis in symptomatic patients. *Digestive Diseases and Sciences*, 54: 1257-1264.

Not in PICO

Martinez, A. D., Alonso Aguirre, P. A., Martin-Granizo, B., I, Cid, G. L. & Pallares, P. A. (2008) [Usefulness of ultrasonography in diagnosing patients suspect for digestive tract neoplasms]. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 100: 545-551.

Not in PICO

Masselli, G., Casciani, E., Poletti, E., Laghi, F. & Gualdi, G. (2013) Magnetic resonance imaging of small bowel neoplasms. *Cancer Imaging*, 13: 92-99.

Narrative review

Matowicka-Karna, J., Kamocki, Z., Polinska, B., Osada, J. & Kemonia, H. (2013) Platelets and inflammatory markers in patients with gastric cancer. *Clinical & Developmental Immunology*, 2013: 401623.

Not in PICO

Matsueda, K. (1998) Guidelines for dyspepsia treatment in Japan. *Clinical Therapeutics*, 20: D13-D22. Guideline

Mc Loughlin, R. M., Sebastian, S. S., O'Connor, H. J., Buckley, M. & O'Morain, C. A. (2003) Review article: test and treat or test and scope for Helicobacter pylori infection. Any change in gastric cancer prevention?. [Review] [71 refs]. *Alimentary Pharmacology & Therapeutics*, 17: Suppl-8.

Narrative review

- McCulloch, P., Williams, E., McCulloch, C. & Mullins, D. (1998) Can we improve the uptake of gastroscopy in the population at risk for gastric cancer? The effect of home letter information. *Journal of the Royal College of Surgeons of Edinburgh*, 43: 385-389.
Not in PICO
- McCulloch, P., Brown, P., Martin, B. & Williams, E. (2003) The effects of an awareness-raising program for patients and primary care physicians on the early detection of gastro-oesophageal cancer. *Surgery*, 133: 154-161.
Not in PICO
- McLean, R. H. & Sardi, A. (1998) Gastric cancer: an overview with emphasis on early gastric cancer. [Review] [26 refs]. *Maryland Medical Journal*, 47: 191-194.
Narrative review
- Medina-Franco, H., Ramirez-Luna, M. A., Cabrera-Mendoza, F., Almaguer-Rosales, S. G. & Guillen-Perez, F. (2011) [Gastric duplication in adults: a case report and literature review]. [Spanish]. *Revista de Gastroenterologia de Mexico*, 76: 260-263.
Not in PICO
- Melleney, E. M. & Willoughby, C. P. (2002) Audit of a nurse endoscopist based one stop dyspepsia clinic. *Postgraduate Medical Journal*, 78: 161-164.
Not in PICO
- Melleney, E. M., Subhani, J. M. & Willoughby, C. P. (2004) Dysphagia referrals to a district general hospital gastroenterology unit: hard to swallow. *Dysphagia*, 19: 78-82.
Not in PICO
- Meng, X. M., Zhou, Y., Dang, T., Tian, X. Y. & Kong, J. (2013) Magnifying chromoendoscopy combined with immunohistochemical staining for early diagnosis of gastric cancer. *World Journal of Gastroenterology*, 19: 404-410.
Not in PICO
- Menon, S., Dhar, A., Hoare, J. M. & Trudgill, N. (2012) How commonly is gastric cancer missed at endoscopy: A UK primary care based study. *Gastrointestinal Endoscopy*, 75: AB139.
Not in PICO
- Mikulin, T. & Hardcastle, J. D. (1987) Gastric cancer--delay in diagnosis and its causes. *European Journal of Cancer & Clinical Oncology*, 23: 1683-1690.
Not in PICO
- Miller, G. & Gloor, F. (1986) Early stomach carcinoma. [German]. *Schweizerische medizinische Wochenschrift*, 116: 1366-1370.
Narrative review
- Misawa, S., Takeda, M., Sakamoto, H., Kirii, Y., Ota, H. & Takagi, H. (2014) - Spontaneous rupture of a giant gastrointestinal stromal tumor of the jejunum: a case report and literature review. - *World Journal of Surgical Oncology*, 12: 153.
Not in PICO
- Mitsudomi, T., Matsusaka, T., Wakasugi, K., Takenaka, M., Kume, K., Fujinaga, Y., Teraoka, H. & Iwashita, A. (2010) A clinicopathological study of gastric cancer with special reference to age of the patients: an analysis of 1,630 cases. *World Journal of Surgery*, 13: 225-230.
Not in PICO
- Mizoue, T., Takano, Y. & Yoshimura, T. (1992) [A population based survey of attendance at screenings in urban areas]. [Japanese]. *Nippon Koshu Eisei Zasshi - Japanese Journal of Public Health*, 39: 269-277.
Not in PICO
- Molina, M. C., Porta, S. M., Malats, N., Jariod, M., Pinol, J. L. & Fernandez, E. (1994) Perception of the initiation and evolution of symptomatology in hospitalized patients with cancer of the digestive tract. [Spanish]. *Neoplasia*, 11: 119-125.
Not in PICO

- Moreno-Otero, R., Rodriguez, S., Carbo, J., Mearin, F. & Pajares, J. M. (1987) Acute upper gastrointestinal bleeding as primary symptom of gastric carcinoma. *Journal of Surgical Oncology*, 36: 130-133.
Not in PICO
- Mori, M., Kitagawa, S., Iida, M., Sakurai, T., Enjoji, M., Sugimachi, K. & Ooiwa, T. (1987) Early carcinoma of the gastric cardia. A clinicopathologic study of 21 cases. *Cancer*, 59: 1758-1766.
Not in PICO
- Mori, M., Adachi, Y., Kakeji, Y., Korenaga, D., Sugimachi, K., Motooka, M. & Ooiwa, T. (1992) Superficial flat-type early carcinoma of the stomach. *Cancer*, 69: 306-313.
Not in PICO
- Motta, C. R., Cunha, M. P., Queiroz, D. M., Cruz, F. W., Guerra, E. J., Mota, R. M. & Braga, L. L. (2008) Gastric precancerous lesions and Helicobacter pylori infection in relatives of gastric cancer patients from Northeastern Brazil. *Digestion*, 78: 3-8.
Not in PICO
- Mudawi, H. M. Y., Mahmoud, A. O. A., El Tahir, M. A., Suliman, S. H. & Ibrahim, S. Z. (2010) Use of endoscopy in diagnosis and management of patients with dysphagia in an African setting. *Diseases of the Esophagus*, 23: 196-200.
Not in PICO
- Munk, E. M., Drewes, A. M., Gorst-Rasmussen, A., Funch-Jensen, P., Gregersen, H. & Norgard, B. (2007) Risk of gastrointestinal cancer in patients with unexplained chest/epigastric pain and normal upper endoscopy: a Danish 10-year follow-up study. *Digestive Diseases & Sciences*, 52: 1730-1737.
Not in PICO
- Muris, J. W. M., Starmans, R., Pop, P., Crebolder, H. F. J. M. & Knottnerus, J. A. (1994) Discriminant value of symptoms in patients with dyspepsia. *Journal of Family Practice*, 38: 139-143.
Not in PICO
- Murray, I. A., Palmer, J., Waters, C. & Dalton, H. R. (2012) Predictive value of symptoms and demographics in diagnosing malignancy or peptic stricture. *World Journal of Gastroenterology*, 18: 4357-4362.
Not in PICO
- Musana, A. K., Yale, S. H. & Lang, K. A. (2006) Managing dyspepsia in a primary care setting. *Clinical Medicine and Research*, 4: 337-342.
Narrative review
- Nago, N. A. (1995) [Early gastric cancer]. [Spanish]. *Revista de Gastroenterologia del Peru*, 15: 255-264.
Not in PICO
- Nakamura, T., Mori, H., Mine, M., Kondo, H., Okajima, S., Morikawa, A. & Toyoda, S. (1982) Long-term trend of haemoglobin decrease in stomach cancer. *Medical Informatics*, 7: 29-38.
Not in PICO
- Nakayama, Y., Kadowaki, K., Higure, A., Hisaoka, M. & Yamaguchi, K. (2013) Synchronous sporadic gastrointestinal stromal tumors in the stomach and jejunum: report of a case. *Case Reports Gastroenterology*, 7: 69-74.
Not in PICO
- Ndububa, D. A., Agbakwuru, A. E., Adebayo, R. A., Olasode, B. J., Olaomi, O. O., Adeosun, O. A. & Arigbabu, A. O. (2001) Upper gastrointestinal findings and incidence of Helicobacter pylori infection among Nigerian patients with dyspepsia. *West African Journal of Medicine*, 20: 140-145.
Not in PICO
- Ndububa, D. A., Agbakwuru, E. A., Olasode, B. J., Aladegbaiye, A. O., Adekanle, O. & Arigbabu, A. O. (2007) Correlation between endoscopic suspicion of gastric cancer and histology in Nigerian patients with dyspepsia. *Tropical Gastroenterology*, 28: 69-71.
Not in PICO

- Niang, A., Mbengue, M., Diouf, M. L., Diouf, B., Ka, M. M., Pouye, A., Diallo, S., Ndiaye, M. F. & Bao, O. (1996) [Current aspects of gastric cancer in Senegal. Epidemiological and clinical study of 220 cases (1984-1991)]. [French]. *Dakar Medical*, 41: 99-103.
Not in PICO
- Niederle, M. B. & Niederle, B. (2011) Diagnosis and treatment of gastroenteropancreatic neuroendocrine tumors: current data on a prospectively collected, retrospectively analyzed clinical multicenter investigation. *The Oncologist*, 16: 602-613.
Not in PICO
- Nkrumah, K. N. (2002) Endoscopic evaluation of upper abdominal symptoms in adult patients, Saudi Aramco-Ai Hasa Health Center, Saudi Arabia. *West African Journal of Medicine*, 21: 1-4.
Not in PICO
- Nogi, S., Hashimoto, A., Iwata, K., Futami, H., Takaoka, H., Arinuma, Y., Shimada, K., Nakayama, H., Matsui, T., Komiya, A., Furukawa, H., Tamama, S., Kinoshita, S., Moriya, H. & Tohma, S. (2012) [A case of immunosuppressant-resistant clinically amyopathic dermatomyositis with rapidly progressive interstitial pneumonia ameliorated after resection of gastric cancer]. [Japanese]. *Nihon Rinsho Meneki Gakkai Kaishi*, 35: 188-193.
Not in PICO
- Nogueira, C., Silva, A. S., Santos, J. N., Silva, A. G., Ferreira, J., Matos, E. & Vilaca, H. (2002) Early gastric cancer: ten years of experience. *World Journal of Surgery*, 26: 330-334.
Narrative review
- Numans, M. E., van der Graaf, Y., de Wit, N. J. & de Melker, R. A. (2001) How useful is selection based on alarm symptoms in requesting gastroscopy? An evaluation of diagnostic determinants for gastro-oesophageal malignancy. *Scandinavian Journal of Gastroenterology*, 36: 437-443.
Not in PICO
- Oberle, E., Brunner, K. & Rhyner, K. (1993) [Gastrointestinal hemorrhage: how much evaluation is necessary?]. [German]. *Schweizerische Rundschau fur Medizin Praxis*, 82: 1244-1252.
Not in PICO
- Ofman, J. J. & Rabeneck, L. (1999) The effectiveness of endoscopy in the management of dyspepsia: A qualitative systematic review. *American Journal of Medicine*, 106: 335-346.
Not in PICO
- Ogawa, F., Genevay, M., Lisovsky, M., Mino-Kenudson, M., Deshpande, V., Odze, R. D. & Lauwers, G. Y. (2009) Natural history of sporadic gastric dysplasia in the U.S.A: Follow up study of 54 patients. *Laboratory Investigation*, 89: 142A.
Not in PICO
- Ogoshi, K., Okamoto, Y., Morita, M., Nabeshima, K., Nakamura, K., Iwata, K., Kondoh, Y. & Makuuchi, H. (2003) Symptoms and cancer patients' outcome: How important is screening for asymptomatic gastric cancer patients? *Annals of Cancer Research and Therapy*, 11: 153-168.
Not in PICO
- Okadome, M., Saito, T., Tsukamoto, N., Nishi, K., Nishiyama, N. & Nagata, E. (2006) Endometrial scraping cytology in women with extragenital malignancies. *Acta Cytologica*, 50: 158-163.
Not in PICO
- Oleagoitia, J. M., Echevarria, A., Santidrian, J. I., Ullacia, M. A. & Hernandez-Calvo, J. (1986) Early gastric cancer. *British Journal of Surgery*, 73: 804-806.
Not in PICO
- Ollier, J. C. (1996) [Stomach cancers. Epidemiology, symptomatology]. [French]. *Soins - Chirurgie*.(180):5, 1996 Dec., 5.
Narrative review
- Ott, J. J., Ullrich, A. & Miller, A. B. (2009) The importance of early symptom recognition in the context of early detection and cancer survival. *European Journal of Cancer*, 45: 2743-2748.
Narrative review

- Ovaska, J., Kruuna, O., Saario, I., Nordling, S., Lempinen, M. & Schroder, T. (1990) Early gastric cancer. A report of 57 consecutive patients over a 20-year period. *Surgical Research Communications*, 8: 123-129.
Not in PICO
- Padma, S., Sundaram, P. S. & Marmattom, B. V. (2011) PET/CT in the evaluation of anti-NMDA-receptor encephalitis: What we need to know as a NM physician. *Indian Journal of Nuclear Medicine*, 26: 99-101.
Not in PICO
- Panter, S. J., O'Flanagan, H., Bramble, M. G. & Hungin, A. P. (2004) Empirical use of antisecretory drug therapy delays diagnosis of upper gastrointestinal adenocarcinoma but does not effect outcome. *Alimentary Pharmacology & Therapeutics*, 19: 981-988.
Not in PICO
- Panter, S. J., Bramble, M. G., O'Flanagan, H. & Hungin, A. P. S. (2004) Urgent cancer referral guidelines: a retrospective cohort study of referrals for upper gastrointestinal adenocarcinoma. *British Journal of General Practice*, 54: 611-613.
Not in PICO
- Park, J. S., Park, D. I., Park, S. K., Choi, J. S., Kim, Y. H., Chang, D. K., Son, H. J., Kim, J. E., Kim, J. O., Lee, S. H., Kim, H. S., Sin, J. E., Lee, S. G., Lee, S. Y., Park, S. J., Park, C. H., Baek, I. H., Jang, B. I., Jeon, Y. T. & Huh, K. C. (2009) Endoscopic evaluation of significant gastrointestinal lesions in patients with iron deficiency with and without anaemia: a Korean Association for the Study of Intestinal Disease study. *Internal Medicine Journal*, 39: 441-446.
Not in PICO
- Paterson, H. M., McCole, D. & Auld, C. D. (2006) Impact of open-access endoscopy on detection of early oesophageal and gastric cancer 1994 - 2003: population-based study. *Endoscopy*, 38: 503-507.
Not in PICO
- Patterson, R. N. & Johnston, S. D. (2003) Iron deficiency anaemia: Are the British Society of Gastroenterology guidelines being adhered to? *Postgraduate Medical Journal*, 79: 226-228.
- Pavone, G., Lombardi, M., Troiani, R., Isoppi, E., Vinciguerra, G., Ambrogi, M., Muttini, M. P., Torri, T. & Sicari, A. (1995) [Early gastric cancer]. [Italian]. *Minerva Chirurgica*, 50: 535-539.
Not in PICO
- Pera, M., Riera, E., Lopez, R., Vinolas, N., Romagosa, C. & Miquel, R. (2001) Metastatic carcinoma of the breast resembling early gastric carcinoma. *Mayo Clinic Proceedings*, 76: 205-207.
Not in PICO
- Perez Lopez de Brinas JM (1993) [Early gastric cancer at a third-level hospital in Barcelona in 1981-1990. Clinical considerations]. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 84: 90-94.
Not in PICO
- Peschl, L. & Munda, W. (1987) [Early clinical diagnosis of stomach and large intestine cancer]. [German]. *ZFA - Zeitschrift fur Alternsforschung*, 42: 155-164.
Narrative review
- Petkowicz, B., Berger, M., Szeszko, L. & Piotrkowicz, J. (2011) Acanthosis nigricans maligna in oral cavity as a symptom of malignant neoplasm of the gastrointestinal tract. [Polish]. *Gastroenterologia Polska*, 18: 41-44.
Narrative review
- Phull, P. S., Salmon, C. A., Park, K. G., Rapson, T., Thompson, A. M. & Gilbert, F. J. (2006) Age threshold for endoscopy and risk of missing upper gastrointestinal malignancy--data from the Scottish audit of gastric and oesophageal cancer. *Alimentary Pharmacology & Therapeutics*, 23: 229-233.
Not in PICO

- Phung, N., Kalantar, J. & Talley, N. J. (1998) Management of dyspepsia in general practice. *Modern Medicine of Australia*, 41: 10-19.
Narrative review
- Pierzchajlo, R. P., Ackermann, R. J. & Vogel, R. L. (1998) Esophagogastroduodenoscopy performed by a family physician. A case series of 793 procedures. *Journal of Family Practice*, 46: 41-46.
Not in PICO
- Pimentel-Nunes, P., Ferreira, A., Veloso, N. & Dinis-Ribeiro, M. (2013) Narrow-Band Imaging for the Diagnosis of Gastric Preneoplastic and Neoplastic Lesions. *Video Journal and Encyclopedia of GI Endoscopy*, 1: 191-193.
Narrative review
- Pisano, R. & Venturelli, A. (1990) Early stomach cancer: the experience of the Hospital John Kennedy in Valdivia. 1976-1989. [Spanish]. *Revista Medica de Chile*, 118: 1111-1115.
Not in PICO
- Plummer, J. M., Gibson, T. N., McFarlane, M. E. C., Hanchard, B., Martin, A. & McDonald, A. H. (2005) Clinicopathologic profile of gastric carcinomas at the University Hospital of the West Indies. *West Indian Medical Journal*, 54: 364-368.
Not in PICO
- Porta, M., Gallen, M., Belloc, J. & Malats, N. (1996) Predictors of the interval between onset of symptoms and first medical visit in patients with digestive tract cancer. *International Journal of Oncology*, 8: 941-949.
Not in PICO
- Quine, M. A., Bell, G. D., McCloy, R. F., Devlin, H. B. & Hopkins, A. (1994) Appropriate use of upper gastrointestinal endoscopy--a prospective audit. Steering Group of the Upper Gastrointestinal Endoscopy Audit Committee.[Erratum appears in Gut 1995 Jan;36(1):157]. *Gut*, 35: 1209-1214.
Not in PICO
- Qureshi, N. A., Hallissey, M. T. & Fielding, J. W. (2007) Outcome of index upper gastrointestinal endoscopy in patients presenting with dysphagia in a tertiary care hospital - A 10 years review. *Bmc Gastroenterology*, 7.
Not in PICO
- Raghuram, A., Holub, J. L. & Lieberman, D. A. (2011) Trends in endoscopic diagnosis of gastric cancer 2000-2008: Decline in prevalence among women. *Gastrointestinal Endoscopy*, 73: AB229.
Not in PICO
- Raju, G. S., Bardhan, K. D., Royston, C. & Beresford, J. (1999) Giant gastric ulcer: its natural history and outcome in the H2RA era. *American Journal of Gastroenterology*, 94: 3478-3486.
Not in PICO
- Read, L., Pass, T. M. & Komaroff, A. L. (1982) Diagnosis and treatment of dyspepsia. A cost-effectiveness analysis. *Medical Decision Making*, 2: 415-438.
Not in PICO
- Rebai, W., Fterich, F., Makni, A., Ksantini, R., Bedioui, H., Daghfous, A., Chebbi, F., Jouini, M., Ammous, A., Kacem, M. & Ben, S. Z. (2010) [Early gastric adenocarcinoma]. [French]. *Tunisie Medicale*, 88: 1-4.
Not in PICO
- Rehs, H. U. (1994) Early gastric carcinoma - Experience in gastroenterological practice. [German]. *Verdauungskrankheiten*, 12: 216-218.
Not in PICO
- Ribichini, P., Piccinini, E., Perrucci, A., Stancanelli, V., Fiorentini, G., Campi, R. & Campagnoni, R. (1984) Early gastric cancer: evaluation of diagnostic, clinicopathologic and therapeutic aspects in 60 cases. *International Surgery*, 69: 325-330.
Not in PICO

- Robinson, M. (2001) Dyspepsia: Challenges in diagnosis and selection of treatment. *Clinical Therapeutics*, 23: 1130-1144.
Narrative review
- Robles-Medranda, C., Lukashok, H. P., Del Valle, R. S., Mariscal, C., Chung Sang, M. A., Rubio, G. & Robles-Jara, C. (2011) Capsule endoscopy for detection of gastritis and gastric lesions in dyspeptic patients: A pilot study. *Gastrointestinal Endoscopy*, 73: AB446-AB447.
Not in PICO
- Rogers, K., Roberts, G. M. & Williams, G. T. (1981) Gastric-juice enzymes--an aid in the diagnosis of gastric cancer? *Lancet*, 1: 1124-1125.
Not in PICO
- Rubay, J., Fievez, M., Daubresse, D. & Grenier, P. (1983) [Surgical experience in 48 cases of early gastric carcinoma]. [French]. *Acta Chirurgica Belgica*, 83: 32-40.
Not in PICO
- Ruggiero, R. P. & Fischer, S. (1982) Gastric malignancy: ten year experience at a community teaching hospital. *Journal of Surgical Oncology*, 20: 129-130.
Not in PICO
- Ryan, J. & Murkies, A. (2006) Diagnosis of upper gastrointestinal malignancy. [Review] [3 refs]. *Australian Family Physician*, 35: 200-201.
Narrative review
- Sadler, G. J., Jothimani, D., Zanetto, U. & Anderson, M. R. (2009) The effect of ethnicity on the presentation and management of oesophageal and gastric cancers: a UK perspective. *European Journal of Gastroenterology & Hepatology*, 21: 996-1000.
Not in PICO
- Sagar, N. & Bhala, N. (2014) Detection rates of gastric cancer at the Queen Elizabeth Hospital Birmingham 2009-2013. *Gut*, 63: A111.
Not in PICO
- Saha, A. K., Maitra, S. & Hazra, S. C. (2013) Epidemiology of gastric cancer in the gangetic areas of west bengal. *ISRN Gastroenterology*, 2013.
Not in PICO
- Sahn, S. A. (1998) Malignancy metastatic to the pleura. [Review] [101 refs]. *Clinics in Chest Medicine*, 19: 351-361.
Narrative review
- Salo, M., Collin, P., Kyronpalo, S., Rasmussen, M., Huhtala, H. & Kaukinen, K. (2008) Age, symptoms and upper gastrointestinal malignancy in primary care endoscopy. *Scandinavian Journal of Gastroenterology*, 43: 122-127.
Not in PICO
- Sato, T., Peiper, M., Fritscher-Ravens, A., Gocht, A., Soehendra, N. & Knoefel, W. T. (2005) Strategy of treatment of submucosal gastric tumors. *European Journal of Medical Research*, 10: 292-295.
Not in PICO
- Saubier, E. C., Partensky, C., Gouillat, C., Berger, F. & Moulinier, B. (1982) [Superficial gastric cancer. Results of surgery in 30 cases (author's transl)]. [French]. *Journal de Chirurgie*, 119: 13-20.
Not in PICO
- Scherubl, H., Faiss, S., Knoefel, W. T. & Wardelmann, E. (2014) - Management of early asymptomatic gastrointestinal stromal tumors of the stomach. - *World Journal of Gastrointestinal Endoscopy*, 6: 266-271.
Narrative review
- Schmidt, N., Peitz, U., Lippert, H. & Malfertheiner, P. (2005) Missing gastric cancer in dyspepsia. *Alimentary Pharmacology & Therapeutics*, 21: 813-820.
Not in PICO

- Schroder, J., Wesner, F. & Kremer, B. (2000) Diagnostic procedures in patients with the principal sign of weight loss. [German]. *Chirurgische Gastroenterologie Interdisziplinär*, 16: 61-64.
Narrative review
- Schumpelick, V., Dreuw, B., Ophoff, K. & Fass, J. (1979) [Adenocarcinoma of the esophagogastric junction: association with Barrett esophagus and gastroesophageal reflux--surgical results in 122 patients]. [German]. *Leber, Magen, Darm*, 26: 75-76.
Not in PICO
- Selgrad, M., Kandulski, A. & Malfertheiner, P. (2008) Dyspepsia and Helicobacter pylori. [Review] [45 refs]. *Digestive Diseases*, 26: 210-214.
Narrative review
- Sharpe, D., Williams, R. N., Ubhi, S. S., Sutton, C. D. & Bowrey, D. J. (2010) The "two-week wait" referral pathway allows prompt treatment but does not improve outcome for patients with oesophago-gastric cancer. *European Journal of Surgical Oncology*, 36: 977-981.
Not in PICO
- Shawihdi, M., Stern, N., Thompson, E., Sturgess, R., Kapoor, N., Pearson, M. G. & Bodger, K. (2011) Emergency admission as a route for oesophagogastric cancer diagnosis: A marker of poor outcome and a candidate quality indicator for local services. *Gut*, 60: A30-A31.
Not in PICO
- Sheen-Chen, S. M., Chou, F. F., Chen, Y. S., Chen, M. J., Chen, F. C., Chen, J. J. & Wan, Y. L. (1992) Early gastric cancer in southern Taiwan. [Review] [35 refs]. *Journal of Clinical Gastroenterology*, 15: 302-305.
Not in PICO
- Siersema, P. D., Dees, J., Tilanus, H. W., Kok, T. C., Hordijk, M. L. & van, B. M. (1995) Early detection and treatment of oesophageal and gastric cancer. The Rotterdam Oesophageal Tumour Study Group. [Review] [69 refs]. *Netherlands Journal of Medicine*, 47: 76-86.
Narrative review
- Sigon, R., Canzonieri, V., Cannizzaro, R., Pasquotti, B., Cattelan, A., Rossi, C. & Carbone, A. (1998) Early gastric cancer: diagnosis, surgical treatment and follow-up of 45 cases. *Tumori*, 84: 547-551.
Not in PICO
- Sigon, R., Canzonieri, V. & Rossi, C. (2003) Early gastric cancer: a single-institution experience on 60 cases. *Supplementi di Tumori: Official Journal of Societa Italiana di Cancerologia*, 2: S23-S26.
Not in PICO
- Sileri, P., D'Ugo, S., Blanco, G., V, Lolli, E., Franceschilli, L., Formica, V., Anemona, L., De, L. C. & Gaspari, A. L. (2012) Solitary metachronous gastric metastasis from pulmonary adenocarcinoma: Report of a case. *International Journal of Surgery Case Reports*, 3: 385-388.
Not in PICO
- Singhal, T., Doddi, S., Leake, T., Parsi, S., Hussain, A., Chandra, A., Smedley, F. & Ellul, J. (2010) Upper gastrointestinal bleeding due to gastric stromal tumour: a case report. *Cases journal*, 3: 58.
Not in PICO
- Siriyuyuen, U., Charatcharoenwiththaya, P., Pausawasdi, N., Maneerattanaporn, M., Leelakusolvong, S. & Kachintorn, U. (2012) The diagnostic value of upper endoscopy in patients with dyspepsia lacking alarm features on acid suppression therapy. *Journal of Gastroenterology and Hepatology*, 27: 437.
Not in PICO
- Sjoblom, S. M., Sipponen, P. & Jarvinen, H. (1993) Gastroscopic follow up of pernicious anaemia patients. *Gut*, 34: 28-32.
Not in PICO
- Smith, G. (1936) Red flags are key to managing dyspepsia. [Review] [8 refs]. *Practitioner*, 251: 31-34.
Narrative review
- Smithers, B. M., Fahey, P. P., Corish, T., Gotley, D. C., Falk, G. L., Smith, G. S., Kiroff, G. K., Clouston, A. D., Watson, D. I. & Whiteman, D. C. (2010) Symptoms, investigations and management of

patients with cancer of the oesophagus and gastro-oesophageal junction in Australia. *Medical Journal of Australia*, 193: 572-577.

Not in PICO

So, J. B. Y., Samarasinghe, K., Raju, G. C. & Ti, T.-K. (2001) Clinical and pathological features of early gastric cancer in Singapore. *Annals of the College of Surgeons of Hong Kong*, 5: 10-13.

Not in PICO

Sorour, M. A., Kassem, M. I., Ghazal, A., El-Riwini, M. T. & Abu, N. A. (2014) - Gastrointestinal stromal tumors (GIST) related emergencies. - *International Journal Of Surgery*, 12: 269-280.

Not in PICO

Sperber, A. D., Fich, A., Eidelman, L., Krugliak, P., Odes, H. S., Hilzenrat, N., Gaspar, N. & Zilberman, A. (1997) Open access endoscopy for hospitalized patients. *American Journal of Gastroenterology*, 92: 1823-1826.

Not in PICO

Stanghellini, V., Tosetti, C., Barbara, G., De, G. R., Salvioli, B. & Corinaldesi, R. (2000) Review article: The continuing dilemma of dyspepsia. *Alimentary Pharmacology and Therapeutics, Supplement*, 14: 23-30.

Narrative review

Stawowy, M., Kruse, A., Mortensen, F. V. & Funch-Jensen, P. (2007) Endoscopic stenting for malignant gastric outlet obstruction. *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques*, 17: 5-9.

Not in PICO

Stella, S. & Bruzzese, A. (1990) [Early gastric cancer: staging and diagnostic-therapeutic trends]. [Italian]. *Giornale di Chirurgia*, 11: 471-474.

Narrative review

Stiel, D. & Barratt, P. J. (1982) Early gastric cancer. *Medical Journal of Australia*, 2: 369-371.

Not in PICO

Sue-Ling, H. M., Martin, I., Griffith, J., Ward, D. C., Quirke, P., Dixon, M. F., Axon, A. T., McMahon, M. J. & Johnston, D. (1992) Early gastric cancer: 46 cases treated in one surgical department. *Gut*, 33: 1318-1322.

Not in PICO

Summers, A. & Khan, Z. (2009) Managing dyspepsia in primary care. *Practitioner*, 253: 23-27.

Narrative review

Sundar, N., Muraleedharan, V., Pandit, J., Green, J. T., Crimmins, R. & Swift, G. L. (2006) Does endoscopy diagnose early gastrointestinal cancer in patients with uncomplicated dyspepsia? *Postgraduate Medical Journal*, 82: 52-54.

Not in PICO

Suvakovic, Z., Bramble, M. G., Jones, R., Wilson, C., Idle, N. & Ryott, J. (1997) Improving the detection rate of early gastric cancer requires more than open access gastroscopy: a five year study. *Gut*, 41: 308-313.

Not in PICO

Suzuki, H., Gotoda, T., Sasako, M. & Saito, D. (2006) Detection of early gastric cancer: misunderstanding the role of mass screening. *Gastric Cancer*, 9: 315-319.

Not in PICO

Tachi, K. & Nkrumah, K. N. (2011) Appropriateness and diagnostic yield of referrals for oesophagogastroduodenoscopy at the Korle Bu teaching hospital. *West African Journal of Medicine*, 30: 158-163.

Not in PICO

Tachibana, M., Takemoto, Y., Monden, N., Nakashima, Y., Kinugasa, S., Dhar, D. K., Kotoh, T., Kubota, H., Kohno, H. & Nagasue, N. (1999) Clinicopathological features of early gastric cancer: results of 100 cases from a rural general hospital. *European Journal of Surgery*, 165: 319-325.

Not in PICO

- Talley, N. J. (1986) Dyspepsia and non-ulcer dyspepsia: An historical perspective. *Medical Journal of Australia*, 145: 614-618.
Narrative review
- Talley, N. J. (1996) Modern management of dyspepsia. [Review] [6 refs]. *Australian Family Physician*, 25: 47-52.
Narrative review
- Talley, N. J., Axon, A., Bytzer, P., Holtmann, G., Lam, S. K. & van Zanten, S. V. (1999) Management of uninvestigated and functional dyspepsia: a working party report for the World Congresses of Gastroenterology 1998. *Alimentary Pharmacology & Therapeutics*, 13: 1135-1148.
Guideline
- Tambo, M., Fujimoto, K., Miyake, M., Hoshiyama, F., Matsushita, C. & Hirao, Y. (2007) Clinicopathological review of 46 primary retroperitoneal tumors. *International Journal of Urology*, 14: 785-788.
Not in PICO
- Tan, Y. K. & Fielding, J. W. (2006) Early diagnosis of early gastric cancer. [Review] [132 refs]. *European Journal of Gastroenterology & Hepatology*, 18: 821-829.
Narrative review
- Tanko, M. N., Manasseh, A. N., Echejoh, G. O., Mandong, B. M., Malu, A. O., Okeke, E. N., Ladep, N. & Agaba, E. I. (2008) Relation between *Helicobacter pylori*, inflammatory (neutrophil) activity, chronic gastritis, gastric atrophy and intestinal metaplasia. *Nigerian Journal of Clinical Practice*, 11: 270-274.
Not in PICO
- Tao, G., Xing-Hua, L., Ai-Ming, Y., Wei-Xun, Z., Fang, Y., Xi, W., Li-Yin, W., Chong-Mei, L., Gui-Jun, F., Hui-Jun, S., Dong-Sheng, W., Yue, L., Xiao-Qing, L. & Jia-Ming, Q. (2014) Enhanced magnifying endoscopy for differential diagnosis of superficial gastric lesions identified with white-light endoscopy. *Gastric Cancer*, 17: 122-129.
Not in PICO
- Tartaglia, A., Bianchini, S. & Vezzadini, P. (2003) Biochemical diagnosis of gastroenteropancreatic endocrine tumors. *Minerva Medica*, 94: 1-7.
Narrative review
- Taylor, K. M., Powell, N., Foxton, M. R. & McNair, A. (2010) Follow-up of patients with iron deficiency anemia subsequent to negative upper and lower gastrointestinal investigations. *Gastroenterology*, 138: S636.
Not in PICO
- Teixeira, G. A., Marchini, J. S. & de Carvalho da Cunha, S. F. Gastric neoplasia misdiagnosed as an eating disorder. [References]. *Revista Brasileira de Psiquiatria* 33[3], 307-309. 2011.
Not in PICO
- Tey, J., Back, M. F., Shakespeare, T. P., Mukherjee, R. K., Lu, J. J., Lee, K. M., Wong, L. C., Leong, C. N. & Zhu, M. (2007) The role of palliative radiation therapy in symptomatic locally advanced gastric cancer. *International Journal of Radiation Oncology, Biology, Physics*, 67: 385-388.
Not in PICO
- Tey, J., Koh, W., Leong, C., Choo, B., Wong, L. & Lu, J. (2012) Clinical outcome of palliative radiation therapy in locally advanced, symptomatic gastric cancer in the modern era. *International Journal of Radiation Oncology Biology Physics*, 84: S315.
Not in PICO
- Tomba, C., Elli, L., Bardella, M. T., Soncini, M., Contiero, P., Locatelli, M. & Conte, D. (2013) Role of capsule endoscopy and double-balloon enteroscopy in early diagnosis of gastrointestinal malignancies in celiac patients at risk. *Digestive and Liver Disease*, 45: S138.
Not in PICO

- Towpik, E. (1982) [Early symptoms of cancer of the esophagus and cardia]. [Polish]. *Wiadomosci Lekarskie*, 35: 1209-1212.
Not in PICO
- Traynor, O. J., Lennon, J., Dervan, P. & Corrigan, T. (1987) Diagnostic and prognostic problems in early gastric cancer. *American Journal of Surgery*, 154: 516-519.
Not in PICO
- Tytgat, G. N., Bartelink, H., Bernards, R., Giaccone, G., van Lanschot, J. J., Offerhaus, G. J. & Peters, G. J. (2004) Cancer of the esophagus and gastric cardia: recent advances. [Review] [109 refs]. *Diseases of the Esophagus*, 17: 10-26.
Narrative review
- Tytgat, G. N. J. (2002) Role of endoscopy and biopsy in the work up of dyspepsia. *Gut*, 50: 13-16.
Narrative review
- Uehara, G., Nago, A., Espinoza, R., Vargas, G., Astete, M., Moran, L., Nunez, N., Mayuri, C., Valdivia, M., Chavez, M. & Moreno, C. (2007) [Optimal age for gastric cancer screening in patients with dyspepsia without alarm symptoms]. [Spanish]. *Revista de Gastroenterologia del Peru*, 27: 339-348.
Not in PICO
- Umeyama, K., Sowa, M., Kamino, K., Kato, Y. & Satake, K. (1982) Gastric carcinoma in young adults in Japan. *Anticancer Research*, 2: 283-286.
Not in PICO
- Unek, I. T., Celtik, A., Alacacioglu, A., Cokmert, S., Yavuzsen, T., Dogan, N. S., Oztop, I., Demirkan, B. & Yilmaz, U. (2007) Gastric carcinoma during pregnancy: Report of a case. *Turkish Journal of Gastroenterology*, 18: 41-43.
Not in PICO
- Uno, K., Iijima, K., Koike, T., Ara, N., Hatta, W., Kusaka, G. & Shimosegawa, T. (2011) The direct measurement of non-acid reflux episodes in patients with or without squamous cell carcinoma by 24 hours pH-impedance monitoring. *Gastroenterology*, 140: S669.
Not in PICO
- Urushizaki, I. (1990) [Palliative therapy in cancer. 3. Palliation of the symptoms from a malignant tumor (1)]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 17: 1383-1392.
Narrative review
- Vaira, D. (1996) How to manage the dyspeptic patient. *Helicobacter*, 1: 261-262.
Comment
- van Kerkhoven, L. A. S., van Rijswijk, S. J., van Rossum, L. G. M., Laheij, R. J. F., Witteman, E. M., Tan, A. C. I. T. & Jansen, J. B. M. J. (2007) Is there any association between referral indications for open-access upper gastrointestinal endoscopy and endoscopic findings? *Endoscopy*, 39: 502-506.
Not in PICO
- Vanis, N., Mesihovic, R., Ibricevic, L. & Dobrila-Dintinjana, R. (2013) Predictive value of endoscopic ultrasound in diagnosis and staging of primary gastric lymphoma. *Collegium Antropologicum*, 37: Suppl-7.
Not in PICO
- Vargas, C. G., Chavez, R. M., Sanchez, V., Rojas, R. P. & Verona, R. R. (2012) [Therapy for early gastric cancer with submucosal endoscopic dissection using the IT-Knife 2]. [Spanish]. *Revista de Gastroenterologia del Peru*, 32: 297-302.
Not in PICO
- Vilaichone, R.-K., Ratanachu-Ek, T. & Mahachai, V. (2010) Gastric adenocarcinoma and Helicobacter pylori infection in Thailand. *Gastrointestinal Endoscopy*, 71: AB359.
Not in PICO
- Vinagre, R. M., Campos, B. P. & Sousa, R. M. (2012) Case study of stomach adenocarcinoma conducted at a cancer referral hospital in northern Brazil. *Arquivos de Gastroenterologia*, 49: 125-

129.

Not in PICO

Voutilainen, M., Sipponen, P., Mecklin, J.-P., Juhola, M. & Farkkila, M. (2000) Gastroesophageal reflux disease: Prevalence, clinical, endoscopic and histopathological findings in 1128 consecutive patients referred for endoscopy due to dyspeptic and reflux symptoms. *Digestion*, 61: 6-13.

Not in PICO

Voutilainen, M., Mantynen, T., Kunnamo, I., Juhola, M., Mecklin, J. P. & Farkkila, M. (2003) Impact of clinical symptoms and referral volume on endoscopy for detecting peptic ulcer and gastric neoplasms. *Scandinavian Journal of Gastroenterology*, 38: 109-113.

Not in PICO

Voutilainen, M., Mantynen, T., Mauranen, K., Kunnamo, I. & Juhola, M. (2005) Is it possible to reduce endoscopy workload using age, alarm symptoms and H. pylori as predictors of peptic ulcer and oesophagogastric cancers? *Digestive & Liver Disease*, 37: 526-532.

Not in PICO

Wada, T., Tanabe, S., Ishido, K., Higuchi, K., Sasaki, T., Katada, C., Azuma, M., Naruke, A., Kim, M., Koizumi, W. & Mikami, T. (2013) DOG1 is useful for diagnosis of KIT-negative gastrointestinal stromal tumor of stomach. *World Journal of Gastroenterology*, 19: 9133-9136.

Not in PICO

Wafula, J. M., Lule, G. N., Otieno, C. F., Nyong'o, A. & Sayed, S. M. (2002) Upper gastrointestinal findings in diabetic outpatients at Kenyatta National Hospital, Nairobi. *East African Medical Journal*, 79: 232-236.

Not in PICO

Wang, P.-W., Jiang, H.-Q. & Wu, J.-J. (2010) Clinicopathologic and endoscopic characteristics of primary gastric malignant lymphoma: An analysis of 24 cases. [Chinese]. *World Chinese Journal of Digestology*, 18: 3352-3355.

Not in PICO

Wayman, J., Hayes, N., Raimes, S. A. & Griffin, S. M. (2000) Prescription of proton pump inhibitors before endoscopy: A potential cause of missed diagnosis of early gastric cancers. *Archives of Family Medicine*, 9: 385-388.

Not in PICO

Wiener, Y., Gold, R., Zehavy, S., Sandbank, J. & Halevy, A. (1956) [Primary gastrointestinal stromal tumors]. [Hebrew]. *Harefuah*, 140: 377-380.

Not in PICO

Williams, B., Luckas, M., Ellingham, J. H., Dain, A. & Wicks, A. C. (1988) Do young patients with dyspepsia need investigation? *Lancet*, 2: 1349-1351.

Not in PICO

Xia, B., Xia, H. H., Ma, C. W., Wong, K. W., Fung, F. M., Hui, C. K., Chan, C. K., Chan, A. O., Lai, K. C., Yuen, M. F. & Wong, B. C. (2005) Trends in the prevalence of peptic ulcer disease and Helicobacter pylori infection in family physician-referred uninvestigated dyspeptic patients in Hong Kong. *Alimentary Pharmacology & Therapeutics*, 22: 243-249.

Not in PICO

Xu, G., Gan, T., Rao, N., Liu, D. Y., Li, B. Y. & Li, Y. (2013) Detection of upper gastrointestinal early cancers based on gastroscopic images. *Journal of Investigative Medicine*, 61: S12-S13.

Not in PICO

Yalamarthi, S., Witherspoon, P., McCole, D. & Auld, C. D. (2004) Missed diagnoses in patients with upper gastrointestinal cancers. *Endoscopy*, 36: 874-879.

Not in PICO

Yamada, Y., Yoshino, K. & Matsumoto, S. (1980) Studies on clinical, histopathological characteristics and prognosis of patients with small-sized gastric carcinoma. [Japanese]. *Japanese Journal of Gastroenterology*, 77: 9-17.

Not in PICO

Yamada, S., Doyama, H., Yao, K., Uedo, N., Ezoe, Y., Oda, I., Kaneko, K., Kawahara, Y., Yokoi, C., Sugiura, Y., Ishikawa, H., Takeuchi, Y., Saito, Y. & Muto, M. (2014) An efficient diagnostic strategy for small, depressed early gastric cancer with magnifying narrow-band imaging: a post-hoc analysis of a prospective randomized controlled trial. *Gastrointestinal Endoscopy*, 79: 55-63.
Not in PICO

Yoon, D. W., Lee, B. J., Lee, J. H., Park, J. J., Kim, J. S., Bak, Y. T., Choi, W. J. & Mok, Y. J. (2012) A case of giant inflammatory ileal polyp removed by double-balloon enteroscopy. *Clinical Endoscopy*, 45: 198-201.
Not in PICO

Yun, G. W., Yang, Y. J., Song, I. C., Park, K. U., Baek, S. W., Yun, H. J., Kim, S., Jo, D. Y. & Lee, H. J. (2011) A prospective evaluation of adult men with iron-deficiency anemia in Korea. *Internal Medicine*, 50: 1371-1375.
Not in PICO

Zaninotto, G., Avellini, C., Barbazza, R., Baruchello, G., Battaglia, G. & Benedetti, E. (2001) Prevalence of intestinal metaplasia in the distal oesophagus, oesophagogastric junction and gastric cardia in symptomatic patients in north-east Italy: a prospective, descriptive survey. *Digestive and Liver Disease*, 33: 316-321.
Not in PICO

Zeeneldin, A. A., Saber, M. M., Seif El-Din, I. A. & Frag, S. A. (2013) Small intestinal cancers among adults in an Egyptian district: a clinicopathological study using a population-based cancer registry. *Journal of Egyptian National Cancer Institute*, 25: 107-114.
Not in PICO

Zhang, B., Cai, J. & Chen, G. (1999) Diagnosis and treatment of early gastric cancer: an experience from 61 cases. [Chinese]. *Zhonghua zhong liu za zhi [Chinese journal of oncology]*, 21: 383-385.
Not in PICO

Zou, X. M., Wang, X. S., Li, Y. L., Jin, Z. X., Piao, D. X., Li, X. Y., Huang, D. W., Liu, W. X., Zhang, J. G., Zhang, G. L., Zhang, H. M., Yu, Z. G., Zhang, J., Fan, D., Liu, W. Y., Xue, Y. W. & Xu, J. (2009) [Analysis of clinical characteristics of gastrointestinal cancer in Heilongjiang province, China 1998 to 2007]. [Chinese]. *Zhonghua Weichang Waike Zazhi*, 12: 577-580.
Not in PICO

Zullo, A., Hassan, C., Cristofari, F., Iegri, C., Villiva, N., Andriani, A. & Morini, S. (2010) Can we eradicate gastric MALT-lymphoma?. [Italian]. *Italian Journal of Medicine*, 4: 154-158.
Not in PICO

Review question:

Which investigations of symptoms of suspected stomach cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	2648	137	23/05/2013
<i>Premedline</i>	1980-2013	143	20	23/05/2013
<i>Embase</i>	1980-2013	3279	120	23/05/2013
<i>Cochrane Library</i>	1980-2013	151	7	23/05/2013
<i>Psychinfo</i>	1980-2013	1	0	23/05/2013
<i>Web of Science (SCI &</i>	1980-2013	147	34	23/05/2013

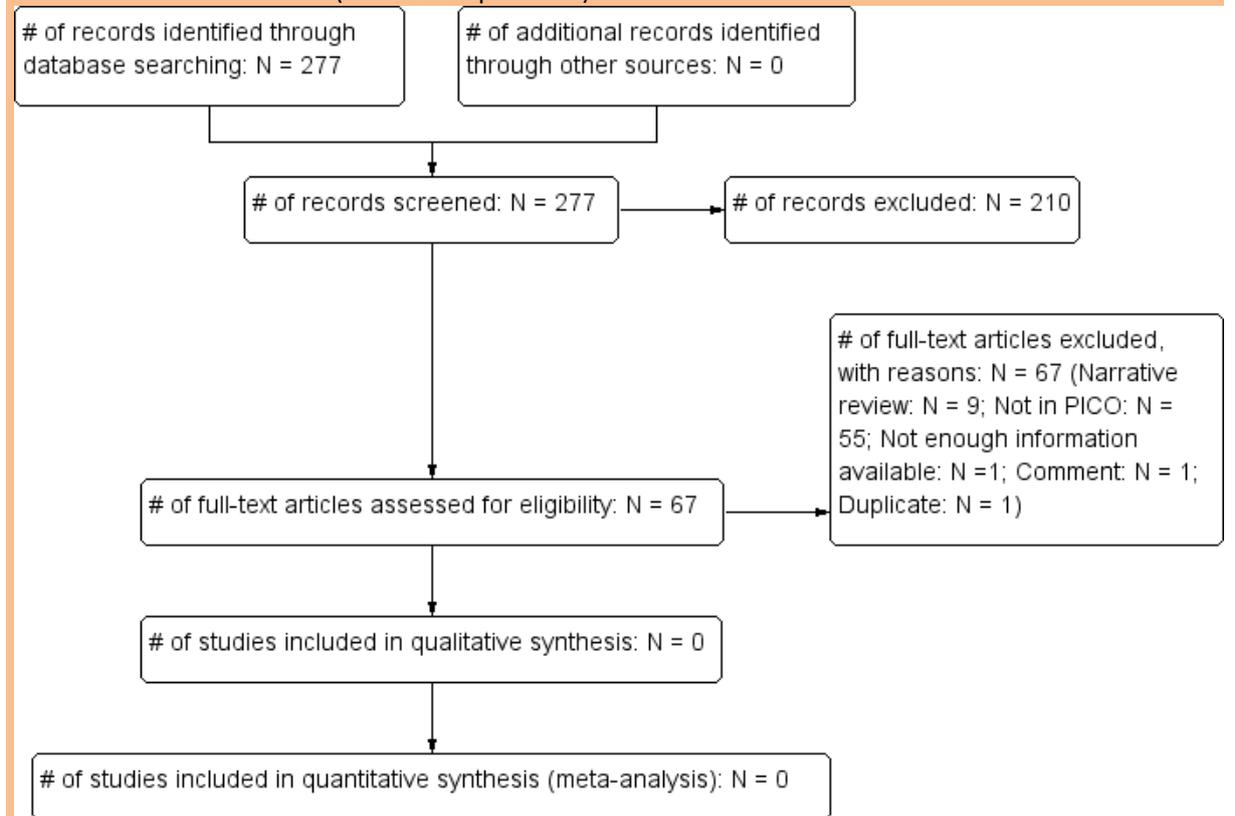
SSCI) and ISI Proceedings				
----------------------------------	--	--	--	--

Total References retrieved (after de-duplication): 256

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	5/2013-26/08/2014	17	4	26/08/2014
Premedline	5/2013-26/08/2014	109	8	26/08/2014
Embase	5/2013-26/08/2014	65	14	26/08/2014
Cochrane Library	5/2013-26/08/2014	54	0	26/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	5/2013-26/08/2014	13	0	26/08/2014

Total References retrieved (after de-duplication): 21



Study results

No evidence was identified pertaining to the diagnostic accuracy of upper gastrointestinal endoscopy, barium meal or abdominal ultrasound in patients with suspected stomach cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

- (1982) Value of biopsy and brush cytology in the diagnosis of gastric cancer. Shanghai Gastrointestinal Endoscopy Cooperative Group, People's Republic of China
126. *Gut*, 23: 774-776.
Not in PICO
- (2003) Information from your family doctor. Dyspepsia. *American Family Physician*, 68: 2040-2041.
Narrative review
- Abahussain, E. A., Hasan, F. A. & Nicholls, P. J. (1998) Dyspepsia and Helicobacter pylori infection: Analysis of 200 Kuwaiti patients referred for endoscopy. *Annals of Saudi Medicine*, 18: 502-505.
Not in PICO
- Abdel-Wahab, M., Attallah, A. M., Elshal, M. F., Eldousoky, I., Zalata, K. R., el-Ghawalby, N. A., Gad el-Hak, N., el-Ebidy, G. & Ezzat, F. (1996) Correlation between endoscopy, histopathology, and DNA flow cytometry in patients with gastric dyspepsia. *Hepato-Gastroenterology*, 43: 1313-1320.
Not in PICO
- Aberra, F., Ates, F., Li, Z., Slaughter, J. C., Higginbotham, T. & Vaezi, M. F. (2014) Appropriateness of upper endoscopy referrals in patients with GERD by specialty. *Gastroenterology*, 146: S749-S750.
Published as abstract only. Not enough information can be extracted to ascertain relevance.
- Aibe, T., Fujimura, H., Noguchi, T., Ohtani, T., Tanaka, T., Ito, T., Fuji, T. & Takemoto, T. (1989) Endosonographic detection and staging of early gastric cancer. *Zeitschrift fur Gastroenterologie*, 27: 71-78.
Not available, but I think it is not in PICO
- Akhtar, A. J. & Shaheen, M. A. (2004) Dyspepsia in African-American and Hispanic patients. *Journal of the National Medical Association*, 96: 635-640.
Not in PICO
- Allum, W. H., Blazeby, J. M., Griffin, S. M., Cunningham, D., Jankowski, J. A. & Wong, R. (2011) Guidelines for the management of oesophageal and gastric cancer. *Gut*, 60: 1449-1472.
Guideline
- Amin, I., Steer, P. & Madhotra, R. (2009) Appropriateness of the "straight to test" gastroscopy request for patients with suspected gastrointestinal cancers. *Gut*, 58: A150.
Not in PICO
- An, J. W., Cheung, D. Y., Seo, M. W., Lee, H. J., Lee, I. K., Kim, T. J., Kim, J. I. & Kim, J. K. (2013) [A case of spindle cell carcinoma of the stomach presenting with hematochezia and weight loss due to fistulous tract formation with colon]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 62: 126-130.
Not in PICO
- Anderson, W. D., III & Strayer, S. M. (2013) Evaluation of nausea and vomiting: a case-based approach. *American Family Physician*, 88: 371-379.
Narrative review
- Andrade, B., Alvarado, L., Zurita, M. & Andrade, S. (2013) Early and advanced gastric cancer: Clinical, endoscopy, histopathology and comparative study. *Journal of Gastroenterology and Hepatology*, 28: 652-653.
Not in PICO
- Ang, T. L., Fock, K. M., Kiong, T. E., Tan, J., Poh, C. H., Ong, J., Ang, D., Kwek, A., Tan, P. S. & Lim, K. B. (2010) Does narrow band imaging provide incremental diagnostic yield over white light endoscopy in the detection and differentiation of premalignant and malignant gastric lesions in a Chinese population with intermediate gastric cancer risk? *Gastrointestinal Endoscopy*, 71: AB202.
Same data as Ang (2012)
- Ang, T. L., Fock, K. M., Teo, E. K., Tan, J., Poh, C. H., Ong, J. & Ang, D. (2012) The diagnostic utility of narrow band imaging magnifying endoscopy in clinical practice in a population with intermediate gastric cancer risk. *European Journal of Gastroenterology & Hepatology*, 24: 362-367.

- Setting is unclear, but don't think population is in PICO
- Ansari, S. & Ford, A. C. (2013) Initial management of dyspepsia in primary care: An evidence-based approach. *British Journal of General Practice*, 63: 498-499.
Narrative review
- Aparcero, M. (1989) [Chromoscopy in the diagnosis of gastric cancer]. [Spanish]. *Gen*, 43: 120-123.
Narrative review
- Ares, D. M., Aguirre, P. A. A., Barrenechea, I. M. G., Gomez, L. C. & Peral, A. P. (2008) Usefulness of ultrasonography in diagnosing patients suspect for digestive tract neoplasms. *Revista Espanola de Enfermedades Digestivas*, 100: 545-551.
Not in PICO
- Asano, N., Iijima, K., Terai, S., Uno, K., Endo, H., Koike, T., Iwai, W., Iwabuchi, T., Hatta, W., Abe, Y., Imatani, A. & Shimosegawa, T. (2011) Signet Ring Cell Gastric Cancer Occurring after Radiation Therapy for Helicobacter pylori-Uninfected Mucosa-Associated Lymphoid Tissue Lymphoma. *Case Reports Gastroenterology*, 5: 325-329.
Not in PICO
- Atoba, M. A., Ayoola, E. A. & Olubuyide, I. O. (1986) Radiological and endoscopic correlation in upper gastrointestinal haemorrhage and malignancy. *Scandinavian Journal of Gastroenterology - Supplement*, 124: 149-151.
Not in PICO
- Axon, A. (2006) Symptoms and diagnosis of gastric cancer at early curable stage. [Review] [37 refs]. *Best Practice & Research in Clinical Gastroenterology*, 20: 697-708.
Narrative review
- Axon, A. T. R. (1997) Chronic dyspepsia: Who needs endoscopy? *Gastroenterology*, 112: 1376-1380.
Narrative review
- Bai, Y., Li, Z. S., Zou, D. W., Wu, R. P., Yao, Y. Z., Jin, Z. D., Ye, P., Li, S. D., Zhang, W. J., Du, Y. Q., Zhan, X. B., Liu, F., Gao, J. & Xu, G. M. (2010) Alarm features and age for predicting upper gastrointestinal malignancy in Chinese patients with dyspepsia with high background prevalence of Helicobacter pylori infection and upper gastrointestinal malignancy: an endoscopic database review of 102 665 patients from 1996 to 2006. *Gut*, 59: 722-728.
Not in PICO
- Ballantyne, K. C., Morris, D. L., Jones, J. A., Gregson, R. H. & Hardcastle, J. D. (1987) Accuracy of identification of early gastric cancer. *British Journal of Surgery*, 74: 618-619.
Not in PICO
- Balogh, I. (1992) Three decades of roentgen-diagnosis of the upper digestive tract in the light of modern endoscopy. [Hungarian]. *Orvosi Hetilap*, 133: 3127-3133.
Narrative review
- Bane, A., Ashenafi, S. & Kassa, E. (2009) Pattern of upper gastrointestinal tumors at Tikur Anbessa Teaching Hospital in Addis Ababa, Ethiopia: a ten-year review. *Ethiopian Medical Journal*, 47: 33-38.
Not in PICO
- Barenys De, L. M., Rota, R., Moreno, V., Villafila, R., Garcia-Bayo, I., Abad, A., Pons, J. M. V. & Pique, J. M. (2003) Prospective validation of a clinical scoring system for the diagnosis of organic dyspepsia. [Spanish]. *Medicina Clinica*, 121: 766-771.
Not in PICO
- Barndt, J. (1987) General practice related significance of the cocard phenomenon in the ultrasound image. [German]. *Zeitschrift fur Arztliche Fortbildung*, 81: 177-180.
Not in PICO
- Bergholt, M. S., Zheng, W., Lin, K., Ho, K. Y., Teh, M., Yeoh, K. G., So, J. B. & Huang, Z. (2011) Characterizing variability in in vivo Raman spectra of different anatomical locations in the upper gastrointestinal tract toward cancer detection. *Journal of Biomedical Optics*, 16: 037003.
Not in PICO

- Berndt, H. & Neumann, P. (1983) [Early detection of malignant tumors of the gastrointestinal organs]. [German]. *Zeitschrift für Ärztliche Fortbildung (Jena)*, 77: 16-20.
Narrative review
- Blackstone, M. O. (1984) The endoscopic diagnosis of early gastric cancer. *Gastrointestinal Endoscopy*, 30: 105-106.
Narrative review
- Boldys, H., Marek, T. A., Wanczura, P., Matusik, P. & Nowak, A. (2003) Even young patients with no alarm symptoms should undergo endoscopy for earlier diagnosis of gastric cancer. *Endoscopy*, 35: 61-67.
Not in PICO
- Bones, J., Byrne, J. C., O'Donoghue, N., McManus, C., Scaife, C., Boissin, H., Nastase, A. & Rudd, P. M. (2011) Glycomic and glycoproteomic analysis of serum from patients with stomach cancer reveals potential markers arising from host defense response mechanisms. *Journal of Proteome Research*, 10: 1246-1265.
Not in PICO
- Borchard-Tuch, C. (2007) Early detection of cancer: Effectiveness of current tests. [German]. *Pharmazeutische Zeitung*, 152: 18-25.
Narrative review
- Boroumand-Noughabi, S., Sima, H. R., Ghaffarzadehgan, K., Jafarzadeh, M., Raziee, H. R., Hosseinneshad, H., Moaven, O., Rajabi-Mashhadi, M. T., Azarian, A. A., Mashhadinejad, M. & Tavakkol-Afshari, J. (2010) Soluble Fas might serve as a diagnostic tool for gastric adenocarcinoma. *BMC Cancer*, 10: 275.
Not in PICO
- Bosseckert, H. (1999) Advances in gastric carcinoma - Endoscopic up-to-date diagnostic. [German]. *Verdauungskrankheiten*, 17: 31-36.
Not in PICO
- Bovio, G., Fonte, M. L. & Baiardi, P. (2014) Prevalence of upper gastrointestinal symptoms and their influence on nutritional state and performance status in patients with different primary tumors receiving palliative care. *American Journal of Hospice & Palliative Medicine*, 31: 20-26.
Not in PICO
- Brandt, D., Muramatsu, Y., Ushio, K., Mizuguchi, Y., Itabashi, M., Yoshida, S., Moriyama, N., Nawano, S., Ishikawa, T., Yamada, T., Hirota, T. & Maruyama, K. (1989) Synchronous early gastric cancer. *Radiology*, 173: 649-652.
Not in PICO
- Brignoli, R., Watkins, P. & Halter, F. (1997) The Omega-Project - A comparison of two diagnostic strategies for risk- and cost-oriented management of dyspepsia. *European Journal of Gastroenterology & Hepatology*, 9: 337-343.
Not in PICO
- Broe, M., Barry, M., Patchett, S. & Hill, A. D. (2013) Evaluating the clinical efficacy and cost effectiveness of direct access endoscopy. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 11: 304-308.
Not in PICO
- Bundhoo, K., Aravinthan, A., Lithgo, K., Price, T. & Johnson, M. (2014) Cost efficiency of faecal calprotectin in assessing new referrals with altered bowel habit. *Gut*, 63: A81.
Not in PICO
- Bustamante, M., Devesa, F., Borghol, A., Ortuno, J. & Ferrando, M. J. (2002) Accuracy of the initial endoscopic diagnosis in the discrimination of gastric ulcers: is endoscopic follow-up study always needed? *Journal of Clinical Gastroenterology*, 35: 25-28.
Not in PICO

- Bytzer, P. (1998) How should new-onset dyspepsia be managed in general and specialist practice? *Baillieres Clinical Gastroenterology*, 12: 587-599.
Narrative review
- Bytzer, P. (2004) Diagnostic approach to dyspepsia. *Best Practice & Research in Clinical Gastroenterology*, 18: 681-693.
Narrative review
- Can, M. F., Yagci, G. & Cetiner, S. (2011) Sentinel lymph node biopsy for gastric cancer: Where do we stand? *World Journal of Gastrointestinal Surgery*, 3: 131-137.
Not in PICO
- Cardillo, M. R. & Agnello, M. (1990) Endoscopic brush cytology in the diagnosis of gastric malignancy 245. *Journal of Experimental and Clinical Cancer Research*, 9: 113-120.
Not in PICO
- Cardin, F., Zorzi, M. & Terranova, O. (2007) Implementation of a guideline versus use of individual prognostic factors to prioritize waiting lists for upper gastrointestinal endoscopy. *European Journal of Gastroenterology & Hepatology*, 19: 549-553.
Not in PICO
- Casadei, A., Simone, A., Cavargini, E., De, V. E. & Ricci, E. (2011) Advanced endoscopy (FICE NBI). How to improve gastric and duodenal tumor diagnosis. [Italian]. *Giornale Italiano di Endoscopia Digestiva*, 34: 131-135.
Narrative review
- Cerqueira, R., Fernandes, C., Correia, M. & Manso, M. C. (2008) Indications for upper gastrointestinal endoscopy: The accuracy of the American Society for Gastrointestinal Endoscopy guidelines in a Portuguese hospital. *Acta Medica Portuguesa*, 21: 427-432.
Not in PICO
- Chang, F. Y., Lee, O. & Lee, S. D. (1994) Coexistent duodenal ulcer among patients with gastric carcinoma. *South African Medical Journal.Suid-Afrikaanse Tydskrif Vir Geneeskunde*, 84: 618-621.
Not in PICO
- Chen, J., Zhuo, S., Chen, G., Yan, J., Yang, H., Liu, N., Zheng, L., Jiang, X. & Xie, S. (2011) Establishing diagnostic features for identifying the mucosa and submucosa of normal and cancerous gastric tissues by multiphoton microscopy. *Gastrointestinal Endoscopy*, 73: 802-807.
Not in PICO
- Chey, W. D. & Moayyedi, P. (2004) Review article: uninvestigated dyspepsia and non-ulcer dyspepsia - the use of endoscopy and the roles of Helicobacter pylori eradication and antisecretory therapy. *Alimentary Pharmacology & Therapeutics*, 19: 1-8.
Narrative review
- Chin, S. Y., Lee, B. H., Kim, K. H., Park, S. T., Do, Y. S. & Cho, K. J. (1994) Radiological prediction of the depth of invasion and histologic type in early gastric cancer. *Abdominal Imaging*, 19: 521-526.
Not in PICO
- Chiodaroli, R., Pancaldi, R., Bruni, G. C., Avogadri, C., Procino, M., Angelini, O. & Tirro, P. (1987) Digestive endoscopy in the diagnosis of early gastric cancer. Personal case series. [Italian]. *Minerva Chirurgica*, 42: 735-737.
Not in PICO
- Christie, J., Shepherd, N. A., Codling, B. W. & Valori, R. M. (1997) Gastric cancer below the age of 55: implications for screening patients with uncomplicated dyspepsia. *Gut*, 41: 513-517.
Not in PICO
- Christinaz, D., Meyer, P., Moser, G. & Rohner, A. (1984) [25 cases of gastric smooth muscle tumors and review of the literature]. [French]. *Schweizerische Medizinische Wochenschrift.Journal Suisse de Medecine*, 114: 708-710.
Not in PICO

- Christinaz, D., Meyer, P., Moser, G. & Rohner, A. (1984) Gastric smooth muscle tumors: 25 cases. [French]. *Schweizerische Medizinische Wochenschrift*, 114: 708-710.
Not in PICO
- da Silva, J. B., Mauricio, S. F., Bering, T. & Correia, M. I. (2013) The relationship between nutritional status and the Glasgow prognostic score in patients with cancer of the esophagus and stomach. *Nutrition & Cancer*, 65: 25-33.
Not in PICO
- Dakubo, J. C., Clegg-Lampthey, J. N. & Sowah, P. (2011) Appropriateness of referrals for upper gastrointestinal endoscopy. *West African Journal of Medicine*, 30: 342-347.
Not in PICO
- Deakin, M., Colin-Jones, D. G. & Vessey, M. P. (1988) Routine practice in the diagnosis of adenocarcinoma of the stomach: a survey of tumours diagnosed in the Portsmouth and Oxford Health Districts 1979-1980. *Postgraduate Medical Journal*, 64: 33-37.
Not in PICO
- Deltenre, M. (2000) [Dyspepsia in general medicine: current diagnostic approach]. [Review] [16 refs] [French]. *Revue Medicale de Bruxelles*, 21: A309-A313.
Narrative review
- Demirci, S. & Gohchi, A. (1990) A comparative study for fiberoptic and video endoscopic determination of the extent in minimal changes of gastric mucosa using indigo dye spraying. *Surgical Endoscopy*, 4: 80-82.
Not in PICO
- Dettoni, G., Noya, G., Bacciu, P. P., Meloni, G., Niolu, P., Cossu, M. L., Chironi, G. & Marogna, P. (1990) [Early gastric cancer: radiologic, endoscopic or combined diagnosis?]. [Review] [21 refs] [Italian]. *Minerva Chirurgica*, 45: 615-618.
Narrative review
- Di Giulio, E., Hassan, C., Marmo, R., Zullo, A. & Annibale, B. (2010) Appropriateness of the indication for upper endoscopy: A meta-analysis. *Digestive and Liver Disease*, 42: 122-126.
Not in PICO
- Diaz-Zorrilla, C., Grube-Pagola, P., Remes-Troche, J. M. & Ramos-De la Medina, A. (2012) Glomus tumour of the stomach: an unusual cause of gastrointestinal bleeding. *BMJ Case Reports*, 2012, 2012.
Not in PICO
- Dobronte, Z., Karacsony, G., Nafradi, J., Pap, A. & Varro, V. (1980) [Early gastric carcinoma detection by endoscopy and biopsy; clinical experiences (author's transl)]. [German] 136. *Wiener Klinische Wochenschrift*, 92: 118-122.
Not in PICO
- Dominguez, R. L., Crockett, S. D., Lund, J. L., Suazo, L. P., Heidt, P., Martin, C. & Morgan, D. R. (2013) Gastric cancer incidence estimation in a resource-limited nation: use of endoscopy registry methodology. *Cancer Causes & Control*, 24: 233-239.
Not in PICO
- Eckardt, V. F., Giessler, W., Kanzler, G., Remmele, W. & Bernhard, G. (1990) Clinical and morphological characteristics of early gastric cancer. A case-control study. *Gastroenterology*, 98: 708-714.
Not in PICO
- Edenholm, M., Gustavsson, R. & Jansson, O. (1985) Endoscopic findings in patients with ulcer-like dyspepsia. *Scandinavian Journal of Gastroenterology, Supplement*, 20: 163-171.
Not in PICO
- El, A. R. & Gerke, H. (2012) Gastric cancer: endoscopic diagnosis and staging. [Review]. *Surgical Oncology Clinics of North America*, 21: 1-19.
Narrative review

- Falt, P., Hanousek, M., Kundratova, E. & Urban, O. (2013) [Precancerous conditions and lesions of the stomach]. [Czech]. *Klinicka Onkologie*, 26: Suppl-8.
Narrative review
- Fashner, J. & Gitu, A. C. (2013) Common Gastrointestinal Symptoms: dyspepsia and *Helicobacter pylori*. [Review]. *Fp Essentials*, 413: 24-28.
Narrative review
- Ferrari, F., Fagioli, Z. A., Nucci, C., Sereni, P., Ceccherini, E. & Baldi, C. (1987) [Echographic identification of symptomatic gastric carcinoma and its lymph node metastases]. [Italian]. *Radiologia Medica*, 73: 417-420.
Not in PICO
- Finch, P. J., Ryan, F. P., Rogers, K. & Holt, S. (1987) Gastric enzymes as a screening test for gastric cancer
113. *Gut*, 28: 319-322.
Not in PICO
- Ford, A. C. & Moayyedi, P. (2009) Should we step-up or step-down in the treatment of new-onset dyspepsia in primary care? *Polskie Archiwum Medycyny Wewnetrznej-Polish Archives of Internal Medicine*, 119: 391-396.
Narrative review
- Fraser, G. M. & Earnshaw, P. M. (1983) The double-contrast barium meal: a correlation with endoscopy. *Clinical Radiology*, 34: 121-131.
Not in PICO
- Fridman, E. G. & Slesareva, I. (1988) [The role of x-ray examination in the detection of early cancer of the stomach]. [Russian]. *Sovetskaia Meditsina*.(9):86-9, 1988., 86-89.
In Russian, not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Froehlich, F., Bochud, M., Gonvers, J. J., Dubois, R. W., Vader, J. P., Wietlisbach, V. & Burnand, B. (1999) 1. Appropriateness of gastroscopy: dyspepsia. [Review] [167 refs]. *Endoscopy*, 31: 579-595.
Narrative review
- Garcia, C. F., Basterra, R. G., Lopez Barbarin, J. M., Razquin, M. J., Diaz de, O. R., Bautista, R. G. & Merino, A. A. (1980) [Early gastric cancer. Clinical, radiological and endoscopically guided biopsy evaluation. Report of 8 cases]. [Spanish]. *Revista Clinica Espanola*, 157: 29-33.
Not in PICO
- Ge, Z. Z., Hu, Y. B. & Xiao, S. D. (2004) Capsule endoscopy and push enteroscopy in the diagnosis of obscure gastrointestinal bleeding. *Chinese Medical Journal*, 117: 1045-1049.
Not in PICO
- Ghita, D., Glavici, A., Saftoiu, A., Plesea, I. E., Cazacu, S., Georgescu, C. & Ciurea, T. (2011) The role of endoscopic examination accompanied by histological examination on biopsy samples in the diagnosis of gastric carcinoma. *Romanian Journal of Morphology & Embryology*, 52: Suppl-62.
Not in PICO
- Goldstein, F., Kline, T. S., Kline, I. K., Thornton, J. J., III, Abramson, J. & Bell, L. (1983) Early gastric cancer in a United States hospital. *American Journal of Gastroenterology*, 78: 715-719.
Not in PICO
- Gong, J.-S., Liu, T., Chen, J., Zhu, J. & Xu, J.-M. (2011) Multi-slice CT virtual gastroscopy in demonstrating gastric cancer: Comparison with optical gastroscopy and pathology. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 27: 345-348.
Not in PICO
- Goodman, K. J., Munday, R., Cheung, J., Girgis, S., Geary, J., Keng, A. B., Chang, H. & Veldhuyzen Van, Z. S. (2011) Symptomatic manifestations of *H. pylori*-associated disease in a Northern Canadian community. *Helicobacter*, 16: 104.
Not in PICO

- Gorshkov, A. N., Meshkov, V. M., Gracheva, N. I. & Zaritskaia, V. A. (2001) [Possibilities of radiologic methods (ultrasonography, computed tomography) in the preoperative evaluation of intramural invasion of gastric cancer]. [Russian]. *Vestnik Rentgenologii i Radiologii*.(2):27-34, 2001 Mar-Apr., 27-34.
Not in PICO
- Gorshkov, A. N. (2003) [Potential of abdominal computed tomography and ultrasonography for the complex diagnosis of early gastric cancer]. [Russian]. *Voprosy Onkologii*, 49: 217-223.
Not in PICO
- Gotoda, T. (2012) Diagnosis of early gastric cancer-chromoendoscopy, NBI and magnification. *Journal of Gastroenterology and Hepatology*, 27: 33.
Narrative review
- Grassini, M., Cavanenghi, D., Sorisio, V. & Amerio, G. M. (1990) Early gastric cancer. A follow-up of 20 cases. [Italian]. *Minerva Chirurgica*, 45: 943-945.
Not in PICO
- Grenacher, L. & Hansmann, J. (2007) [Radiological imaging of the upper gastrointestinal tract. Part II. The stomach]. [Review] [34 refs] [German]. *Radiologe*, 47: 71-88.
Narrative review
- Guirguis, E. M. (1989) Gastric cancer in primary care: how hard should you look? *Canadian Family Physician*, 35: 243-248.
Narrative review
- Gurzu, S., Copotoiu, C., Azamfirei, L. & Jung, I. (2013) A Caliber Persistent Artery (Dieulafoy's Lesion) which is Associated with an Early-Stage Gastric Stump Cancer Following a Distal Gastrectomy. *Journal of Clinical and Diagnostic Research JCDR*, 7: 1717-1719.
Not in PICO
- Hanamure, Y. (1991) [Gastric mucosa investigated by endoscopic biopsy and functional study]. [Japanese]. *Nippon Ika Daigaku Zasshi - Journal of the Nippon Medical School*, 58: 640-652.
Not in PICO
- Harmon, R. C. & Peura, D. A. (2010) Evaluation and management of dyspepsia. *Therapeutic Advances in Gastroenterology*, 3: 87-98.
Narrative review
- Haruma, K., Suzuki, T., Tsuda, T., Yoshihara, M., Sumii, K. & Kajiyama, G. (1991) Evaluation of tumor growth rate in patients with early gastric carcinoma of the elevated type. *Gastrointestinal Radiology*, 16: 289-292.
Not in PICO
- Hedenbro, J. L., Ekelund, M. & Wetterberg, P. (1991) Endoscopic diagnosis of submucosal gastric lesions. The results after routine endoscopy. *Surgical Endoscopy*, 5: 20-23.
Not in PICO
- Holdstock, G. & Bruce, S. (1981) Endoscopy and gastric cancer. *Gut*, 22: 673-676.
Not in PICO
- Hosokawa, O., Tsuda, S., Kidani, E., Watanabe, K., Tanigawa, Y., Shirasaki, S., Hayashi, H. & Hinoshita, T. (1998) Diagnosis of gastric cancer up to three years after negative upper gastrointestinal endoscopy. *Endoscopy*, 30: 669-674.
Unclear setting, but think population not in PICO
- Hsu, Y. C., Yang, T. H., Liou, J. M., Hsu, W. L., Lin, H. J., Wu, H. T., Lin, J. T., Wang, H. P. & Wu, M. S. (2012) Can clinical features stratify use of endoscopy for dyspeptic patients with high background prevalence of upper gastrointestinal cancer? *Digestive and Liver Disease*, 44: 218-223.
Not in PICO
- Hu, J., Zhang, X., Li, B., Zhang, M., Wang, C. & Chen, G. (2013) The clinical value of 18F-FDG PET/CT in the evaluation of bone metastases undetermined origin. *Clinical Imaging*, 37: 922-924.
Not in PICO

- Huang, J. Y., Jiang, H. P., Chen, D. & Tang, H. L. (2011) Primary gastric signet ring cell carcinoma presenting as cardiac tamponade. *World Journal of Gastrointestinal Oncology*, 3: 67-70.
Not in PICO
- Hungin, A. P. S., Rubin, G. P., Russell, A. J. & Convery, B. (1997) Guidelines for dyspepsia management in general practice using focus groups. *British Journal of General Practice*, 47: 275-279.
Not in PICO
- Hungin, A. P. S. & Rubin, G. P. (2001) Management of dyspepsia across the primary-secondary healthcare interface. *Digestive Diseases*, 19: 219-224.
Narrative review
- Hwang, E. J., Jang, J. Y., Kim, Y. W., Dong, S. H., Kim, H. J., Kim, B. H. & Chang, Y. W. (2013) A case of early gastric cancer with solitary metastasis to the pleura. *Clinical Endoscopy*, 46: 666-670.
Not in PICO
- Ichikawa, H., Yamada, T., Horikoshi, H., Doi, H., Matsue, H., Tobayashi, K., Sasagawa, M. & Higa, A. (2010) X-ray diagnosis of early gastric cancer. *Japanese Journal of Clinical Oncology*, 40: e1-e18.
Not in PICO
- Ihara, E., Matsuzaka, H., Honda, K., Hata, Y., Sumida, Y., Akiho, H., Misawa, T., Toyoshima, S., Chijiwa, Y., Nakamura, K. & Takayanagi, R. (2013) Mucosal-incision assisted biopsy for suspected gastric gastrointestinal stromal tumors. *World Journal of Gastrointestinal Endoscopy*, 5: 191-196.
Not in PICO
- Ihara, E., Matsuzaka, H., Honda, K., Hata, Y., Sumida, Y., Akiho, H., Misawa, T., Toyoshima, S., Chijiwa, Y., Nakamura, K. & Takayanagi, R. (2013) Mucosal-incision assisted biopsy for suspected gastric gastrointestinal stromal tumors. *World Journal of Gastrointestinal Endoscopy*, 5: 191-196.
Not in PICO
- Iishi, H. & Tatsuta, M. (1985) Endoscopic diagnosis of early gastric cancer with less malignant appearance. [Japanese]. *Gastroenterological Endoscopy*, 27: 1056-1057.
Not in PICO
- Irving, M. J., Lamb, P. J., Irving, R. J. & Raimes, S. A. (2002) Speeding up the diagnosis of oesophago-gastric cancer. *Nursing Times*, 98: 35-37.
Not in PICO
- Ivanov, S. & Karanov, S. (1986) [Current diagnostic methods of examination in early ascertaining diagnosis of stomach carcinoma]. [Bulgarian]. *Khirurgiia*, 39: 56-59.
Not in PICO
- Jones, R. (1986) Upper gastrointestinal endoscopy--a view from general practice. *Journal of the Royal College of General Practitioners*, 36: 6-8.
Not in PICO
- Kadowaki, Y., Nishimura, T., Komoto, S., Yuasa, T., Tamura, R., Okamoto, T. & Ishido, N. (2014) - Gastroduodenal intussusception caused by a gastric collision tumor consisting of adenocarcinoma and neuroendocrine carcinoma. - *Case Reports Gastroenterology*, 8: 89-94.
Not in PICO
- Kagevi, I., Lofstedt, S. & Persson, L. G. (1989) Endoscopic findings and diagnoses in unselected dyspeptic patients at a primary health care center. *Scandinavian Journal of Gastroenterology*, 24: 145-150.
Not in PICO
- Kakeji, Y., Yamaguchi, S., Yoshida, D., Tanoue, K., Ueda, M., Masunari, A., Utsunomiya, T., Imamura, M., Honda, H., Maehara, Y. & Hashizume, M. (2006) Development and assessment of morphologic criteria for diagnosing gastric cancer using confocal endomicroscopy: an ex vivo and in vivo study. *Endoscopy*, 38: 886-890.
Not in PICO
- Kapoor, N., Bassi, A., Sturgess, R. & Bodger, K. (2005) Predictive value of alarm features in a rapid access upper gastrointestinal cancer service. *Gut*, 54: 40-45.

Not in PICO

Karbasi, A., Karbasi-Afshar, R., Ahmadi, J. & Saburi, A. (2013) Retroperitoneal fibrosis as a result of signet ring cell gastric cancer: a case-based review. *Journal of Gastrointestinal Cancer*, 44: 94-97.

Not in PICO

Kataoka, M., Kawai, T., Yagi, K., Sugimoto, H., Yamamoto, K., Hayama, Y., Nonaka, M., Aoki, T., Fukuzawa, M., Fukuzawa, M., Itoi, T. & Moriyasu, F. (2013) Mucosal cutting biopsy technique for histological diagnosis of suspected gastrointestinal stromal tumors of the stomach. *Digestive Endoscopy*, 25: 274-280.

Not in PICO

Kato, M., Kaise, M., Yonezawa, J., Goda, K., Toyozumi, H., Yoshimura, N., Yoshida, Y., Kawamura, M. & Tajiri, H. (2009) Trimodal imaging endoscopy may improve diagnostic accuracy of early gastric neoplasia: a feasibility study. *Gastrointestinal Endoscopy*, 70: 899-906.

Not in PICO

Kato, M., Kaise, M., Yonezawa, J., Toyozumi, H., Yoshimura, N., Yoshida, Y., Kawamura, M. & Tajiri, H. (2010) Magnifying endoscopy with narrow-band imaging achieves superior accuracy in the differential diagnosis of superficial gastric lesions identified with white-light endoscopy: a prospective study. *Gastrointestinal Endoscopy*, 72: 523-529.

Not in PICO

Kawada, K. (2012) [Diagnosis of early gastric cancer using transnasal endoscope]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 70: 1748-1751.

Narrative review

Kaya, Z. R., Caliskan, F. A., Ekmekcioglu, O., Vural, T. O., Sager, M. S., Halac, M. & Sonmezoglu, K. (2012) Is there any clinical benefit to obtain delayed FDG-PET/CT Scan in patients with signet ring cell gastric carcinoma? *European Journal of Nuclear Medicine and Molecular Imaging*, 39: S583.

Not in PICO

Kelessis, N. G., Vassilopoulos, P. P., Tsamakidis, K. G., Bai, M. G., Avital, S. & Rosenthal, R. J. (2003) Is gastroscopy still a valid diagnostic tool in detecting gastric MALT lymphomas? A dilemma beyond the eye. Mucosa-associated lymphoid tissue. *Surgical Endoscopy*, 17: 469-474.

Not in PICO

Khademi, H., Radmard, A.-R., Malekzadeh, F., Kamangar, F., Nasseri-Moghaddam, S., Johansson, M., Byrnes, G., Brennan, P. & Malekzadeh, R. (2012) Diagnostic accuracy of age and alarm symptoms for upper GI malignancy in patients with dyspepsia in a GI clinic: A 7-year cross-sectional study. *PLoS ONE*, 7.

Not in PICO

Kim, S. H., Han, J. K., Lee, K. H., Chung, J. W., Yang, H. K. & Choi, B. I. (2003) Computed tomography gastrography with volume-rendering technique: correlation with double-contrast barium study and conventional gastroscopy. *Journal of Computer Assisted Tomography*, 27: 140-149.

Narrative review

Kobayashi, M., Tajiri, H., Seike, E., Shitaya, M., Tounou, S., Mine, M. & Oba, K. (2001) Detection of early gastric cancer by a real-time autofluorescence imaging system. *Cancer Letters*, 165: 155-159.

Not in PICO

Kochhar, R., Rajwanshi, A., Malik, A. K., Gupta, S. K. & Mehta, S. K. (1988) Endoscopic fine needle aspiration biopsy of gastroesophageal malignancies
107. *Gastrointestinal Endoscopy*, 34: 321-323.

Not in PICO

Koontz, M. Z., Visser, B. M. & Kunz, P. L. (2012) Neoadjuvant imatinib for borderline resectable GIST. *Journal of the National Comprehensive Cancer Network*, 10: 1477-1482.

Not in PICO

Korstanje, A., den Hartog, G., Biemond, I. & Lamers, C. B. H. W. (2002) The serological gastric biopsy: a non-endoscopical diagnostic approach in management of the dyspeptic patient - Significance

- for primary care based on a survey of the literature. *Scandinavian Journal of Gastroenterology*, 37: 22-26.
Narrative review
- Korstanje, A., van, E. S., Offerhaus, J. A., Waltman, F. L., Hartog, G., Roelandse, F. W., Souverijn, J. H., Biemond, I. & Lamers, C. B. (2008) Comparison between serology and histology in the diagnosis of advanced gastric body atrophy: a study in a Dutch primary community. *Journal of Clinical Gastroenterology*, 42: 18-22.
Not in PICO
- Krauss, E., Agaimy, A., Douplik, A., Albrecht, H., Neumann, H., Hartmann, A., Hohenstein, R., Raithel, M., Hahn, E. G., Neurath, M. F. & Mudter, J. (2012) Normalized autofluorescence imaging diagnostics in upper GI tract: a new method to improve specificity in neoplasia detection. *International Journal of Clinical & Experimental Pathology*, 5: 956-964.
Not in PICO
- Kurihara, M., Shirakabe, H., Yarita, T., Izumi, T., Miyasaka, K., Maruyama, T. & Kobayashi, S. (1981) Diagnosis of small early gastric cancer by X-ray, endoscopy, and biopsy. *Cancer Detection & Prevention*, 4: 377-383.
Not in PICO
- Kurmanov, D., Inshakov, L. N., Aisarova, A. M., Vorontsov, I. I. & Aleksandrova, N. M. (1982) Diagnosis of precancerous changes and early cancer of the stomach on a background of atrophic gastritis (based on data from the Kazakh Research Institute of Oncology and Radiology). [Russian]. *Voprosy Onkologii*, 28: 60-63.
Not in PICO
- Kusano, M. (2004) Review article: diagnosis and investigation of gastro-oesophageal reflux disease in Japanese patients. [Review] [26 refs]. *Alimentary Pharmacology & Therapeutics*, 20: Suppl-8.
Narrative review
- Lam, E. C., Rego, R. R., Paquin, S. C., Chua, T. S., Raymond, G. & Sahai, A. V. (2007) In patients referred for investigation because computed tomography suggests thickened gastric folds, endoscopic ultrasound is superfluous if gastroscopy is normal. *American Journal of Gastroenterology*, 102: 1200-1203.
Not in PICO
- Lee, D. H. (1998) Three-dimensional imaging of the stomach by spiral CT. *Journal of Computer Assisted Tomography*, 22: 52-58.
Narrative review
- Lee, S.-W., Chang, C.-S., Yeh, H.-J., Lien, H.-C., Lee, T.-Y. & Chou, M.-C. (2012) The diagnostic value of alarm features for identifying types and stages of upper gastrointestinal malignancies: One medical center's experience. *Journal of Gastroenterology and Hepatology*, 27: 350.
Not in PICO
- Lee, S. H., Ryu, C. B., Jang, J. Y. & Cho, J. Y. (2006) [Magnifying endoscopy in upper gastrointestinal tract]. [Review] [26 refs] [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 48: 145-155.
Narrative review
- Li, R., Hong, J. & Jin, J. (2010) CT diagnosis of gastric stromal tumor: Analysis of 24 cases. [Chinese]. *Chinese Journal of Gastroenterology*, 15: 106-108.
Not in PICO
- Li, W. B., Zuo, X. L., Li, C. Q., Zuo, F., Gu, X. M., Yu, T., Chu, C. L., Zhang, T. G. & Li, Y. Q. (2011) Diagnostic value of confocal laser endomicroscopy for gastric superficial cancerous lesions. *Gut*, 60: 299-306.
Not in PICO
- Lieberman, D., Fennerty, M. B., Morris, C. D., Holub, J., Eisen, G. & Sonnenberg, A. (2004) Endoscopic evaluation of patients with dyspepsia: results from the national endoscopic data repository. *Gastroenterology*, 127: 1067-1075.

Not in PICO

Liou, J.-M., Lin, J.-T., Wang, H.-P., Huang, S.-P., Lee, Y.-C., Shun, C.-T., Lin, M.-T. & Wu, M.-S. (2005) The optimal age threshold for screening upper endoscopy for uninvestigated dyspepsia in Taiwan, an area with a higher prevalence of gastric cancer in young adults. *Gastrointestinal Endoscopy*, 61: 819-825.

Not in PICO

Liu, H., Qiao, P., Wu, X., Wang, L., Ao, Y., Jia, Z. & Pi, X. (2014) - A smart capsule system of gastric occult blood detection. - *Bio-Medical Materials & Engineering*, 24: 519-528.

Not in PICO

Loffeld, R. J. & van der Putten, A. B. (2003) The yield of UGIE: a study of a ten-year period in the 'Zaanstreek'. *Netherlands Journal of Medicine*, 61: 14-18.

Not in PICO

Lomba-Viana, R., Dinis-Ribeiro, M., Fonseca, F., Vieira, A. S., Bento, M. J. & Lomba-Viana, H. (2012) Serum pepsinogen test for early detection of gastric cancer in a European country. *European Journal of Gastroenterology & Hepatology*, 24: 37-41.

Not in PICO

Longo, W. E., Zucker, K. A., Zdon, M. J. & Modlin, I. M. (1989) Detection of early gastric cancer in an aggressive endoscopy unit. *American Surgeon*, 55: 100-104.

Not in PICO

Luman, W. & Ng, K. L. (2003) Audit of Investigations in Patients with Iron Deficiency Anaemia. *Singapore Medical Journal*, 44: 504-510.

Not in PICO

Ly, Y. (1981) [X-ray analysis of 29 cases of early gastric carcinoma (author's transl)]. [Chinese]. *Chung-Hua Fang She Hsueh Tsa Chih Chinese Journal of Radiology*, 15: 13-15.

Not in PICO

Ma, Q., Xin, J., Zhao, Z., Guo, Q., Yu, S., Xu, W., Liu, C. & Zhai, W. (2013) Value of 18F-FDG PET/CT in the diagnosis of primary gastric cancer via stomach distension. *European Journal of Radiology*, 82: e302-e306.

Not in PICO

Ma, Q., Xin, J., Zhao, Z., Guo, Q., Yu, S., Xu, W., Liu, C. & Zhai, W. (2013) Value of 8F-FDG PET/CT in the diagnosis of primary gastric cancer via stomach distension. *European Journal of Radiology*, 82: e302-e306.

Not in PICO

Maconi, G., Manes, G. & Porro, G. B. (2008) Role of symptoms in diagnosis and outcome of gastric cancer. *World Journal of Gastroenterology*, 14: 1149-1155.

Narrative review

Madsen, L. G. & Bytzer, P. (2000) The value of alarm features in identifying organic causes of dyspepsia. [Review] [106 refs]. *Canadian Journal of Gastroenterology*, 14: 713-720.

Narrative review

Mahadeva, S., Chia, Y. C., Vinothini, A., Mohazmi, M. & Goh, K. L. (2008) Cost-effectiveness of and satisfaction with a Helicobacter pylori "test and treat" strategy compared with prompt endoscopy in young Asians with dyspepsia. *Gut*, 57: 1214-1220.

Not in PICO

Mahadeva, S. & Goh, K. L. (2012) Clinically Significant Endoscopic Findings in a Multi-Ethnic Population With Uninvestigated Dyspepsia. *Digestive Diseases and Sciences*, 57: 3205-3212.

Not in PICO

Makis, W., Ciarallo, A., Hickeson, M., Derbekyan, V., Novales-Diaz, J. A. & Lisbona, R. (2013) Gastric Neuroendocrine Carcinoma Staged and Followed With 18F-FDG PET/CT-A Report of 3 Cases. *Clinical Nuclear Medicine*, 38: 447-450.

Not in PICO

- Manes, G., Balzano, A., Marone, P., Lioniello, M. & Mosca, S. (2002) Appropriateness and diagnostic yield of upper gastrointestinal endoscopy in an open-access endoscopy system: a prospective observational study based on the Maastricht guidelines. *Alimentary Pharmacology & Therapeutics*, 16: 105-110.
Not in PICO
- Marmo, R., Rotondano, G., Piscopo, R., Bianco, M. A., Russo, P., Capobianco, P. & Cipolletta, L. (2005) Combination of age and sex improves the ability to predict upper gastrointestinal malignancy in patients with uncomplicated dyspepsia: A prospective multicentre database study. *American Journal of Gastroenterology*, 100: 784-791.
Not in PICO
- Martinez-Ares, D., Aguirre, P. A., Lopez, J. Y., Barrenechea, I. M., Cadilla, J. M., Martinez, D. R. & Peral, A. P. (2009) Sensitivity of ultrasonography for gastric cancer diagnosis in symptomatic patients. *Digestive Diseases & Sciences*, 54: 1257-1264.
Not in PICO
- Masselli, G., Casciani, E., Polettini, E., Laghi, F. & Gualdi, G. (2013) Magnetic resonance imaging of small bowel neoplasms. *Cancer Imaging*, 13: 92-99.
Narrative review
- Masselli, G., Casciani, E., Polettini, E., Laghi, F. & Gualdi, G. (2013) Magnetic resonance imaging of small bowel neoplasms. *Cancer Imaging*, 13: 92-99.
Narrative review
- Matowicka-Karna, J., Kamocki, Z., Polinska, B., Osada, J. & Kemon, H. (2013) Platelets and inflammatory markers in patients with gastric cancer. *Clinical & Developmental Immunology*, 2013: 401623.
Not in PICO
- Mayinger, B., Horner, P., Jordan, M., Gerlach, C., Horbach, T., Hohenberger, W. & Hahn, E. G. (2001) Endoscopic fluorescence spectroscopy in the upper GI tract for the detection of GI cancer: initial experience. *American Journal of Gastroenterology*, 96: 2616-2621.
Not in PICO
- Meenan, J., Harris, K., Oppong, K., McKay, C., Penman, I., Carroll, N. & Norton, S. (2011) Service provision and training for endoscopic ultrasound in the UK. *Frontline Gastroenterology*, 2: 188-194.
Narrative review
- Menon, S., Dhar, A., Hoare, J. & Trudgill, N. (2012) How Commonly Is Gastric Cancer Missed at Endoscopy: A Uk Primary Care Based Study. *Gut*, 61: A43.
Not in PICO
- Mihailovici, M. S., Danciu, M., Teleman, S., Stanciu, C., Stan, M., Balan, G. & Potoroaca, A. (2002) Diagnosis of gastric cancer on endobiopsies using the WHO classification. [Romanian] 209. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 106: 725-729.
Not in PICO
- Mironiuk, N. V. & Andrun', P. K. (1983) Diagnosis of stomach polyp in a polyclinic. [Russian]. *Klinicheskaia khirurgiia*, 39-40.
Not in PICO
- Miwa, H. & Sato, N. (2001) Shed light again on magnifying endoscopy for diagnosis of early gastric cancer. *Digestive Endoscopy*, 13: 127-128.
Narrative review
- Mochizuki, K., Ueda, M., Shiozawa, S., Ishigame, H., Hasegawa, M., Koiwai, K., Watanabe, T. & Kadoya, M. (2003) [Imaging of gastrointestinal stromal tumor (GIST): relation between CT findings and grade of malignancy]. [Japanese]. *Nippon Igaku Hoshasen Gakkai Zasshi - Nippon Acta Radiologica*, 63: 210-213.
Not in PICO

- Moehler, M., Voigt, J., Kastor, M., Heil, M., Sengespeick, C., Biesterfeld, S., Dippold, W., Kanzler, S. & Galle, P. R. (2011) Endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) as primary diagnostic tool for unclear lesions in the upper gastrointestinal tract. *Deutsche Medizinische Wochenschrift*, 136: 303-308.
Not in PICO
- Mollmann, K. M. (1981) Early diagnosis of gastric cancer. The possibility of delimiting high risk groups. *Danish Medical Bulletin*, 28: 89-92.
Not in PICO
- Mollmann, K. M. (1981) Endoscopic service for general practice. Organisation and experience. *Danish Medical Bulletin*, 28: 96-99.
Not in PICO
- Mollmann, K. M. (1985) Cooperation between hospital and general practice in multipractice studies. Personal experiences from a study on early diagnosis for gastric cancer. *Scandinavian Journal of Primary Health Care*, 3: 121-125.
Narrative review
- Moreno, O. R., Martinez, R. A., Cantero, J. & Pajares, J. M. (1983) Exfoliative cytodiagnosis of gastric adenocarcinoma. Comparison with biopsy and endoscopy. *Acta Cytologica*, 27: 485-488.
Not in PICO
- Mori, M., Kitagawa, S. & Iida, M. (1987) Early carcinoma of the gastric cardia. A clinicopathologic study of 21 cases. *Cancer*, 59: 1758-1766.
Not in PICO
- Mori, M., Adachi, Y., Kakeji, Y., Korenaga, D., Sugimachi, K., Motooka, M. & Ooiwa, T. (1992) Superficial flat-type early carcinoma of the stomach. *Cancer*, 69: 306-313.
Not in PICO
- Muralee, M., Ahamed, I., Somanathan, T. & Anila, K. S. (2011) Hepatoid Adenocarcinoma of the Stomach - A rare pathological entity. *The gulf journal of oncology*, 1: 78-81.
Not in PICO
- Muretto, P., Graziano, F., Staccioli, M. P., Barbanti, I., Bartolucci, A., Paolini, G., Giordano, D., Testa, E. & De, G. A. (2003) An endogastric capsule for measuring tumor markers in gastric juice: an evaluation of the safety and efficacy of a new diagnostic tool. *Annals of Oncology*, 14: 105-109.
Not in PICO
- Muris, J. W. M., Starmans, R., Pop, P., Crebolder, H. F. J. M. & Knottnerus, J. A. (1994) Discriminant value of symptoms in patients with dyspepsia. *Journal of Family Practice*, 38: 139-143.
Not in PICO
- Ndububa, D. A., Agbakwuru, E. A., Olasode, B. J., Aladegbaiye, A. O., Adekanle, O. & Arigbabu, A. O. (2007) Correlation between endoscopic suspicion of gastric cancer and histology in Nigerian patients with dyspepsia. *Tropical Gastroenterology*, 28: 69-71.
Not in PICO
- Neeman, A., Shoenfeld, Y. & Kadish, U. (1987) Does duodenal ulcer lead to an early diagnosis of gastric cancer? *Journal of Clinical Gastroenterology*, 9: 37-39.
Not in PICO
- Niang, A., Mbengue, M., Diouf, M. L., Diouf, B., Ka, M. M., Pouye, A., Diallo, S., Ndiaye, M. F. & Bao, O. (1996) [Current aspects of gastric cancer in Senegal. Epidemiological and clinical study of 220 cases (1984-1991)]. [French]. *Dakar Medical*, 41: 99-103.
Not in PICO
- Nishida, T., Kumano, S., Sugiura, T., Ikushima, H., Nishikawa, K., Ito, T. & Matsuda, H. (2003) Multidetector CT of high-risk patients with occult gastrointestinal stromal tumors. *AJR.American Journal of Roentgenology*, 180: 185-189.
Not in PICO

- Niwa, Y., Ohashi, A., Miyahara, R., Ohmiya, N. & Goto, H. (2005) Differential diagnosis of gastric lesions by magnifying endoscopy. *Digestive Endoscopy*, 17: S20-S22.
Not in PICO
- Nyren, O. (1991) Therapeutic Trial in Dyspepsia - Its Role in the Primary Care Setting. *Scandinavian Journal of Gastroenterology*, 26: 61-69.
Narrative review
- Oberle, E., Brunner, K. & Rhyner, K. (1993) [Gastrointestinal hemorrhage: how much evaluation is necessary?]. [German]. *Schweizerische Rundschau fur Medizin Praxis*, 82: 1244-1252.
Not in PICO
- Ofman, J. J. & Rabeneck, L. (1999) The effectiveness of endoscopy in the management of dyspepsia: A qualitative systematic review. *American Journal of Medicine*, 106: 335-346.
Not in PICO
- Ogata, I., Komohara, Y., Yamashita, Y., Mitsuzaki, K., Takahashi, M. & Ogawa, M. (1999) CT evaluation of gastric lesions with three-dimensional display and interactive virtual endoscopy: comparison with conventional barium study and endoscopy. *AJR.American Journal of Roentgenology*, 172: 1263-1270.
Not in PICO
- Oguro, Y. (1981) Does early gastric cancer really look different from what it used to be? From the viewpoint of endoscopic diagnosis. [Japanese]. *Stomach and Intestine*, 16: 47-56.
Narrative review
- Oiwa, T., Mori, M., Sugimachi, K. & Enjoji, M. (1986) Diagnostics of small gastric carcinoma. *Journal of Surgical Oncology*, 33: 170-175.
Not in PICO
- Osawa, H., Yamamoto, H., Miura, Y., Ajibe, H., Shinhata, H., Yoshizawa, M., Sunada, K., Toma, S., Satoh, K. & Sugano, K. (2012) Diagnosis of depressed-type early gastric cancer using small-caliber endoscopy with flexible spectral imaging color enhancement. *Digestive Endoscopy*, 24: 231-236.
Not in PICO
- Padmavathy, F., Siddaraju, N. & Sistla, S. C. (2011) Distinction of intestinal and diffuse types of gastric adenocarcinoma on brush cytology. *Acta Cytologica*, 55: 187-192.
Not in PICO
- Papp, I., Bajtai, A., Szentirmay, Z., Szerjan, E. & Figus, I. A. (1992) [Diagnostic possibilities of endoscopic ultrasonography in the detection of gastric cancer]. [Hungarian]. *Orvosi Hetilap*, 133: 2163-2166.
Not in PICO
- Parente, F., Bargiggia, S. & Bianchi, P. G. (2002) Prospective audit of gastroscopy under the 'three-day rule': a regional initiative in Italy to reduce waiting time for suspected malignancy. *Alimentary Pharmacology & Therapeutics*, 16: 1011-1014.
Not in PICO
- Park, J. S., Park, D. I., Park, S. K., Choi, J. S., Kim, Y. H., Chang, D. K., Son, H. J., Kim, J. E., Kim, J. O., Lee, S. H., Kim, H. S., Sin, J. E., Lee, S. G., Lee, S. Y., Park, S. J., Park, C. H., Baek, I. H., Jang, B. I., Jeon, Y. T. & Huh, K. C. (2009) Endoscopic evaluation of significant gastrointestinal lesions in patients with iron deficiency with and without anaemia: a Korean Association for the Study of Intestinal Disease study. *Internal Medicine Journal*, 39: 441-446.
Not in PICO
- Park, S. H., Song, C. W., Kim, Y. B., Kim, Y. S., Chun, H. R., Lee, J. H., Seol, W. J., Yoon, H. S., Lee, M. K., Lee, J. H., Bhang, C. S., Park, J. H., Park, Y. H., Do, B. H., Park, Y. D., Yoon, S. J., Park, C. W., Kim, J. P., Choi, J. H., Shin, K. C. & Park, S. M. (2012) [Clinicopathologic characteristics of superficial gastric cancer diagnosed at primary health care institutions in 2011]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 60: 285-291.
Not in PICO

- Perez Lopez de Brinas JM (1993) [Early gastric cancer at a third-level hospital in Barcelona in 1981-1990. Clinical considerations]. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 84: 90-94.
Not in PICO
- Perri, F., Ricciardi, R., Merla, A., Piepoli, A., Gasperi, V., Quitadamo, M. & Andriulli, A. (2002) Appropriateness of urea breath test: a prospective observational study based on Maastricht 2000 guidelines. *Alimentary Pharmacology & Therapeutics*, 16: 1443-1447.
Not in PICO
- Peschl, L. & Munda, W. (1987) [Early clinical diagnosis of stomach and large intestine cancer]. [German]. *ZFA - Zeitschrift fur Alternsforschung*, 42: 155-164.
Narrative review
- Phung, N., Kalantar, J. & Talley, N. J. (1998) Management of dyspepsia in general practice. *Modern Medicine of Australia*, 41: 10-19.
Narrative review
- Pierzchajlo, R. P. J., Ackermann, R. J. & Vogel, R. L. (1998) Esophagogastroduodenoscopy performed by a family physician: A case series of 793 procedures. *Journal of Family Practice*, 46: 41-46.
Not in PICO
- Pimanov, S. I. & Krylov, I. V. (1991) Improvement of ultrasonographic diagnosis of stomach cancer. [Russian]. *Voprosy Onkologii*, 37: 588-592.
Not in PICO
- Pimentel-Nunes, P., Ferreira, A., Veloso, N. & Dinis-Ribeiro, M. (2013) Narrow-Band Imaging for the Diagnosis of Gastric Preneoplastic and Neoplastic Lesions. *Video Journal and Encyclopedia of GI Endoscopy*, 1: 191-193.
Narrative review
- Podolsky, I., Storms, P. R., Richardson, C. T., Peterson, W. L. & Fordtran, J. S. (1988) Gastric adenocarcinoma masquerading endoscopically as benign gastric ulcer. A five-year experience. *Digestive Diseases and Sciences*, 33: 1057-1063.
Not in PICO
- Portnoi, L. M. & Kazantseva, I. A. (1995) [Gastric cancer: diagnostic problems]. [Russian]. *Vestnik Rentgenologii i Radiologii*.(3):27-33, 1995 May-Jun., 27-33.
Narrative review
- Portnoi, L. M., Legostaeva, T. B., Iaurova, N. V., Tripathki, S., Emel'ianova, L. N. & Gaganov, L. E. (1997) Role of ultrasound study in present-day diagnosis of gastric endophytic carcinoma. [Russian]. *Vestnik Rentgenologii i Radiologii*, 26-32.
Narrative review
- Portnoi, L. M., Legostaeva, T. B., Iaurova, N. V., Tripathki, S., Emel'ianova, L. N. & Gaganov, L. E. (1997) [Role of ultrasound study in present-day diagnosis of gastric endophytic carcinoma]. [Russian]. *Vestnik Rentgenologii i Radiologii*.(6):26-32, 1997 Nov-Dec., 26-32.
Narrative review
- Portnoi, L. M., Kazantseva, I. A. & Isakov, V. A. (1997) [The diagnosis of stomach cancer: the status of the problem, the outlook for improvement and the clinico-morphological aspects]. [Russian]. *Terapevticheskii Arkhiv*, 69: 42-48.
Narrative review
- Pruitt, R. E. & Truss, C. D. (1993) Endoscopy, gastric ulcer, and gastric cancer. Follow-up endoscopy for all gastric ulcers? *Digestive Diseases & Sciences*, 38: 284-288.
Not in PICO
- Qizilbash, A. H., Castelli, M., Kowalski, M. A. & Churly, A. (1980) Endoscopic brush cytology and biopsy in the diagnosis of cancer of the upper gastrointestinal tract
135. *Acta Cytologica*, 24: 313-318.
Not in PICO

- Raker, J. & Sadler, G. (2014) Two week rule referrals for upper GI cancer: Right patients, wrong test? *Gut*, 63: A52.
Not in PICO
- Richter, G. M., Dux, M., Roeren, T., Heuschen, U. & Kauffmann, G. W. (1996) Gastrointestinal imaging with hydrosoneography and hydro-CT. Part 1: Gastric carcinoma. [German]. *RoFo Fortschritte auf dem Gebiete der Rontgenstrahlen und der Neuen Bildgebenden Verfahren*, 164: 281-289.
Not in PICO
- Rogers, K., Roberts, G. M. & Williams, G. T. (1981) Gastric-juice enzymes--an aid in the diagnosis of gastric cancer? *Lancet*, 1: 1124-1125.
Not in PICO
- Sacco, R., Sammarco, G., De, V. R., Vescio, G., Scarpelli, A., Lucisano, A. M., Pata, F., Mascia, E. & Martines, V. (2007) [Relief of gastric cancer with an electromagnetic interaction system (TRIMprob) in outpatients]. [Italian]. *Chirurgia Italiana*, 59: 823-828.
Not in PICO
- Sagar, N. & Bhala, N. (2014) Detection rates of gastric cancer at the Queen Elizabeth Hospital Birmingham 2009-2013. *Gut*, 63: A111.
Not in PICO
- Saha, A. K., Maitra, S. & Hazra, S. C. (2013) Epidemiology of gastric cancer in the gangetic areas of west bengal. *ISRN Gastroenterology*, 2013.
Not in PICO
- Salo, M., Collin, P., Kyronpalo, S., Rasmussen, M., Huhtala, H. & Kaukinen, K. (2008) Age, symptoms and upper gastrointestinal malignancy in primary care endoscopy. *Scandinavian Journal of Gastroenterology*, 43: 122-127.
Not in PICO
- Savides, T. (2000) A blind comparison of the effectiveness of endoscopic ultrasonography and endoscopy in staging early gastric cancer. *Gastrointestinal Endoscopy*, 51: 635-636.
Not in PICO
- Schlemper, R. (1999) [Early cancer detection: what makes the Japanese so good?]. [German]. *MMW Fortschritte der Medizin*, 141: 20.
Narrative review
- Schmidt, N., Peitz, U., Lippert, H. & Malfertheiner, P. (2005) Missing gastric cancer in dyspepsia. *Alimentary Pharmacology & Therapeutics*, 21: 813-820.
Not in PICO
- Schonfeld, J. V. (2008) [Endoscopic options for early gastric cancer]. [German]. *MMW Fortschritte der Medizin*, 150: 29-31.
Narrative review
- Schwartz, G. D. & Barkin, J. S. (2007) Small-bowel tumors detected by wireless capsule endoscopy. *Digestive Diseases & Sciences*, 52: 1026-1030.
Not in PICO
- Shen, Y., Kang, H. K., Jeong, Y. Y., Heo, S. H., Han, S. M., Chen, K. & Liu, Y. (2011) Evaluation of early gastric cancer at multidetector CT with multiplanar reformation and virtual endoscopy. [Review]. *Radiographics*, 31: 189-199.
Narrative review
- Shimizu, K., Ito, K., Matsunaga, N., Shimizu, A. & Kawakami, Y. (2005) Diagnosis of gastric cancer with MDCT using the water-filling method and multiplanar reconstruction: CT-histologic correlation. *AJR.American Journal of Roentgenology*, 185: 1152-1158.
Not in PICO
- Shimizu, S., Tada, M. & Kawai, K. (1994) Endoscopic ultrasonography for early gastric cancer. *Endoscopy*, 26: 767-768.
Not in PICO

- Shimoda, T., Nimura, S., Tominaga, K., Ogawa, M., Fujimoto, Y. & Nakanishi, Y. (2001) Clinicopathological findings and histological appearance of early gastric cancer. [Japanese]. *Nippon rinsho*, Japanese: 142-155.
Not in PICO
- Shimuzu, S., Tada, M. & Kawai, K. (1994) Endoscopic ultrasonography for early gastric cancer. *Endoscopy*, 26: 767-768.
Duplicate
- Singh, S. & Sharma, P. (2005) Magnification endoscopy in the upper GI tract. *Digestive Endoscopy*, 17: S17-S19.
Narrative review
- Singhal, T., Doddi, S., Leake, T., Parsi, S., Hussain, A., Chandra, A., Smedley, F. & Ellul, J. (2010) Upper gastrointestinal bleeding due to gastric stromal tumour: a case report. *Cases journal*, 3: 58.
Not in PICO
- Sjoblom, S. M., Sipponen, P. & Jarvinen, H. (1993) Gastroscopic follow up of pernicious anaemia patients. *Gut*, 34: 28-32.
Not in PICO
- Smith, G. (1936) Red flags are key to managing dyspepsia. [Review] [8 refs]. *Practitioner*, 251: 31-34.
Narrative review
- Sokolov, L. K., Nikiforov, P. A., Vasil'ev, I. D., Gul'kevich, K. I., Sklianskaia, O. A. & Iarushnikov, K. I. (1990) [Gastroscopy in follow-up studies of patients with chronic atrophic gastritis and diagnosis of early gastric cancer]. [Russian]. *Klinicheskaia Meditsina*, 68: 108-111.
Not in PICO
- Stabile Ianora, A. A., Wolowiec, A., Francioso, G., Scardapane, A., Rotondo, A. & Angelelli, G. (2001) [Benign and malignant gastric ulcer: CT findings]. [Italian]. *Radiologia Medica*, 102: 32-36.
Not in PICO
- Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M. & Hamilton, W. (2013) The risk of oesophago-gastric cancer in symptomatic patients in primary care: A large case-control study using electronic records. *British Journal of Cancer*, 108: 25-31.
Not in PICO
- Stepp, H., Sroka, R. & Baumgartner, R. (1998) Fluorescence endoscopy of gastrointestinal diseases: Basic principles, techniques, and clinical experience. *Endoscopy*, 30: 379-386.
Narrative review
- Stromar, I. K., Jakic-Razumovic, J., Knezevic-Obad, A. & Knezevic, J. (2004) [Comparison of cytological and histological analysis of gastric mucosa biopsy in diagnosing malignant diseases]. [Croatian]. *Lijecnicki Vjesnik*, 126: 287-290.
Not in PICO
- Sturgeon, C. M., Duffy, M. J., Hofmann, B. R., Lamerz, R., Fritsche, H. A., Gaarenstroom, K., Bonfrer, J., Ecke, T. H., Grossman, H. B., Hayes, P., Hoffmann, R.-T., Lerner, S. P., Lohe, F., Louhimo, J., Sawczuk, I., Taketa, K. & Diamandis, E. P. (2010) National academy of clinical biochemistry laboratory medicine practice guidelines for use of tumor markers in liver, bladder, cervical, and gastric cancers. *Clinical Chemistry*, 56: e1-e48.
Guideline
- Sudasna Na, A. N., Luengrojanakul, P. & Suwanagool, P. (1994) The advantages of upper gastrointestinal tract brush cytology. *Journal of the Medical Association of Thailand*, 77: 7-11.
Not in PICO
- Sumathi, B., Navaneethan, U. & Jayanthi, V. (2008) Appropriateness of indications for diagnostic upper gastrointestinal endoscopy in India. *Singapore Medical Journal*, 49: 970-976.
Not in PICO
- Swaroop, V. S., Mohandas, K. M., Swaroop, V. D., Soman, C. S., Krishnamurthi, S., Nagral, A., Jagannath, P. & Desouza, L. J. (1994) Comparative endoscopic study of primary gastric lymphoma

- vs. gastric carcinoma. *Journal of Surgical Oncology*, 56: 94-97.
Not in PICO
- Tafner, G. (1994) Gastric ulcer as a pre-cancerous condition. *Italian Journal of Gastroenterology*, 26: Suppl-8.
Narrative review
- Takasu, S., Tsuchiya, H., Kitamura, A., Yoshida, S., Ito, M., Sakurai, Y., Funatomi, T. & Ikegami, F. (1984) Detection of early gastric cancer by panendoscopy
121. *Japanese Journal of Clinical Oncology*, 14: 243-252.
Not in PICO
- Talley, N. J. (1986) Dyspepsia and non-ulcer dyspepsia: An historical perspective. *Medical Journal of Australia*, 145: 614-618.
Narrative review
- Talley, N. J., Lam, S. K., Goh, K. L. & Fock, K. M. (1998) Management guidelines for uninvestigated and functional dyspepsia in the Asia-Pacific region: First Asian Pacific working party on functional dyspepsia. *Journal of Gastroenterology and Hepatology*, 13: 335-353.
Narrative review
- Talley, N. J. (2002) Review article: dyspepsia: how to manage and how to treat? *Alimentary Pharmacology & Therapeutics*, 16: 95-104.
Narrative review
- Tao, G., Xing-Hua, L., Ai-Ming, Y., Wei-Xun, Z., Fang, Y., Xi, W., Li-Yin, W., Chong-Mei, L., Gui-Jun, F., Hui-Jun, S., Dong-Sheng, W., Yue, L., Xiao-Qing, L. & Jia-Ming, Q. (2014) - Enhanced magnifying endoscopy for differential diagnosis of superficial gastric lesions identified with white-light endoscopy. - *Gastric Cancer*, 17: 122-129.
Not in PICO
- Thijs, J. C., Arents, N. L. A., van Zwet, A. A. & Kleibeuker, J. H. (2003) Dyspepsia management in primary care. *Scandinavian Journal of Gastroenterology*, 38: 44-50.
Narrative review
- Tomizawa, Y., Seki, M. & Mori, M. (2012) Unusual presentation of localized gastric mucosa-associated lymphoid tissue lymphoma mimicking poorly differentiated gastric adenocarcinoma. *Case Reports Gastroenterology*, 6: 47-51.
Not in PICO
- Tragardh, B., Wehlin, L. & Lindstrom, C. (1980) The yield of endoscopy and double contrast radiography for the detection of early gastric cancer in Malmo. *Acta Chirurgica Scandinavica*, 146: 357-362.
Not in PICO
- Trillo, S. E., Lopez Fananas, M. S., Villaverde Royo, M. V. & Isanta, P. C. (2005) Study of the gastroscopies requested at a health centre. [Spanish]. *Atencion Primaria*, 35: 375-377.
Not in PICO
- Tsukada, T., Nakano, T., Miyata, T., Sasaki, S. & Higashi, K. (2012) Xanthogranulomatous gastritis mimicking malignant GIST on F-18 FDG PET. *Annals of Nuclear Medicine*, 26: 752-756.
Not in PICO
- Tytgat, G. N. J. (2002) Role of endoscopy and biopsy in the work up of dyspepsia. *Gut*, 50: 13-16.
Narrative review
- Uehara, G., Nago, A., Espinoza, R., Vargas, G., Astete, M., Moran, L., Nunez, N., Mayuri, C., Valdivia, M., Chavez, M. & Moreno, C. (2007) [Optimal age for gastric cancer screening in patients with dyspepsia without alarm symptoms]. [Spanish]. *Revista de Gastroenterologia del Peru*, 27: 339-348.
Not in PICO
- Vakil, N., Talley, N., van Zanten, S. V., Flook, N., Persson, T., Bjorck, E., Lind, T. & Bolling-Sternevald, E. (2009) Cost of Detecting Malignant Lesions by Endoscopy in 2741 Primary Care Dyspeptic Patients Without Alarm Symptoms. *Clinical Gastroenterology and Hepatology*, 7: 756-761.

Not in PICO

Valori, R. M., Brown, C. M., Strangeways, P. & Bradburn, M. (2001) Reducing community dyspepsia drug costs: a controlled trial. *Gut*, 49: 495-501.

Not in PICO

Vanis, N., Mesihovic, R., Ibricevic, L. & Dobrila-Dintinjana, R. (2013) Predictive value of endoscopic ultrasound in diagnosis and staging of primary gastric lymphoma. *Collegium Antropologicum*, 37: Suppl-7.

Not in PICO

Vannella, L., Spiriti, M. A. A., Di, G. E., Lahner, E., Corleto, V. D., Monarca, B., Delle, F. G. & Annibale, B. (2010) Upper and lower gastrointestinal causes of iron deficiency anemia in elderly compared with adult outpatients. *Minerva Gastroenterologica e Dietologica*, 56: 397-404.

Not in PICO

Vidyavathi, K., Harendrakumar, M. & Lakshmana, K. Y. (2008) Correlation of endoscopic brush cytology with biopsy in diagnosis of upper gastrointestinal neoplasms. *Indian Journal of Pathology and Microbiology*, 51: 489-492.

Not in PICO

Vigoni, A., Marcato, M. & Mandelli, L. (1987) [Our experience in carcinoma of the stomach (clinico-statistical contribution)]. [Italian]. *Chirurgia Italiana*, 39: 284-290.

Not in PICO

Vinner, M. G. & Beloded, V. M. (1988) [Diagnosis of ulcerous early cancer of the stomach]. [Russian]. *Voprosy Onkologii*, 34: 721-725.

Not in PICO

Vinner, M. G. & Beloded, V. M. (1988) Differential diagnosis of ulcerated forms of early cancer of the stomach. [Russian]. *Vestnik khirurgii imeni I*, 1.: 18-22.

Not in PICO

Vinner, M. G., Beloded, V. M. & Gerasimov, V. B. (1990) Roentgeno-endoscopic diagnosis of elevated early cancer of the stomach. [Russian]. *Khirurgiia*, 47-50.

In Russian, not enough information can be extracted to ascertain relevance, but think it is not in PICO

Voutilainen, M., Mantynen, T., Kunnamo, I., Juhola, M., Mecklin, J. P. & Farkkila, M. (2003) Impact of clinical symptoms and referral volume on endoscopy for detecting peptic ulcer and gastric neoplasms. *Scandinavian Journal of Gastroenterology*, 38: 109-113.

Not in PICO

Voutilainen, M. & Kunnamo, I. (2005) A survey of open-access endoscopy in primary health care centres: outcome of gastric carcinoma patients diagnosed by general practitioners compared with hospital-referred endoscopy. *Digestive & Liver Disease*, 37: 119-123.

Not in PICO

Voutilainen, M. & Kunnamo, I. (2005) A survey of open-access endoscopy in primary health care centres: outcome of gastric carcinoma patients diagnosed by general practitioners compared with hospital-referred endoscopy. *Digestive and Liver Disease*, 37: 119-123.

Duplicate

Voutilainen, M., Mantynen, T., Mauranen, K., Kunnamo, I. & Juhola, M. (2005) Is it possible to reduce endoscopy workload using age, alarm symptoms and H-pylori as predictors of peptic ulcer and oesophagogastric cancers? *Digestive and Liver Disease*, 37: 526-532.

Not in PICO

Vradelis, S., Maynard, N., Warren, B. F., Keshav, S. & Travis, S. P. (2011) Quality control in upper gastrointestinal endoscopy: detection rates of gastric cancer in Oxford 2005-2008. *Postgraduate Medical Journal*, 87: 335-339.

Not in PICO

Wada, T., Tanabe, S., Ishido, K., Higuchi, K., Sasaki, T., Katada, C., Azuma, M., Naruke, A., Kim, M., Koizumi, W. & Mikami, T. (2013) DOG1 is useful for diagnosis of KIT-negative gastrointestinal

- stromal tumor of stomach. *World Journal of Gastroenterology*, 19: 9133-9136.
Not in PICO
- Williams, B., Luckas, M., Ellingham, J. H., Dain, A. & Wicks, A. C. (1988) Do young patients with dyspepsia need investigation? *Lancet*, 2: 1349-1351.
Not in PICO
- Worliceck, H. (1986) [Sonographic diagnosis of the fluid-filled stomach]. [German][Erratum appears in *Ultraschall Med* 1987 Feb;8(1):56]. *Ultraschall in der Medizin*, 7: 259-263.
Not in PICO
- Xia, B., Xia, H. H., Ma, C. W., Wong, K. W., Fung, F. M., Hui, C. K., Chan, C. K., Chan, A. O., Lai, K. C., Yuen, M. F. & Wong, B. C. (2005) Trends in the prevalence of peptic ulcer disease and *Helicobacter pylori* infection in family physician-referred uninvestigated dyspeptic patients in Hong Kong. *Alimentary Pharmacology & Therapeutics*, 22: 243-249.
Not in PICO
- Xirouchakis, E., Laoudi, F., Tsartsali, L., Spiliadi, C. & Georgopoulos, S. D. (2013) Screening for gastric premalignant lesions with narrow band imaging, white light and updated Sydney protocol or both? *Digestive Diseases & Sciences*, 58: 1084-1090.
Not in PICO
- Xu, G., Gan, T., Rao, N., Liu, D. Y., Li, B. Y. & Li, Y. (2013) Detection of upper gastrointestinal early cancers based on gastroscopic images. *Journal of Investigative Medicine*, 61: S12-S13.
Not in PICO
- Yamada, S., Doyama, H., Yao, K., Uedo, N., Ezoe, Y., Oda, I., Kaneko, K., Kawahara, Y., Yokoi, C., Sugiura, Y., Ishikawa, H., Takeuchi, Y., Saito, Y. & Muto, M. (2014) An efficient diagnostic strategy for small, depressed early gastric cancer with magnifying narrow-band imaging: a post-hoc analysis of a prospective randomized controlled trial. *Gastrointestinal Endoscopy*, 79: 55-63.
Not in PICO
- Yamaji, Y., Mitsushima, T., Ikuma, H., Okamoto, M., Yoshida, H., Kawabe, T., Shiratori, Y., Saito, K., Yokouchi, K. & Omata, M. (2002) Weak response of *Helicobacter pylori* antibody is high risk for gastric cancer: a cross-sectional study of 10,234 endoscoped Japanese. *Scandinavian Journal of Gastroenterology*, 37: 148-153.
Not in PICO
- Yamamoto, S., Nishida, T., Kato, M., Inoue, T., Hayashi, Y., Kondo, J., Akasaka, T., Yamada, T., Shinzaki, S., Iijima, H., Tsujii, M. & Takehara, T. (2012) Evaluation of endoscopic ultrasound image quality is necessary in endosonographic assessment of early gastric cancer invasion depth. *Gastroenterology Research and Practice*.
Not in PICO
- Yanai, H., Noguchi, T., Mizumachi, S., Tokiyama, H., Nakamura, H., Tada, M. & Okita, K. (1999) A blind comparison of the effectiveness of endoscopic ultrasonography and endoscopy in staging early gastric cancer. *Gut*, 44: 361-365.
Not in PICO
- Yanakiev, A. & Andonov, C. (1999) Possibilities of transabdominal ultrasonography in diagnosing cancer of the stomach. [Greek]. *Rentgenologiya i Radiologiya*, 38: 33-36.
Foreign language, not enough information can be extracted to definitely ascertain relevance, but I strongly think it is not in PICO
- Yang, K.-C. & Liu, Y.-H. (1992) Endoscopic ultrasonography in the diagnosis of gastric submucosal tumor. *Chinese Journal of Gastroenterology*, 9: 15-21.
Unavailable, but I think it is not in PICO
- Yao, K., Iwashita, A. & Yao, T. (2004) Early gastric cancer: Proposal for a new diagnostic system based on microvascular architecture as visualized by magnified endoscopy. *Digestive Endoscopy*, 16: S110-S117.
Not in PICO

- Yao, K. (2013) The endoscopic diagnosis of early gastric cancer. *Annals of Gastroenterology*, 26: 11-22.
Narrative review
- Yasuda, K. (2002) EUS in the detection of early gastric cancer. [Review] [3 refs]. *Gastrointestinal Endoscopy*, 56: Suppl-75.
Narrative review
- Zambelli, A. (2010) Can virtual chromoendoscopy measure up to histology in early gastric cancer? *Digestive & Liver Disease*, 42: 677-678.
Comment
- Zaninotto, G., Avellini, C., Barbazza, R., Baruchello, G., Battaglia, G., Benedetti, E., Bernardi, A., Boccu, C., Bonoldi, E., Bottona, E., Bozzola, L., Canizzaro, R., Canzonieri, V., Caroli, A., Carta, A., Colonna, A., Costa-Biedo, F., Dal, B. N., De, B. R., De, B. M., De, B. F., De, P. G., Di, M. F., Doglioni, C., Donisi, P. M., Franceschi, M., Furlanetto, A., Germana, B., Grassi, S. A., Macor, V., Marcon, V., Marin, R., Meggiato, T., Melina, V., Menghi, A., Milan, R., Militello, C., Molena, D., Monica, F., Murer, B., Nisi, E., Olivieri, P., Orzes, N., Parenti, A., Paternello, E., Penelli, N., Pilotto, A., Pisciolli, F., Pozzato, F., Ronzani, G., Rugge, M., Saggiaro, A., Stracca-Pansa, V., Togni, R., Valiante, F. & Vianello, F. (2001) Prevalence of intestinal metaplasia in the distal oesophagus, oesophagogastric junction and gastric cardia in symptomatic patients in north-east Italy: a prospective, descriptive survey. The Italian Ulcer Study Group "GISU". *Digestive & Liver Disease*, 33: 316-321.
Not in PICO
- Zeeneldin, A. A., Saber, M. M., Seif El-Din, I. A. & Frag, S. A. (2013) Small intestinal cancers among adults in an Egyptian district: a clinicopathological study using a population-based cancer registry. *Journal of Egyptian National Cancer Institute*, 25: 107-114.
Not in PICO
- Yagi, K., Nozawa, Y., Endou, S. & Nakamura, A. (2012) Diagnosis of early gastric cancer by magnifying endoscopy with NBI from viewpoint of histological imaging: Mucosal patterning in terms of white zone visibility and its relationship to histology. *Diagnostic and Therapeutic Endoscopy*.
Not in PICO
- Zhang, J., Guo, S. B. & Duan, Z. J. (2011) Application of magnifying narrow-band imaging endoscopy for diagnosis of early gastric cancer and precancerous lesion. *BMC Gastroenterology*, 11: 135.
Not in PICO
- Zhang, J. N., Yu, T., Li, Y. Q., Guo, Y. T., Liu, H. & Zhang, J. P. (2007) [Confocal endomicroscopy for differential diagnosis of indented gastric lesions]. [Chinese]. *Chung-Hua Nei Ke Tsa Chih Chinese Journal of Internal Medicine*, 46: 835-837.
Not in PICO
- Zhong, L., Li, L., Sun, J. H. & Xu, J. R. (2005) Preoperative diagnosis of gastric cancer using 2-D magnetic resonance imaging with 3-D reconstruction techniques. *Chinese Journal of Digestive Diseases*, 6: 159-164.
Not in PICO
- Zuo-Rong, S. & Da-Li, C. (1985) Endoscopic diagnosis of gastric cancer: An analysis of 872 cases in China. *Gastrointestinal Endoscopy*, 31: 191-195.
Not in PICO

SMALL INTESTINAL CANCER

Review question:

What is the risk of small intestine cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

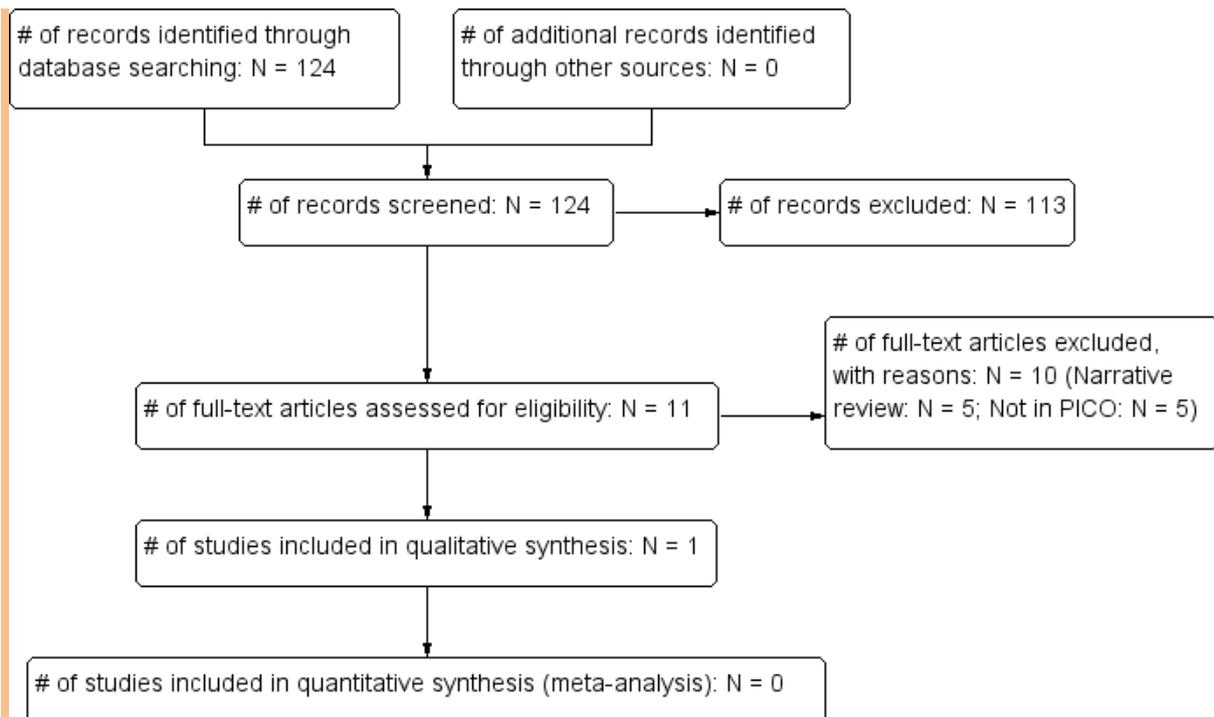
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	344	68	29/10/2012
<i>Premedline</i>	All-2012	2	1	29/10/2012
<i>Embase</i>	All-2012	398	53	01/11/2012
<i>Cochrane Library</i>	All-2012	172	0	01/11/2012
<i>Psychinfo</i>	All-2012	0	0	01/11/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	211	3	01/11/2012
<i>Biomed Central</i>	All-2012	217	5	05/11/2012

Total References retrieved (after de-duplication): 117

Update Search

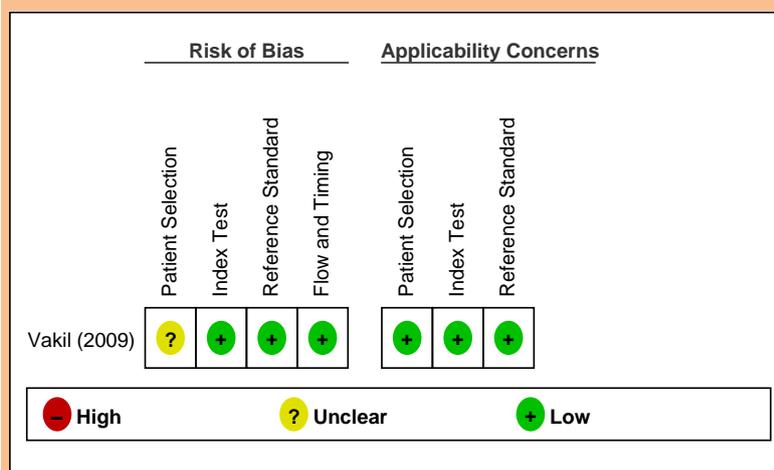
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	11/2012-26/08/2014	25	2	26/08/2014
<i>Premedline</i>	11/2012-26/08/2014	4	3	26/08/2014
<i>Embase</i>	11/2012-26/08/2014	40	2	26/08/2014
<i>Cochrane Library</i>	11/2012-26/08/2014	155	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	11/2012-26/08/2014	23	0	26/08/2014

Total References retrieved (after de-duplication): 7



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included study in the figure below. The main issue to note is that the patient recruitment method is unclear and that the study patients may therefore not be directly representative of an unselected symptomatic population of patients presenting to the UK-based GP.



Study results

Table 1: Small intestinal cancer: Study results.

Study	Symptom(s)	Patient group	PPVs % (95% CI); prevalence
Vakil (2009)	Dyspepsia without alarm symptoms	All included patients	0.2 (0.09-0.5) 6/2741 Cancer:

			Oesophagus: N = 3 Stomach: N = 3
Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 45 years old	0.4 (0.2-1.1) 5/1127 Cancer: Oesophagus: N = 2 Stomach: N = 3
Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 50 years old	0.6 (0.2-1.5) 5/829 Cancer: Oesophagus: N = 2 Stomach: N = 3
Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 55 years old	0.2 (0.009-1.2) 1/554 Cancer: Oesophagus: N = 1 Stomach: N = 0
Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 60 years old	0.3 (0.02-2) 1/323 Cancer: Oesophagus: N = 1 Stomach: N = 0

TP = True positives, FP = False positives.

Evidence statement(s):

Dyspepsia without accompanying alarm features (1 study, N = 2741) presenting in a primary care setting do not appear to confer an increased risk of small intestine cancer, although the study population is probably not directly representative of the typical unselected symptomatic UK GP population (see also Table 1).

Evidence tables

Vakil (2009)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2741, mean (range) age = not reported (not reported) years, numbers of females/males: Not reported. <u>Inclusion criteria:</u> Patients aged 18-70 years who met Rome II criteria for dyspepsia (intermittent or continuous pain or burning centered in the upper abdomen for ≥ 3 months). <u>Exclusion criteria:</u> Past diagnosis of gastro-oesophageal reflux disease,

	<p>predominant symptom of heartburn or regurgitation, history of heartburn or regurgitation > 2 days/week, treatment > 2 days/week with non-steroidal anti-inflammatory drugs or cyclooxygenase-2 selective inhibitors or aspirin (except for cardiovascular prophylaxis at doses ≤ 325 mg/day), concurrent alarm features (e.g., dysphagia, recurrent vomiting, unexplained anaemia, gastro-intestinal bleeding), H pylori eradication treatment within 12 months, maintenance therapy with either a proton pump or an H2-receptor antagonist within 6 months.</p> <p><u>Clinical setting:</u> The study was conducted in 190 primary care health centers in 17 countries (Argentina, Belgium, Brazil, Canada, Denmark, France, Germany, Greece, Iceland, Italy, Norway, Romania, Singapore, South Africa, Spain, Sweden, Switzerland). Patients were recruited from primary care clinics where flyers publicising the study were placed and the primary care physicians recruited patients presenting to their offices with dyspepsia [random or consecutive sampling unlikely].</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia/ intermittent or continuous pain or burning centered in the upper abdomen for ≥ 3 months. Symptoms were evaluated using a scale validated in a number of languages
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	All patients received outpatient endoscopy
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes (probably)

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Supported by AstraZeneca R&D Sweden. The authors state that “The sponsor did not play any role in the calculations or in the writing of the manuscript”.

References

Included studies

Vakil, N., Talley, N., van Zanten, S. V., Flook, N., Persson, T., Bjorck, E., Lind, T., and Bolling-Sternevald, E. Cost of Detecting Malignant Lesions by Endoscopy in 2741 Primary Care Dyspeptic Patients Without Alarm Symptoms. *Clinical Gastroenterology and Hepatology* 7[7], 756-761. 2009.

Excluded studies (with excl reason)

Amin, M. A., Khan, M. A., Ayub, M., Mahmood, M., Ashraf, M., and Choudhry, A. R. Delay in the diagnosis and prognosis of caecal carcinoma--a study of 20 cases. *Journal of Ayub Medical College, Abbottabad : JAMC* 13[2], 28-31. 2001.

Excl reason: Not in PICO

Andersson, J., Sihto, H., Meis-Kindblom, J. M., Joensuu, H., Nupponen, N., and Kindblom, L. G. NF1-associated gastrointestinal stromal tumors have unique clinical, phenotypic, and genotypic characteristics. *American Journal of Surgical Pathology* 29[9], 1170-1176. 2005.

Excl reason: Not in PICO

Awrich, A. E., Irish, C. E., Vetto, R. M., and Fletcher, W. S. A twenty-five year experience with primary malignant tumors of the small intestine. *Surgery Gynecology and Obstetrics* 151[1], 9-14. 1980.

Excl reason: Not in PICO

Bailey, A. A., Debinski, H. S., Appleyard, M. N., Remedios, M. L., Hooper, J. E., Walsh, A. J., and Selby, W. S. Diagnosis and outcome of small bowel tumors found by capsule endoscopy: a three-center Australian experience. *American Journal of Gastroenterology* 101[10], 2237-2243. 2006.

Excl reason: Not in PICO

Bianchi, E., De, Monti M., Miani, S., Stringhi, E., and Scorza, R. Malignancies of the small intestine: Seven cases. Clinical discussion and review of the literature. [Italian]. *Minerva Chirurgica* 53[4], 289-298. 1998.

Excl reason: Not in PICO

Bolanowski, M., Jarzab, B., Handkiewicz-Junak, D., Jeziorski, A., Kos-Kudla, B., Zajecki, W., and oraz Pozostali Uczestnicy Konferencji Okraglego Stolu. [Neuroendocrine tumors of the small intestine and the appendix - management guidelines (recommended by The Polish Network of Neuroendocrine Tumors)]. [Polish]. *Endokrynologia Polska* 59[1], 87-96. 2008.

Excl reason: Not in PICO

Brophy, C. and Cahow, C. E. Primary small bowel malignant tumors. Unrecognized until emergent laparotomy. *American Surgeon* 55[7], 408-412. 1989.

Excl reason: Not in PICO

Broughton, M., Bailey, J., and Linney, J. How can experiences of patients and carers influence the clinical care of large bowel cancer? *European Journal of Cancer Care* 13[4], 318-327. 2004.

Excl reason: Not in PICO

Call, Jerry, Walentas, Christopher, Eickhoff, Jens, and Scherzer, Norman. Survival of gastrointestinal stromal tumor patients in the imatinib era: life raft group observational registry. *BMC Cancer* 12[1], 90. 2012.

Excl reason: Not in PICO

Catena, Fausto, Di Saverio, Salomone, Kelly, Michael, Biffi, Walter, Ansaloni, Luca, Mandala, Vincenzo, Velmahos, George, Sartelli, Massimo, Tugnoli, Gregorio, Lupo, Massimo, Mandala,

Stefano, Pinna, Antonio, Sugarbaker, Paul, Van Goor, Harry, Moore, Ernest, and Jeekel, Johannes. Bologna Guidelines for Diagnosis and Management of Adhesive Small Bowel Obstruction (ASBO): 2010 Evidence-Based Guidelines of the World Society of Emergency Surgery. *World Journal of Emergency Surgery* 6[1], 5. 2011.

Excl reason: Guideline

Cazzato, I. A., Cammarota, G., Nista, E. C., Cesaro, P., Sparano, L., Bonomo, V., Gasbarrini, G. B., and Gasbarrini, A. Diagnostic and therapeutic impact of double-balloon enteroscopy (DBE) in a series of 100 patients with suspected small bowel diseases. *Digestive & Liver Disease* 39[5], 483-487. 2007.

Excl reason: Not in PICO

Cerame, M. A. A 25-year review of adenocarcinoma of the appendix. A frequently perforating carcinoma. *Diseases of the Colon and Rectum* 31[2], 145-150. 1988.

Excl reason: Not in PICO

Chao, C. C., Ng Jao, Y. T., and Mo, L. R. Capsule endoscopy for gastrointestinal bleeding with an obscure etiology. *Journal of the Formosan Medical Association* 104[9], 659-665. 2005.

Excl reason: Not in PICO

Ciresi, D. L. and Scholten, D. J. The continuing clinical dilemma of primary tumors of the small intestine. *American Surgeon* 61[8], 698-702. 702.

Excl reason: Not in PICO

Cobrin, G. M., Pittman, R. H., and Lewis, B. S. Increased diagnostic yield of small bowel tumors with capsule endoscopy. *Cancer* 107[1], 22-27. 1-7-2006.

Excl reason: Not in PICO

Cockburn, J., Paul, C., Tzelepis, F., McElduff, P., and Byles, J. Delay in seeking advice for symptoms that potentially indicate bowel cancer. *American Journal of Health Behavior* 27[4], 401-407. 2003.

Excl reason: Not in PICO

Comandone, A. and Boglione, A. Biology, diagnosis and therapeutic options in gastrointestinal stromal tumours. [Review] [18 refs]. *Minerva Chirurgica* 60[4], 197-203. 2005.

Excl reason: Narrative review

Crusco, F., Pugliese, F., Maselli, A., Pelliccia, G., Mariani, E., Farroni, F., and Giovagnoni, A. Malignant small-bowel neoplasms: spectrum of disease on MR imaging. [Review]. *Radiologia Medica* 115[8], 1279-1291. 2010.

Excl reason: Narrative review

Cui, T., Elgue, G., Li, S. C., Hurtig, M., Veronesi, ., Pelosi, G., Essaghir, A., Demoulin, J. B., Oberg, K., and Giandomenico, V. Paraneoplastic antigen Ma2 (PNMA2) auto-antibodies as biomarkers for early small intestine neuroendocrine tumors detection. *Neuroendocrinology* 92[1], 5. 2010. S. Karger AG.

Excl reason: Not in PICO

Dabaja, B. S., Suki, D., Pro, B., Bonnen, M., and Ajani, J. Adenocarcinoma of the small bowel: presentation, prognostic factors, and outcome of 217 patients. *Cancer* 101[3], 518-526. 1-8-2004.

Excl reason: Not in PICO

De, Monti M., Mangoni, I., Gobatti, D., Ghilardi, G., and Scorza, R. [Primary jejunal liposarcoma]. [Italian]. *Minerva Gastroenterologica e Dietologica* 46[2], 119-122. 2000.

Excl reason: Not in PICO

Debnath, D., Rees, J., and Myint, F. Are we missing diagnostic opportunities in cases of carcinoid tumours of the appendix? *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland* 6[5], 266-272. 2008.

Excl reason: Not in PICO

Donohue, J. H. Malignant tumours of the small bowel. [Review] [60 refs]. *Surgical Oncology* 3[2], 61-68. 1994.
 Excl reason: Narrative review

Droogendijk, J., Beukers, R., Berendes, P. B., Tax, M. G. H. M., Sonneveld, P., and Levin, M. D. Screening for gastrointestinal malignancy in patients with iron deficiency anemia by general practitioners: An observational study. *Scandinavian Journal of Gastroenterology* 46[9], 1105-1110. 2011.
 Excl reason: Not in PICO (but include for colorectal)

Egberts, J. H., Scharrer, M. L., Hinz, S., Schafmayer, C., Klomp, H. J., Faendrich, F., and Tepel, J. Small bowel cancer: single-centre results over a period of 12 years. *Hepato-Gastroenterology* 54[73], 129-134. 2007.
 Excl reason: Not in PICO

Einstein, D. M., Lieberman, J. M., Paushter, D. M., Chilcote, W. A., Yagan, R., Desberg, A. L., and Motta, A. O. Gastrointestinal radiology: current indications and referral patterns. *Abdominal Imaging* 18[1], 2-6. 1993.
 Excl reason: Not in PICO

Eliakim, R. Video capsule endoscopy of the small bowel. [Review] [39 refs]. *Current Opinion in Gastroenterology* 26[2], 129-133. 2010.
 Excl reason: Narrative review

Estevez, E., Gonzalez-Conde, B., Vazquez-Iglesias, J. L., Alonso, P. A., Vazquez-Millan, Mde L., and Pardeiro, R. Incidence of tumoral pathology according to study using capsule endoscopy for patients with obscure gastrointestinal bleeding. *Surgical Endoscopy* 21[10], 1776-1780. 2007.
 Excl reason: Not in PICPO

Farnbacher, M. J., Reisch, A., Lederer, R., and Schneider, T. [Video capsule endoscopy in a group of networked users: effective and cost saving]. [German]. *Zeitschrift fur Gastroenterologie* 42[6], 505-508. 2004.
 Excl reason: Not in PICO

Feil, W. and Schulz, F. Tumors of the small intestine--diagnosis, therapy and prognosis. [German]. *Langenbecks Archiv fur Chirurgie* 365[1], 25-35. 1985.
 Excl reason: Not in PICO

Feinberg, Y., Law, C. H. L., Singh, S., and Wright, F. C. Patient experiences of having a rare cancer: A qualitative study. *European Journal of Cancer* 47, S477. 2011. Elsevier Ltd.
 Excl reason: Not in PICO

Fischer, H. P. and Zhou, H. [Pathogenesis and histomorphology of ampullary carcinomas and their precursor lesions. Review and individual findings]. [Review] [35 refs] [German]. *Pathologie* 24[3], 196-203. 2003.
 Excl reason: Not in PICO

Flashman, K., O'Leary, D. P., Senapati, A., and Thompson, M. R. The Department of Health's "two week standard" for bowel cancer: is it working? *Gut* 53[3], 387-391. 2004.
 Excl reason: Not in PICO

Garcia Latorre, F. J., Stoduto, Garcia P., Monserrat Blasco, M. T., Muniesa Cuenca, M. P., Hernandez Navarrete, M. J., Garcia Mata, J. R., and Arribas Llorente, J. L. Digestive tract neoplasm. A descriptive study and approximation to the symptom diagnosis interval through a hospital-based tumor registry. [Spanish]. *Oncologia* 17[2], 23-33. 1994.
 Excl reason: Not in PICO

Ge, Z. Z., Hu, Y. B., and Xiao, S. D. Capsule endoscopy and push enteroscopy in the diagnosis of obscure gastrointestinal bleeding. *Chinese Medical Journal* 117[7], 1045-1049. 2004.
 Excl reason: Not in PICO

Goh, B. K., Chow, P. K., Kesavan, S. M., Yap, W. M., Chung, Y. F., and Wong, W. K. A single-institution experience with eight CD117-positive primary extragastrointestinal stromal tumors: critical appraisal and a comparison with their gastrointestinal counterparts. *Journal of Gastrointestinal*

Surgery 13[6], 1094-1098. 2009.
 Excl reason: Not in PICO

Gore, R. M. Small bowel cancer. Clinical and pathologic features. [Review] [83 refs]. Radiologic Clinics of North America 35[2], 351-360. 1997.
 Excl reason: Narrative review

Gore, R. M., Mehta, U. K., Berlin, J. W., Rao, V., and Newmark, G. M. Diagnosis and staging of small bowel tumours. [Review] [14 refs]. Cancer Imaging 6, 209-212. 2006.
 Excl reason: Narrative review

Gourlay, K., Win, May K., and Wiggins, J. Bowelscreen Australia: An opportunity to maximise early detection of bowel cancer through community pharmacy. Asia-Pacific Journal of Clinical Oncology 7, 188. 2011. Blackwell Publishing Ltd.
 Excl reason: Not in PICO

Grill, W. Prognosis of carcinomata of the efferent biliary tracts. [German]. Fortschritte der Medizin 99[30], 1174-1177. 1981.
 Excl reason: Not in PICO

Guivarc'h, M., Kabbej, M., Roullet-Audy, J. C., Mosnier, H., and Boche, O. [Adenocarcinoma of the duodenum. 17 cases]. [French]. Presse Medicale 19[29], 1351-1354. 15-9-1990.
 Excl reason: Not in PICO

Gumustas, O. G., Gumustas, A., Yalcin, R., Savci, G., and Soylu, R. A. Unusual causes of small bowel obstruction and contemporary diagnostic algorithm. [Review] [30 refs]. Journal of Medical Imaging & Radiation Oncology 52[3], 208-215. 2008.
 Excl reason: Narrative review

Harada, J., Taniai, N., Ueda, J., Yoshida, H., Mineta, S., Yoshioka, M., Kawano, Y., Mizuse, M., and Uchida, E. Malignant hepatic epithelioid hemangioendothelioma with abdominal pain due to rapid progression. Hepatology International 5[1], 399. 2011. Springer New York.
 Excl reason: Not in PICO

Harmon, Rhonda and Sugarbaker, Paul. Prognostic indicators in peritoneal carcinomatosis from gastrointestinal cancer. International Seminars in Surgical Oncology 2[1], 3. 2005.
 Excl reason: Narrative review

Hartenfels, I. M., Dukat, A., Burg, J., Hansen, M., and Jung, M. [Adenomas of Vater's ampulla and of the duodenum. Presentation of diagnosis and therapy by endoscopic interventional and surgical methods]. [Review] [38 refs] [German]. Chirurg 73[3], 235-240. 2002.
 Excl reason: Not in PICO

Heyn, G. Prevention of intestinal cancer - Early detection. [German]. Pharmazeutische Zeitung 149[9], 22-28. 26-2-2004.
 Excl reason: Narrative review

Hinz, S., Pauser, U., Egberts, J. H., Schafmayer, C., Tepel, J., and Fandrich, F. Audit of a series of 40 gastrointestinal stromal tumour cases. European Journal of Surgical Oncology 32[10], 1125-1129. 2006.
 Excl reason: Not in PICO

Holzinger, F., Schilling, M., Baer, H. U., and Buchler, M. W. Chronic anaemia caused by small-bowel adenocarcinoma: Case report. [German]. Chirurgische Gastroenterologie 11[2], 174-177. 1995.
 Excl reason: Not in PICO

Howard, R. A., Dores, G. M., Curtis, R. E., Anderson, W. F., and Travis, L. B. Merkel cell carcinoma and multiple primary cancers. Cancer Epidemiology Biomarkers and Prevention 15[8], 1545-1549. 2006.
 Excl reason: Not in PICO

Hundt, S., Haug, U., and Brenner, H. Early detection of intestinal cancer: Comparison of stool tests. [German]. Gynakologe 43[2], 173-175. 2010.
 Excl reason: Narrative review

- Jones, Sian, D'Souza, Charles, and Haboubi, Nadim. Patterns of clinical presentation of adult coeliac disease in a rural setting. *Nutrition Journal* 5[1], 24. 2006.
Excl reason: Not in PICO
- Kamaoui, I., De-Luca, V., Ficarelli, S., Mennesson, N., Lombard-Bohas, C., and Pilleul, F. Value of CT enteroclysis in suspected small-bowel carcinoid tumors. *AJR.American Journal of Roentgenology* 194[3], 629-633. 2010.
Excl reason: Not in PICO
- Kennington, E. How community pharmacists can help in the early detection of bowel cancer. *Pharmaceutical Journal* 288[7702], 497. 21-4-2012.
Excl reason: Not in PICO
- Kloppel, G., Dege, K., Remmele, W., Kapran, Y., Tuzlali, S., and Modlin, I. M. Siegfried Oberndorfer: A tribute to his work and life between Munich, Kiel, Geneva, and Istanbul. *Virchows Archiv* 451, S3-S7. 2007.
Excl reason: Narrative review
- Kok, L., Elias, S. G., Witteman, B. J., Goedhard, J. G., Muris, J. W., Moons, K. G., and de Wit, N. J. Diagnostic accuracy of point-of-care fecal calprotectin and immunochemical occult blood tests for diagnosis of organic bowel disease in primary care: the Cost-Effectiveness of a Decision Rule for Abdominal Complaints in Primary Care (CEDAR) study. *Clinical Chemistry* 58[6], 989-998. 2012.
Excl reason: Not in PICO
- Kovacs, M., Pak, P., Pak, G., and Feher, J. [Capsule endoscopy for the diagnostics of small intestine tumours]. [Review] [38 refs] [Hungarian]. *Orvosi Hetilap* 149[42], 1997-2001. 19-10-2008.
Excl reason: Narrative review
- Lakatos, P. L., Fuszek, P., Horvath, H. C., Zubek, L., Haller, P., and Papp, J. Double-balloon enteroscopy for the diagnosis and treatment of obscure bleeding, inflammatory bowel diseases and polyposis syndromes: we see more but do we know more? *Hepato-Gastroenterology* 55[81], 133-137. 2008.
Excl reason: Not in PICO
- Lee, B. I., Choi, H., Choi, K. Y., Byeon, J. S., Jang, H. J., Eun, C. S., Cheon, J. H., Shin, S. J., Kim, J. O., Lee, M. S., and Choi, J. H. Clinical characteristics of small bowel tumors diagnosed by double-balloon endoscopy: KASID multi-center study. *Digestive Diseases & Sciences* 56[10], 2920-2927. 2011.
Excl reason: Not in PICO
- Li, C.-H., Bair, M.-J., Chang, W.-H., Lin, S.-C., Chen, C.-J., and Liao, W.-S. Primary malignant tumors of the small intestine: 11-year experience in a regional hospital in Taitung. [Chinese]. *Journal of Internal Medicine of Taiwan* 18[1], 29-34. 2007.
Excl reason: Not in PICO
- Li, C. Y., Zhang, B. L., Chen, C. X., and Li, Y. M. OMOM capsule endoscopy in diagnosis of small bowel disease. *Journal of Zhejiang University SCIENCE B* 9[11], 857-862. 2008.
Excl reason: Not in PICO
- Makino, S., Okada, K., Wada, Y., Kato, R., Takeoka, T., Yanagisawa, T., Okamura, S., Fukuchi, N., Ebisui, C., Murata, K., Yokouchi, H., Kinuta, M., Nakagomi, N. & Tamai, M. (2013) [A case of jejunum cancer diagnosed by anemia]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 40: 1720-1722.
Not in PICO
- Maruyama, M. Early gastrointestinal cancers. *Abdominal Imaging* 28[4], 456-463. 2003.
Excl reason: Narrative review
- Mazzarello, M. G. [Occult blood in the feces for the early diagnosis of tumors of the digestive system]. [Italian]. *Minerva Medica* 81[10], 687-690. 1990.
Excl reason: Not in PICO

- McMurrick, P., Dorien, S., and Shapiro, J. Bowel cancer - guide for the GP. [Review] [7 refs]. Australian Family Physician 35[4], 192-197. 2006.
Excl reason: Narrative review
- Michels, J. and Pelfrene, E. Screening campaign for the detection of intestinal and prostate cancer by the general practitioner. [Dutch]. Huisarts Nu 18[1], 14-18. 1989.
Excl reason: Not in PICO
- Miike, T.; Yamamoto, S.; Tahara, Y.; Hasuike, S.; Funagayama, M.; Maehara, N.; Tanaka, H.; Akiyama, Y.; Chijiwa, K.; Shimoda, K. (2014). A case report of gastrointestinal stromal tumor of the small intestine presenting with liver abscesses caused by Streptococcus constellatus. *Nippon Shokakibyō Gakkai Zasshi - Japanese Journal of Gastroenterology*, 111, 1376-83.
Not in PICO
- Mitchell, K. J., Williams, E. S., and Leffall, L. D., Jr. Primary malignant small bowel tumors: an atypical abdominal emergency. Journal of the National Medical Association 87[4], 276-279. 1995.
Excl reason: Not in PICO
- Mitsui, K., Tanaka, S., Yamamoto, H., Kobayashi, T., Ehara, A., Yano, T., Goto, H., Nakase, H., Tanaka, S., Matsui, T., Iida, M., Sugano, K., and Sakamoto, C. Role of double-balloon endoscopy in the diagnosis of small-bowel tumors: the first Japanese multicenter study. *Gastrointestinal Endoscopy* 70[3], 498-504. 2009.
Excl reason: Not in PICO
- Morgan, B. K., Compton, C., Talbert, M., Gallagher, W. J., and Wood, W. C. Benign smooth muscle tumors of the gastrointestinal tract. A 24-year experience. *Annals of Surgery* 211[1], 63-66. 1990.
Excl reason: Not in PICO
- Mori, S. Useful cutaneous markers of internal malignancy in the early stage. [Japanese]. *Japanese Journal of Cancer and Chemotherapy* 15[4 II-3], 1564-1568. 1988.
Excl reason: Not in PICO
- Nicholl, M. B., Ahuja, V., Conway, C., Sim, M. S., and Singh, G. Small Bowel Adenocarcinoma: Understaged and Undertreated? *Annals of Surgical Oncology* 17[10], 2728-2732. 2010.
Excl reason: Not in PICO
- Nordkild, P. and Kjaergard, H. Primary tumours of the small intestine--the diagnostic problem. *Annales Chirurgiae et Gynaecologiae* 75[1], 31-36. 1986.
Excl reason: Not in PICO
- North, Jr and Pack, M. S. Malignant tumors of the small intestine: A review of 144 cases. *American Surgeon* 66[1], 46-51. 2000.
Excl reason: Not in PICO
- O'Donnell, M. E., Carson, J., and Garstin, W. I. H. Surgical treatment of malignant carcinoid tumours of the appendix. *International Journal of Clinical Practice* 61[3], 431-437. 2007.
Excl reason: Not in PICO
- Oberle, E., Brunner, K., and Rhyner, K. [Gastrointestinal hemorrhage: how much evaluation is necessary?]. [German]. *Schweizerische Rundschau für Medizin Praxis* 82[44], 1244-1252. 2-11-1993.
Excl reason: Not in PICO
- Ojha, A., Zacherl, J., Scheuba, C., Jakesz, R., and Wenzl, E. Primary small bowel malignancies: single-center results of three decades. *Journal of Clinical Gastroenterology* 30[3], 289-293. 2000.
Excl reason: Not in PICO
- Oka, S., Tanaka, S., Nagata, S., Hiyama, T., Ito, M., Kitadai, Y., Yoshihara, M., Haruma, K., and Chayama, K. Clinicopathologic Features and Endoscopic Resection of Early Primary Nonampullary Duodenal Carcinoma. *Journal of Clinical Gastroenterology* 37[5], 381-386. 2003.
Excl reason: Not in PICO
- Okada, E., Araki, A., Suzuki, S., Watanabe, H., Ikeda, T., Watanabe, T., Kurata, M., Eishi, Y. & Watanabe, M. (2013) Histological diagnosis of follicular lymphoma by biopsy of small intestinal

normal mucosa. *Digestive Endoscopy*, 25: 544-546.

Not in PICO

Okadome, M., Saito, T., Tsukamoto, N., Nishi, K., Nishiyama, N., and Nagata, E. Endometrial scraping cytology in women with extragenital malignancies. *Acta Cytologica* 50[2], 158-163. 2006.

Excl reason: Not in PICO

Orlandi, M. and Inauen, W. [Chronic gastrointestinal bleeding]. [Review] [6 refs] [German].

Therapeutische Umschau 63[5], 327-332. 2006.

Excl reason: Narrative review

Osawa, H. & Yamamoto, H. (2014) Present and future status of flexible spectral imaging color enhancement and blue laser imaging technology. *Digestive Endoscopy*, 26: Suppl-15.

Narrative review

Peacock, O., Blackwell, J., Hanna, N., Muhammad, N., Watts, E., Robinson, M., Tierney, G. & Lund, J. (2012) Regional 2 week wait referrals to the lower gastrointestinal clinic for iron deficiency anaemia. *Colorectal Disease*, 14: 56.

Not in PICO

Peacock, O., Watts, E. S., Faimali, M., Makandidze, L., Tazeen, U., Robinson, M. & Lund, J. N. (2012) Up to 92% of patients referred via the 2WW for iron deficiency anaemia pathway are inadequately investigated before referral or inappropriately referred. *Colorectal Disease*, 14: 14.

Not in PICO

Potter, D. D., Murray, J. A., Donohue, J. H., Burgart, L. J., Nagorney, D. M., van Heerden, J. A., Plevak, M. F., Zinsmeister, A. R., and Thibodeau, S. N. The role of defective mismatch repair in small bowel adenocarcinoma in celiac disease. *Cancer Research* 64[19], 7073-7077. 1-10-2004.

Excl reason: Not in PICO

Reiter, J., Kaufmann, W., and Saeger, H. D. Primary duodenal tumors. [German]. *Der Chirurg; Zeitschrift für alle Gebiete der operativen Medizin* 52[7], 457-461. 1981.

Excl reason: Narrative review

Ribeiro, M. B., Greenstein, A. J., Heimann, T. M., Yamazaki, Y., and Aufses, Jr. Adenocarcinoma of the small intestine in Crohn's disease. *Surgery Gynecology and Obstetrics* 173[5], 343-349. 1991.

Excl reason: Not in PICO

Riccioni, M. E., Urgesi, R., Cianci, R., Spada, C., Nista, E. C., and Costamagna, G. Single-balloon push-and-pull enteroscopy system: does it work? A single-center, 3-year experience. *Surgical Endoscopy* 25[9], 3050-3056. 2011.

Excl reason: Not in PICO

Riccioni, M. E., Cianci, R., Urgesi, R., Bizzotto, A., Spada, C., Rizzo, G., Coco, C., and Costamagna, G. Advance in diagnosis and treatment of small bowel tumors: a single-center report. *Surgical Endoscopy* 26[2], 438-441. 2012.

Excl reason: Not in PICO

Sailer, J., Zacherl, J., and Schima, W. MDCT of small bowel tumours. [Review] [30 refs]. *Cancer Imaging* 7, 224-233. 2007.

Excl reason: Narrative review

Santoro, E., Sacchi, M., Scutari, F., Carboni, F., and Graziano, F. Primary adenocarcinoma of the duodenum: treatment and survival in 89 patients. *Hepato-Gastroenterology* 44[16], 1157-1163. 1997.

Excl reason: Not in PICO

Schwartz, G. D. and Barkin, J. S. Small-bowel tumors detected by wireless capsule endoscopy. *Digestive Diseases & Sciences* 52[4], 1026-1030. 2007.

Excl reason: Not in PICO

Scialpi, C., Mosca, S., Malaguti, A., Orsi, I., Vezzadini, C., and Toni, R. Acromegaly and intestinal neoplasms. *Minerva Endocrinologica* 24[3-4], 123-127. 1999.

Excl reason: Narrative review

Sharma, M., Mallows, K., West, S., Hodges, G., and Budhoo, M. Bowel symptoms don't predict cancer in bowel cancer screening. *Colorectal Disease* 12, 15. 2010. Blackwell Publishing Ltd.
Excl reason: Not in PICO (abstract: Screened population, not split by symptom or cancer)

Shyung, L. R., Lin, S. C., Shih, S. C., Chang, W. H., Chu, C. H., and Wang, T. E. Proposed scoring system to determine small bowel mass lesions using capsule endoscopy. *Journal of the Formosan Medical Association* 108[7], 533-538. 2009.
Excl reason: Not in PICO

Slavin, T. P. and Wiesner, G. L. Developmental defects and childhood cancer. *Current Opinion in Pediatrics* 21[6], 717-723. 2009.
Excl reason: Narrative review

Solem, C. A., Harmsen, W. S., Zinsmeister, A. R., and Loftus, E. V., Jr. Small intestinal adenocarcinoma in Crohn's disease: a case-control study. *Inflammatory Bowel Diseases* 10[1], 32-35. 2004.
Excl reason: Not in PICO

Sorour, M.A.; Kassem, M.I.; Ghazal, Ael; El-Riwini, M.T.; Abu, Nasr A. (2014). Gastrointestinal stromal tumors (GIST) related emergencies. *International Journal of Surgery*, 12, 269-80.
Not in PICO

Spada, C., Riccioni, M. E., Familiari, P., Marchese, M., Bizzotto, A., and Costamagna, G. Video capsule endoscopy in small-bowel tumours: a single centre experience. *Scandinavian Journal of Gastroenterology* 43[4], 497-505. 2008.
Excl reason: Not in PICO

Spelsberg, F. and Schmidtler, F. Primary malignant tumours in the small bowel. (A report about 43 of our own cases and 1134 cases from literature). *Acta Chirurgica Iugoslavica* 27[1], 39-46. 1980.
Excl reason: Not in PICO

Spunt, S. L., Pratt, C. B., Rao, B. N., Pritchard, M., Jenkins, J. J., Hill, D. A., Cain, A. M., and Pappo, A. S. Childhood carcinoid tumors: the St Jude Children's Research Hospital experience. *Journal of Pediatric Surgery* 35[9], 1282-1286. 2000.
Excl reason: Not in PICO

Srirajaskanthan, R., Toumpanakis, C., Sogbodjor, A., Desai, K., Krepska, A., Marelli, L., Winslett, M., Ogunbyi, G., and Caplin, M. Mesenteric fibrosis in patients with small bowel carcinoid tumours: Impact on quality of life and survival. *Gut* 58, A119. 2009. BMJ Publishing Group.
Excl reason: Not in PICO

Steckelberg, A. and Bunge, M. Informed decision in the early detection of intestinal cancer: Way out of immaturity. [German]. *Public Health Forum* 20[1], 23. 2012.
Excl reason: Narrative review

Strodel, W. E., Talpos, G., Eckhauser, F., and Thompson, N. Surgical therapy for small-bowel carcinoid tumors. *Archives of Surgery* 118[4], 391-397. 1983.
Excl reason: Not in PICO

Sturniolo, G. C., Di, Leo, V., Vettorato, M. G., and D'Inca, R. Clinical relevance of small-bowel findings detected by wireless capsule endoscopy. *Scandinavian Journal of Gastroenterology* 40[6], 725-733. 2005.
Excl reason: Not in PICO

Sugawara, G., Yamaguchi, A., Isogai, M., Harada, T., Kaneoka, Y., Suzuki, M., Akutagawa, A., Suzumura, K., and Usui, T. A clinicopathological study on primary carcinoma of the duodenum. [Japanese]. *Japanese Journal of Gastroenterological Surgery* 34[8], 1283-1288. 2001.
Excl reason: Not in PICO

Sugita, A., Koganei, K., Tatsumi, K., Yamada, K., Futatsuki, R., Kuroki, H., Arai, K., Kimura, H., Kitoh, F., and Fukushima, T. Optimal diagnosis for fistula-associated anal cancer with Crohn's disease. [Japanese]. *Gastroenterological Endoscopy* 54[1], 66-72. 2012.
Excl reason: Narrative review

Szodoray, P., Barta, Z., Lakos, G., Szakall, S., and Zeher, M. Coeliac disease in Sjogren's syndrome--a study of 111 Hungarian patients. *Rheumatology International* 24[5], 278-282. 2004.
Excl reason: Not in PICO

Thang, N. N., Cochet, S., George, A. C., Betz, M., and Roth, A. [Management of anal canal carcinoma]. [French]. *Revue Medicale Suisse* 7[296], 1144-1148. 25-5-2011.
Excl reason: Narrative review

Thompson, M. R., Heath, I., Ellis, B. G., Swarbrick, E. T., Faulds, Wood L., and Atkin, W. S. Identifying and managing patients at low risk of bowel cancer in general practice. *British Medical Journal* 327[7409], 263-265. 2-8-2003.
Excl reason: Narrative review

Thompson, M. R., Heath, I., Swarbrick, E. T., Wood, L. F., and Ellis, B. G. Earlier diagnosis and treatment of symptomatic bowel cancer: can it be achieved and how much will it improve survival?. [Review]. *Colorectal Disease* 13[1], 6-16. 2011.
Excl reason: Not in PICO

Thompson, M. R., Asiimwe, A., Flashman, K., and Tsavellas, G. Is earlier referral and investigation of bowel cancer patients presenting with rectal bleeding associated with better survival? *Colorectal Disease* 13[11], 1242-1248. 2011.
Excl reason: Not in PICO

Tran, Thang N. N., Cochet, S., George, A.-C., Betz, M., and Roth, A. Management of anal canal carcinoma. [French]. *Revue Medicale Suisse* 7[296], 1144-1148. 25-5-2011.
Excl reason: Narrative review

Tsuji, Y., Ohata, K., Umezawa, S., Takeuchi, S., Sekiguchi, M., Ohno, A., Ito, T., Chiba, H., Yamawaki, M., Hisatomi, K., Teratani, T., and Matsushashi, N. [Diagnosis of small bowel carcinoma by capsule endoscopy]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]* 37[8], 1440-1445. 2010.
Excl reason: Narrative review

Ugurly, M. M., Asoglu, O., Potter, D. D., Barnes, S. A., Harmsen, W. S., and Donohue, J. H. Adenocarcinomas of the jejunum and ileum: a 25-year experience. *Journal of Gastrointestinal Surgery* 9[8], 1182-1188. 2005.
Excl reason: Not in PICO

Urgesi, R., Riccioni, M. E., Bizzotto, A., Cianci, R., Spada, C., Pelecca, G., Ricci, R. M., and Costamagna, G. Increased diagnostic yield of small bowel tumors with PillCam: the role of capsule endoscopy in the diagnosis and treatment of gastrointestinal stromal tumors (GISTs). Italian single-center experience. *Tumori* 98[3], 357-363. 2012.
Excl reason: Not in PICO

Varras, Michail, Vlachakos, Nikolaos, Akrivis, Christodoulos, Vasilakaki, Thivi, and Skafida, Evangelia. Malignant gastrointestinal stromal tumor presenting with hemoperitoneum in puerperium: report of a case with review of the literature. *World Journal of Surgical Oncology* 8[1], 95. 2010.
Excl reason: Not in PICO

Voderholzer, W. A., Ortner, M., Rogalla, P., Beinholzl, J., and Lochs, H. Diagnostic yield of wireless capsule enteroscopy in comparison with computed tomography enteroclysis. *Endoscopy* 35[12], 1009-1014. 2003.
Excl reason: Not in PICO

Wang, J., Gao, J. D., and Shao, Y. F. [Diagnosis and surgical treatment of primary duodenal carcinoma]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]* 41[1], 30-32. 2003.
Excl reason: Not in PICO

Ward, S. M., Mobsby, C. J., and Wilkinson, S. Capsule endoscopy: a surgical perspective. *ANZ Journal of Surgery* 78[1-2], 28-33. 2008.
Excl reason: Not in PICO

Williamson, J.M.; Williamson, R.C. (2014). Small bowel tumors: pathology and management. *Journal of the Medical Association of Thailand*, 97, 126-37.

Narrative review

Yakan, S., Caliskan, C., Makay, O., Denecli, A. G., and Korkut, M. A. Intussusception in adults: clinical characteristics, diagnosis and operative strategies. *World Journal of Gastroenterology* 15[16], 1985-1989. 28-4-2009.

Excl reason: Not in PICO

Yang, W. L., Zhang, X. C., Yan, Z. Q., Zhang, H. M., Zhao, Z., Zhang, J. G., and Wang, Y. J. [Clinical analysis of primary small intestinal neoplasms in 305 cases]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]* 29[10], 781-783. 2007.

Excl reason: Not in PICO

Yun, G. W., Yang, Y. J., Song, I. C., Park, K. U., Baek, S. W., Yun, H. J., Kim, S., Jo, D. Y., and Lee, H. J. A prospective evaluation of adult men with iron-deficiency anemia in Korea. *Internal Medicine* 50[13], 1371-1375. 2011.

Excl reason: Not in PICO

Zeeneldin, A. A., Saber, M. M., Seif El-Din, I. A. & Frag, S. A. (2013) Small intestinal cancers among adults in an Egyptian district: a clinicopathological study using a population-based cancer registry. *Journal of Egyptian National Cancer Institute*, 25: 107-114.

Not in PICO

Zollei, I. and Balogh, A. About the primary malignant tumors of small bowel. *Acta Chirurgica Hungarica* 36[1-4], 406-408. 1997.

Excl reason: Not in PICO

Review question:

Which investigations of symptoms of suspected small intestine cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	299	59	03/06/2013
Premedline	1980-2013	15	10	03/06/2013
Embase	1980-2013	114	48	03/06/2013
Cochrane Library	1980-2013	79	0	03/06/2013
Psychinfo	1980-2013	0	0	03/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	27	6	03/06/2013

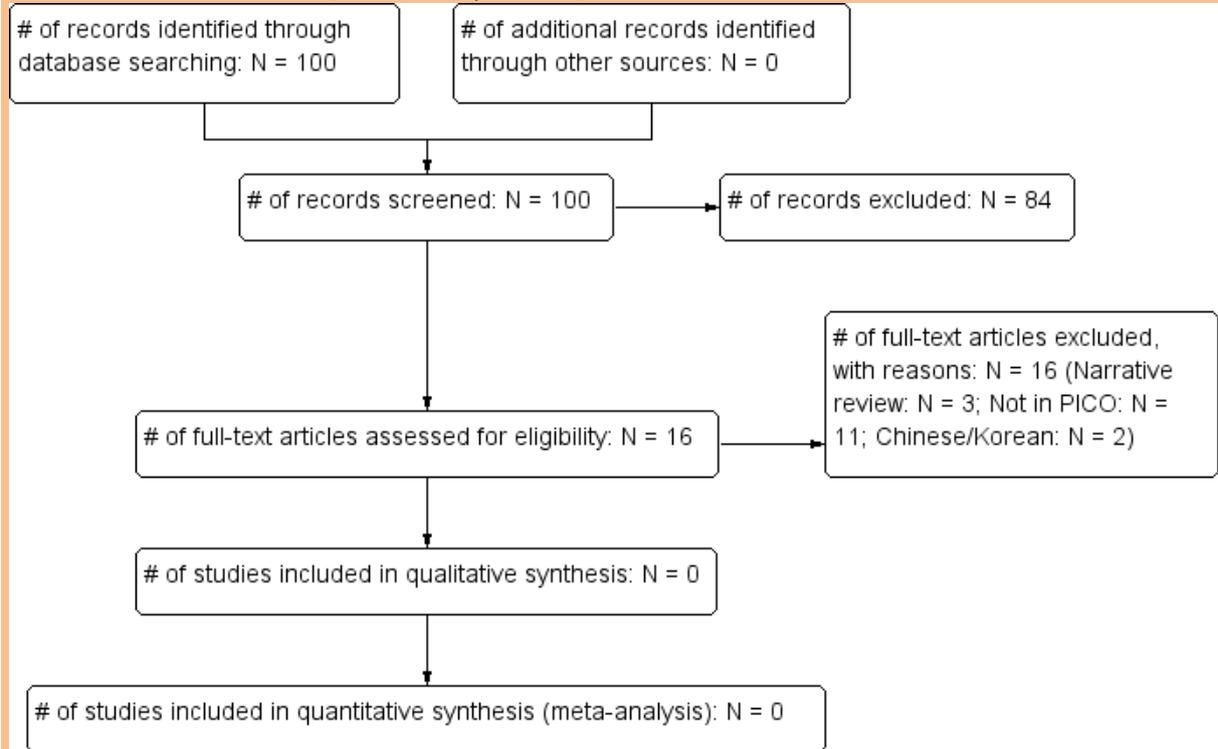
Total References retrieved (after de-duplication): 95

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	6/2013-26/08/2014	14	0	26/08/2014
Premedline	6/2013-26/08/2014	37	4	26/08/2014
Embase	6/2013-26/08/2014	15	1	26/08/2014

Cochrane Library	6/2013-26/08/2014	12	0	26/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	6/2013-26/08/2014	1	1	26/08/2014

Total References retrieved (after de-duplication): 5



Study results

No evidence was identified pertaining to the diagnostic accuracy of CT scan, barium follow through or capsule endoscopy in patients with suspected small intestine cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Apostolopoulos, P., Liatsos, C., Gralnek, I. M., Giannakouloupoulou, E., Alexandrakis, G., Kalantzis, C., Gabriel, P. & Kalantzis, N. (2006) The role of wireless capsule endoscopy in investigating unexplained iron deficiency anemia after negative endoscopic evaluation of the upper and lower gastrointestinal tract. *Endoscopy*, 38: 1127-1132.

Not in PICO

Barney, S. P., Muller, C. Y. & Bradshaw, K. D. (2008) Pelvic Masses. *Medical Clinics of North America*, 92: 1143-1161.

Narrative review

Benis, E., Szilagyi, A., Izbeki, F., Varga, I. & Altorjay, A. (2014) - [Intestinal bleeding and obstruction in the small intestine caused by metastatic thyroid angiosarcoma. Case report]. [Hungarian]. - *Orvosi Hetilap*, 155: 918-921.

Not in PICO

- Bocker, U., Dinter, D., Litterer, C., Hummel, F., Knebel, P., Franke, A., Weiss, C., Singer, M. V. & Lohr, J. M. (2010) Comparison of magnetic resonance imaging and video capsule enteroscopy in diagnosing small-bowel pathology: localization-dependent diagnostic yield. *Scandinavian Journal of Gastroenterology*, 45: 490-500.
Not in PICO
- Borchard-Tuch, C. (2007) Early detection of cancer: Effectiveness of current tests. [German]. *Pharmazeutische Zeitung*, 152: 18-25.
Narrative review
- Boudiaf, M., Jaff, A., Soyer, P., Bouhnik, Y., Hamzi, L. & Rymer, R. (2004) Small-bowel diseases: prospective evaluation of multi-detector row helical CT enteroclysis in 107 consecutive patients. *Radiology*, 233: 338-344.
Not in PICO
- Casadei, A., Simone, A., Cavargini, E., De, V. E. & Ricci, E. (2011) Advanced endoscopy (FICE NBI). How to improve gastric and duodenal tumor diagnosis. [Italian]. *Giornale Italiano di Endoscopia Digestiva*, 34: 131-135.
Narrative review
- Chao, C. C., Ng Jao, Y. T. & Mo, L. R. (2005) Capsule endoscopy for gastrointestinal bleeding with an obscure etiology. *Journal of the Formosan Medical Association*, 104: 659-665.
Not in PICO
- Chelimilla, H., Ihimoyan, A., Carvajal, S. & Bhavna, B. (2012) Ileoileal intussusception secondary to an ileal fibroma. *Case Reports Gastroenterology*, 6: 734-740.
Not in PICO
- Choda, Y., Ninomiya, M., Fujiwara, Y., Kanazawa, T., Harano, M., Matsukawa, H., Ojima, Y., Shiozaki, S. & Ohno, S. (2011) [A case report of multiple adenocarcinoma in small intestine after total gastrectomy by Roux-en-Y re-construction]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 38: 2042-2044.
Not in PICO
- Cichoż-Lach, H. & Celinński, K. (2007) Modern methods of endoscopic diagnosis of gastrointestinal tract. [Review] [53 refs]. *Journal of Physiology & Pharmacology*, 58: Suppl-31.
Narrative review
- Clemençon, G. H. (1980) Endoscopy in ambulant practice. *Endoscopy.(Suppl):69-89, 1980.*, 69-89.
Narrative review
- Cobrin, G. M., Pittman, R. H. & Lewis, B. S. (2006) Increased diagnostic yield of small bowel tumors with capsule endoscopy. *Cancer*, 107: 22-27.
Not in PICO
- Costamagna, G., Gabrielli, A., Mutignani, M., Perri, V., Buononato, M. & Crucitti, F. (1993) Endoscopic diagnosis and treatment of malignant biliary strictures: review of 505 patients. *Acta Gastroenterologica Belgica*, 56: 201-206.
Not in PICO
- Crusco, F., Pugliese, F., Maselli, A., Pelliccia, G., Mariani, E., Farroni, F. & Giovagnoni, A. (2010) Malignant small-bowel neoplasms: spectrum of disease on MR imaging. [Review]. *Radiologia Medica*, 115: 1279-1291.
Narrative review
- Cwikel, W. & Andren-Sandberg, A. (1991) Diagnostic difficulties with duodenal malignancies revisited: A new strategy. *Gastrointestinal Radiology*, 16: 301-304.
Not in PICO
- El Alaoui, M., D'Halluin, P. N., Boustiere, C., Bretagne, J. F. & Heresbach, D. (2006) Clinical impact of patients examined by PILLCAM SB (R) videocapsule: one-year follow-up of patients consecutively included in two French centers in 2003. *Acta Endoscopica*, 36: 149-162.
Not in PICO

- Eliakim, A. R. (2006) Video capsule endoscopy of the small bowel (PillCam SB). [Review] [22 refs]. *Current Opinion in Gastroenterology*, 22: 124-127.
Narrative review
- Ell, C., Remke, S., May, A. & Brown, R. D. (2003) Capsule endoscopy has higher diagnostic yield than push enteroscopy in patients with chronic gastrointestinal bleeding: Comment. *Evidence-Based Gastroenterology*, 4: 52-53.
Comment
- Estevez, E., Gonzalez-Conde, B., Vazquez-Iglesias, J. L., Alonso, P. A., Vazquez-Millan, M. L. & Pardeiro, R. (2007) Incidence of tumoral pathology according to study using capsule endoscopy for patients with obscure gastrointestinal bleeding. *Surgical Endoscopy*, 21: 1776-1780.
Not in PICO
- Farnbacher, M. J., Reisch, A., Lederer, R. & Schneider, T. (2004) Cooperative use of video capsule endoscopy: Effective and economic. [German]. *Zeitschrift fur Gastroenterologie*, 42: 505-508.
Not in PICO
- Farnbacher, M. J., Reisch, A., Lederer, R. & Schneider, T. (2004) [Video capsule endoscopy in a group of networked users: effective and cost saving]. [German]. *Zeitschrift fur Gastroenterologie*, 42: 505-508.
Not in PICO
- Fataar, S. & Schulman, A. (1983) Small-bowel obstruction masking synchronous large-bowel obstruction: a need for emergency barium enema. *AJR.American Journal of Roentgenology*, 140: 1159-1162.
Not in PICO
- Frantz, D. J., Dellon, E. S., Grimm, I. S. & Morgan, D. R. (2010) Single-balloon enteroscopy: results from an initial experience at a U.S. tertiary-care center. *Gastrointestinal Endoscopy*, 72: 422-426.
Not in PICO
- Galniche, J.-P. & Tygat (1999) Treat or investigate? *European Journal of Gastroenterology and Hepatology, Supplement*, 11: S11-S15.
Narrative review
- Gay, G., Delvaux, M. & Fassler, I. (2006) Outcome of capsule endoscopy in determining indication and route for push-and-pull enteroscopy. *Endoscopy*, 38: 49-58.
Not in PICO
- Ge, Z. Z., Hu, Y. B. & Xiao, S. D. (2004) Capsule endoscopy and push enteroscopy in the diagnosis of obscure gastrointestinal bleeding. *Chinese Medical Journal*, 117: 1045-1049.
Not in PICO
- Ghaderi, H., Jafarian, A., Aminian, A. & Daryasari, S. A. M. (2010) Clinical presentations, diagnosis and treatment of adult intussusception, a 20 years survey. *International Journal of Surgery*, 8: 318-320.
Not in PICO
- Goodfellow, P. B., Fretwell, I. A. & Simms, J. M. (2003) Nurse endoscopy in a district general hospital. *Annals of the Royal College of Surgeons of England*, 85: 181-184.
Not in PICO
- Gyokeres, T. (2011) [Symptoms and diagnosis of neuroendocrine tumors of the digestive system]. [Review] [Hungarian]. *Orvosi Hetilap*, 152: 371-378.
Narrative review
- Hale, M. F., Sidhu, R. & McAlindon, M. E. (2014) - Capsule endoscopy: current practice and future directions. [Review]. - *World Journal of Gastroenterology*, 20: 7752-7759.
Narrative review
- Haug, A. R., Cindea-Drimus, R., Auernhammer, C. J., Reincke, M., Wangler, B., Uebleis, C., Schmidt, G. P., Goke, B., Bartenstein, P. & Hacker, M. (2012) The role of 68Ga-DOTATATE PET/CT in suspected neuroendocrine tumors. *Journal of Nuclear Medicine*, 53: 1686-1692.
Not in PICO

- Hedayati, A. A., Bandurski, J. & Lewandowski, A. (2013) Bifocal metastasis of melanoma to the small intestine from an unknown primary with intestinal obstruction - case report. *Wspolczesna Onkologia-Contemporary Oncology*, 17: 317-320.
Not in PICO
- Hizawa, K., Iida, M., Matsumoto, T., Kohrogi, N., Suekane, H., Yao, T. & Fujishima, M. (1994) Gastrointestinal manifestations of Cowden's disease. Report of four cases. *Journal of Clinical Gastroenterology*, 18: 13-18.
Not in PICO
- Hong, X., Choi, H., Loyer, E. M., Benjamin, R. S., Trent, J. C. & Charnsangavej, C. (2006) Gastrointestinal stromal tumor: role of CT in diagnosis and in response evaluation and surveillance after treatment with imatinib. [Review] [22 refs]. *Radiographics*, 26: 481-495.
Narrative review
- Jo, J. Y., Byeon, J. S., Choi, K. D., Park, H. W., Lee, G. H., Myung, S. J., Jung, H. Y., Yang, S. K., Hong, W. S., Kim, J. H. & Ha, H. K. (2006) [Comparison of double balloon enteroscopy and small bowel series for the evaluation of small bowel lesions]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 48: 25-31.
In Korean, not enough information can be extracted, but it appears to be "Not in PICO".
- Jones, R. H. (1996) Clinical economics review: Gastrointestinal disease in primary care. *Alimentary Pharmacology and Therapeutics*, 10: 233-239.
Narrative review
- Katsinelos, P., Fasoylas, K., Chatzimavroudis, G., Lazaraki, G., Zavos, C., Pilpilidis, I., Terzoudis, S., Kokonis, G., Patsis, I., Beltsis, A., Paroutoglou, G. & Kountouras, J. (2010) Diagnostic yield and clinical management after capsule endoscopy in daily clinical practice: A single-center experience. *Hippokratia*, 14: 271-276.
Not in PICO
- Kawamoto, K., Ueyama, T., Iwashita, I., Utsunomiya, T., Honda, H., Onitsuka, H., Haraguchi, Y., Kojima, N., Takano, H. & Masuda, K. (1994) Colonic submucosal tumors: comparison of endoscopic US and target air-enema CT with barium enema study and colonoscopy. *Radiology*, 192: 697-702.
Not in PICO
- Khademi, H., Radmard, A.-R., Malekzadeh, F., Kamangar, F., Nasser-Moghaddam, S., Johansson, M., Byrnes, G., Brennan, P. & Malekzadeh, R. (2012) Diagnostic accuracy of age and alarm symptoms for upper GI malignancy in patients with dyspepsia in a GI clinic: A 7-year cross-sectional study. *PLoS ONE*, 7.
Not in PICO
- Kimchi, N. A., Mindrul, V., Broide, E. & Scapa, E. (1998) The contribution of endoscopy and biopsy to the diagnosis of periampullary tumors. *Endoscopy*, 30: 538-543.
Not in PICO
- Kok, L., Elias, S. G., Witteman, B. J. M., Goedhard, J. G., Muris, J. W. M., Moons, K. G. M. & De Wit, N. J. (2012) Diagnostic accuracy of point-of-care fecal calprotectin and immunochemical occult blood tests for diagnosis of organic bowel disease in primary care: The cost-effectiveness of a decision rule for abdominal complaints in primary care (CEDAR) study. *Clinical Chemistry*, 58: 989-998.
Not in PICO
- Kolodziej, M., Annabhani, A. & Sasiadek, M. (2010) CT enteroclysis in the diagnostics of small bowel diseases. *Polish Journal of Radiology*, 75: 66-72.
Not in PICO
- Lakatos, P. L., Horvath, H. C., Zubek, L., Pak, G., Pak, P., Fuszek, P., Nagypal, A. & Papp, J. (2010) Double-balloon endoscopy for small intestinal disease: a single-center experience in Hungary. *Medical Science Monitor*, 16: MT22-MT27.
Not in PICO

- Lee, C. H., Kim, P. S., Lee, J. I., Jeong, S., Lee, J. W., Kwon, K. S., Lee, D. H., Kim, H. G., Shin, Y. W., Kim, Y. S., Kim, J. M. & Jeon, Y. S. (2006) [A case of primary jejunal adenocarcinoma diagnosed by enteroscopy using pediatric colonoscope]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwaagi Hakhoe Chi*, 48: 365-368.
Not in PICO
- Levy, A. D. & Sobin, L. H. (2007) From the archives of the AFIP: Gastrointestinal carcinoids: imaging features with clinicopathologic comparison. [Review] [61 refs]. *Radiographics*, 27: 237-257.
Narrative review
- Li, C.-Y., Zhang, B.-L., Chen, C.-X. & Li, Y.-M. (2008) OMOM capsule endoscopy in diagnosis of small bowel disease. *Journal of Zhejiang University: Science B*, 9: 857-862.
Not in PICO
- Liao, Z., Gao, R., Xu, C. & Li, Z. S. (2010) Indications and detection, completion, and retention rates of small-bowel capsule endoscopy: a systematic review. [Review] [36 refs]. *Gastrointestinal Endoscopy*, 71: 280-286.
Not in PICO
- Lingohr, P., Knoefel, W. T., Kleimann, E. & Rheinwald, K. P. (2007) [Laparoscopic coincidental finding in a case of incomplete ileus: adenocarcinoma of the small intestine as first manifestation of Crohn's disease]. [German]. *Zentralblatt fur Chirurgie*, 132: 564-568.
Narrative review
- Maruyama, M. (2003) Early gastrointestinal cancers. [Review] [40 refs]. *Abdominal Imaging*, 28: 456-463.
Narrative review
- Masselli, G., Casciani, E., Poletini, E., Laghi, F. & Gualdi, G. (2013) Magnetic resonance imaging of small bowel neoplasms. *Cancer Imaging*, 13: 92-99.
Narrative review
- McIntyre, A. S. & Long, R. G. (1993) Prospective survey of investigations in outpatients referred with iron deficiency anaemia. *Gut*, 34: 1102-1107.
Not in PICO
- Mitsui, K., Tanaka, S., Yamamoto, H., Kobayashi, T., Ehara, A., Yano, T., Goto, H., Nakase, H., Tanaka, S., Matsui, T., Iida, M., Sugano, K. & Sakamoto, C. (2009) Role of double-balloon endoscopy in the diagnosis of small-bowel tumors: the first Japanese multicenter study. *Gastrointestinal Endoscopy*, 70: 498-504.
Not in PICO
- Neely, D., Ong, J., Patterson, J., Kirkpatrick, D. & Skelly, R. (2013) Small intestinal adenocarcinoma: rarely considered, often missed? *Postgraduate Medical Journal*, 89: 197-201.
Narrative review
- Ning, S., Jin, X., Tang, J., Zhu, M., Cao, C., Zhao, J. & Mao, G. (2010) Diagnostic value of double-balloon enteroscopy in small bowel tumor. [Chinese]. *Chinese Journal of Gastroenterology*, 15: 609-611.
in Chinese, not enough information can be extracted, but it appears to be "Not in PICO".
- Nordkild, P. & Kjaergard, H. (1986) Primary tumours of the small intestine--the diagnostic problem. *Annales Chirurgiae et Gynaecologiae*, 75: 31-36.
Not in PICO
- Omori, K., Tetsuhara, K., Hiramoto, H., Shoda, H., Sanefuji, H. & Okamoto, N. (2010) [A case of primary small intestinal malignant lymphoma found based on multiple pulmonary nodules with cavitation]. [Japanese]. *Nihon Kokyuki Gakkai Zasshi*, 48: 497-501.
Not in PICO
- Osawa, H. & Yamamoto, H. (2014) - Present and future status of flexible spectral imaging color enhancement and blue laser imaging technology. - *Digestive Endoscopy*, 26 Suppl 1: 105-115.
Narrative review

- Paulsen, S. R., Huprich, J. E., Fletcher, J. G., Booya, F., Young, B. M., Fidler, J. L., Johnson, C. D., Barlow, J. M. & Earnest, F. (657) CT enterography as a diagnostic tool in evaluating small bowel disorders: review of clinical experience with over 700 cases. [Review] [53 refs]. *Radiographics*, 26: 641-657.
Narrative review
- Pennazio, M. (2006) Capsule endoscopy: Where are we after 6 years of clinical use? *Digestive and Liver Disease*, 38: 867-878.
Narrative review
- Perez-Cuadrado, E., Mas, P., Hallal, H., Shanabo, J., Munoz, E., Ortega, I., Lopez, M. A., Torrella, E., Lopez, H. A., Martin, A. & Carballo, F. (2006) Double-balloon enteroscopy: a descriptive study of 50 explorations. *Revista Espanola de Enfermedades Digestivas*, 98: 73-81.
Not in PICO
- Petras, R. E. (1995) Comments on the proceedings of the Endoscopy Masters Forum: Endoscopy in precancerous and early-stage cancerous conditions of the gastrointestinal tract. *Endoscopy*, 27: 58-63.
Comment
- Poddar, N., Raza, S., Sharma, B., Liu, M., Gohari, A. & Kalavar, M. (2011) Small bowel adenocarcinoma presenting with refractory iron deficiency anemia - case report and review of literature. *Case Reports Oncology*, 4: 458-463.
Not in PICO
- Rey, J. F., Ladas, S., Alhassani, A. & Kuznetsov, K. (2006) European Society of Gastrointestinal Endoscopy (ESGE) video capsule endoscopy: Update to guidelines (May 2006). *Endoscopy*, 38: 1047-1053.
Guideline
- Riccioni, M. E., Urgesi, R., Cianci, R., Spada, C., Nista, E. C. & Costamagna, G. (2011) Single-balloon push-and-pull enteroscopy system: does it work? A single-center, 3-year experience. *Surgical Endoscopy*, 25: 3050-3056.
Not in PICO
- Rogalla, P. (2005) CT of the small intestine. [Review] [6 refs]. *European Radiology*, 15: Suppl-8.
Narrative review
- Salo, M., Collin, P., Kyronpalo, S., Rasmussen, M., Huhtala, H. & Kaukinen, K. (2008) Age, symptoms and upper gastrointestinal malignancy in primary care endoscopy. *Scandinavian Journal of Gastroenterology*, 43: 122-127.
Not in PICO
- Schwartz, G. D. & Barkin, J. S. (2006) Small bowel tumors. [Review] [33 refs]. *Gastrointestinal Endoscopy Clinics of North America*, 16: 267-275.
Narrative review
- Schwartz, G. D. & Barkin, J. S. (2007) Small-bowel tumors detected by wireless capsule endoscopy. *Digestive Diseases & Sciences*, 52: 1026-1030.
Not in PICO
- Shah, I. A., Dolan, W. V., Ramirez, F. C. & Iqbal, J. (1997) Diagnosis of early peri-ampullary carcinoma. *Digestive Surgery*, 14: 323-326.
Narrative review
- Shyung, L. R., Lin, S. C., Shih, S. C., Chang, W. H., Chu, C. H. & Wang, T. E. (2009) Proposed scoring system to determine small bowel mass lesions using capsule endoscopy. *Journal of the Formosan Medical Association*, 108: 533-538.
Not in PICO
- Sidhu, R., McAlindon, M. E., Drew, K., Hardcastle, S., Cameron, I. C. & Sanders, D. S. (2012) Evaluating the role of small-bowel endoscopy in clinical practice: The largest single-centre experience. *European Journal of Gastroenterology and Hepatology*, 24: 513-519.
Not in PICO

- Sokolov, L. K., Zakharov, P. I. & Kandinov, I. A. (1986) Endoscopy during the ambulatory care of patients with multiple polyps of the digestive organs. [Russian]. *Klinicheskaja Meditsina*, 64: 87-90.
Not in PICO
- Spiegel, B. M. R., Farid, M., Van Oijen, M. G. H., Laine, L., Howden, C. W. & Esrailian, E. (2009) Adherence to best practice guidelines in dyspepsia: A survey comparing dyspepsia experts, community gastroenterologists and primary-care providers. *Alimentary Pharmacology and Therapeutics*, 29: 871-881.
Not in PICO
- Steine, S., Stordahl, A., Lunde, O. C., Loken, K. & Laerum, E. (1993) Double-contrast barium enema versus colonoscopy in the diagnosis of neoplastic disorders: aspects of decision-making in general practice. *Family Practice*, 10: 288-291.
Not in PICO
- Stiefelhagen, P. (2007) [Gentle methods for early intestinal cancer diagnosis. Conventional colonoscopy--an obsolete model?]. [German]. *MMW Fortschritte der Medizin*, 149: 18.
Not in PICO
- Storey, R., Gatt, M. & Bradford, I. (2009) Mucosa associated lymphoid tissue lymphoma presenting within a solitary anti-mesenteric dilated segment of ileum: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 3: 6.
Not in PICO
- Stringer, D. A., Cloutier, S., Daneman, A. & Durie, P. (1986) The value of the small bowel enema in children. *Canadian Association of Radiologists Journal*, 37: 13-16.
Not in PICO
- Sturniolo, G. C., Di, L., V, Vettorato, M. G., De, B. M., Lamboglia, F., De, B. M., Bellumat, A., Martines, D. & D'Inca, R. (2006) Small bowel exploration by wireless capsule endoscopy: results from 314 procedures. *American Journal of Medicine*, 119: 341-347.
Not in PICO
- Suzuki, H., Yamada, A., Watabe, H., Kobayashi, Y., Hirata, Y., Yamaji, Y., Yoshida, H. & Koike, K. (2012) Successful treatment of early-stage jejunum adenocarcinoma by endoscopic mucosal resection using double-balloon endoscopy: a case report. *Diagnostic & Therapeutic Endoscopy*, 2012: 521960.
Not in PICO
- Tanaka, K., Toyoda, H., Inoue, H., Hamada, Y., Aoki, M., Kosaka, R., Takamura, M. & Imoto, I. (2007) Depressed-type early duodenal carcinoma (carcinoma in situ) observed by enhanced magnification endoscopy. *Endoscopy*, 39: Suppl-6.
Not in PICO
- Taricco, M. T., Macchia, G., Marra, V. & Temporelli, A. (1990) [Role of ultrasonic diagnosis as a complementary method in contrast radiography of the intestines]. [Italian]. *Radiologia Medica*, 80: 886-888.
Not in PICO
- Terauchi, S., Snowberger, N. & Demarco, D. (2006) Double-balloon endoscopy and Peutz-Jeghers syndrome: a new look at an old disease. *Baylor University Medical Center Proceedings*, 19: 335-337.
Narrative review
- Tirkes, A. T. & Duerinckx, A. J. (2005) Adenocarcinoma of the ileum in Crohn disease. *Abdominal Imaging*, 30: 671-673.
Not in PICO
- Tomba, C., Elli, L., Bardella, M. T., Soncini, M., Contiero, P., Locatelli, M. & Conte, D. (2013) Role of capsule endoscopy and double-balloon enteroscopy in early diagnosis of gastrointestinal malignancies in celiac patients at risk. *Digestive and Liver Disease*, 45: S138.
Not in PICO

- Tomba, C., Elli, L., Bardella, M. T., Soncini, M., Contiero, P., Roncoroni, L., Locatelli, M. & Conte, D. (2014) - Enteroscopy for the early detection of small bowel tumours in at-risk celiac patients. - *Digestive & Liver Disease*, 46: 400-404.
Not in PICO
- Torre-Bravo, A., Dominguez-Perez, A. E., Bermudes-Ruiz, H., Torres-Vargas, S. & Alfaro-Fattel, L. G. (2001) Endoscopic diagnosis of ampulla of Vater tumors. [Spanish]. *Gaceta Medica de Mexico*, 137: 9-14.
Not in PICO
- Triadafilopoulos, G. (2012) Management of lower gastrointestinal bleeding in older adults. *Drugs & Aging*, 29: 707-715.
Narrative review
- Troppmann, M., Lippert, E., Hamer, O. W., Kirchner, G. & Endlicher, E. (2012) Colonic bowel wall thickening: is there a need for endoscopic evaluation? *International Journal of Colorectal Disease*, 27: 601-604.
Not in PICO
- Tsuji, Y., Ohata, K., Umezawa, S., Takeuchi, S., Sekiguchi, M., Ohno, A., Ito, T., Chiba, H., Yamawaki, M., Hisatomi, K., Teratani, T. & Matsushashi, N. (2010) [Diagnosis of small bowel carcinoma by capsule endoscopy]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 37: 1440-1445.
Narrative review
- Uedo, N., Iishi, H., Ishihara, R., Higashino, K. & Takeuchi, Y. (2006) Novel autofluorescence videoendoscopy imaging system for diagnosis of cancers in the digestive tract. *Digestive Endoscopy*, 18: S131-S136.
Narrative review
- Urbain, D., De, L. D., Demedts, I., Louis, E., Dewit, O., Macken, E. & Van, G. A. (2006) Video capsule endoscopy in small-bowel malignancy: a multicenter Belgian study. *Endoscopy*, 38: 408-411.
Not in PICO
- Voderholzer, W. A., Ortner, M., Rogalla, P., Beinholzl, J. & Lochs, H. (2003) Diagnostic yield of wireless capsule enteroscopy in comparison with computed tomography enteroclysis. *Endoscopy*, 35: 1009-1014.
Not in PICO
- Wahnschaffe, U., Ullrich, R., Mayerle, J., Lerch, M. M., Zeitz, M. & Faiss, S. (2009) EUS-guided Trucut needle biopsies as first-line diagnostic method for patients with intestinal or extraintestinal mass lesions. *Surgical Endoscopy*, 23: 2351-2355.
Not in PICO
- Wang, H. Y. & Lin, W. Y. (2006) Jejunal tuberculosis: incidental finding on an FDG-PET scan. *Kaohsiung Journal of Medical Sciences*, 22: 34-38.
Not in PICO
- Waterman, M. & Eliakim, R. (2009) Capsule enteroscopy of the small intestine. [Review] [50 refs]. *Abdominal Imaging*, 34: 452-458.
Narrative review
- Wilkins, T., Jarvis, K. & Patel, J. (2011) Diagnosis and management of Crohn's disease. [Review][Summary for patients in Am Fam Physician. 2011 Dec 15;84(12):1379-80; PMID: 22230272]. *American Family Physician*, 84: 1365-1375.
Narrative review
- Yamamoto, H. (2005) Double balloon endoscopy-cutting edge in the diagnosis and treatment of small bowel disease. [Japanese]. *Endoscopic Forum for Digestive Disease*, 21: 136-142.
Narrative review
- Yang, C. J., Hwang, J. J., Kang, W. Y., Chong, I. W., Wang, T. H., Sheu, C. C., Tsai, J. R. & Huang, M. S. (2006) Gastro-intestinal metastasis of primary lung carcinoma: clinical presentations and

outcome. *Lung Cancer*, 54: 319-323.

Not in PICO

Zinsser, E., Oelzner, P., Bartunek, R. & Adam, G. (2000) [Metastatic small intestine carcinoma--delayed diagnosis due to misinterpretation of diagnostic imaging and symptom confusion due to Bechterew disease and duodenal ulcer]. [German]. *Zeitschrift fur Gastroenterologie*, 38: 495-498.

Not in PICO

GALL BLADDER CANCER

Review question:

What is the risk of gall bladder cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

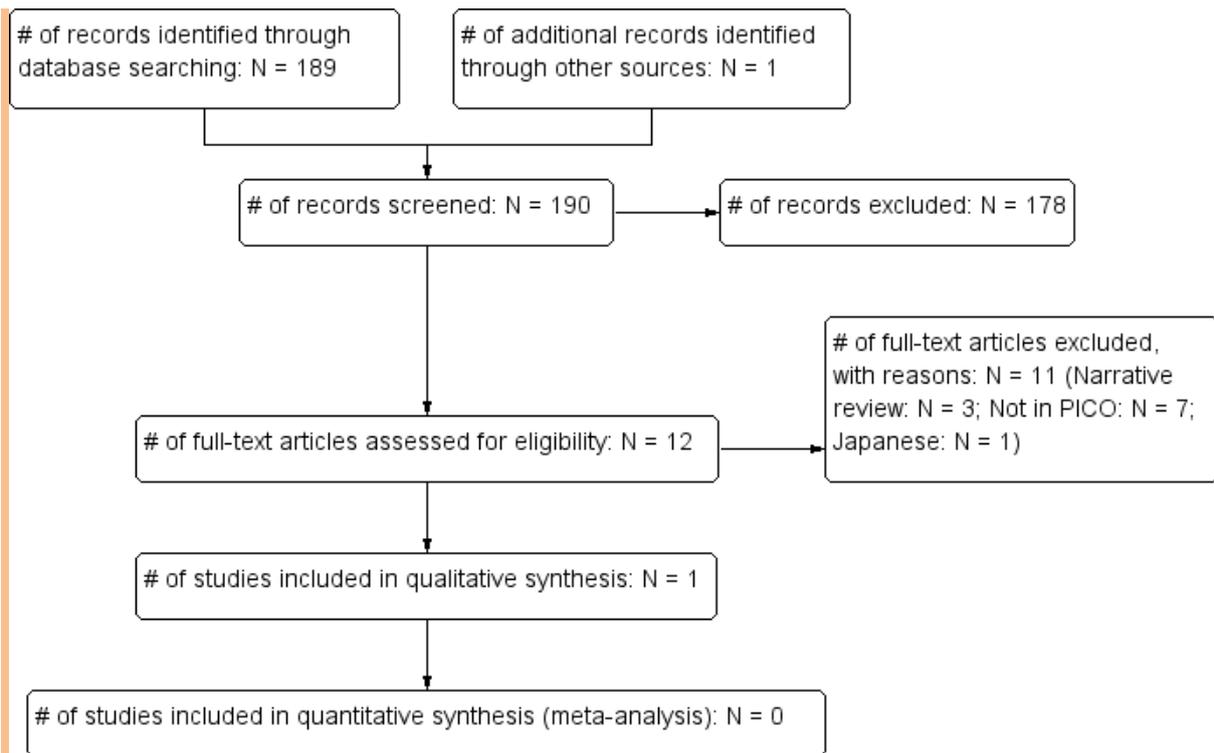
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	691	113	05/11/2012
<i>Premedline</i>	All-2012	24	6	05/11/2012
<i>Embase</i>	All-2012	1010	94	07/11/2012
<i>Cochrane Library</i>	All-2012	160	0	07/11/2012
<i>Psychinfo</i>	All-2012	1	1	05/11/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	75	7	07/11/2012
<i>Biomed Central</i>	All-2012	82	0	07/11/2012

Total References retrieved (after de-duplication): 182

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	11/2012-26/08/2014	35	1	26/08/2014
<i>Premedline</i>	11/2012-26/08/2014	59	2	26/08/2014
<i>Embase</i>	11/2012-26/08/2014	200	4	26/08/2014
<i>Cochrane Library</i>	11/2012-26/08/2014	38	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	11/2012-26/08/2014	20	0	26/08/2014

Total References retrieved (after de-duplication): 7



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included study in the figure below. The main issue to note is that the patient sample may not be directly applicable to the current question.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Hallissey (1990)	+	+	+	+	?	+	+

⊖ High	?	Unclear	+	Low
--------	---	---------	---	-----

Study results

Table 1: Gall bladder cancer: Positive predictive values for gall bladder cancer

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)
Hallissey (1990)	Dyspepsia	All patients	0.04 (0.002-0.3) 1/2585

Evidence statement(s):

The positive predictive value of having gall bladder cancer was 0.04% (for dyspepsia) for patients aged > 40 years (1 study, N = 2585). The included study was associated with 1 applicability concern (see also Table 1).

Evidence tables**Hallissey (1990)**

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Propective consecutive patient series from a group of 10 general practices in England.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia. <u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, England.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia of any degree
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its	Low risk

interpretation have introduced bias?	
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	2659 patients were seen and 2585 attended for investigation
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), cirrhomatosis of unknown primary (7).

References

Included studies

Hallissey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.

Excluded studies (with excl reason)

Acalovschi, M. (2004) Cholangiocarcinoma: risk factors, diagnosis and management. *Romanian journal of internal medicine = Revue roumaine de medecine interne*, 42: 41-58.

Narrative review

Adsay, N. V., Bagci, P., Tajiri, T., Oliva, I., Ohike, N., Balci, S., Gonzalez, R. S., Basturk, O., Jang, K.-T. & Roa, J. C. (2012) Pathologic staging of pancreatic, ampullary, biliary, and gallbladder cancers: Pitfalls and practical limitations of the current AJCC/UICC TNM staging system and opportunities for improvement. *Seminars in Diagnostic Pathology*, 29: 127-141.

Narrative review

Albazaz, R., Patel, C. N., Chowdhury, F. U. & Scarsbrook, A. F. (2013) Clinical impact of FDG PET-CT on management decisions for patients with primary biliary tumours. *Insights Into Imaging*, 4: 691-700.

Not in PICO

Albores-Saavedra, J., Chable-Montero, F., Angeles-Albores, D., Schwartz, A., Klimstra, D. S. & Henson, D. E. (2011) Early gallbladder carcinoma: A clinicopathologic study of 13 cases of intramucosal carcinoma. *American Journal of Clinical Pathology*, 135: 637-642.

Not in PICO

Aldridge, M. C., Gruffaz, F., Castaing, D. & Bismuth, H. (1991) Adenomyomatosis of the gallbladder. A premalignant lesion? *Surgery*, 109: 107-110.

Not in PICO

Barr, L. H. & Wright, F. H. (1984) Carcinoma of the gallbladder. *American Surgeon*, 50: 275-276.

Not in PICO

Bartlett, D. L. (2000) Gallbladder cancer. *Seminars in Surgical Oncology*, 19: 145-155.

Narrative review

- Bartolucci, R., Leo, G., Baselice, P. F., Di, P. R., Angelici, G. & Valle, M. (1989) Carcinoma of the gallbladder. [Italian]. *Chirurgia*, 2: 400-405.
Not in PICO
- Belli, G., Cioffi, L., D'Agostino, A., Limongelli, P., Belli, A., Russo, G. & Fantini, C. (2011) Revision surgery for incidentally detected early gallbladder cancer in laparoscopic era. *Journal of Laparoendoscopic & Advanced Surgical Techniques.Part A*, 21: 531-534.
Not in PICO
- Bismuth, H. & Krissat, J. (1999) Choledochal cystic malignancies. *Annals of Oncology*, 10: Suppl-8.
Narrative review
- Biswas, P. K. (2010) Carcinoma gallbladder. [Review]. *Mymensingh Medical Journal: MMJ*, 19: 477-481.
Narrative review
- Brown, K. M. (2009) Multidisciplinary approach to tumors of the pancreas and biliary tree. [Review] [77 refs]. *Surgical Clinics of North America*, 89: 115-131.
Narrative review
- Burlefinger, R. J. (1992) Early carcinoma of the gallbladder: Macroscopic features and US-findings. [German]. *Endoskopie Heute*, 5: 144-146.
Not in PICO
- Cha, J. M., Kim, M. H., Lee, S. K., Seo, D. W., Lee, S. S., Lee, J. H., Lee, S. G. & Jang, S. J. (2006) Clinicopathological review of 61 patients with early bile duct cancer. *Clinical Oncology (Royal College of Radiologists)*, 18: 669-677.
Not in PICO
- Cha, J. M., Kim, M. H. & Jang, S. J. (2007) Early bile duct cancer. [Review] [53 refs]. *World Journal of Gastroenterology*, 13: 3409-3416.
Narrative review
- Chan, K.-M., Yeh, T.-S., Tseng, J.-H., Liu, N.-J., Jan, Y.-Y. & Chen, M.-F. (2005) Clinicopathological analysis of cystic duct carcinoma. *Hepato-Gastroenterology*, 52: 691-694.
Not in PICO
- Chang, B. J., Kim, S. H., Park, H. Y., Lim, S. W., Kim, J., Lee, K. H., Lee, K. T., Rhee, J. C., Lim, J. H. & Lee, J. K. (2010) Distinguishing xanthogranulomatous cholecystitis from the wall-thickening type of early-stage gallbladder cancer. *Gut & Liver*, 4: 518-523.
Not in PICO
- Chaudhary, A., Dhar, P., Sachdev, A. & Agarwal, A. (1999) Gastric outlet obstruction in carcinoma gall bladder. *Indian Journal of Gastroenterology*, 18: 101-103.
Not in PICO
- Chen, M., Dong, B., Zhu, Q., Li, J., Wang, B., Wang, M., Choiji, K., Sato, Y., Kishimoto, R. & Fujita, N. (1995) A new method for early diagnosis of carcinoma in bile duct-sonography of common bile duct before and after injection of ceosunin. *Chinese Medical Journal*, 108: 355-360.
Not in PICO
- Chen, Y. L., Huang, Z. Q., Zhou, N. X., Zhang, W. Z., Huang, X. Q., Duan, W. D., Liu, R. & Liu, Y. (2007) [Clinical analysis of 110 patients with primary gallbladder carcinoma]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 29: 704-706.
Not in PICO
- Chianakwana, G. U., Okafor, P. I. & Anyanwu, S. N. (2005) Carcinoma of the gallbladder at the Nnamdi Azikiwe University Teaching Hospital--a 5-year retrospective study. *Nigerian Journal of Clinical Practice*, 8: 10-13.
Not in PICO
- Chijiwa, K. & Tanaka, M. (1994) Polypoid lesion of the gallbladder: Indications of carcinoma and outcome after surgery for malignant polypoid lesion. *International Surgery*, 79: 106-109.
Not in PICO

- Chin, K. F., Mohammad, A. A., Khoo, Y. Y. & Krishnasamy, T. (2012) The impact of routine histopathological examination on cholecystectomy specimens from an Asian demographic. *Annals of the Royal College of Surgeons of England*, 94: 165-169.
Not in PICO
- Costi, R., Randone, B., Violi, V., Scatton, O., Sarli, L., Soubrane, O., Dousset, B. & Montariol, T. (2009) Cholecystocolonic fistula: facts and myths. A review of the 231 published cases. [Review] [168 refs]. *Journal of Hepato-Biliary-Pancreatic Surgery*, 16: 8-18.
Not in PICO
- Csendes, A., Alvarez, F., Medina, E., Campos, A., Blanco, C., Guell, M. L. & Jeria, M. (1995) [Prevalence of digestive symptoms in normal adult women and its association with cholelithiasis]. [Spanish]. *Revista Medica de Chile*, 122: 531-536.
Not in PICO (non-symptomatic, randomly selected women for prevalence study)
- Csendes, A., Becerra, M., Rojas, J. & Medina, E. (2000) Number and size of stones in patients with asymptomatic and symptomatic gallstones and gallbladder carcinoma: a prospective study of 592 cases. *Journal of Gastrointestinal Surgery*, 4: 481-485.
Not in PICO
- Cubertafond, P., Gainant, A. & Raymond, J. (1984) [Gallbladder cancer in its early stages: current aspects of diagnosis, prognosis and treatment. Apropos of 30 cases]. [French]. *Chirurgie*, 110: 729-733.
Not in PICO
- Cubertafond, P., Gainant, A. & Raymond, J. (1984) Early stage gallbladder cancer. Update review of diagnosis, prognosis, and treatment. Report on 30 cases. [French]. *Chirurgie - Memoires de l'Academie de Chirurgie*, 110: 729-733.
Not in PICO
- Daines, W. P., Rajagopalan, V., Grossbard, M. L. & Kozuch, P. (2004) Gallbladder and biliary tract carcinoma: A comprehensive update, part 2. *Oncology-New York*, 18: 1049-1059.
Narrative review
- Das, D. K., Tripathi, R. P., Bhambhani, S., Chachra, K. L., Sodhani, P. & Malhotra, V. (1998) Ultrasound-guided fine-needle aspiration cytology diagnosis of gallbladder lesions: a study of 82 cases. *Diagnostic Cytopathology*, 18: 258-264.
Not in PICO
- De Zoysa, M. I., De Silva, S. K. & Illeperuma, A. (2010) Is routine histological examination of gall bladder specimens justifiable? *Ceylon Medical Journal*, 55: 13-16.
Not in PICO
- de, A., X, Roa, I. & Burgos, L. (1999) Gallbladder cancer, management of early tumors. [Review] [29 refs]. *Hepato-Gastroenterology*, 46: 1547-1551.
Narrative review
- de, A., X, Roa, I., Hepp, J., Maluenda, F., Mordojovich, G., Leon, J. & Roa, J. C. (2009) Early gallbladder cancer: is further treatment necessary? *Journal of Surgical Oncology*, 100: 589-593.
Not in PICO
- Diaz, J. A., Tantalean, E. A., Vilela, C., Urtecho, F. A., Angulo, M. H. & Guzman, C. (1996) Primary cancer of the gallbladder. [Spanish]. *Revista de gastroenterologia del Peru : organo oficial de la Sociedad de Gastroenterologia del Peru*, 16: 142-147.
Not in PICO
- Diehl, A. K. (1992) Symptoms of gallstone disease. [Review] [68 refs]. *Baillieres Clinical Gastroenterology*, 6: 635-657.
Narrative review
- Dixit, V. K., Prakash, A., Gupta, A., Pandey, M., Gautam, A., Kumar, M. & Shukla, V. K. (1998) Xanthogranulomatous cholecystitis. *Digestive Diseases & Sciences*, 43: 940-942.
Narrative review

- Donohue, J. H., Stewart, A. K. & Menck, H. R. (1998) The National Cancer Data Base report on carcinoma of the gallbladder, 1989-1995. *Cancer*, 83: 2618-2628.
Not in PICO
- Donohue, J. H. (2001) Present status of the diagnosis and treatment of gallbladder carcinoma. [Review] [40 refs]. *Journal of Hepato-Biliary-Pancreatic Surgery*, 8: 530-534.
Narrative review
- Downing, S. R., Cadogan, K. A., Ortega, G., Oyetunji, T. A., Siram, S. M., Chang, D. C., Ahuja, N., Leffall, L. D., Jr. & Frederick, W. A. (2011) Early-stage gallbladder cancer in the Surveillance, Epidemiology, and End Results database: effect of extended surgical resection. *Archives of Surgery*, 146: 734-738.
Not in PICO
- Dwivedi, M., Misra, S. P. & Misra, V. (2000) Clinical and ultrasonographic findings of carcinoma of gallbladder in Indian patients. *Journal of the Association of Physicians of India*, 48: 192-195.
Not in PICO
- Erdas, E., Licheri, S., Pulix, N., Lai, M. L., Pisano, G., Pomata, M. & Daniele, G. M. (2002) [Adenomyomatosis of the gallbladder. Personal experience and analysis of the literature]. [Italian]. *Chirurgia Italiana*, 54: 673-684.
Not in PICO
- Erkol, B., Oven, B. B., Bayoglu, V., Paker, N., Kochan, K., Ozkara, S., Tilki, M., Surmelioglu, A., Yesil, A. & Gonen, C. (2013) The sensitivity and specificity of DR-70 as a tumor marker for gastrointestinal cancers. *Journal of Clinical Oncology*, 31.
Not in PICO
- Friend, E., Yadegarfar, G., Byrne, C., Johnson, C. D., Sezer, O., Pucciarelli, S., Pereira, S. P., Chie, W. C., Banfield, A., Ramage, J. K. & EORTC Quality of Life Group (2011) Development of a questionnaire (EORTC module) to measure quality of life in patients with cholangiocarcinoma and gallbladder cancer, the EORTC QLQ-BIL21. *British Journal of Cancer*, 104: 587-592.
Not in PICO
- Fuji, T., Amano, H. & Aibe, T. (1983) Early diagnosis of carcinoma of the gallbladder. [Japanese]. *Stomach and Intestine*, 18: 1063-1068.
Not in PICO
- Fujita, R., Hirata, N., Takekuma, Y. & Yamamura, M. (1996) Non surgical approach to obstructive jaundice. [Japanese]. *Endoscopic Forum for Digestive Disease*, 12: 9-13.
Narrative review
- Gabrielli, A., Frulloni, L., Ruffini, M., Bernardoni, L., Castagnini, A., Angelini, G., Benini, L. & Vantini, I. (2011) Involvement of bile duct in autoimmune pancreatitis. ERCP Verona experience. *Digestive and Liver Disease*, 43: S241.
Not in PICO
- Gautam, A., Sood, B. P., Pandey, M., Dixit, V. K., Shukla, R. C., Agrawal, A. K. & Shukla, V. K. (1997) Sonographic morphology of carcinoma of the gallbladder: A review of 173 cases. *Indian Journal of Radiology and Imaging*, 7: 159-163.
Not in PICO
- Ghadimi, B. M., Horstmann, O., Jacobsen, K., Feth, J. & Becker, H. (2002) Delay of diagnosis in pancreatic cancer due to suspected symptomatic cholelithiasis. *Scandinavian Journal of Gastroenterology*, 37: 1437-1439.
Not in PICO
- Ghevariya, V., Ahluwalia, M., Krishnaiah, M. & Anand, S. (2010) Adenocarcinoma of duodenum mimics choledocholithiasis! *American Journal of Gastroenterology*, 105: S241.
Not in PICO
- Gholson, C. F. & Burton, F. R. (1991) Obstructive jaundice: Nonsurgical options for 'surgical' jaundice. *Postgraduate Medicine*, 90: 107-114+116.
Narrative review

- Giang, T. H., Ngoc, T. T. & Hassell, L. A. (2012) Carcinoma involving the gallbladder: a retrospective review of 23 cases - pitfalls in diagnosis of gallbladder carcinoma. *Diagnostic Pathology*, 7: 10.
Not in PICO
- Giatromanolaki, A., Sivridis, E., Simopoulos, C., Polychronidis, A., Gatter, K. C., Harris, A. L. & Koukourakis, M. I. (2006) Hypoxia inducible factors 1alpha and 2alpha are associated with VEGF expression and angiogenesis in gallbladder carcinomas. *Journal of Surgical Oncology*, 94: 242-247.
Not in PICO
- Goh, M. H. & Low, J. K. (2012) Mirizzi syndrome and incidence of gallbladder cancer: A single institution's experience. *HPB*, 14: 375-376.
Not in PICO
- Gomez, F. C., Acea, N. B., Fraguera, M. J., Taboada, F. L., Freire, R. D. & Aguirrezabalaga, G. J. (1995) [Carcinoma in situ of the gallbladder. The prognostic and therapeutic implications]. [Spanish]. *Gastroenterologia y Hepatologia*, 18: 457-459.
Not in PICO
- Gomez, N. A., Leon, C. J. & Monserrate, J. O. (1995) Carcinoma of the gallbladder: A review of 15 patients. [Spanish]. *Oncologia*, 4: 55-60.
Not in PICO
- Goto, A., Ishimine, Y., Hirata, T., Naito, T., Yabana, T., Adachi, T., Kondo, Y. & Kasai, K. (2014) - [Gallbladder Cancer with Elevated Serum a-Fetoprotein, a-Fetoprotein-L3, and Human Chorionic Gonadotropin Levels]. [Japanese]. - *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 41: 1021-1025.
Not in PICO
- Grill, W. (1981) [The prognosis of cancers of the efferent bile ducts]. [German]. *Fortschritte der Medizin*, 99: 1174-1177.
Narrative review
- Gurleyik, G., Gurleyik, E., Ozturk, A. & Unalmiser, S. (2002) Gallbladder carcinoma associated with gallstones. *Acta Chirurgica Belgica*, 102: 203-206.
Not in PICO
- Hamid, F., Yousef, O., Al-Zoubi, R. & Sadeddin, E. (2012) Primary hepatic neuroendocrine tumor. *American Journal of Gastroenterology*, 107: S406.
Not in PICO
- Hasegawa, H., Makuuchi, M. & Yamazaki, S. (1982) The dawn of early detection of biliary tract carcinoma. *Asian Medical Journal*, 25: 655-664.
Narrative review
- Heavey, S. F., Roeland, E. J., Tipps, A. M., Datnow, B. & Sicklick, J. K. (2014) - Rapidly progressive subcutaneous metastases from gallbladder cancer: insight into a rare presentation in gastrointestinal malignancies. - *Journal of Gastrointestinal Oncology*, 5: E58-E64.
Not in PICO
- Hsieh, J. P., Tsao, W. L., Tang, H. S., Hsu, C. T. & Wu, K. L. (1993) Primary carcinoma of the gallbladder: a review of 10 years of experience at Tri-Service General Hospital. *Chung Hua i Hsueh Tsa Chih - Chinese Medical Journal*, 51: 193-199.
Not in PICO
- Huang, J. Q., Bao, X. J. & Lu, X. H. (1993) [The common causes and differential diagnosis of malignant jaundice]. [Chinese]. *Chung-Hua Nei Ko Tsa Chih Chinese Journal of Internal Medicine*, 32: 400-404.
Not in PICO
- Huang, Z. Q., Zhou, N. X., Liu, Y. X., Li, W. H. & Yu, G. (1992) Surgical treatment of hilar bile duct carcinoma. Clinical and pathological studies. *Chinese Medical Journal*, 105: 635-640.
Not in PICO

- Interlandi, A., Andreotti, A. & Chiavilli, S. (1999) [Gallbladder carcinoma. Personal case histories]. [Italian]. *Minerva Chirurgica*, 54: 491-494.
Not in PICO
- Inui, K. (2006) [Biliary tract cancer: present status in early diagnosis and treatment]. [Review] [49 refs] [Japanese]. *Nippon Shokakibyō Gakkai Zasshi - Japanese Journal of Gastroenterology*, 103: 495-500.
Narrative review/not in PICO
- Inui, K., Yoshino, J. & Miyoshi, H. (2011) Diagnosis of gallbladder tumors. [Review]. *Internal Medicine*, 50: 1133-1136.
Not in PICO
- Isayama, H., Sasaki, T., Nakai, Y., Togawa, O., Kogure, H., Sasahira, N., Yashima, Y., Kawakubo, K., Ito, Y., Hirano, K., Tsujino, T., Toda, N., Tada, M., Omata, M. & Koike, K. (2012) Management of malignant gastric outlet obstruction with a modified triple-layer covered metal stent. *Gastrointestinal Endoscopy*, 75: 757-763.
Not in PICO
- Iseki, J., Ushiyama, K. & Beppu, T. (1982) Early carcinoma of the gallbladder. A clinical and pathological study. [Japanese]. *Japanese Journal of Gastroenterology*, 79: 2112-2120.
Not in PICO
- Ishak, G., Ribeiro, F. S., Costa, D. S., Bahia, L. A., Dias, E. M. & Assumpcao, P. P. (2011) Gallbladder cancer: 10 years of experience at an Amazon reference hospital. *Revista do Colegio Brasileiro de Cirurgioes*, 38: 100-104.
Not in PICO
- Ito, Y., Kenmochi, T., Irino, T., Egawa, T., Hayashi, S., Nagashima, A. & Kitagawa, Y. (2012) Clinicopathological feature of extrahepatic cholangiocarcinoma without jaundice: A single-center experience. *Hepato-Gastroenterology*, 59: 1744-1747.
Not in PICO
- Jablonska-Kaszewska, I., Bielawski, W., Bilczuk, B. & Stech-Golian, J. (1984) [Difficulties in the early diagnosis of cancer of the gallbladder]. [Polish]. *Wiadomosci Lekarskie*, 37: 12-20.
Not in PICO
- Joo, I. & Lee, J. M. (2013) Imaging bile duct tumors: Pathologic concepts, classification, and early tumor detection. *Abdominal Imaging*, 38: 1334-1350.
Narrative review
- Juntermanns, B., Kaiser, G. M., Reis, H., Saner, F. H., Radunz, S., Vernadakis, S., Heuer, M., Kuehl, H., Paul, A. & Treckmann, J. (2011) Klatskin-mimicking lesions: still a diagnostic and therapeutic dilemma? *Hepato-Gastroenterology*, 58: 265-269.
Not in PICO
- Juul Nielsen, L. B., Schultz, N. A., Hasselby, J. P. & Wettergren, A. (2013) [Benign gallbladder polyp is a rare cause of haemobilia]. [Danish]. *Ugeskrift for Laeger*, 175: 2117-2118.
Not in PICO
- Kai, K., Ide, T., Masuda, M., Kitahara, K., Miyoshi, A., Miyazaki, K., Noshiro, H. & Tokunaga, O. (2011) Clinicopathologic features of advanced gallbladder cancer associated with adenomyomatosis. *Virchows Archiv*, 459: 573-580.
Not in PICO
- Kamisawa, T., Tu, Y., Egawa, N., Nakajima, H., Horiguchi, S., Tsuruta, K. & Okamoto, A. (2006) Clinicopathologic features of ampullary carcinoma without jaundice. *Journal of Clinical Gastroenterology*, 40: 162-166.
Not in PICO
- Kamisawa, T., Ando, H., Suyama, M., Shimada, M., Morine, Y. & Shimada, H. (2012) Japanese clinical practice guidelines for pancreaticobiliary maljunction. *Journal of Gastroenterology*, 47: 731-759.
Guideline

- Kapoor, A., Kapoor, A. & Mahajan, G. (2011) Differentiating malignant from benign thickening of the gallbladder wall by the use of acoustic radiation force impulse elastography. *Journal of Ultrasound in Medicine*, 30: 1499-1507.
Not in PICO
- Kapoor, V. K., Pradeep, R., Haribhakti, S. P., Sikora, S. S. & Kaushik, S. P. (1996) Early carcinoma of the gallbladder: an elusive disease. *Journal of Surgical Oncology*, 62: 284-287.
Narrative review
- Kasahara, Y., Sonobe, N., Tomiyoshi, H., Imano, M., Nakatani, M., Urata, T., Morishita, A., Ueda, S., Takemoto, M. & Yamada, Y. (1992) Adenomyomatosis of the gallbladder: a clinical survey of 30 surgically treated patients. *Nippon Geka Hokan - Archiv fur Japanische Chirurgie*, 61: 190-198.
Not in PICO
- Kaushik, S. P. (2001) Current perspectives in gallbladder carcinoma. *Journal of Gastroenterology and Hepatology*, 16: 848-854.
Narrative review
- Khan, M. R., Raza, S. A., Ahmad, Z., Naeem, S., Pervez, S., Siddiqui, A. A., Ahmed, M. & Azami, R. (2011) Gallbladder intestinal metaplasia in Pakistani patients with gallstones. *International Journal Of Surgery*, 9: 482-485.
Not in PICO
- Khan, R. A., Wahab, S., Khan, M. A., Siddiqui, S. & Maheshwari, V. (2010) Advanced presentation of gallbladder cancer: epidemioclinicopathological study to evaluate the risk factors and assess the outcome. *JPMA - Journal of the Pakistan Medical Association*, 60: 217-219.
Not in PICO
- Khoo, J. J. & Nurul, A. M. (2008) A clinicopathological study of nine cases of gallbladder carcinoma in 1122 cholecystectomies in Johor, Malaysia. *Malaysian Journal of Pathology*, 30: 21-26.
Not in PICO
- Kianmanesh, R., Scaringi, S., Castel, B., Flamant, Y. & Msika, S. (2007) [Precancerous lesions of the gallbladder]. [Review] [99 refs] [French][Erratum appears in J Chir (Paris). 2007 Nov-Dec;144(6):566]. *Journal de Chirurgie*, 144: 278-286.
Narrative review
- Kijima, H., Ishihara, N., Iwafuchi, M. & Watanabe, H. (1986) [Characteristics of early carcinoma of the gallbladder--clinico-pathological study]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 32: 1240-1245.
Not in PICO
- Kijima, H., Watanabe, H., Iwafuchi, M. & Ishihara, N. (1989) Histogenesis of gallbladder carcinoma from investigation of early carcinoma and microcarcinoma. *Acta Pathologica Japonica*, 39: 235-244.
Not in PICO
- Kimura, W., Shimada, H., Kuroda, A. & Morioka, Y. (1989) Carcinoma of the gallbladder and extrahepatic bile duct in autopsy cases of the aged, with special reference to its relationship to gallstones. *American Journal of Gastroenterology*, 84: 386-390.
Not in PICO
- Kitagawa, H., Nagakawa, T., Ueno, K., Ohta, T., Kayahara, M. & Miyazaki, I. (1996) Early carcinoma of the biliary tract. [Japanese]. *Nippon rinsho*, Japanese: 1385-1389.
Narrative review
- Kobayashi, T. & Kawakubo, T. (1994) Prospective investigation of tumor markers and risk assessment in early cancer screening. *Cancer*, 73: 1946-1953.
Not in PICO
- Koga, A., Yamauchi, S., Izumi, Y. & Hamanaka, N. (1985) Ultrasonographic detection of early and curable carcinoma of the gallbladder. *British Journal of Surgery*, 72: 728-730.
Not in PICO

- Koga, A., Yamauchi, S. & Nakayama, F. (1985) Primary carcinoma of the gallbladder. *American Surgeon*, 51: 529-533.
Not in PICO
- Kositchaiwat, S., Kositchaiwat, C., Kanchanapitak, A., Lerkpatanakit, P. & Tinnakornrasamee, C. (2000) Diagnostic value of endoscopic transampullary biopsy for malignant bile duct stricture. *Journal of the Medical Association of Thailand*, 83: 992-998.
Not in PICO
- Kumar, S., Masood, N., Shaikh, A. J., Valimhammad, A. T., Haider, G., Lal, A. & Niamatullah, N. (2009) Clinical Presentation and Outcomes of Patients with Biliary Malignancies: the Aga Khan University Experience. *Asian Pacific Journal of Cancer Prevention*, 10: 463-466.
Not in PICO
- Lai, C. H. & Lau, W. Y. (2008) Gallbladder cancer--a comprehensive review. [Review] [143 refs]. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 6: 101-110.
Not in PICO
- Larsen, A. C., Dabrowski, T., Fisker, R. V., Kristensen, S. R., Moller, B. K. & Thorlacius-Ussing, O. (2012) Venous thromboembolism and haemostatic disturbances in patients with upper gastrointestinal cancer. *Thrombosis Research*, 129: S165.
Not in PICO
- Lee, K. F., Wong, J., Li, J. C. & Lai, P. B. (2004) Polypoid lesions of the gallbladder. [Review] [30 refs]. *American Journal of Surgery*, 188: 186-190.
Not in PICO
- Li, W. H. (1993) Carcinoma of the hilar bile duct: a clinical and pathological study. [Chinese]. *Zhonghua wai ke za zhi [Chinese journal of surgery]*, 31: 536-538.
Not in PICO
- Lim, E. & Rosenthal, M. A. (2007) Diagnosing cancer: Changing patterns of care. *Internal Medicine Journal*, 37: 124-126.
Not in PICO
- Lim, J. H., Jang, K. T., Choi, D., Lee, W. J. & Lim, H. K. (2006) Early bile duct carcinoma: comparison of imaging features with pathologic findings. *Radiology*, 238: 542-548.
Not in PICO
- Lim, K. S., Peters, C. C., Kow, A. & Tan, C. H. (2012) The varying faces of gall bladder carcinoma: pictorial essay. [Review]. *Acta Radiologica*, 53: 494-500.
Narrative review
- Lin, W. R., Lin, D. Y., Tai, D. I., Hsieh, S. Y., Lin, C. Y., Sheen, I. S. & Chiu, C. T. (2008) Prevalence of and risk factors for gallbladder polyps detected by ultrasonography among healthy Chinese: analysis of 34 669 cases. *Journal of Gastroenterology & Hepatology*, 23: 965-969.
Not in PICO
- Lorenzo-Zuniga, V., Moreno, D. V., V, Domenech, E. & Boix, J. (2009) [Diagnosis and treatment of ampullary tumors]. [Review] [57 refs] [Spanish]. *Gastroenterologia y Hepatologia*, 32: 101-108.
Narrative review
- Lubashev, I., Abdulaev, R. A., Bagaudinov, K. G., Saidov, S. S., Ratnikov, V. A. & Udalov, I. (2006) [The early diagnosis of gallbladder polypiform neoplasm in the flying staff]. [Russian]. *Voenno-Meditsinskii Zhurnal*, 327: 65-68.
Russian, no English abstract. Probably not in PICO based on title.
- Matos, A. S., Baptista, H. N., Pinheiro, C. & Martinho, F. (2010) [Gallbladder polyps: how should they be treated and when?]. [Review]. *Revista da Associacao Medica Brasileira*, 56: 318-321.
Not in PICO
- Mazer, L. M., Losada, H. F., Chaudhry, R. M., Velazquez-Ramirez, G. A., Donohue, J. H., Kooby, D. A., Nagorney, D. M., Adsay, N. V. & Sarmiento, J. M. (2012) Tumor characteristics and survival analysis of incidental versus suspected gallbladder carcinoma. *Journal of Gastrointestinal Surgery*,

16: 1311-1317.

Not in PICO

Meara, R. S., Jhala, D., Eloubeidi, M. A., Eltoun, I., Chhieng, D. C., Crowe, D. R., Varadarajulu, S. & Jhala, N. (2006) Endoscopic ultrasound-guided FNA biopsy of bile duct and gallbladder: analysis of 53 cases. *Cytopathology*, 17: 42-49.

Not in PICO

Miller, G. & Jarnagin, W. R. (2008) Gallbladder carcinoma. [Review] [55 refs]. *European Journal of Surgical Oncology*, 34: 306-312.

Narrative review

Misra, S., Chaturvedi, A., Misra, N. C. & Sharma, I. D. (2003) Carcinoma of the gallbladder. [Review] [79 refs]. *Lancet Oncology*, 4: 167-176.

Narrative review

Miyakawa, S., Ishihara, S., Takada, T., Miyazaki, M., Tsukada, K., Nagino, M., Kondo, S., Furuse, J., Saito, H., Tsuyuguchi, T., Kimura, F., Yoshitomi, H., Nozawa, S., Yoshida, M., Wada, K., Amano, H. & Miura, F. (2008) Flowcharts for the management of biliary tract and ampullary carcinomas. *Journal of Hepato-Biliary-Pancreatic Surgery*, 15: 7-14.

Narrative review

Miyazaki, M., Takada, T., Miyakawa, S., Tsukada, K., Nagino, M., Kondo, S., Furuse, J., Saito, H., Tsuyuguchi, T., Chijiwa, K., Kimura, F., Yoshitomi, H., Nozawa, S., Yoshida, M., Wada, K., Amano, H. & Miura, F. (2008) Risk factors for biliary tract and ampullary carcinomas and prophylactic surgery for these factors. *Journal of Hepato-Biliary-Pancreatic Surgery*, 15: 15-24.

Narrative review

Mizumoto, R., Ogura, Y. & Matsuda, S. (1988) [Clinical characteristics and imaging diagnosis of early cancer in the hepatobiliary and pancreatic region]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1342-1348.

Narrative review

Mizumoto, R., Ogura, Y. & Kusuda, T. (1993) Definition and diagnosis of early cancer of the biliary tract. *Hepato-Gastroenterology*, 40: 69-77.

Narrative review

Moore, S. & Grossman, E. (2010) A case of symptomatic hypercalcemia associated with primary cholangiocarcinoma. *Journal of General Internal Medicine*, 25: S477.

Not in PICO

Morera Ocon, F. J., Ballestin, V. J., Ripoll, O. F., Landete, M. F., Garcia-Granero, X. M., Millan, T. J., Tursi, R. L. & Bernal Sprekelsen, J. C. (2009) [Gallbladder cancer in a regional hospital]. [Spanish]. *Cirugia Espanola*, 86: 219-223.

Not in PICO

Mouzas, I. A., Skordilis, P., Frangiadakis, N., Leondidis, C., Alexandrakis, G., Potamianos, S., Kouroumalis, E. & Manousos, O. N. (1999) Carcinoma of the ampulla of Vater in Crete. A clinical and ERCP registry over eight years. *Anticancer Research*, 19: 4501-4505.

Not in PICO

Murata, I., Makiyama, K., Funatsu, S., Kubo, K., Mizuta, Y., Nishihata, S., Imanishi, T., Hara, K., Nakamura, N. & Murase, K. (1988) A study involving early carcinomas of the gall bladder. [Japanese]. *Gan no rinsho*, Japan: 867-874.

Not in PICO

Nagashima, H., Watanabe, A. & Hayashi, S. (1982) Primary carcinoma of the gallbladder and the extrahepatic bile duct. *Gastroenterologia Japonica*, 17: 246-253.

Not in PICO

Nesanelis, D., Charpentier, J., Kheder, J. & Wassef, W. (2012) Primary gallbladder carcinoma in a patient with ulcerative colitis and primary sclerosing cholangitis (PSC). *American Journal of Gastroenterology*, 107: S79.

Not in PICO

- Noorullah, O., Wadsworth, C. A., Brougham, K., Lekharaju, V. P., Hood, S. V., Stern, N., Kaltsidis, C., Terlizzo, M. & Sturgess, R. (2013) A systematic approach to standard endoscopic sampling of bile duct strictures is highly accurate in the diagnosis of peri-hilar cholangiocarcinoma. A single UK tertiary centre experience. *Gastrointestinal Endoscopy*, 77: AB304.
Not in PICO
- Ohta, T., Nagakawa, T. & Miyazaki, I. (1989) [Definition, diagnosis and treatment of early carcinoma of the biliary tract]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 47: 1130-1134.
Japanese (no English abstract).
- Okaniwa, S., Fujita, N., Noda, Y., Kobayashi, G., Kimura, K., Yago, A., Mochizuki, F., Yamazaki, T. & Sawai, T. (1996) [A clinico-pathological study of early gallbladder carcinoma]. [Japanese]. *Nippon Shokakibyō Gakkai Zasshi - Japanese Journal of Gastroenterology*, 93: 628-633.
Not in PICO
- Ono, S., Fumino, S., Shimadera, S. & Iwai, N. (2010) Long-term outcomes after hepaticojejunostomy for choledochal cyst: a 10- to 27-year follow-up. *Journal of Pediatric Surgery*, 45: 376-378.
Not in PICO
- Palaniappan, K., Narashiman, G., Shanmugam, V., Perumalla, R., Reddy, S., Cherian, T., Kaliamoorthy, I., Vij, M. & Rela, M. (2014) Neuroendocrine tumors of gallbladder & extra hepatic biliary tract. *HPB*, 16: 331.
Not in PICO
- Park, J. Y., Hong, S. P., Kim, Y. J., Kim, H. J., Kim, H. M., Cho, J. H., Park, S. W., Song, S. Y., Chung, J. B. & Bang, S. (2009) Long-term follow up of gallbladder polyps. *Journal of Gastroenterology & Hepatology*, 24: 219-222.
Not in PICO
- Patel, S., Roa, J. C., Tapia, O., Dursun, N., Bagci, P., Basturk, O., Cakir, A., Losada, H., Sarmiento, J. & Adsay, V. (2011) Hyalinizing cholecystitis and associated carcinomas: clinicopathologic analysis of a distinctive variant of cholecystitis with porcelain-like features and accompanying diagnostically challenging carcinomas. *American Journal of Surgical Pathology*, 35: 1104-1113.
Not in PICO
- Potente, F., Ghiron, U., Caramia, M., Seglie, E., Fava, F. & Rolfo, F. (1994) [Gallbladder carcinoma. Our experience]. [Italian]. *Minerva Chirurgica*, 49: 787-790.
Not in PICO
- Renard, P., Boutron, M. C., Faivre, J., Milan, C., Bedenne, L., Hillon, P. & Klepping, C. (1987) Biliary tract cancers in Cote-d'Or (France): incidence and natural history. *Journal of Epidemiology & Community Health*, 41: 344-348.
Not in PICO
- Riener, M. O. (2011) [Diagnosis of tumours of the liver and the biliary tract: new tissue and serum markers]. [Review] [German]. *Pathologe*, 32: Suppl-9.
Narrative review
- Rizwan, K. M., Ahsan, R. S., Ahmad, Z., Naeem, S., Pervez, S., Siddiqui, A. A., Ahmed, M. & Azami, R. (2011) Gallbladder intestinal metaplasia in Pakistani patients with gallstones. *International Journal Of Surgery*, 9: 482-485.
Not in PICO
- Roa, I., Araya, J. C., Villaseca, M., Roa, J., de, A., X & Ibacache, G. (1999) Gallbladder cancer in a high risk area: morphological features and spread patterns. *Hepato-Gastroenterology*, 46: 1540-1546.
Not in PICO
- Roa, I., de, A., X, Araya, J. C., Villaseca, M., Roa, J. & Guzman, P. (2001) [Incipient gallbladder carcinoma. Clinical and pathological study and prognosis in 196 cases]. [Spanish]. *Revista Medica de Chile*, 129: 1113-1120.
Not in PICO

- Roa, I., de, A., X, Roa, J., Araya, J. C., Villaseca, M., Guzman, P. & Burgos, L. (2002) [Is gallbladder cancer a disease with bad prognosis?]. [Spanish]. *Revista Medica de Chile*, 130: 1295-1302.
Narrative review
- Roa, I., de, A., X, Araya, J. C., Villaseca, M., Roa, J., Gilda, I. T., Burgos, L. & Munoz, S. (2002) [Morphological prognostic elements in gallbladder cancer]. [Spanish]. *Revista Medica de Chile*, 130: 387-395.
Not in PICO
- Roa, I., de, A., X, Roa, J., Araya, J. C., Villaseca, M., Guzman, P. & Burgos, L. (2002) Is gallbladder cancer a disease with bad prognosis?. [Spanish]. *Revista Medica de Chile*, 130: 1295-1302.
Narrative review
- Roa, I., de, A., X, Araya, J. C. & Roa, J. (2006) Preneoplastic lesions in gallbladder cancer. [Review] [86 refs]. *Journal of Surgical Oncology*, 93: 615-623.
Narrative review/Not in PICO
- Ruys, A., Heuts, S., Rauws, E., Busch, O., Gouma, D. & Van, G. T. (2012) The impact of delay in treatment of hilar cholangiocarcinoma on resectability and survival. *HPB*, 14: 128.
Not in PICO
- Ruys, A. T., Heuts, S. G., Rauws, E. A., Busch, O. R. C., Gouma, D. J. & van Gulik, T. M. (2014) Delay in surgical treatment of patients with hilar cholangiocarcinoma: Does time impact outcomes? *HPB*, 16: 469-474.
Not in PICO
- Ryu, J., Ahn, D., Yoon, W., Kim, Y. & Yoon, Y. (2010) Clinicopathologic features and prognosis of early bile duct cancer. *Internal Medicine Journal*, 40: 159.
Not in PICO
- Sakellaridis, T., Mathioulakis, S. & Antiochos, C. (2005) Synchronous early primary adenocarcinoma of both rectum and gallbladder. Report of a case. *International Seminars in Surgical Oncology*, 2: 19.
Not in PICO
- Samad, A. (2005) Gall bladder carcinoma in patients undergoing cholecystectomy for cholelithiasis. *JPMA - Journal of the Pakistan Medical Association*, 55: 497-499.
Not in PICO
- Sarkut, P., Kilicturgay, S., Ozer, A., Ozturk, E. & Yilmazlar, T. (2013) The incidence of malignancy in gallbladder polyps: How useful is ultrasound findings? *European Surgical Research*, 50: 76.
Not in PICO
- Sato, T., Koyama, K., Yamauchi, H. & Matsuno, S. (1981) Early carcinoma of the gallbladder. *Gastroenterologia Japonica*, 16: 459-464.
Not in PICO
- Sautereau, D., Sava, P., Dupuy, J. F., Cessot, F., Cubertafond, P., Claude, R. & Pillegand, B. (1989) Carcinoma of the biliary tract and long common channel. [French]. *Gastroenterologie Clinique et Biologique*, 13: 298-301.
Not in PICO
- Secchi, M. A., Rossi, L., Quadrelli, L., Cantaberta, M., Carossi, I. & Mateljan, E. (2014) Malignant periampullary tumors. *HPB*, 16: 617.
Not in PICO
- Sen'ko, V. P., Kharitonov, V. N. & Solodnikova, L. D. (1984) Malignant tumors of the gallbladder. [Russian]. *Vestnik khirurgii imeni I*, 1: 46-49.
Not in PICO
- Shi, J. S., Wang, J. S., Liu, G., Yu, Y. L., Lu, Y., Jiao, X. Y., Yang, Y. J., Li, G. C. & Han, Y. (2002) Early diagnosis of primary gallbladder carcinoma. *Hepatobiliary & Pancreatic Diseases International*, 1: 273-275.
Not in PICO

- Shirai, Y., Yoshida, K., Tsukada, K., Muto, T. & Watanabe, H. (1992) Early carcinoma of the gallbladder. *European Journal of Surgery*, 158: 545-548.
Not in PICO
- Siddiqui, A. A., Mehendiratta, V., Jackson, W. E., Loren, D. E., Kowalski, T. E. & Eloubeidi, M. A. (2012) SpyGlass peroral cholangioscopy and cholangioscopic forceps biopsy for the diagnosis of extrahepatic cholangiocarcinoma after negative ERCP brush cytology and negative EUS-guided FNA results. *Gastrointestinal Endoscopy*, 75: AB390.
Not in PICO
- Sirishinha, S. (1989) Tumor markers for early diagnosis of cholangiocarcinoma. *Asian Pacific Journal of Allergy and Immunology*, 7: 1-3.
Narrative review
- Slaar, A., Eshuis, W. J., van der Gaag, N. A., Nio, C. Y., Busch, O. R., van Gulik, T. M., Reitsma, J. B. & Gouma, D. J. (2011) Predicting distant metastasis in patients with suspected pancreatic and periampullary tumors for selective use of staging laparoscopy. *World Journal of Surgery*, 35: 2528-2534.
Not in PICO
- Smok, G., Bentjerodt, R. & Csendes, A. (1992) [Benign polypoid lesions of the gallbladder. Their relation to gallbladder adenocarcinoma]. [Spanish]. *Revista Medica de Chile*, 120: 31-35.
Not in PICO
- Sokolowski, J., Placzkowski, J., Karon, J. & Sowier, J. (1990) Our experience with surgical treatment of primary cancer of the gallbladder. [Polish]. *Polski tygodnik lekarski (Warsaw, Poland : 1960)*, 45: 709-711.
Not in PICO
- Sowula, A. & Fryc, B. (2001) [Gallbladder carcinoma detected accidentally by histopathologic examination]. [Polish]. *Wiadomosci Lekarskie*, 54: 51-55.
Not in PICO
- Spisni, R., Nervi, M., Lijoi, C., Matronola, M., Della, G. C. & Caldarelli, G. F. (1989) [Primary carcinoma of the gallbladder]. [Italian]. *Minerva Chirurgica*, 44: 991-993.
Not in PICO
- Stefanovic, D., Novakovic, R., Perisic-Savic, M., Djordjevic, Z., Zivanovic, M. & Stajic, S. (1993) The evaluation of tumor markers levels in determination of surgical procedure in patients with gallbladder carcinoma. *Medicinski Pregled*, 46: 58-59.
Not in PICO
- Stender, S., Frikke-Schmidt, R., Nordestgaard, B. G. & Tybjaerg-Hansen, A. (2011) Sterol transporter adenosine triphosphate-binding cassette transporter G8, gallstones, and biliary cancer in 62,000 individuals from the general population. *Hepatology*, 53: 640-648.
Not in PICO
- Stewart, C. J., Mills, P. R., Carter, R., O'Donohue, J., Fullarton, G., Imrie, C. W. & Murray, W. R. (2001) Brush cytology in the assessment of pancreatico-biliary strictures: a review of 406 cases. *Journal of Clinical Pathology*, 54: 449-455.
Not in PICO
- Sugiyama, M., Atomi, Y., Kuroda, A. & Muto, T. (1997) Bile duct carcinoma without jaundice: clues to early diagnosis. *Hepato-Gastroenterology*, 44: 1477-1483.
Not in PICO
- Takemoto, T. & Fuji, T. (1982) Definition and diagnosis of early cancer of the biliary tract from the clinical viewpoint. [Japanese]. *Stomach and Intestine*, 17: 613-618.
Not in PICO
- Tan, Y., Ma, S. Y., Wang, F. Q., Meng, H. P., Mei, C., Liu, A. & Wu, H. R. (2011) Proteomic-based analysis for identification of potential serum biomarkers in gallbladder cancer. *Oncology Reports*, 26: 853-859.
Not in PICO

- Tanaka, K., Nishimura, A., Yamada, K., Ishibe, R., Ishizaki, N., Yoshimine, M., Hamada, N. & Taira, A. (1993) Cancer of the gallbladder associated with anomalous junction of the pancreatobiliary duct system without bile duct dilatation. *British Journal of Surgery*, 80: 622-624.
Not in PICO
- Tanaka, K. & Kida, M. (2009) Role of endoscopy in screening of early pancreatic cancer and bile duct cancer. [Review] [7 refs]. *Digestive Endoscopy*, 21: Suppl-S100.
Narrative review
- Taner, C. B., Nagorney, D. M. & Donohue, J. H. (1989) Surgical treatment of gallbladder cancer. *Journal of Gastrointestinal Surgery*, 8: 83-89.
Not in PICO
- Taylor, A., Stapley, S. & Hamilton, W. (2012) Jaundice in primary care: a cohort study of adults aged >45 years using electronic medical records. *Family Practice*, 29: 416-420.
Not in PICO (but use for pancreatic)
- Tazuma, S. & Kajiyama, G. (2001) Carcinogenesis of malignant lesions of the gall bladder. The impact of chronic inflammation and gallstones. [Review] [45 refs]. *Langenbecks Archives of Surgery*, 386: 224-229.
Narrative review
- Tessler, D. A., Catanzaro, A., Velanovich, V., Havstad, S. & Goel, S. (2006) Predictors of cancer in patients with suspected pancreatic malignancy without a tissue diagnosis. *American Journal of Surgery*, 191: 191-197.
Not in PICO
- Thompson, J. S., Murayama, K. M., Edney, J. A. & Rikkers, L. F. (573) Pancreaticoduodenectomy for suspected but unproven malignancy. *American Journal of Surgery*, 168: 571-573.
Not in PICO
- Tsankov, N. (1990) The diagnosis and treatment of cancer of the papilla of Vater. [Bulgarian]. *Khirurgiia*, 43: 42-44.
Not in PICO/narrative review
- Tsuchiya, Y. (1991) Early carcinoma of the gallbladder: macroscopic features and US findings. *Radiology*, 179: 171-175.
Not in PICO
- Tsukada, K., Takada, T., Miyazaki, M., Miyakawa, S., Nagino, M., Kondo, S., Furuse, J., Saito, H., Tsuyuguchi, T., Kimura, F., Yoshitomi, H., Nozawa, S., Yoshida, M., Wada, K., Amano, H., Miura, F., Japanese Association of Biliary Surgery, Japanese Society of Hepato-Biliary-Pancreatic Surgery & Japan Society of Clinical Oncology (2008) Diagnosis of biliary tract and ampullary carcinomas. *Journal of Hepato-Biliary-Pancreatic Surgery*, 15: 31-40.
Narrative review
- Tsunoda, T., Eto, T., Koga, M., Tomioka, T., Moroshima, K., Yamaguchi, T., Izawa, K. & Tsuchiya, R. (1989) Early carcinoma of the extrahepatic bile duct. *Japanese Journal of Surgery*, 19: 691-698.
Not in PICO
- Uttaravichien, T. & Buddhisawasdi, V. (1990) Experience of non-jaundiced cholangiocarcinoma. *Hepato-Gastroenterology*, 37: 608-611.
Not in PICO
- Vallilengua, C., Otero, J. C. R., Proske, S. A. & Celoria, G. C. (1995) Imprint cytology of the gallbladder mucosa: Its use in diagnosing macroscopically inapparent carcinoma. *Acta Cytologica*, 39: 19-22.
Not in PICO
- van Leeuwen, D. J., Verbeek, P. C., Smits, N. J. & Gonzalez, G. D. (1990) Guideline in (suspected) malignant obstruction of the proximal bile ducts. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 134: 2524-2529.
Guideline

- Wacha, H. & Ungeheuer, E. (1987) [Symptomless gallstone disease--when to treat surgically?]. [Review] [22 refs] [German]. *Zentralblatt fur Chirurgie*, 112: 843-848.
Narrative review
- Wacha, W. & Ungeheuer, E. (1987) Silent gallstone disease - Timing of surgery. [German]. *Zentralblatt fur Chirurgie*, 112: 843-848.
Narrative review
- Wakai, T., Ajioka, Y., Nagino, N., Yamaguchi, N., Shirai, Y. & Hatakeyama, K. (2012) Morphological features of early gallbladder carcinoma. *Hepato-Gastroenterology*, 59: 1013-1017.
Not in PICO
- Wang, B. S., Qin, J., Deng, J., Zhang, B. H., Han, T. Q., Shen, M. C., Rashid, A., Hsing, A. W. & Gao, Y. T. (2005) A survey on the diagnosis and treatment of biliary tract cancers in Shanghai. [Chinese]. *Zhonghua wai ke za zhi [Chinese journal of surgery]*, 43: 455-459.
Not in PICO
- Watanabe, H., Yamagiwa, I. & Iwashita, A. (1982) Definition and diagnosis of early carcinoma of the biliary tract. From the pathological viewpoint. [Japanese]. *Stomach and Intestine*, 17: 608-612.
Not in PICO
- Watanabe, H., Taguchi, Y. & Ajioka, Y. (1986) Comparative morphological study on early carcinoma of the stomach, large intestine and gallbladder. [Japanese]. *Stomach and Intestine*, 21: 57-63.
Not in PICO
- Weilert, F., Bhat, Y. M., Binmoeller, K. F., Kane, S., Jaffee, I. M., Cameron, R., Hashimoto, Y. & Shah, J. N. (2013) EUS-FNA is superior to ERCP tissue sampling in suspected malignant biliary obstruction-direct comparison in single session. *Journal of Gastroenterology and Hepatology*, 28: 51.
Not in PICO
- Weilert, F., Bhat, Y. M., Binmoeller, K., Kane, S., Jaffee, I. M., Cameron, R. G., Hashimoto, Y. & Shah, J. N. (2013) EUS-FNA is superior to ERCP tissue sampling in suspected malignant biliary obstruction. *Gastrointestinal Endoscopy*, 77: AB423.
Not in PICO
- Wernberg, J. A. & Lucarelli, D. D. (2014) - Gallbladder cancer. [Review]. - *Surgical Clinics of North America*, 94: 343-360.
Narrative review
- Wernberg, J. A. & Lucarelli, D. D. (2014) Gallbladder cancer. *Surgical Clinics of North America*, 94: 343-360.
Duplicate
- Wohlauer, M. V., McManus, M. C., Brauer, B., Hedges, J. & Gajdos, C. (2012) Synchronous presentation of ampullary adenocarcinoma and common bile duct cancer: report of a case and review of literature. *Jop: Journal of the Pancreas [Electronic Resource]*, 13: 536-539.
Not in PICO
- Xiaodong, H., Yi, X., Chaoji, Z., Zhenhuan, Z. & Jianxi, Z. (2000) Overview for the diagnosis and treatment of gallbladder carcinoma. *Chinese Medical Sciences Journal*, 15: 115-118.
Not in PICO
- Xie, J. X. (1989) Current status and prospects of the early diagnosis of gallbladder cancer. [Chinese]. *Zhonghua fang she xue za zhi Chinese journal of radiology*, 23: 371-373.
Narrative review
- Yamagiwa, H. & Yoshimura, H. (1986) [Clinico-pathological studies of gallbladder diseases-6 early carcinoma of the gallbladder]. [Japanese]. *Rinsho Byori - Japanese Journal of Clinical Pathology*, 34: 1437-1441.
Not in PICO
- Yamagiwa, H. (1989) Mucosal dysplasia of gallbladder: Isolated and adjacent lesions to carcinoma. *Japanese Journal of Cancer Research*, 80: 238-243.
Not in PICO

Yamaguchi, K. & Enjoji, M. (1988) Carcinoma of the gallbladder. A clinicopathology of 103 patients and a newly proposed staging. *Cancer*, 62: 1425-1432.

Not in PICO

Yamaguchi, K. (1992) Early bile duct carcinoma. *Australian & New Zealand Journal of Surgery*, 62: 525-529.

Not in PICO

Yang, Z., Yang, Z., Xiong, L., Huang, S., Liu, J., Yang, L. & Miao, X. (2011) Expression of VHL and HIF-1alpha and Their Clinicopathologic Significance in Benign and Malignant Lesions of the Gallbladder. *Applied Immunohistochemistry & Molecular Morphology*, 19: 534-539.

Not in PICO

Yeh, C. N., Jan, Y. Y., Chao, T. C. & Chen, M. F. (2001) Laparoscopic cholecystectomy for polypoid lesions of the gallbladder: a clinicopathologic study. *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques*, 11: 176-181.

Not in PICO

Yoshioka, M., Watanabe, G., Uchinami, H., Miyazawa, H., Ise, N., Abe, Y., Nakagawa, Y., Kudoh, K., Takahashi, K., Ishiyama, K., Hashimoto, M., Nakamura, A. & Yamamoto, Y. (2013) Differential diagnosis of inflammatory diseases in gallbladder lesions using diffusion weighted MRI. *European Surgical Research*, 50: 191.

Not in PICO

Youssef, F., Khan, A. W. & Davidson, B. R. (2003) Disseminated bony metastases following incidental gallbladder cancer detected after laparoscopic cholecystectomy. *HPB*, 5: 258-260.

Not in PICO

Zulke, C. & Schlitt, H. J. (2007) [Incidentalomas of the liver and gallbladder. Evaluation and therapeutic procedure]. [German]. *Chirurg*, 78: 698-712.

Narrative review

Review question:

Which investigations of symptoms of suspected gall bladder cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	348	100	08/05/2013
<i>Premedline</i>	1980-2013	19	4	08/05/2013
<i>Embase</i>	1980-2013	509	69	09/05/2013
<i>Cochrane Library</i>	1980-2013	31	0	09/05/2013
<i>Psychinfo</i>	1980-2013	0	0	09/05/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	21	5	09/05/2013

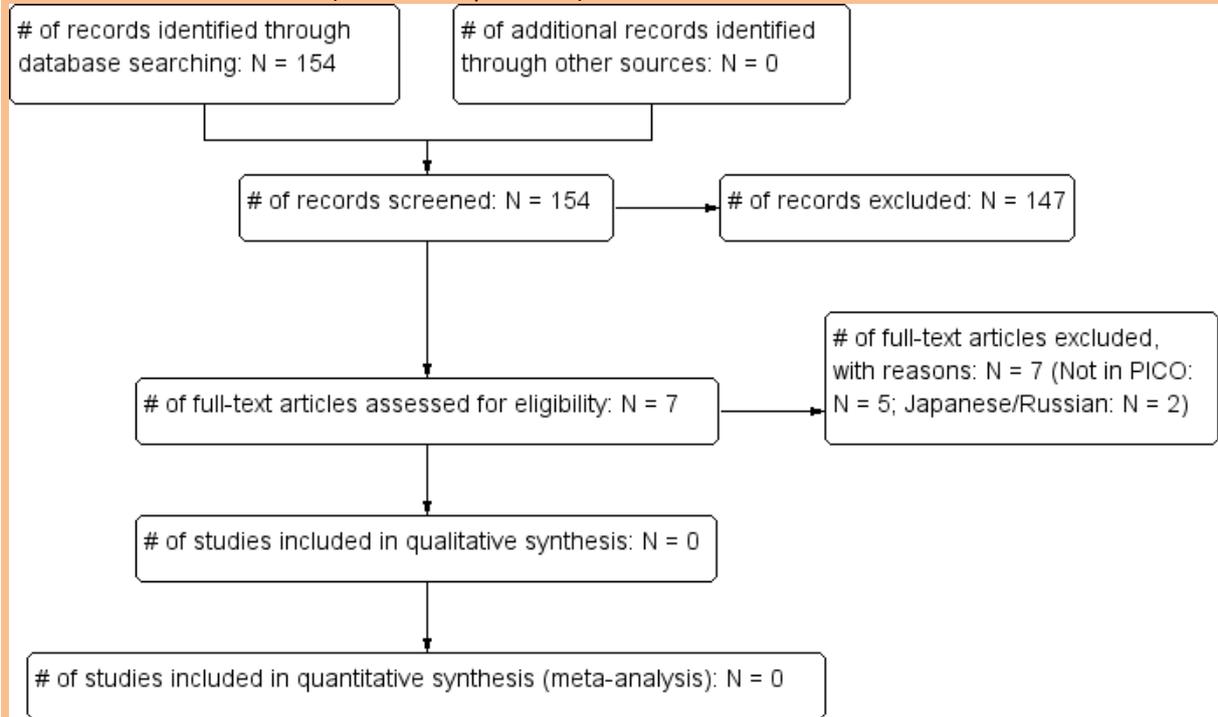
Total References retrieved (after de-duplication): 142

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-26/08/2014	9	0	26/08/2014
<i>Premedline</i>	5/2013-26/08/2014	16	3	26/08/2014

Embase	5/2013-26/08/2014	75	11	26/08/2014
Cochrane Library	5/2013-26/08/2014	34	0	26/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	5/2013-26/08/2014	9	0	26/08/2014

Total References retrieved (after de-duplication): 12



Study results

No evidence was identified pertaining to the diagnostic accuracy of CT scan, ultrasound, liver function tests or tumour marker CA19-9 in patients with suspected gall bladder cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Abu-Hamda, E. M. & Baron, T. H. (2004) Endoscopic management of cholangiocarcinoma. *Seminars in Liver Disease*, 24: 165-175.

Narrative review

Akatsu, T., Aiura, K., Shimazu, M., Ueda, M., Wakabayashi, G., Tanabe, M., Kawachi, S. & Kitajima, M. (2006) Can endoscopic ultrasonography differentiate nonneoplastic from neoplastic gallbladder polyps? *Digestive Diseases & Sciences*, 51: 416-421.

Not in PICO

Albazaz, R., Patel, C. N., Chowdhury, F. U. & Scarsbrook, A. F. (2013) Clinical impact of FDG PET-CT on management decisions for patients with primary biliary tumours. *Insights Into Imaging*, 4: 691-

700.

Not in PICO

Andersson, M., Kostic, S., Johansson, M., Lundell, L., Asztely, M. & Hellstrom, M. (2005) MRI combined with MR cholangiopancreatography versus helical CT in the evaluation of patients with suspected periampullary tumors: a prospective comparative study. *Acta Radiologica*, 46: 16-27.

Not in PICO

Arabul, M., Karakus, F., Alper, E., Kandemir, A., Celik, M., Karakus, V., Yucel, K. & Unsal, B. (2012) Comparison of multidetector CT and endoscopic ultrasonography in malignant pancreatic mass lesions. *Hepato-Gastroenterology*, 59: 1599-1603.

Not in PICO

Bartlett, D. L. (2000) Gallbladder cancer. *Seminars in Surgical Oncology*, 19: 145-155.

Narrative review

Brugge, W. R. (2006) Advances in the endoscopic management of patients with pancreatic and biliary malignancies. [Review] [46 refs]. *Southern Medical Journal*, 99: 1358-1366.

Narrative review

Burlefinger, R. J. (1992) Early carcinoma of the gallbladder: Macroscopic features and US-findings. [German]. *Endoskopie Heute*, 5: 144-146.

Not in PICO

Chan, K.-M., Yeh, T.-S., Tseng, J.-H., Liu, N.-J., Jan, Y.-Y. & Chen, M.-F. (2005) Clinicopathological analysis of cystic duct carcinoma. *Hepato-Gastroenterology*, 52: 691-694.

Not in PICO

Chen, W. X., Xie, Q. G., Zhang, W. F., Zhang, X., Hu, T. T., Xu, P. & Gu, Z. Y. (2008) Multiple imaging techniques in the diagnosis of ampullary carcinoma. *Hepatobiliary & Pancreatic Diseases International*, 7: 649-653.

Not in PICO

Chen, Y. L., Huang, Z. Q., Zhou, N. X., Zhang, W. Z., Huang, X. Q., Duan, W. D., Liu, R. & Liu, Y. (2007) [Clinical analysis of 110 patients with primary gallbladder carcinoma]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 29: 704-706.

Not in PICO

Cohan, R. H., Illescas, F. F. & Braun, S. D. (1986) Fine needle aspiration biopsy in malignant obstructive jaundice. *Gastrointestinal Radiology*, 11: 145-150.

Not in PICO

Colli, A., Cocciolo, M., Mumoli, N., Cesarini, L., Prisco, A., Gaffuri, I. & Martinez, E. (1998) Peripheral intrahepatic cholangiocarcinoma: ultrasound findings and differential diagnosis from hepatocellular carcinoma. *European Journal of Ultrasound*, 7: 93-99.

Not in PICO

Costamagna, G., Boskoski, I., Familiari, P., Tringali, A., Cesaro, P. & Perri, V. (2011) Update in biliary endoscopy. [Review]. *Digestive Diseases*, 29: Suppl-8.

Narrative review

Craanen, M. E., Van, W. J. H., Van Der Peet, D. L., Loffeld, R. J. L. F., Cuesta, M. A. & Mulder, C. J. J. (2006) Endoscopic ultrasound in patients with obstructive jaundice and inconclusive ultrasound and computer tomography findings. *European Journal of Gastroenterology and Hepatology*, 18: 1289-1292.

Not in PICO

Cubertafond, P., Gainant, A. & Raymond, J. (1984) Early stage gallbladder cancer. Update review of diagnosis, prognosis, and treatment. Report on 30 cases. [French]. *Chirurgie - Memoires de l'Academie de Chirurgie*, 110: 729-733.

Not in PICO

Curcio, G., Traina, M., Mocciaro, F., Liotta, R., Gentile, R., Tarantino, I., Barresi, L., Granata, A., Tuzzolino, F. & Gridelli, B. (2012) Intraductal aspiration: a promising new tissue-sampling technique for the diagnosis of suspected malignant biliary strictures. *Gastrointestinal Endoscopy*,

75: 798-804.

Not in PICO

Dancygier, H. (1991) Endoscopic ultrasonography of the upper gastrointestinal tract. [Review] [38 refs]. *Baillieres Clinical Gastroenterology*, 5: 19-36.

Narrative review

Darmas, B., Mahmud, S., Abbas, A. & Baker, A. L. (2007) Is there any justification for the routine histological examination of straightforward cholecystectomy specimens? *Annals of the Royal College of Surgeons of England*, 89: 238-241.

Not in PICO

Das, D. K., Tripathi, R. P., Bhambhani, S., Chachra, K. L., Sodhani, P. & Malhotra, V. (1998) Ultrasound-guided fine-needle aspiration cytology diagnosis of gallbladder lesions: a study of 82 cases. *Diagnostic Cytopathology*, 18: 258-264.

Not in PICO

De Zoysa, M. I., De Silva, S. K. & Illeperuma, A. (2010) Is routine histological examination of gall bladder specimens justifiable? *The Ceylon medical journal*, 55: 13-16.

Not in PICO

de, A., X, Roa, I. & Burgos, L. (1999) Gallbladder cancer, management of early tumors. [Review] [29 refs]. *Hepato-Gastroenterology*, 46: 1547-1551.

Narrative review

Defrain, C., Chang, C. Y., Srikureja, W., Nguyen, P. T. & Gu, M. (2005) Cytologic features and diagnostic pitfalls of primary ampullary tumors by endoscopic ultrasound-guided fine-needle aspiration biopsy. *Cancer*, 105: 289-297.

Not in PICO

Donohue, J. H. (2001) Present status of the diagnosis and treatment of gallbladder carcinoma. [Review] [40 refs]. *Journal of Hepato-Biliary-Pancreatic Surgery*, 8: 530-534.

Narrative review

Dwivedi, M., Misra, S. P. & Misra, V. (2000) Clinical and ultrasonographic findings of carcinoma of gallbladder in Indian patients. *Journal of the Association of Physicians of India*, 48: 192-195.

Not in PICO

Eloubeidi, M. A., Chen, V. K., Jhala, N. C., Eltoun, I. E., Jhala, D., Chhieng, D. C., Syed, S. A., Vickers, S. M. & Mel, W. C. (2004) Endoscopic ultrasound-guided fine needle aspiration biopsy of suspected cholangiocarcinoma. *Clinical Gastroenterology & Hepatology*, 2: 209-213.

Not in PICO

Eloubeidi, M. A., Tamhane, A., Jhala, N., Chhieng, D., Jhala, D., Crowe, R. & Eltoun, I. A. (2006) Agreement between rapid onsite and final cytologic interpretations of EUS-guided FNA specimens: Implications for the endosonographer and patient management. *American Journal of Gastroenterology*, 101: 2841-2847.

Not in PICO

Elvin, A., Erwald, R., Muren, C. & Mare, K. (1989) Gallbladder carcinoma. Diagnostic procedures with emphasis on ultrasound diagnosis. *Annales de Radiologie*, 32: 282-287.

Not in PICO

Erdas, E., Licheri, S., Pulix, N., Lai, M. L., Pisano, G., Pomata, M. & Daniele, G. M. (2002) Adenomyomatosis of the gallbladder. Personal experience and analysis of the literature. [Italian]. *Chirurgia Italiana*, 54: 673-684.

Not in PICO

Erkol, B., Oven, B. B., Bayoglu, V., Paker, N., Kochan, K., Ozkara, S., Tilki, M., Surmelioglu, A., Yesil, A. & Gonen, C. (2013) The sensitivity and specificity of DR-70 as a tumor marker for gastrointestinal cancers. *Journal of Clinical Oncology*, 31.

Not in PICO

- Fickling, W. E. & Wallace, M. B. (2003) Endoscopic ultrasound and upper gastrointestinal disorders. [Review] [68 refs]. *Journal of Clinical Gastroenterology*, 36: 103-110.
Narrative review
- Fiegler, W., Schorner, W. & Felix, R. (1984) [Value of sonography, computer tomography, hepatobiliary scintigraphy and nuclear magnetic tomography in diseases of the gallbladder and bile ducts]. [German]. *Rontgen-Blatter*, 37: 327-332.
Narrative review
- Fleischer, G. M. & Dittrich, S. (1992) [Therapy and prognosis of gallbladder cancer]. [German]. *Zentralblatt fur Chirurgie*, 117: 81-86.
Not in PICO
- Frank, W., Graf, O., Jantsch, H., Lechner, G., Maier, A. & Pichler, W. (1989) [Sonography of gallbladder carcinoma. Correlation with surgical findings in 60 cases]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 150: 556-561.
Not in PICO
- Fuji, T., Amano, H. & Aibe, T. (1983) Early diagnosis of carcinoma of the gallbladder. [Japanese]. *Stomach and Intestine*, 18: 1063-1068.
Not in PICO
- Gerber, S. & Schweizer, W. (2000) Surgical therapy of juxtapapillary tumors. *Swiss surgery = Schweizer Chirurgie = Chirurgie suisse = Chirurgia svizzera*, 6: 271-274.
Narrative review
- Gertsch, P., Thomas, P., Baer, H., Lerut, J., Zimmermann, A. & Blumgart, L. H. (1990) Multiple tumors of the biliary tract. [Review] [18 refs]. *American Journal of Surgery*, 159: 386-388.
Not in PICO
- Giang, T. H., Ngoc, T. T. & Hassell, L. A. (2012) Carcinoma involving the gallbladder: a retrospective review of 23 cases - pitfalls in diagnosis of gallbladder carcinoma. *Diagnostic Pathology*, 7: 10.
Not in PICO
- Goh, M. H. & Low, J. K. (2012) Mirizzi syndrome and incidence of gallbladder cancer: A single institution's experience. *HPB*, 14: 375-376.
Not in PICO
- Haenle, M. M., Voegtli, A., Mason, R. A., Akinli, A. S., Hirschbuehl, K., Schuler, A., Kaechele, V., Beckh, K., Bilger, B., Dinkel, A., Flegel, W. A., Frosch, M., Gaus, W., Gottstein, B., Hay, B., Jenne, L., Kern, P., Kilwinski, J., Kimmig, P., Koerner, K., Kratzer, W., Kron, M., Lucius, R., Merkle, P., Merli, M., Naser, K., Orth, M., Romig, T., Seitz, H. M., Sigel, H. & Wagner, F. F. (2008) Ultrasonographically detected gallbladder polyps: A reason for concern? A seven-year follow-up study. *BMC Gastroenterology*, 8.
Not in PICO
- Hall-Craggs, M. A. & Lees, W. R. (1986) Fine-needle aspiration biopsy: Pancreatic and biliary tumors. *American Journal of Roentgenology*, 147: 399-403.
Not in PICO
- Handa, U., Nanda, A., Mohan, H., Kochhar, S. & Sachdev, A. (2010) Cytologic diagnosis of gallbladder lesions - A study of 150 cases. *Indian Journal of Surgery*, 72: 181-184.
Not in PICO
- Hartenfels, I. M., Dukat, A., Burg, J., Hansen, M. & Jung, M. (2002) [Adenomas of Vater's ampulla and of the duodenum. Presentation of diagnosis and therapy by endoscopic interventional and surgical methods]. [Review] [38 refs] [German]. *Chirurg*, 73: 235-240.
Not in PICO
- Hatanaka, K., Kudo, M., Minami, Y. & Maekawa, K. (2008) Sonazoid-enhanced ultrasonography for diagnosis of hepatic malignancies: Comparison with contrast-enhanced CT. *Oncology*, 75: 42-47.
Not in PICO
- Heinzow, H., Uphoff, M.-A., Domagk, D. & Meister, T. (2014) Clinical predictors to identify malignancy in indeterminate bile duct strictures by ERCP-results of a cohort analysis with 1135

- patients. *Gastroenterology*, 146: S-605.
Not in PICO
- Heinzow, H. S., Lenz, P., Lallier, S., Lenze, F., Domagk, D., Domschke, W. & Meister, T. (2011) Ampulla of Vater tumors: impact of intraductal ultrasound and transpapillary endoscopic biopsies on diagnostic accuracy and therapy. *Acta Gastroenterologica Belgica*, 74: 509-515.
Not in PICO
- Hsieh, J. P., Tsao, W. L., Tang, H. S., Hsu, C. T. & Wu, K. L. (1993) Primary carcinoma of the gallbladder: a review of 10 years of experience at Tri-Service General Hospital. *Chung Hua i Hsueh Tsa Chih - Chinese Medical Journal*, 51: 193-199.
Not in PICO
- Hsu, M. H., Tummuru, R. & Patil, A. (2012) Endobiliary jumbo forceps biopsy as a technique for diagnosing bile duct malignancies. *Journal of Clinical Oncology*, 30.
Not in PICO
- Huibregtse, K. & Tytgat, G. N. (1988) Carcinoma of the ampulla of Vater: the endoscopic approach. *Endoscopy*, 20: Suppl-6.
Narrative review
- Inui, K. (2006) [Biliary tract cancer: present status in early diagnosis and treatment]. [Review] [49 refs] [Japanese]. *Nippon Shokakibyo Gakkai Zasshi - Japanese Journal of Gastroenterology*, 103: 495-500.
Narrative review
- Inui, K., Yoshino, J. & Miyoshi, H. (2011) Diagnosis of gallbladder tumors. [Review]. *Internal Medicine*, 50: 1133-1136.
Not in PICO
- Iqbal, S. & Stevens, P. D. (2009) Cholangiopancreatography for targeted biopsies of the bile and pancreatic ducts. [Review] [46 refs]. *Gastrointestinal Endoscopy Clinics of North America*, 19: 567-577.
Narrative review
- Iseki, J., Ushiyama, K. & Beppu, T. (1982) Early carcinoma of the gallbladder. A clinical and pathological study. [Japanese]. *Japanese Journal of Gastroenterology*, 79: 2112-2120.
Not in PICO
- Ishak, G., Ribeiro, F. S., Costa, D. S., Bahia, L. A., Dias, E. M. & Assumpcao, P. P. (2011) Gallbladder cancer: 10 years of experience at an Amazon reference hospital. *Revista do Colegio Brasileiro de Cirurgioes*, 38: 100-104.
Not in PICO
- Iwama, A., Tadatashi, T., Mituka, Y., Mamamichi, M., Tokio, H. & Shintaro, Y. (2012) Imaging modality of reformatted longitudinal image by multi-detector row CT in the diagnosis for gallbladder cancer. *HPB*, 14: 340.
Not in PICO
- Jang, J. Y., Kim, S. W., Lee, S. E., Hwang, D. W., Kim, E. J., Lee, J. Y., Kim, S. J., Ryu, J. K. & Kim, Y. T. (2009) Differential diagnostic and staging accuracies of high resolution ultrasonography, endoscopic ultrasonography, and multidetector computed tomography for gallbladder polypoid lesions and gallbladder cancer. *Annals of Surgery*, 250: 943-949.
Not in PICO
- Jin, K., Lan, H., Zhu, T., He, K. & Teng, L. (2011) Gallbladder carcinoma incidentally encountered during laparoscopic cholecystectomy: how to deal with it. [Review]. *Clinical & Translational Oncology: Official Publication of the Federation of Spanish Oncology Societies & of the National Cancer Institute of Mexico*, 13: 25-33.
Narrative review
- Jin, W., Zhang, C., He, X., Xu, Y., Wang, L. & Zhao, Z. (2013) Differences between images of large adenoma and protruding type of gallbladder carcinoma. *Oncology Letters*, 5: 1629-1632.
Not in PICO

- Joo, I. & Lee, J. M. (2013) Imaging bile duct tumors: Pathologic concepts, classification, and early tumor detection. *Abdominal Imaging*, 38: 1334-1350.
Narrative review
- Jung, G.-S., Huh, J.-D., Lee, S. U., Han, B. H., Chang, H.-K. & Cho, Y. D. (2002) Bile duct: Analysis of percutaneous transluminal forceps biopsy in 130 patients suspected of having malignant biliary obstruction. *Radiology*, 224: 725-730.
Not in PICO
- Juntermanns, B., Kaiser, G. M., Reis, H., Saner, F. H., Radunz, S., Vernadakis, S., Heuer, M., Kuehl, H., Paul, A. & Treckmann, J. (2011) Klatskin-mimicking lesions: still a diagnostical and therapeutical dilemma? *Hepato-Gastroenterology*, 58: 265-269.
Not in PICO
- Juul Nielsen, L. B., Schultz, N. A., Hasselby, J. P. & Wettergren, A. (2013) [Benign gallbladder polyp is a rare cause of haemobilia]. [Danish]. *Ugeskrift for Laeger*, 175: 2117-2118.
Not in PICO
- Kamisawa, T., Tu, Y., Egawa, N., Nakajima, H., Horiguchi, S., Tsuruta, K. & Okamoto, A. (2006) Clinicopathologic features of ampullary carcinoma without jaundice. *Journal of Clinical Gastroenterology*, 40: 162-166.
Not in PICO
- Kapoor, V. K., Pradeep, R., Haribhakti, S. P., Sikora, S. S. & Kaushik, S. P. (1996) Early carcinoma of the gallbladder: an elusive disease. *Journal of Surgical Oncology*, 62: 284-287.
Not in PICO
- Kimchi, N. A., Mindrul, V., Broide, E. & Scapa, E. (1998) The contribution of endoscopy and biopsy to the diagnosis of periampullary tumors. *Endoscopy*, 30: 538-543.
Not in PICO
- Kimura, K., Fujita, N., Noda, Y., Kobayashi, G., Yago, A., Okaniwa, S., Chonan, A., Matsunaga, A., Ando, M., Yuki, T., Tominaga, G., Nomura, M., Ishida, K., Inoue, S., Kisara, N., Yamada, N., Rin, T., Mochizuki, F. & Yamazaki, T. (1996) [Diagnosis of superficial-type early carcinoma of the gallbladder by endoscopic ultrasonography--comparison with ultrasonography]. [Japanese]. *Nippon Shokakibyō Gakkai Zasshi - Japanese Journal of Gastroenterology*, 93: 462-469.
Not in PICO
- Kinoshita, H., Nakayama, T., Imayama, H. & Okuda, K. (1998) [Diagnosis of extension and treatment of carcinoma of the gallbladder]. [Japanese]. *Nippon Geka Gakkai Zasshi. Journal of Japan Surgical Society*, 99: 700-705.
Narrative review
- Klein, H. M. & Gunther, R. W. (2004) Carcinoma of the gallbladder and biliary ducts - What is the value of CT, MRI, and magnetic resonance cholangiography?. [German]. *Chirurgische Gastroenterologie Interdisziplinär*, 20: 250-258.
Narrative review
- Klimkiewicz-Wiesiolek, E., Dybicki, J., Jackiewicz, Z., Dybkowski, J., Lacki, M. & Grabicki, R. (1989) [Gallbladder carcinoma--results of treatment]. [Polish]. *Wiadomości Lekarskie*, 42: 711-716.
Not in PICO
- Koga, A., Yamauchi, S., Izumi, Y. & Hamanaka, N. (1985) Ultrasonographic detection of early and curable carcinoma of the gallbladder. *British Journal of Surgery*, 72: 728-730.
Not in PICO
- Koga, A., Yamauchi, S. & Nakayama, F. (1985) Primary carcinoma of the gallbladder. *American Surgeon*, 51: 529-533.
Not in PICO
- Koga, F., Tanaka, H., Takamatsu, S., Baba, S., Takihara, H., Hasegawa, A., Yanagihara, E., Inoue, T., Nakano, T., Ueda, C. & Ono, W. (2012) A case of very large intrahepatic bile duct adenoma followed for 7 years. *World Journal of Clinical Oncology*, 3: 63-66.
Not in PICO

- Kohno, A., Yoshikawa, W. & Yunoki, M. (1996) [Contrast enhanced CT]. [Review] [14 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 54: 1249-1254.
Narrative review
- Konno, T. (1985) [Diagnostic criteria for early detection of cancer of the gallbladder by angiography]. [Japanese]. *Rinsho Hoshasen - Japanese Journal of Clinical Radiology*, 30: 705-712.
In Japanese. Not enough information can be extracted, but it appears to be "Not in PICO".
- Kositchaiwat, S., Kositchaiwat, C., Kanchanapitak, A., Lerkpatanakit, P. & Tinnakornrasamee, C. (2000) Diagnostic value of endoscopic transampullary biopsy for malignant bile duct stricture. *Journal of the Medical Association of Thailand*, 83: 992-998.
Not in PICO
- Kriplani, A. K., Jayant, S. & Kapur, B. M. (1992) Laparoscopy in primary carcinoma of the gallbladder. *Gastrointestinal Endoscopy*, 38: 326-329.
Not in PICO
- Kulaksiz, H., Strnad, P., Rompp, A., von, F. G., Barth, T., Esposito, I., Schirmacher, P., Henne-Bruns, D., Adler, G. & Stiehl, A. (2011) A novel method of forceps biopsy improves the diagnosis of proximal biliary malignancies. *Digestive Diseases & Sciences*, 56: 596-601.
Not in PICO
- Lahde, S. (1996) Helical CT in the examination of bile duct obstruction. *Acta Radiologica*, 37: 660-664.
Not in PICO
- Lee, D. H., Lee, J. M., Kim, K. W., Park, H. S., Kim, S. H., Lee, J. Y., Han, J. K. & Choi, B. I. (2008) MR imaging findings of early bile duct cancer. *Journal of Magnetic Resonance Imaging*, 28: 1466-1475.
Not in PICO
- Lee, S. W., Kim, H. J., Park, J. H., Park, D. I., Cho, Y. K., Sohn, C. I., Jeon, W. K. & Kim, B. I. (2010) Clinical usefulness of 18F-FDG PET-CT for patients with gallbladder cancer and cholangiocarcinoma. *Journal of Gastroenterology*, 45: 560-566.
Not in PICO
- Lim, J. H., Jang, K. T., Choi, D., Lee, W. J. & Lim, H. K. (2006) Early bile duct carcinoma: comparison of imaging features with pathologic findings. *Radiology*, 238: 542-548.
Not in PICO
- Lim, K. S., Peters, C. C., Kow, A. & Tan, C. H. (2012) The varying faces of gall bladder carcinoma: pictorial essay. [Review]. *Acta Radiologica*, 53: 494-500.
Narrative review
- Lin, C., Liao, Y. & He, C.-Y. (2007) Clinical value of combined serum tumor marker CA199 and spiral CT in the diagnosis of gallbladder carcinoma: An analysis of 33 cases. [Chinese]. *World Chinese Journal of Digestology*, 15: 3641-3643.
Not in PICO
- Lubashev, I., Abdulaev, R. A., Bagaudinov, K. G., Saidov, S. S., Ratnikov, V. A. & Udalov, I. (2006) [The early diagnosis of gallbladder polypiform neoplasm in the flying staff]. [Russian]. *Voenno-Meditsinskii Zhurnal*, 327: 65-68.
Russian, no English abstract. Probably not in PICO based on title.
- Magnuson, T. H., Bender, J. S., Duncan, M. D., Ahrendt, S. A., Harmon, J. W. & Regan, F. (1971) Utility of magnetic resonance cholangiography in the evaluation of biliary obstruction. *Journal of the American College of Surgeons*, 189: 63-71.
Not in PICO
- Manta, R., Conigliaro, R., Castellani, D., Messerotti, A., Bertani, H., Sabatino, G., Vetrucchio, E., Losi, L., Villanacci, V. & Bassotti, G. (2010) Linear endoscopic ultrasonography vs magnetic resonance imaging in ampullary tumors. *World Journal of Gastroenterology*, 16: 5592-5597.
Not in PICO

- Manu, N. K., Derek, M. M., Viney, W. & Kofi, O. E. (2011) Role of EUS/EUS-guided FNA in the management of proximal biliary strictures. *Hepato-Gastroenterology*, 58: 1862-1865.
Not in PICO
- Marangoni, G., Hakeem, A., Toogood, G. J., Lodge, J. P. & Prasad, K. R. (2012) Treatment and surveillance of polypoid lesions of the gallbladder in the United Kingdom. *HPB*, 14: 435-440.
Not in PICO
- McIntosh, D. M. & Penney, H. F. (1980) Gray-scale ultrasonography as a screening procedure in the detection of gallbladder disease. *Radiology*, 136: 725-727.
Not in PICO
- Meara, R. S., Jhala, D., Eloubeidi, M. A., Eltoun, I., Chhieng, D. C., Crowe, D. R., Varadarajulu, S. & Jhala, N. (2006) Endoscopic ultrasound-guided FNA biopsy of bile duct and gallbladder: analysis of 53 cases. *Cytopathology*, 17: 42-49.
Not in PICO
- Meister, T., Heinzow, H. S., Woestmeyer, C., Lenz, P., Menzel, J., Kucharzik, T., Domschke, W. & Domagk, D. (2013) Intraductal ultrasound substantiates diagnostics of bile duct strictures of uncertain etiology. *World Journal of Gastroenterology*, 19: 874-881.
Not in PICO
- Miller, G. & Jarnagin, W. R. (2008) Gallbladder carcinoma. [Review] [55 refs]. *European Journal of Surgical Oncology*, 34: 306-312.
Narrative review
- Mitake, M., Nakazawa, S., Naitoh, Y., Kimoto, E., Tsukamoto, Y., Asai, T., Yamao, K., Inui, K., Morita, K. & Hayashi, Y. (1990) Endoscopic ultrasonography in diagnosis of the extent of gallbladder carcinoma. *Gastrointestinal Endoscopy*, 36: 562-566.
Not in PICO
- Miyakawa, S., Ishihara, S., Takada, T., Miyazaki, M., Tsukada, K., Nagino, M., Kondo, S., Furuse, J., Saito, H., Tsuyuguchi, T., Kimura, F., Yoshitomi, H., Nozawa, S., Yoshida, M., Wada, K., Amano, H. & Miura, F. (2008) Flowcharts for the management of biliary tract and ampullary carcinomas. *Journal of Hepato-Biliary-Pancreatic Surgery*, 15: 7-14.
Narrative review
- Mizumoto, R., Ogura, Y. & Matsuda, S. (1988) [Clinical characteristics and imaging diagnosis of early cancer in the hepatobiliary and pancreatic region]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1342-1348.
Narrative review
- Mori, T., Souda, S., Hashimoto, J., Yoshikawa, Y. & Ohshima, M. (1997) Unsuspected gallbladder cancer diagnosed by laparoscopic cholecystectomy: a clinicopathological study. *Surgery Today*, 27: 710-713.
Not in PICO
- Mortele, K. J., Ji, H. & Ros, P. R. (2002) CT and magnetic resonance imaging in pancreatic and biliary tract malignancies. *Gastrointestinal Endoscopy*, 56: S206-S212.
Narrative review
- Murata, I., Makiyama, K., Funatsu, S., Kubo, K., Mizuta, Y., Nishihata, S., Imanishi, T., Hara, K., Nakamura, N. & Murase, K. (1988) [A study involving early carcinomas of the gall bladder]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 867-874.
Not in PICO
- Murohisa, B. & Kida, H. (1986) [Ultrasonic diagnosis of early gallbladder cancer]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 32: 1235-1239.
Not in PICO
- Nishiyama, Y., Yamamoto, Y., Fukunaga, K., Kimura, N., Miki, A., Sasakawa, Y., Wakabayashi, H., Satoh, K. & Ohkawa, M. (2006) Dual-time-point 18F-FDG PET for the evaluation of gallbladder carcinoma.[Erratum appears in J Nucl Med. 2006 Aug;47(8):1266]. *Journal of Nuclear Medicine*,

- 47: 633-638.
Not in PICO
- Noorullah, O., Wadsworth, C. A., Brougham, K., Lekharaju, V. P., Hood, S. V., Stern, N., Kaltsidis, C., Terlizzo, M. & Sturgess, R. (2013) A systematic approach to standard endoscopic sampling of bile duct strictures is highly accurate in the diagnosis of peri-hilar cholangiocarcinoma. A single UK tertiary centre experience. *Gastrointestinal Endoscopy*, 77: AB304.
Not in PICO
- Ohshima, Y., Yasuda, I., Kawakami, H., Kuwatani, M., Mukai, T., Iwashita, T., Doi, S., Nakashima, M., Hirose, Y., Asaka, M. & Moriwaki, H. (2011) EUS-FNA for suspected malignant biliary strictures after negative endoscopic transpapillary brush cytology and forceps biopsy. *Journal of Gastroenterology*, 46: 921-928.
Not in PICO
- Oikarinen, H. (2006) Diagnostic imaging of carcinomas of the gallbladder and the bile ducts. [Review] [97 refs]. *Acta Radiologica*, 47: 345-358.
Narrative review
- Okamoto, M., Okamoto, H., Kitahara, F., Kobayashi, K., Karikome, K., Miura, K., Matsumoto, Y. & Fujino, M. A. (1999) Ultrasonographic evidence of association of polyps and stones with gallbladder cancer. *American Journal of Gastroenterology*, 94: 446-450.
Not in PICO
- Okuda, K., Ohto, M. & Tsuchiya, Y. (1988) The role of ultrasound, percutaneous transhepatic cholangiography, computed tomographic scanning, and magnetic resonance imaging in the preoperative assessment of bile duct cancer. *World Journal of Surgery*, 12: 18-26.
Narrative review
- Onoyama, H., Yamamoto, M., Takada, M., Urakawa, T., Ajiki, T., Yamada, I., Fujita, T. & Saitoh, Y. (1999) Diagnostic imaging of early gallbladder cancer: retrospective study of 53 cases. *World Journal of Surgery*, 23: 708-712.
Not in PICO
- Palaniappan, K., Narashiman, G., Shanmugam, V., Perumalla, R., Reddy, S., Cherian, T., Kaliamoorthy, I., Vij, M. & Rela, M. (2014) Neuroendocrine tumors of gallbladder & extra hepatic biliary tract. *HPB*, 16: 331.
Not in PICO
- Pelsang, R. E. & Johlin, F. C. (1997) A percutaneous biopsy technique for patients with suspected biliary or pancreatic cancer without a radiographic mass. *Abdominal Imaging*, 22: 307-312.
Not in PICO
- Polverosi, R., Zambelli, C., Sbeghen, R., Caracciolo, F. & Berlanda, G. (1994) [Ultrasonography and computerized tomography in the diagnosis of gallbladder carcinoma]. [Italian]. *Radiologia Medica*, 87: 643-647.
Not in PICO
- Potente, F., Ghiron, U., Caramia, M., Seglie, E., Fava, F. & Rolfo, F. (1994) [Gallbladder carcinoma. Our experience]. [Italian]. *Minerva Chirurgica*, 49: 787-790.
Not in PICO
- Puhalla, H. & Laengle, F. (2006) Gallbladder cancer - Only surgery is curative. *European Surgery - Acta Chirurgica Austriaca*, 38: 100-106.
Narrative review
- Qualman, S. J., Haupt, H. M., Bauer, T. W. & Taxy, J. B. (1984) Adenocarcinoma of the hepatic duct junction. A reappraisal of the histologic criteria of malignancy. *Cancer*, 53: 1545-1551.
Not in PICO
- Riener, M. O. (2011) [Diagnosis of tumours of the liver and the biliary tract: new tissue and serum markers]. [Review] [German]. *Pathologe*, 32: Suppl-9.
Narrative review

- Ritts, J., Nagorney, D. M., Jacobsen, D. J., Talbot, R. W. & Zurawski, J. (1994) Comparison of preoperative serum CA19-9 levels with results of diagnostic imaging modalities in patients undergoing laparotomy for suspected pancreatic or gallbladder disease. *Pancreas*, 9: 707-716.
Not in PICO
- Rupesh, P., Manoj, P. & Vijay, K. S. (2008) Biomarkers in carcinoma of the gallbladder. *Expert Opinion on Medical Diagnostics*, 2: 511-526.
Narrative review
- Saotome, N. & Karasawa, E. (1991) [Imaging diagnosis of cancer of the gallbladder]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 18: 1252-1257.
Narrative review
- Sarkut, P., Kilicturgay, S., Ozer, A., Ozturk, E. & Yilmazlar, T. (2013) The incidence of malignancy in gallbladder polyps: How useful is ultrasound findings? *European Surgical Research*, 50: 76.
Not in PICO
- Sasson, A., Kim, E., Ly, Q. & Are, C. (2010) The benefit of intra-operative ultrasound in the management of suspected gallbladder cancer. *HPB*, 12: 71.
Not in PICO
- Sato, T., Koyama, K., Yamauchi, H. & Matsuno, S. (1981) Early carcinoma of the gallbladder. *Gastroenterologia Japonica*, 16: 459-464.
Not in PICO
- Sheth, S., Bedford, A. & Chopra, S. (2000) Primary gallbladder cancer: recognition of risk factors and the role of prophylactic cholecystectomy. *American Journal of Gastroenterology*, 95: 1402-1410.
Narrative review
- Shi, J.-S., Wang, J.-S., Liu, G., Yu, Y.-L., Lu, Y., Jiao, X.-Y., Yang, Y.-J., Li, G.-C. & Han, Y. (2002) Early diagnosis of primary gallbladder carcinoma. *Hepatobiliary and Pancreatic Diseases International*, 1: 273-275.
Not in PICO
- Shirai, Y., Yoshida, K., Tsukada, K., Muto, T. & Watanabe, H. (1992) Early carcinoma of the gallbladder. *European Journal of Surgery*, 158: 545-548.
Not in PICO
- Sriwanitchrak, P., Viyanant, V., Chaijaroenkul, W., Srivatanakul, P., Gram, H. R., Eursiddhichai, V. & Na-Bangchang, K. (2011) Proteomics analysis and evaluation of biomarkers for detection of cholangiocarcinoma. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 12: 1503-1510.
Not in PICO
- Sugiyama, M., Atomi, Y., Kuroda, A. & Muto, T. (1997) Bile duct carcinoma without jaundice: clues to early diagnosis. *Hepato-Gastroenterology*, 44: 1477-1483.
Not in PICO
- Sun, X.-J., Shi, J.-S., Han, Y., Wang, J.-S. & Ren, H. (2004) Diagnosis and treatment of polypoid lesions of the gallbladder: Report of 194 cases. *Hepatobiliary and Pancreatic Diseases International*, 3: 591-594.
Not in PICO
- Takemoto, T. & Fuji, T. (1982) Definition and diagnosis of early cancer of the biliary tract from the clinical viewpoint. [Japanese]. *Stomach and Intestine*, 17: 613-618.
Not in PICO
- Tapping, C. R., Byass, O. R. & Cast, J. E. (2012) Cytological sampling versus forceps biopsy during percutaneous transhepatic biliary drainage and analysis of factors predicting success. *Cardiovascular & Interventional Radiology*, 35: 883-889.
Not in PICO
- Tazuma, S. & Kajiyama, G. (2001) Carcinogenesis of malignant lesions of the gall bladder. The impact of chronic inflammation and gallstones. [Review] [45 refs]. *Langenbecks Archives of Surgery*, 386: 224-229.
Narrative review

- Testoni, P. A. & Mangiavillano, B. (2008) Optical coherence tomography in detection of dysplasia and cancer of the gastrointestinal tract and bilio-pancreatic ductal system. [Review] [40 refs]. *World Journal of Gastroenterology*, 14: 6444-6452.
Narrative review
- Tilleman, E. H., Phoa, S. S., Van Delden, O. M., Rauws, E. A., van Gulik, T. M., Lameris, J. S. & Gouma, D. J. (2003) Reinterpretation of radiological imaging in patients referred to a tertiary referral centre with a suspected pancreatic or hepatobiliary malignancy: impact on treatment strategy. *European Radiology*, 13: 1095-1099.
Not in PICO
- Tomita, M., Onoyama, H., Sako, T., Ajiki, T., Ohara, S., Yamazaki, I., Yamamoto, M. & Saito, Y. (1994) [Diagnosis of gallbladder cancer by imaging techniques: problems, limitations and their explanations, especially with ss invasive cancer]. [Japanese]. *Nippon Shokakibyō Gakkai Zasshi - Japanese Journal of Gastroenterology*, 91: 2065-2072.
Not in PICO
- Tsai, P. J., Wang, S. E., Shyr, Y. M., Chen, T. H., Su, C. H. & Wu, C. W. (2012) Diagnostic and therapeutic dilemmas in periampullary lesions. *Hepato-Gastroenterology*, 59: 1621-1625.
Not in PICO
- Tsugeno, H., Nunoue, T., Inokuchi, T., Seki, H., Kubota, J., Miyoshi, K., Takemoto, K., Takenaka, R., Taira, A. & Fujiki, S. (2010) A comparison of the diagnostic capability between Magnetic Resonance Imaging (MRI) with Diffusion Weighted Imaging (DWI) and 18-fluoro-2-dglucose positron emission tomography (FDG-PET/CT) for pancreaticobiliary malignancies. *Gastroenterology*, 138: S509-S510.
Not in PICO
- Tsukada, K., Takada, T., Miyazaki, M., Miyakawa, S., Nagino, M., Kondo, S., Furuse, J., Saito, H., Tsuyuguchi, T., Kimura, F., Yoshitomi, H., Nozawa, S., Yoshida, M., Wada, K., Amano, H., Miura, F., Japanese Association of Biliary Surgery, Japanese Society of Hepato-Biliary-Pancreatic Surgery & Japan Society of Clinical Oncology (2008) Diagnosis of biliary tract and ampullary carcinomas. *Journal of Hepato-Biliary-Pancreatic Surgery*, 15: 31-40.
Narrative review
- Venkataramu, N. K., Sood, B. P., Gupta, S., Gulati, M., Khandelwal, N. & Suri, S. (1999) Ultrasound-guided fine needle aspiration biopsy of gall bladder malignancies. *Acta Radiologica*, 40: 436-439.
Not in PICO
- Wachter, G. (1993) [Determining the value of ultrasound in diagnosis of the gallbladder and bile ducts]. [Review] [13 refs] [German]. *Bildgebung*, 60: 248-250.
Narrative review
- Wachter, G. (1993) Current status of ultrasound in the diagnosis of gallbladder and biliary tract. [German]. *Bildgebung/Imaging*, 60: 248-250.
Narrative review
- Walsh, R. M., Connelly, M. & Baker, M. (2003) Imaging for the diagnosis and staging of periampullary carcinomas. [Review] [61 refs]. *Surgical Endoscopy*, 17: 1514-1520.
Narrative review
- Wang, J., Xu, W., Dai, D., Zhu, Y., Men, X. & Liu, B. (2013) Diagnostic value and advantage of 18F-FDG PET/CT imaging in patients with primary gallbladder carcinoma. [Chinese]. *Chinese Journal of Clinical Oncology*, 40: 103-106.
Not in PICO
- Wang, Y.-F., Feng, F.-L., Zhao, X.-H., Ye, Z.-X., Zeng, H.-P., Li, Z., Jiang, X.-Q. & Peng, Z.-H. (2014) Combined detection tumor markers for diagnosis and prognosis of gallbladder cancer. *World Journal of Gastroenterology*, 20: 4085-4092.
Not in PICO

- Watanabe, H., Yamagiwa, I. & Iwashita, A. (1982) Definition and diagnosis of early carcinoma of the biliary tract. From the pathological viewpoint. [Japanese]. *Stomach and Intestine*, 17: 608-612.
Not in PICO
- Weber, A., von, W. C., Fend, F., Schneider, J., Neu, B., Meining, A., Weidenbach, H., Schmid, R. M. & Prinz, C. (2008) Endoscopic transpapillary brush cytology and forceps biopsy in patients with hilar cholangiocarcinoma. *World Journal of Gastroenterology*, 14: 1097-1101.
Not in PICO
- Weilert, F., Bhat, Y. M., Binmoeller, K. F., Kane, S., Jaffee, I. M., Cameron, R., Hashimoto, Y. & Shah, J. N. (2013) EUS-FNA is superior to ERCP tissue sampling in suspected malignant biliary obstruction-direct comparison in single session. *Journal of Gastroenterology and Hepatology*, 28: 51.
Not in PICO
- Weilert, F., Bhat, Y. M., Binmoeller, K., Kane, S., Jaffee, I. M., Cameron, R. G., Hashimoto, Y. & Shah, J. N. (2013) EUS-FNA is superior to ERCP tissue sampling in suspected malignant biliary obstruction. *Gastrointestinal Endoscopy*, 77: AB423.
Not in PICO
- Weiner, S. N., Koenigsberg, M., Morehouse, H. & Hoffman, J. (1984) Sonography and computed tomography in the diagnosis of carcinoma of the gallbladder. *AJR.American Journal of Roentgenology*, 142: 735-739.
Not in PICO
- Weiss, H., Deck, G., Weiss, A. & Rethel, R. (1981) Gallbladder carcinoma: Does ultrasonography give an early enough diagnosis?. [German]. *Therapiewoche*, 31: 8547-8552.
Narrative review
- Will, U., Bosseckert, H. & Meyer, F. (2008) Correlation of endoscopic ultrasonography (EUS) for differential diagnostics between inflammatory and neoplastic lesions of the papilla of Vater and the peripapillary region with results of histologic investigation. *Ultraschall in der Medizin*, 29: 275-280.
Not in PICO
- Wright, E. R., Bakis, G., Srinivasan, R., Raju, R., Vittal, H., Sanders, M. K., Bernadino, K., Stefan, A., Blaszyk, H. & Howell, D. A. (2011) Intraprocedural tissue diagnosis during ERCP employing a new cytology preparation of forceps biopsy (Smash protocol). *American Journal of Gastroenterology*, 106: 294-299.
Not in PICO
- Yamaguchi, K. & Enjoji, M. (1988) Carcinoma of the gallbladder. A clinicopathology of 103 patients and a newly proposed staging. *Cancer*, 62: 1425-1432.
Not in PICO
- Yamaguchi, K. (1992) Early bile duct carcinoma. *Australian and New Zealand Journal of Surgery*, 62: 525-529.
Not in PICO
- Yamakawa, T. & Honda, H. (1991) [Image diagnostics for carcinoma of the biliary tract]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 18: 1258-1263.
Narrative review
- Yoshioka, M., Watanabe, G., Uchinami, H., Miyazawa, H., Ise, N., Abe, Y., Nakagawa, Y., Kudoh, K., Takahashi, K., Ishiyama, K., Hashimoto, M., Nakamura, A. & Yamamoto, Y. (2013) Differential diagnosis of inflammatory diseases in gallbladder lesions using diffusion weighted MRI. *European Surgical Research*, 50: 191.
Not in PICO
- Zbar, A. P., Maor, Y. & Czerniak, A. (2012) Imaging tumours of the ampulla of Vater. [Review]. *Surgical Oncology*, 21: 293-298.
Narrative review

Zevallos, M. C., Ruiz Lopez, M. J., Gonzalez Valverde, F. M., Alarcon, S. F., Pastor, Q. F. & Garcia, M., V (2014) - Ultrasound findings associated to gallbladder carcinoma. - *Cirugia Espanola*, 92: 348-355.

Not in PICO

Zhang, H.-Y. & Dou, K.-F. (2014) Effect of ultrasound combined with determination of CA19-9 and hs-CRP on the accuracy of early diagnosis of gallbladder cancer. *Medical Journal of Chinese People's Liberation Army*, 39: 222-225.

Not in PICO

Zulke, C. & Schlitt, H. J. (2007) [Incidentalomas of the liver and gallbladder. Evaluation and therapeutic procedure]. [German]. *Chirurg*, 78: 698-712.

Narrative review

LIVER CANCER

Review question:

What is the risk of liver cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

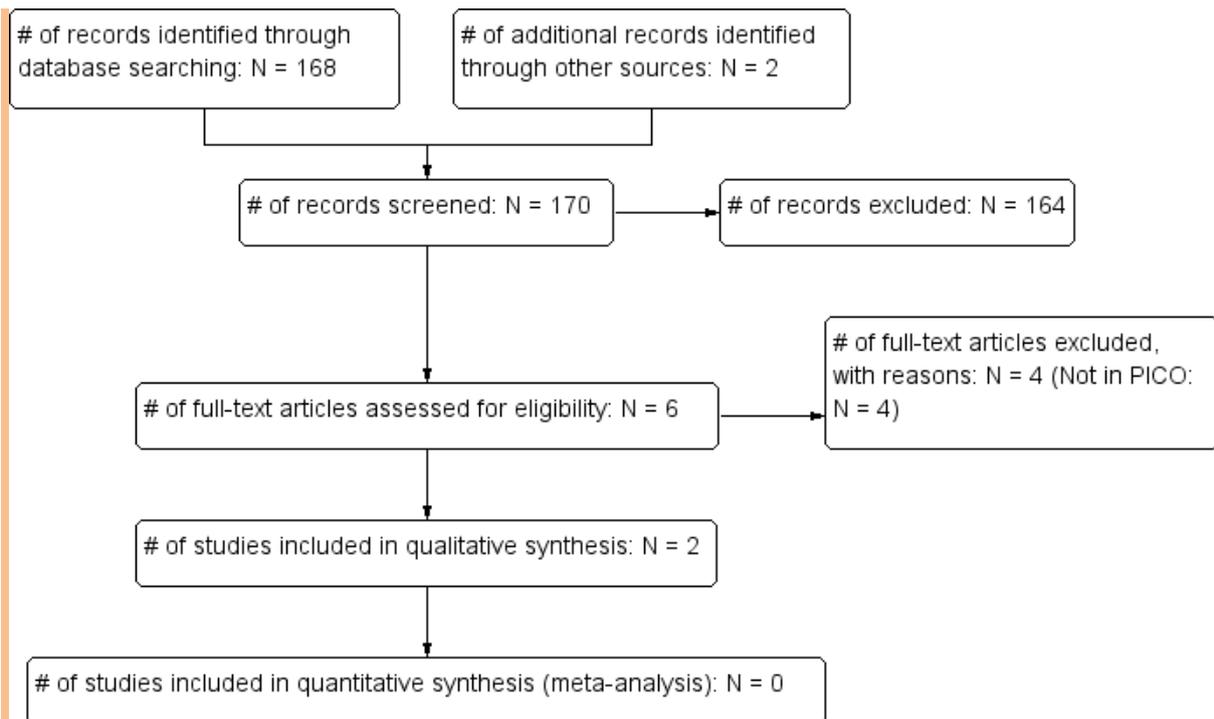
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	1073	71	30/04/2013
<i>Premedline</i>	All-2012	155	9	01/05/2013
<i>Embase</i>	All-2012	1305	93	02/05/2013
<i>Cochrane Library</i>	All-2012	459	0	03/05/2013
<i>Psychinfo</i>	All-2012	20	2	30/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	771	31	03/05/2013

Total References retrieved (after de-duplication): 164

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-19/08/2014	28	1	19/08/2014
<i>Premedline</i>	5/2013-19/08/2014	101	2	19/08/2014
<i>Embase</i>	5/2013-19/08/2014	163	2	19/08/2014
<i>Cochrane Library</i>	5/2013-19/08/2014	202	0	19/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	5/2013-19/08/2014	139	0	19/08/2014

Total References retrieved (after de-duplication): 4



Study results

Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included studies in the figure below. In one of the included studies, the main issue to note is that the population in the study comprises a mix of 'old' and 'new' investigated or uninvestigated symptoms, and it is unclear how directly applicable this sample is to the current question. In the other included study, it is unclear whether the patient selection was consecutive. This study also used a sub-optimal reference standard and was also subject to varying degrees of missing data; all of which challenges the validity of the reported results.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Hallissey (1990)	+	+	+	+	?	+	+
Lilford (2013)	?	+	?	-	+	+	+

⊖ High	⊕ Unclear	⊕ Low
--------	-----------	-------

Study results

Table 1: Liver cancer: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI)
Hallissey (1990)	Dyspepsia	All patients	0.04 (0.002-0.25) 1/2585
Lilford (2013)	LFT: Abnormal alanine aminotransferase	All patients	0.46 (0.08-1.8) 2/438
Lilford (2013)	LFT: Abnormal aspartate aminotransferase	All patients	0.39 (0.02-2.5) 1/255
Lilford (2013)	LFT: Abnormal γ -glutamyltransferase	All patients	0.92 (0.43-1.9) 8/867
Lilford (2013)	LFT: Abnormal bilirubin	All patients	0 (0-3.2) 0/148
Lilford (2013)	LFT: Abnormal alkaline phosphatase	All patients	1.59 (0.41-4.9) 3/189
Lilford (2013)	LFT: Abnormal albumin	All patients	0 (0-14) 0/30
Lilford (2013)	LFT: Abnormal globulin	All patients	0 (0-8.1) 0/55
Lilford (2013)	LFT: Abnormal total protein	All patients	0 (0-4.7) 0/97

Evidence statement(s):

The positive predictive value for liver cancer ranged from 0% (for abnormal bilirubin/ albumin/ globulin/ total [hepatic] protein) to 1.59% (for abnormal alkaline phosphatase; 2 studies, N = 3875) presenting in primary care was 0.04%. The included studies were associated with 1-3 bias/applicability concerns (see also Table 1).

Evidence tables

Hallissey (1990)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive patient series from a group of 10 general practices in England.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia. <u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, England.

Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia of any degree
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	2659 patients were seen and 2585 attended for investigation
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), carcinomatosis of unknown primary (7).
Lilford (2013)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective UK study of patients with an abnormal LFT panel across eight primary care practices in Birmingham and three in the Lambeth area of London, UK.
Was a consecutive or random sample of patients enrolled?	Unclear

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1290; 724 males / 566 females; aged ≤ 34 years: N = 106; 35-44 years: N = 165; 45-54 years: N = 240; 55-64 years: N = 325; 65-74 years: N = 273; 75+ years: N = 181. Reason for testing: Signs and symptoms: N = 406; chronic disease review: N = 884; alcohol at follow up (unit/week): 0: N = 547; 1-14: N = 352; 15-29: N = 153; 30-49: N = 122; 50-99: N = 84; 100+: N = 24; not known: N = 8. <u>Inclusion criteria:</u> Primary care patients without obvious or pre-existing liver disease, and one or more of the eight analytes in an index LFT panel was abnormal. Recruitment took place from 2005 to 2008. Eligible patients were invited to join the study and attend a first follow-up session. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, England.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	“The index panel comprised: alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyltransferase (GGT), bilirubin (Bili), alkaline phosphatase (ALP), albumin (Alb), globulin (Glob), and total protein (Tprot). Analyte abnormality was determined using standard laboratory reference ranges, which are routinely adjusted for age and gender where appropriate.” The measurement of these was repeated at a first follow up session (taking place a median of 30 days post-first LFT measures (IQR 21-51 days).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Diagnosis of any tumours of the hepatobiliary system based on ultrasound of the upper abdomen + exclusion of other hepatic diseases and hepatologist’s opinion along with follow up.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined	Low concern

by the reference standard does not match the question?	
FLOW AND TIMING	
A. risk of bias	
Flow and timing	The authors report the results both for the initial testing (that identified the patients in the first place) and for the follow up session (a median of 30 days later). The results reported here are limited to the former, which across the panel of 8 LFTs varied between 977 and 1278 of the included 1290.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	

References

Included studies

- Hallisey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.
- Lilford, R.J., Bentham, L.M., Armstrong, M.J., Neuberger, J., Girling, A.L. What is the best strategy for investigating abnormal liver function tests in primary care? Implications from a prospective study. *BMJ Open* 3, e003099. Doi:10.1136/bmjopen-2013-003099. 2013.

Excluded studies (with excl reason)

Reference List

- Abdel, W. M., Fathy, O., Elghwalby, N., Sultan, A., Mostafa, M., El, B. M., Elsaadany, M., Elshobary, M. & Ezzat, F. (2006) Primary hepatic carcinoid tumor: One Egyptian center experience. *Hepato-Gastroenterology*, 53: January/February.
Not in PICO
- Acalovschi, M. (2004) Cholangiocarcinoma: risk factors, diagnosis and management. [Review] [28 refs]. *Romanian Journal of Internal Medicine*, 42: 41-58.
Narrative review
- Akinyinka, O. O., Falade, A. G., Ogunbiyi, O. & Johnson, A. O. K. (2001) Hepatocellular carcinoma in Nigerian children. *Annals of Tropical Paediatrics*, 21: 165-168.
Not in PICO
- Altaf, F. J. (2001) Hepatocellular carcinoma. *Saudi Medical Journal*, 22: 416-418.
Not in PICO
- Andrade, B., Alvarado, L., Zurita, M. & Andrade, S. (2013) Early and advanced gastric cancer: Clinical, endoscopy, histopathology and comparative study. *Journal of Gastroenterology and Hepatology*, 28: 652-653.
Not in PICO
- Andrzejewska, M., Pacho, R. & Malkowski, P. (2006) [Radiological imaging of hepatocellular carcinoma]. [Review] [12 refs] [Polish]. *Przegląd Epidemiologiczny*, 60: 741-748.
Narrative review
- Anthony, P. P. (2001) Hepatocellular carcinoma: an overview. *Histopathology*, 39: 109-118.
Narrative review

- Aramaki, M., Kawano, K., Sasaki, A., Ohno, T., Tahara, K., Kai, S., Iwashita, Y. & Kitano, S. (2005) Hepatocellular carcinoma in young adults. *Hepato-Gastroenterology*, 52: 1795-1797.
Not in PICO
- Arterburn, D. E. & Richardson, W. S. (2000) Evidence-based case review - Should we look further for cancer in a patient with venous thromboembolism? *Western Journal of Medicine*, 172: 325-328.
Not in PICO
- Berasain, C., Castillo, J., Perugorria, M. J., Latasa, M. U., Prieto, J. & Avila, M. A. (2009) Inflammation and liver cancer: new molecular links . [Review] [106 refs]. *Annals of the New York Academy of Sciences*, 1155: 206-221.
Narrative review
- Bergquist, A., Glaumann, H., Persson, B. & Broome, U. (1998) Risk factors and clinical presentation of hepatobiliary carcinoma in patients with primary sclerosing cholangitis: A case-control study. *Hepatology*, 27: 311-316.
Not in PICO
- Bleyer, A. (2009) CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology*, 36: June.
Narrative review
- Brancatelli, G., Federle, M. P., Grazioli, L. & Carr, B. I. (2002) Hepatocellular carcinoma in noncirrhotic liver: CT, clinical, and pathologic findings in 39 U.S. residents. *Radiology*, 222: 89-94.
Not in PICO
- Caballeria, L. & Toran, P. (2012) Early detection of chronic liver disease in primary care in the apparently health adult population. [Spanish]. *Gastroenterologia y Hepatologia*, 35: December.
Narrative review
- Cardona, D., Grobmyer, S., Crawford, J. M. & Liu, C. (2007) Hepatocellular carcinoma arising from ectopic liver tissue in the pancreas. *Virchows Archiv*, 450: February.
Not in PICO
- Castells, L., Vargas, V., Comas, P., Sureda, D. G., Vidal, X., Esteban, R. & Guardia, J. (1993) Hepatocellular-Carcinoma - Clinical Manifestations, Diagnosis and Survival in 140 Cases. *Medicina Clinica*, 100: 441-446.
Not in PICO
- Chen, D. S., Sheu, J. C. & Sung, J. L. (1982) Small hepatocellular carcinoma: A clinicopathological study in thirteen patients. *Gastroenterology*, 83.
Not in PICO
- Cherian, P. T., Dent, H., Sreenivasan, P., Prachalias, A., Heaton, N. D. & Rela, M. (2010) Double duct dilatation-what does it mean in the absence of a periampullary mass? A review of 737 patients. *HPB.Conference: 9th World Congress of the International Hepato-Pancreato-Biliary Association Buenos Aires Argentina.Conference Start: 20100418 Conference End: 20100422.Conference Publication: (var.pagings)*, 12: April.
Not in PICO
- Choi, J., Lee, Y.-J., Hwang, D. W., Chon, S.-H., Nagpal, A. & Park, K.-M. (2011) Surgical treatment of giant hepatic hemangiomas: Technical point of view. *American Surgeon*, 77: January.
Not in PICO
- Chu, J.-S., Yang, K.-C., Hsu, T.-C., Kao, C.-R., Chou, S.-Y. & Shih, S.-C. (1993) Concomitant digestive malignancy in pregnancy. *Chinese Journal of Gastroenterology*, 10.
Not in PICO
- Cioffi-Pretti, J. L., Kalof, A. N., Ebert, G. & McCahill, L. E. (2009) Hepatic angiosarcoma five years following spontaneous intraperitoneal bleed of a hepatic mass. *Rare Tumors*, 1: e33.
Not in PICO
- Crowe, A., Knight, C. S., Jhala, D., Bynon, S. J. & Jhala, N. C. (2011) Diagnosis of metastatic fibrolamellar hepatocellular carcinoma by endoscopic ultrasound-guided fine needle aspiration.

- Cytojournal*, 8: 2.
Not in PICO
- Crownover, B. K. & Covey, C. J. (2013) Hereditary hemochromatosis. [Review]. *American Family Physician*, 87: 183-190.
Narrative review
- Czako, L., Takacs, T., Morvay, Z., Csernay, L. & Lonovics, J. (2004) Diagnostic role of secretin-enhanced MRCP in patients with unsuccessful ERCP. *World Journal of Gastroenterology*, 10: 3034-3038.
Not in PICO
- Czako, L., Takacs, T., Morvay, Z., Csernay, L. & Lonovics, J. (2004) [Diagnostic value of secretin-enhanced magnetic resonance cholangiopancreatography (S-MRCP) after unsuccessful endoscopic retrograde cholangiopancreatography (ERCP)]. [Hungarian]. *Orvosi Hetilap*, 145: 529-534.
Not in PICO
- Daker, C., Kalkan, C. G., Belman, D., Van Someren, N. M. & Besherdas, K. (2010) Straight to endoscopy triage saves significant time for cancer diagnosis. *Gastroenterology.Conference: Digestive Disease Week, DDW 2011 Chicago, IL United States.Conference Start: 20110507 Conference End: 20110510.Conference Publication: (var.pagings)*, 140: May.
Not in PICO
- Dalla, P. L., Ricci, C. & Magnaldi, S. (1995) Referral criteria for selection of patients and diagnostic procedures. *Radiation Protection Dosimetry*, 57.
Narrative review
- Daniels, I. R. & Layer, G. T. (2003) How should gynaecomastia be managed? *ANZ Journal of Surgery*, 73: 213.
Not in PICO
- Das, B. C. & Khan, Z. R. (2013) Periampullary carcinoma: better prognosis with early pre-stenting referral to surgery. *Mymensingh Medical Journal: MMJ*, 22: 110-115.
Not in PICO
- De, S., I, Castellano, L., Calandra, M., Romano, M., Persico, M. & Del Vecchio-Blanco, C. (1995) Liver and biliary. Ultrasound-guided fine needle aspiration biopsy of portal vein thrombosis in liver cirrhosis: Results in 15 patients. *Journal of Gastroenterology and Hepatology*, 10.
Not in PICO
- Dechene, A., Hilgard, P. A., El, F. A., Gerken, G. & Zoepf, T. (2009) It looks like cholangiocarcinoma - But is it? Cholangioscopy using a cholangioscopy system for diagnosis of cholangiocarcinoma in patients with primary sclerosing cholangitis. *Gastrointestinal Endoscopy.Conference: Digestive Disease Week, DDW 2009 Chicago, IL United States.Conference Start: 20090530 Conference End: 20090604.Conference Publication: (var.pagings)*, 69: April.
Not in PICO
- Dewan, R., Sarma, M. P., Asim, M. & Kar, P. (2012) Demographic, clinical, biochemical, radiological, and etiological profile and the risk factors associated with 357 hepatocellular carcinoma cases from India. *Journal of Clinical and Experimental Hepatology.Conference: 20th Annual Conference of Indian National Association for the Study of Liver, INASL 2012 Guwahati India.Conference Start: 20120302 Conference End: 20120304.Conference Publication: (var.pagings)*, 2: March.
Not in PICO
- Dohmen, K., Shigematsu, H., Irie, K. & Ishibashi, H. (2003) Trends in clinical characteristics, treatment and prognosis of hepatocellular carcinoma. *Hepato-Gastroenterology*, 50: 1872-1877.
Not in PICO
- Dunkelberg, J. C., Barakat, J. & Deutsch, J. (2005) Gastrointestinal, pancreatic, and hepatic cancer during pregnancy. [Review] [112 refs]. *Obstetrics & Gynecology Clinics of North America*, 32: 641-660.
Narrative review

- Dunn, A. L. (2010) Malignancy in patients with haemophilia: A review of the literature. *Haemophilia*, 16: May.
Narrative review
- Dusan, J. (1111) The suggestions for prevention, screening, diagnosis and treatment of hepatocellular carcinoma. [Serbian, English]. *Archives of Gastroenterohepatology*, 23: July/December.
Narrative review
- Elhajj, M. & Elhajj, I. (2002) Evaluation for hepatic diseases in a primary care setting. *Primary Care Update for Ob/Gyns*, 9.
Narrative review
- Eloubeidi, M. A., Chen, V. K., Jhala, N. C., Eltoun, I. E., Jhala, D., Chhieng, D. C., Syed, S. A., Vickers, S. M. & Wilcox, C. M. (2004) Endoscopic ultrasound-guided fine needle aspiration biopsy of suspected cholangiocarcinoma. *Clinical Gastroenterology and Hepatology*, 2: March.
Not in PICO
- Erdogan, D., Busch, O. R. C., Van Delden, O. M., Bennink, R. J., Ten Kate, F. J. W., Gouma, D. J. & Van Gulik, T. M. (2007) Management of liver hemangiomas according to size and symptoms. *Journal of Gastroenterology and Hepatology*, 22: November.
Not in PICO
- Etemadi, A., Golozar, A., Ghassabian, A., Zarei, M., Hashemi Taheri, A. P., Dawsey, S. M. & Malekzadeh, R. (2011) Cavernous hemangioma of the liver: factors affecting disease progression in general hepatology practice. *European Journal of Gastroenterology & Hepatology*, 23: 354-358.
Not in PICO
- Fallon, H. J. (1999) Hepatitis C: implications for the general physician. [Review] [8 refs]. *Comprehensive Therapy*, 25: 253-257.
Narrative review
- Farghaly, M. M., Abdul-Ghaffar, N. U. & Almanee, M. S. (1998) Ruptured hepatoma: Report of 5 cases in Arabs. *Medical Principles and Practice*, 7: October/December.
Not in PICO
- Farrer, F. (2010) Cancer screening in primary care. *SA Pharmaceutical Journal*, 77: October.
Narrative review
- Fassio, E. (2010) Hepatitis C and hepatocellular carcinoma. *Annals of Hepatology*, 9: Suppl-22.
Narrative review
- Ferenci, P., Fried, M., Labrecque, D., Bruix, J., Sherman, M., Omata, M., Heathcote, J., Piratsivuth, T., Kew, M., Otegbayo, J. A., Zheng, S. S., Sarin, S., Hamid, S. S., Modawi, S. B., Fleig, W., Fedail, S., Thomson, A., Khan, A., Malfertheiner, P., Lau, G., Carillo, F. J., Krabshuis, J., Le, M. A. & World Gastroenterology Organization (2010) Hepatocellular carcinoma (HCC): a global perspective. *Journal of Clinical Gastroenterology*, 44: 239-245.
Not in PICO
- Fermelia, D. & Berci, G. (1987) Diagnostic and therapeutic laparoscopy. An entity often overlooked by the surgeon. *Surgical Endoscopy*, 1: 73-77.
Narrative review
- Ferrante, J. M., Winston, D. G., Chen, P. H. & de la Torre, A. N. (2008) Family physicians' knowledge and screening of chronic hepatitis and liver cancer. *Family Medicine*, 40: 345-351.
Not in PICO
- Fleming, K. M., West, J., Aithal, G. P. & Fletcher, A. E. (2011) Abnormal liver tests in people aged 75 and above: prevalence and association with mortality. *Alimentary Pharmacology & Therapeutics*, 34: 324-334.
Not in PICO (not symptomatic patients presenting to primary care)
- Follador, A., Fanzutti, M., Adami, G., Merlo, V., Rijavec, E., Belvedere, O., Pertoldi, F. & Piga, A. (2008) An audit of non-urgent attendances of cancer patients (PTS) to the emergency department (ED) of a District General Hospital in North-Eastern. *Annals of Oncology.Conference: 34th*

- Congress of the European Society for Medical Oncology (ESMO) Stockholm Sweden. Conference Start: 20080912 Conference End: 20080916. Conference Publication: (var.pagings), 19: September.
Not in PICO
- Fujimoto, K., Sawabe, M., Sasaki, M., Kino, K. & Arai, T. (2008) Undiagnosed cirrhosis occurs frequently in the elderly and requires periodic follow ups and medical treatments. *Geriatrics & gerontology international*, 8: 198-203.
Not in PICO
- Gabbrielli, A., Frulloni, L., Ruffini, M., Bernardoni, L., Castagnini, A., Angelini, G., Benini, L. & Vantini, I. (2011) Involvement of bile duct in autoimmune pancreatitis. ERCP Verona experience. *Digestive and Liver Disease. Conference: 17th National Congress of Digestive Diseases - Italian Federation of Societies of Digestive Diseases, FISMAD Turin Italy. Conference Start: 20110305 Conference End: 20110309. Conference Publication: (var.pagings)*, 43: March.
Not in PICO
- Gennari, R., Veronesi, U., Andreoli, C., Betka, J., Castelli, A., Gatti, G., Hugosson, J., Llovet, J. M., Melia, J., Nakhosteen, J. A., Pastorino, U., Sideri, M., Stephan, C., Veronesi, P. & Zurrada, S. (2007) Early detection of cancer: ideas for a debate. [Review] [40 refs]. *Critical Reviews in Oncology-Hematology*, 61: 97-103.
Narrative review
- Gervain, J. (2010) [Symptoms of hepatocellular carcinoma. Laboratory tests used for its diagnosis and screening]. [Hungarian]. *Orvosi Hetilap*, 151: 1415-1417.
Narrative review
- Giannini, E., Romagnoli, P., Fasoli, A., Botta, F., Risso, D. & Testa, R. (2002) Influence of age on clinical presentation, therapeutic options, and prognosis in anti-HCV positive cirrhotic patients with hepatocellular carcinoma. *Age and Ageing*, 31: November.
Not in PICO
- Giannini, E. G., Risso, D., Testa, R., Trevisani, F., Di Nolfo, M. A., Del, P. P., Benvegna, L., Ludovico, R. G., Farinati, F., Zoli, M., Borzio, F. & Caturelli, E. (2006) Prevalence and Prognostic Significance of the Presence of Esophageal Varices in Patients With Hepatocellular Carcinoma. *Clinical Gastroenterology and Hepatology*, 4: November.
Not in PICO
- Gomez, V., Walser, E., Nakhleh, R. & Michel, J. A. (2012) IgG4-related sclerosing disease: The great mimicker. *American Journal of Gastroenterology. Conference: 77th Annual Scientific Meeting of the American College of Gastroenterology Las Vegas, NV United States. Conference Start: 20121019 Conference End: 20121024. Conference Publication: (var.pagings)*, 107: October.
Not in PICO
- Hannam, S., McDonnell, M. & Rennie, J. M. (2000) Investigation of prolonged neonatal jaundice. *Acta Paediatrica*, 89: 694-697.
Not in PICO
- Harrison, H. & Adams, P. C. (2002) Hemochromatosis. Common genes, uncommon illness?. [Review] [26 refs]. *Canadian Family Physician*, 48: 1326-1333.
Not in PICO
- Hassett, M., Yopp, A. C. & Singal, A. G. (2013) Surveillance for hepatocellular carcinoma: how can we do better? *American Journal of the Medical Sciences*, 346: 308-313.
Narrative review
- Hidajat, N., Stobbe, H., Griesshaber, V., Schroder, R. J. & Felix, R. (2005) Portal vein thrombosis: etiology, diagnostic strategy, therapy and management. [Review] [139 refs]. *Vasa*, 34: 81-92.
Narrative review
- Higashi, H., Matsumata, T., Utsunomiya, T., Koyanagi, N., Hashizume, M. & Sugimachi, K. (402) Successful treatment of early hepatocellular carcinoma and concomitant esophageal varices. *World Journal of Surgery*, 17: 398-402.
Not in PICO

- Ho, H.-Y., Wu, T.-H., Yu, M.-C., Lee, W.-C., Chao, T. C. & Chen, M.-F. (2011) Surgical management of giant hepatic hemangiomas: Complications and review of literature. *HPB.Conference: 3rd Biennial Congress of the Asian-Pacific HPBA 2011 Melbourne, VIC Australia.Conference Start: 20110927 Conference End: 20110930.Conference Publication: (var.pagings)*, 13: October.
Not in PICO
- Hojo, A., Nakayama, H., Aramaki, O., Higaki, T., Moriguchi, M., Sugitani, M., Miura, K., Takeuchi, J., Nishiyama, R., Moriyama, M. & Takayama, T. (2013) Diagnostic value of open biopsy for malignant T-cell lymphoma of the liver. *International Surgery*, 98: 13-18.
Not in PICO
- Hsieh, M. S., Liang, P. C., Kao, Y. C. & Shun, C. T. (2010) Hepatic Epithelioid Hemangioendothelioma in Taiwan: A Clinicopathologic Study of Six Cases in a Single Institution Over a 15-Year Period. *Journal of the Formosan Medical Association*, 109: 219-227.
Not in PICO
- Huang, J. Q., Bao, X. J. & Lu, X. H. (1993) [The common causes and differential diagnosis of malignant jaundice]. [Chinese]. *Chung-Hua Nei Ko Tsa Chih Chinese Journal of Internal Medicine*, 32: 400-404.
Not in PICO
- Hucke, F., Sieghart, W., Schoniger-Hekele, M., Peck-Radosavljevic, M. & Muller, C. (2011) Clinical characteristics of patients with hepatocellular carcinoma in Austria - is there a need for a structured screening program? *Wiener Klinische Wochenschrift*, 123: 542-551.
Not in PICO
- Husain, A., Bezjak, A. & Easson, A. (2010) Malignant ascites symptom cluster in patients referred for paracentesis. *Annals of Surgical Oncology*, 17: February.
Not in PICO
- Iloh, G. U. P. & Ikwudinma, A. O. (2013) Sero-epidemiology of Hepatitis B surface antigenaemia among adult Nigerians with clinical features of liver diseases attending a primary-care clinic in a resource-constrained setting of eastern Nigeria. *North American Journal of Medical Sciences*, 5: April.
Not in PICO
- Inoue, Y., Lefor, A. T. & Yasuda, Y. (2012) Intrahepatic cholangiocarcinoma with sarcomatous changes. *Case Reports Gastroenterology*, 6: 1-4.
Not in PICO
- Ioannou, G. N., Splan, M. F., Weiss, N. S., McDonald, G. B., Beretta, L. & Lee, S. P. (2007) Incidence and predictors of hepatocellular carcinoma in patients with cirrhosis. *Clinical Gastroenterology and Hepatology*, 5: 938-945.
Not in PICO
- Ito, Y., Kenmochi, T., Irino, T., Egawa, T., Hayashi, S., Nagashima, A. & Kitagawa, Y. (2012) Clinicopathological feature of extrahepatic cholangiocarcinoma without jaundice: a single-center experience. *Hepato-Gastroenterology*, 59: 1744-1747.
Not in PICO
- Iwamura, K. (1982) Clinicopathological aspects of primary hepatocellular carcinoma occurring in patients with liver cirrhosis. *Tokai Journal of Experimental & Clinical Medicine*, 7: 589-605.
Not in PICO
- Jaeger, H. J., MacFie, J., Mitchell, C. J., Couse, N. & Wai, D. (1990) Diagnosis of abdominal masses with percutaneous biopsy guided by ultrasound. *BMJ*, 301: 1188-1191.
Not in PICO
- Jeffers, L. (2000) Hepatocellular carcinoma: an emerging problem with hepatitis C. *Journal of the National Medical Association*, 92: 369-371.
Narrative review
- Jiang, G. Q., Qian, J. J., Yao, J., Jin, S. J. & Bai, D. S. (2014) - Acute pancreatitis and obstructive jaundice as initial complaints of hepatocellular carcinoma: case report. - *World Journal of Surgical*

- Oncology*, 12: 13.
Not in PICO
- Joo, I. & Lee, J. M. (2013) Imaging bile duct tumors: pathologic concepts, classification, and early tumor detection. *Abdominal Imaging*, 38: 1334-1350.
Narrative review
- Juan, L. B. (2008) Cholangiocarcinoma. *Revista Medica de Chile*, 136: 240-248.
Narrative review
- Jubelirer, S. J., Talkington, A. & Bailey, D. (1991) Hepatocellular carcinoma: a review of 30 years experience. *West Virginia Medical Journal*, 87: 400-402.
Not in PICO
- Jung, G. S., Huh, J. D., Lee, S. U., Han, B. H., Chang, H. K. & Cho, Y. D. (2002) Bile duct: analysis of percutaneous transluminal forceps biopsy in 130 patients suspected of having malignant biliary obstruction. *Radiology*, 224: 725-730.
Not in PICO
- Kammula U.S., Buell, J. F., Labow, D. M., Rosen, S., Millis, J. M. & Posner, M. C. (2001) Surgical management of benign tumors of the liver. *International Journal of Gastrointestinal Cancer*, 30.
Not in PICO
- Kanematsu, T. & Inokuchi, K. (1983) [Treatment of liver cancer and concomitant esophageal varices]. [Japanese]. *Nippon Geka Gakkai Zasshi. Journal of Japan Surgical Society*, 84: 923-926.
Not in PICO
- Karnabatidis, D., Spiliopoulos, S., Katsakiori, P., Romanos, O., Katsanos, K. & Siablis, D. (2013) Percutaneous trans-hepatic bilateral biliary stenting in Bismuth IV malignant obstruction. *World Journal of Hepatology*, 5: 114-119.
Not in PICO
- Kee, K.-M., Lu, S.-N., Wang, J.-H., Wang, C.-C., Chen, T.-Y. & Huang, Y.-J. (2012) Difference of stage, treatment strategy and survival of hepatocellular carcinoma patients between past and recent periods: Analysis of 7852 cases from 1986 to 2010. *Journal of Hepatology. Conference: 47th Annual Meeting of the European Association for the Study of the Liver, International Liver Congress 2012 Barcelona Spain. Conference Start: 20120418 Conference End: 20120422. Conference Publication: (var.pagings)*, 56: April.
Not in PICO
- Klein, H. M. & Gunther, R. W. (1111) Carcinoma of the gallbladder and biliary ducts - What is the value of CT, MRI, and magnetic resonance cholangiography?. [German]. *Chirurgische Gastroenterologie Interdisziplinär*, 20: December.
Narrative review
- Kubo, S., Uenishi, T., Yamamoto, S., Hai, S., Yamamoto, K., Ogawa, M., Takemura, S., Shuto, T., Tanaka, H., Yamazaki, O., Hirohashi, K. & Kinoshita, H. (2004) Clinicopathologic characteristics of small intrahepatic cholangiocarcinomas of mass-forming type. *Hepatology Research*, 29: 223-227.
Not in PICO
- Kudo, M. (2006) Early detection and characterization of hepatocellular carcinoma: value of imaging multistep human hepatocarcinogenesis. [Review] [40 refs]. *Intervirolgy*, 49: 64-69.
Narrative review
- Kudo, M., Han, K. H., Kokudo, N., Cheng, A. L., Choi, B. I., Furuse, J., Izumi, N., Park, J. W., Poon, R. T. & Sakamoto, M. (2010) Liver Cancer Working Group report. *Japanese Journal of Clinical Oncology*, 40: Suppl-27.
Narrative review
- Lack, E. E. & Ornvold, K. (1986) Focal nodular hyperplasia and hepatic adenoma: a review of eight cases in the pediatric age group. *Journal of Surgical Oncology*, 33: 129-135.
Not in PICO

- Lai, C. L., Lam, K. C., Wong, K. P., Wu, P. C. & Todd, D. (1981) Clinical features of hepatocellular carcinoma: review of 211 patients in Hong Kong. *Cancer*, 47: 2746-2755.
Not in PICO
- Larsen, A. C., Dabrowski, T., Fisker, R. V., Kristensen, S. R., Moller, B. K. & Thorlacius-Ussing, O. (2012) Venous thromboembolism and haemostatic disturbances in patients with upper gastrointestinal cancer. *Thrombosis Research. Conference: 6th International Conference on Thrombosis and Hemostasis Issues in Cancer Bergamo Italy. Conference Start: 20120420 Conference End: 20120422. Conference Publication: (var.pagings)*, 129: April.
Not in PICO
- Le, S. J., Durupt, S., Bailly, F., Rode, A. & Seve, P. (2009) A strange Evans syndrome: a case report. *Cases journal*, 2: 8001.
Not in PICO
- Lemoine, A., Azoulay, D., Jezequel-Cuer, M. & Debuire, B. (1999) [Hepatocellular carcinoma]. [Review] [71 refs] [French]. *Pathologie Biologie*, 47: 903-910.
Narrative review
- Lertpipommetha, K. & Auewarakul, C. U. (2011) High Incidence of Hepatitis B Infection-Associated Cirrhosis and Hepatocellular Carcinoma in the Southeast Asian Patients with Portal Vein Thrombosis. *Bmc Gastroenterology*, 11.
Not in PICO
- Li, Z. Y., Cai, J. Q., Bi, X. Y., Zhao, J. J., Zhao, H., Huang, Z. & Zheng, X. C. (2012) [Surgical management of nodular hyperplasia tumor-like hepatic lesions: a study of 72 cases]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]*, 50: 97-100.
Not in PICO
- Liu, Y., Liu, A., Li, H., Li, C. & Lin, J. (2011) Celecoxib inhibits interleukin-6/interleukin-6 receptor-induced JAK2/STAT3 phosphorylation in human hepatocellular carcinoma cells. *Cancer Prevention Research*, 4: 1296-1305.
Not in PICO
- Lok, K. H., Li, K. F., Li, K. K. & Szeto, M. L. (2008) Pyogenic liver abscess: clinical profile, microbiological characteristics, and management in a Hong Kong hospital. *Journal of Microbiology Immunology and Infection*, 41: 483-490.
Not in PICO
- Lupberger, J. & Hildt, E. (2007) Hepatitis B virus-induced oncogenesis. [Review] [111 refs]. *World Journal of Gastroenterology*, 13: 74-81.
Narrative review
- Marrero, J. A. (2006) Hepatocellular carcinoma. [Review] [42 refs]. *Current Opinion in Gastroenterology*, 22: 248-253.
Narrative review
- Masterton, G., Chatterjee, S. & Nylander, D. (2009) More cancers are diagnosed in patients with symptoms compliant with the 2 week referral guidance than originally predicted. *Gut. Conference: Annual Meeting of the British Society of Gastroenterology Glasgow United Kingdom. Conference Start: 20090323 Conference End: 20090326. Conference Publication: (var.pagings)*, 58: April.
Not in PICO
- McGahan, J. P., Bishop, J., Webb, J., Howell, L., Torok, N., Lamba, R. & Corwin, M. T. (2013) Role of FNA and Core Biopsy of Primary and Metastatic Liver Disease. *International Journal of Hepatology*, 2013: 174103.
Not in PICO
- McMahon, B. J. (2008) Implementing evidenced-based practice guidelines for the management of chronic hepatitis B virus infection. *American Journal of Medicine*, 121: Suppl-52.
Narrative review

- Molina, E. & Hernandez, A. (2003) Clinical manifestations of primary hepatic angiosarcoma. *Digestive Diseases and Sciences*, 48: 677-682.
Not in PICO
- Morisawa, Y., Tanaka, A., Miura, R., Fukami, M., Goto, H., Negoro, S., Hanawa, N., Aiso, M., Kuyama, Y. & Takikawa, H. (1111) The etiology of liver cirrhosis in the Department of Medicine at Teikyo University Hospital. [Japanese]. *Teikyo Medical Journal*, 31: September.
Not in PICO
- Morita, R., Yoshii, M., Nakajima, K., Kohsaka, T., Miki, M. & Torizuka, K. (1981) Clinical evaluation of serum ferritin to iron ratio in malignant diseases. *European Journal of Nuclear Medicine*, 6: 331-336.
Not in PICO
- Munk, E. M., Drewes, A. M., Gorst-Rasmussen, A., Funch-Jensen, P., Gregersen, H. & Norgard, B. (2007) Risk of gastrointestinal cancer in patients with unexplained chest/epigastric pain and normal upper endoscopy: a Danish 10-year follow-up study. *Digestive Diseases & Sciences*, 52: 1730-1737.
Not in PICO
- Murata, K., Shiraki, K., Kawakita, T., Yamamoto, N., Okano, H., Sakai, T., Ohmori, S., Deguchi, M., Shimizu, A. & Nakano, T. (2003) Hepatocellular carcinoma presenting with obstructive jaundice: a clinicopathological study of eight cases. *Hepato-Gastroenterology*, 50: 2057-2060.
Not in PICO
- Muto, Y., Moriwaki, H., Shimazaki, M., Fukutomi, Y., Adachi, S., Kawai, K., Okuno, M., Hoshiyama, N., Yamada, M. & Shimizu, M. (1989) [A high risk group of hepatocellular carcinoma in man, with special reference to its clinical significance for the screening of early liver cancer. Gifu Study Group for Early Liver Cancer]. [Japanese]. *Nippon Shokakibyo Gakkai Zasshi - Japanese Journal of Gastroenterology*, 86: 2833-2838.
Not in PICO
- Nawara, C., Wolkersdorfer, G., Ofner-Velano, D. & Emmanuel, K. (2011) Recent developments in the diagnosis and treatment of bile duct cysts: A review. *European Surgery - Acta Chirurgica Austriaca*, 43: October.
Narrative review
- Nguyen, L., Shandling, B., Ein, S. & Stephens, C. (1982) Hepatic hemangioma in childhood: medical management or surgical management? *Journal of Pediatric Surgery*, 17: 576-579.
Not in PICO
- Ni, Y. H., Chang, M. H., Hsu, H. Y., Hsu, H. C., Chen, C. C., Chen, W. J. & Lee, C. Y. (1991) Hepatocellular-Carcinoma in Childhood - Clinical Manifestations and Prognosis. *Cancer*, 68: 1737-1741.
Not in PICO
- Nonomura, A., Mizukami, Y. & Kadoya, M. (1994) Angiomyolipoma of the liver: a collective review. [Review] [46 refs]. *Journal of Gastroenterology*, 29: 95-105.
Narrative review
- Olah, A., Issekutz, A., Toth, G., Haulik, L. & Banga, P. (2002) [Surgical treatment of giant hemangiomas of the liver]. [Hungarian]. *Magyar Sebeszet*, 55: 57-62.
Not in PICO
- Omoniyi-Esan, G. O., Famurewa, O. C., Omonisi, A. E., Titiloye, N. A., Pelemo, O. E. & Olasode, B. J. (2011) The role of ultrasound guided fine needle aspiration cytology in the diagnosis of hepatocellular carcinoma: A tertiary hospital experience. *Journal of Pathology.Conference: 6th Joint Meeting of the British Division of the International Academy of Pathology and the Pathological Society of Great Britain and Ireland, Ghent Pathology 2011 Ghent Belgium.Conference Start: 20110510 Conference End: 224: July.*
Not in PICO

- Ott, J. J., Ullrich, A. & Miller, A. B. (2009) The importance of early symptom recognition in the context of early detection and cancer survival. *European Journal of Cancer*, 45: November.
Narrative review
- Ozer, B., Serin, E., Yilmaz, U., Gumurdulu, Y., Saygili, O. B., Kayaselcuk, F. & Boyacioglu, S. (2003) Clinicopathologic features and risk factors for hepatocellular carcinoma: Results from a single center in southern Turkey. *Turkish Journal of Gastroenterology*, 14: June.
Not in PICO
- Patiakas, S., Xiropoulou, E., Mylona, T., Barbantonakis, N. & Kipeni, D. (2009) Comparative study of tumor markers sensitivity in cases of patients with liver disease. *European Journal of Immunology.Conference: 2nd European Congress of Immunology Berlin Germany.Conference Start: 20090913 Conference End: 20090916.Conference Publication: (var.pagings)*, 39: September.
Not in PICO
- Paul, S. B., Gulati, M. S., Sreenivas, V., Madan, K., Gupta, A. K., Mukhopadhyay, S. & Acharya, S. K. (2007) Evaluating patients with cirrhosis for hepatocellular carcinoma: value of clinical symptomatology, imaging and alpha-fetoprotein. *Oncology*, 72: Suppl-23.
Not in PICO
- Putterman, D., Safadi, R., Ilan, Y., Rivkind, A. I. & Benchetrit, E. (1994) Pulmonary-Embolism As the Presenting Feature of Hepatocellular-Carcinoma. *Presse Medicale*, 23: 474-476.
Not in PICO
- Rabe, C., Pilz, T., Klostermann, C., Berna, M., Schild, H. H., Sauerbruch, T. & Caselmann, W. H. (2001) Clinical characteristics and outcome of a cohort of 101 patients with hepatocellular carcinoma. *World Journal of Gastroenterology*, 7: 208-215.
Not in PICO
- Reisman, Y., Gips, C. H., Lavelle, S. M. & Wilson, J. H. P. (1996) Clinical presentation of (subclinical) jaundice - The Euricterus project in The Netherlands. *Hepato-Gastroenterology*, 43: 1190-1195.
Not in PICO
- Robotin, M., Patton, Y., Putha, V., Tipper, S. & George, J. (2010) Collaborating with general practitioners in cancer control: Lessons from the B positive project. *Asia-Pacific Journal of Clinical Oncology.Conference: 37th Annual Scientific Meeting of the Clinical Oncological Society of Australia, COSA Melbourne, VIC Australia.Conference Start: 20101109 Conference End: 20101111.Conference Publication: (var.paging)*, 6: November.
Not in PICO
- Rodriguez, R. G., Gutierrez, M. R., de Frutos, C. G., Varasa, T. D., Perez, G. D., Dopazo, J. J. C., Perez, C. L. & Moreno, A. Z. G. (2011) Clinical characteristics, staging and treatment of patients with hepatocellular carcinoma in clinical practice. Prospective study of 136 patients. *Gastroenterologia y Hepatologia*, 34: 524-531.
Not in PICO
- Roganovic, J. (1111) Hepatic tumours. [Croatian]. *Paediatrica Croatica, Supplement*, 50: 2006.
Narrative review
- Ryder, S. D. & British Society of Gastroenterology (2003) Guidelines for the diagnosis and treatment of hepatocellular carcinoma (HCC) in adults. *Gut*, 52: Suppl-8.
Guideline
- Sada, Y., David, E., El-Serag, H., Singh, H. & Davila, J. (2013) Guideline adherence for diagnosis of liver cancer in veterans. *Journal of Clinical Oncology*, 31.
Not in PICO
- Salvador, V. B., Samrao, P., Leytin, A. & Basith, M. (2013) Atypical presentation of an advanced obstructive biliary cancer without jaundice. *The American Journal of Case Reports*, 14: 462-466.
Not in PICO
- Sands, R. G. & Greenberg, R. A. (1987) Reported vague symptoms and at-risk status: the case of polyvinyl chloride workers in Louisville. *Public Health Reports*, 102: 438-444.
Not in PICO

- Santambrogio, R., Opocher, E., Costa, M., Bruno, S., Ceretti, A. P. & Spina, G. P. (2006) Natural history of a randomized trial comparing distal splenorenal shunt with endoscopic sclerotherapy in the prevention of variceal rebleeding: A lesson from the past. *World Journal of Gastroenterology*, 12: 21.
Not in PICO
- Santi, V., Buccione, D., Fatti, G., DiMicoli, A., Farinati, F., Del, P. P., Rapaccini, G., DiNolfo, M. A., Benvegno, L., Zoli, M., Borzio, F., Giannini, E. G., Caturelli, E., Chiaramonte, M., Bernardi, M. & Trevisani, F. (1111) The evolving clinical scenario of hepatocellular carcinoma over the last 20 years in Italy. *Digestive and Liver Disease.Conference: Italian Association for the Study of the Liver, A.I.S.F.- Annual Meeting 2011 Rome Italy.Conference Start: 20110224 Conference End: 20110225.Conference Publication: (var.pagings)*, 43: February.
Not in PICO
- Santi, V., Buccione, D., Fatti, G., Di, M. A., Frigerio, M., Grignaschi, A., Farinati, F., Del, P. P., Rapaccini, G., Di Nolfo, M. A., Benvegno, L., Zoli, M., Borzio, F., Giannini, E. G., Caturelli, E., Chiaramonte, M., Bernardi, M. & Trevisani, F. (2011) The evolving clinical scenario of hepatocellular carcinoma over the last 20 years in Italy. *Journal of Hepatology.Conference: 46th Annual Meeting of the European Association for the Study of the Liver, International Liver Congress 2011 Berlin Germany.Conference Start: 20110330 Conference End: 20110403.Conference Publication: (var.pagings)*, 54: March.
Not in PICO
- Santi, V., Buccione, D., Di, M. A., Fatti, G., Frigerio, M., Farinati, F., Del, P. P., Rapaccini, G., Di Nolfo, M. A., Benvegno, L., Zoli, M., Borzio, F., Giannini, E. G., Caturelli, E., Chiaramonte, M., Bernardi, M. & Trevisani, F. (2012) The changing scenario of hepatocellular carcinoma over the last two decades in Italy. *Journal of Hepatology*, 56: 397-405.
Not in PICO
- Schoniger-Hekele, M., Muller, C., Kutilek, M., Oesterreicher, C., Ferenci, P. & Gangl, A. (2000) Hepatocellular carcinoma in Austria: aetiological and clinical characteristics at presentation. *European Journal of Gastroenterology & Hepatology*, 12: 941-948.
Not in PICO
- Sherman, M. (1995) Hepatocellular carcinoma. [Review] [174 refs]. *Gastroenterologist*, 3: 55-66.
Narrative review
- Shimauchi, Y., Tanaka, M., Koga, K., Itano, S., Ishii, K., Kumashiro, R., Sakisaka, S. & Sata, M. (2000) Clinical characteristics of patients in their 40s with HCV antibody-positive hepatocellular carcinoma. *Alcoholism-Clinical and Experimental Research*, 24: 64S-67S.
Not in PICO
- Siddique, K., Mirza, S., Ali, Q. & Zafar, P. A. (2011) Evaluation of the aetiological spectrum of obstructive jaundice. *Hepatology International.Conference: 21st Conference of the Asian Pacific Association for the Study of the Liver, APASL 2011 Bangkok Thailand.Conference Start: 20110217 Conference End: 20110220.Conference Publication: (var.pagings)*, 5: March.
Not in PICO
- Siddiqui, A. A., Mehendiratta, V., Jackson, W. E., Loren, D. E., Kowalski, T. E. & Eloubeidi, M. A. (2012) SpyGlass peroral cholangioscopy and cholangioscopic forceps biopsy for the diagnosis of extrahepatic cholangiocarcinoma after negative ERCP brush cytology and negative EUS-guided FNA results. *Gastrointestinal Endoscopy.Conference: Digestive Disease Week 2012, DDW 2012 San Diego, CA United States.Conference Start: 20120519 Conference End: 20120522.Conference Publication: (var.pagings)*, 75: April.
Not in PICO
- Siddiqui, I., Bhally, H. S., Niaz, Q. & Burney, I. A. (2002) Tumor-induced hypercalcemia: predictors of early mortality. *JPMA - Journal of the Pakistan Medical Association*, 52: 361-364.
Not in PICO

- Silva, M. A., Tekin, K., Aytakin, F., Bramhall, S. R., Buckels, J. A. C. & Mirza, D. F. (2005) Surgery for hilar cholangiocarcinoma; a 10 year experience of a tertiary referral centre in the UK. *European Journal of Surgical Oncology*, 31: June.
Not in PICO
- Sithinamsuwan, P., Piratvisuth, T., Tanomkiat, W., Apakupakul, N. & Tongyoo, S. (2000) Review of 336 patients with hepatocellular carcinoma at Songklanagarind Hospital. *World Journal of Gastroenterology*, 6: 339-343.
Not in PICO
- Sorensen, H. T., Moller-Petersen, J. F., Felding, P., Andreasen, C. & Nielsen, J. O. (1991) Epidemiology of abnormal liver function tests in general practice in a defined population in Denmark. *Danish Medical Bulletin*, 38: 420-422.
Not in PICO
- Speets, A. M., Kalmijn, S., Hoes, A. W., Van Der Graaf, Y. & Mali, W. P. T. (2006) Yield of abdominal ultrasound in patients with abdominal pain referred by general practitioners. *European Journal of General Practice*, 12: November.
Not in PICO
- Stephen, F. O. & Rossaro, L. (2008) 12th Update in Gastroenterology and Hepatology for the Primary Care Practitioner. *Expert review of gastroenterology & hepatology*, 2: 635-637.
Narrative review
- Stephenson, D. (2000) Detecting hereditary hemochromatosis. [Review] [31 refs]. *Nurse Practitioner*, 25: 64-66.
Narrative review
- Sugita, M., Masuda, Y. & Tsuchiya, K. (1986) Early detection and signs of hepatoangiosarcoma among vinyl chloride workers. *American Journal of Industrial Medicine*, 10: 411-417.
Not in PICO
- Takeda, J., Toyonaga, A., Koufujii, K., Kodama, I., Tsuji, Y., Aoyagi, K. & Kakegawa, T. (1994) Surgical management of gastric cancer patients with liver cirrhosis. *The Kurume medical journal*, 41.
Not in PICO
- Tang, L., Lai, E. C., Cong, W. M., Li, A. J., Fu, S. Y., Pan, Z. Y., Zhou, W. P., Lau, W. Y. & Wu, M. C. (2010) Inflammatory myofibroblastic tumor of the liver: a cohort study. *World Journal of Surgery*, 34: 309-313.
Not in PICO
- Tapping, C. R., Byass, O. R. & Cast, J. E. (2012) Cytological sampling versus forceps biopsy during percutaneous transhepatic biliary drainage and analysis of factors predicting success. *Cardiovascular & Interventional Radiology*, 35: 883-889.
Not in PICO
- Taylor, A., Stapley, S. & Hamilton, W. (2012) Jaundice in primary care: a cohort study of adults aged >45 years using electronic medical records. *Family Practice*, 29: 416-420.
Not in PICO
- Tiftikci, A., Vardareli, E. N., Kaban, K., Peker, O., Akansel, S. & Tozun, N. (2008) Actinomycotic hepatic abscess. *Hepatology International*, 2: 133-135.
Not in PICO
- Tsalis, K., Zacharakis, E., Sapidis, N., Lambrou, I., Zacharakis, E. & Betsis, D. (2005) Adrenal metastasis as first presentation of hepatocellular carcinoma. *World Journal of Surgical Oncology*, 3: 50.
Not in PICO
- Uttaravichien, T. & Buddhisawasdi, V. (1990) Experience of non-jaundiced cholangiocarcinoma. *Hepato-Gastroenterology*, 37.
Not in PICO
- Van Roey, G., Fevery, J. & Van Steenberghe, W. (2000) Hepatocellular carcinoma in Belgium: clinical and virological characteristics of 154 consecutive cirrhotic and non-cirrhotic patients. *European*

Journal of Gastroenterology & Hepatology, 12: 61-66.

Not in PICO

Van, C. J., Devine, P. & Odom-Ball, P. (1999) Multidisciplinary care of hepatocellular carcinoma. *Cancer Practice*, 7: 302-308.

Not in PICO

Villa, E. & Fattovich, G. (2010) No inflammation? No cancer! Clear HBV early and live happily. *Journal of Hepatology*, 52: 768-770.

Comment

Voll, R. A rare differential diagnosis of a somatoform autonomous disorder of the gastro-intestinal tract: The hepatocellular liver carcinoma in childhood. [German]. [References]. *Zeitschrift für Kinder- und Jugendpsychiatrie und Psychotherapie* 36[4], 275-278. 2008.

Not in PICO

Weiser, M. A., Cabanillas, M., Vu, K., Tamm, E. P., Wallace, M. J., Escalante, C. P. & Bresalier, R. S. (2005) Diagnostic evaluation of patients with a high suspicion of malignancy: Comorbidities and clinical predictors of cancer. *American Journal of the Medical Sciences*, 330: July.

Not in PICO

Weiss, E., Kirtich, S., Markowitz, B., Ramachandran, R., Dasari, V. & Aytaman, A. (2012) Occult cirrhosis can be uncovered by evaluation of unexplained thrombocytopenia. *American Journal of Gastroenterology.Conference: 77th Annual Scientific Meeting of the American College of Gastroenterology Las Vegas, NV United States.Conference Start: 20121019 Conference End: 20121024.Conference Publication: (var.pagings)*, 107: October.

Not in PICO

Wiedermann, K. H. (2009) [Hepatocellular carcinoma--an increasing problem in the Western world]. [German]. *MMW Fortschritte der Medizin*, 151: 40-43.

Narrative review

Wiener, Y., Gold, R., Zehavy, S., Sandbank, J. & Halevy, A. (456) [Primary gastrointestinal stromal tumors]. [Hebrew]. *Harefuah*, 140: 377-380.

Not in PICO

Wilkins, T., Zimmerman, D. & Schade, R. R. (2010) Hepatitis B: Diagnosis and treatment. *American Family Physician*, 81: 965-972.

Narrative review

Wiwanitkit, V. (2003) Clinical findings among 62 Thais with cholangiocarcinoma. *Tropical Medicine & International Health*, 8: 228-230.

Not in PICO

Wu, C. X., Guo, H., Gong, J. P., Liu, Q. & Sun, H. (2013) The role of high mobility group box chromosomal protein 1 expression in the differential diagnosis of hepatic actinomycosis: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 7: 31.

Not in PICO

Yakoob, J., Jafri, W., Asim, M. B., Abbas, Z., Naz, S., Islam, M., Khalid, A. B., Khan, R. & Ahmad, Z. (2010) Emerging parasitic infection mimicking functional bowel disease. *Gastroenterology.Conference: Digestive Disease Week, DDW 2010 New Orleans, LA United States.Conference Start: 20100501 Conference End: 20100506.Conference Publication: (var.pagings)*, 138: May.

Not in PICO

Yamaguchi, K., Nakano, K., Nagai, E., Chijiwa, K., Kinoshita, M., Ohta, M. & Tanaka, M. (2005) Ki-ras mutations in codon 12 and p53 mutations (biomarkers) and cytology in bile in patients with hepatobiliary-pancreatic carcinoma. *Hepato-Gastroenterology*, 52: May/June.

Not in PICO

Yamazaki, Y., Kakizaki, S., Sohara, N., Sato, K., Takagi, H., Arai, H., Abe, T., Katakai, K., Kojima, A., Matsuzaki, Y. & Mori, M. (2007) Hepatocellular carcinoma in young adults: The clinical characteristics, prognosis, and findings of a patient survival analysis. *Digestive Diseases and*

Sciences, 52: 1103-1107.

Not in PICO

Yang, B. H., Xia, J. L., Huang, L. W., Tang, Z. Y., Chen, M. S., Li, J. Q., Liang, A. M., Mo, Q. G., Lu, H. S., Dai, C. L., Yan, L. N., Yu, Z. J., Rao, R. S., Li, L. Q., Su, Z. X. & Fang, Z. W. (2004) Changed clinical aspects of primary liver cancer in China during the past 30 years. *Hepatobiliary & Pancreatic Diseases International*, 3: 194-198.

Not in PICO

Yang, W. L., Zhang, X. C., Zhang, D. W. & Tong, B. F. (2007) Diagnosis and surgical treatment of hepatic hilar cholangiocarcinoma. *Hepatobiliary & Pancreatic Diseases International*, 6: 631-635.

Not in PICO

Yeoman, A. D., Al-Chalabi, T., Karani, J. B., Quaglia, A., Devlin, J., Mieli-Vergani, G., Bomford, A., O'Grady, J. G., Harrison, P. M. & Heneghan, M. A. (2008) Evaluation of risk factors in the development of hepatocellular carcinoma in autoimmune hepatitis: Implications for follow-up and screening. *Hepatology*, 48: 863-870.

Not in PICO

Yoon, S. S., Charny, C. K., Fong, Y., Jarnagin, W. R., Schwartz, L. H., Blumgart, L. H. & DeMatteo, R. P. (2003) Diagnosis, management, and outcomes of 115 patients with hepatic hemangioma. *Journal of the American College of Surgeons*, 197: 392-402.

Not in PICO

Yopp, A. C., Subramanian, M., Jain, M. K., Mansour, J. C., Schwarz, R. E., Balch, G. C. & Singal, A. G. (2012) Presentation, treatment, and clinical outcomes of patients with hepatocellular carcinoma, with and without human immunodeficiency virus infection. *Clinical Gastroenterology & Hepatology*, 10: 1284-1290.

Not in PICO

Young, K., Dundas, P., Vijayan, B. & Fraser, A. (2011) Fast track jaundice clinic: The standard of care for hepatobiliary malignancy? *Gut.Conference: British Association for the Study of the Liver Annual Meeting, BASL 2011 London United Kingdom.Conference Start: 20110907 Conference End: 20110909.Conference Publication: (var.pagings)*, 60: September.

Not in PICO

Zaheer, A., Anwar, M. M., Donohoe, C. L., O'Keefe, S., Mushtaq, H., Barry, K. T., Clarke, E., Kirca, M., Mac, M. P. & O'Toole, D. (2011) EUS significantly reduces the burden of ERCP and accurately predicts CBD stones in patients with suspected biliary obstruction: Consecutive analysis of 418 patients. *Gastrointestinal Endoscopy.Conference: Digestive Disease Week, DDW 2011 Chicago, IL United States.Conference Start: 20110507 Conference End: 20110510.Conference Publication: (var.pagings)*, 73: April.

Not in PICO

Zhang, G.-D., Zou, D.-D., Wang, H., He, Y. & Huang, D. (2013) Value of contrast-enhanced ultrasound in diagnosis of liver metastases: Analysis of 55 cases. *World Chinese Journal of Digestology*, 21: 2849-2853.

Not in PICO

Zhang, Z., Chen, H. J., Yang, W. J., Bu, H., Wei, B., Long, X. Y., Fu, J., Zhang, R., Ni, Y. B. & Zhang, H. Y. (2010) Infantile hepatic hemangioendothelioma: A clinicopathologic study in a Chinese population. *World Journal of Gastroenterology*, 16: 4549-4557.

Not in PICO

Zhu, K., Dai, Z. & Zhou, J. (2013) Biomarkers for hepatocellular carcinoma: progression in early diagnosis, prognosis, and personalized therapy. *Biomarker Research*, 1: 10.

Narrative review

Review question:

Which investigations of symptoms of suspected liver cancer should be done with clinical responsibility retained by primary care?

Results**Literature search**

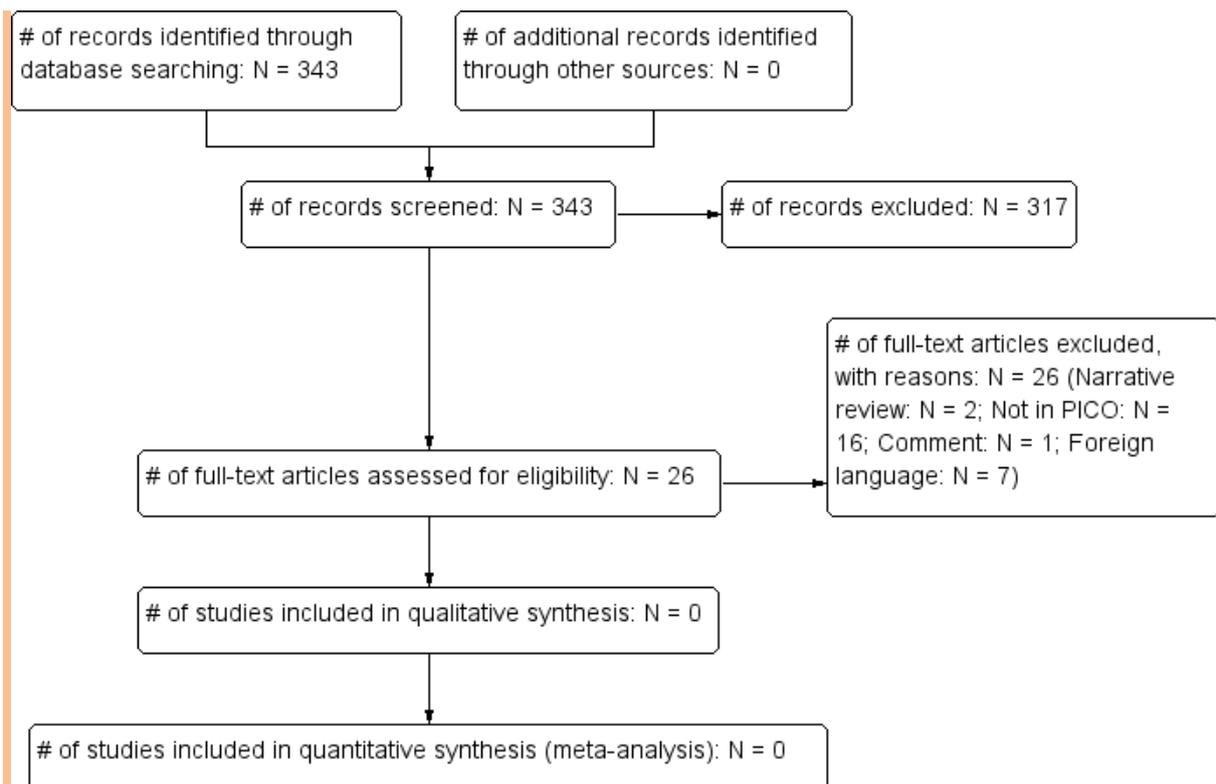
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	992	190	21/05/2013
<i>Premedline</i>	1980-2013	75	19	22/05/2013
<i>Embase</i>	1980-2013	1742	176	22/05/2013
<i>Cochrane Library</i>	1980-2013	182	2	22/05/2013
<i>Psychinfo</i>	1980-2013	1	0	22/05/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	108	10	22/05/2013

Total References retrieved (after de-duplication): 329

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-19/08/2014	23	2	19/08/2014
<i>Premedline</i>	5/2013-19/08/2014	73	5	19/08/2014
<i>Embase</i>	5/2013-19/08/2014	70	5	19/08/2014
<i>Cochrane Library</i>	5/2013-19/08/2014	92	0	19/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	5/2013-19/08/2014	25	4	19/08/2014

Total References retrieved (after de-duplication): 14



Study results

No evidence was identified pertaining to the diagnostic accuracy of ultrasound, CT, MRI or alpha feta protein in patients with suspected liver cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

(1984) Early detection of primary hepatocellular carcinoma - Alaska. *Journal of the American Medical Association*, 251: 1134.

Not in PICO

Abbasi, A., Bhutto, A. R., Butt, N. & Munir, S. M. (2012) Correlation of serum alpha fetoprotein and tumor size in hepatocellular carcinoma. *JPMA - Journal of the Pakistan Medical Association*, 62: 33-36.

Not in PICO

Ali, S., Shah, P., Shah, U. J., Shah, A., Zargar, S., Bashir, A., Dhar, S. & Ali, M. (2008) Primary fibrosarcoma of the liver: we don't know much: a case report. *Case Reports Gastroenterology*, 2: 384-389.

Not in PICO

Andrade, B., Alvarado, L., Zurita, M. & Andrade, S. (2013) Early and advanced gastric cancer: Clinical, endoscopy, histopathology and comparative study. *Journal of Gastroenterology and Hepatology*, 28: 652-653.

Not in PICO

- Andreana, L., Isgro, G., Pleguezuelo, M., Germani, G. & Burroughs, A. K. (2009) Surveillance and diagnosis of hepatocellular carcinoma in patients with cirrhosis. *World Journal of Hepatology*, 1: 48-61.
Narrative review
- Andrzejewska, M., Pacho, R. & Malkowski, P. (2006) [Radiological imaging of hepatocellular carcinoma]. [Review] [12 refs] [Polish]. *Przegląd Epidemiologiczny*, 60: 741-748.
Narrative review
- Aoki, K., Takayasu, K., Kawano, T., Muramatsu, Y., Moriyama, N., Wakao, F., Yamamoto, J., Shimada, K., Takayama, T. & Kosuge, T. (1993) Combined hepatocellular carcinoma and cholangiocarcinoma: clinical features and computed tomographic findings. *Hepatology*, 18: 1090-1095.
Not in PICO
- Aoyagi, Y., Yanagi, M. & Asakura, H. (1995) Early diagnosis of hepatocellular carcinoma by serum AFP and PIVKA-II analysis. [Japanese]. *Nihon Naika Gakkai zasshi*, The: 2003-2007.
In Japanese. Not enough information can be extracted, but don't think it is in PICO
- Aoyagi, Y. (1995) Carbohydrate-based measurements on alpha-fetoprotein in the early diagnosis of hepatocellular carcinoma. *Glycoconjugate Journal*, 12: 194-199.
Narrative review
- Aoyagi, Y., Mita, Y., Kuroiwa, T., Wakuri, N., Kawai, H., Kobayashi, M., Igarashi, M. & Suda, T. (2001) Alpha-fetoprotein and its fucosylation index in the early diagnosis of hepatocellular carcinoma. [Japanese]. *Nippon rinsho*, Japanese: 342-348.
In Japanese, not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Aoyagi, Y. & Kubota, T. (2005) Measurement of alpha-fetoprotein with L3 fraction in the early diagnosis of patients with hepatocellular carcinoma. [Japanese]. *Nippon rinsho*, Japanese: 625-628.
Not in PICO
- Aribas, B. K., Arda, K., Ciledag, N., Aktas, E., Yakut, F., Kavak, S., Sahin, G. & Kaygusuz, H. (2012) Accuracy and safety of percutaneous US-guided needle biopsies in specific focal liver lesions: comparison of large and small needles in 1300 patients. *Panminerva Medica*, 54: 233-239.
Not in PICO
- Arrigoni, A., Andriulli, A., Gindro, T., Piantino, P., Capussotti, L. & Rizzetto, M. (1988) Pattern analysis of serum alpha-fetoprotein in the early diagnosis of hepatocellular carcinoma in liver cirrhosis. *International Journal of Biological Markers*, 3: 172-176.
Not in PICO
- Aschoff, P., Plathow, C., Beyer, T., Lichy, M. P., Erb, G., Oksuz, M. O., Claussen, C. D. & Pfannenber, C. (2012) Multiphase contrast-enhanced CT with highly concentrated contrast agent can be used for PET attenuation correction in integrated PET/CT imaging. *European Journal of Nuclear Medicine & Molecular Imaging*, 39: 316-325.
Not in PICO
- Ashraf, S. J., Arya, S. C. & El-Sayed, M. (1986) A profile of primary hepatocellular carcinoma patients in the Gizan Area of Saudi Arabia. *Cancer*, 58: 2163-2168.
Not in PICO
- Asrih, M., Lenglet, S., Mach, F. & Montecucco, D. (2013) Alpha-fetoprotein: A controversial prognostic biomarker for small hepatocellular carcinoma. *World Journal of Gastroenterology*, 19: 328-330.
Narrative review
- Aube, C. & Lebigot, J. (2003) [Contrast ultrasonography: value in diagnosis and characterisation of hepatic tumors]. [Review] [28 refs] [French]. *Gastroenterologie Clinique et Biologique*, 27: Suppl-70.
Narrative review

- Ba-Ssalamah, A., Happel, B., Kettenbach, J., Dirisamer, A., Wrba, F., Langle, F. & Schima, W. (2004) [MRT of the liver. Clinical significance of nonspecific and liver-specific MRT contrast agents]. [Review] [39 refs] [German]. *Radiologe*, 44: 1170-1184.
Narrative review
- Ba, M. C., Long, H., Tang, Y. Q. & Cui, S. Z. (2012) GP73 expression and its significance in the diagnosis of hepatocellular carcinoma: a review. [Review]. *International Journal of Clinical & Experimental Pathology*, 5: 874-881.
Narrative review
- Ballesta, A. M., Calvet, X., Filella, X., Bruix, J., Bru, C., Molina, R. & Rodes, J. (1989) Alpha-fetoprotein in the early diagnosis of hepatocellular carcinoma. *The Journal of nuclear medicine and allied sciences*, 33: 39-41.
Narrative review
- Bartolozzi, C. (2012) Imaging diagnosis of suspected HCC lesions. *Cardiovascular and Interventional Radiology*, 35: S146-S147.
Narrative review
- Bauditz, J., Schade, T. & Wermke, W. (2007) [Sonographic diagnosis of hilar cholangiocarcinomas by the use of contrast agents]. [German]. *Ultraschall in der Medizin*, 28: 161-167.
Not in PICO
- Ben, H. L., Daghfous, M. H., Mami, A., Chammakhi-Jemli, C., Zouaoui, W., Saddoud, W., Miaoui, A., Kharrat, J., Ghorbal, A. & Sehili-Briki, S. (2007) [Imaging in the screening and diagnosis of hepatocellular carcinoma in cirrhosis liver in Tunisia. A series of 30 cases]. [French]. *Tunisie Medicale*, 85: 421-426.
Not in PICO
- Bernardino, M. E., Erwin, B. C., Steinberg, H. V., Baumgartner, B. R., Torres, W. E. & Gedgudas-McClees, R. K. (1986) Delayed hepatic CT scanning: increased confidence and improved detection of hepatic metastases. *Radiology*, 159: 71-74.
Not in PICO
- Bertino, G., Ardiri, A., Malaguarnera, M., Malaguarnera, G., Bertino, N. & Calvagno, G. S. (2012) Hepatocellular carcinoma serum markers. [Review]. *Seminars in Oncology*, 39: 410-433.
Narrative review
- Bhatavdekar, J. M., Trivedi, S. N., Desai, N. D., Balar, D. B., Patel, G. H. & Sheth, J. J. (1984) Tumor markers in primary and metastatic liver cancer: possible value in early detection and differentiation. *Indian Journal of Cancer*, 21: 95-98.
Not in PICO
- Bhosale, P., Szklaruk, J. & Silverman, P. M. (2006) Current staging of hepatocellular carcinoma: imaging implications. [Review] [22 refs]. *Cancer Imaging*, 6: 83-94.
Narrative review
- Biwole-Sida, M., Amvene, N., Oyono, E., Mbakop, A., Manfo, C., Tapko, J. B., Edzoa, T. & Ngu, K. B. (1992) [Screening of hepatocellular carcinoma in the middle of a high risk population in Cameroon]. [French]. *Annales de Gastroenterologie et d Hepatologie*, 28: 213-216.
Not in PICO
- Bjornsson, E., Ismael, S., Nejdert, S. & Kilander, A. (2003) Severe jaundice in Sweden in the new millennium: Causes, investigations, treatment and prognosis. *Scandinavian Journal of Gastroenterology*, 38: 86-94.
Not in PICO
- Block, T. M., Marrero, J., Gish, R. G., Sherman, M., London, W. T., Srivastava, S. & Wagner, P. D. (2008) The degree of readiness of selected biomarkers for the early detection of hepatocellular carcinoma: Notes from a recent workshop. *Cancer Biomarkers*, 4: 19-33.
Narrative review
- Borzio, M., Trete, D., Borzio, F., Ferrari, A. R., Bruno, S., Roncalli, M., Colloredo, G., Leandro, G., Oliveri, F. & Derenzini, M. (1998) Hepatocyte proliferation rate is a powerful parameter for

predicting hepatocellular carcinoma development in liver cirrhosis. *Molecular Pathology*, 51: 96-101.

Not in PICO

Bottelli, R., Tibballs, J., Hochhauser, D., Watkinson, A., Dick, R. & Burroughs, A. K. (1998) Ultrasound screening for hepatocellular carcinoma (HCC) in cirrhosis: the evidence for an established clinical practice. [Review] [34 refs]. *Clinical Radiology*, 53: 713-716.

Narrative review

Brancatelli, G., Federle, M. P., Grazioli, L. & Carr, B. I. (2002) Hepatocellular carcinoma in noncirrhotic liver: CT, clinical, and pathologic findings in 39 U.S. residents. *Radiology*, 222: 89-94.

Not in PICO

Bressler, E. L., Alpern, M. B. & Glazer, G. M. (1987) Hypervascular hepatic metastases: CT evaluation. *Radiology*, 162: 49-51.

Not in PICO

Bruno, S., Silini, E., Crosignani, A., Borzio, F., Leandro, G., Bono, F., Asti, M., Rossi, S., Larghi, A., Cerino, A., Podda, M. & Mondelli, M. U. (1997) Hepatitis C virus genotypes and risk of hepatocellular carcinoma in cirrhosis: a prospective study. *Hepatology*, 25: 754-758.

Not in PICO

Buadu, A. & Meyer, M. A. (2013) Small liver nodule detection with a high-frequency transducer in patients with chronic liver disease: report of 3 cases. *Journal of Ultrasound in Medicine*, 32: 355-359.

Not in PICO

Cabibbo, G. & Craxi, A. (2010) Epidemiology, risk factors and surveillance of hepatocellular carcinoma. [Review] [26 refs]. *European Review for Medical & Pharmacological Sciences*, 14: 352-355.

Narrative review

Catalano, O., Sandomenico, F., Nunziata, A., Vallone, P., Raso, M. M., Setola, S. V. & D'Errico, A. G. (2011) Source and clinical motivation of orders for contrast-enhanced sonography (CEUS) of the liver: A prospective single-center survey. *Journal of Ultrasound*, 14: 66-74.

Not in PICO

Caturelli, E., Solmi, L., Anti, M., Fusilli, S., Roselli, P., Andriulli, A., Fornari, F., Del Vecchio, B. C. & de, S., I (2004) Ultrasound guided fine needle biopsy of early hepatocellular carcinoma complicating liver cirrhosis: a multicentre study. *Gut*, 53: 1356-1362.

Not in PICO

Celli, N., Gaiani, S., Piscaglia, F., Zironi, G., Camaggi, V., Leoni, S., Righini, R. & Bolondi, L. (2007) Characterization of liver lesions by real-time contrast-enhanced ultrasonography. *European Journal of Gastroenterology & Hepatology*, 19: 3-14.

Not in PICO

Chalasani, N., Said, A., Ness, R., Hoen, H. & Lumeng, L. (1999) Screening for hepatocellular carcinoma in patients with cirrhosis in the United States: results of a national survey. *American Journal of Gastroenterology*, 94: 2224-2229.

Not in PICO

Cheng, H. T., Chang, Y. H., Chen, Y. Y., Lee, T. H., Tai, D. I. & Lin, D. Y. (2007) AFP-L3 in chronic liver diseases with persistent elevation of alpha-fetoprotein. *Journal of the Chinese Medical Association: JCMA*, 70: 310-317.

Not in PICO

Choi, B. I., Takayasu, K. & Han, M. C. (1993) Small hepatocellular carcinomas and associated nodular lesions of the liver: pathology, pathogenesis, and imaging findings. [Review] [89 refs]. *AJR. American Journal of Roentgenology*, 160: 1177-1187.

Narrative review

Choi, B. I. (2010) Advances of imaging for hepatocellular carcinoma. *Oncology*, 78: Suppl-52.

Narrative review

- Claudon, M., Dietrich, C. F., Choi, B. I., Cosgrove, D. O., Kudo, M., Nolsoe, C. P., Piscaglia, F., Wilson, S. R., Barr, R. G., Chammass, M. C., Chaubal, N. G., Chen, M. H., Clevert, D. A., Correas, J. M., Ding, H., Forsberg, F., Fowlkes, J. B., Gibson, R. N., Goldberg, B. B., Lassau, N., Leen, E. L. S., Mattrey, R. F., Moriyasu, F., Solbiati, L., Weskott, H. P. & Xu, H. X. (2013) Guidelines and Good Clinical Practice Recommendations for Contrast Enhanced Ultrasound (CEUS) in the Liver - Update 2012 A WFUMB-EFSUMB Initiative in Cooperation With Representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS. *Ultraschall in der Medizin*, 34: 11-29.
Guideline
- Claudon, M., Dietrich, C. F., Choi, B. I., Cosgrove, D. O., Kudo, M., Nolsoe, C. P., Piscaglia, F., Wilson, S. R., Barr, R. G., Chammass, M. C., Chaubal, N. G., Chen, M. H., Clevert, D. A., Correas, J. M., Ding, H., Forsberg, F., Fowlkes, J. B., Gibson, R. N., Goldberg, B. B., Lassau, N., Leen, E. L. S., Mattrey, R. F., Moriyasu, F., Solbiati, L., Weskott, H. P. & Xu, H. X. (2013) Guidelines and Good Clinical Practice Recommendations for Contrast Enhanced Ultrasound (Ceus) in the Liver - Update 2012 A Wfumb-Efsumb Initiative in Cooperation with Representatives of Afsumb, Aium, Asum, Flaus and Icus. *Ultrasound in Medicine and Biology*, 39: 187-210.
Guideline/duplicate
- Claudon, M., Dietrich, C. F., Choi, B. I., Cosgrove, D. O., Kudo, M., Nolsoe, C. P., Piscaglia, F., Wilson, S. R., Barr, R. G., Chammass, M. C., Chaubal, N. G., Chen, M. H., Clevert, D. A., Correas, J. M., Ding, H., Forsberg, F., Fowlkes, J. B., Gibson, R. N., Goldberg, B. B., Lassau, N., Leen, E. L. S., Mattrey, R. F., Moriyasu, F., Solbiati, L., Weskott, H. P. & Xu, H. X. (2013) Guidelines and Good Clinical Practice Recommendations for Contrast Enhanced Ultrasound (CEUS) in the Liver - Update 2012 A WFUMB-EFSUMB Initiative in Cooperation With Representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS. *Ultraschall in der Medizin*, 34: 11-29.
Guideline
- Clevert, D. A., Helck, A., Paprottka, P. M., Zengel, P., Trumm, C. & Reiser, M. F. (2012) [Ultrasound-guided image fusion with computed tomography and magnetic resonance imaging. Clinical utility for imaging and interventional diagnostics of hepatic lesions]. [German]. *Radiologe*, 52: 63-69.
Narrative review
- Colli, A., Cocciolo, M., Mumoli, N., Cesarini, L., Prisco, A., Gaffuri, I. & Martinez, E. (1998) Peripheral intrahepatic cholangiocarcinoma: ultrasound findings and differential diagnosis from hepatocellular carcinoma. *European Journal of Ultrasound*, 7: 93-99.
Not in PICO
- Colombo, M. (2009) Screening and diagnosis of hepatocellular carcinoma. [Review] [26 refs]. *Liver International*, 29: Suppl-7.
Narrative review
- Colombo, M. (2011) Small liver nodule (1-2 cm) in cirrhosis: Biopsy or follow up? *Hepatology International*, 5: 43-44.
Narrative review
- Colombo, S., Del, P. P., Zabbialini, G., Di Nolfo, M. A., Rapaccini, G. L., Benvegna, L., Borzio, F., Farinati, F., Zoli, M., Giannini, E. G., Caturelli, E., Chiaramonte, M. & Trevisani, F. (2011) Failure of ultrasound surveillance in detecting early stage hepatocellular carcinoma (HCC): Analysis of causes. *Hepatology*, 54: 1376A-1377A.
Not in PICO
- Coon, J. T., Rogers, G., Hewson, P., Wright, D., Anderson, R., Cramp, M., Jackson, S., Ryder, S., Price, A. & Stein, K. (2007) Surveillance of cirrhosis for hepatocellular carcinoma: systematic review and economic analysis. *Health Technology Assessment*, 11: 1-+.
Not in PICO
- Cottone, M., Marceno, M. P., Maringhini, A., Rinaldi, F., Russo, G., Sciarrino, E., Turri, M. & Pagliaro, L. (1983) Ultrasound in the diagnosis of hepatocellular carcinoma associated with cirrhosis. *Radiology*, 147: 517-519.
Not in PICO

- Cottone, M., Turri, M., Caltagirone, M., Maringhini, A., Sciarrino, E., Virdone, R., Fusco, G., Orlando, A., Marino, L. & Pagliaro, L. (1988) Early detection of hepatocellular carcinoma associated with cirrhosis by ultrasound and alfafetoprotein: a prospective study. *Hepato-Gastroenterology*, 35: 101-103.
Not in PICO
- Cottone, M., Turri, M., Caltagirone, M., Parisi, P., Orlando, A., Fiorentino, G., Virdone, R., Fusco, G., Grasso, R. & Simonetti, R. G. (1994) Screening for hepatocellular carcinoma in patients with Child's A cirrhosis: an 8-year prospective study by ultrasound and alfafetoprotein. *Journal of Hepatology*, 21: 1029-1034.
Not in PICO
- Cross, T. J. S., Ding, W., Richardson, P. D., Yousef, F., Palmer, D., Joekes, E., Farrell, C. & Evans, J. (2014) Surveillance leads to improved outcomes for patients with hepatocellular carcinoma (HCC). *Gut*, 63: A16.
Not in PICO
- Crowe, A., Knight, C. S., Jhala, D., Bynon, S. J. & Jhala, N. C. (2011) Diagnosis of metastatic fibrolamellar hepatocellular carcinoma by endoscopic ultrasound-guided fine needle aspiration. *Cytojournal*, 8: 2.
Not in PICO
- Crowe, D. R., Eloubeidi, M. A., Chhieng, D. C., Jhala, N. C., Jhala, D. & Eltoun, I. A. (2006) Fine-needle aspiration biopsy of hepatic lesions: computerized tomographic-guided versus endoscopic ultrasound-guided FNA. *Cancer*, 108: 180-185.
Not in PICO
- Curley, S. A., Izzo, F., Gallipoli, A., de, B. M., Cremona, F. & Parisi, V. (380) Identification and screening of 416 patients with chronic hepatitis at high risk to develop hepatocellular cancer. *Annals of Surgery*, 222: 375-380.
Not in PICO
- Das, B. C. & Khan, Z. R. (2013) Periampullary carcinoma: better prognosis with early pre-stenting referral to surgery. *Mymensingh Medical Journal: MMJ*, 22: 110-115.
Not in PICO
- Davila, J. A., Weston, A., Smalley, W. & El-Serag, H. B. (2007) Utilization of screening for hepatocellular carcinoma in the United States. *Journal of Clinical Gastroenterology*, 41: 777-782.
Not in PICO
- Davila, J. A., Morgan, R. O., Richardson, P. A., Du, X. L., McGlynn, K. A. & El-Serag, H. B. (2010) Use of surveillance for hepatocellular carcinoma among patients with cirrhosis in the United States. *Hepatology*, 52: 132-141.
Not in PICO
- De Pauw, F. F., Francque, S. M., Bogers, J. P., Duysburgh, I. K., Pelckmans, P. A., Van Marck, E. A. & Michielsen, P. P. (2007) Fine needle trucut biopsy in focal liver lesions: a reliable and safe method in identifying the malignant nature of liver lesions. *Acta Gastroenterologica Belgica*, 70: 1-5.
Not in PICO
- de Wilt, J. H., de Man, R. A., Lameris, J. S. & Ijzermans, J. N. (1996) [Focal nodular hyperplasia of the liver: assessment of diagnosis and treatment in 31 patients in 15 years]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 140: 18-22.
Not in PICO
- De, M. S., Tosti, M. E. & Mele, A. (2005) Screening for hepatocellular carcinoma. *Digestive & Liver Disease*, 37: 260-268.
Not in PICO
- de, S., I, Castellano, L., Calandra, M., Romano, M., Persico, M. & Del Vecchio-Blanco, C. (1995) Ultrasound-guided fine needle aspiration biopsy of portal vein thrombosis in liver cirrhosis: results in 15 patients. *Journal of Gastroenterology & Hepatology*, 10: 662-665.
Not in PICO

- Della, C. C. & Colombo, M. (2012) Surveillance for hepatocellular carcinoma. [Review]. *Seminars in Oncology*, 39: 384-398.
Narrative review
- Delorme, S. (2012) [Ultrasound in oncology: screening and staging]. [Review] [German]. *Internist*, 53: 271-281.
Narrative review
- Denies, L., Ernst, O., Sergent-Baudson, G., Duvet, S. & L'hermine, C. (2002) [Contribution of spiral CT for the early diagnosis of hepato-cellular carcinoma in cirrhotic patients]. [French]. *Journal de Radiologie*, 83: 635-640.
Not in PICO
- Di Bisceglie, A. M. (2004) Issues in screening and surveillance for hepatocellular carcinoma. [Review] [19 refs]. *Gastroenterology*, 127: Suppl-7.
Narrative review
- Donati, O. F., Fischer, M. A., Chuck, N., Hunziker, R., Weishaupt, D. & Reiner, C. S. (2013) Accuracy and confidence of Gd-EOB-DTPA enhanced MRI and diffusion-weighted imaging alone and in combination for the diagnosis of liver metastases. *European Journal of Radiology*, 82: 822-828.
Not in PICO
- Duchmann, J. C. & Joly, J. P. (1996) [Ambulatory ultrasound-guided puncture in abdominal tumoral pathology. Study of 131 cases]. [French]. *Gastroenterologie Clinique et Biologique*, 20: 258-262.
Not in PICO
- Dumas, O., Barthelemy, C. & Audigier, J. C. (1990) [Is detection of primary hepatocellular carcinoma in cirrhosis useful?]. [Review] [138 refs] [French]. *Gastroenterologie Clinique et Biologique*, 14: 715-726.
Narrative review
- Edoute, Y., Tibon-Fisher, O., Ben-Haim, S. A. & Malberger, E. (1991) Imaging-guided and nonimaging-guided fine needle aspiration of liver lesions: experience with 406 patients. *Journal of Surgical Oncology*, 48: 246-251.
Not in PICO
- Edoute, Y., Tibon-Fisher, O., Ben, H. S. & Malberger, E. (1992) Ultrasonically guided fine-needle aspiration of liver lesions. *American Journal of Gastroenterology*, 87: 1138-1141.
Not in PICO
- Edoute, Y., Osamah, H., Malberger, E., Yerushalmi, R., Tibon-Fisher, O. & Assy, N. (2001) Diagnostic accuracy of direct fine-needle aspiration of liver lesions: A prospective study of 107 patients in peripheral community center with limited technological capability. *Archives of Gastroenterohepatology*, 20: 19-24.
Not in PICO
- El-Aneed, A. & Banoub, J. (2006) Proteomics in the diagnosis of hepatocellular carcinoma: focus on high risk hepatitis B and C patients. [Review] [49 refs]. *Anticancer Research*, 26: 3293-3300.
Narrative review
- Ertle, J. M., Wichert, M., Kuper, R., Hilgard, P., Gerken, G. & Schlaak, J. (2011) Sensitivity and specificity of alpha-feto protein (AFP), lens culinaris agglutinin-reactive AFP (AFP-L3) and desgamma-carboxyprothrombin (DCP) as tumor markers in patients with hepatocellular carcinoma (HCC). *Journal of Hepatology*, 54: S385.
Not in PICO
- Fang, F., Wang, H.-Y. & Wu, X.-J. (2007) Significance of GPC3 protein in diagnosis of primary liver cancer. [Chinese]. *Academic Journal of Second Military Medical University*, 28: 568-570.
In Chinese. Not enough information can be extracted, but I don't think it is in PICO
- Federle, M. P. (2002) Use of radiologic techniques to screen for hepatocellular carcinoma. *Journal of Clinical Gastroenterology*, 35: Suppl-S100.
Narrative review

- Fenkel, J. M. & Navarro, V. J. (2011) Assessment of adherence to guidelines for hepatocellular carcinoma screening in HIV/HCV coinfecting patients. *Gastroenterology*, 140: S922.
Not in PICO
- Ferenci, P., Fried, M., Labrecque, D., Bruix, J., Sherman, M., Omata, M., Heathcote, J., Piratsivuth, T., Kew, M., Otegbayo, J. A., Zheng, S. S., Sarin, S., Hamid, S. S., Modawi, S. B., Fleig, W., Fedail, S., Thomson, A., Khan, A., Malfertheiner, P., Lau, G., Carillo, F. J., Krabshuis, J. & Le, M. A. (2010) Hepatocellular carcinoma (HCC): A global perspective. *Journal of Clinical Gastroenterology*, 44: 239-245.
Not in PICO
- Ferrucci, J. T. (1991) Liver tumor imaging. [Review] [25 refs]. *Cancer*, 67: Suppl-95.
Narrative review
- Fiegler, W., Schorner, W. & Felix, R. (1984) Value of sonography, computer tomography, hepatobiliary scintigraphy and nuclear magnetic tomography in diseases of the gallbladder and bile ducts. [German]. *Rontgen-Blatter; Zeitschrift fur Rontgen-Technik und medizinisch-wissenschaftliche Photographie*, 37: 327-332.
Narrative review
- Filmus, J. & Capurro, M. (2004) Glypican-3 and alphafetoprotein as diagnostic tests for hepatocellular carcinoma. [Review] [66 refs]. *Molecular Diagnosis*, 8: 207-212.
Narrative review
- Foley, W. D. & Quiroz, F. A. (2007) The role of sonography in imaging of the biliary tract. [Review] [45 refs]. *Ultrasound Quarterly*, 23: 123-135.
Narrative review
- Fornari, F., Civardi, G., Cavanna, L., Rossi, S., Buscarini, E., Di, S. M., Sbolli, G. & Buscarini, L. (1990) Ultrasonically guided fine-needle aspiration biopsy: a highly diagnostic procedure for hepatic tumors. *American Journal of Gastroenterology*, 85: 1009-1013.
Not in PICO
- Forner, A., Rodriguez de, L. C., Reig, M., Rimola, J. & Varela, M. (2008) [Early diagnosis of primary liver cancer: imaging versus genetics]. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 100: 423-429.
Narrative review
- Fracanzani, A. L., Burdick, L., Borzio, M., Roncalli, M., Bonelli, N., Borzio, F., Maraschi, A., Fiorelli, G. & Fargion, S. (2001) Contrast-enhanced Doppler ultrasonography in the diagnosis of hepatocellular carcinoma and premalignant lesions in patients with cirrhosis. *Hepatology*, 34: 1109-1112.
Not in PICO
- Friedman, M. L. & Esposito, F. S. (1980) Comparison of CT scanning and radionuclide imaging in liver disease. *Critical Reviews in Diagnostic Imaging*, 14: 143-189.
Narrative review
- Gervain, J. (2010) [Symptoms of hepatocellular carcinoma. Laboratory tests used for its diagnosis and screening]. [Hungarian]. *Orvosi Hetilap*, 151: 1415-1417.
Narrative review
- Giannelli, G. & Antonaci, S. (2006) New frontiers in biomarkers for hepatocellular carcinoma. *Digestive and Liver Disease*, 38: 854-859.
Narrative review
- Giannini, E. G., Erroi, V. & Trevisani, F. (2012) Effectiveness of alpha-fetoprotein for hepatocellular carcinoma surveillance: The return of the living-dead? *Expert Review of Gastroenterology and Hepatology*, 6: 441-444.
Not in PICO
- Gilmore, I. T., Burroughs, A., Murray-Lyon, I. M., Williams, R., Jenkins, D. & Hopkins, A. (1995) Indications, methods, and outcomes of percutaneous liver biopsy in England and Wales: an audit by the British Society of Gastroenterology and the Royal College of Physicians of London. *Gut*, 36:

- 437-441.
Not in PICO
- Giorgio, A., Calisti, G., Di, S. A., Farella, N., De, S. G., Scognamiglio, U. & Giorgio, V. (2011) Characterization of dysplastic nodules, early hepatocellular carcinoma and progressed hepatocellular carcinoma in cirrhosis with contrast-enhanced ultrasound. *Anticancer Research*, 31: 3977-3982.
Not in PICO
- Gish, R. G. (2014) Early detection of hepatocellular carcinoma through surveillance using biomarkers. *Gastroenterology and Hepatology*, 10: 121-123.
Narrative review
- Gohel, T., Dosanjh, G., Patel, C., Theethira, T., Dhingani, D. & Lankaala, P. (2012) A multicenter survey to determine hepatocellular carcinoma screening awareness among physicians. *American Journal of Gastroenterology*, 107: S172-S173.
Not in PICO
- Goulet, R. J., Jr., Seekri, I., Inman, M., Kopecky, K. K., Madura, J. A. & Grosfeld, J. L. (700) The diagnosis and definition of hepatic malignancies by use of arterial enhanced computerized tomographic scanning. *Surgery*, 108: 694-700.
Not in PICO
- Gowda, G. A. (2010) Human bile as a rich source of biomarkers for hepatopancreatobiliary cancers. [Review] [106 refs]. *Biomarkers in Medicine*, 4: 299-314.
Narrative review
- Gritzmann, N. (2003) Small hepatocellular carcinomas in patients with liver cirrhosis: potentials and limitations of contrast-enhanced power Doppler sonography. *European Journal of Gastroenterology & Hepatology*, 15: 881-883.
Narrative review
- Guyader, D., Gandon, Y., Sapey, T., Turlin, B., Mendler, M. H., Brissot, P. & Deugnier, Y. (1999) Magnetic resonance iron-free nodules in genetic hemochromatosis. *American Journal of Gastroenterology*, 94: 1083-1086.
Not in PICO
- Halvorsen, J. & Thompson, W. M. (1991) Imaging primary and metastatic cancer of the liver. *Seminars in Oncology*, 18: 111-122.
Narrative review
- Hamed, M., El-Etreby, S., Bahgat, M., Attia, M., Abdaziz, S., Salem, D. & Kamr, W. (2012) Is plasma proteasome level a reliable marker of hepatocellular carcinoma in hepatitis C virus related cirrhosis. *Journal of Hepatology*, 56: S281.
Not in PICO
- Haradome, H., Grazioli, L., Tinti, R., Morone, M., Motosugi, U., Sano, K., Ichikawa, T., Kwee, T. C. & Colagrande, S. (2011) Additional value of gadoxetic acid-DTPA-enhanced hepatobiliary phase MR imaging in the diagnosis of early-stage hepatocellular carcinoma: comparison with dynamic triple-phase multidetector CT imaging. *Journal of Magnetic Resonance Imaging*, 34: 69-78.
Not in PICO
- Hassett, M., Yopp, A. C. & Singal, A. G. (2013) Surveillance for hepatocellular carcinoma: how can we do better? *American Journal of the Medical Sciences*, 346: 308-313.
Narrative review
- He, Y. M., Wang, X. Y., Gao, S. D., Yu, L. Y., Lin, X. D. & Lin, L. W. (2005) Ultrasound-guided fine needle biopsy of intrahepatic nodules and low elevation of AFP in early diagnosis of hepatocellular carcinoma. *Hepatobiliary & Pancreatic Diseases International*, 4: 50-54.
Not in PICO
- Herszenyi, L., Farinati, F., Cecchetto, A., Marafin, C., de, M. N., Cardin, R. & Naccarato, R. (1995) Fine-needle biopsy in focal liver lesions: the usefulness of a screening programme and the role of

- cytology and microhistology. *Italian Journal of Gastroenterology*, 27: 473-478.
Not in PICO
- Herszenyi, L., Farinati, F., Cecchetto, A., Marafin, C., de, M. N., Cardin, R., Della, L. G. & Naccarato, R. (1995) [Ultrasound guided fine-needle aspiration biopsy in the diagnosis of hepatocellular carcinoma]. [Review] [50 refs] [Hungarian]. *Orvosi Hetilap*, 136: 1545-1549.
Not in PICO
- Hippo, Y., Watanabe, K., Watanabe, A., Midorikawa, Y., Yamamoto, S., Ihara, S., Tokita, S., Iwanari, H., Ito, Y., Nakano, K., Nezu, J.-I., Tsunoda, H., Yoshino, T., Ohizumi, I., Tsuchiya, M., Ohnishi, S., Makuuchi, M., Hamakubo, T., Kodama, T. & Aburatani, H. (2004) Identification of Soluble NH2-Terminal Fragment of Glypican-3 as a Serological Marker for Early-Stage Hepatocellular Carcinoma. *Cancer Research*, 64: 2418-2423.
Not in PICO
- Hirohashi, S., Tanaka, M., Uchida, H., Kitano, S., Ohmichi, R., Iwasaki, S. & Ohishi, H. (1991) [Utility of MRI in the early diagnosis of hepatocellular carcinoma--comparison with US, CT and DSA]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 49: 1805-1809.
In Japanese. Not enough information can be extracted to ascertain eligibility status
- Ho, C. S., McLoughlin, M. J., Tao, L. C., Blendis, L. & Evans, W. K. (1981) Guided percutaneous fine-needle aspiration biopsy of the liver. *Cancer*, 47: 1781-1785.
Not in PICO
- Hohmann, J., Albrecht, T., Oldenburg, A., Skrok, J. & Wolf, K. J. (2004) Liver metastases in cancer: detection with contrast-enhanced ultrasonography. [Review] [61 refs]. *Abdominal Imaging*, 29: 669-681.
Narrative review
- Hojo, A., Nakayama, H., Aramaki, O., Higaki, T., Moriguchi, M., Sugitani, M., Miura, K., Takeuchi, J., Nishiyama, R., Moriyama, M. & Takayama, T. (2013) Diagnostic value of open biopsy for malignant T-cell lymphoma of the liver. *International Surgery*, 98: 13-18.
Not in PICO
- Hojo, A., Nakayama, H., Aramaki, O., Higaki, T., Moriguchi, M., Sugitani, M., Miura, K., Takeuchi, J., Nishiyama, R., Moriyama, M. & Takayama, T. (2013) Diagnostic value of open biopsy for malignant T-cell lymphoma of the liver. *International Surgery*, 98: 13-18.
Not in PICO
- Holm, J. & Jacobsen, B. (1986) Accuracy of dynamic ultrasonography in the diagnosis of malignant liver lesions. *Journal of Ultrasound in Medicine*, 5: 1-4.
Not in PICO
- Hotta, N., Tagaya, T., Maeno, T., Ayada, M., Sato, K., Ishikawa, T., Okumura, A., Fukuzawa, Y. & Kakumu, S. (2005) Advanced dynamic flow imaging with contrast-enhanced ultrasonography for the evaluation of tumor vascularity in liver tumors. *Clinical Imaging*, 29: 34-41.
Not in PICO
- Hou, D. J., Rastegar, R., Harris, A. C., Klass, D., Yoshida, E., Ho, S. & Liu, D. M. (2012) Investigation of suspected hepatocellular carcinoma: A pictorial review of HCC and the 2010 revised American Association for the Study of Liver Disease (AASLD) criteria. *Journal of Vascular and Interventional Radiology*, 23: S145.
Narrative review
- Huijie, J. (2011) Functional computed tomography with perfusion imaging in the assessment of tumor vascularization in cirrhotic liver disease. *Hepatology International*, 5: 478-479.
Not in PICO
- Ichikawa, T. & Kumazaki, T. (2000) Clinical usefulness of computed tomography arteriography and computed tomography during arterial portography for the diagnosis of early and early advanced hepatocellular carcinoma. *Journal of Nippon Medical School = Nihon Ika Daigaku Zasshi*, 67: 105-109.
Not in PICO

- Ichikawa, T., Kitamura, T., Nakajima, H., Sou, H., Tsukamoto, T., Ikenaga, S. & Araki, T. (2002) Hypervascular hepatocellular carcinoma: can double arterial phase imaging with multidetector CT improve tumor depiction in the cirrhotic liver? *AJR.American Journal of Roentgenology*, 179: 751-758.
Not in PICO
- Inoue, Y., Lefor, A. T. & Yasuda, Y. (2012) Intrahepatic cholangiocarcinoma with sarcomatous changes. *Case Reports Gastroenterology*, 6: 1-4.
Not in PICO
- Ippolito, D., Sironi, S., Pozzi, M., Antolini, L., Ratti, L., Meloni, F., Invernizzi, F., Valsecchi, M. G. & Fazio, F. (2008) Perfusion computed tomographic assessment of early hepatocellular carcinoma in cirrhotic liver disease: initial observations. *Journal of Computer Assisted Tomography*, 32: 855-858.
Not in PICO
- Ippolito, D., Sironi, S., Pozzi, M., Antolini, L., Invernizzi, F., Ratti, L., Leone, E. B. & Fazio, F. (2010) Perfusion CT in cirrhotic patients with early stage hepatocellular carcinoma: Assessment of tumor-related vascularization. *European Journal of Radiology*, 73: 148-152.
Not in PICO
- Irshad, A., Anis, M. & Ackerman, S. J. (2012) Current role of ultrasound in chronic liver disease: surveillance, diagnosis and management of hepatic neoplasms. [Review]. *Current Problems in Diagnostic Radiology*, 41: 43-51.
Narrative review
- Ito, K., Choji, T., Nakada, T., Nakanishi, T., Kurokawa, F. & Okita, K. (1993) Multislice dynamic MRI of hepatic tumors. *Journal of Computer Assisted Tomography*, 17: 390-396.
Not in PICO
- Ito, K., Fujita, T., Shimizu, A., Koike, S., Sasaki, K., Matsunaga, N., Hibino, S. & Yuhara, M. (2004) Multiarterial phase dynamic MRI of small early enhancing hepatic lesions in cirrhosis or chronic hepatitis: Differentiating between hypervascular hepatocellular carcinomas and pseudolesions. *American Journal of Roentgenology*, 183: 699-705.
Not in PICO
- Iwamura, K. (1982) Clinicopathological aspects of primary hepatocellular carcinoma occurring in patients with liver cirrhosis. *The Tokai journal of experimental and clinical medicine*, 7: 589-605.
Not in PICO
- Iwamura, K. (1982) A contribution to early diagnosis of primary hepatic cell carcinoma occurring in patients with liver cirrhosis. *Tokai Journal of Experimental and Clinical Medicine*, 7: 397-411.
Not in PICO
- Iwamura, K. (1988) [Capsule formation in hepatocellular carcinomas arising from liver cirrhosis]. [German]. *Leber, Magen, Darm*, 18: 56-60.
Not in PICO
- Izzo, F., Cremona, F., Ruffolo, F., Palaia, R., Parisi, V. & Curley, S. A. (1998) Outcome of 67 patients with hepatocellular cancer detected during screening of 1125 patients with chronic hepatitis. *Annals of Surgery*, 227: 513-518.
Not in PICO
- Jacobsen, G. K., Gammelgaard, J. & Fuglo, M. (1983) Coarse needle biopsy versus fine needle aspiration biopsy in the diagnosis of focal lesions of the liver. Ultrasonically guided needle biopsy in suspected hepatic malignancy. *Acta Cytologica*, 27: 152-156.
Not in PICO
- Jakab, Z. (2010) [Diagnostic imaging for the screening of hepatocellular carcinoma]. [Review] [29 refs] [Hungarian]. *Orvosi Hetilap*, 151: 1083-1090.
Narrative review
- Jang, J. Y., Kim, J. N., Jeong, S. W., Choo, J. W., Kwon, S. H., Lim, D. S., Park, E. J., Lee, S. H., Kim, S. G., Cha, S.-W., Kim, Y. S., Cho, Y. D., Kim, H. S., Kim, B. S., Choi, D. & Jin, S. Y. (2012) The comparison

- of radiologic findings and histopathology for the diagnosis of hepatocellular carcinoma. *Hepatology*, 56: 484A.
Not in PICO
- Jaray, B., Turanyi, E., Szalay, K. & Winternitz, T. (1997) [Ultrasound-guided fine-needle aspiration biopsy of focal liver lesions]. [Hungarian]. *Orvosi Hetilap*, 138: 1731-1736.
Not in PICO
- Jenkins, D., Gilmore, I. T., Doel, C. & Gallivan, S. (1995) Liver biopsy in the diagnosis of malignancy. *QJM*, 88: 819-825.
Not in PICO
- Jiang, J., Wu, C., Shen, Y., Xu, B., Zheng, X., Li, X. & Xu, N. (2011) Clinical application of determining serum AFP-IgM complexes for diagnosis of small hepatocellular carcinoma. *Anticancer Research*, 31: 687-691.
Not in PICO
- Johnson, C. D. (1993) Magnetic resonance imaging of the liver: current clinical applications. [Review] [55 refs]. *Mayo Clinic Proceedings*, 68: 147-156.
Narrative review
- Joo, I. & Lee, J. M. (2013) Imaging bile duct tumors: pathologic concepts, classification, and early tumor detection. *Abdominal Imaging*, 38: 1334-1350.
Narrative review
- Kameda, Y. & Shinji, Y. (1992) Early detection of hepatocellular carcinoma by laparoscopy: Yellow nodules as diagnostic indicators. *Gastrointestinal Endoscopy*, 38: 554-559.
Narrative review
- Kanda, T., Yoshikawa, T., Ohno, Y., Kanata, N., Koyama, H., Takenaka, D. & Sugimura, K. (2012) CT hepatic perfusion measurement: comparison of three analytic methods. *European Journal of Radiology*, 81: 2075-2079.
Not in PICO
- Kanematsu, T., Sonoda, T., Takenaka, K., Matsumata, T., Sugimachi, K. & Inokuchi, K. (1985) The value of ultrasound in the diagnosis and treatment of small hepatocellular carcinoma. *British Journal of Surgery*, 72: 23-25.
Not in PICO
- Kanmura, S., Uto, H., Kusumoto, K., Ishida, Y., Hasuike, S., Nagata, K. & et al (2007) Early detection of hepatocellular carcinoma. *Liver Transplantation*, 13: 1196-1197.
Not in PICO
- Kaude, J. V., Felman, A. H. & Hawkins, I. F., Jr. (1980) Ultrasonography in primary hepatic tumors in early childhood. *Pediatric Radiology*, 9: 77-83.
Not in PICO
- Kchaou-Ouakaa, A., Belhadjrik, N., Elloumi, H., Gargouri, D., Kochlef, A., Kilani, A., Romani, M., Kharrat, J. & Ghorbel, A. (2007) [Surveillance for hepatocellular carcinoma: does it work?]. [French]. *Tunisie Medicale*, 85: 866-870.
Not in PICO
- Kempf, J. S., Hudak, R., Abdel-Dayem, H. M., Freiman, H. & Cheung, Y. (1996) Tl-201 chloride SPECT imaging of hepatocellular carcinoma. *Clinical Nuclear Medicine*, 21: 953-957.
Not in PICO
- Khong, P. L., Chau, M. T., Fan, S. T. & Leong, L. L. (1999) Ultrasound contrast agent Levovist in colour Doppler sonography of hepatocellular carcinoma in Chinese patients. *Australasian Radiology*, 43: 156-159.
Not in PICO
- Kim, D. Y., Kim, J. W., Kuromatsu, R., Ahn, S. H., Torimura, T. & Sherman, M. (2011) Controversies in surveillance and early diagnosis of hepatocellular carcinoma. *Oncology*, 81: 56-60.
Narrative review

- Kim, H. C., Kim, T. K., Sung, K. B., Yoon, H. K., Kim, P. N., Ha, H. K., Kim, A. Y., Kim, H. J. & Lee, M. G. (2003) Preoperative evaluation of hepatocellular carcinoma: combined use of CT with arterial portography and hepatic arteriography. *AJR.American Journal of Roentgenology*, 180: 1593-1599.
Not in PICO
- Kim, J. H., Kim, M. J., Suh, S. H., Chung, J. J., Yoo, H. S. & Lee, J. T. (2002) Characterization of focal hepatic lesions with ferumoxides-enhanced MR imaging: utility of T1-weighted spoiled gradient recalled echo images using different echo times. *Journal of Magnetic Resonance Imaging*, 15: 573-583.
Not in PICO
- Kim, S. H., Na, K., Kim, D. Y., Choi, G. H., Ahn, S. H., Choi, J. S., Kim, K. S. & Back, Y. K. (2011) The validation of HCE1 as tumor marker in HCC with low AFP or pivka-II levels - Preliminary results. *HPB*, 13: 85.
Not in PICO
- Klein, H. M. & Gunther, R. W. (2004) Carcinoma of the gallbladder and biliary ducts - What is the value of CT, MRI, and magnetic resonance cholangiography?. [German]. *Chirurgische Gastroenterologie Interdisziplinär*, 20: 250-258.
Narrative review
- Kobayashi, S., Kim, S. R., Imoto, S., Ando, K., Hirakawa, M., Saito, J., Fukuda, K., Otono, Y., Sakaki, M., Tsuchida, S., Kim, S. K., Hayashi, Y., Nakano, M. & Kudo, M. (2012) Histopathological diagnosis of early HCC through biopsy: efficacy of victoria blue and cytokeratin 7 staining. *Digestive Diseases*, 30: 574-579.
Not in PICO
- Kojiro, M., Wanless, I. R., Alves, V., Badve, S., Balabaud, C., Bedosa, P., Bhathal, P., Bioulac-Sage, P., Brunt, E. M., Burt, A. D., Craig, J. R., Dhillion, A., Ferrell, L., Geller, S. A., Goodman, Z. D., Gouw, A. S. H., Guido, M., Guindi, M., Hytiroglou, P., Kage, M., Kondo, F., Kudo, M., Lauwers, G. Y., Nakano, M., Paradis, V., Park, Y.-N., Quaglia, A., Roncalli, M., Roskams, T., Ruebner, B., Sakamoto, M., Saxena, R., Theise, N. D., Thung, S. & Taniakos, D. (2009) Pathologic diagnosis of early hepatocellular carcinoma: A report of the International Consensus Group for Hepatocellular Neoplasia. *Hepatology*, 49: 658-664.
Not in PICO
- Kolligs, F. T., Zech, C. J., Schonberg, S. O., Schirral, J., Thasler, W., Graebl, C., Beuers, U., Wilkowskil, R., Jacobs, T., Bock, S., Berster, J., Heinerann, V. & Schafer, C. (2008) Interdisciplinary diagnosis of and therapy for cholangiocarcinoma. *Zeitschrift für Gastroenterologie*, 46: 58-68.
Narrative review
- Kudo, M. (2005) Early detection and curative treatment of early-stage hepatocellular carcinoma. [Review] [31 refs]. *Clinical Gastroenterology & Hepatology*, 3: Suppl-8.
Narrative review
- Kudo, M., Hatanaka, K., Inoue, T. & Maekawa, K. (2010) Depiction of portal supply in early hepatocellular carcinoma and dysplastic nodule: value of pure arterial ultrasound imaging in hepatocellular carcinoma. *Oncology*, 78: Suppl-7.
Not in PICO
- Kudo, M. (2010) Will Gd-EOB-MRI change the diagnostic algorithm in hepatocellular carcinoma? *Oncology*, 78: 87-93.
Narrative review
- Kudo, M. (2011) Diagnostic imaging of hepatocellular carcinoma: recent progress. [Review]. *Oncology*, 81: Suppl-85.
Narrative review
- Kung, K., Lam, A. & Li, P. K. T. (2004) Screening in chronic hepatitis B carriers - A retrospective study in a primary care clinic. *Hong Kong Practitioner*, 26: 221-227.
Not in PICO

- Kuwahara, T., Sakai, T., Majima, Y., Hirai, K. & Tanikawa, K. (1993) Serial changes in serum alpha-fetoprotein prior to detection of hepatocellular carcinoma in liver cirrhosis. *Hepato-Gastroenterology*, 40: 347-351.
Not in PICO
- Laurent, V., Mathias, J., Ganne, P. A., Bruot, O. & Regent, D. (2008) [Diagnostic approach for suspected benign tumor of the liver]. [French]. *Gastroenterologie Clinique et Biologique*, 32: t-93.
Not in PICO
- Lee, H.-S., Chung, Y. H. & Kim, C. Y. (1991) Specificities of serum alpha-fetoprotein in HBsAg+ and HBsAg- patients in the diagnosis of hepatocellular carcinoma. *Hepatology*, 14: 68-72.
Not in PICO
- Lee, S. W., Kim, H. J., Park, J. H., Park, D. I., Cho, Y. K., Sohn, C. I., Jeon, W. K. & Kim, B. I. (2010) Clinical usefulness of 18F-FDG PET-CT for patients with gallbladder cancer and cholangiocarcinoma. *Journal of Gastroenterology*, 45: 560-566.
Not in PICO
- Lee, W. J. (2005) [Imaging diagnosis of hepatocellular carcinoma]. [Review] [45 refs] [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 45: 234-246.
Narrative review
- Leerapun, A., Suravarapu, S. V., Bida, J. P., Clark, R. J., Sanders, E. L., Mettler, T. A., Stadheim, L. M., Aderca, I., Moser, C. D., Nagorney, D. M., LaRusso, N. F., de Groen, P. C., Menon, K. V., Lazaridis, K. N., Gores, G. J., Charlton, M. R., Roberts, R. O., Therneau, T. M., Katzmann, J. A. & Roberts, L. R. (2007) The utility of Lens culinaris agglutinin-reactive alpha-fetoprotein in the diagnosis of hepatocellular carcinoma: evaluation in a United States referral population. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*, 5: 394-402.
Not in PICO
- Lemoine, A., Azoulay, D., Jezequel-Cuer, M. & Debuire, B. (1999) [Hepatocellular carcinoma]. [Review] [71 refs] [French]. *Pathologie Biologie*, 47: 903-910.
Narrative review
- Lencioni, R., Della, P. C., Bruix, J., Majno, P., Grazioli, L., Morana, G., Filippone, A., Laghi, A. & Bartolozzi, C. (2005) Clinical management of hepatic malignancies: ferucarbotran-enhanced magnetic resonance imaging versus contrast-enhanced spiral computed tomography. *Digestive Diseases & Sciences*, 50: 533-537.
Not in PICO
- Lencioni, R. & European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) (2006) Impact of European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines on the use of contrast agents in liver ultrasound. *European Radiology*, 16: 1610-1613.
Narrative review
- Lencioni, R., Crocetti, L., Della Pina, M. C. & Cioni, D. (2008) Guidelines for imaging focal lesions in liver cirrhosis. [Review] [52 refs]. *Expert review of gastroenterology & hepatology*, 2: 697-703.
Narrative review
- Lencioni, R. (2010) Surveillance and early diagnosis of hepatocellular carcinoma. *Digestive & Liver Disease*, 42: Suppl-7.
Narrative review
- Leone, N. & Rizzetto, M. (2005) [Screening for hepatocellular carcinoma]. [Review] [84 refs] [Italian]. *Minerva Medica*, 96: 95-108.
Narrative review
- Li, J.-P., Zhao, D.-L., Jiang, H.-J., Huang, Y.-H., Li, D.-Q., Wan, Y., Liu, X.-D. & Wang, J.-E. (2011) Assessment of tumor vascularization with functional computed tomography perfusion imaging in patients with cirrhotic liver disease. *Hepatobiliary and Pancreatic Diseases International*, 10: 43-

49.

Not in PICO

Li, P., Zhai, Y., Liu, H., Lv, F.-D., Li, N. & Ding, H.-G. (2010) Diagnostic value of serum AFP alone or in combination with glypican 3, VEGF or IGF-II for patients with primary hepatocellular carcinoma. [Chinese]. *World Chinese Journal of Digestology*, 18: 2702-2706.

Not in PICO

Li, X., Wu, K. & Fan, D. (2009) Serum Golgi phosphoprotein 2 level: A better marker than alpha-fetoprotein for diagnosing early hepatocellular carcinoma (*Hepatology* (2009) 50, 1, (325) DOI:10.1002/hep.23028). *Hepatology*, 50: 1682.

Comment

Li, Y. L., Ma, H. B., Guo, J. X., Shi, J. B., Xu, J., Liu, A. X., Yang, L. H., Li, B. A. & Mao, Y. L. (2008) The studies on early warning of Lens culinaris-reactive alpha-Fetoprotein (AFP-L3) detecting in primary hepatocellular carcinoma. [Chinese]. *Zhonghua shi yan he lin chuang bing du xue za zhi = Zhonghua shiyan he linchuang bingduxue zazhi = Chinese journal of experimental and clinical virology*, 22: 336-338.

Not in PICO

Liaw, Y. F., Tai, D. I., Chu, C. M., Lin, D. Y., Sheen, I. S., Chen, T. J. & Pao, C. C. (1986) Early detection of hepatocellular carcinoma in patients with chronic type B hepatitis. A prospective study. *Gastroenterology*, 90: 263-267.

Not in PICO

Lilford, R. J., Bentham, L., Girling, A., Litchfield, I., Lancashire, R., Armstrong, D., Jones, R., Marteau, T., Neuberger, J., Gill, P., Cramb, R., Olliff, S., Arnold, D., Khan, K., Armstrong, M. J., Houlihan, D. D., Newsome, P. N., Chilton, P. J., Moons, K. & Altman, D. (2013) Birmingham and Lambeth Liver Evaluation Testing Strategies (BALETS): a prospective cohort study. *Health Technology Assessment*, 17: 1-+.

Same data as other included Lilford paper

Lilford, R. J., Bentham, L. M., Armstrong, M. J., Neuberger, J. & Girling, A. J. (2013) What is the best strategy for investigating abnormal liver function tests in primary care? Implications from a prospective study. *BMJ Open*, 3.

Asked Willie 9/1290 had cancer, but these may be known cancers (4 metastatic), i.e. patients selected who LFTs done to

Limaye, A. R. & Cabrera, R. (2010) Imaging of hepatocellular carcinoma and early diagnosis. [Review]. *Minerva Medica*, 101: 395-404.

Narrative review

Lin, B. P., Chu, J. M. & Rose, R. A. (1987) Ultrasound-guided fine needle aspiration biopsy of the liver. *Pathology*, 19: 173-177.

Not in PICO

Liu, W.-Y., Jin, Y., Rong, R.-H., Ta, X. & Zhu, X.-S. (2003) Multi-phase helical CT in diagnosis of early hepatocellular carcinoma. *Hepatobiliary and Pancreatic Diseases International*, 2: 73-76.

Not in PICO

Liu, X., Wan, X., Li, Z., Lin, C., Zhan, Y. & Lu, X. (2011) Golgi protein 73(GP73), a useful serum marker in liver diseases. *Clinical Chemistry and Laboratory Medicine*, 49: 1311-1316.

Not in PICO

Liu, Y., Wang, X. Q., Jiang, K., Zhang, W. Z. & Dong, J. H. (2014) The Diagnostic Value of Tumor Biomarkers for Detecting Hepatocellular Carcinoma Accompanied by Portal Vein Tumor Thrombosis. *Cell Biochemistry and Biophysics*, 69: 455-459.

Not in PICO

Lok, A. S., Sterling, R. K., Everhart, J. E., Wright, E. C., Hoefs, J. C., Di Bisceglie, A. M., Morgan, T. R., Kim, H. Y., Lee, W. M., Bonkovsky, H. L., Dienstag, J. L. & HALT, C. (2010) Des-gamma-carboxy prothrombin and alpha-fetoprotein as biomarkers for the early detection of hepatocellular

- carcinoma. *Gastroenterology*, 138: 493-502.
Not in PICO
- Luo, W., Numata, K., Morimoto, M., Nozaki, A., Nagano, Y., Sugimori, K., Zhou, X. & Tanaka, K. (2009) Clinical utility of contrast-enhanced three-dimensional ultrasound imaging with Sonazoid: findings on hepatocellular carcinoma lesions. *European Journal of Radiology*, 72: 425-431.
Not in PICO
- Ma, Y., Zhang, X. L., Li, X. Y., Zhang, L., Su, H. H. & Zhan, C. Y. (2008) Value of computed tomography and magnetic resonance imaging in diagnosis and differential diagnosis of small hepatocellular carcinoma. [Chinese]. *Nan fang yi ke da xue xue bao = Journal of Southern Medical University*, 28: 2235-2238.
Not in PICO
- MacKinnon, J. & Orellana, P. (1985) [The neoplastic liver. Scintigraphy or echotomography? Experience in 58 patients with clinically suspected hepatic neoplasm]. [Spanish]. *Revista Medica de Chile*, 113: 661-664.
Not in PICO
- Maier, K. P. (2002) [Hepatocellular carcinoma: risk groups--screening]. [Review] [23 refs] [German]. *Praxis*, 91: 1380-1386.
Narrative review
- Mandai, M., Koda, M., Matono, T., Nagahara, T., Sugihara, T., Ueki, M., Ohyama, K. & Murawaki, Y. (2011) Assessment of hepatocellular carcinoma by contrast-enhanced ultrasound with perfluorobutane microbubbles: comparison with dynamic CT. *British Journal of Radiology*, 84: 499-507.
Not in PICO
- Maringhini, A., Cottone, M., Sciarrino, E., Marceno, M. P., La, S. F., Rinaldi, F. & Pagliaro, L. (1984) Ultrasonographic and radionuclide detection of hepatocellular carcinoma in cirrhotics with low alpha-fetoprotein levels. *Cancer*, 54: 2924-2926.
Not in PICO
- Marinucci, G., Muglia, M. & Di, G. C. (1981) Early detection of developing hepatocellular carcinoma by means of determination of alpha fetoprotein (RIA). [Italian]. *Giornale Italiano di Oncologia*, 1: 161-162.
Unavailable, but I think it is not in PICO
- Marrero, J. A. (2005) Screening tests for hepatocellular carcinoma. [Review] [97 refs]. *Clinics in Liver Disease*, 9: 235-251.
Narrative review
- Massarweh, N. N., Park, J. O., Bruix, J., Yeung, R. S., Etzioni, R. B., Symons, R. G., Baldwin, L. M. & Flum, D. R. (2011) Diagnostic imaging and biopsy use among elderly medicare beneficiaries with hepatocellular carcinoma. *Journal of oncology practice/American Society of Clinical Oncology*, 7: 155-160.
Not in PICO
- Matsuda, H., Abe, K. & Freeny, P. C. (1996) Utility of bolus dynamic CT for the detection of hypervascular malignant hepatic tumors: mainly referring to the comparison with delayed phase contrast-enhanced CT. [Japanese]. *Nihon Igaku Hoshasen Gakkai zasshi*, Nippon: 167-172.
Not in PICO
- Matsushiro, Y., Ebara, M., Ohto, M. & Kondo, F. (1993) [Usefulness of percutaneous biopsy under sonographic control and histological examination in the early diagnosis of hepatocellular carcinoma]. [Japanese]. *Nippon Shokakibyō Gakkai Zasshi - Japanese Journal of Gastroenterology*, 90: 655-664.
Not in PICO
- Matsutani, S., Fukuzawa, T., Ebara, M. & Ohto, M. (1994) [Ultrasonography in the diagnosis of liver cirrhosis]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 52: 56-62.
Narrative review

- McGahan, J. P., Bishop, J., Webb, J., Howell, L., Torok, N., Lamba, R. & Corwin, M. T. (2013) Role of FNA and Core Biopsy of Primary and Metastatic Liver Disease. *International Journal of Hepatology*, 2013: 174103.
Not in PICO
- McMahon, B. J. (2008) Implementing evidenced-based practice guidelines for the management of chronic hepatitis B virus infection. *American Journal of Medicine*, 121: Suppl-52.
Narrative review
- McMahon, B. J. (2014) - Chronic hepatitis B virus infection. [Review]. - *Medical Clinics of North America*, 98: 39-54.
Narrative review
- Messner, M., Deugnier, Y., Bernard-Griffiths, I., Delamaire, D., Estable, P., Friguet, J. L., Le, G. M., Brissot, P. & Bourel, M. (1985) [Value of ultrasound-guided cytopuncture in the diagnosis of tumors in cirrhosis. Study of 29 cases]. [French]. *Gastroenterologie Clinique et Biologique*, 9: 42-46.
Not in PICO
- Messner, M., Deugnier, Y. & Bernard-Griffiths, I. (1985) Value of fine needle aspiration biopsy with ultrasound guidance in the diagnosis of hepatic tumors associated with cirrhosis. [French]. *Gastroenterologie Clinique et Biologique*, 9: 42-46.
Not in PICO
- Michielsen, P. P., Duysburgh, I. K., Francque, S. M., Van der Planken, M., Van Marck, E. A. & Pelckmans, P. A. (1998) Ultrasonically guided fine needle puncture of focal liver lesions. Review and personal experience. *Acta Gastroenterologica Belgica*, 61: 158-163.
Not in PICO
- Midia, M., Ruo, L., Landers, S. & Midia, R. (2013) Role of IR in obtaining tissue diagnosis in patients with suspected biliary lesions and inconclusive endoscopic biopsy. *Journal of Vascular and Interventional Radiology*, 24: 145.
Not in PICO
- Miller, J. C., Hahn, P. F., Chung, R. T., Thrall, J. H. & Lee, S. I. (2008) Screening for hepatocellular carcinoma in cirrhotic patients. *Journal of the American College of Radiology*, 5: 1012-1014.
Not in PICO
- Mito, M., Kusano, M. & Kohno, T. (1989) [Early liver cancer--definition, diagnosis and treatment]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 47: 1121-1129.
In Japanese. Not enough information can be extracted to ascertain eligibility status, but I think it is a narrative review
- Moehler, M., Voigt, J., Kastor, M., Heil, M., Sengespeick, C., Biesterfeld, S., Dippold, W., Kanzler, S. & Galle, P. R. (2011) Endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) as primary diagnostic tool for unclear lesions in the upper gastrointestinal tract. *Deutsche Medizinische Wochenschrift*, 136: 303-308.
Not in PICO
- Molina, R., Bosch, X., Auge, J. M., Filella, X., Escudero, J. M., Molina, V., Sole, M. & Lopez-Soto, A. (2012) Utility of serum tumor markers as an aid in the differential diagnosis of patients with clinical suspicion of cancer and in patients with cancer of unknown primary site. *Tumor Biology*, 33: 463-474.
Not in PICO
- Moriya, S., Morimoto, M., Numata, K., Nozaki, A., Shimoyama, Y., Kondo, M., Nakano, M., Maeda, S. & Tanaka, K. (2013) Fucosylated fraction of alpha-fetoprotein as a serological marker of early hepatocellular carcinoma. *Anticancer Research*, 33: 997-1001.
Not in PICO
- Moriyama, N. (1995) [Early diagnosis of hepatocellular carcinoma using computed tomography and magnetic resonance imaging]. [Review] [4 refs] [Japanese]. *Nippon Naika Gakkai Zasshi - Journal*

- of Japanese Society of Internal Medicine, 84: 1997-2002.
Narrative review
- Murakami, K. (2011) FDG-PET for hepatobiliary and pancreatic cancer: Advances and current limitations. *World Journal of Clinical Oncology*, 2: 229-236.
Narrative review
- Murakami, T., Mochizuki, K. & Nakamura, H. (2001) Imaging evaluation of the cirrhotic liver. [Review] [67 refs]. *Seminars in Liver Disease*, 21: 213-224.
Narrative review
- Murakami, T., Hori, M., Kim, T., Kawata, S., Abe, H. & Nakamura, H. (2004) Multidetector row CT and MR imaging in diagnosing hepatocellular carcinoma. [Review] [62 refs]. *Intervirolgy*, 47: 209-226.
Narrative review
- Muramatsu, Y., Nawano, S., Moriyama, N. & Takayasu, K. (1991) [MR image of early hepatocellular carcinoma and hepatocellular carcinoma with early components]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 49: 1815-1820.
Not in PICO
- Muramatsu, Y., Nawano, S., Takayasu, K., Moriyama, N., Yamada, T., Yamasaki, S. & Hirohashi, S. (1991) Early hepatocellular carcinoma: MR imaging. *Radiology*, 181: 209-213.
Not in PICO
- Murata, K., Shiraki, K., Kawakita, T., Yamamoto, N., Okano, H., Sakai, T., Ohmori, S., Deguchi, M., Shimizu, A. & Nakano, T. (2003) Hepatocellular carcinoma presenting with obstructive jaundice: a clinicopathological study of eight cases. *Hepato-Gastroenterology*, 50: 2057-2060.
Not in PICO
- Murray, M. J. & Nicholson, J. C. (2011) -Fetoprotein. *Archives of Disease in Childhood Education & Practice*, 96: 141-147.
Narrative review
- N'Dri, K., D'Horpock, A. F., Konan, A., Attia, A., Gbazi, G. C., Mensah, G. D. & Abby, B. C. (1996) [Ultrasonically guided fine needle biopsy in the diagnosis of malignant liver tumors]. [French]. *Medecine Tropicale*, 56: 51-53.
Not in PICO
- Nishio, H., Sakuma, T. & Nakamura, S. (1985) Diagnostic value of liver function tests in the detection of hepatic metastases in lung cancer patients. [Japanese]. *Japanese Journal of Lung Cancer*, 25: 609-615.
Not in PICO
- Noone, T. C., Semelka, R. C., Balci, N. C. & Graham, M. L. (1999) Common occurrence of benign liver lesions in patients with newly diagnosed breast cancer investigated by MRI for suspected liver metastases. *Journal of Magnetic Resonance Imaging*, 10: 165-169.
Not in PICO
- Oancea, R., Georgescu, S., Dumitrescu, M., Antonescu, S. & Timis, E. (1986) [Comparative study of the value of the hepatic scintigram, echography and x-ray computed tomography in the early diagnosis of hepatic tumors]. [Romanian]. *Revista de Medicina Interna, Neurologie, Psihiatrie, Neurochirurgie, Dermato-Venerologie. Medicina Interna*, 38: 49-59.
Not in PICO (The study refers to 45 patients with liver tumors, including 12 with malignant tumors primitive, 15 with liver metastases and 18 with benign liver tumors.)
- Oda, K., Ido, A., Tamai, T., Matsushita, M., Kumagai, K., Mawatari, S.-I., Saishoji, A., Kure, T., Ohno, K., Toyokura, E., Imanaka, D., Moriuchi, A., Uto, H., Oketani, M., Hashiguchi, T. & Tsubouchi, H. (2011) Highly sensitive lens culinaris agglutinin-reactive alpha-fetoprotein is useful for early detection of hepatocellular carcinoma in patients with chronic liver disease. *Oncology Reports*, 26: 1227-1233.
Not in PICO

- Odano, I., Hinata, H., Hara, K. & Sakai, K. (1983) [Theoretical analysis of early detection of hepatocellular carcinoma by medical imaging procedure]. [Japanese]. *Nippon Igaku Hoshasen Gakkai Zasshi - Nippon Acta Radiologica*, 43: 582-588.
Not in PICO
- Ohtomo, K., Matsuoka, Y., Abe, O., Okada, M., Amo, K., Minami, M., Kawauchi, N. & Sasaki, Y. (1997) High-resolution MR imaging evaluation of hepatocellular carcinoma. *Abdominal Imaging*, 22: 182-186.
Not in PICO
- Oka, H., Kurioka, N., Kim, K., Kanno, T., Kuroki, T., Mizoguchi, Y. & Kobayashi, K. (1990) Prospective study of early detection of hepatocellular carcinoma in patients with cirrhosis. *Hepatology*, 12: 680-687.
Not in PICO
- Okazaki, N., Yoshino, M., Yoshida, T., Takayasu, K., Moriyama, N., Makuuchi, M., Yamazaki, S., Hasegawa, H., Noguchi, M. & Hirohashi, S. (1990) Early diagnosis of hepatocellular carcinoma. *Hepato-Gastroenterology*, 37: 480-483.
Not in PICO
- Ola, O. S., Ogunbiyi, O. J., Olaleye, O. D. & Ayoola, E. A. (2006) Tumour markers and hepatitis C virus infection in Nigerian patients with liver diseases. *Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria*, 15: 417-420.
Not in PICO
- Oliva, M. R. & Saini, S. (2004) Liver cancer imaging: role of CT, MRI, US and PET. *Cancer Imaging*, 4: Spec-6.
Narrative review
- Omer, M., Majmundar, K., Siddiqui, M., Khan, M. Z., Port, J. & Ayub, K. (2009) Endoscopic ultrasound (EUS) guided fine needle aspiration of hepatic lesions: Efficacy, safety and impact on management. *Gastroenterology*, 136: A517.
Not in PICO
- Omoniyi-Esan, G. O., Famurewa, O. C., Omonisi, A. E., Titiloye, N. A., Pelemo, O. E. & Olasode, B. J. (2011) The role of ultrasound guided fine needle aspiration cytology in the diagnosis of hepatocellular carcinoma: A tertiary hospital experience. *Journal of Pathology*, 224: S23.
Not in PICO
- Oyunsuren, T., Sanduijav, R., Davaadorj, D. & Nansalmaa, D. (2006) Hepatocellular carcinoma and its early detection by AFP testing in Mongolia. *Asian Pacific journal of cancer prevention : APJCP*, 7: 460-462.
Not in PICO
- Ozer, B., Serin, E., Yilmaz, U., Gumurdulu, Y., Saygili, O. B., Kayaselcuk, F. & Boyacioglu, S. (2003) Clinicopathologic features and risk factors for hepatocellular carcinoma: Results from a single center in southern Turkey. *Turkish Journal of Gastroenterology*, 14: 85-90.
Not in PICO
- Ozkan, H., Erdal, H., Tutkak, H., Karaeren, Z., Yakut, M., Yuksel, O. & Koklu, S. (2010) Diagnostic and prognostic validity of Golgi protein 73 in hepatocellular carcinoma. *Digestion*, 83: 83-88.
Not in PICO
- Palmer, L. B., Kappelman, M., Porter, C. Q., Sandler, R. S. & Hayashi, P. H. (2010) Screening for hepatocellular carcinoma in a medicaid cirrhotic population: Opportunities for improvement. *Gastroenterology*, 138: S796.
Not in PICO
- Park, J. O., Stephen, Z., Sun, C., Veisoh, O., Kievit, F. M., Fang, C., Leung, M., Mok, H. & Zhang, M. (2011) Glypican-3 targeting of liver cancer cells using multifunctional nanoparticles. *Molecular Imaging*, 10: 69-77.
Not in PICO

- Patel, M., Shariff, M. I., Ladeb, N. G., Thillainayagam, A. V., Thomas, H. C., Khan, S. A. & Taylor-Robinson, S. D. (2012) Hepatocellular carcinoma: diagnostics and screening. [Review]. *Journal of Evaluation in Clinical Practice*, 18: 335-342.
Narrative review
- Patten, R. M., Byun, J. Y. & Freeny, P. C. (1993) CT of hypervascular hepatic tumors: are unenhanced scans necessary for diagnosis? *AJR.American Journal of Roentgenology*, 161: 979-984.
Not in PICO
- Patwardhan, V., Paul, S., Corey, K. E., Mazhar, S. M., Richter, J. M., Thiim, M. & Chung, R. T. (2011) Hepatocellular Carcinoma Screening Rates Vary by Etiology of Cirrhosis and Involvement of Gastrointestinal Sub-specialists. *Digestive Diseases and Sciences*, 56: 3316-3322.
Not in PICO
- Paul, S. B., Gulati, M. S., Sreenivas, V., Madan, K., Gupta, A. K., Mukhopadhyay, S. & Acharya, S. K. (2007) Evaluating patients with cirrhosis for hepatocellular carcinoma: value of clinical symptomatology, imaging and alpha-fetoprotein. *Oncology*, 72: Suppl-23.
Not in PICO
- Peck-Radosavljevic, M. (2011) Imaging and early diagnosis of hepatocellular carcinoma. *Minerva Gastroenterologica e Dietologica*, 57: 273-286.
Narrative review
- Phulpoto, J. A., Shah, I. A. & Bhatti, Z. (2012) Prevalence of hepatocellular carcinoma in cirrhotic patients of Northern Sindh attending liver clinics at Ghulam Mohammad Mahar Medical College Hospitals Sukkur and Khairpur. *Journal of the Liaquat University of Medical and Health Sciences*, 11: 29-33.
Not in PICO
- Piscaglia, F., Lencioni, R., Sagrini, E., Pina, C. D., Cioni, D., Vidili, G. & Bolondi, L. (2010) Characterization of focal liver lesions with contrast-enhanced ultrasound. [Review] [98 refs]. *Ultrasound in Medicine & Biology*, 36: 531-550.
Narrative review
- Piwkowski, P., Kolodziejczyk, A., Zebrowski, J. & Macioszek, A. (2011) PET-CT in metastatic liver tumor of unknown origin - Verification of primary diagnosis, influence on final diagnosis and place in diagnostics algorithm. *European Journal of Nuclear Medicine and Molecular Imaging*, 38: S371.
Not in PICO
- Rand, D., Ortiz, V., Liu, Y., Derdak, Z., Wands, J. R., Taticek, M. & Rose-Petruck, C. (2011) Nanomaterials for X-ray imaging: gold nanoparticle enhancement of X-ray scatter imaging of hepatocellular carcinoma. *Nano Letters*, 11: 2678-2683.
Not in PICO
- Rastegar, R. F., Hou, D., Harris, A., Yoshida, E., Lum, B., Ho, S., Ford, J. A., Chung, S., Soulez, G., Lee, E. & Liu, D. (2012) Is a liver biopsy necessary? Investigation of a suspected hepatocellular carcinoma: a pictorial essay of hepatocellular carcinoma and the revised American Association for the Study of Liver Disease criteria. [Review]. *Canadian Association of Radiologists Journal*, 63: 329-340.
Narrative review
- Ren, F.-Y., Piao, X.-X. & Jin, A.-L. (2006) Efficacy of ultrasonography and alpha-fetoprotein on early detection of hepatocellular carcinoma. *World Journal of Gastroenterology*, 12: 4656-4659.
Not in PICO
- Riley, T. R. & Smith, J. P. (1999) Preventive care in chronic liver disease. [Review] [55 refs]. *Journal of General Internal Medicine*, 14: 699-704.
Not in PICO
- Robinson, P. J., Arnold, P. & Wilson, D. (2003) Small "indeterminate" lesions on CT of the liver: a follow-up study of stability. *British Journal of Radiology*, 76: 866-874.
Not in PICO

- Rode, A. (2011) [Radiological diagnosis of hepatocellular carcinoma in 2010]. [Review] [French]. *Cancer Radiotherapie*, 15: 7-12.
Narrative review
- Roebuck, D. J. (2009) Assessment of malignant liver tumors in children. [Review] [26 refs]. *Cancer Imaging*, 9: Spec-S103.
Narrative review
- Roncalli, M., Borzio, M. & Di, T. L. (2007) Hepatocellular dysplastic nodules. *Hepatology Research*, 37: Suppl-34.
Narrative review
- Rugge, J. B., Lochner, J. & Judkins, D. (155) What is the best surveillance for hepatocellular carcinoma in chronic carriers of hepatitis B?. [Review] [6 refs]. *Journal of Family Practice*, 55: 155-156.
Not in PICO
- Rummeny, E. J. & Marchal, G. (1997) Liver imaging - Clinical applications and future perspectives. *Acta Radiologica*, 38: 626-630.
Narrative review
- Ruzek, V. & Vanecek, T. (1992) [Present views on the diagnosis of cavernous hemangioma of the liver using ultrasound]. [Czech]. *Vnitřní Lekarství*, 38: 395-401.
Narrative review
- Sada, Y., David, E., El-Serag, H., Singh, H. & Davila, J. (2013) Guideline adherence for diagnosis of liver cancer in veterans. *Journal of Clinical Oncology*, 31.
Not in PICO
- Saito, A. (2001) [Early diagnosis of hepatocellular carcinoma using ultrasonography]. [Review] [3 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 59: Suppl-7.
In Japanese, not enough information can be extracted to ascertain relevance
- Sakamoto, M., Mori, T., Masugi, Y., Effendi, K., Rie, I. & Du, W. (2008) Candidate molecular markers for histological diagnosis of early hepatocellular carcinoma. *Intervirology*, 51: 42-45.
Narrative review
- Sakuma, S. & Ishigaki, T. (1989) Imaging diagnosis of early cancer: prospect and problems of present investigation. [Japanese]. *Nippon rinsho*, Japanese: 983-989.
Not in PICO
- Salvador, V. B., Samrao, P., Leytin, A. & Basith, M. (2013) Atypical presentation of an advanced obstructive biliary cancer without jaundice. *The American Journal of Case Reports*, 14: 462-466.
Not in PICO
- Sano, K., Ichikawa, T., Motosugi, U., Sou, H., Muhi, A. M., Matsuda, M., Nakano, M., Sakamoto, M., Nakazawa, T., Asakawa, M., Fujii, H., Kitamura, T., Enomoto, N. & Araki, T. (2011) Imaging study of early hepatocellular carcinoma: usefulness of gadoteric acid-enhanced MR imaging. *Radiology*, 261: 834-844.
Not in PICO
- Sato, T., Tateishi, R., Yoshida, H., Ohki, T., Masuzaki, R., Imamura, J., Goto, T., Kanai, F., Obi, S., Kato, N., Shiina, S., Kawabe, T. & Omata, M. (2009) Ultrasound surveillance for early detection of hepatocellular carcinoma among patients with chronic hepatitis C. *Hepatology International*, 3: 544-550.
Not in PICO
- Sato, Y., Nakata, K., Kato, Y., Shima, M., Ishii, N., Koji, T., Taketa, K., Endo, Y. & Nagataki, S. (1993) Early recognition of hepatocellular carcinoma based on altered profiles of alpha-fetoprotein. *New England Journal of Medicine*, 328: 1802-1806.
Not in PICO
- Schima, W. (2002) Organ specific MRI contrast media in general practice. [German]. *Wiener Medizinische Wochenschrift*, Supplement.: 8-11.
Narrative review

- Schima, W., Hammerstingl, R., Catalano, C., Marti-Bonmati, L., Rummeny, E. J., Montero, F. T., Dirisamer, A., Westermayer, B., Bellomi, M., Brisbois, D., Chevallier, P., Dobritz, M., Drouillard, J., Fraioli, F., Martinez, M. J., Morassut, S. & Vogl, T. J. (2006) Quadruple-phase MDCT of the liver in patients with suspected hepatocellular carcinoma: Effect of contrast material flow rate. *American Journal of Roentgenology*, 186: 1571-1579.
Not in PICO
- Schmillevitch, J., Szutan, L. A., Ferreira, F. G., Santos, M. F., Mincis, R. & Gorski, A. (2011) Prospective study of ultrasound with perflutrene contrast compared to magnetic resonance imaging in the diagnosis of hepatic hemangiomas. *Arquivos de Gastroenterologia*, 48: 119-123.
Not in PICO
- Scholmerich, J., Volk, B. A. & Gerok, W. (1987) Value and limitations of abdominal ultrasound in tumour staging--liver metastasis and lymphoma. *European Journal of Radiology*, 7: 243-245.
Not in PICO
- Schwerk, W. B., Durr, H. K. & Schmitz-Moormann, P. (1983) Ultrasound guided fine-needle biopsies in pancreatic and hepatic neoplasms. *Gastrointestinal Radiology*, 8: 219-225.
Not in PICO
- Sekiguchi, R., Kuwajima, A., Nagamoto, M., Ohno, H. & Tamura, M. (1993) Hepatocellular carcinoma: the diagnostic difficulties of ultrasonography and analysis of risk factors in MHTS. *Journal of Medical Systems*, 17: 133-137.
Not in PICO
- Shaan, U. F., El-Halafawy, K. A. & Raouf, A. A. (2010) Molecular approach for early diagnosis of hepatocellular carcinoma in egyptian patients by Alpha fetoprotein (AFP) and Vascular Endothelial Growth Factor (VEGF). *Pakistan Journal of Biotechnology*, 7: 67-74.
Not in PICO
- Shah, A. J., Parsons, B., Pope, I., Callaway, M., Finch-Jones, M. D. & Thomas, M. G. (2009) The clinical impact of magnetic resonance imaging in diagnosing focal hepatic lesions and suspected cancer. *Clinical Imaging*, 33: 209-212.
Not in PICO
- Shariff, M. I., Ladep, N. G., Cox, I. J., Williams, H. R., Okeke, E., Malu, A., Thillainayagam, A. V., Crossey, M. M., Khan, S. A., Thomas, H. C. & Taylor-Robinson, S. D. (2010) Characterization of urinary biomarkers of hepatocellular carcinoma using magnetic resonance spectroscopy in a Nigerian population. *Journal of Proteome Research*, 9: 1096-1103.
Not in PICO
- Sherman, M. (2005) Approaches to the diagnosis of hepatocellular carcinoma. [Review] [42 refs]. *Current Gastroenterology Reports*, 7: 11-18.
Narrative review
- Sherman, M. (2007) Surveillance for hepatocellular carcinoma and early diagnosis. [Review] [125 refs]. *Clinics in Liver Disease*, 11: 817-837.
Narrative review
- Sheu, J. C., Sung, J. L., Chen, D. S., Lai, M. Y., Wang, T. H., Yu, J. Y., Yang, P. M., Chuang, C. N., Yang, P. C. & Lee, C. S. (1985) Early detection of hepatocellular carcinoma by real-time ultrasonography. A prospective study. *Cancer*, 56: 660-666.
Not in PICO
- Simon, K., Serafinska, S. & Pazgan-Simon, M. (2012) Surveillance programmes for early detection of hepatocellular carcinoma. *Wspolczesna Onkologia*, 16: 295-299.
Narrative review
- Singal, A., Volk, M. L., Waljee, A., Salgia, R., Higgins, P., Rogers, M. A. & Marrero, J. A. (2009) Meta-analysis: surveillance with ultrasound for early-stage hepatocellular carcinoma in patients with cirrhosis. *Alimentary Pharmacology & Therapeutics*, 30: 37-47.
Not in PICO

- Singal, A., Conjeevaram, H. S., Fontana, R. J., Fu, S., Wright, W., Askari, F., Su, G. L., Lok, A. S. & Marrero, J. A. (2009) Risk factors for the development of hepato-Cellular carcinoma (HCC) in a prospective cohort of 446 American patients with cirrhosis undergoing surveillance. *Hepatology*, 50: 1075A-1076A.
Not in PICO
- Sinn, D. H., Yi, J., Choi, M. S., Eo, S. J., Kim, Y. J., Gwka, G.-Y., Lee, J. H., Koh, K. C., Paik, S. W. & Yoo, B. C. (2012) A significant additional role of serum alpha-fetoprotein in surveillance of hepatocellular carcinoma in a hepatitis B endemic area. *Hepatology International*, 6: 214.
Not in PICO
- Smith, A., Miller, M., Groome, M. & Dillon, J. F. (2011) Predictors of neoplasia in patients presenting with obstructive jaundice. *Hepatology*, 54: 1423A-1424A.
Not in PICO
- Snarska, J., Szajda, S. D., Puchalski, Z., Szmitkowski, M., Chabielska, E., Kaminski, F., Zwierz, P. & Zwierz, K. (2006) Usefulness of examination of some tumor markers in diagnostics of liver cancer. *Hepato-Gastroenterology*, 53: 271-274.
Not in PICO
- Song, J. & Kim, J. (2011) Significance of alpha fetoprotein in the surveillance of HBV-associated hepatocellular carcinoma. *Hepatology*, 54: 1419A.
Not in PICO
- Songsivilai, S., Dharakul, T. & Senawong, S. (1995) Hepatitis B- and hepatitis C-associated hepatocellular carcinoma: Evaluation of alpha-fetoprotein as a diagnostic marker. *Asian Pacific Journal of Allergy and Immunology*, 13: 167-171.
Not in PICO
- Sonu, I. S., Nguyen, L. H., Chen, C., Kin, K. C., Ha, N. B., Trinh, H. N., Ahmed, A., Li, J., Zhang, J. Q. & Nguyen, M. H. (2012) Incidence and risk factors in the development of hepatocellular carcinoma (HCC) in non-cirrhotic and cirrhotic patients with chronic hepatitis B (CHB): Results of a multicenter U.S. Cohort study. *Hepatology*, 56: 478A-479A.
Not in PICO
- Speets, A. M., Kalmijn, S., Hoes, A. W., Van Der Graaf, Y. & Mali, W. P. T. (2006) Yield of abdominal ultrasound in patients with abdominal pain referred by general practitioners. *European Journal of General Practice*, 12: 135-137.
Not in PICO
- Sporea, I., Badea, R., Martie, A., Dumitru, E., Ioanimescu, S., Sirli, R., Socaciu, M., Popescu, A., Danila, M. & Voiculescu, M. (2012) Contrast Enhanced Ultrasound for the evaluation of focal liver lesions in daily practice. A multicentre study. *Medical Ultrasonography*, 14: 95-100.
Not in PICO
- Sturgeon, C. M., Duffy, M. J., Hofmann, B. R., Lamerz, R., Fritsche, H. A., Gaarenstroom, K., Bonfrer, J., Ecke, T. H., Grossman, H. B., Hayes, P., Hoffmann, R. T., Lerner, S. P., Lohe, F., Louhimo, J., Sawczuk, I., Taketa, K., Diamandis, E. P. & National Academy of Clinical Biochemistry (2010) National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines for use of tumor markers in liver, bladder, cervical, and gastric cancers. *Clinical Chemistry*, 56: e1-48.
Narrative review
- Sun, S., Day, P. J., Lee, N. P. & Luk, J. M. (2009) Biomarkers for early detection of liver cancer: focus on clinical evaluation. [Review] [52 refs]. *Protein & Peptide Letters*, 16: 473-478.
Narrative review
- Tada, S., Miura, S., Miznuma, K., Kurisu, Y. & Yasuda, M. (1988) Differential diagnosis of the early cancer: imaging diagnosis "CT". [Japanese]. *Gan no rinsho*, Japan: 1223-1226.
Narrative review
- Taga, H., Hirai, H., Ishizuka, H. & Kaneda, H. (1988) Early diagnosis of hepatocellular carcinoma with lectin electrophoresis of serum alpha-fetoprotein. *Tumor Biology*, 9: 110-115.
Narrative review

- Takahashi, M., Sakamoto, Y., Kojima, R. & Wakamatsu, J. (1988) [Diagnosis of cancer with magnetic resonance imaging (MRI)]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1237-1246.
Narrative review
- Takayasu, K., Furukawa, H., Wakao, F., Muramatsu, Y., Abe, H., Terauchi, T., Winter, T. C., III, Sakamoto, M. & Hirohashi, S. (1995) CT diagnosis of early hepatocellular carcinoma: sensitivity, findings, and CT-pathologic correlation. *AJR.American Journal of Roentgenology*, 164: 885-890.
Not in PICO
- Takayasu, K., Muramatsu, Y., Furukawa, H., Wakao, F., Moriyama, N., Takayama, T., Yamasaki, S., Sakamoto, M. & Hirohashi, S. (1995) Early hepatocellular carcinoma: appearance at CT during arterial portography and CT arteriography with pathologic correlation. *Radiology*, 194: 101-105.
Not in PICO
- Takayasu, K., Muramatsu, Y., Mizuguchi, Y., Moriyama, N. & Ojima, H. (2004) Imaging of early hepatocellular carcinoma and adenomatous hyperplasia (dysplastic nodules) with dynamic ct and a combination of CT and angiography: experience with resected liver specimens. [Review] [39 refs]. *Intervirolgy*, 47: 199-208.
Narrative review
- Tanaka, H., Nouse, K., Kobashi, H., Kobayashi, Y., Nakamura, S., Miyake, Y., Ohnishi, H., Miyoshi, K., Iwado, S., Iwasaki, Y., Sakaguchi, K. & Shiratori, Y. (2006) Surveillance of hepatocellular carcinoma in patients with hepatitis C virus infection may improve patient survival. *Liver International*, 26: 543-551.
Not in PICO
- Tangkijvanich, P., Chanmee, T., Komtong, S., Mahachai, V., Wisedopas, N., Pothacharoen, P. & Kongtawelert, P. (2010) Diagnostic role of serum glypican-3 in differentiating hepatocellular carcinoma from non-malignant chronic liver disease and other liver cancers. *Journal of Gastroenterology and Hepatology*, 25: 129-137.
Not in PICO
- Taniai, M., Hashimoto, E., Noto, H., Tobari, M., Yatsuji, S., Tokushige, K. & Shiratori, K. (2009) Clinicopathological evaluation of hepatocellular carcinoma arising in patients without a known underlying liver disease. *Gastroenterology*, 136: A863-A864.
Not in PICO
- Tannapfel, A. & Wittekind, C. (2000) Biopsy of focal lesions of the liver necessary - Useful - or waste of time? *Leber Magen Darm*, 30: 157-160.
Narrative review
- Tanwandee, T., Setthasin, S., Charatcharoenwitthaya, P., Chainuvati, S., Leelakusolvong, S., Pausawasdi, N., Srikureja, W., Pongprasobchai, S., Manatsathit, S., Kachintorn, U., Ekpo, P. & Senawong, S. (2009) Clinical utility of lens culinaris agglutinin-reactive alpha-fetoprotein in the diagnosis of hepatocellular carcinoma: evaluation in a Thai referral population. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet*, 92: S49-S56.
Not in PICO
- Terada, T. (2011) Hepatocellular carcinoma metastatic to the gingiva as a first manifestation of hepatocellular carcinoma. *Journal of Maxillofacial & Oral Surgery*, 10: 271-274.
Not in PICO
- Tilleman, E. H., Phoa, S. S., Van Delden, O. M., Rauws, E. A., van Gulik, T. M., Lameris, J. S. & Gouma, D. J. (2003) Reinterpretation of radiological imaging in patients referred to a tertiary referral centre with a suspected pancreatic or hepatobiliary malignancy: impact on treatment strategy. *European Radiology*, 13: 1095-1099.
Not in PICO
- Tinkle, C. L. & Haas-Kogan, D. (2012) Hepatocellular carcinoma: natural history, current management, and emerging tools. *Biologics*, 6: 207-219.
Narrative review

- Trape, J., Botargues, J. M., Porta, F., Ricos, C., Badal, J. M., Salinas, R., Sala, M. & Roca, A. (2003) Reference change value for alpha-fetoprotein and its application in early detection of hepatocellular carcinoma in patients with hepatic disease. *Clinical Chemistry*, 49: 1209-1211.
Not in PICO
- Tremolda, F., Benevegna, L., Drago, C., Casarin, C., Cechetto, A., Realdi, G. & Ruol, A. (1989) Early detection of hepatocellular carcinoma in patients with cirrhosis by alphafetoprotein, ultrasound and fine-needle biopsy. *Hepato-Gastroenterology*, 36: 519-521.
Not in PICO
- Tremosini, S., Forner, A., Boix, L., Vilana, R., Bianchi, L., Reig, M., Rimola, J., Rodriguez-Lope, C., Ayuso, C., Sole, M. & Bruix, J. (2012) Prospective validation of an immunohistochemical panel (glypican 3, heat shock protein 70 and glutamine synthetase) in liver biopsies for diagnosis of very early hepatocellular carcinoma. *Gut*, 61: 1481-1487.
Not in PICO
- Tsai, S.-L., Huang, G.-T., Yang, P.-M., Sheu, J.-C., Sung, J.-L. & Chen, D.-S. (1990) Plasma des--carboxyprothrombin in the early stage of hepatocellular carcinoma. *Hepatology*, 11: 481-488.
Not in PICO
- Tu, Z. X., Wu, M. C. & Cui, Z. F. (1986) The early detection of hepatocellular cancer by using alpha-feto-protein microheterogeneity. [Chinese]. *Zhonghua nei ke za zhi [Chinese journal of internal medicine]*, 25: 272-318.
In Chinese. Not enough information can be extracted to ascertain eligibility status
- Uchino, K., Tateishi, R., Nakagawa, H., Shindoh, J., Sugawara, Y., Akahane, M., Shibahara, J., Yoshida, H. & Koike, K. (2013) Uninodular combined hepatocellular and cholangiocarcinoma with multiple non-neoplastic hypervascular lesions appearing in the liver of a patient with HIV and HCV coinfection. *Journal of Clinical Virology*, 57: 173-177.
Not in PICO
- Vajragupta, L., Tumkosit, M., Pantongrag-Brown, L. & Wangsuphachart, S. (2008) Detection of small primary and secondary malignant hepatic tumors with Superparamagnetic iron oxideenhanced magnetic resonance imaging. *Asian Biomedicine*, 2: 135-139.
Not in PICO
- Vargas, C., Jeffers, L. J., Bernstein, D., Reddy, K. R., Munnangi, S., Behar, S., Scott, C., Parker, T. & Schiff, E. R. (1995) Diagnostic laparoscopy: A 5-year experience in a hepatology training program. *American Journal of Gastroenterology*, 90: 1258-1263.
Not in PICO
- Vera Sempere, F. J., Camanas, S. A., Prieto, R. M., Navarro, H. M., Ramos, F., V & Artes, M. J. (1994) [The diagnostic value of liver aspiration puncture with echographic control]. [Spanish]. *Revista Espanola de Enfermedades Digestivas*, 85: 440-444.
Not in PICO
- Verhoef, C., Valkema, R., de Man, R. A., Krenning, E. P. & Yzermans, J. N. (2002) Fluorine-18 FDG imaging in hepatocellular carcinoma using positron coincidence detection and single photon emission computed tomography. *Liver*, 22: 51-56.
Not in PICO
- Villa, E. & Fattovich, G. (2010) No inflammation? No cancer! Clear HBV early and live happily. *Journal of Hepatology*, 52: 768-770.
Comment
- Vogt, W. (2005) [Value of ultrasound and doppler sonography in chronic hepatitis and liver cirrhosis]. [Review] [17 refs] [German]. *Praxis*, 94: 639-643.
Narrative review
- Vutrapongwatana, U., Juiklom, W., Wilaipraphakorn, N., Suratako, S., Sarasamkan, J., Wongsa, P., Boonkawin, N., Keeratipiriyakul, S., Kongsakorn, P., Chanachai, R. & Chotipanich, C. (2011) Diagnosis in hepatocellular carcinoma using 11C-Choline PET/CT by comparison with 18F-FDG:

- Pilot study. *European Journal of Nuclear Medicine and Molecular Imaging*, 38: S373.
Not in PICO
- Wang, J.-X., Zhang, B., Yu, J.-K., Liu, J., Yang, M.-Q. & Zheng, S. (2005) Application of serum protein fingerprinting coupled with artificial neural network model in diagnosis of hepatocellular carcinoma. *Chinese Medical Journal*, 118: 1278-1286.
Not in PICO
- Wang, L. & Gao, C.-F. (2007) Clinical significance of tumor markers for diagnosis of hepatocellular carcinoma. [Chinese]. *Academic Journal of Second Military Medical University*, 28: 1314-1319.
Narrative review
- Wang, W., Zhao, L.-J., Wang, Y., Tao, Q.-Y., Feitelson, M. A., Zhao, P., Ren, H. & Qi, Z.-T. (2012) Application of HBx-induced anti-URGs as early warning biomarker of cirrhosis and HCC. *Cancer Biomarkers*, 11: 29-39.
Not in PICO
- Ward, D. G., Cheng, Y., N'Kontchou, G., Thar, T. T., Barget, N., Wei, W., Billingham, L. J., Martin, A., Beaugrand, M. & Johnson, P. J. (2006) Changes in the serum proteome associated with the development of hepatocellular carcinoma in hepatitis C-related cirrhosis. *British Journal of Cancer*, 94: 287-292.
Not in PICO
- Weber, A., von, W. C., Fend, F., Schneider, J., Neu, B., Meining, A., Weidenbach, H., Schmid, R. M. & Prinz, C. (2008) Endoscopic transpapillary brush cytology and forceps biopsy in patients with hilar cholangiocarcinoma. *World Journal of Gastroenterology*, 14: 1097-1101.
Not in PICO
- Weiss, A. & Weiss, H. (1995) Early detection of cancer through ultrasonic screening. [German]. *Onkologie*, 18: 10-13.
Narrative review
- Weiss, E., Kirtich, S., Parakh, P. K., Kaufman, M. S., McFarlane, S. & Aytaman, A. (2011) Hepatocellular carcinoma surveillance rates: Results from a large cirrhotic database analysis of a VA medical center. *Gastroenterology*, 140: S923.
Not in PICO
- Westwood, M., Joore, M., Grutters, J., Redekop, K., Armstrong, N., Lee, K., Gloy, V., Raatz, H., Misso, K., Severens, J. & Kleijnen, J. (2013) Contrast-enhanced ultrasound using SonoVue (sulphur hexafluoride microbubbles) compared with contrast-enhanced computed tomography and contrast-enhanced magnetic resonance imaging for the characterisation of focal liver lesions and detection of liver metastases: a systematic review and cost-effectiveness analysis. *Health Technology Assessment (Winchester, England)*, 17: 1-243.
Not in PICO
- Wongjitrat, C., Pattanaphapan, A., Wongjitrat, N. & Burivong, W. (2011) Common bile duct size in patients with cirrhosis. *Hepatology International*, 5: 479.
Not in PICO
- Wu, C.-S., Yen, C.-J., Chou, R.-H., Li, S.-T., Huang, W.-C., Ren, C.-T., Wu, C.-Y. & Yu, Y.-L. (2012) Cancer-associated carbohydrate antigens as potential biomarkers for hepatocellular carcinoma. *PLoS ONE*, 7.
Not in PICO
- Wu, J. C., Lee, S. D., Hsiao, K. J., Wang, S. S., Chou, P., Tsao, D., Tsai, Y. T., Lui, W. Y., Chiang, J. H. & Lo, K. J. (1988) Mass screening of primary hepatocellular carcinoma by alpha-fetoprotein in a rural area of Taiwan--a dried blood spot method. *Liver*, 8: 100-104.
Not in PICO
- Wu, N. H., Wang, C. C., Huang, G. T., Yang, P. M., Sheu, J. C. & Chen, D. S. (1999) A different experience of hepatic adenoma in Taiwan with emphasis on clinical manifestations and ultrasonographic features. *Hepato-Gastroenterology*, 46: 3197-3200.
Not in PICO

- Wu, Q. P., Xie, F. Y., Meng, Q. L. & Mu, Y. Y. (2012) [Value of combined detection of GP73 and alpha-fetoprotein in diagnosis of hepatocellular carcinoma]. [Chinese]. *Zhonghua shi yan he lin chuang bing du xue za zhi = Zhonghua shiyan he linchuang bingduxue zazhi = Chinese journal of experimental and clinical virology*, 26: 148-149.
Not in PICO
- Wu, W., Chen, M. H., Yin, S. S., Yan, K., Fan, Z. H., Yang, W., Dai, Y., Huo, L. & Li, J. Y. (2006) The role of contrast-enhanced sonography of focal liver lesions before percutaneous biopsy. *AJR.American Journal of Roentgenology*, 187: 752-761.
Not in PICO
- Xing, G.-S., Wang, S., Ouyang, H., Ma, X.-H. & Zhou, C.-W. (2010) Comparison of CT and dynamic-enhancement MRI for the diagnosis of hepatocellular carcinoma. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 26: 1-4.
Not in PICO
- Yamamoto, K., Shiraki, K., Nakanishi, S., Deguchi, M., Sugimoto, K., Sakai, T., Ohmori, S., Murata, K., Fuke, H., Hashimoto, A., Shimizu, A., Okuda, Y. & Nakano, T. (2003) The usefulness of digital subtraction imaging with Levovist in the diagnosis of focal hepatic tumors. *International Journal of Oncology*, 22: 353-358.
Not in PICO
- Yang, B., Zhang, B., Xu, Y., Wang, W., Shen, Y., Zhang, A. & Xu, Z. (1997) Prospective study of early detection for primary liver cancer. *Journal of Cancer Research & Clinical Oncology*, 123: 357-360.
Not in PICO
- Yang, B., Zhang, B. & Tang, Z. (1999) Screening and early diagnosis of primary liver cancer. [Japanese]. *Zhonghua gan zang bing za zhi = Zhonghua ganzangbing zazhi = Chinese journal of hepatology*, 7: 130-131.
Not in PICO
- Yaqoob, J., Bari, V., Usman, M. U., Munir, K., Mosharaf, F. & Akhtar, W. (2004) The evaluation of hepatocellular carcinoma with biphasic contrast enhanced helical CT scan. *JPMA - Journal of the Pakistan Medical Association*, 54: 123-127.
Not in PICO
- Yu, E. W., Chie, W. C. & Chen, T. H. (2004) Does screening or surveillance for primary hepatocellular carcinoma with ultrasonography improve the prognosis of patients? *Cancer Journal*, 10: 317-325.
Not in PICO
- Yu, J.-S., Cho, E.-S., Kim, K.-H., Chung, W.-S., Park, M.-S. & Kim, K. W. (2006) Newly developed hepatocellular carcinoma (HCC) in chronic liver disease: MR imaging findings before the diagnosis of HCC. *Journal of Computer Assisted Tomography*, 30: 765-771.
Not in PICO
- Yuen, M. F. & Lai, C. L. (2003) Screening for hepatocellular carcinoma: survival benefit and cost-effectiveness. [Review] [38 refs]. *Annals of Oncology*, 14: 1463-1467.
Not in PICO
- Zarski, J. P., Doffoel, M., Filoche, B., Marcellin, P., Samuel, D. & Bedossa, P. (2008) [Hepatitis C, cirrhosis and hepatocellular carcinoma]. [Review] [20 refs] [French]. *Gastroenterologie Clinique et Biologique*, 32: t-20.
Narrative review
- Zhang, B. & Yang, B. (1999) Combined alpha fetoprotein testing and ultrasonography as a screening test for primary liver cancer. *Journal of Medical Screening*, 6: 108-110.
Not in PICO
- Zhang, G.-D., Zou, D.-D., Wang, H., He, Y. & Huang, D. (2013) Value of contrast-enhanced ultrasound in diagnosis of liver metastases: Analysis of 55 cases. *World Chinese Journal of Digestology*, 21: 2849-2853.
Not in PICO

- Zhao, Y., Zhang, L., Li, H., Cui, C. & Wu, X. (2013) Clinical significance of serum GP73, AFP, and CA199 test in the diagnosis of hepatic cancer. [Chinese]. *Chinese Journal of Clinical Oncology*, 40: 29-31+40.
Not in PICO
- Zhao, Y.-Z., Meng, J., Zhang, F.-J., Ji, X.-H., Yang, Y. & Han, R.-L. (2006) Comparison of contrast-enhanced ultrasound and contrast-enhanced CT in detecting liver tumors. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 22: 183-185.
Not in PICO
- Zhou, W., Guo, X., Cao, Z.-G., Zhao, X.-T. & Tu, H. (2007) Detection of glypican 3 in serum and its clinical significance on the diagnosis of hepatocellular carcinoma. [Chinese]. *Tumor*, 27: 679-682.
Not in PICO
- Zhou, Z., Xia, D., Wang, C., Lin, C., Zhao, W. & Dong, C. (2012) Clinical evaluation of single or joint of golgi protein 73 and alpha-fetoprotein in hepatocellular carcinoma diagnosing. *Chinese-German Journal of Clinical Oncology*, 11: 650-654.
Not in PICO
- Zhu, K., Dai, Z. & Zhou, J. (2013) Biomarkers for hepatocellular carcinoma: progression in early diagnosis, prognosis, and personalized therapy. *Biomarker Research*, 1: 10.
Narrative review
- Zhu, X.-L. & Feng, S.-T. (2005) Analysis of artery computed tomography angiography for digestive tumor in 83 cases. [Chinese]. *World Chinese Journal of Digestology*, 13: 2398-2401.
Not in PICO
- Zoli, M., Magalotti, D., Bianchi, G., Gueli, C., Marchesini, G. & Pisi, E. (1996) Efficacy of a surveillance program for early detection of hepatocellular carcinoma. *Cancer*, 78: 977-985.
Not in PICO
- Zorger, N., Jung, E. M., Schreyer, A. G., Heiss, P., Mueller-Wille, R., Wiest, R., Feuerbach, S. & Rennert, J. (2010) Ultrasound-arteriportography (US-AP): A new technical approach to perform detection of liver lesions. *Clinical Hemorheology & Microcirculation*, 46: 117-126.
Not in PICO

LOWER GASTRO-INTESTINAL TRACT CANCERS

COLORECTAL CANCER

Review question:

What is the risk of colorectal cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

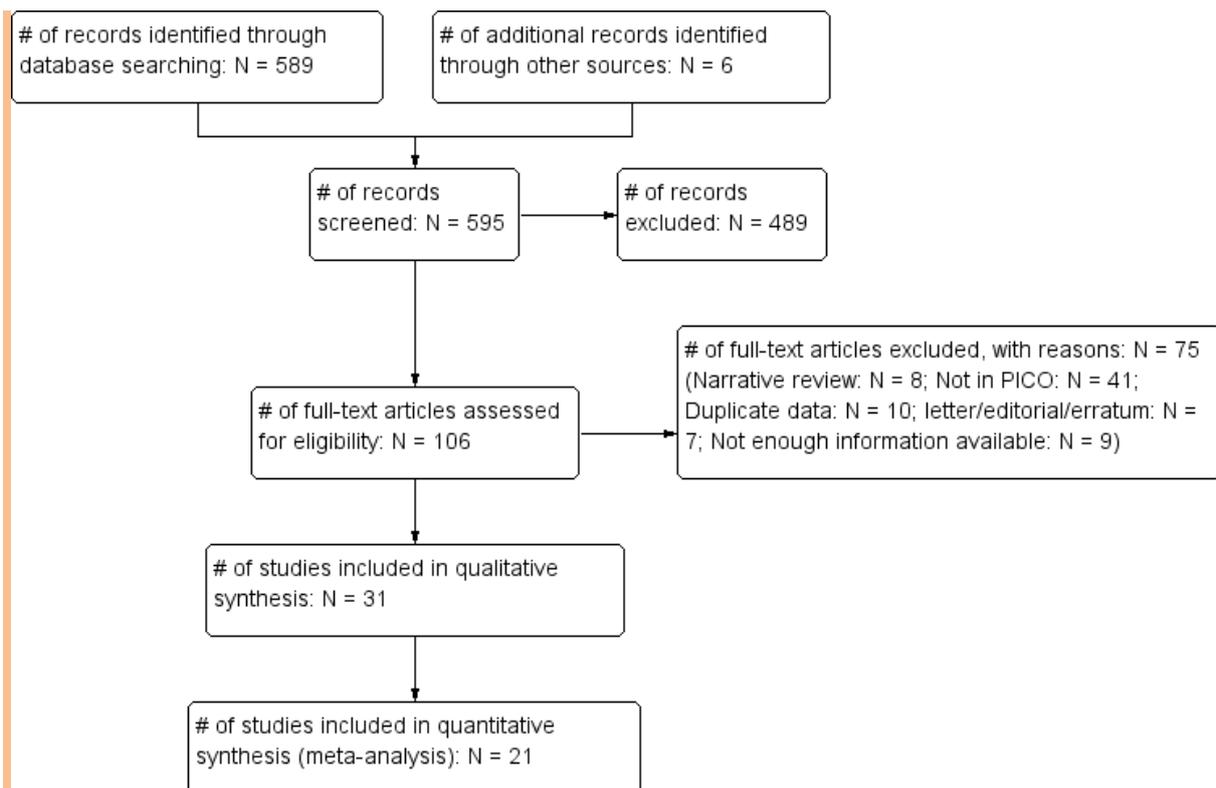
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All - 2012	3575	329	10/08/2012
<i>Premedline</i>	All - 2012	16	12	11/07/2012
<i>Embase</i>	All - 2012	4169	279	18/07/2012
<i>Cochrane Library</i>	All - 2012	725	5	18/07/2012
<i>Psychinfo</i>	All - 2012	12	4	18/07/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All - 2012	1207	53	18/07/2012
<i>Biomed Central</i>	All - 2012	1680	1	18/07/2012

Total References retrieved (after de-duplication): 519

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	7/2012-13/08/2014	172	24	13/08/2014
<i>Premedline</i>	7/2012-13/08/2014	98	20	13/08/2014
<i>Embase</i>	7/2012-13/08/2014	655	31	13/08/2014
<i>Cochrane Library</i>	7/2012-13/08/2014	23	0	13/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	7/2012-13/08/2014	297	3	13/08/2014

Total References retrieved (after de-duplication): 70



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main bias and validity issues to note relates to patient selection and applicability with some studies employing non-consecutive patient sampling, e.g., case-control designs (which has been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection), and others being conducted in setting or with patients that may not directly translate to the current question and UK-based primary care. The other main issues of concern relates to missing data (and the concern that this may not be missing at random) and under specification of symptoms and reference standards, which makes it difficult to ascertain their applicability and/or validity.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Bellentani (1990)	+	+	+	+	?	?	+
Collins (2012)	+	+	+	+	+	+	+
Droogendijk (2011)	+	+	+	?	?	+	+
Du Toit (2006)	+	+	+	+	+	+	+
Ellis (2005)	?	+	+	+	+	+	+
Farrus Palou (2000)	+	+	?	-	?	+	?
Fijten (1995)	+	+	?	?	?	+	+
Hallissey (1990)	+	+	+	+	?	+	+
Hamilton (2005)	-	+	+	+	+	+	+
Hamilton (2008)	-	+	+	?	+	+	+
Hamilton (2009)	-	+	+	+	+	+	+
Heikkinen (1995)	+	+	+	+	?	+	+
Heintze (2005)	-	+	+	-	+	+	+
Helfand (1997)	+	+	+	+	-	+	+
Hippisley-Cox (2012)	+	+	+	+	+	+	+
Jones (2007)	+	+	+	+	+	+	+
Lawrenson (2006)	+	+	+	+	+	+	+
Lucas (1996)	+	+	+	+	?	+	+
Mant (1989)	+	+	+	+	?	+	+
Meineche-Schmidt (2002)	+	+	+	+	?	+	+
Metcalf (1996)	+	+	+	+	+	+	+
Muris (1993)	+	+	+	+	?	?	+
Muris (1995)	-	+	+	+	-	-	+
Nørrelund (1996)	?	+	+	+	+	+	+
Oudega (2006)	+	+	+	+	?	+	+
Panzuto (2003)	-	+	+	?	?	+	+
Parker (2007)	+	+	+	+	+	+	+
Robertson (2006)	+	+	+	+	+	+	+
Stellon (1997)	+	+	+	+	+	+	+
Wauters (2000)	?	+	+	+	?	+	+
Yates (2004)	+	+	+	+	?	+	+

High

Unclear

Low

Study results

Table 1: Colorectal cancer: Meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Collins (2012) Du Toit (2006) Ellis (2005) Fijten (1995) Heintze (2005) Helfand (1997) Hippisley-Cox (2012) Jones (2007, at 6 months) Mant (1989) Metcalf (1996) Nørrelund (1996) Panzuto (2003) Parker (2007) Robertson (2006) Wauters (2000)	Rectal bleeding	All patients N = 132701	4.79 (3.37-6.77)
		Without Heintze (2005) and Panzuto (2003) N = 132187	4.41 (3.1-6.28)
Collins (2012) Du Toit (2006) Ellis (2005) Fijten (1995) Heintze (2005) Helfand (1997) Hippisley-Cox (2012) Jones (2007, at 3 years) Mant (1989) Metcalf (1996) Nørrelund (1996) Panzuto (2003) Parker (2007) Robertson (2006) Wauters (2000)	Rectal bleeding	All patients N = 132701	4.88 (3.48-6.79)
		Without Heintze (2005) and Panzuto (2003) N = 132187	4.5 (3.2-6.3)
Collins (2012) Bellentani (1990) Hippisley-Cox (2012) Panzuto (2003)	Abdominal pain	All patients N = 371703	2.04 (0.53-7.55)
		Without Panzuto (2003) N = 371480	1.02 (0.38-2.69)
Collins (2012) Droogendijk (2011) Farrus Palou (2000) Hippisley-Cox (2012) Lucas (1996) Panzuto (2003) Stellon (1997) Yates (2004)	Anaemia	All patients N = 35949	5.87 (2.64-12.)
		Without Panzuto (2003) N = 35880	4.09 (2.24-7.34)

Collins (2012) Hippisley-Cox (2012) Panzuto (2003)	Weight loss	All patients N = 42338	3 (0.32-22.89)
		Collins (2012) N = 28289	0.8 (0.7-0.9)
		Hippisley-Cox (2012) N = 14007	0.8 (0.7-0.9)
Hallissey (1990) Heikkinen (1995) Meineche-Schmidt (2002)	Dyspepsia	All patients N = 4476	0.6 (0.27-1.35)

Please note that the data from Hamilton (2005, 2008, 2009) are not included in these meta-analyses due to the case-control design of the studies. These data are instead reported in the table below. In addition, sensitivity analyses were conducted where the studies with a high risk of patient selection bias were excluded. When the number of studies was < 3, the data were not meta-analysed, but presented for the individual studies instead.

Table 2: Colorectal cancer: Individual positive predictive values from the meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Collins (2012)	Rectal bleeding	All patients	2.4 (2.3-2.6) 1362/56234
Du Toit (2006)	Rectal bleeding	All patients	5.7 (3.3-9.4) 15/265
Ellis (2005),	Rectal bleeding	All patients	3.4 (1.8-6.3) 11/319
Fijten (1995),	Rectal bleeding	All patients	3.3 (1.6-6.5) 9/269
Heintze (2005)	Rectal bleeding	All patients	4.3 (2.6-6.9) 17/400
Helfand (1997)	Rectal bleeding	All patients	6.5 (3.6-11.1) 13/201
Hippisley-Cox (2012)	Rectal bleeding	All patients	2.9 (2.7-3.1) 841/28952
Jones (2007, at 6 months)	Rectal bleeding	All patients	1.7 (1.5-1.9) 257/15289
Jones (2007, at 3 years)	Rectal bleeding	All patients	2.2 (2-2.5) 338/15289
Mant (1989)	Rectal bleeding	All patients	11.7 (7.2-18.4) 17/145
Metcalf (1996)	Rectal bleeding	All patients	8.1 (3.8-15.8) 8/99
Nørrelund (1996)	Rectal bleeding	All patients	13.7 (10.6-17.4) 57/417
Panzuto (2003)	Rectal bleeding	All patients	15.8 (9.9-24.1) 18/114
Parker (2007)	Rectal bleeding	All patients	2.2 (2.1-2.4) 645/29007
Robertson (2006)	Rectal bleeding	All patients	3.6 (2.4-5.6) 22/604
Wauters (2000)	Rectal bleeding	All patients	7 (4.7-10.1) 27/386

Bellentani (1990)	Abdominal pain	All patients	3.9 (2-7.3) 10/254
Collins (2012)	Abdominal pain	All patients	0.5 (0.5-0.5) 1220/245989
Hippisley-Cox (2012)	Abdominal pain	All patients	0.7 (0.6-0.7) 845/125237
Panzuto (2003)	Abdominal pain	All patients	13.5 (9.4-18.8) 30/223
Collins (2012)	Anaemia	All patients	1.7 (1.5-1.9) 308/18125
Droogendijk (2011)	Anaemia	All patients	8.4 (5.5-12.3) 24/287
Farrus Palou (2000)	Anaemia	All patients	3.4 (0.6-13) 2/58
Hippisley-Cox (2012)	Anaemia	All patients	1.5 (1.3-1.7) 247/16823
Lucas (1996)	Anaemia	All patients	6.9 (3.4-13.1) 9/130
Panzuto (2003)	Anaemia	All patients	40.6 (29.1-53.1) 28/69
Stellon (1997)	Anaemia	All patients	7.7 (1.3-26.6) 2/26
Yates (2004)	Anaemia	All patients	8.6 (6.2-11.7) 37/431
Collins (2012)	Weight loss	All patients	0.8 (0.7-0.9) 215/28289
Hippisley-Cox (2012)	Weight loss	All patients	0.8 (0.7-0.9) 106/14007
Panzuto (2003)	Weight loss	All patients	35.7 (22-52) 15/42
Hallissey (1990)	Dyspepsia	All patients	0.5 (0.3-0.9) 14/2585
Heikkinen (1995)	Dyspepsia	All patients	0 (0-1.2) 0/400
Meineche-Schmidt (2002)	Dyspepsia	All patients	1.14 (0.7-1.9) 17/1491

Table 3: Colorectal cancer: Additional results reported by the individual papers: Individual symptoms

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Hamilton (2005)	Rectal bleeding (reported once)	All patients	2.4 (1.9-3.2) Cases: 148/349 Controls: 73/1744
Hamilton (2005)	Rectal bleeding (reported twice)	All patients	6.8 (NR)
Hamilton (2005)	Constipation (reported once)	All patients	0.42 (0.3-0.5) Cases: 91/349 Controls: 258/1744
Hamilton (2005)	Constipation (reported twice)	All patients	0.81 (0.5-1.3)

Panzuto (2003)	Constipation	All patients	15.7 (10.2-23.2) 21/134
Hamilton (2005)	Diarrhoea (reported once)	All patients	0.94 (0.7-1.1) Cases: 132/349 Controls: 171/1744
Panzuto (2003)	Diarrhoea	All patients	11.8 (6.1-21) 10/85
Hamilton (2005)	Diarrhoea (reported twice)	All patients	1.5 (1-2.2)
Panzuto (2003)	Bloating	All patients	13.2 (8.6-19.5) 22/167
Panzuto (2003)	Change in bowel habit	All patients	14 (6.7-26.3) 8/57
Hamilton (2005)	Loss of weight (reported once)	All patients	1.2 (0.9-1.6) Cases: 94/349 Controls: 92/1744
Hamilton (2005)	Loss of weight (reported twice)	All patients	1.4 (0.8-2.6)
Collins (2012)	Loss of appetite	All patients	0.8 (0.6-1.1) 44/5732
Hippisley-Cox (2012)	Loss of appetite	All patients	0.9 (0.6-1.2) 46/5316
Hamilton (2005)	Abdominal pain (reported once)	All patients	1.1 (0.9-1.3) Cases: 148/349 Controls: 163/1744
Hamilton (2005)	Abdominal pain (reported twice)	All patients	3 (1.8-5.2)
Hamilton (2005)	Abdominal tenderness (reported once)	All patients	1.1 (0.8-1.5) Cases: 62/349 Controls: 67/1744
Muris (1993)	Non-acute abdominal complaints	All patients	0.52 (0.1-1.6) 3/578
Muris (1995)	Non-acute abdominal complaints	All patients	0.43 (0.1-1.2) 4/933
Hamilton (2005)	Abnormal rectal exam (reported once)	All patients	1.5 (1-2.2) Cases: 51/349 Controls: 14/1744
Hamilton (2005)	Haemoglobin 10-13 g dl ⁻¹ (reported once)	All patients	0.97 (0.8-1.3) Cases: 55/349 Controls: 69/1744
Hamilton (2008)	Haemoglobin 10-12.9 g dl ⁻¹	All patients	0.3 (0.2-0.3) Cases: 503/3421 Controls: 996/23928
Hamilton (2005)	Haemoglobin < 10 g dl ⁻¹ (reported once)	All patients	2.3 (1.6-3.1) Cases: 40/349 Controls: 21/1744
Hamilton (2008)	Haemoglobin < 9.9 g dl ⁻¹	All patients	2 (1.7-2.3) Cases: 296/3421 Controls: 96/23928
Hamilton (2005)	Haemoglobin 12-12.9 g dl ⁻¹	All patients	Cases: 17/349 Controls: 20/1744

Hamilton (2005)	Haemoglobin 10-11.9 g dl ⁻¹	All patients	Cases: 38/349 Controls: 49/1744
Hamilton (2005)	Haemoglobin < 10 g dl ⁻¹	All patients	Cases: 40/349 Controls: 21/1744
Hamilton (2005)	Positive faecal occult blood	All patients	Cases: 31/79 Controls: 5/47
Hamilton (2005)	Blood sugar > 10 mmol l ⁻¹	All patients	Cases: 25/349 Controls: 39/1744
Oudega (2006)	Deep vein thrombosis	All patients	0.7 (0.2-2.2) 3/430
Hamilton (2005)	History of diabetes	All patients	Cases: 37/349 Controls: 119/1744

Please note:

- Lawrenson (2006) calculated the positive predictive values of colorectal cancer being diagnosed within 12 months of initial symptoms per 100 patients presenting by using Kaplan-Maier curves, and it is unclear how and if these calculations differ from those of the other studies.

- The calculations of the positive predictive values differ between the remaining studies using (TP)/(TP+FP) and Hamilton (2005, 2008, 2009) using other statistics due to the case-control design of these studies. NR = Not reported.

Table 4: Colorectal cancer: Additional results reported by the individual papers: Rectal bleeding with other symptoms/signs

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Hamilton (2005)	Rectal bleeding and constipation	All patients	2.4 (1.4-4.4)
Metcalf (1996)	Rectal bleeding and constipation	All patients	2.6 (0.1-15.1) 1/39
Hamilton (2005)	Rectal bleeding and diarrhoea	All patients	3.4 (2.1-6)
Metcalf (1996)	Rectal bleeding and diarrhoea	All patients	7.4 (1.3-25.8) 2/27
Hamilton (2005)	Rectal bleeding and abdominal tenderness	All patients	4.5 (NR)
Hamilton (2005)	Rectal bleeding and abnormal rectal exam	All patients	8.5 (NR)
Wauters (2000)	Rectal bleeding and fatigue	All patients	7.1 (??)
Hamilton (2005)	Rectal bleeding and haemoglobin 10-13 g dl ⁻¹	All patients	3.6 (NR)
Hamilton (2005)	Rectal bleeding and haemoglobin < 10 g dl ⁻¹	All patients	3.2 (NR)
Ellis (2005)	Rectal bleeding and change in bowel habit	Patients with flexible sigmoidoscopy/ questionnaire data	9.2 (4.9-16.3) 11/119
Mant (1989)	Rectal bleeding and change in bowel habit	All patients	11 (NR)
Metcalf (1996)	Rectal bleeding and change in bowel habit	All patients	10.3 (3.3-25.2) 4/39
Nørrelund (1996)	New onset or changed	All patients	26.85 (19-36.4)

	pattern rectal bleeding and change in bowel habit		29/108
Nørrelund (1996)	New onset or changed pattern rectal bleeding and uncertain change in bowel habit	All patients	25 (8.3-52.6) 4/16
Nørrelund (1996)	New onset or changed pattern rectal bleeding and no change in bowel habit	All patients	8.75 (5.6-13.2) 21/240
Ellis (2005)	Rectal bleeding and no change in bowel habit	Patients with flexible sigmoidoscopy/ questionnaire data	0 0/147
Mant (1989)	Rectal bleeding and no change in bowel habit	All patients	11 (NR)
Ellis (2005)	Rectal bleeding and change in bowel habit (loose ± frequent)	Patients with flexible sigmoidoscopy/ questionnaire data	12 (6.2-21.5) 10/83
Robertson (2006)	Rectal bleeding and increased frequency/loose motions	All patients	4.8 (2.7-8.3) 13/269
Robertson (2006)	Rectal bleeding and no 'increased frequency/loose motions'	All patients	2.8 (1.4-5.5) 9/319
Ellis (2005)	Rectal bleeding and change in bowel habit (hard ± infrequent)	Patients with flexible sigmoidoscopy/ questionnaire data	2.8 (0.1-16.2) 1/36
Ellis (2005)	Rectal bleeding and no perianal symptoms	Patients with flexible sigmoidoscopy/ questionnaire data	11.1 (5-22.2) 7/63
Ellis (2005)	Rectal bleeding and perianal symptoms	Patients with flexible sigmoidoscopy/ questionnaire data	1.97 (0.6-5.3) 4/203
Mant (1989)	Rectal bleeding and feeling of incomplete evacuation of rectum	All patients	12 (NR)
Mant (1989)	Rectal bleeding and no feeling of incomplete evacuation of rectum	All patients	11 (NR)
Mant (1989)	Rectal bleeding and pain on defecation	All patients	7 (NR)
Mant (1989)	Rectal bleeding and no pain on defecation	All patients	12 (NR)
Wauters (2000)	Rectal bleeding and spasm	All patients	5.4 (2-11.4)
Nørrelund (1996)	New onset or changed pattern rectal bleeding and discomfort	All patients	16.67 (10.1-26) 16/96

Nørrelund (1996)	New onset or changed pattern rectal bleeding and uncertain discomfort	All patients	23.08 (9.8-44.1) 6/26
Nørrelund (1996)	New onset or changed pattern rectal bleeding and no discomfort	All patients	13.22 (9.3-18.3) 32/242
Ellis (2005)	Rectal bleeding and change in bowel habit and abdominal pain	Patients with flexible sigmoidoscopy/ questionnaire data	9 (3.7-19.1) 6/67
Ellis (2005)	Rectal bleeding and change in bowel habit and no abdominal pain	Patients with flexible sigmoidoscopy/ questionnaire data	9.6 (3.6-21.8) 5/52
Ellis (2005)	Rectal bleeding: Dark blood	Patients with flexible sigmoidoscopy/ questionnaire data	9.7 (2.5-26.9) 3/31
Mant (1989)	Rectal bleeding: Dark blood	All patients	19 (NR)
Robertson (2006)	Rectal bleeding: Dark blood	All patients	7.4 (3.7-14) 9/121
Metcalf (1996)	Rectal bleeding: Dark red blood loss	All patients	9.7 (2.5-26.9) 3/31
Robertson (2006)	Rectal bleeding: No/not dark blood	All patients	2.7 (1.5-4.7) 13/483
Ellis (2005)	Rectal bleeding: Bright blood	Patients with flexible sigmoidoscopy/ questionnaire data	4 (1.9-8.1) 8/199
Mant (1989)	Rectal bleeding: Bright blood	All patients	10 (NR)
Metcalf (1996)	Rectal bleeding: Bright red blood loss	All patients	8.6 (3.5-18.4) 6/70
Ellis (2005)	Rectal bleeding: Blood on paper only	Patients with flexible sigmoidoscopy/ questionnaire data	2.4 (0.4-9.4) 2/82
Mant (1989)	Rectal bleeding: Blood seen on paper	All patients	9 (NR)
Metcalf (1996)	Rectal bleeding: Blood only on paper	All patients	8.3 (1.5-28.5) 2/24
Mant (1989)	Rectal bleeding: Blood seen in toilet bowl	All patients	14 (NR)
Ellis (2005)	Rectal bleeding: Blood in pan and on paper	Patients with flexible sigmoidoscopy/ questionnaire data	4.9 (2.4-9.4) 9/184
Mant (1989)	Rectal bleeding: Blood seen on paper and in toilet bowl	All patients	11 (NR)
Ellis (2005)	Rectal bleeding: Large volume of blood	Patients with flexible sigmoidoscopy/ questionnaire data	1.3 (0.07-7.8) 1/79
Ellis (2005)	Rectal bleeding: Small volume of blood	Patients with flexible sigmoidoscopy/ questionnaire data	5.3 (2.7-9.9) 10/187

		questionnaire data	
Ellis (2005)	Rectal bleeding: First time	Patients with flexible sigmoidoscopy/ questionnaire data	4.7 (1.7-11.2) 5/106
Nørrelund (1996)	Rectal bleeding: New onset	All patients	14.24 (10.7-18.7) 45/316
Ellis (2005)	Rectal bleeding: Not first time	Patients with flexible sigmoidoscopy/ questionnaire data	3.8 (1.5-8.3) 6/160
Nørrelund (1996)	Rectal bleeding: Not first time, unchanged bleeding pattern	All patients	4.4 (0.8-16.4) 2/45
Nørrelund (1996)	Rectal bleeding: Not first time, changed bleeding pattern	All patients	18.75 (9.4-33.1) 9/48
Fijten (1995)	Rectal bleeding: Blood on stool or mixed with only	All patients	7 (NR) Total positives N = 54
Fijten (1995)	Rectal bleeding: Blood mixed with stool only	All patients	14 (NR) Total positives N = 14
Mant (1989)	Rectal bleeding: Blood seen mixed with faeces	All patients	21 (NR)
Metcalfe (1996)	Rectal bleeding: Blood mixed with stool	All patients	10.9 (4.1-24.4) 5/46
Ellis (2005)	Rectal bleeding: Blood mixed with the stool	Patients with flexible sigmoidoscopy/ questionnaire data	3 (0.2-17.5) 1/33
Robertson (2006)	Rectal bleeding: Blood mixed with stool	All patients	5.4 (3.3-8.7) 17/314
Fijten (1995)	Rectal bleeding: Others or combinations apart from "blood on stool or mixed with stool only"	All patients	1 (NR) Total positives N = 122
Robertson (2006)	Rectal bleeding: Dark blood and blood mixed with stool	All patients	10.2 (5.1-19) 9/88
Robertson (2006)	Rectal bleeding: Not 'dark blood and blood mixed with stool'	All patients	2.5 (1.4-4.4) 13/516
Robertson (2006)	Rectal bleeding: Blood neither dark nor mixed with stool	All patients	1.9 (0.7-4.7) 5/257
Robertson (2006)	Rectal bleeding: Not 'blood neither dark nor mixed with stool'	All patients	4.9 (3-7.9) 17/347
Fijten (1995)	Rectal bleeding: Unknown how blood was seen	All patients	7 (NR) Total positives N = 54

Ellis (2005)	Rectal bleeding: Blood not mixed with the stool	Patients with flexible sigmoidoscopy/ questionnaire data	4.3 (2.2-8) 10/233
Robertson (2006)	Rectal bleeding: Blood not mixed with stool	All patients	1.7 (0.6-4.2) 5/290
Mant (1989)	Rectal bleeding: Blood seen separate from faeces	All patients	7 (NR)
Metcalf (1996)	Rectal bleeding and associated slime	All patients	10.7 (2.8-29.4) 3/28
Fijten (1995)	Rectal bleeding and nausea	All patients	2 (NR) Total positives N = 68
Fijten (1995)	Rectal bleeding and abdominal pain	All patients	2 (NR) Total positives N = 135
Hamilton (2005)	Rectal bleeding and abdominal pain	All patients	3.1 (1.9-5.3)
Mant (1989)	Rectal bleeding and abdominal pain	All patients	9 (NR)
Metcalf (1996)	Rectal bleeding and abdominal pain	All patients	7.1 (1.9-20.6) 3/42
Robertson (2006)	Rectal bleeding and abdominal pain	All patients	1.7 (0.6-4.6) 4/232
Nørrelund (1996)	New onset or changed pattern rectal bleeding and abdominal pain	All patients	23.33 (15.3-33.7) 21/90
Meineche-Schmidt (2002)	Rectal bleeding and dyspepsia	All patients	2.6 (1.1-5.9) 6/227
Meineche-Schmidt (2002)	Rectal bleeding (visible blood in stools only) and dyspepsia	All patients	4 (1.5-9.6) 5/124
Nørrelund (1996)	New onset or changed pattern rectal bleeding and uncertain abdominal pain	All patients	22.22 (3.9-59.8) 2/9
Mant (1989)	Rectal bleeding and no abdominal pain	All patients	12 (NR)
Robertson (2006)	Rectal bleeding and no abdominal pain	All patients	4.5 (2.7-7.3) 16/358
Nørrelund (1996)	New onset or changed pattern rectal bleeding and no abdominal pain	All patients	11.7 (8.2-16.3) 31/265
Fijten (1995)	Rectal bleeding and decreased appetite	All patients	2 (NR) Total positives N = 42
Fijten (1995)	Rectal bleeding and pain at night	All patients	0 (0-8.9) Total positives N = 50
Wauters (2000)	Rectal bleeding and pain	All patients	0 (0-10.2) 0/386
Fijten (1995)	Rectal bleeding and weight loss	All patients	10 (NR) Total positives N = 42
Hamilton (2005)	Rectal bleeding and	All patients	4.7 (NR)

	weight loss		
Robertson (2006)	Rectal bleeding and weight loss	All patients	4.8 (1.3-14.4) 3/62
Mant (1989)	Rectal bleeding and weight loss	All patients	13 (NR)
Metcalfe (1996)	Rectal bleeding and weight loss	All patients	13.3 (2.3-41.6) 2/15
Nørrelund (1996)	New onset or changed pattern rectal bleeding and weight loss	All patients	22.73 (12-38.2) 10/44
Wauters (2000)	Rectal bleeding and weight loss	All patients	16 (4.5-36.1)
Nørrelund (1996)	New onset or changed pattern rectal bleeding and uncertain weight loss	All patients	28.57 (9.6-58) 4/14
Mant (1989)	Rectal bleeding and no weight loss	All patients	11 (NR)
Robertson (2006)	Rectal bleeding and no weight loss	All patients	3.6 (2.2-5.6) 19/531
Nørrelund (1996)	New onset or changed pattern rectal bleeding and no weight loss	All patients	13.07 (9.6-17.5) 40/306
Fijten (1995)	Rectal bleeding and pale conjunctivae	All patients	17 (NR) Total positives N = 6
Mant (1989)	Rectal bleeding and nongastrointestinal symptoms	All patients	5 (NR)
Mant (1989)	Rectal bleeding and no nongastrointestinal symptoms	All patients	12 (NR)
Fijten (1995)	Rectal bleeding and perianal eczema	All patients	18 (NR) Total positives N = 17
Mant (1989)	Rectal bleeding and anal itch	All patients	3 (NR)
Mant (1989)	Rectal bleeding and no anal itch	All patients	14 (NR)
Fijten (1995)	Rectal bleeding and haemorrhoid on rectal palpation	All patients	10 (NR) Total positives N = 20 (but out of 208, not 269)
Mant (1989)	Rectal bleeding and haemorrhoids identified by GP	All patients	5 (NR)
Robertson (2006)	Rectal bleeding and haemorrhoids	All patients	3.1 (1.6-5.9) 10/320
Robertson (2006)	Rectal bleeding and haemorrhoids and bright red blood not mixed with stools	All patients	1.9 (0.5-5.8) 3/159
Robertson (2006)	Rectal bleeding and	All patients	3.3 (0.9-10.1)

	haemorrhoids and no other symptoms except bright non-mixed bleeding		3/90
Mant (1989)	Rectal bleeding and no haemorrhoids identified by GP	All patients	17 (NR)
Robertson (2006)	Rectal bleeding and no haemorrhoids	All patients	4.6 (2.4-8.3) 11/239
Robertson (2006)	Rectal bleeding and no 'haemorrhoids and bright red blood not mixed with stools'	All patients	4.5 (2.8-7.2) 18/400
Robertson (2006)	Rectal bleeding and no 'haemorrhoids and no other symptoms except bright non-mixed bleeding'	All patients	3.8 (2.4-6.1) 18/469
Fijten (1995)	Rectal bleeding and tumour on rectal palpation	All patients	100 (NR) Total positives N = 1 (but out of 208, not 269)
Wauters (2000)	Rectal bleeding and palpable tumour	All patients	31.5 (12.5-56.5)
Mant (1989)	Rectal bleeding and anal protrusion noticed by patient	All patients	3 (NR)
Mant (1989)	Rectal bleeding and no anal protrusion noticed by patient	All patients	13 (NR)
Fijten (1995)	Rectal bleeding and abnormal prostate on rectal palpation	All patients	50 (NR) Total positive N = 2 (but out of 208, not 269)
Fijten (1995)	Rectal bleeding and previous history of rectal bleeding	All patients	0 (0-4.8) Total positives N = 96
Mant (1989)	Rectal bleeding and first degree relative with colorectal cancer	All patients	10 (NR)
Mant (1989)	Rectal bleeding and no first degree relative with colorectal cancer	All patients	11 (NR)
Metcalfe (1996)	Rectal bleeding and family history of bowel cancer	All patients	0 (0-40.2) 0/8
Fijten (1995)	Rectal bleeding and family history of abdominal disease	All patients	0 (0-5.5) Total positives N = 83
Robertson (2006)	Rectal bleeding and history of irritable bowel	All patients	0 (0-4.8) 0/96

	syndrome		
Robertson (2006)	Rectal bleeding and no history of irritable bowel syndrome	All patients	4.4 (2.8-6.7) 21/481
Robertson (2006)	Rectal bleeding and history of diverticular disease	All patients	0 (0-12.6) 0/34
Robertson (2006)	Rectal bleeding and no history of diverticular disease	All patients	3.9 (2.5-6) 21/536
Fijten (1995)	Rectal bleeding and abnormal proctoscopy	All patients	0 (0-14.1) Total positives N = 30 (but out of 45, not 269)
Robertson (2006)	Rectal bleeding and deprivation category (deprivation category 1 = least deprived, deprivation category 7 = most deprived)	Deprivation category 1	4.1 (1.1-12.2) 3/74
		Deprivation category 2	3.4 (1.1-8.9) 4/119
		Deprivation category 3	2.6 (0.8-6.9) 4/155
		Deprivation category 4	5.8 (2.7-11.6) 8/137
		Deprivation category 5	0/53 (0-8.4)
		Deprivation category 6	0/25 (0-16.6)
		Deprivation category 7	5.3 (0.3-28.1) 1/19

Please note:

- The calculations of the positive predictive values differ between the remaining studies using (TP)/(TP+FP) and Hamilton (2005, 2008, 2009) using other statistics due to the case-control design of these studies. NR = Not reported.

Table 5: Colorectal cancer: Additional results reported by the individual papers: Other symptom combinations

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Hamilton (2005)	Constipation and diarrhoea	All patients	1.1 (0.6-1.8)
Hamilton (2005)	Constipation and loss of weight	All patients	3 (1.7-5.4)
Hamilton (2005)	Constipation and abdominal pain	All patients	1.5 (1-2.2)
Hamilton (2005)	Constipation and abdominal tenderness	All patients	1.7 (0.9-3.4)
Hamilton (2005)	Constipation and abnormal rectal exam	All patients	2.6 (NR)
Hamilton (2005)	Constipation and haemoglobin 10-13 g dl ⁻¹	All patients	1.2 (0.6-2.7)
Hamilton (2005)	Constipation and haemoglobin < 10 g dl ⁻¹	All patients	2.6 (NR)

Hamilton (2005)	Diarrhoea and loss of weight	All patients	3.1 (1.8-5.5)
Hamilton (2005)	Diarrhoea and abdominal pain	All patients	1.9 (1.4-2.7)
Hamilton (2005)	Diarrhoea and abdominal tenderness	All patients	2.4 (1.3-4.8)
Hamilton (2005)	Diarrhoea and abnormal rectal exam	All patients	11 (NR)
Hamilton (2005)	Diarrhoea and haemoglobin 10-13 g dl ⁻¹	All patients	2.2 (1.2-4.3)
Hamilton (2005)	Diarrhoea and haemoglobin < 10 g dl ⁻¹	All patients	2.9 (NR)
Hamilton (2005)	Abdominal pain and loss of weight	All patients	3.4 (2.1-6)
Hamilton (2005)	Abdominal pain and abdominal tenderness	All patients	1.4 (0.3-2.2)
Hamilton (2005)	Abdominal pain and abnormal rectal exam	All patients	3.3 (NR)
Hamilton (2005)	Abdominal pain and haemoglobin 10-13 g dl ⁻¹	All patients	2.2 (1.1-4.5)
Hamilton (2005)	Abdominal pain and haemoglobin < 10 g dl ⁻¹	All patients	6.9 (NR)
Hamilton (2005)	Abdominal tenderness and loss of weight	All patients	6.4 (NR)
Hamilton (2005)	Abdominal tenderness and abnormal rectal exam	All patients	5.8 (NR)
Hamilton (2005)	Abdominal tenderness and haemoglobin 10-13 g dl ⁻¹	All patients	2.7 (NR)
Hamilton (2005)	Abdominal tenderness and haemoglobin < 10 g dl ⁻¹	All patients	>10 (NR) (no controls had this pair of symptoms)
Hamilton (2005)	Loss of weight and abnormal rectal exam	All patients	7.4 (NR)
Hamilton (2005)	Loss of weight and haemoglobin 10-13 g dl ⁻¹	All patients	1.3 (0.7-2.6)
Hamilton (2005)	Loss of weight and haemoglobin < 10 g dl ⁻¹	All patients	4.7 (NR)
Meineche-Schmidt (2002)	Dyspepsia and anaemia	All patients	13.51 (5-29.57) 5/37
Meineche-Schmidt (2002)	Dyspepsia and dysphagia	All patients	0 (0-2.2) 0/215
Meineche-Schmidt (2002)	Dyspepsia and jaundice	All patients	0 (0-48.32) 0/6
Meineche-Schmidt (2002)	Dyspepsia and weight loss	All patients	1.37 (0.35-4.28) 3/219

Please note:

- The calculations of the positive predictive values differ between the remaining studies using (TP)/(TP+FP) and Hamilton (2005, 2008, 2009) using other statistics due to the case-control design of these studies. NR = not reported.

Table 6: Colorectal cancer: Additional results reported by the individual papers: Age

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Du Toit (2006)	Rectal bleeding	Patients 45-54 years	3.9 (0.7-14.6) 2/51
		Patients 55-64 years	1.3 (0.07-8.2) 1/75
		Patients 65-74 years	9.5 (3.9-20.2) 6/63
		Patients ≥ 75 years	7.9 (3.3-17) 6/76
Ellis (2005)	Rectal bleeding and aged ≥ 60 years	Patients with flexible sigmoidoscopy/ questionnaire data	5.2 (2.4-10.3) 8/155
	Rectal bleeding and aged ≤ 59 years		1.8 (0.5-5.7) 3/164
Fijten (1995)	Rectal bleeding	Patients 18-59 years	0.4 (0.03-2.8) 1/229
		Patients 60-75 years	20 (9.6-36.1) 8/40
Nørrelund (1996)	New onset or changed pattern rectal bleeding	Patients 40-69 years	7.87 (5-12.1) 20/254
		Patients 70-79 years	34.12 (24.4-45.3) 29/85
		Patients 80+ years	20 (7.6-41.3) 5/25
Hamilton (2005)	Rectal bleeding	Patients 40-69 years	1.4 (NR)
		Patients ≥ 70 years	4.8 (NR)
Heintze (2005)	Rectal bleeding	Patients < 50 years	2/≤153*
		Patients ≥ 50 years	15/≤268*
Mant (1989)	Rectal bleeding	Patients 40-60 years	8 (NR)
		Patients > 60 years	16 (NR)
Parker (2007)	Rectal bleeding	Patients 25-34 years	0.1 3/4717
		Patients 35-44 years	0.3 17/5301
		Patients 45-54 years	1.5 (1.2-1.8) 75/5120
		Patients 55-64 years	2.8 (2.3-3.3) 137/4927
		Patients 65-74 years	4.3 (3.7-5) 189/4383
		Patients 75-84 years	5.5 (4.7-6.3) 173/3168
		Patients ≥ 85 years	3.7 (2.8-4.8) 51/1391
Robertson (2006)	Rectal bleeding	Patients < 50 years	1.1 (0.3-3.5) 3/270
		Patients 50-69 years	4.8 (2.6-8.7)

			11/227
		Patients ≥ 70 years	7.5 (3.5-14.6) 8/107
Wauters (2000)	Rectal bleeding	Patients < 50 years	0.7 (0-4.9) 1/141
		Patients 50-59 years	1.7 (0-9.4) 1/57
		Patients 60-69 years	11.2 (5-21) 8/71
		Patients 70-79 50 years	21.2 (12-33) 14/66
		Patients ≥ 80 years	5.8 (1.2-16.2) 3/51
Nørrelund (1996)	New onset or changed pattern rectal bleeding and change in bowel habit	Patients 40-69 years	16.13 (8.4-28.1) 10/62
		Patients 70-79 years	42.5 (27.4-59) 17/40
		Patients 80+ years	33.3 (6-75.9) 2/6
Nørrelund (1996)	New onset or changed pattern rectal bleeding and uncertain change in bowel habit	Patients 40-69 years	18.18 (3.2-52.2) 2/11
		Patients 70-79 years	66.7 (12.5-98.2) 2/3
		Patients 80+ years	0 (0-80.2) 0/2
Nørrelund (1996)	New onset or changed pattern rectal bleeding and no change in bowel habit	Patients 40-69 years	4.42 (2.1-8.8) 8/181
		Patients 70-79 years	23.81 (12.6-39.8) 10/42
		Patients 80+ years	17.65 (4.7-44.2) 3/17
Hamilton (2005)	Abdominal pain	Patients 40-69 years	0.65 (NR)
		Patients ≥ 70 years	2 (NR)
Hamilton (2005)	Diarrhoea	Patients 40-69 years	0.63 (NR)
		Patients ≥ 70 years	1.7 (NR)
Hamilton (2005)	Constipation	Patients 40-69 years	0.2 (NR)
		Patients ≥ 70 years	1.3 (NR)
Hamilton (2005)	Weight loss	Patients 40-69 years	0.74 (NR)
		Patients ≥ 70 years	2.5 (NR)

*Data missing from 22/422 patients, but it is unclear which of the age subgroups the missing data belongs to.

Please note:

- Lawrenson (2006) calculated the positive predictive values of colorectal cancer being diagnosed within 12 months of initial symptoms per 100 patients presenting by using Kaplan-Maier curves, and it is unclear how and if these calculations differ from those of the other studies.

- The calculations of the positive predictive values differ between the remaining studies using (TP)/(TP+FP) and Hamilton (2005, 2008, 2009) using other statistics due to the case-control design of these studies.

Table 7: Colorectal cancer: Additional results reported by the individual papers: Men

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Collins (2012)	Rectal bleeding	Men 30-84 years	2.8 (2.6-3) 791/28423
Jones (2007)	Rectal bleeding at 6 months	Men (all ages)	1.8 (1.5-2.2) 138/7523
Fijten (1995)	Rectal bleeding	Men (all ages)	5.9 (2.6-12.3) 7/118
Jones (2007)	Rectal bleeding at 3 years	Men (all ages)	2.4 (2.1-2.8) 184/7523
Mant (1989)	Rectal bleeding	Men ≥ 40 years	9 (NR)
Nørrelund (1996)	New onset or changed pattern rectal bleeding	Men ≥ 40 years	17.26 (12-24) 29/168
Robertson (2006)	Rectal bleeding	Men (all ages)	4.8 (2.7-8.2) 13/273
Jones (2007)	Rectal bleeding at 3 years	Men < 45 years	0.07 (0.01-0.27) 2/2701
		Men 45-54 years	1.56 (1-2.31) 24/1542
		Men 55-64 years	3.38 (2.47-4.51) 44/1302
		Men 65-74 years	4.8 (3.65-6.17) 57/1188
		Men 75-84 years	7.74 (5.78-10.1) 49/633
		Men ≥ 85 years	5.1 (2.23-9.79) 8/157
Hamilton (2009)	Rectal bleeding at 2 years (read off graph)	Men < 60 years	0.5 (0.3-0.7)
		Men 60-69 years	2.4 (1.8-3.2)
		Men 70-79 years	3.5 (2.8-4.6)
		Men ≥ 80 years	4.5 (3.3-5.9)
Lawrenson (2006)	Rectal bleeding	Men 40-49 years	0.92 (NR)
		Men 50-59 years	2.75 (NR)
		Men 60-69 years	5.99 (NR)
		Men 70-79 years	7.69 (NR)
		Men 80-89 years	9.13 (NR)
Helfand (1007)	Rectal bleeding	Men < 50 years	0 (0-7.7) 0/58
Collins (2012)	Change in bowel habit	Men 30-84 years	2.9 (2.2-3.9) 49/1670
Hippisley-Cox (2012)	Change in bowel habit	Men 30-84 years	2.8 (1.8-4.2) 21/763
Hamilton (2009)	Change in bowel habit (read off graph)	Men < 60 years	1.1 (0.6-2.4)
		Men 60-69 years	3 (2.1-4.2)
		Men 70-79 years	4.2 (3.2-5.4)
		Men ≥ 80 years	3.9 (2.8-5.6)
Lawrenson (2006)	Change in bowel habit	Men 40-49 years	0.89 (NR)
		Men 50-59 years	4.07 (NR)
		Men 60-69 years	6.89 (NR)
		Men 70-79 years	8.48 (NR)

		Men 80-89 years	7.73 (NR)
Collins (2012)	Abdominal pain	Men 30-84 years	0.6 (0.6-0.7) 622/102192
Hamilton (2009)	Abdominal pain (read off graph)	Men < 60 years	0.15 (0.1-0.15)
		Men 60-69 years	0.9 (0.7-1)
		Men 70-79 years	1.1 (0.9-1.3)
		Men ≥ 80 years	1.2 (1-1.5)
Hamilton (2009)	Diarrhoea (read off graph)	Men < 60 years	0.1 (0.1-0.1)
		Men 60-69 years	0.9 (0.7-1.1)
		Men 70-79 years	1.3 (1.1-1.5)
		Men ≥ 80 years	1.2 (1-1.5)
Hamilton (2009)	Constipation (read off graph)	Men < 60 years	0.2 (0.2-0.2)
		Men 60-69 years	0.8 (0.6-0.9)
		Men 70-79 years	0.8 (0.7-0.9)
		Men ≥ 80 years	0.7 (0.6-0.8)
Collins (2012)	Appetite loss	Men 30-84 years	1 (0.6-1.5) 24/2481
Collins (2012)	Weight loss	Men 30-84 years	1 (0.8-1.1) 124/12891
Hamilton (2009)	Weight loss 5-10% (read off graph)	Men aged < 60 years	0.1 (0.05-0.2)
		Men aged 60-69 years	0.3 (0.2-0.4)
		Men aged 70-79 years	0.7 (0.5-0.8)
		Men aged ≥ 80 years	0.5 (0.3-0.8)
Hamilton (2009)	Weight loss ≥ 10% (read off graph)	Men < 60 years	0.2 (0.1-0.3)
		Men 60-69 years	0.7 (0.4-0.9)
		Men 70-79 years	1.5 (1.2-1.8)
		Men ≥ 80 years	0.8 (0.6-1.4)
Hamilton (2008)	Haemoglobin ≥ 13 g dl ⁻¹	Men 30-59 years	0.1 (0.1-0.1)
		Men 60-69 years	0.3 (0.3-0.3)
		Men 70-79 years	0.4 (0.3-0.4)
		Men ≥ 80 years	0.4 (0.3-0.5)
Hamilton (2008)	Haemoglobin 12-12.9 g dl ⁻¹	Men 30-59 years	0.2 (0.1-0.3)
		Men 60-69 years	0.7 (0.5-1)
		Men 70-79 years	1 (0.7-1.2)
		Men ≥ 80 years	0.6 (0.5-0.8)
Hamilton (2008)	Haemoglobin 11-11.9 g dl ⁻¹	Men 30-59 years	0.8 (0.2-2.9)
		Men 60-69 years	1.4 (0.9-2.3)
		Men 70-79 years	1.5 (1.2-2)
		Men ≥ 80 years	1 (0.8-1.4)
Hamilton (2008)	Haemoglobin 10-10.9 g dl ⁻¹	Men 30-59 years	0.8 (0.3-2.2)
		Men 60-69 years	2.3 (1.1-4.8)
		Men 70-79 years	3.2 (2.2-4.8)
		Men ≥ 80 years	1.6 (1.1-2.2)
Hamilton (2008)	Haemoglobin 9-9.9 g dl ⁻¹	Men 30-59 years	1.4 (0.2-10)
		Men 60-69 years	7.2 (2.9-17)
		Men 70-79 years	4 (2.5-6.3)
		Men ≥ 80 years	6 (3.4-10)
Hamilton (2008)	Haemoglobin < 9 g dl ⁻¹	Men 30-59 years	1.3 (0.4-4.3)
		Men 60-69 years	7.6 (3.4-16)
		Men 70-79 years	8.8 (5.4-14)

		Men ≥ 80 years	6.8 (4.2-11)
Hamilton (2008)	Haemoglobin ≥ 13 g dl ⁻¹ + indicators of iron deficiency**	Men 60-69 years	1.4 (0.6-3.6)
		Men 70-79 years	1.7 (0.9-3.1)
		Men ≥ 80 years	1.4 (0.6-3.1)
Hamilton (2008)	Haemoglobin 12-12.9 g dl ⁻¹ + indicators of iron deficiency**	Men 60-69 years	1.8 (0.7-4.2)
		Men 70-79 years	3.9 (1.8-8.5)
		Men ≥ 80 years	1.5 (0.5-4.2)
Hamilton (2008)	Haemoglobin 11-11.9 g dl ⁻¹ + indicators of iron deficiency**	Men 60-69 years	6.5 (2-19)
		Men 70-79 years	4.1 (2.1-8)
		Men ≥ 80 years	4 (1.6-9.3)
Hamilton (2008)	Haemoglobin 10-10.9 g dl ⁻¹ + indicators of iron deficiency**	Men 60-69 years	5.5 (1.2-21)
		Men 70-79 years	14 (5.9-29)
		Men ≥ 80 years	8.2 (3.7-17)
Hamilton (2008)	Haemoglobin 9-9.9 g dl ⁻¹ + indicators of iron deficiency**	Men 60-69 years	12 (3.1-37)
		Men 70-79 years	16 (6.3-35)
		Men ≥ 80 years	31 (5.6-77)
Hamilton (2008)	Haemoglobin < 9 g dl ⁻¹ + indicators of iron deficiency**	Men 60-69 years	>5 (30 cases, 0 controls)
		Men 70-79 years	18 (8.7-34)
		Men ≥ 80 years	15 (7.3-28)
Hamilton (2008)	Haemoglobin < 11 g dl ⁻¹ + indicators of iron deficiency	Men > 60 years	13.3 (9.7-18)
Collins (2012)	Anaemia	Men 30-84 years	3 (2.5-3.6) 135/4466
Yates (2004)	Anaemia	Men > 20 years	18.2 (12.6-25.4) 28/154
Lawrenson (2006)	Anaemia	Men 40-49 years	1.07 (NR)
		Men 50-59 years	1.86 (NR)
		Men 60-69 years	3.02 (NR)
		Men 70-79 years	3.38 (NR)
		Men 80-89 years	2.98 (NR)

**For the 30-59 years group 64 cases, but only 11 controls had markers of iron deficiency making meaningful analysis impossible.

Please note:

- Lawrenson (2006) calculated the positive predictive values of colorectal cancer being diagnosed within 12 months of initial symptoms per 100 patients presenting by using Kaplan-Maier curves, and it is unclear how and if these calculations differ from those of the other studies.

- The calculations of the positive predictive values differ between the remaining studies using (TP)/(TP+FP) and Hamilton (2005, 2008, 2009) using other statistics due to the case-control design of these studies. NP = Not reported.

Table 8: Colorectal cancer: Additional results reported by the individual papers: Women

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Collins (2012)	Rectal bleeding	Women 30-84 years	2.1 (1.9-2.2) 571/27811
Jones (2007)	Rectal bleeding at 6 months	Women (all ages)	1.5 (1.3-1.8) 119/7766

Fijten (1995)	Rectal bleeding	Women (all ages)	1.3 (0.2-5.2) 2/151
Jones (2007)	Rectal bleeding at 3 years	Women (all ages)	2 (1.7-2.3) 154/7766
Mant (1989)	Rectal bleeding	Women ≥ 40 years	13 (NR)
Nørrelund (1996)	New onset or changed pattern rectal bleeding	Women ≥ 40 years	12.76 (8.6-18.4) 25/196
Robertson (2006)	Rectal bleeding	Women (all ages)	2.7 (1.3-5.3) 9/331
Jones (2007)	Rectal bleeding at 3 years	Women < 45 years	0.22 (0.08-0.47) 6/2780
		Women 45-54 years	0.63 (0.27-1.24) 8/1270
		Women 55-64 years	2.75 (1.9-3.84) 33/1200
		Women 65-74 years	2.42 (1.62-3.48) 28/1156
		Women 75-84 years	7.2 (5.63-9.06) 67/930
		Women > 85 years	2.79 (1.45-4.82) 12/430
Hamilton (2009)	Rectal bleeding at 2 years (read off graph)	Women < 60 years	0.4 (0.3-0.5)
		Women 60-69 years	2.1 (1.4-3.1)
		Women 70-79 years	2.2 (1.7-2.9)
		Women ≥ 80 years	2.9 (2.1-3.8)
Lawrenson (2006)	Rectal bleeding	Women 40-49 years	0.87 (NR)
		Women 50-59 years	2.16 (NR)
		Women 60-69 years	3.5 (NR)
		Women 70-79 years	4.61 (NR)
		Women 80-89 years	4.89 (NR)
Hamilton (2009)	Change in bowel habit (read off graph)	Women < 60 years	0.4 (0.3-0.5)
		Women 60-69 years	1.3 (0.8-1.9)
		Women 70-79 years	1.5 (1.1-1.9)
		Women ≥ 80 years	1.9 (1.3-2.7)
Lawrenson (2006)	Change in bowel habit	Women 40-49 years	0.64 (NR)
		Women 50-59 years	1.64 (NR)
		Women 60-69 years	2.42 (NR)
		Women 70-79 years	3.25 (NR)
		Women 80-89 years	4.09 (NR)
Collins (2012)	Abdominal pain	Women 30-84 years	0.4 (0.4-0.5) 598/143797
Hamilton (2009)	Abdominal pain (read off graph)	Women < 60 years	0.01 (0.1-0.1)
		Women 60-69 years	0.4 (0.35-0.5)
		Women 70-79 years	0.7 (0.6-0.75)
		Women ≥ 80 years	0.9 (0.8-1)
Hamilton (2009)	Diarrhoea (read off graph)	Women < 60 years	0.01 (0.1-0.1)
		Women 60-69 years	0.35 (0.25-0.4)
		Women 70-79 years	0.5 (0.4-0.6)
		Women ≥ 80 years	0.7 (0.6-0.8)
Hamilton (2009)	Constipation (read off	Women < 60 years	0.1 (0.1-0.1)

	graph)	Women 60-69 years	0.5 (0.4-0.6)
		Women 70-79 years	0.5 (0.4-0.6)
		Women aged ≥ 80 years	0.5 (0.4-0.6)
Collins (2012)	Appetite loss	Women 30-84 years	0.6 (0.4-1) 20/3295
Collins (2012)	Weight loss	Women 30-84 years	0.6 (0.5-0.7) 91/15398
Hamilton (2009)	Weight loss 5-10% (read off graph)	Women < 60 years	0.05 (0.05-0.05)
		Women 60-69 years	0.2 (0.1-0.3)
		Women 70-79 years	0.4 (0.3-0.6)
		Women ≥ 80 years	0.4 (0.3-0.6)
Hamilton (2009)	Weight loss ≥ 10% (read off graph)	Women < 60 years	0.06 (0.06-0.08)
		Women 60-69 years	0.5 (0.3-0.7)
		Women 70-79 years	0.8 (0.6-1.1)
		Women ≥ 80 years	0.8 (0.6-1.1)
Hamilton (2008)	Haemoglobin ≥ 13 g dl ⁻¹	Women 30-59 years	0 (0-0)
		Women 60-69 years	0.1 (0.1-0.2)
		Women 70-79 years	0.2 (0.2-0.2)
		Women ≥ 80 years	0.2 (0.2-0.3)
Hamilton (2008)	Haemoglobin 12-12.9 g dl ⁻¹	Women 30-59 years	0.0 (0.0-0.1)
		Women 60-69 years	0.2 (0.1-0.2)
		Women 70-79 years	0.3 (0.3-0.4)
		Women ≥ 80 years	0.3 (0.2-0.4)
Hamilton (2008)	Haemoglobin 11-11.9 g dl ⁻¹	Women 30-59 years	0.1 (0.1-0.2)
		Women 60-69 years	0.4 (0.3-0.6)
		Women 70-79 years	0.5 (0.4-0.6)
		Women ≥ 80 years	0.6 (0.5-0.8)
Hamilton (2008)	Haemoglobin 10-10.9 g dl ⁻¹	Women 30-59 years	0.4 (0.2-0.8)
		Women 60-69 years	1.2 (0.7-2)
		Women 70-79 years	1.9 (1.4-2.6)
		Women ≥ 80 years	1.2 (0.9-1.5)
Hamilton (2008)	Haemoglobin 9-9.9 g dl ⁻¹	Women 30-59 years	0.3 (0.1-0.6)
		Women 60-69 years	2.7 (1.2-5.9)
		Women 70-79 years	3.6 (2.1-6)
		Women ≥ 80 years	2.2 (1.5-3.1)
Hamilton (2008)	Haemoglobin < 9 g dl ⁻¹	Women 30-59 years	0.9 (0.3-2.9)
		Women 60-69 years	>5 (41 cases, 0 controls)
		Women 70-79 years	8.6 (5.4-14)
		Women ≥ 80 years	7.1 (4.5-11)
Hamilton (2008)	Haemoglobin ≥ 13 g dl ⁻¹ + indicators of iron deficiency	Women 30-59 years	0.1 (0-0.3)
		Women 60-69 years	2.9 (0.6-12)
		Women 70-79 years	0.4 (0.2-1.1)
		Women ≥ 80 years	0.8 (0.3-1.8)
Hamilton (2008)	Haemoglobin 12-12.9 g dl ⁻¹ + indicators of iron deficiency	Women 30-59 years	0.1 (0.0-0.3)
		Women 60-69 years	0.1 (0.0-0.8)
		Women 70-79 years	0.8 (0.4-1.7)
		Women ≥ 80 years	1.5 (0.5-4.2)
Hamilton (2008)	Haemoglobin 11-11.9 g	Women 30-59 years	0.2 (0.1-0.4)

	dl ⁻¹ + indicators of iron deficiency	Women 60-69 years	1.5 (0.7-3.3)
		Women 70-79 years	2.1 (1.1-4)
		Women ≥ 80 years	3.6 (2-6.5)
Hamilton (2008)	Haemoglobin 10-10.9 g dl ⁻¹ + indicators of iron deficiency	Women 30-59 years	0.6 (0.2-2.1)
		Women 60-69 years	2.4 (1-5.7)
		Women 70-79 years	5.9 (3-11)
		Women ≥ 80 years	2.5 (1.5-4.1)
Hamilton (2008)	Haemoglobin 9-9.9 g dl ⁻¹ + indicators of iron deficiency	Women 30-59 years	0.3 (0.1-0.8)
		Women 60-69 years	3.5 (1.1-11)
		Women 70-79 years	8.6 (3.8-18)
		Women ≥ 80 years	5.7 (3-11)
Hamilton (2008)	Haemoglobin < 9 g dl ⁻¹ + indicators of iron deficiency	Women 30-59 years	0.6 (0.2-2.2)
		Women 60-69 years	>5 (36 cases, 0 controls)
		Women 70-79 years	10 (5.2-19)
		Women ≥ 80 years	10 (5.6-17)
Hamilton (2008)	Haemoglobin < 10 g dl ⁻¹	Women > 60 years	7.7 (5.7-11) Cases: 367/3021 Controls: 121/21138
Collins (2012)	Anaemia	Women 30-84 years	1.3 (1.1-1.5) 173/13659
Yates (2004)	Anaemia	Women > 50 years	3.2 (1.6-6.3) 9/277
Lawrenson (2006)	Anaemia	Women 40-49 years	0.08 (NR)
		Women 50-59 years	0.56 (NR)
		Women 60-69 years	1.38 (NR)
		Women 70-79 years	1.99 (NR)
		Women 80-89 years	2.01 (NR)

Please note:

- Lawrenson (2006) calculated the positive predictive values of colorectal cancer being diagnosed within 12 months of initial symptoms per 100 patients presenting by using Kaplan-Maier curves, and it is unclear how and if these calculations differ from those of the other studies.
- The calculations of the positive predictive values differ between the remaining studies using (TP)/(TP+FP) and Hamilton (2005, 2008, 2009) using other statistics due to the case-control design of these studies. NR = Not reported

Evidence statement(s):

Rectal bleeding (16 studies, N = 134794) presenting in a primary care setting is associated with an overall positive predictive value of up to 4.88% for colorectal cancer, which tended to increase with age (10 studies, N = 33874) both in men (3 studies, N = 103846) and in women (3 studies, N = 103846). All the studies were associated with ≤ 2 bias or applicability concerns (see also Tables 1-3, 6-8).

Abdominal pain (5 studies, N = 373796) presenting in a primary care setting is associated with an overall positive predictive value of up to 2.04% for colorectal cancer, which tended to increase with age (1 study, N = 2093) both in men (1 study, N = 43791) and in women (1 study, N = 43791). All the studies were associated with ≤ 2 bias or applicability concerns (see also Tables 1-3, 6-8).

Anaemia (10 studies, N = 89550) presenting in a primary care setting is associated with an overall positive predictive value of up to 5.87% for colorectal cancer, which tended to increase with age (1 study, N = 2093) both in men (2 studies, N = 118672) and in women (2 studies, N = 118672). Seven of the studies were associated with ≤ 2 bias or applicability concern, while the remaining two studies were associated with 3 and 4 bias or applicability concerns, respectively (see also Tables 1-3, 7-8).

Constipation (2 studies, N = 2373) presenting in a primary care setting is associated with an overall positive predictive value of up to 15.7% for colorectal cancer in a very small study (N = 280) in selected patients that contrasts with the estimates of 0.42-0.81% reported by another study (N = 2093) that also showed that the positive predictive values increase with age, which seems to be the case for both men (1 study, N = 43791) and for women (1 study, N = 43791). All the studies were associated with ≤ 3 bias or applicability concerns (see also Tables 3, 6-8).

Diarrhoea (2 studies, N = 2373) presenting in a primary care setting is associated with an overall positive predictive value of up to 11.8% for colorectal cancer in a very small study (N = 280) in selected patients that contrasts with the estimates of 0.94-1.5% reported by another study (N = 2093) that also showed that the positive predictive values increase with age, which seems to be the case for both men (1 study, N = 43791) and for women (1 study, N = 43791). All the studies were associated with ≤ 3 bias or applicability concerns (see also Tables 3, 6-8).

Change in bowel habit (3 studies, N = 621601) presenting in a primary care setting is associated with an overall positive predictive value of up to 14% for colorectal cancer in a very small study (N = 280) in selected patients that contrasts with the estimates of 2.8% and 2.9% reported by two other studies in men only (N = 621321). The positive predictive values of change in bowel habit for colorectal cancer also appears to increase with age in men (2 studies, N = 71315) and in women (2 studies, N = 71315). All the studies were associated with ≤ 3 bias or applicability concerns (see also Tables 3, 7-8).

Weight loss (4 studies, N = 44431) presenting in a primary care setting is associated with an overall positive predictive value of up to 3% for colorectal cancer which tended to increase with age (1 study, N = 2093) both in men (1 study, N = 43791) and in women (1 study, N = 43791). All the studies were associated with ≤ 3 bias or applicability concerns (see also Tables 1-3, 6-8).

Dyspepsia (3 studies, N = 4476) presenting in a primary care setting is associated with an overall positive predictive value of 0.6% for colorectal cancer. All the studies were associated with 1 applicability concerns (see also Table 3).

Other single symptoms (8 studies, N = 1245637) presenting in a primary care setting are associated with overall positive predictive values of up to 13.2% for colorectal cancer, but this estimate comes from a small study (N = 280) of selected patients and may therefore be inflated. All the studies were associated with ≤ 3 bias or applicability concerns (see also Table 3).

Rectal bleeding presenting with other symptoms (9 studies, N = 5770) in a primary care setting are associated with overall positive predictive values ranging from 0-100%, but many of these estimates are artificially inflated due to small numbers of patients in the calculations. All the studies were associated with ≤ 2 bias or applicability concerns (see also Table 4).

Other symptom combinations (2 studies, N = 3494) presenting in a primary care setting are associated with overall positive predictive values for colorectal cancer ranging from 0% for dyspepsia with dysphagia or jaundice to 13.51% for dyspepsia and anaemia. Both studies were associated with 1 bias/applicability concern (see also Table 5).

Evidence tables

Bellentani (1990)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive patient series
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 254 (103 males/151 females); mean (SD) age of patients = Not reported; N = 140 were studied in primary care, N = 114 were referred to the gastroenterology services. It is unclear from the publication whether the patients who were referred to secondary care were a subset of "254 consecutive patients who presented to their GP during the study period for chronic abdominal pain" or whether they are recruited directly from secondary care (see Inclusion criteria).</p> <p><u>Inclusion criteria:</u> All consecutive patients consulting 14 GPs of the local health district, taking care of 14000 citizens, or referred to the outpatient clinic of the Gastroenterology Unit, either complaining of recurrent abdominal pain or having intestinal problems (as judged by the GP), between January 1987 and March 1988.</p> <p><u>Exclusion criteria:</u> Patients with acute abdomen, acute gastroenteritis or a clear cut diagnosis of upper gastrointestinal tract disease (gastritis, oesophagitis, peptic ulcer, or dyspepsia).</p> <p><u>Clinical setting:</u> Primary/secondary care, Italy.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Recurrent abdominal pain or intestinal problems (as judged by the GP; not further specified)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Double-contrast barium enema or colonoscopy no more than 2 months after the enrolment in the study.
Is the reference standard likely to correctly classify the target condition?	Yes

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results but the number of true negatives and false negatives could not be ascertained from the reported results.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Collins (2012)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2135540 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Rectal bleeding (N = 56234; 28423 men, 27811 women), abdominal pain (N = 245989; 102192 men, 143797 women), appetite loss (N = 5776; 2481 men, 3295 women), weight loss (N = 28289; 12891 men, 15398 women), anaemia (N = 18125; 4466 men, 13659 women), change in bowel habit (men only, N = 1670).</p> <p><u>Incident cases of colorectal cancer during the 2-year follow up period:</u> N = 3712 (2036 men, 1676 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of colorectal cancer at baseline, and patients with a recorded 'red-flag' symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>

Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Rectal bleeding, loss of appetite, weight loss, abdominal pain, change in bowel habit (men only), and anaemia.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	The is <i>very large, if not complete, overlap</i> of the data used in this study with those used in Hamilton (2008 [for anaemia], 2009)

Droogendijk (2011)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective peripheral hospital laboratory database study serving 265 GPs in Dordrecht (Holland).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	N = 287; 129 men, 158 women; median (range) age = 70 (19-87) years. <u>Inclusion criteria:</u> All women aged > 50 years and all men aged ≥ 18 years who between January 2004 and December 2005 were diagnosed with iron-deficiency anaemia (haemoglobin < 13.7 g/dl in men and < 12.1 g/dl in women, and a serum ferritin level < 25 µg/l for men and < 20 µg/l for women). <u>Exclusion criteria:</u> Patients with a known history of iron-deficiency anaemia in the previous 2 years, a history of gastrointestinal malignancy or congenital haemoglobinopathy. <u>Clinical setting:</u> GPs in Holland
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	New onset iron-deficiency anaemia (haemoglobin < 13.7 g/dl in men and < 12.1 g/dl in women, and a serum ferritin level < 25 µg/l for men and < 20 µg/l for women).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy and 12-month follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	It is unclear if all patients are accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Unclear
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

NOTES	In addition to the 24 patients with colorectal cancer, 3 patients had gastric cancer, 1 patient had oesophageal cancer and 1 patient had locally invasive endometrial cancer.	
Du Toit (2006)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	10-year prospective consecutive patient sample from a rural UK GP practice (four doctors and 1 registrar; mean list size 4426 patients over the decade).	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	N = 265; age: 45-54 years: N = 51; 55-64 years: N = 75; 65-74 years: N = 63; ≥ 75 years: N = 76. <u>Inclusion criteria:</u> Patients aged ≥ 45 years reporting new onset rectal bleeding with or without diarrhoea, during a 10-year period. <u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> Primary care, UK.	
Are there concerns that the included patients and setting do not match the review question?	Low concern	
INDEX TEST		
A. Risk of bias		
Index test	New onset rectal bleeding	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Rigid sigmoidoscopy with barium enema or flexible sigmoidoscopy or colonoscopy.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	

FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	13/265 patients had adenoma and 15/265 had colorectal cancer. 2/15 patients with cancer and 4/13 patients with adenoma had diarrhoea.

Ellis (2005)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 19 GPs in 3 practices (1 in each of the following: market town/rural community, suburban area and inner-city).
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 319 (143 males/176 females); mean (range) age of male patients = 56 (35-84) years, mean (range) age of female patients = 62 (35-84) years. Patients accepting a flexible sigmoidoscopy: 219/319; patients filling out questionnaire: 47/319; patients declining both sigmoidoscopy and questionnaire: 57/319. 61/219 patients had either a barium-enema (37) or a colonoscopy (24).</p> <p><u>Inclusion criteria:</u> GPs were asked to identify patients (aged > 34 years) whose primary complaint was rectal bleeding and those with other lower gastrointestinal symptoms who, on questioning, also had rectal bleeding. The patients were asked if they were willing to fill out a postal questionnaire and/or accept a flexible sigmoidoscopy.</p> <p><u>Exclusion criteria:</u> None listed.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Rectal bleeding
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or	Low concern

interpretation differ from the review question?		
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Flexible sigmoidoscopy/barium enema/colonoscopy and follow up	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients are accounted for and included in the results for rectal bleeding alone. However, for the analyses based on other symptoms presenting with rectal bleeding only those patients who received flexible sigmoidoscopy (N = 219) or who filled in a patient questionnaire (N = 47) were included.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	No	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES		
Farrus Palou (2000)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective consecutive patient series from urban general practice covering a population of 24000.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 87 of whom the data from 29 were unavailable as no etiological diagnosis was found (due to patient refusal of further investigation [?; 8], lost to follow up [7], patient deterioration rendering them unsuitable for further investigation [14]); of the remaining 58 patients there were 14 males, 44 females; mean (SD) age = 54.26 (19.95) years.</p> <p><u>Inclusion criteria:</u> Patients aged > 14 years who attended the health centre between 1 October 1995 and 31 September 1996 who were found to have new onset (previously unknown) anaemia (haemoglobin < 13 g/dl for men</p>	

	and 12 g/dl for women). Exclusion criteria: Pregnant women. Clinical setting: Spanish GP	
Are there concerns that the included patients and setting do not match the review question?		Unclear concern
INDEX TEST		
A. Risk of bias		
Index test	Anaemia (haemoglobin < 13 g/dl for men and 12 g/dl for women)	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up I think	
Is the reference standard likely to correctly classify the target condition?		Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?		No
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Unclear concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	No diagnosis available for 29/87 patients	
Was there an appropriate interval between index test and reference standard?		Unclear
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		No
Could the patient flow have introduced bias?		High risk
NOTES	This paper is published in Spanish	
Fijten (1995)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective consecutive patient series	
Was a consecutive or random sample of patients enrolled?		Yes
Was a case-control design avoided?		Yes
Did the study avoid inappropriate exclusions?		Yes
Could the selection of patients have introduced bias?		Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 269 (118 males/151 females), mean (SD, range) age = 42 (15, 18-75). Mean (SD) follow up time = 20 (5) months. For 51% rectal bleeding was the main reason for the encounter, and 49% had another reason (e.g., abdominal complaints), but blood loss per rectum was seen and mentioned by the patients. N = 8 used anticoagulants.</p> <p><u>Inclusion criteria:</u> From September 1988 to April 1990, patients with rectal bleeding were recruited by 83 GPs in Limburg, with an average duration of participation of 11 months per doctor. Patients were included when overt rectal bleeding was the reason for encounter or when there was a history of recent (within the previous three months) rectal blood loss visible for the patient.</p> <p><u>Exclusion criteria:</u> Aged below 18 or above 75 years, pregnancy, urgent admission to hospital (for, e.g., a massive bleeding or acute abdominal pain), and if follow-up data were not available.</p> <p><u>Clinical setting:</u> Primary care, Netherlands</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Rectal bleeding
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up for min 1 year.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 290 patients were recruited, however 21/290 were excluded as they were lost to follow-up (moved to an unknown destination).
Was there an appropriate interval between index test and reference standard?	Unclear

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk
NOTES	
Hallissey (1990)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Propective consecutive patient series from a group of 10 general practices in England.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia. <u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, England.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia of any degree
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	2659 patients were seen and 2585 attended for investigation	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), circinomatosis of unknown primary (7).	

Hamilton (2005)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Population-based matched case-control study involving all 21 general practices in Exeter, Devon, UK.	
Was a consecutive or random sample of patients enrolled?	No	
Was a case-control design avoided?	No	
Did the study avoid inappropriate exclusions?	Yes	
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes	
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes	
Could the selection of patients have introduced bias?		High risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p><u>Cases:</u> N = 349 (177 males/172 females), age at diagnosis: < 60 years: N = 45, 60-69 years: N = 97, 70-79 years: N = 113, 80+ years: N = 94. 210/349 had tumours at or distal to the splenic flexure, and 126/349 had tumours proximal to the splenic flexure, the remaining 13/349 has tumours in multiple or unknown sites. Duke's staging was known for 305/349: 170/305 were Duke's A or B, and 135/305 were Duke's C or D.</p> <p><u>Controls:</u> N = 1744 (885 males/859 females), age at diagnosis: < 60 years: N = 225, 60-69 years: N = 487, 70-79 years: N = 555, 80+ years: N = 477.</p> <p><u>Inclusion criteria:</u> Cases: All patients aged ≥ 40 years with a primary colorectal cancer, diagnosed from 1998 to 2002, were identified from the cancer registry at the Royal Devon and Exeter Hospital combined with computerised searches at every practice in Devon to identify any cases missing from the cancer</p>	

	<p>register.</p> <p>Controls: Five controls were matched to each case on sex, general practice, and age (to 1-year bands if possible, increased in 1-year multiples to a maximum of 5 years). Controls were eligible if they were alive at the time of diagnosis of their case.</p> <p><u>Exclusion criteria:</u></p> <p>Cases and controls: Unobtainable records; no consultations in the 2 years before diagnosis; previous colorectal cancer; or residence outside Exeter at the time of diagnosis.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
<u>A. Risk of bias</u>	
Index test	Anonymised photocopies of the full primary care records for 2 years before diagnosis were coded (blinded to case/control status) for all entries using the International Classification of Primary Care-2. Additional codes were created to incorporate all possible clinical features. Only variables occurring in $\geq 2.5\%$ of cases or controls were analysed.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
<u>A. risk of bias</u>	
Reference standard(s)	Colorectal cancer diagnosis in the cancer registry at the Royal Devon and Exeter Hospital or practice notes.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
<u>A. risk of bias</u>	
Flow and timing	All the patients are accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes

Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Hamilton (2008)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Matched case-control study using patients in the Health Improvement Network (THIN), which uploads electronic medical records from GP practices using the VISION computer system. The records contain patient characteristics, all consultations, diagnoses, and primary care investigations. The database has 2.2 million currently active patients in over 300 practices; 4.7 million patients when historical data are included. Laboratory results have been transmitted electronically to most practices from the year 2000.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> 6442 cases of colorectal cancer (3421 men, 3021 women) of whom 3183 cases (1604 males, 1579 females) had a haemoglobin value measured in the year before the index date. Age of patients with a haemoglobin estimation: 30-59 years: N = 489; 60-69 years: N = 748; 70-79: N = 1085; 80+ years: N = 861. The haemoglobin results were taken in a median (interquartile range) of 62 (28- 122) days before the index date. A mean cell volume (MVC) result was available in 2951 cases of which 764 results showed microcytosis. Ferritin results were available for 723 and 353 of these were low.</p> <p>Haemoglobin > 12.9 g dl⁻¹: Men/women (N = 805/459); Haemoglobin 12-12.9 g dl⁻¹: Men/women (N = 203/289) Haemoglobin 11-11.9 g dl⁻¹: Men/women (N = 171/238) Haemoglobin 10-10.9 g dl⁻¹: Men/women (N = 129/226) Haemoglobin 9-9.9 g dl⁻¹: Men/women (N = 118/146) Haemoglobin < 9 g dl⁻¹: Men/women (N = 178/221)</p> <p><u>Controls:</u> 45066 matched controls were available, of whom 10514 controls (5223 males, 5291 females) had a haemoglobin value measured in the year before the index date. Age of patients with a haemoglobin estimation: 30-59 years: N = 1158; 60-69 years: N = 2215; 70-79: N = 3823; 80+ years: N = 3318. Haemoglobin results were taken in a median (interquartile range) of 134 (59-235) days before the index date. AN MVC result was available in 9648 controls of which 210 results showed microcytosis. Ferritin results were</p>

	<p>available for 825 and 129 of these were low. Haemoglobin > 12.9 g dl⁻¹: Men/women (N = 4131/2992); Haemoglobin 12-12.9 g dl⁻¹: Men/women (N = 572/1337) Haemoglobin 11-11.9 g dl⁻¹: Men/women (N = 293/616) Haemoglobin 10-10.9 g dl⁻¹: Men/women (N = 131/225) Haemoglobin 9-9.9 g dl⁻¹: Men/women (N = 49/85) Haemoglobin < 9 g dl⁻¹: Men/women (N = 47/36)</p> <p><u>Inclusion criteria:</u> Cases: All patients with colorectal cancer were identified, who were aged 30 years or older, and diagnosed between January 2000 and July 2006. All participants had at least 2 years of electronic records prior to the date of diagnosis of the case (the index date). Controls: Up to seven controls were randomly selected for each case, using a computerised random numbers sequence. Controls were free from colorectal cancer and were matched for practice, sex, and age. Where possible controls were born in the same year as cases, if none were available within 1 year of the cases, the range was expanded to 2 years, continuing to a maximum of 5 years. All participants had at least 2 years of electronic records prior to the date of diagnosis of the case (the index date). <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Haemoglobin results were taken in the year before the index dates were studied. If more than one haemoglobin measurement had been taken, the final value was used for analysis. MCV and ferritin results for the same year were also collated. Microcytosis was defined as an MCV < 80.0 fl, and a low ferritin as < 20 ng ml ⁻¹ .
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Colorectal cancer code in the THIN database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its	Low risk

interpretation have introduced bias?		
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	The MVC and ferritin data was not available for all included cases and controls, which may bias the results reported for the combined haemoglobin + iron deficiency estimates.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Could the patient flow have introduced bias?	Unclear risk	
NOTES	The is very large, if not complete, overlap of the data used in this study with those used in Collins (2012) and Hamilton (2009)	

Hamilton (2009)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Matched case-control study using patients in the Health Improvement Network (THIN), which uploads electronic medical records from GP practices using the VISION computer system. The records contain patient characteristics, all consultations, diagnoses, and primary care investigations. The database has 2.2 million currently active patients in over 300 practices; 4.7 million patients when historical data are included. Laboratory results have been transmitted electronically to most practices from the year 2000.	
Was a consecutive or random sample of patients enrolled?	No	
Was a case-control design avoided?	No	
Did the study avoid inappropriate exclusions?	Yes	
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes	
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes	
Could the selection of patients have introduced bias?	High risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p><u>Cases:</u> 5477 cases of colorectal cancer from 317 practices (2911 men, 2566 women); median (inter-quartile range) age at diagnosis: 72 (63-79) years. Constipation: N = 1477/27%; Diarrhoea: N = 988/18%; Change in bowel habit: N = 615/11.2%; Rectal bleeding: N = 853/15.6%; Weight loss 5-9.9%: N = 210/3.8%; Weight loss ≥ 10%: N = 351/6.4%; Abdominal pain: N = 1629/29.7%; Haemoglobin < 12 g dl⁻¹: N = 1424/26%; Mean red cell volume < 80 fl: N = 363/6.6%; Irritable bowel syndrome: N = 135/2.5%; Diabetes: N =</p>	

	<p>626/11.4%; Obesity: N = 510/9.3%.</p> <p><u>Controls:</u> 38314 matched controls (with only seven very elderly cases having fewer than seven controls available). 36925 (96.4%) controls were matched to the same year of birth, and 1150 to the adjoining year, leaving only 239 controls 2 to 5 years different in age.</p> <p>Constipation: N = 4051/10.6%; Diarrhoea: N = 2171/5.7%; Change in bowel habit: N = 375/1%; Rectal bleeding: N = 460/1.2%; Weight loss 5-9.9%: N = 852/2.2%; Weight loss \geq 10%: N = 678/1.8%; Abdominal pain: N = 3121/8.1%; Haemoglobin $<$ 12 g dl⁻¹: N = 1803/4.7%; Mean red cell volume $<$ 80 fl: N = 923/2.4%; Irritable bowel syndrome: N = 325/0.8%; Diabetes: N = 3679/9.6%; Obesity: N = 3510/9.2%.</p> <p><u>Inclusion criteria:</u> Cases: All patients with colorectal cancer were identified, who were aged 30 years or older, and diagnosed between January 2001 and July 2006. All participants had at least 2 years of electronic records prior to the date of diagnosis of the case (the index date). Controls: Up to seven controls were randomly selected for each case, using a computerised random numbers sequence. Controls were free from colorectal cancer and were matched for practice, sex, and age. Where possible controls were born in the same year as cases, if none were available within 1 year of the cases, the range was expanded to 2 years, continuing to a maximum of 5 years. All participants had at least 2 years of electronic records prior to the date of diagnosis of the case (the index date).</p> <p><u>Exclusion criteria:</u> None listed.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	<p>From a review of the literature, 23 candidate variables (features) were identified, either a symptom, or an abnormal primary care investigation, or a predisposing risk marker such as obesity. Codes for irritable bowel syndrome as a potential misdiagnosis were also identified. For some symptoms the availability of data on related prescriptions were also used, for example, prescriptions for antidiarrhoeals and laxatives were obtained as possible surrogates for the relevant symptoms, and similarly antispasmodic drugs for irritable bowel syndrome. Features were designated as new if there were no similar symptoms or prescriptions observed previously in the 2 years before the index date. Weight loss was calculated from the change between the last recorded weight and the highest weight in the previous 2 years, separated into two categories: \geq 10% weight loss or 5-10% weight loss. Patients were assigned to their maximum weight loss category. Obesity was defined as a body mass index $>$ 30 kg/m² within 2 years of the index date. Diabetes was considered to be present if it had ever been diagnosed.</p> <p>$<$ 2.5% cases or controls had an abnormal rectal examination (15 cases, 2 controls), abdominal masses (86 cases, 19 controls), a positive FOB (7 cases, 2 controls), or thrombo-embolism (24 cases, 74 controls), and these features were therefore not analysed any further.</p>
Were the index test results interpreted without knowledge	Yes

of the results of the reference standard?	
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Colorectal cancer code in the THIN database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the participants are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	The is very large, if not complete, overlap of the data used in this study with those used in Collins (2012) and Hamilton (2008, for anaemia)
Heikkinen (1995)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Consecutive patient series from 11 GPs (from 3 rural health centres) and from the catchment area of 6 physicians in the health centre of an urban area (population [individuals > 14 years old] of study area = 24600) in Finland.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient	N = 400; 152 males, 248 females; 77% were > 44 years.

characteristics and setting	<p><u>Inclusion criteria:</u> Consecutive patients who consulted their GP from January 11th 1993 to January 12th 1994 for dyspepsia (defined as upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptoms considered to be referable to the proximal alimentary tract).</p> <p><u>Exclusion criteria:</u> Patients with symptoms of an acute condition within the abdomen or who had had an upper intestinal endoscopy performed within the last 3 months or aged < 15 years</p> <p><u>Clinical setting:</u> Primary care, Finland.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia (defined as upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptoms considered to be referable to the proximal alimentary tract).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy, upper abdominal ultrasound, more detailed interview, blood count, serum screening (creatinine, alkaline phosphatase, alanine aminotransferase, amylase, and C-reactive protein), lactose intolerance test, and follow up of ≥ 1 month.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 9 had cancer: 0 colorectal, 2 oesophageal and 7 stomach (of which 3 were lymphomas of the MALT type (Mucosa-associated lymphoid

	tissue).
Heintze (2005)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 422 (222 males/199 females); aged < 50 years: N = 153, aged ≥ 50 years: N = 268. The most common accompanying symptoms associated with rectal bleeding were: Abdominal pain > 3 weeks (N = 97), change in bowel habit > 3 weeks (N = 73), anaemia (N = 23), and weight loss (N = 13). <u>Inclusion criteria:</u> Patients aged ≥ 15 years presenting with ≥ 1 bowel symptom to one of the participating 116 GP. The present analyses only included patients who presented with the first sign of rectal bleeding and associated symptoms, but without any pre-existing bowel diseases. <u>Exclusion criteria:</u> ≤ minimum level of data entry for each patient by the participating physician. <u>Clinical setting:</u> Primary care, Germany.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Rectal bleeding, abdominal pain > 3 weeks, change in bowel habit > 3 weeks, anaemia, and weight loss.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	A number of different diagnostic investigations, although some patients did not undergo any, - their explanatory notes were examined instead
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	93 patients did not undergo any investigations, and in 22/93 the course of disease and the diagnostics could not be assessed with the data provided in the explanatory notes. The results are therefore only reported for the 400 patients for whom the data are known
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	Over the course of 1 year, 2239 patients with chronic bowel symptoms and diseases were registered by 116 participating GPs. 24/116 GPs withdrew from the study before study completion (due to personal reasons (12) or lack of cooperation (10)), leaving 1696 patients registered by 94 GPs of whom 1584 met the minimum requirements for inclusion. 422/1584 patients presented with rectal bleeding.

Helfand (1997)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive patient series from the walk-in and general medical clinics of the Veterans Affairs Medical Center, Palo Alto, California.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 201; 200 males, 1 female; mean ages (SD; 3 values given based on final diagnostic category): "None" (N = 49) = 53.8 (15.4) years; "anorectal" (N = 104) = 54.6 (13.6) years; "serious" (N = 48) = 58.3 (11.3) years.</p> <p><u>Inclusion criteria:</u> Patients who between January 1981 and October 1983 presented to the walk-in and general medical clinics of the Veterans Affairs Medical Center, Palo Alto, California were given a questionnaire after by the nursing personnel after their vital signs had been measured. Patients who according to their answers had experienced rectal bleeding within the last 3 months and not sought medical attention for it were invited to take part in the study.</p> <p><u>Exclusion criteria:</u> Patients with no data available at 6 and 12 months follow up.</p> <p><u>Clinical setting:</u> Walk-in and general medical clinics of the Veterans Affairs Medical Center, Palo Alto, California</p>
Are there concerns that the included patients and setting	High concern

do not match the review question?		
INDEX TEST		
A. Risk of bias		
Index test	New onset (within 3-months) rectal bleeding (blood in stool or on toilet paper)	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up 6-12 months and examination of medical records 8-10 years after study entry.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	The authors mention that between 2 and 10 years after study entry 3 patients developed colorectal cancer. These patients do not appear to be included as true positives.	
Hippisley-Cox (2012)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	

B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1236601 patients were identified from 189 practices (620240 males, 616361 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Symptoms:</u> Current rectal bleeding (N = 29118), current abdominal pain (N = 125816), current appetite loss (N = 5358), current weight loss (N = 14065), recent change in bowel habit (N = 1821).</p> <p><u>Incident cases of colorectal cancer during the 2-year follow up period:</u> N = 2603 (1562 colon and 1041 rectum).</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000); 12 months after the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of colorectal cancer at baseline, and patients with a recorded 'red-flag' symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: First onset rectal bleeding, first onset loss of appetite, first onset weight loss, first onset abdominal pain, first onset change in bowel habit (in the past 12 months), and anaemia (recorded haemoglobin < 11 g/dl in the past 12 months).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear

Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	A total of 1342329 patients were initially identified of whom 105728 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of colorectal cancer (N = 2908), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 31973), leaving 1236601 patients. However, data is presented for 1235547/1236601 patients for all symptoms apart from change in bowel habit, which is only presented for 619651/620240 of the male patients. The missing data does not appear to include any of the cancer cases (although this cannot be ascertained for change in bowel habit), but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Could the patient flow have introduced bias?	Low risk	
NOTES	Please note there is some overlap between this patient sample and that of Parker (2007)	
Jones (2007)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective consecutive patient series using patients in the UK's General Practice Research Database.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	A total of 923605 patients were identified, of whom 762325 were aged \geq 15 years. <u>Number of first occurrences in patients with no previous diagnosis of cancer:</u> <u>Haematuria:</u> N = 11138, mean (SD) age at first symptom = 58.5 (18.9) years. Patients excluded due to incomplete dates for their first symptom: N = 30. Sex (of final sample): 6385 males, 4723 females. <u>Haemoptysis:</u> N = 4822, mean (SD) age at first symptom = 61.6 (18) years. Patients excluded due to incomplete dates for their first symptom: N = 10. Sex (of final sample): 2930 males, 1882 females. <u>Dysphagia:</u> N = 6003, mean (SD) age at first symptom = 54.5 (19.4) years. Patients excluded due to incomplete dates for their first symptom: N = 4. Sex (of final sample): 2628 males, 3371 females.	

	<p><u>Rectal bleeding</u>: N = 15314, mean (SD) age at first symptom = 52.5 (18.8) years. Patients excluded due to incomplete dates for their first symptom: N = 25. Sex (of final sample): 7523 males, 7766 females.</p> <p><u>Inclusion criteria</u>: All patients from 128 general practices that provided data of a sufficient standard from 1 January 1994 to 31 December 2000 and which provided exclusively Read coded data, who were aged between 15 and 100 years, whose first ever recorded occurrence of each alarm symptom (haematuria, haemoptysis, dysphagia, or rectal bleeding) was after 31 December 1994 and who had not previously been diagnosed as having any cancer.</p> <p><u>Exclusion criteria</u>: Patients whose date of first symptom or first relevant diagnosis of cancer was before 1 January 1995 and patients with a diagnosis of any other cancer than the ones of interest before the date of the first recorded symptom or before the index cancer diagnosis date if the related symptom was not recorded.</p> <p><u>Clinical setting</u>: Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Identification of all patients who ever had symptoms recorded for haematuria, haemoptysis, dysphagia, or rectal bleeding.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	<p>Cancer code in the UK's General Practice Research Database:</p> <p><u>Haematuria</u>: Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs.</p> <p><u>Haemoptysis</u>: Respiratory tract neoplasms.</p> <p><u>Dysphagia</u>: Oesophageal neoplasms.</p> <p><u>Rectal bleeding</u>: Colorectal neoplasms.</p>
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	<p>Diagnoses of cancer were most often made in the first three months after the onset of alarm symptoms; very few diagnoses of cancer were made later than three years after symptom onset. In the 4th and 5th years of study, the small number of observed occurrences of cancer was similar to the number expected from background incidence rates.</p> <p>Secondary analyses evaluating whether the incidence of neoplasms other than those prespecified was increased after the occurrence of alarm symptoms showed for:</p> <p><u>Haematuria</u>: Inclusion of cancers of the reproductive organs yielded 21 additional cancers in women and 158 cancers in men, mostly cancers of the prostate. Inclusion of these cancers in the analysis would give a positive predictive value of 3.9% in women and 9.9% in men.</p> <p><u>Dysphagia</u>: Inclusion of gastric cancers yielded 17 additional cancer diagnoses in women and 30 in men. Inclusion of these cancers gave positive predictive values of 5.2% in women and 6.9% in men.</p> <p><i>Estimates based on the pre-specified cancers may be thus conservative for these symptoms.</i></p> <p><u>Haemoptysis</u>: Extension of the diagnostic criteria yielded 6 additional cancers.</p> <p><u>Rectal bleeding</u>: Extension of the diagnostic criteria yielded 2 additional cancers.</p>

Lawrenson (2006)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Database study using patients from a sample of UK practices contributing data to the General Practice Research Database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>Anaemia cases: N = 67164 (18896 males, 48268 females) Changes in bowel habit cases: N = 27524 (10934 males, 16590 females) Rectal bleeding cases: N = 44741 (21472 males, 23269 females) Colorectal cancer cases: N = 9143</p> <p><u>Inclusion criteria</u>: All patients aged 40-89 years presenting to their GP between 1 January 1992 and 31 December 1999 with new symptoms of anaemia, change in bowel habit or rectal bleeding, who had ≥ 1 year of data. <u>Exclusion criteria</u>: Patients with colorectal cancer, or a diagnosis of colorectal</p>

	cancer within 1 year of presentation. Clinical setting: Primary care, UK.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Anaemia, change in bowel habit or rectal bleeding as identified by their diagnostic codes
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up from presenting symptom until diagnosis of colorectal cancer, death or the end of the patient record.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes (probably)
Could the patient flow have introduced bias?	Low risk
NOTES	The authors state that the positive predictive values were derived from Kaplan-Maier curves constructed for men and women for each symptom cohort in 10-year age bands and report the positive predictive values of colorectal cancer being diagnosed within 12 months of initial symptoms per 100 patients presenting. It is unclear to me why this method was chosen over just calculating the values by dividing the true positives by the total positives and how and if these calculations differ from those of the other studies. The raw data is not presented and these data can therefore not be included in the meta-analysis.

Lucas (1996)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective laboratory database (recording all full blood counts analysed in the district) study from one UK health district (population 290000).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 130 of whom 21 were clearly attributable to non-gastrointestinal disease (e.g., urinary tract bleeding, uterine/respiratory/surgical blood loss and sideroblastic anaemia). In the remaining 109 patients with a presumed gastrointestinal cause N = 29 were aged < 65 years, N = 51 were aged 65-79 years and N = 29 were aged > 80 years.</p> <p><u>Inclusion criteria:</u> Women aged > 50 years and all men who between October 1991 and March 1992 were found to have probable iron-deficiency anaemia (haemoglobin < 11 g/dl in women and < 12 g/dl in men, and men cell volume < 83 fl) where the date of the first abnormal full blood count fell either within or 3 months prior to the study period and where there had been no other episode of anaemia within the previous 2 years.</p> <p><u>Exclusion criteria:</u> None listed.</p> <p><u>Clinical setting:</u> UK primary and beyond</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	New onset iron-deficiency anaemia. Hypochronic microcytic anaemia was presumed to be due to iron-deficiency anaemia unless proven otherwise through appropriate investigation.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up using hospital and general practice records until 18 months after study period finish.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk
NOTES	In addition to the 9 patients with colorectal cancer, 5 patients had gastric cancer.	
Mant (1989)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective consecutive patient series from 58 general practitioners in New South Wales, Australia.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 145; 77 males, 68 females; mean age (SD, range) = 57.7 (11.9, 40-95) years.</p> <p><u>Inclusion criteria:</u> All patients aged ≥ 40 years who consulted the GP with rectal bleeding.</p> <p><u>Exclusion criteria:</u> Patients (1) for whom it was considered that their age or general medical condition precluded colonoscopy, (2) who were known to have inflammatory bowel disease, colorectal cancer or polyposis coli, (3) with a coagulation defect or haemalogic disorder, (4) where the bleeding was melanic, or (5) who refused investigation.</p> <p><u>Clinical setting:</u> General practice in New South Wales, Australia.</p>	
Are there concerns that the included patients and setting do not match the review question?		Unclear concern
INDEX TEST		
A. Risk of bias		
Index test	New onset (within 6-months) rectal bleeding (blood in stool or on toilet paper)	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		

Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Flexible sigmoidoscopy and air-contrast barium enema ± colonoscopy	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes (probably)	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	In addition to the 15 patients with colorectal cancer, 1 patient had anal cancer and 1 patient had lymphoma of the ascending colon. Both of these are included in the meta-analyses, but only the lymphoma patient is included in the subgroup analyses reported by the authors.	
Meineche-Schmidt (2002)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Consecutive patient series from 82 GPs in Denmark.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	N = 1491; 688 males, 803 females; age groups: 18-37 years: N = 377; 38-50 years: N = 369; 51-64 years: N = 338; 65- years: N = 402. Inclusion criteria: Consecutive patients who consulted their GP between June 1991 and May 1993 for dyspepsia (defined as pain or discomfort in the abdomen judged by the GP to be related to the gastrointestinal tract). Exclusion criteria: None listed. Clinical setting: Primary care, Denmark.	
Are there concerns that the included patients and setting	Unclear concern	

do not match the review question?		
INDEX TEST		
A. Risk of bias		
Index test	Dyspepsia (defined as pain or discomfort in the abdomen judged by the GP to be related to the gastrointestinal tract).	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	18 months-3 years and 10 months follow up.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	In total N = 31 had cancer: 17 colorectal, 8 gastro-oesophageal (no subgroup analyses presented for these patients) and 6 other.	
Metcalf (1996)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective consecutive patient sample from UK GPs.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient	N = 99, 42 males, 57 females; median age (range) = 58 (40-86) years.	

characteristics and setting	<u>Inclusion criteria:</u> Patients aged > 40 years presenting with rectal bleeding of recent onset (< 1 year). <u>Exclusion criteria:</u> Patients refusing colonoscopy. <u>Clinical setting:</u> Primary care, UK	
Are there concerns that the included patients and setting do not match the review question?	Low concern	
INDEX TEST		
A. Risk of bias		
Index test	Recent onset (< 1 year) rectal bleeding	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Colonoscopy ± barium enema	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES		
Muris (1993)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective consecutive patient series from 11 general practitioners in Maastricht (Holland)	
Was a consecutive or random sample of patients enrolled?	Yes	

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 578; 212 males, 342 females; age groups: 18-39 years: N = 295; 40-49 years: N = 80; 50-59 years: N = 91; 60-75 years: N = 88. <u>Inclusion criteria:</u> Patients who during a 3-month period consulted one of the participating GPs for abdominal complaints. <u>Exclusion criteria:</u> Patients aged < 18 years and patients with a condition necessitating immediate referral or admission to hospital. <u>Clinical setting:</u> GPs in Holland
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Abdominal complaints. Not further specified, but the authors do report that the duration of pain before the patient presented for the first time for the evaluation of abdominal pain varied from some days to more than 1 year.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up for 15 months.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

NOTES	Although not explicitly stated by the authors it is implied that the patients included were those presenting with the abdominal complaint for the first time.	
Muris (1995)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series from 80/460 general practitioners in Limburg (Holland)	
Was a consecutive or random sample of patients enrolled?	No	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?	High risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 933; 335 males, 598 females; age range = 18-75, aged > 30 years: N = 712, aged > 40 years: N = 517, aged > 60 years: N = 171.</p> <p><u>Inclusion criteria</u>: Patients who in 1989 consulted one of the participating GPs for new abdominal complaints lasting ≥ 2 weeks and with whom the GPs had a diagnostic problem.</p> <p><u>Exclusion criteria</u>: None listed.</p> <p><u>Clinical setting</u>: GPs in Holland</p>	
Are there concerns that the included patients and setting do not match the review question?	High concern	
INDEX TEST		
A. Risk of bias		
Index test	New abdominal complaints lasting ≥ 2 weeks. Not further specified.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up for ≥ 12 months (mean = 18 months).	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	

FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Other cancers diagnosed in these patients were: Stomach (2/933), pancreas (2/933), trachea/bronchus/lung (2/933), kidney (1/933), cervix (1/933), other cancer of the female genital system (2/933), and other and unspecified sites (2/933).
Nørrelund (1996)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient sample from GPs in Denmark.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 417, but no demographic data reported for 45 patients who presented with similar rectal bleeding patterns to previously experienced rectal bleeding or for 8 patients with non-reported rectal bleeding pattern. The characteristics for the 364 patients with new onset or changed pattern rectal bleeding are as follows: 168 males, 196 females; age groups: 40-69 years: N = 254; 70-79 years: N = 85; 80+ years: N = 25. <u>Inclusion criteria</u> : Patients aged ≥ 40 years who between August 1989 and October 1992 presented to the participating GPs with rectal bleeding. <u>Exclusion criteria</u> : Known inflammatory bowel disease, colonic polyps, polyposis coli, colorectal cancer, predisposition to haemorrhage, and melaena stool. <u>Clinical setting</u> : Primary care, Denmark
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Rectal bleeding subclassified into: First episode (within 6-months) rectal bleeding (blood in/on stool, in the toilet or on toilet paper), change in rectal bleeding pattern, and no change in rectal bleeding pattern
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up (range = 22-57 months)	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES		
Oudega (2006)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective study of all primary care physicians (N = 50) within a catchment area (ca 130000 inhabitants) of a non-teaching hospital in Holland.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 430; 162 males, 268 females; mean age (SD) = 60.7 (18.2) years.</p> <p><u>Inclusion criteria</u>: Consecutive patients who consulted their GP between January 1996 and July 2002 and who, after investigation (not referral) was confirmed to have deep vein thrombosis.</p> <p><u>Exclusion criteria</u>: Patients with a known malignancy or a malignancy detected within 2 weeks of deep vein thrombosis diagnosis.</p> <p><u>Clinical setting</u>: Primary care, Holland.</p>	
Are there concerns that the included patients and setting do not match the review question?	Unclear concern	

INDEX TEST	
A. Risk of bias	
Index test	Deep vein thrombosis (suspicion based on painful swollen leg \leq 30 days). Patients were classified as having secondary deep vein thrombosis if \geq 1 of the following risk factors for deep vein thrombosis were present: Recent surgery, prolonged immobilisation, use of oral contraceptives or hormonal replacement therapy. If no risk factors were present patients were classified as having idiopathic deep vein thrombosis.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2 years follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 19 had cancer: 3 colorectal, 5 urogenital (not further subgrouped), 4 breast, 3 lung and 4 other. The urogenital data is added to the renal cancer evidence review.
Panzuto (2003)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective 8-week study of patients presenting to 159 primary care physicians (approximately 63600 patient visits during the study period in total) in Italy.
Was a consecutive or random sample of patients enrolled?	No

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 280; 120 males, 160 females; median age (range) = 61 (18-87) years. <u>Inclusion criteria:</u> Consecutive patients who consulted their GP “with symptoms considered suspicious for the presence of a colon disease to rule out the presence of colorectal cancer” and who were investigated with a colonoscopy or double-contrast barium enema [The decision of how (colonoscopy or double-contrast barium enema) and when to investigate the colon was made only by the physicians on the basis of the clinical evaluation during the visit]. <u>Exclusion criteria:</u> Patients with previous diagnoses of colorectal disorders or a recent large bowel examination. <u>Clinical setting:</u> Primary care, Italy.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Abdominal pain, bloating, constipation, rectal bleeding, diarrhoea, iron-deficiency anaemia (haemoglobin levels < 14 g/dl for males and < 12 g/dl for females, in the presence of ferritin < 30 µg/l and a median corpuscular value < 80 fl), change in bowel habits (onset of diarrhoea or constipation or altered stool in the previous 3 months) and weight loss (decrease of ≥ 3 kg in the 3 months prior to the visit).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histology
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	

A. risk of bias	
Flow and timing	56/332 patients were excluded due to lack of mandatory fields (age, sex, clinical history, presenting symptoms and procedure results) in the database (N = 35) or violation of exclusion criteria (N = 18)
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	
Parker (2007)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>Rectal bleeding: N = 29007 (13931, males, 15076 females); median age (inter-quartile range) = 54 (40-69) years.</p> <p>Post-menopausal bleeding: N = 10122 (10122 females); median age (inter-quartile range) = 58 (54-67) years.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system before 1 April 1998 and had complete data up to 1 April 2005. Patients were included if they were registered with an eligible practice at any time between 1 April 1998 and 31 March 2003, had been registered with the practice for ≥ 12 months and had a first-ever consultation for rectal bleeding and were aged ≥ 25 years, or post-menopausal bleeding and were aged ≥ 40 years, between 1 April 1998 and 31 March 2003.</p> <p><u>Exclusion criteria:</u> Previous record of colorectal cancer (for patients presenting with rectal bleeding) and endometrial cancer (for patients presenting with post-menopausal bleeding)</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	First ever presentation of rectal bleeding, first ever presentation of post-menopausal bleeding.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	2-year follow up	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	Please note there is some overlap between this patient sample and that of Hippisley-Cox (2012).	
Robertson (2006)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective consecutive patient sample from UK GPs.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 604, 273 males, 331 females; median age (range) = 52 (18-97) years.</p> <p><u>Inclusion criteria</u>: Patients who between September 1996 and June 1999 presented to the participating GPs with rectal bleeding.</p> <p><u>Exclusion criteria</u>: Patients with ulcerative colitis, current warfarin treatment or missing data for the kind of bleeding.</p> <p>Clinical setting: Primary care, UK</p>	
Are there concerns that the included patients and setting do not match the review question?	Low concern	
INDEX TEST		
A. Risk of bias		

Index test	Rectal bleeding	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up (min 4 years)	
Is the reference standard likely to correctly classify the target condition?		Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?		No
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?		Yes
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		Yes
Could the patient flow have introduced bias?		Low risk
NOTES	Deprivation categories were allocated to participants by mapping their postcodes with national deprivation categories (septiles) derived from the Carstairs scores generated by MIMAS at Manchester University using 1991 census data.	

Stellon (1997)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective? consecutive patient series from semi-rural UK general practice with a patient list between 2400-3400 during the study period.	
Was a consecutive or random sample of patients enrolled?		Yes
Was a case-control design avoided?		Yes
Did the study avoid inappropriate exclusions?		Yes
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient	N = 26; 5 males, 21 females; age range = 51-87 years.	

characteristics and setting	<u>Inclusion criteria:</u> All patients aged > 50 years found to have iron deficiency anaemia between January 1989 and March 1994. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> UK GP	
Are there concerns that the included patients and setting do not match the review question?	Low concern	
INDEX TEST		
A. Risk of bias		
Index test	Iron deficiency anaemia (< 12 g/dl haemoglobin and/or mean corpuscular volume < 80 fl with ferritin ≤ 16 ng/l)	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up during 5 year study period.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES		
Wauters (2000)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective study of a network of sentinel Belgian general practices (covering 1% of the Belgian population) registering epidemiological data.	

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 386; gender distribution not reported; age groups: < 50 years: N = 141; 50-59 years: N = 57; 60-69 years: N = 71; 70-79 years: N = 66; ≥ 80 years: N = 51. <u>Inclusion criteria:</u> All patients who in 1993-4 presented with rectal bleeding. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> GPs in Belgium
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Rectal bleeding (any blood of rectal origin on stool, underwear or toilet paper irrespective of duration)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	18-30 months follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes (probably)
Could the patient flow have introduced bias?	Low risk

NOTES	
Yates (2004)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective database study using the laboratory databases of two district general hospitals including all the general practices using these laboratories.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 431; 154 males, 277 females; median age (inter-quartile range) = 75 (65-81) years. <u>Inclusion criteria:</u> All female patients aged > 50 years and male patients aged > 20, with haemoglobin concentrations ≤ 110 g/l (women) or ≤ 120 g/l (men), and mean cell volume < 82 fl (district 1) or 78 fl (district 2), and red cell count ≤ 5.5 x 10 ¹² /l between June 1997 and May 1998. <u>Exclusion criteria:</u> History of anaemia within previous 12 months, known haematological abnormalities (e.g., haemoglobinopathy), unavailable notes at follow up. <i>That is, patients with a history of cancer were not excluded.</i> <u>Clinical setting:</u> UK GP
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Iron deficiency anaemia (haemoglobin concentrations ≤ 110 g/l (women) or ≤ 120 g/l (men), and mean cell volume < 82 fl (district 1) or 78 fl (district 2), and red cell count ≤ 5.5 x 10 ¹² /l)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Minimum 3 years follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 48 had gastrointestinal cancer (11 upper, 2 small bowel and 35 lower, including recurrent tumours) and N = 23 had non-gastrointestinal cancers, but the study only reports the type of some of these cancers (3 lung + 1 lung tumour secondary to a previous breast tumour, 1 ovary, 2 bladder, 1 Hodgkin's, 1 Non-Hodgkin's, 1 endometrial sarcoma, 1 lymphoma, 1 endometrial) and has therefore not been added to the evidence reviews for the non-gastrointestinal cancers. The paper considers both the lower gastrointestinal cancers and the small bowel cancers as colorectal cancer and in order to present subgroup analyses by gender I have maintained this grouping and not added this paper to the evidence review for small intestine.

References

Included studies

- Bellentani, S., Baldoni, P., Petrella, S., Tata, C., Armocida, C., Marchegiano, P., Saccoccio, G., and Manenti, F. A simple score for the identification of patients at high risk of organic diseases of the colon in the family doctor consulting room. The Local IBS Study Group. *Family Practice* 7[4], 307-312. 1990.
- Collins, G.S., Altman, D.G. Identifying patients with undetected colorectal cancer: An independent validation of QCancer (Colorectal). *British Journal of Cancer* 107, 260-265. 2012.
- Droogendijk, J., Beukers, R., Berendes, P. B., Tax, M. G. H. M., Sonneveld, P., and Levin, M. D. Screening for gastrointestinal malignancy in patients with iron deficiency anemia by general practitioners: An observational study. *Scandinavian Journal of Gastroenterology* 46[9], 1105-1110. 2011.
- du Toit, J., Hamilton, W., and Barraclough, K. Risk in primary care of colorectal cancer from new onset rectal bleeding: 10 year prospective study. *British Medical Journal* 333[7558], 69-70. 2006.
- Ellis, B. G. and Thompson, M. R. Factors identifying higher risk rectal bleeding in general practice. *British Journal of General Practice* 55[521], 949-955. 2005.
- Farrus, Palou M., Perez, Ocana A., Mayer Pujadas, M. A., Piquer, Gibert M., Mundet, Tuduri, X, and Iglesias, Rodal M. [Anemia in primary care: etiology and morphological characteristics]. [Spanish]. *Atencion Primaria* 25[4], 230-235. 15-3-2000.
- Fijten, G. H., Starmans, R., Muris, J. W., Schouten, H. J., Blijham, G. H., and Knottnerus, J. A. Predictive value of signs and symptoms for colorectal cancer in patients with rectal bleeding in general practice. *Family Practice* 12[3], 279-286. 1995.
- Hallissey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.

- Hamilton, W., Round, A., Sharp, D., and Peters, T. J. Clinical features of colorectal cancer before diagnosis: a population-based case-control study. *British Journal of Cancer* 93[4], 399-405. 22-8-2005.
- Hamilton, W., Lancashire, R., Sharp, D., Peters, T. J., Cheng, K. K., and Marshall, T. The importance of anaemia in diagnosing colorectal cancer: a case-control study using electronic primary care records. *British Journal of Cancer* 98[2], 323-327. 29-1-2008.
- Hamilton, W., Lancashire, R., Sharp, D., Peters, T. J., Cheng, K., and Marshall, T. The risk of colorectal cancer with symptoms at different ages and between the sexes: a case-control study. *BMC Medicine* 7, 17. 2009.
- Heikkinen, M., Pikkarainen, P., Takala, J., and Rasanen, H. Julkunen R. Etiology of dyspepsia: Four hundred unselected consecutive patients in general practice. *Scandinavian Journal of Gastroenterology* 30[6], 519-523. 1995.
- Heintze, C., Matysiak-Klose, D., Krohn, T., Wolf, U., Brand, A., Meisner, C., Fischer, I., Wehrmeyer, H., and Braun, V. Diagnostic work-up of rectal bleeding in general practice. *British Journal of General Practice* 55[510], 14-19. 20-1-2005.
- Helfand, M., Marton, K. I., Zimmer-Gembeck, M. J., and Sox, H. C., Jr. History of visible rectal bleeding in a primary care population. Initial assessment and 10-year follow-up. *JAMA* 277[1], 44-48. 1-1-1997.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected colorectal cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice* 62[594], e29-e37. 2012.
- Jones, R., Latinovic, R., Charlton, J., and Gulliford, M. C. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *BMJ* 334[7602], 1040. 19-5-2007.
- Lawrenson, R., Logie, J., and Marks, C. Risk of colorectal cancer in general practice patients presenting with rectal bleeding, change in bowel habit or anaemia. *European Journal of Cancer Care* 15[3], 267-271. 2006.
- Lucas, C. A., Logan, E. C., and Logan, R. F. Audit of the investigation and outcome of iron-deficiency anaemia in one health district. *Journal of the Royal College of Physicians of London* 30[1], 33-36. 1996.
- Mant, A., Bokey, E. L., Chapuis, P. H., Killingback, M., Hughes, W., Koorey, S. G., Cook, I., Goulston, K. J., and Dent, O. F. Rectal bleeding. Do other symptoms aid in diagnosis? *Diseases of the Colon & Rectum* 32[3], 191-196. 1989.
- Meineche-Schmidt, V. and Jorgensen, T. 'Alarm symptoms' in patients with dyspepsia: a three-year prospective study from general practice. *Scandinavian Journal of Gastroenterology* 37[9], 999-1007. 2002.
- Metcalfe, J. V., Smith, J., Jones, R., and Record, C. O. Incidence and causes of rectal bleeding in general practice as detected by colonoscopy. *British Journal of General Practice* 46[404], 161-164. 1996.
- Muris, J.W.M., Starmans, R., Fijten, G.H., Crebolder, F.J.M., Krebber, T.F.W.A., and Knottnerus, J.A., Abdominal pain in general practice. *Family Practice* 10[4], 387-390. 1993.
- Muris, J. W., Starmans, R., Fijten, G. H., Crebolder, H. F., Schouten, H. J., and Knottnerus, J. A. Non-acute abdominal complaints in general practice: diagnostic value of signs and symptoms. *British Journal of General Practice* 45[395], 313-316. 1995.
- Nørrelund, N. and Nørrelund, H. Colorectal cancer and polyps in patients aged 40 years and over who consult a GP with rectal bleeding. *Family Practice* 13[2], 160-165. 1996.
- Oudega, R., Moons, K. G. M., Nieuwenhuis, H. K., van Nierop, F. L., and Hoes, A. W. Deep vein thrombosis in primary care: Possible malignancy? *British Journal of General Practice* 56[530], 693-696. 2006.
- Panzuto, F., Chiriatti, A., Bevilacqua, S., Giovannetti, P., Russo, G., Impinna, S., Pistilli, F., Capurso, G., Annibale, B., Delle, Fave G., and Digestive and Liver Disease and Primary Care Medicine Lazio

Group. Symptom-based approach to colorectal cancer: survey of primary care physicians in Italy. *Digestive & Liver Disease* 35[12], 869-875. 2003.

Parker, C., Hippisley-Cox, J., Coupland, C., and Vinogradova, Y. Rectal and postmenopausal bleeding: consultation and referral of patients with and without severe mental health problems. *British Journal of General Practice* 57[538], 371-376. 2007.

Robertson, R., Campbell, C., Weller, D. P., Elton, R., Mant, D., Primrose, J., Nugent, K., Macleod, U., and Sharma, R. Predicting colorectal cancer risk in patients with rectal bleeding. *British Journal of General Practice* 56[531], 763-767. 2006.

Stellon, A. J. and Kenwright, S. E. Iron deficiency anaemia in general practice: Presentations and investigations. *British Journal of Clinical Practice* 51[2], 78-80. 1997.

Wauters, H., Van, Casteren, V, and Buntinx, F. Rectal bleeding and colorectal cancer in general practice: diagnostic study.[Erratum appears in *BMJ*. 2001 Feb 24;322(7284):488]. *BMJ* 321[7267], 998-999. 21-10-2000.

Yates, J. M., Logan, E. C., and Stewart, R. M. Iron deficiency anaemia in general practice: clinical outcomes over three years and factors influencing diagnostic investigations. *Postgraduate Medical Journal* 80[945], 405-410. 2004.

Excluded studies (with excl reason)

(1996) American Academy of Family Physicians releases a procedural skills paper on EGD by family physicians. *American Family Physician*, 53: 1429-1433.
Not in PICO

(2009) The Dutch College of General Practitioners guideline for rectal bleeding. [Dutch]. *Huisarts en Wetenschap*, 52: 23-38.
Guideline

(2013) EUS-guided deep biopsy and EMR in the early diagnosis and treatment of rectal carcinoid tumors. *Journal of Gastroenterology and Hepatology*, 28: 718-719.
Not in PICO

Acar-Vaizoglu, S., Turhan, T., Temel, F., Bolat, O., Baydar, O., Bacanli, A., Asarcikli, F. & Guler, C. (2010) Determination of risk factors associated with colorectal cancer and compliance with fecal occult blood testing among patients aged 50 years and over in primary health care. [Turkish]. *Turk Geriatri Dergisi*, 13: 79-86.
Not in PICO

Acher, P. L., Al-Mishlab, T., Rahman, M. & Bates, T. (2003) Iron-deficiency anaemia and delay in the diagnosis of colorectal cancer. *Colorectal Disease*, 5: 145-148.
Not in PICO

Adam, Z., Pour, L., Krejci, M., Koristek, Z., Navratil, M., Krivanova, A., Zahradova, L. & Hajek, R. (2009) [Treatment of Waldenstrom macroglobulinaemia--the experience of one centre]. [Czech]. *Vnitřní Lekarství*, 55: 9-17.
Not in PICO

Adell, R., Marcote, E., Segarra, M. A., Pellicer, V., Gamon, R., Bayon, A. M., Canales, M. & Torner, A. (2002) [Is mucinous colorectal adenocarcinoma a distinct entity?]. [Spanish]. *Gastroenterologia y Hepatologia*, 25: 534-540.
Not in PICO

Adelstein, B., Macaskill, P., Chan, S. F., Katelaris, P. H. & Irwig, L. (2011) Most bowel cancer symptoms do not indicate colorectal cancer and polyps: A systematic review. *BMC Gastroenterology*, 11.
Mixed secondary care, primary care and screening; results cannot be extracted separately for primary care

Aderka, D., Hausmann, M., Santo, M., Weinberger, A. & Pinkhas, J. (1985) Unexplained episodes of fever: an early manifestation of colorectal carcinoma. *Israel Journal of Medical Sciences*, 21: 421-

424.

Not in PICO

Ahlquist, D. A., Klee, G. G., McGill, D. B. & Ellesfon, R. D. (1990) Colorectal cancer detection in the practice setting. Impact of fecal blood testing. *Archives of Internal Medicine*, 150: 1041-1045.

Not in PICO

Ahmed, A., Myers, E. & Kirwan, W. O. (2011) Clinic screening-rapid access colorectal clinic experience. *Irish Journal of Medical Science*, 180: S282.

Not in PICO

Ahmed, S., Leslie, A., Thaha, M. A., Carey, F. A. & Steele, R. J. (2005) Lower gastrointestinal symptoms are not predictive of colorectal neoplasia in a faecal occult blood screen-positive population. *British Journal of Surgery*, 92: 478-481.

Not in PICO

Ahnen, D. J., Wade, S. W., Jones, W. F., Sifri, R., Mendoza, S. J., Greenamyre, J., Guiffre, S., Axilbund, J., Spiegel, A. & You, Y. N. (2014) The increasing incidence of young-onset colorectal cancer: a call to action. *Mayo Clinic Proceedings*, 89: 216-224.

Narrative review

Akhtar, M., Boshnaq, M., Creamer, A., Doughan, S. & Marzouk, D. (2013) Assessment of efficiency of tissue biopsy process in the diagnosis of rectal cancer; current practice and the outcome. *Colorectal Disease*, 15: 66.

Not in PICO

Al-Mashat, F. & Sibiany, A. M. (2010) Sister Mary Joseph's nodule of the umbilicus: is it always of gastric origin? A review of eight cases at different sites of origin. *Indian Journal of Cancer*, 47: 65-69.

Not in PICO

Aljarabah, M. M., Borley, N. R., Goodman, A. J. & Wheeler, J. M. (2009) Referral letters for 2-week wait suspected colorectal cancer do not allow a 'straight-to-test' pathway. *Annals of the Royal College of Surgeons of England*, 91: 106-109.

Not in PICO

Allen, A. S., Orav, E. J., Lee, T. H. & Sequist, T. D. (2011) Clinician personality and the evaluation of higher-risk patient symptoms. *Journal of patient safety*, 7: 122-126.

Not in PICO

Allen, E., Nicolaidis, C. & Helfand, M. (2005) The evaluation of rectal bleeding in adults: A cost-effectiveness analysis comparing four diagnostic strategies. *Journal of General Internal Medicine*, 20: 81-90.

Not in PICO

Allgar, V. L., Neal, R. D., Ali, N., Leese, B., Heywood, P., Proctor, G. & Evans, J. (2006) Urgent GP referrals for suspected lung, colorectal, prostate and ovarian cancer. *British Journal of General Practice*, 56: 355-362.

Not in PICO

Alonso-Abreu, I., Alarcon-Fernandez, O., Gonzalez-Mendez, Y., Jimenez-Sosa, A. & Quintero, E. (2010) Diagnostic predictive value of indications for prompt referral colonoscopy. *Gastroenterology*, 138: S285-S286.

Not in PICO

Alpert, J. B., Fantauzzi, J. P., Melamud, K., Greenwood, H., Naidich, D. P. & Ko, J. P. (2012) Clinical significance of lung nodules reported on abdominal CT. *American Journal of Roentgenology*, 198: 793-799.

Not in PICO

Alzubi, A., Zollei, I., Krenacs, L., Intzedy, K. & Hudak, J. (2008) [Primary T-cell lymphoma of the small bowel]. [Hungarian]. *Magyar Sebeszet*, 61: 79-83.

Not in PICO

- An, J. W., Cheung, D. Y., Seo, M. W., Lee, H. J., Lee, I. K., Kim, T. J., Kim, J. I. & Kim, J. K. (2013) [A case of spindle cell carcinoma of the stomach presenting with hematochezia and weight loss due to fistulous tract formation with colon]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 62: 126-130.
Not in PICO
- Andersson, A. & Bergdahl, L. (1976) Carcinoma of the colon in children: a report of six new cases and a review of the literature. *Journal of Pediatric Surgery*, 11: 967-971.
Pre-1980
- Andrejic, B., Djolai, M. & Ivanov, D. (2011) Lipoma of the colon clinically mimicking malignant tumor. *Virchows Archiv*, 459: S194.
Not in PICO
- Arafa, M. A., Sallam, S. & Jriesat, S. (2011) Colorectal cancer screening amongst first degree relatives of colon cancer cases in Jordan. *Asian Pacific Journal of Cancer Prevention*, 12: 1007-1011.
Not in PICO
- Arcangeli, P. & Digiesi, V. (1975) [Symptomatology of gastric carcinoma]. [Italian]. *Minerva Medica*, 66: 3498-3508.
Pre-1980
- Arrangoiz, R., Papavasiliou, P., Dushkin, H. & Farma, J. M. (2011) Case report and literature review: Metastatic lobular carcinoma of the breast an unusual presentation. *International Journal of Surgery Case Reports*, 2: 301-305.
Not in PICO
- Asensio Lahoz, L. A., Abaitua, B. J. & Palazuelos, C. M. (1995) [Rectal hemorrhage as the first manifestation of prostatic carcinoma]. [Spanish]. *Archivos Espanoles de Urologia*, 48: 640-641.
Not in PICO
- Astin, M., Griffin, T., Neal, R. D., Rose, P. & Hamilton, W. (2011) The diagnostic value of symptoms for colorectal cancer in primary care: a systematic review. [Review]. *British Journal of General Practice*, 61: e231-e243.
Systematic review, but current review updates it
- Ata, R. M. (2013) Clinical and histopathologic profile of patients with early & late-onset colorectal cancer. *Journal of Gastroenterology and Hepatology*, 28: 110.
Not in PICO
- Atkin, W., Dadswell, E., Wooldrage, K., Kralj-Hans, I., von, W. C., Edwards, R., Yao, G., Kay, C., Burling, D., Faiz, O., Teare, J., Lilford, R. J., Morton, D., Wardle, J., Halligan, S. & SIGGAR, i. (2013) Computed tomographic colonography versus colonoscopy for investigation of patients with symptoms suggestive of colorectal cancer (SIGGAR): a multicentre randomised trial. *Lancet*, 381: 1194-1202.
Same as Halligan 2013
- Badiani, S., Desai, A. & Chapman, M. A. (2012) Is whole colonic imaging necessary for symptoms of change in bowel habit and/or rectal bleeding? *Colorectal Disease*, 14: 1197-1200.
Not in PICO
- Bae, S. H., Park, W., Choi, D. H., Nam, H., Kang, W. K., Park, Y. S., Park, J. O., Chun, H. K., Lee, W. Y., Yun, S. H. & Kim, H. C. (2011) Palliative radiotherapy in patients with a symptomatic pelvic mass of metastatic colorectal cancer. *Radiation Oncology*, 6: 52.
Not in PICO
- Bafandeh, Y., Khoshbaten, M., Eftekhar-Sadat, A. T. & Farhang, S. (2007) Colorectal neoplasms in symptomatic patients without evidence of bleeding: a prospective study in an Iranian population. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 8: 485-488.
Not in PICO (referred population)
- Bafandeh, Y., Khoshbaten, M., Eftekhar Sadat, A. T. & Farhang, S. (2008) Clinical predictors of colorectal polyps and carcinoma in a low prevalence region: results of a colonoscopy based study.

World Journal of Gastroenterology, 14: 1534-1538.

Not in PICO

Baker, J. W., Mitchell, S. J. & Dixon, A. R. (2002) Early diagnosis of colonic carcinoma: a haemorrhagic complication after the use of tissue plasminogen activator. *Postgraduate Medical Journal*, 78: 429.

Not in PICO

Ballinger, A. (2007) Gastroenterology and anaemia. *Medicine*, 35: 142-146.

Narrative review

BANCHIERI, F. R. & RIZZELLO, N. (1964) [Urinary symptomatology in recto-sigmoid cancer]. [Italian]. *Minerva Urologica*, 16: 159-162.

Pre-1980

Barchetti, F., Al, A. N., De, M., V, Caravani, F. & Broglia, L. (2010) Giant lipoma of descending colon diagnosed at CT: report of a case. *European Review for Medical & Pharmacological Sciences*, 14: 573-575.

Not in PICO

Barillari, P., de, A. R., Valabrega, S., Indinnimeo, M., Gozzo, P., Ramacciato, G. & Fegiz, G. (1989) Relationship of symptom duration and survival in patients with colorectal carcinoma. *European Journal of Surgical Oncology*, 15: 441-445.

Not in PICO

Barney, S. P., Muller, C. Y. & Bradshaw, K. D. (2008) Pelvic Masses. *Medical Clinics of North America*, 92: 1143-1161.

Narrative review

Barracough, K. (2010) The predictive value of cancer symptoms in primary care. *British Journal of General Practice*, 60: 639-640.

Letter/narrative review

Barrett, J., Jiwa, M., Rose, P. & Hamilton, W. (2006) Pathways to the diagnosis of colorectal cancer: an observational study in three UK cities. *Family Practice*, 23: 15-19.

Not in PICO

Bartoszewicz, L., Kalicki, B., Grad, A. & Koszycka, A. (2008) Differentiation of pathological states in children with high fever - Meaning of procalcitonin. [Polish]. *Pediatrics i Medycyna Rodzinna*, 4: 113-117.

Not in PICO

Barwick, T. W., Scott, S. B. & Ambrose, N. S. (2004) The two week referral for colorectal cancer: a retrospective analysis. *Colorectal Disease*, 6: 85-91.

Not in PICO

Bassett, M. L., Bennett, S. A. & Goulston, K. J. (1979) Colorectal cancer. A study of 230 patients. *Medical Journal of Australia*, 1: 589-592.

Pre-1980

Bates, A. W. & Baithun, S. I. (2002) Secondary solid neoplasms of the prostate: a clinico-pathological series of 51 cases. *Virchows Archiv*, 440: 392-396.

Not in PICO

Batko, B. (1974) [2 cases of anemia as an early sign of colonic carcinoma]. [Polish]. *Wiadomosci Lekarskie*, 27: 277-280.

Pre-1980

Bekkink, O. M., McCowan, C., Falk, G. A., Teljeur, C., Van de Laar, F. A. & Fahey, T. (2010) Diagnostic accuracy systematic review of rectal bleeding in combination with other symptoms, signs and tests in relation to colorectal cancer. *British Journal of Cancer*, 102: 48-58.

SR, but include 8 studies that are all included in this review

Benjazia, E., Turki, H., Atig, A., Khalifa, M., Letaief, A., Bahri, F. & Braham, A. (2011) Bloom syndrome complicated by colonic cancer in a young Tunisian woman. *Clinics & Research in Hepatology &*

- Gastroenterology*, 35: 682-684.
Not in PICO
- Benoit, M. F., Hannigan, E. V., Smith, R. P., Smith, E. R. & Byers, L. J. (2004) Primary gastrointestinal cancers presenting as gynecologic malignancies. *Gynecologic Oncology*, 95: 388-392.
Not in PICO
- Berger, M., De, W. N., Vogelenzang, R., Wetzels, R., Van Rijn-Van, K. N. & Opstelten, W. (2011) The NHG guideline diverticulitis. [Dutch]. *Huisarts en Wetenschap*, 54: 492-499.
Guideline
- Betzler, M. (2010) Successes in early detection of cancer. More and more curable colorectal carcinomas. [German]. *MMW-Fortschritte der Medizin*, 152: 26.
Letter
- Bhangu, A., Khan, M., Roberts, L., Reynolds, A., Desai, A. & Mathew, G. (2011) Detection and survival of colorectal cancer from a 2 week wait service. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 9: 78-82.
Not in PICO
- Bhargava, A., Aldameh, A., Stewart, J. & Hill, A. G. (2007) Prioritization of patients with rectal bleeding for urgent outpatient colonoscopy--a pilot study. *New Zealand Medical Journal*, 120: U2637.
Not in PICO
- Biswas, S., Willington, A. & Ellis, A. J. (2013) Impact of primary care education on the two week wait referral process for GI cancers. *Gastroenterology*, 144: S581-S582.
Not in PICO
- Bjerregaard, N. C., Tottrup, A., Sorensen, H. T. & Laurberg, S. (2007) Diagnostic value of self-reported symptoms in Danish outpatients referred with symptoms consistent with colorectal cancer. *Colorectal Disease*, 9: 443-451.
Not in PICO
- Bjerregaard, N. C., Tottrup, A., Sorensen, H. T. & Laurberg, S. (2009) Detection of colorectal cancer in symptomatic outpatients without visible rectal bleeding: Validity of the fecal occult blood test. *Clinical Epidemiology*, 1: 119-124.
Not in PICO
- Bjoernsen, L. P. & Lindsay, M. B. (2011) An unusual case of pediatric abdominal pain. *CJEM Canadian Journal of Emergency Medical Care*, 13: 133-138.
Not in PICO
- Boellaard, T. N., De Haan, M. C., Venema, H. W. & Stoker, J. (2013) Colon distension and scan protocol for CT-colonography: An overview. *European Journal of Radiology*, 82: 1144-1158.
Narrative review
- Boffa, C., Wright, H., Nickinson, A., Barker, T., Lamparelli, M. & Lewis, M. (2012) The effect of the bowel cancer symptoms pilot media campaign on colorectal referrals to a district general hospital. *Colorectal Disease*, 14: 37-38.
Not in PICO
- Boldys, H., Marek, T. A., Wanczura, P., Matusik, P. & Nowak, A. (2003) Even young patients with no alarm symptoms should undergo endoscopy for earlier diagnosis of gastric cancer. *Endoscopy*, 35: 61-67.
Not in PICO
- Bonde, P., Sachithanandan, A., Graham, A. N., Richardson, S. G. & Gladstone, D. J. (2002) Right atrial myxoma arising from the Eustachian valve in a patient with colonic polyposis. *Journal of Heart Valve Disease*, 11: 601-602.
Not in PICO
- Borhan-Manesh, F. (2009) "Low caliber stool" and "pencil thin stool" are not signs of colo-rectal cancer. [Review] [30 refs]. *Digestive Diseases & Sciences*, 54: 208-211.
Narrative review

- Borjeson, S., Starkhammar, H., Unosson, M. & Bertero, C. (2012) Common Symptoms and Distress Experienced Among Patients with Colorectal Cancer: A Qualitative part of Mixed Method Design. *The Open Nursing Journal*, 6: 100-107.
Not in PICO
- Bosch, X., Foix, A., Jordan, A., Coca, A. & Lopez-Soto, A. (2011) Outpatient Quick Diagnosis Units for the evaluation of suspected severe diseases: an observational, descriptive study. *Clinics (Sao Paulo, Brazil)*, 66: 737-741.
Not in PICO
- Bowman, M. A. & Neale, A. V. (2011) Family practice is a highly complex business. *Journal of the American Board of Family Medicine: JABFM*, 24: 1-3.
Not in PICO
- Bowrey, D. J., Otter, M. I. & Billings, P. J. (2003) Rectal infiltration by prostatic adenocarcinoma: report on six patients and review of the literature. [Review] [37 refs]. *Annals of the Royal College of Surgeons of England*, 85: 382-385.
Not in PICO
- Bowrey, D. J., Griffin, S. M., Wayman, J., Karat, D., Hayes, N. & Rames, S. A. (2006) Use of alarm symptoms to select dyspeptics for endoscopy causes patients with curable esophagogastric cancer to be overlooked. *Surgical Endoscopy*, 20: 1725-1728.
Not in PICO
- Brandenburg, D., Roorda, C., Groenhof, F., Havenga, K., Berger, M. Y., de Bock, G. H. & Berendsen, A. J. (2014) - Increased primary health care use in the first year after colorectal cancer diagnosis. - *Scandinavian Journal of Primary Health Care*, 32: 55-61.
Not in PICO
- Bratucu, E., Marincas, M. & Boru, C. (2004) [Particular evolution of a jejunal tumor in one patient with multiples neoplasia]. [Hungarian]. *Chirurgia (Bucuresti)*, 99: 57-60.
Not in PICO
- Brooks, J. (2006) Clinical update on oncology treatments and trends. *American Journal of Managed Care*, 12: S45-S70.
Not in PICO
- Brophy, C. & Cahow, C. E. (1989) Primary small bowel malignant tumors. Unrecognized until emergent laparotomy. *American Surgeon*, 55: 408-412.
Not in PICO
- Browne, S., Dowie, A., Mitchell, L., Wyke, S., Ziebland, S., Campbell, N. & Macleod, U. (2011) Patients' needs following colorectal cancer diagnosis: where does primary care fit in? *British Journal of General Practice*, 61: e692-e699.
Not in PICO
- Budzynski, J., Manerowski, M. & Swiatkowski, M. (2007) The comparison of symptoms of the colorectal cancer and extraintestinal digestive tract neoplasms in patients referred by family doctors to gastroenterology department. [Polish]. *Family Medicine and Primary Care Review*, 9: 381-383.
Not in PICO
- Bull-Henry, K. & Al-Kawas, F. H. (2013) Evaluation of occult gastrointestinal bleeding. *American Family Physician*, 87: 430-436.
Narrative review
- Byles, J. E., Redman, S., Hennrikus, D., Sanson-Fisher, R. W. & Dickinson, J. (1992) Delay in consulting a medical practitioner about rectal bleeding. *Journal of Epidemiology and Community Health*, 46: 241-244.
Not in PICO
- Byles, J. E., Sanson-Fisher, R. W., Redman, S., Reid, A. L. & Agrez, M. (1992) Early detection of colorectal cancer: a profile of current practice. *Cancer Detection & Prevention*, 16: 245-252.
Not in PICO

- Cai, S. R., Zheng, S. & Zhang, S. Z. (2005) [Multivariate analysis of prognostic factors in colorectal cancer patients with different ages]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 27: 483-485.
Not in PICO
- Calogero, A., Cirillo, M., Gennarelli, N., Buonomo, M. & Lobello, R. (2012) Cancer colon test: Evolution and prospects in colorectal cancer screening. *Digestive and Liver Disease*, 44: S202.
Not in PICO
- Capell, S., Comas, P., Piella, T., Rigau, J., Pruna, X., Martinez, F. & Montull, S. (2004) [Quick and early diagnostic outpatient unit: an effective and efficient assistential model. Five years experience]. [Spanish]. *Medicina Clinica*, 123: 247-250.
Not in PICO
- Cappell, M. S. (2003) Colon cancer during pregnancy. [Review] [323 refs]. *Gastroenterology Clinics of North America*, 32: 341-383.
Not in PICO
- Carlsson, L., Hakansson, A. & Nordenskjold, B. (2001) Common cancer-related symptoms among GP patients - Opportunistic screening in primary health care. *Scandinavian Journal of Primary Health Care*, 19: 199-203.
Symptoms not linked with cancer, not patients presenting with symptoms unprompted (patients prompted to attend)
- Cathomas, R. (2007) Oncology for the general practitioner - Update 2007. [German]. *Schweizerische Rundschau fur Medizin - Praxis*, 96: 1989-1995.
Narrative review
- Cavallaro, A., Lauretta, A., Pennisi, S. & Cavallaro, V. (2005) Iron deficiency anemia: Often early sign of ascending colorectal cancer. [Italian]. *Chirurgia*, 18: 81-84.
Not in PICO
- Celestino, A., Castillo, T., Frisancho, O., Contardo, C., Espejo, H., Tomioka, C. & Navarrete, J. (1996) [Colorectal cancer: study on 365 cases]. [Review] [37 refs] [Spanish]. *Revista de Gastroenterologia del Peru*, 16: 187-196.
Not in PICO
- Cerdan-Santacruz, C., Cano-Valderrama, O., Cardenas-Crespo, S., Torres-Garcia, A. J. & Cerdan-Miguel, J. (2011) Colorectal cancer and its delayed diagnosis: have we improved in the past 25 years? *Revista Espanola de Enfermedades Digestivas*, 103: 458-463.
Not in PICO
- Chan, K.-W., Ng, P. T. K., Chan, C., Ng, C.-L. & Yiu, Y.-K. (2009) The Family Medicine Specialist Surgical Clinic - A new project to benefit the patient, hospital specialist, family physicians and the private sector in the community. *Hong Kong Practitioner*, 31: 24-29.
Not in PICO
- Chan, Y. M., Ngai, S. W. & Lao, T. T. (1999) Colon cancer in pregnancy. A case report. *Journal of Reproductive Medicine*, 44: 733-736.
Not in PICO
- Chattopadhyay, S., Gupta, P., Aich, R. K. & Deb, A. R. (2012) Colorectal carcinoma in a ten-year-old girl: A case report. *Journal of Cancer Research and Therapeutics*, 8: 120-122.
Not in PICO
- Chen, H.-F., Ho, C.-A., Chen, P. & Li, C.-Y. (2011) Higher Risk of colorectal cancers among diabetic patients in Taiwan: A population-based study with age and sex stratification. *Diabetes*, 60: A370.
Not in PICO
- Chen, S. C., Yen, Z. S., Wang, H. P., Lee, C. C., Hsu, C. Y., Chen, W. J., Hsu, C. Y., Lai, H. S., Lin, F. Y. & Chen, W. J. (2006) Ultrasonography in diagnosing colorectal cancers in patients presenting with abdominal distension. *Medical Journal of Australia*, 184: 614-616.
Not in PICO

- Chiao, H., Tsai, F. & Strum, W. (2013) Risks for advanced adenomas in patients with a positive family history of sporadic colorectal cancer have a bimodal age distribution. *American Journal of Gastroenterology*, 108: S171.
Not in PICO
- Chiu, C. T., Chiang, J. M., Yeh, T. S., Tseng, J. H., Chen, T. C., Jan, Y. Y. & Chen, M. F. (2008) Clinicopathological analysis of colorectal cancer liver metastasis and intrahepatic cholangiocarcinoma: are they just apples and oranges? *Digestive & Liver Disease*, 40: 749-754.
Not in PICO
- Chu, J.-S., Yang, K.-C., Hsu, T.-C., Kao, C.-R., Chou, S.-Y. & Shih, S.-C. (1993) Concomitant digestive malignancy in pregnancy. *Chinese Journal of Gastroenterology*, 10: 1-8.
Not in PICO
- Clark, K., Smith, J. M. & Currow, D. C. (2012) The prevalence of bowel problems reported in a palliative care population. *Journal of Pain & Symptom Management*, 43: 993-1000.
Not in PICO
- Clary, P. L. & Lawson, P. (2009) Pharmacologic pearls for end-of-life care. *American Family Physician*, 79: 1059-1065.
Not in PICO
- Cleary, J., Peters, T. J., Sharp, D. & Hamilton, W. (2007) Clinical features of colorectal cancer before emergency presentation: a population-based case-control study. *Family Practice*, 24: 3-6.
Sub-population of Hamilton (2005)
- CLERY, A. P., DOYLE, J. S. & RYAN, M. J. (1963) The early diagnosis of cancer of the colon and rectum. *Journal of the Irish Medical Association*, 53: 18-21.
Pre-1980
- Coco, C., Rizzo, G., Manno, A., Mattana, C. & Verbo, A. (2010) Surgical treatment of small bowel neoplasms. [Review] [51 refs]. *European Review for Medical & Pharmacological Sciences*, 14: 327-333.
Not in PICO
- COLCOCK, B. P. (1964) Early diagnosis in carcinoma of the right colon. *Diseases of the Colon & Rectum*, 7: 482-485.
Pre-1980
- Colecchia, G. & Nardi, M. (1999) [Colorectal cancer in pregnancy. A case report]. [Review] [15 refs] [Italian]. *Giornale di Chirurgia*, 20: 159-161.
Not in PICO
- Collins, P. D., Mpofo, C., Watson, A. J. & Rhodes, J. M. (2006) Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease. *Cochrane Database of Systematic Reviews*.
Not in PICO
- Courtney, R. J., Paul, C. L., Sanson-Fisher, R. W., Macrae, F. A., Attia, J. & McEvoy, M. (2012) Factors associated with consultation behaviour for primary symptoms potentially indicating colorectal cancer: a cross-sectional study on response to symptoms. *BMC Gastroenterology*, 12: 100.
Not in PICO
- Courtney, R. J., Paul, C. L., Sanson-Fisher, R. W., Macrae, F., Attia, J. & McEvoy, M. (2012) Current state of medical-advice-seeking behaviour for symptoms of colorectal cancer: determinants of failure and delay in medical consultation. *Colorectal Disease*, 14: e222-e229.
Not in PICO
- Courtney, R. J., Paul, C. L., Sanson-Fisher, R. W., Macrae, F. A., Carey, M. L., Attia, J. & McEvoy, M. (2012) Colorectal cancer risk assessment and screening recommendation: a community survey of healthcare providers' practice from a patient perspective. *Bmc Family Practice*, 13.
Not in PICO
- Cubas, C. R., Ballarino, E. A., Neiro, P. & Grasso, R. L. (2011) [Hereditary nonpolyposis colorectal cancer: analysis of a case and review of management]. [Review] [Spanish]. *Acta*

- Gastroenterologica Latinoamericana*, 41: 137-141.
Not in PICO
- Curless, R., French, J., Williams, G. V. & James, O. F. (1994) Comparison of gastrointestinal symptoms in colorectal carcinoma patients and community controls with respect to age. *Gut*, 35: 1267-1270.
Not in PICO
- Curless, R., French, J. M., Williams, G. V. & James, O. F. (1994) Colorectal carcinoma: do elderly patients present differently? *Age & Ageing*, 23: 102-107.
Not in PICO
- Currie, A. C., Evans, J., Smith, N. J., Brown, G., Abulafi, A. M. & Swift, R. I. (2012) The impact of the two-week wait referral pathway on rectal cancer survival. *Colorectal Disease*, 14: 848-853.
Not in PICO
- Damery, S., Ryan, R., Wilson, S., Ismail, T., Hobbs, R. & Improving Colorectal Outcomes Group (2011) Iron deficiency anaemia and delayed diagnosis of colorectal cancer: a retrospective cohort study. *Colorectal Disease*, 13: e53-e60.
Not in PICO
- Daniel, W. J. (2010) Anorectal pain, bleeding and lumps. *Australian Family Physician*, 39: 376-381.
Narrative review
- Dattalo, M., Cheng, J. & Levine, R. (2010) History keeps repeating itself: A 21st century case of a centuries old scourge. *Journal of General Internal Medicine*, 25: S518.
Not in PICO
- Davis, A. J. M., Bowman, D. & Shepherd, H. A. (2004) Patients referred from primary care with iron-deficiency anaemia: Analysis of a nurse-led service. An improvement for both doctor and patient? *Quality in Primary Care*, 12: 129-135.
Not in PICO (referred patients)
- de, J. E., Numans, M. E., de Wit, N. J., Heemstra-Borst, C. G., Geijer, R. M. & Burgers, J. S. (2013) [Summary of the Dutch College of General Practitioners' (NHG) practice guideline 'Gastric symptoms']. [Review] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 157: A6101.
Narrative review/guideline
- De, L. R., I, Rodrigo, S. L., Prados, C. D. & Schleiman, H. H. (1989) [Epidemiology of cancer of the colon and the rectum in Asturias (1977-1981)]. [Spanish]. *Revista Espanola de Las Enfermedades del Aparato Digestivo*, 76: t-8.
Not in PICO
- De, N. J., Lechner, L. & De, V. H. (2001) A qualitative study on detecting cancer symptoms and seeking medical help; an application of Andersen's model of total patient delay. *Patient Education and Counseling*, 42: 145-157.
Not in PICO
- Debnath, D., Dielehner, N. & Gunning, K. A. (2002) Guidelines, compliance, and effectiveness: a 12 months' audit in an acute district general healthcare trust on the two week rule for suspected colorectal cancer. *Postgraduate Medical Journal*, 78: 748-751.
Not in PICO
- Deng, S. X., An, W., Gao, J., Yin, J., Cai, Q. C., Yang, M., Hong, S. Y., Fu, X. X., Yu, E. D., Xu, X. D., Zhu, W. & Li, Z. S. (2012) Factors influencing diagnosis of colorectal cancer: a hospital-based survey in China. *Journal of Digestive Diseases*, 13: 517-524.
Not in PICO
- Denis, B., Perrin, P., Cailleret, A. F., Guth, F., Ruetsch, M. & Strentz, P. (2003) [Colorectal cancer screening: a survey of French general practitioners]. [French]. *Gastroenterologie Clinique et Biologique*, 27: 992-997.
Not in PICO
- Denis, B., Schon, G., Ruetsch, M., Grall, J. C., Leveque, M., Meyer, J. M., Moser, S., Tschiember, J. C. & Perrin, P. (2007) Cancer screening by primary care physicians: a chart audit. *Presse Medicale*, 36:

217-223.

Not in PICO

Dennis, R., Tou, S. & Miller, R. (2011) Colorectal cancer: Prevention and early diagnosis. *Medicine*, 39: 243-249.

Narrative review

Dent, B., Coyne, P., Eltringham, M. & Katory, M. (2009) Age, stage, and symptoms: Should the NHS Bowel Cancer Screening Programme be screening earlier? *Colorectal Disease*, 11: 45.

Not in PICO

Dent, O. F., Goulston, K. J., Tennant, C. C., Langeluddecke, P., Mant, A., Chapuis, P. H., Ward, M. & Bokey, E. L. (1990) Rectal bleeding. Patient delay in presentation. *Diseases of the Colon & Rectum*, 33: 851-857.

Not in PICO (outcome)

Denters, M., Bossuyt, P. M., Deutekom, M., Fockens, P. & Dekker, E. (2011) Females, younger persons and persons with a negative family history more often have a false positive FIT result. *Gastroenterology*, 140: S418.

Not in PICO

Diallo Owono, F. K., Nguema, M. R., Ibaba, J., Mihindou, C. & Ondo, N. F. (2011) [Epidemiological and diagnostic features of colorectal cancer in Libreville, Gabon]. [French]. *Medecine Tropicale*, 71: 605-607.

Not in PICO

Diaz-Sanchez, A., Lara, M. A., Ortega, P., Aramendi, T., Gonzalez, C., Alberdi, J. M., Del, V. E., Casado, I., Campos, R. & Aldeguer, M. (2011) [Colorectal melanoma: review of two distinct forms of presentation]. [Spanish]. *Gastroenterologia y Hepatologia*, 34: 83-88.

Not in PICO

Dobie, S., Saver, B. G., Wang, C. Y., Green, P. K. & Baldwin, L. M. (2011) Do Primary Care Physicians Lose Contact with Their Colorectal Cancer Patients? *Journal of the American Board of Family Medicine*, 24: 704-709.

Not in PICO

Dolman, G. E., Wijayasekara, C. M. & Cummings, J. R. F. (2011) Gastrointestinal complications following percutaneous coronary intervention (PCI). *Gut*, 60: A102.

Not in PICO

Dominguez-Ayala, M., Diez-Vallejo, J. & Comas-Fuentes, A. (2012) Missed opportunities in early diagnosis of symptomatic colorectal cancer. *Revista Espanola de Enfermedades Digestivas*, 104: 343-349.

Not in PICO

Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W. & Martin, R. M. (2012) Features of childhood cancer in primary care: a population-based nested case-control study. *British Journal of Cancer*, 106: 982-987.

Not in PICO

Doolabh, N., Anthony, T., Simmang, C., Bieligk, S., Lee, E., Huber, P., Hughes, R. & Turnage, R. (2000) Primary colonic lymphoma. *Journal of Surgical Oncology*, 74: 257-262.

Not in PICO

Dozois, E. J., Boardman, L. A., Suwanthanma, W., Limburg, P. J., Cima, R. R., Bakken, J. L., Vierkant, R. A., Aakre, J. A. & Larson, D. W. (2008) Young-onset colorectal cancer in patients with no known genetic predisposition: can we increase early recognition and improve outcome? *Medicine*, 87: 259-263.

Not in PICO

Draskovic, M., Misovic, S., Kronja, G., Krsic, J., Tomic, A. & Sarac, M. (2005) [Jejuno-jejunal intussusception in adults secondary to submucosal leiomyoma]. [Serbian]. *Medicinski Pregled*, 58: 405-409.

Not in PICO

- Dregan, A., Moller, H., Charlton, J. & Gulliford, M. C. (2013) Are alarm symptoms predictive of cancer survival? Population-based cohort study. *British Journal of General Practice*, 63: e807-e812.
Not in PICO
- Dusek, L., Muzik, J., Gelnarova, E., Finek, J., Vyzula, R. & Abrahamova, J. (2010) Cancer incidence and mortality in the Czech Republic. *Klinicka Onkologie*, 23: 311-324.
Not in PICO
- Edgren, G., Bagnardi, V., Bellocco, R., Hjalgrim, H., Rostgaard, K., Melbye, M., Reilly, M., Adami, H. O., Hall, P. & Nyren, O. (2010) Pattern of declining hemoglobin concentration before cancer diagnosis. *International Journal of Cancer*, 127: 1429-1436.
Not in PICO - Willie has requested we check this, so ordered now
- Edwards, A., Penney, M. & Allison, M. (2004) Using iron deficiency tests for colorectal cancer screening: a feasibility study in one UK general practice. *Journal of Evaluation in Clinical Practice*, 10: 475-479.
Not in PICO
- Ekelund, G., Lindstrom, C. & Rosengren, J. E. (1974) Appearance and growth of early carcinomas of the colon-rectum. *Acta Radiologica: Diagnosis*, 15: 670-679.
Pre-1980
- Eladawy, M., Dominguez, S. R., Anderson, M. S. & Glode, M. P. (2013) Kawasaki disease and the pediatric gastroenterologist: a diagnostic challenge. *Journal of Pediatric Gastroenterology & Nutrition*, 56: 297-299.
Not in PICO
- Elikowski, W., Lewandowska, M., Malek, M., Krokowicz, P., Piotrowska-Stelmaszyk, G. & Zawilska, K. (1267) [Pulmonary embolism as a first manifestation of synchronous occurrence of two neoplasms]. [Polish]. *Kardiologia Polska*, 67: 1262-1266.
Case report
- Ellis, H. (2012) The early days of surgery for cancer of the rectum. *Journal of Perioperative Practice*, 22: 103-104.
Not in PICO
- Elmi, A., Hedgire, S. S., Pargaonkar, V., Cao, K., McDermott, S. & Harisinghani, M. (2013) Is early colonoscopy beneficial in patients with CT-diagnosed diverticulitis? *AJR.American Journal of Roentgenology*, 200: 1269-1274.
Not in PICO
- Emery, J. D., Shaw, K., Williams, B., Mazza, D., Fallon-Ferguson, J., Varlow, M. & Trevena, L. J. (2014) The role of primary care in early detection and follow-up of cancer. *Nature Reviews Clinical Oncology*, 11: 38-48.
Not in PICO
- Emrich, J. & Niemeyer, C. (2002) [The secreting villous adenoma as a rare cause of acute renal failure]. [German]. *Medizinische Klinik*, 97: 619-623.
Not in PICO
- Esteva, M., Leiva, A., Ramos, M., Pita-Fernandez, S., Gonzalez-Lujan, L., Casamitjana, M., Sanchez, M. A., Pertega-Diaz, S., Ruiz, A., Gonzalez-Santamaria, P., Martin-Rabadan, M., Costa-Alcaraz, A. M., Espi, A., Macia, F., Segura, J. M., Lafita, S., Arnal-Monreal, F., Amengual, I., Bosca-Watts, M. M., Hospital, A., Manzano, H. & Magallon, R. (2013) Factors related with symptom duration until diagnosis and treatment of symptomatic colorectal cancer. *Bmc Cancer*, 13.
Not in PICO
- Esteva, M., Leiva, A., Ramos, M., Pita-Fernandez, S., Gonzalez-Lujan, L., Casamitjana, M., Sanchez, M. A., Pertega-Diaz, S., Ruiz, A., Gonzalez-Santamaria, P., Martin-Rabadan, M., Costa-Alcaraz, A. M., Espi, A., Macia, F., Segura, J. M., Lafita, S., Arnal-Monreal, F., Amengual, I., Bosca-Watts, M. M., Hospital, A., Manzano, H., Magallon, R. & DECCIRE GROUP (2013) Factors related with symptom duration until diagnosis and treatment of symptomatic colorectal cancer. *Bmc Cancer*, 13: 87.
Not in PICO

- Exbrayat, C., Poncet, F., Billette, d., V, Garnier, A. & Bureau du, C. P. (2010) Colonoscopy practices, and colorectal cancer and polyp screening, as assessed in the French district of Iserre from May to July in 2004. *Gastroenterologie Clinique et Biologique*, 34: 702-711.
Not in PICO
- Fargo, M. V. & Latimer, K. M. (2012) Evaluation and management of common anorectal conditions. *American Family Physician*, 85: 623-630.
Narrative review
- Farkkila, M., Sarna, S., Valtonen, V. & Sipponen, P. (2004) Does the 'test-and-treat' strategy work in primary health care for management of uninvestigated dyspepsia? A prospective two-year follow-up study of 1552 patients. *Scandinavian Journal of Gastroenterology*, 39: 327-335.
Not in PICO
- Farrer, F. (2010) Cancer screening in primary care. *SA Pharmaceutical Journal*, 77: 41-45.
Narrative review
- Feldstein, A. C., Perrin, N., Liles, E. G., Smith, D. H., Rosales, A. G., Schneider, J. L., Lafata, J. E., Myers, R. E., Mosen, D. M. & Glasgow, R. E. (2012) Primary Care Colorectal Cancer Screening Recommendation Patterns: Associated Factors and Screening Outcomes. *Medical Decision Making*, 32: 198-208.
Not in PICO
- Ferguson, H. J. M., Mak, T., Royle, T. J., Simpson, J. & Bhalerao, S. (2010) The RADAR one-stop clinic for suspected colorectal cancer: An analysis of 1690 patients. *Colorectal Disease*, 12: 17.
Not in PICO
- Fijten, G. H., Muris, J. W., Starmans, R., Knottnerus, J. A., Blijham, G. H. & Krebber, T. F. (1993) The incidence and outcome of rectal bleeding in general practice. *Family Practice*, 10: 283-287.
Publication of data from Fijten 1995
- Fijten, G. H. (1994) Occurrence and clinical significance of overt blood loss per rectum in the general population and in medical practice. *British Journal of General Practice*, 44: 320-325.
"SR", but contain no data from primary care
- Fisch, M. J., Zhao, F., O'Mara, A. M., Wang, X. S., Cella, D. & Cleeland, C. S. (2014) Predictors of significant worsening of patient-reported fatigue over a 1-month timeframe in ambulatory patients with common solid tumors. *Cancer*, 120: 442-450.
Not in PICO
- Fisher, D. A., Martin, C., Galanko, J., Sandler, R. S., Noble, M. D. & Provenzale, D. (2004) Risk factors for advanced disease in colorectal cancer. *American Journal of Gastroenterology*, 99: 2019-2024.
Not in PICO
- Forbes, L. J., Warburton, F., Richards, M. A. & Ramirez, A. J. (2014) - Risk factors for delay in symptomatic presentation: a survey of cancer patients. - *British Journal of Cancer*, 111: 581-588.
Not in PICO
- Ford, A. C., Veldhuyzen van Zanten, S. J., Rodgers, C. C., Talley, N. J., Vakil, N. B. & Moayyedi, P. (2008) Diagnostic utility of alarm features for colorectal cancer: systematic review and meta-analysis. [Review] [37 refs]. *Gut*, 57: 1545-1553.
SR, but majority of included studies are secondary care, the only relevant studies from primary care are already included
- Ford, A. C. & Moayyedi, P. (2013) Dyspepsia. *BMJ (Online)*, 347.
Narrative review
- Fotiadis, C., Manolis, E. N., Troupis, T. G., Gorgoulis, V. G. & Sechas, M. N. (2000) Pelvic cancer pain. *Journal of Surgical Oncology*, 75: 280-300.
Not in PICO
- Freeman, H. J. (2008) Natural history and long-term clinical behavior of segmental colitis associated with diverticulosis (SCAD syndrome). *Digestive Diseases & Sciences*, 53: 2452-2457.
Not in PICO

- Gaj, P., Maryan, N., Hennig, E. E., Ledwon, J. K., Paziewska, A., Majewska, A., Karczmariski, J., Nesteruk, M., Wolski, J., Antoniewicz, A. A., Przytulski, K., Rutkowski, A., Teumer, A., Homuth, G., Starzynska, T., Regula, J. & Ostrowski, J. (2012) Pooled Sample-Based GWAS: A Cost-Effective Alternative for Identifying Colorectal and Prostate Cancer Risk Variants in the Polish Population. *PLoS ONE*, 7.
Not in PICO
- Garcia Marcilla, J. A., Sanchez, B. F., Aguilar, J. & Parrilla, P. P. (1994) Primary small bowel malignant tumors. *European Journal of Surgical Oncology*, 20: 630-634.
Not in PICO
- Gatta, G., Ciccolallo, L., Faivre, J., Bouvier, A. M., Berrino, F. & Gerard, J. P. (2007) Late outcomes of colorectal cancer treatment: a FECS-EUROCARE study. *Journal of Cancer Survivorship*, 1: 247-254.
Not in PICO
- Geboes, K., De, J. E., Rutgeerts, P. & Vantrappen, G. (1988) Symptomatic gastrointestinal metastases from malignant melanoma. A clinical study. *Journal of Clinical Gastroenterology*, 10: 64-70.
Not in PICO
- Ghafoor, A., Jan, M. A. & Bokhari, H. (1998) Clinical presentation and diagnosis of colorectal cancer. *Journal of the College of Physicians and Surgeons Pakistan*, 8: 126-128.
Not in PICO
- Ghanadi, K., Anbari, K., Obeidavi, Z. & Pournia, Y. (2014) - Characteristics of Colorectal Cancer in Khorramabad, Iran during 2013. - *Middle East Journal of Digestive Diseases*, 6: 81-86.
Not in PICO
- Giannattasio, F., Santinelli, C., Troise, R., Varriale, M., Iannacci, G. & Visconti, M. (1995) [Synchronous adenomas of the stomach and rectum with severe protein-losing syndrome]. [Italian]. *Minerva Gastroenterologica e Dietologica*, 41: 187-190.
Not in PICO
- Gifaldi, A. S., Petros, J. G. & Wolfe, G. R. (1992) Metastatic breast carcinoma presenting as persistent diarrhea. *Journal of Surgical Oncology*, 51: 211-215.
Not in PICO
- Girolami, A., Prandoni, P., Zanon, E., Bagatella, P. & Girolami, B. (1999) Venous thromboses of upper limbs are more frequently associated with occult cancer as compared with those of lower limbs. *Blood Coagulation & Fibrinolysis*, 10: 455-457.
Not in PICO (referred population)
- Glushko, Y., Basher, W., Barchana, M. & Zidan, J. (2010) Differences in clinical and pathological characteristics of colorectal cancer in Arab as compared to Jewish patients in Northern Israel. *Familial Cancer*, 9: 327-330.
Not in PICO
- Gonzalez-Hermoso, F., Perez-Palma, J., Marchena-Gomez, J., Lorenzo-Rocha, N. & Medina-Arana, V. (2004) Can early diagnosis of symptomatic colorectal cancer improve the prognosis? *World Journal of Surgery*, 28: 716-720.
Not in PICO
- Gorin, S. S., Gemson, D., Ashford, A., Bloch, S., Lantigua, R., Ahsan, H. & Neugut, A. (2000) Cancer education among primary care physicians in an underserved community. *American Journal of Preventive Medicine*, 19: 53-58.
Not in PICO
- Goulston, K. J., Cook, I. & Dent, O. F. (1986) How important is rectal bleeding in the diagnosis of bowel cancer and polyps? *Lancet*, 2: 261-265.
Same data as Mant, but Mant's got other data too, so just include Mant
- Graham, J. (1978) Problems in family practice. Rectal bleeding. *Journal of Family Practice*, 7: 169-176.
Pre-1980

- Greenwald, D. A. & Brandt, L. J. (1998) Colonic ischemia. [Review] [37 refs]. *Journal of Clinical Gastroenterology*, 27: 122-128.
Not in PICO
- Griggs, R., Cork, T. & Robertson, C. (2013) Rigid sigmoidoscopy: A dinosaur diagnostic tool? *International Journal Of Surgery*, 11: 626.
Abstract only, not enough information can be extracted to ascertain relevance, but I think it is not in PICO.
- Gutierrez, C., Hernansanz, S., Rubiales, A. S., Del Valle, M. L., Cuadrillero, R. F., Flores, L. A. & Garcia, C. (2006) Clinical manifestations and care in tumors with pelvic involvement: Is there a pelvic syndrome in Palliative Care?. [Spanish]. *Medicina Paliativa*, 13: 32-36.
Not in PICO
- Ha, T. H., Jeon, T. J., Park, J. Y., Jang, Y. H., Kim, D. H., Ryu, M. J., Sinn, D. H. & Oh, T. H. (2013) [A case of basaloid squamous cell carcinoma of rectosigmoid colon]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 62: 375-378.
Not in PICO
- Half, E., Bercovich, D. & Rozen, P. (2009) Familial adenomatous polyposis. [Review] [114 refs]. *Orphanet Journal Of Rare Diseases*, 4: 22.
Narrative review
- Halligan, S. (2013) CT colonography for investigation of patients with symptoms potentially suggestive of colorectal cancer: a review of the UK SIGGAR trials. [Review]. *British Journal of Radiology*, 86: 20130137.
Narrative review
- Halligan, S., Wooldrage, K., Dadswell, E., Kralj-Hans, I., von, W. C., Edwards, R., Yao, G., Kay, C., Burling, D., Faiz, O., Teare, J., Lilford, R. J., Morton, D., Wardle, J., Atkin, W. & SIGGAR, i. (2013) Computed tomographic colonography versus barium enema for diagnosis of colorectal cancer or large polyps in symptomatic patients (SIGGAR): a multicentre randomised trial. *Lancet*, 381: 1185-1193.
Not in PICO (referred population)
- Halligan, S. & Atkin, W. S. (2013) CT colonography for diagnosis of symptomatic colorectal cancer: The SIGGAR trials and their implication for service delivery. *Clinical Radiology*, 68: 643-645.
Same as Halligan 2013
- Hamilton, W. & Sharp, D. (2004) Diagnosis of colorectal cancer in primary care: the evidence base for guidelines. *Family Practice*, 21: 99-106.
Narrative review
- Hamilton, W. (2009) The CAPER studies: five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients. *British Journal of Cancer*, 101: Suppl-6.
Review of studies already included
- Hamilton, W. (2010) Cancer diagnosis in primary care. *British Journal of General Practice*, 60: 121-128.
Narrative review
- Hamilton, W., Astin, M., Griffin, T., Neal, R. D. & Rose, P. (2011) Diagnostic value of symptoms for colorectal cancer in primary care: a systematic review. *British Journal of General Practice*, 61: 333-334.
Data already included
- Hancock, B. J. & Vajcner, A. (1988) Lipomas of the colon: a clinicopathologic review. [Review] [29 refs]. *Canadian Journal of Surgery*, 31: 178-181.
Not in PICO
- Hansen, H. J., Morsel-Carlsen, L. & Bulow, S. (1997) [Patients' perception of symptoms in colorectal cancer. A cause of delay in diagnosis and treatment]. [Danish]. *Ugeskrift for Laeger*, 159: 1941-

1944.

Not in PICO

Harinath, G., Somasekar, K. & Haray, P. N. (2002) The effectiveness of new criteria for colorectal fast track clinics. *Colorectal Disease*, 4: 115-117.

Not in PICO

Harmston, C., Hunter, J. & Wong, L. (2009) Does the location of screen detected cancers differ from that seen in the unscreened population? *Colorectal Disease*, 11: 19.

Not in PICO

Harmston, C., Akwei, S., Barnes, R., Goodyear, S. & Wong, L. (2010) Are screen detected colorectal cancers asymptomatic? *Colorectal Disease*, 12: 416-419.

Not in PICO

Harris, G. J. & Simson, J. N. (1998) Causes of late diagnosis in cases of colorectal cancer seen in a district general hospital over a 2-year period. *Annals of the Royal College of Surgeons of England*, 80: 246-248.

Not in PICO

Harris, J. N., Robinson, P., Lawrance, J., Carrington, B. M., Hopwood, P., Dougal, M. & Makin, W. (2003) Symptoms of colorectal liver metastases: correlation with CT findings. *Clinical Oncology (Royal College of Radiologists)*, 15: 78-82.

Not in PICO

Hashim, S. M., Fah, T. S., Omar, K., Rashid, M. R., Shah, S. A. & Sagap, I. (2011) Knowledge of colorectal cancer among patients presenting with rectal bleeding and its association with delay in seeking medical advice. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 12: 2007-2011.

Not in PICO

Hatzell, T. A., Ricketts, T. C., Tropman, S. E., Paskett, E. D. & Cooper, M. R. (1999) Rural physicians' understanding of the state-of-the-art in breast, colon and rectum cancer treatment. *Cancer Causes & Control*, 10: 261-267.

Not in PICO

Heap, T. (1996) Managing diarrhoea. Current thinking. [Review] [11 refs]. *Australian Family Physician*, 25: 38-45.

Narrative review

Heidrich, H., Konau, E. & Hesse, P. (2009) Asymptomatic venous thrombosis in cancer patients--a problem often overlooked. Results of a retrospective and prospective study. *Vasa*, 38: 160-166.

Not in PICO

Heikkinen, M., Pikkarainen, P., Eskelinen, M. & Julkunen, R. (2000) GPs' ability to diagnose dyspepsia based only on physical examination and patient history. *Scandinavian Journal of Primary Health Care*, 18: 99-104.

Does not distinguish between malignancy categories, but companion ref does, so that's included instead.

Heintze, C., Esch, T. & Braun, V. (2006) Computer-based health care research in the competence network inflammatory bowel disease. Handling of bowel diseases in general practice. *Medizinische Klinik*, 101: 357-364.

Not in PICO

Heise, R. H., Van Winter, J. T., Wilson, T. O. & Ogburn, P. L., Jr. (1992) Colonic cancer during pregnancy: case report and review of the literature. [Review] [30 refs]. *Mayo Clinic Proceedings*, 67: 1180-1184.

Not in PICO

Heitland, W. (2010) Colon carcinoma. [German]. *DoctorConsult - The Journal*, Wissen: e183-e189.

Not in PICO

Hillenbrand, A., Barth, T. F., Henne-Bruns, D. & Formentini, A. (2008) Anorectal amelanotic melanoma. *Colorectal Disease*, 10: 612-615.

Not in PICO

- Hippisley-Cox, J. & Coupland, C. (2011) Development and validation of risk prediction algorithm (QThrombosis) to estimate future risk of venous thromboembolism: prospective cohort study. *British Medical Journal*, 343.
Not in PICO
- Hippisley-Cox, J. & Coupland, C. (2013) **Symptoms and risk factors to identify people with suspected cancer in primary care.** *British Journal of General Practice*, 63: 125-126.
Comment
- Hoffenberg, E. J., Sauaia, A., Maltzman, T., Knoll, K. & Ahnen, D. J. (1999) Symptomatic colonic polyps in childhood: not so benign. *Journal of Pediatric Gastroenterology & Nutrition*, 28: 175-181.
Not in PICO
- Hogberg, C., Karling, P., Rutegard, J., Lilja, M. & Ljung, T. (2013) Immunochemical faecal occult blood tests in primary care and the risk of delay in the diagnosis of colorectal cancer. *Scandinavian Journal of Primary Health Care*, 31: 209-214.
Not in PICO
- Holtedahl, K. A. (1990) Probability revision in general practice: Occult blood in stool in patients with indigestion, and daily smoking in patients with cough. *Allgemeinmedizin*, 19: 35-38.
Not in PICO
- Holzinger, F., Schilling, M., Baer, H. U. & Buchler, M. W. (1995) Chronic anaemia caused by small-bowel adenocarcinoma: Case report. [German]. *Chirurgische Gastroenterologie*, 11: 174-177.
Not in PICO
- Hopper, A. D., Leeds, J. S., Hurlstone, D. P., Hadjivassiliou, M., Drew, K. & Sanders, D. S. (2005) Are lower gastrointestinal investigations necessary in patients with coeliac disease? *European Journal of Gastroenterology & Hepatology*, 17: 617-621.
Not in PICO
- Hsiang, J. C., Bai, W. & Lal, D. (2013) Symptom presentations and other characteristics of colorectal cancer patients and the diagnostic performance of the Auckland Regional Grading Criteria for Suspected Colorectal Cancer in the South Auckland population. *New Zealand Medical Journal*, 126: 95-107.
Not in PICO
- Hsing, C. T., Kim, H. Y., Lee, J. H., Han, J. S., Lee, J. H., Chang, J. S., Choi, S. R. & Jeong, J. S. (2012) [Gastrointestinal metastasis from a primary adenocarcinoma of the lung presenting with acute abdominal pain]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 59: 382-385.
Not in PICO
- Huerta, C., Johansson, S., Wallander, M. A. & Garcia Rodriguez, L. A. (2007) Risk factors and short-term mortality of venous thromboembolism diagnosed in the primary care setting in the United Kingdom. *Archives of Internal Medicine*, 167: 935-943.
Not in PICO
- Humphries, A., Clarke, J., Bhatnagar, G., Jenkins, I., Burling, D. & Thomas-Gibson, S. (2013) A new lower gastrointestinal 2-week wait 'direct to test' pathway results in earlier diagnosis of cancer. *Gut*, 62: A262.
Not in PICO
- Husain, A., Bezjak, A. & Easson, A. (2010) Malignant ascites symptom cluster in patients referred for paracentesis. *Annals of Surgical Oncology*, 17: 461-469.
Not in PICO
- Imaoka, H., Higaki, N., Kumagi, T., Miyaike, J., Ohmoto, M., Yamauchi, K., Murakami, T., Murakami, H., Ikeda, Y., Yokota, T., Shibata, N., Ninomiya, T., Abe, M., Hiasa, Y., Matsuura, B., Onji, M., Umeda, M. & Horiike, N. (2011) Characteristics of small bowel tumors detected by double balloon endoscopy. *Digestive Diseases & Sciences*, 56: 2366-2371.
Not in PICO

- Jain, P., Shah, P. & Bhansali, M. (2010) Unusual presentation of an uncommon abdominal pathology. *Annals of the Royal College of Surgeons of England*, 92: W19-W21.
Not in PICO
- Janicke, D. M. & Pundt, M. R. (1996) Anorectal disorders. [Review] [83 refs]. *Emergency Medicine Clinics of North America*, 14: 757-788.
Narrative review
- Jellema, P., van der Windt, D. A., Bruinvels, D. J., Mallen, C. D., van Weyenberg, S. J., Mulder, C. J. & de Vet, H. C. (2010) Value of symptoms and additional diagnostic tests for colorectal cancer in primary care: systematic review and meta-analysis. [Review] [79 refs]. *BMJ*, 340: c1269.
SR, all PC studies included apart from one on haemoccult testing
- Jerkic, S., Rosewich, H., Scharf, J. G., Perske, C., Fuzesi, L., Wilichowski, E. & Gartner, J. (2005) Colorectal cancer in two pre-teenage siblings with familial adenomatous polyposis. *European Journal of Pediatrics*, 164: 306-310.
Not in PICO
- Jiang, L. X., Xu, J., Wang, X. W., Zhou, F. R., Gao, W., Yu, G. H., Lv, Z. C. & Zheng, H. T. (2008) Gastric outlet obstruction caused by heterotopic pancreas: A case report and a quick review. [Review] [21 refs]. *World Journal of Gastroenterology*, 14: 6757-6759.
Not in PICO
- Jiwa, M., Gordon, M., Arnet, H., Ee, H., Bulsara, M. & Colwell, B. (2008) Referring patients to specialists: A structured vignette survey of Australian and British GPs. *Bmc Family Practice*, 9.
Not in PICO
- Jiwa, M., Halkett, G., Arnet, H., Smith, M., McConigley, R., Lim, D., Bulsara, M. & Islam, A. (2009) Advice to consult a general medical practitioner in Western Australia: could it be cancer? *Quality in Primary Care*, 17: 23-29.
Not in PICO
- Jiwa, M., Spilsbury, K. & Duke, J. (2010) Do pharmacists know which patients with bowel symptoms should seek further medical advice? A survey of pharmacists practicing in community pharmacy in Western Australia. *Annals of Pharmacotherapy*, 44: 910-917.
Not in PICO
- Jiwa, M., Sriram, D., Khadaroo, Z. & Ping-Delfos, W. C. (2011) Could community pharmacies offer an opportunity to improve outcomes for patients with bowel cancer? *Quality in Primary Care*, 19: 105-108.
Not in PICO
- John, D. W. (2010) Anorectal pain, bleeding and lumps. *Australian Family Physician*, 39: 376-381.
Narrative review
- John, S. K. P., George, S., Primrose, J. N. & Fozard, J. B. J. (2011) Symptoms and signs in patients with colorectal cancer. *Colorectal Disease*, 13: 17-25.
Narrative review
- Jones, L. S., Nicholson, R. W. & Evans, D. A. (2001) Experience with a one-stop colorectal clinic. *Journal of the Royal College of Surgeons of Edinburgh*, 46: 96-97.
Not in PICO
- Jones, R. (2008) Primary care research and clinical practice: gastroenterology. *Postgraduate Medical Journal*, 84: 454-458.
Narrative review
- Jones, R., Charlton, J., Latinovic, R. & Gulliford, M. C. (2009) Alarm symptoms and identification of non-cancer diagnoses in primary care: cohort study. *British Medical Journal*, 339.
Not in PICO
- Jones, R. H. (1996) Clinical economics review: gastrointestinal disease in primary care. [Review] [38 refs]. *Alimentary Pharmacology & Therapeutics*, 10: 233-239.
Narrative review

- Joosten, E., Meeuwissen, J., Vandewinckele, H. & Hiele, M. (2008) Iron status and colorectal cancer in symptomatic elderly patients. *American Journal of Medicine*, 121: 1072-1077.
Not in PICO
- Jordan, K. P., Hayward, R. A., Blagojevic-Bucknall, M. & Croft, P. (2013) Incidence of prostate, breast, lung and colorectal cancer following new consultation for musculoskeletal pain: a cohort study among UK primary care patients. *International Journal of Cancer*, 133: 713-720.
Cannot extract outcome in PICO (PPVs) as cancer data only reported in total for 10-year follow up
- Joss, R., Nothiger, F., Greiner, R., Goldhirsch, A. & Brunner, K. W. (1981) [Colorectal cancer. Progress and unsolved problems]. [German]. *Schweizerische Medizinische Wochenschrift. Journal Suisse de Medecine*, 111: 697-705.
Narrative review
- Juniku-Shkololli, A. & Haziri, A. (2009) Small-bowel carcinoid with no liver metastases. *Medicinski Arhiv*, 63: 53-54.
Not in PICO
- Kalra, L., Price, W. R., Jones, B. J. & Hamlyn, A. N. (1988) Open access fibresigmoidoscopy: a comparative audit of efficacy. *British Medical Journal Clinical Research Ed.*, 296: 1095-1096.
Not in PICO
- Kam, M. H., Eu, K. W., Barben, C. P. & Seow-Choen, F. (2004) Colorectal cancer in the young: a 12-year review of patients 30 years or less. *Colorectal Disease*, 6: 191-194.
Not in PICO
- Kam, M. H., Barben, C. P., Eu, K. W. & Seow-Choen, F. (2004) Small bowel malignancies: A review of 29 patients at a single centre. *Colorectal Disease*, 6: 195-197.
Not in PICO
- Kang, J.-Y., Rink, E., Sundaram, K. K. & Hartley, I. (2003) Factors associated with the frequency of stool examination: Effect on incidence of reported rectal bleeding. *European Journal of Gastroenterology and Hepatology*, 15: 531-533.
Not in PICO
- Kardaszewicz, S., Rusinowska, Z., Harbut-Grylka, H., Grzesiak, A., Rozek-Lesiak, K., Scieszkowa, M. & Kochanski, L. (1982) [Thrombophlebitis as one of the early signs of neoplastic processes]. [Polish]. *Polski Tygodnik Lekarski*, 37: 493-496.
Not in PICO
- Karnak, I., Ciftci, A. O., Senocak, M. E. & Buyukpamukcu, N. (1999) Colorectal carcinoma in children. *Journal of Pediatric Surgery*, 34: 1499-1504.
Not in PICO
- Kaul, A., Shah, A., Magill, F. H., Hawkins, S. A. & Skaife, P. (2013) Immunological faecal occult blood testing: a discriminatory test to identify colorectal cancer in symptomatic patients. *International Journal Of Surgery*, 11: 329-331.
Not in PICO
- Keane, M. G. & Johnson, G. J. (2002) Early diagnosis improves survival in colorectal cancer. *Practitioner*, 256: 15-18.
Not in PICO
- Keddie, N. (1968) SYMPTOMS OF CARCINOMA OF THE COLON AND RECTUM. *Lancet*, 292: 741-784 .
Pre-1980
- Kemppainen, M., Raiha, I., Rajala, T. & Sourander, L. (1993) Delay in diagnosis of colorectal cancer in elderly patients. *Age & Ageing*, 22: 260-264.
Not in PICO
- Kennington, E., Carter, S., Dear, M., Allen, B. & Patel, N. (2012) Bowel cancer symptom presentation in community pharmacy-an opportunity for early detection? *International Journal of Pharmacy Practice*, 20: 19-20.
Not in PICO

- Kennington, E. (2012) How community pharmacists can help in the early detection of bowel cancer. *Pharmaceutical Journal*, 288: 497.
Not in PICO
- Khan, R., Davis, T., Wilson, L., Daci, K., Gould, M., El-Serag, H. & Singh, H. (2010) Measuring and improving the timeliness of colorectal cancer diagnosis: A mixed-methods approach. *Gastroenterology*, 138: S326.
Not in PICO
- Kibria, R., Khalil, Q., Siraj, U., Ali, S. A. & Akram, S. (2009) Giant ulcerated lipoma of the colon causing iron deficiency anemia successfully treated with endoscopic ultrasound-assisted resection. *Southern Medical Journal*, 102: 1058-1060.
Not in PICO
- Kim, T., Chae, G., Chung, S. S., Sands, D. R., Speranza, J. R., Weiss, E. G., Noguerras, J. J. & Wexner, S. D. (2008) Faecal incontinence in male patients. *Colorectal Disease*, 10: 124-130.
Not in PICO
- Kirchhoff, G. M., Buhmann, S., Kirchhoff, C., Mussack, T., Ladurner, R., Kamal, A. A. M. & Kirchhoff, R. M. (2006) Early diagnosis of colorectal cancer: A preventive task in occupational health. *European Journal of Medical Research*, 11: 279-284.
Narrative review
- Klabunde, C. N., Ambs, A., Keating, N. L., He, Y., Doucette, W. R., Tisnado, D., Clauser, S. & Kahn, K. L. (2009) The Role of Primary Care Physicians in Cancer Care. *Journal of General Internal Medicine*, 24: 1029-1036.
Not in PICO
- Knight, K., Wade, S. & Balducci, L. (2004) Prevalence and outcomes of anemia in cancer: a systematic review of the literature. [Review] [74 refs]. *American Journal of Medicine*, 116: Suppl-26S.
Not in PICO
- Kolb, G. F. (2006) Cancer screening in the elderly: Breast and prostate cancer and colorectal carcinoma. [Spanish]. *Revista Espanola de Geriatria y Gerontologia*, 41: 128-133.
Narrative review
- Koo, J. H., You, M. Y., Liu, K., Athureliya, M. D., Tang, C. W., Redmond, D. M., Connor, S. J. & Leong, R. W. (2012) Colorectal cancer screening practise is influenced by ethnicity of medical practitioner and patient. *Journal of Gastroenterology & Hepatology*, 27: 390-396.
Not in PICO
- Korde, L. A. & Gadalla, S. M. (2009) Cancer Risk Assessment for the Primary Care Physician. *Primary Care - Clinics in Office Practice*, 36: 471-488.
Narrative review
- Kothari, S., Prabhakar, G. & Kalra, V. B. (1998) Colorectal carcinoma. *Indian Journal of Pediatrics*, 65: 913-916.
Not in PICO
- Kozłowska, E., Szewczyk, M. T., Banaszkiwicz, Z., Jawien, A., Cierzniaowska, K. & Jarmocik, P. (2011) Knowledge of symptoms and diagnostic possibilities of cancer diseases. *Archives of Medical Science*, 7: 304-309.
Not in PICO
- Krajcar, N., Mascitti, A. & Simons, K. (2011) Improving primary to acute referrals: the role of the cancer clinical network in developing consistent information for general practitioners. *Asia-Pacific Journal of Clinical Oncology*, 7: 185.
Not in PICO
- Kravarusic, D., Feigin, E., Dlugy, E., Steinberg, R., Baazov, A., Erez, I., Lazar, L., Kapuller, V., Grunspan, M., Ash, S. & Freud, E. (2007) Colorectal carcinoma in childhood: a retrospective multicenter study. *Journal of Pediatric Gastroenterology & Nutrition*, 44: 209-211.
Not in PICO

- Kuester, D., Dalicho, S., Monkemuller, K., Benedix, F., Lippert, H., Guenther, T., Roessner, A. & Meyer, F. (2008) Synchronous multifocal colorectal carcinoma in a patient with delayed diagnosis of ulcerative pancolitis. *Pathology, Research & Practice*, 204: 905-910.
Not in PICO
- Kyle, S. M., Isbister, W. H. & Yeong, M. L. (1991) Presentation, duration of symptoms and staging of colorectal carcinoma. *Australian & New Zealand Journal of Surgery*, 61: 137-140.
Not in PICO
- Ladabaum, U., Fioritto, A., Mitani, A., Desai, M., Kim, J. P., Rex, D. K., Imperiale, T. & Gunaratnam, N. (2013) Real-time optical biopsy of colon polyps with narrow band imaging in community practice does not yet meet key thresholds for clinical decisions. *Gastroenterology*, 144: 81-91.
Not in PICO
- Lahr, C. J., Griffith, J., Subramony, C., Halley, L., Adams, K., Paine, E. R., Schmieg, R., Islam, S., Salameh, J., Spree, D., Kothari, T., Kedar, A., Nikitina, Y. & Abell, T. (2013) Gastric electrical stimulation for abdominal pain in patients with symptoms of gastroparesis. *American Surgeon*, 79: 457-464.
Not in PICO
- Lao, I. H., Chao, H., Wang, Y. J., Mak, C. W., Tzeng, W. S., Wu, R. H., Chang, S. T. & Fang, J. L. (2013) Computed tomography has low sensitivity for the diagnosis of early colon cancer. *Colorectal Disease*, 15: 807-811.
Not in PICO
- LaPorte, D., Farber, S., Sorin, S., Wabba, S., Daneels, E., Korzenko, A. & Kopes-Kerr, C. P. (2003) When deep venous thrombosis fails to respond to therapy. *Journal of the American Board of Family Practice*, 16: 246-250.
Not in PICO
- Larghero, G. C., Scarpettini, S., Pavero, R., Costanzo, A., Cariati, A., Berti, S., Maritato, F. & Zoli, S. (1996) [Adenocarcinoma of the anal glands. Description of a clinical case and review of the literature]. [Italian]. *Minerva Chirurgica*, 51: 573-576.
Not in PICO
- Lawicki, S., Mroczko, B. & Szmikowski, M. (2002) [Neoplasm markers useful for diagnosis and monitoring of colonic neoplasms]. [Review] [87 refs] [Polish]. *Postepy Higieny i Medycyny Doswiadczalnej*, 56: 617-634.
Not in PICO
- Lazarovici, C., Khodabakhshi, R., Leignel, D., Fabre-Guillevin, E., Minard, A. & Gisselbrecht, M. (2011) Factors leading oncologists to refer elderly cancer patients for geriatric assessment. *Journal of Geriatric Oncology*, 2: 194-199.
Not in PICO
- Lazzareschi, I., Barone, G., Mastrangelo, S., Furfaro, I. F., Rando, G. & Riccardi, R. (2009) Could APC gene screening be useful in children with hepatoblastoma? Early onset of adenocarcinoma in a child with familial adenomatous polyposis and hepatoblastoma. *Tumori*, 95: 819-822.
Not in PICO
- Lecoules, S., Carmoi, T., Klotz, C., Rapp, C., Perrot, G., Galeano, C. & Algayres, J. P. (2013) [Fever as the presenting manifestation of colon cancer: a case series of 11 patients]. [French]. *Revue de Medecine Interne*, 34: 136-140.
Not in PICO
- Lee, H. J., Song, I. C., Yun, G. W., Yun, H. J., Kim, S. & Jo, D. Y. (2010) A prospective evaluation of adult men with iron deficiency anemia. *Blood*, 116.
Published as abstract only, not enough information can be extracted to ascertain clinical setting
- Lee, J. S., Rieger, N. A., Stephens, J. H., Hewett, P. J., Rodda, D. J. & Lawrence, M. J. (2007) Six-year prospective analysis of the rectal bleeding clinic at the Queen Elizabeth Hospital, Adelaide, South Australia. *ANZ Journal of Surgery*, 77: 553-556.
Not in PICO (secondary care setting)

- Lee, J. S., Cho, J. H., Kim, K. O., Lee, S. H. & Jang, B. I. (2012) [Clinical significance of the large intestinal wall thickening detected by abdominal computed tomography]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 60: 300-305.
Not in PICO
- Lee, M. G., McFarlane, M., Branday, J. M. & Williams, N. (1988) Primary tumours of the small intestine in Jamaica. *Journal of Tropical Medicine & Hygiene*, 91: 319-322.
Not in PICO
- Lees, A. N. & Reid, D. W. (2008) Management dilemma; a woman with cystic fibrosis and severe lung disease presenting with colonic carcinoma: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 2: 384.
Not in PICO
- Leung, E., Grainger, J., Bandla, N. & Wong, L. (2010) The effectiveness of the '2-week wait' referral service for colorectal cancer. *International Journal of Clinical Practice*, 64: 1671-1674.
Not in PICO
- Levitt, C. A. & Lupea, D. (2009) Provincial primary care and cancer engagement strategy. *Canadian Family Physician*, 55: E55-E59.
Not in PICO
- Lewis, R. (1976) Anemia--a common but never a normal concomitant of aging. *Geriatrics*, 31: 53-60.
Pre-1980
- Li, C.-H., Bair, M.-J., Chang, W.-H., Lin, S.-C., Chen, C.-J. & Liao, W.-S. (2007) Primary malignant tumors of the small intestine: 11-year experience in a regional hospital in Taitung. [Chinese]. *Journal of Internal Medicine of Taiwan*, 18: 29-34.
Not in PICO
- Li, J. N., Zhao, L., Zheng, W. Y., Miao, Z., Tang, X. Y. & Qian, J. M. (2010) [The trends in clinical characteristics of colon cancer in last two decades]. [Chinese]. *Chung-Hua Nei Ke Tsa Chih Chinese Journal of Internal Medicine*, 49: 226-229.
Not in PICO
- Li, Z., Sun, Z., Wang, Z. N., Miao, Z. F., Lv, Z. D., Li, X. X., Yang, J. G. & Xu, H. M. (2012) Iron-deficiency anemia: A predictor of diminished disease-free survival of T3N0M0 stage colon cancer. *Journal of Surgical Oncology*, 105: 371-375.
Not in PICO
- Lieberman, D. A. Screening for colorectal cancer. [References]. *The New England Journal of Medicine* 361[12], 1179-1187. 2009.
Not in PICO
- Lim, C. S., McGeever, L., Grey, J. H., Krishna, A., Jabbar, A. A. & Hendry, W. S. (2009) How important is it to investigate the whole of the colon after initial assessment at a rapid access colorectal clinic? *International Journal of Colorectal Disease*, 24: 1341-1345.
Not in PICO
- Lin, G. A., Halley, M., Rendle, K. A., Tietbohl, C., May, S. G., Trujillo, L. & Frosch, D. L. (2013) An effort to spread decision aids in five California primary care practices yielded low distribution, highlighting hurdles. *Health Affairs*, 32: 311-320.
Not in PICO
- Lizarzabal de, B. M. & Sociedad Venezolana, d. G. (2007) [Gastroenterology in the new century in Venezuela. A first five years situational diagnosis]. [Spanish]. *Investigacion Clinica*, 48: Suppl-127.
Not in PICO
- Llor, X. (2012) When Should We Suspect Hereditary Colorectal Cancer Syndrome? *Clinical Gastroenterology and Hepatology*, 10: 363-367.
Narrative review
- Lloyd, M. (1992) Early diagnosis of gastrointestinal cancer. *Practitioner*, 236: 980-983.
Narrative review

- Logan, E. C., Yates, J. M., Stewart, R. M., Fielding, K. & Kendrick, D. (2002) Investigation and management of iron deficiency anaemia in general practice: a cluster randomised controlled trial of a simple management prompt. *Postgraduate Medical Journal*, 78: 533-537.
Same as Yates (2004)
- Longstreth, G. F. (1998) Sorting out the causes of acute lower GI hemorrhage: When direct evidence is lacking, diagnosis is often presumptive. *Journal of Critical Illness*, 13: 177-185.
Narrative review
- Lorinczi, K., Denheyer, V., Pickard, A., Lee, A. & Mager, D. R. (2012) Referral criteria for assessment and treatment in an ambulatory dysphagia clinic. *Canadian Journal of Dietetic Practice & Research*, 73: 189-194.
Not in PICO
- Loyd, R. A. & McClellan, D. A. (2011) Update on the evaluation and management of functional dyspepsia. *American Family Physician*, 83: 546-552.
Narrative review
- Lu, Y.-Y., Chen, J.-H., Chien, C.-R., Chen, W. T. L., Tsai, S.-C., Lin, W.-Y. & Kao, C.-H. (2013) Use of FDG-PET or PET/CT to detect recurrent colorectal cancer in patients with elevated CEA: A systematic review and meta-analysis. *International Journal of Colorectal Disease*, 28: 1039-1047.
Not in PICO
- Luman, W. & Ng, K. L. (2003) Audit of Investigations in Patients with Iron Deficiency Anaemia. *Singapore Medical Journal*, 44: 504-510.
Not in PICO
- Lupaltsov, V. & Shalkov, Y. (2013) Colorectal cancer: Factors of the early recognition. *Colorectal Disease*, 15: 111.
Abstract only, not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Lynch, B. M., Youlden, D., Fritschi, L., Newman, B., Pakenham, K. I., Leggett, B., Owen, N. & Aitken, J. F. (2008) Self-reported information on the diagnosis of colorectal cancer was reliable but not necessarily valid. *Journal of Clinical Epidemiology*, 61: 498-504.
Not in PICO
- Lyratzopoulos, G., Neal, R. D., Barbiere, J. M., Rubin, G. P. & Abel, G. A. (2012) Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. *Lancet Oncology*, 13: 353-365.
Not in PICO
- MacArthur, C. & Smith, A. (1984) Factors associated with speed of diagnosis, referral, and treatment in colorectal cancer. *Journal of Epidemiology & Community Health*, 38: 122-126.
Narrative review
- MacDonald, L. & Freeling, P. (1986) Bowels: beliefs and behaviour. *Family Practice*, 3: 80-84.
Not in PICO
- MacKenzie, S., Norrie, J., Vella, M., Drummond, I., Walker, A., Molloy, R., Galloway, D. J. & O'Dwyer, P. J. (2003) Randomized clinical trial comparing consultant-led or open access investigation for large bowel symptoms. *British Journal of Surgery*, 90: 941-947.
Not in PICO (secondary care)
- Maggs, J. R., Browning, L. C., Warren, B. F. & Travis, S. P. (2008) Obstructing giant post-inflammatory polyposis in ulcerative colitis: Case report and review of the literature. *Journal of Crohn's & Colitis*, 2: 170-180.
Not in PICO
- Mahadavan, L., Loktionov, A., Daniels, I. R., Shore, A., Cotter, D., Llewelyn, A. H. & Hamilton, W. (2012) Exfoliated colonocyte DNA levels and clinical features in the diagnosis of colorectal cancer: a cohort study in patients referred for investigation. *Colorectal Disease*, 14: 306-313.
Not in PICO

- Majumdar, S. R., Fletcher, R. H. & Evans, A. T. (1999) How does colorectal cancer present? Symptoms, duration, and clues to location. *American Journal of Gastroenterology*, 94: 3039-3045.
Not in PICO
- Mak, T., Iqbal, T., Wilson, S., Holder, R., Lawrence, G., Ryan, R., McManus, R., Hobbs, R., Hamilton, W., Rubin, R., Weller, D. & Ismail, T. (2010) The impact of NICE guidelines on the diagnosis of colorectal cancer from patients with iron deficiency anaemia. *Colorectal Disease*, 12: 17.
Not in PICO (same as other 2 Mak 2010s)
- Mak, T., Wilson, S., Damery, S., Ryan, R., McManus, R., Murray, J., Hamilton, W., Warmington, S., Rubin, G., Hobbs, R. & Ismail, T. (2010) Iron deficiency anaemia and delayed diagnosis of colorectal cancer: A retrospective cohort study. *Colorectal Disease*, 12: 43.
Not in PICO (same as other 2 Mak 2010s)
- Mak, T., Wilson, S., Iqbal, T., Ryan, R., McManus, R., Lawrence, G., Hobbs, R., Rubin, R., Hamilton, W., Weller, D., Holder, R. & Ismail, T. (2010) The impact of referral pattern on the length of diagnosis in colorectal cancer patients with iron deficiency anaemia. *Colorectal Disease*, 12: 17.
Not in PICO (same as other 2 Mak 2010s)
- Makino, S., Okada, K., Wada, Y., Kato, R., Takeoka, T., Yanagisawa, T., Okamura, S., Fukuchi, N., Ebisui, C., Murata, K., Yokouchi, H., Kinuta, M., Nakagomi, N. & Tamai, M. (2013) [A case of jejunum cancer diagnosed by anemia]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 40: 1720-1722.
Not in PICO
- Malfertheiner, P. (1999) The Maastricht recommendations and their impact on general practice. *European Journal of Gastroenterology & Hepatology*, 11: Suppl-7.
Guideline/narrative review
- Manerowski, M., Budzynski, J. & Swiatkowski, M. (2007) Alarm symptoms in patients with colorectal cancer referred by family doctors to the chair of gastroenterology in 2006. [Polish]. *Family Medicine and Primary Care Review*, 9: 516-518.
Not in PICO
- Mankodi, S., Hayee, B. H., O'Donohue, J. & Reffitt, D. (2010) Anaemia investigation in practice: inappropriate, cost inefficient with a risk of missing gastrointestinal cancer. Can we improve? *Clinical Medicine*, 10: 115-118.
Not in PICO
- Manning-Dimmitt, L. L., Dimmitt, S. G. & Wilson, G. R. (2005) Diagnosis of gastrointestinal bleeding in adults. *American Family Physician*, 71: 1339-1346.
Not in PICO
- Mansell, G., Shapley, M., Van Der Windt, D., Sanders, T. & Little, P. (2014) Critical items for assessing risk of lung and colorectal cancer in primary care: A Delphi study. *British Journal of General Practice*, 64: e509-e515.
Not in PICO
- Mansell, G., Shapley, M., Van Der Windt, D., Sanders, T. & Little, P. (2014) - Critical items for assessing risk of lung and colorectal cancer in primary care: a Delphi study. - *British Journal of General Practice*, 64: e509-e515.
Duplicate
- Mansson, J. (1990) The diagnosis of colorectal cancer--experiences from the community of Kungsbacka, Sweden. *Scandinavian Journal of Primary Health Care*, 8: 31-35.
Not in PICO
- Mansson, J., Bjorkelund, C. & Hultborn, R. (1999) Symptom pattern and diagnostic work-up of malignancy at first symptom presentation as related to level of care a retrospective study from the primary health care centre area of Kungsbacka, Sweden. *Neoplasma*, 46: 93-99.
Not in PICO
- Mansson, J., Marklund, B. & Hultborn, R. (2001) The diagnosis of cancer in the "roar" of potential cancer symptoms of patients in primary health care - Research by means of the computerised

- journal. *Scandinavian Journal of Primary Health Care*, 19: 83-89.
Symptoms not linked with cancers; analysis based on number of codes, not patients.
- Mansson, J., Marklund, B. & Carlsson, P. (2006) Costs in primary care of investigating symptoms suspicious of cancer in a defined population. *Scandinavian Journal of Primary Health Care*, 24: 243-250.
Symptoms not linked with cancers; analysis based on number of codes, not patients
- Manzotti, L. N., Bolino, M. C., Braner, M., Cerisoli, C. & Caro, L. E. (2013) Prevalence of rectosigmoid adenomas and adenocarcinomas in patients younger than 50 years old referred for proctorrhagia. *Acta Gastroenterologica Latinoamericana*, 43: 279-283.
Not in PICO
- Mariani, L., Lo Vullo, S. & Bozzetti, F. (2012) Weight loss in cancer patients: a plea for a better awareness of the issue. *Supportive Care in Cancer*, 20: 301-309.
Not in PICO
- Marinis, A., Yiallourou, A., Samanides, L., Dafnios, N., Anastasopoulos, G., Vassiliou, I. & Theodosopoulos, T. (2009) Intussusception of the bowel in adults: a review. [Review] [53 refs]. *World Journal of Gastroenterology*, 15: 407-411.
Not in PICO
- Masson, S., Chinn, D. J., Tabaqchali, M. A., Waddup, G. & Dwarakanath, A. D. (2007) Is anaemia relevant in the referral and diagnosis of colorectal cancer? *Colorectal Disease*, 9: 736-739.
Not in PICO
- Matsui, S., Kibi, M., Anami, E., Anami, T., Inagaki, Y., Kanouda, A., Yoshinaga, H., Watanabe, A., Sugahara, A., Mukai, H., Toyokawa, A., Iwasaki, T., Tachibana, M. & Teramura, K. (2011) A case of Cronkhite-Canada syndrome with multiple colon adenomas and early colon cancers. *Nippon Shokakibyō Gakkai Zasshi - Japanese Journal of Gastroenterology*, 108: 778-786.
Not in PICO
- Mcavoy, B. R. (2007) General practitioners and cancer control. *Medical Journal of Australia*, 187: 115-117.
Narrative review
- McFarlane, M. E., Rhoden, A., Fletcher, P. R. & Carpenter, R. (2004) Cancer of the colon and rectum in a Jamaican population: diagnostic implications of the changing frequency and subsite distribution. *West Indian Medical Journal*, 53: 170-173.
Not in PICO
- McIntyre, A. S. & Long, R. G. (1993) Prospective survey of investigations in outpatients referred with iron deficiency anaemia. *Gut*, 34: 1102-1107.
Not in PICO
- McLaren, G. D., Kolodney, J. A., Doki, N., Chen, W.-P., Khalaghizadeh, S., Novin, M., Cook, J. D., Jamal, M. & McLaren, C. E. (2009) Iron deficiency detected by estimation of body iron in a primary care population: Prevalence and etiology. *American Journal of Hematology*, 84: E357.
Not in PICO
- McMurrick, P., Dorien, S. & Shapiro, J. (2006) Bowel cancer - guide for the GP. [Review] [7 refs]. *Australian Family Physician*, 35: 192-197.
Narrative review
- Mehta, R. S., Ennis, P. & Whitten, J. (2012) Ureterosigmoidostomy associated signet ring colon cancer presenting as hip pain. *Journal of Gastrointestinal Cancer*, 43: 122-127.
Not in PICO
- Miabi, Z. (2011) Metastatic brain tumors: A retrospective review in east azarbyjan (Tabriz). *Acta Medica Iranica*, 49: 115-117.
Not in PICO
- Mijinyawa, M. S., Sani, M. U., Yusuf, S. M., Mohammed, A. Z. & Alhassan, S. U. (2009) Krukenberg's tumour. *Nigerian Journal of Medicine: Journal of the National Association of Resident Doctors of*

Nigeria, 18: 416-419.
Not in PICO

Mila, R., Grille, S., Laurini, M., Lapiedra, D. & Bagattini, J. C. (2008) [McKittrick- Wheelock syndrome: report of one case]. [Spanish]. *Revista Medica de Chile*, 136: 900-904.
Not in PICO

Miles, R. M., Crawford, D. & Duras, S. (1979) The small bowel tumor problem: an assessment based on a 20 year experience with 116 cases. *Annals of Surgery*, 189: 732-740.
Pre-1980

Miner, T. J., Jaques, D. P., Paty, P. B., Guillem, J. G. & Wong, W. D. (2003) Symptom control in patients with locally recurrent rectal cancer. *Annals of Surgical Oncology*, 10: 72-79.
Not in PICO

Mirensky, T. L., Schuster, K. M., Ali, U. A., Reddy, V., Schwartz, P. E. & Longo, W. E. (2012) Outcomes of small bowel obstruction in patients with previous gynecologic malignancies. *American Journal of Surgery*, 203: 472-479.
Not in PICO

Mitchell, E., Macdonald, S., Campbell, N. C., Weller, D. & Macleod, U. (2008) Influences on pre-hospital delay in the diagnosis of colorectal cancer: A systematic review. *British Journal of Cancer*, 98: 60-70.
Not in PICO

Mnif, L., Amouri, A., Masmoudi, M. A., Mezghanni, A., Gouiaa, N., Boudawara, T. & Tahri, N. (2009) Giant lipoma of the transverse colon: a case report and review of the literature. [Review] [26 refs]. *Tunisie Medicale*, 87: 398-402.
Not in PICO

Modiri, A., Makipour, K., Gomez, J. & Friedenberg, F. (2013) Predictors of colorectal cancer testing using the California Health Inventory Survey. *World Journal of Gastroenterology*, 19: 1247-1255.
Not in PICO

Mohamadnejad, M., Al-Haddad, M. A., Sherman, S., McHenry, L., Leblanc, J. K. & DeWitt, J. (2012) Utility of EUS-guided biopsy of extramural pelvic masses. *Gastrointestinal Endoscopy*, 75: 146-151.
Not in PICO

Molina, R. (2011) Tumor markers in personalized medicine. *Tumor Biology*, 32: S49.
Not in PICO

Mongan, J. P., Fadul, C. E., Cole, B. F., Zaki, B. I., Suriawinata, A. A., Ripple, G. H., Tosteson, T. D. & Pipas, J. M. (2009) Brain metastases from colorectal cancer: risk factors, incidence, and the possible role of chemokines. *Clinical Colorectal Cancer*, 8: 100-105.
Not in PICO

Monreal, M., Lafoz, E., Casals, A., Inaraja, L., Montserrat, E., Callejas, J. M. & Martorell, A. (1991) Occult cancer in patients with deep venous thrombosis. A systematic approach. *Cancer*, 67: 541-545.
Not in PICO

Moore, H. & Dodd, N. (2013) Computed tomographic colonography (CTC); Colorectal cancer diagnosis with CTC in an Auckland population. *Journal of Medical Imaging and Radiation Oncology*, 57: 572-575.
Not in PICO

Moran, E. M., Burras, R. W., DaCosta-Iyer, M., Deng, X., Jadus, M., Phan, R. T., Ouyang, Y. & Szabo, S. (2010) Colon cancer: Clinical, biochemical, and pathological, differences between the right (proximal) side and the left (distal) side of involvement. *Annals of Oncology*, 21: vi74.
Not in PICO

Mouton, W., Kienle, Y., Muggli, B., Naef, M. & Wagner, H. (2010) Tumors associated with superficial thrombophlebitis. *Vasa - Journal of Vascular Diseases*, 39: 127.
Published as abstract only, not enough information can be extracted to ascertain setting

- Mulcahy, H. E. & O'Donoghue, D. P. (1997) Duration of colorectal cancer symptoms and survival: the effect of confounding clinical and pathological variables. *European Journal of Cancer*, 33: 1461-1467.
Not in PICO
- Muley, P., Mhapsekar, R. V. & Kumar, R. M. (2012) Constipation in children - is it always benign? *Colorectal Disease*, 14: e272-e273.
Not in PICO
- Munk, E. M., Drewes, A. M., Gorst-Rasmussen, A., Funch-Jensen, P., Gregersen, H. & Norgard, B. (2007) Risk of gastrointestinal cancer in patients with unexplained chest/epigastric pain and normal upper endoscopy: a Danish 10-year follow-up study. *Digestive Diseases & Sciences*, 52: 1730-1737.
Not in PICO (referred v asymptomatic population controls)
- Murchie, P., Campbell, N. C., Delaney, E. K., Dinant, G. J., Hannaford, P. C., Johansson, L., Lee, A. J., Rollano, P. & Spigt, M. (2012) Comparing diagnostic delay in cancer: a cross-sectional study in three European countries with primary care-led health care systems. *Family Practice*, 29: 69-78.
Not in PICO
- Murphy, J., Rangrez, S., Haste, F. & Machesney, M. (2011) UK National Bowel Cancer Screening Programme: Asymptomatic screening or 'straight to test' for symptomatic patients? *Colorectal Disease*, 13: 8.
Not in PICO
- Nacchiero, M., Marzaioli, R., Campanile, L., Incantalupo, F., Loverre, G. & Bonomo, G. M. (2002) [Right abdominal colonic masses. Recent diagnostic and therapeutic advances: personal experience]. [Review] [56 refs] [Italian]. *Annali Italiani di Chirurgia*, 73: 47-57.
Not in PICO
- Nadel, M. R., Berkowitz, Z., Klabunde, C. N., Smith, R. A., Coughlin, S. S. & White, M. C. (2010) Fecal Occult Blood Testing Beliefs and Practices of US Primary Care Physicians: Serious Deviations from Evidence-Based Recommendations. *Journal of General Internal Medicine*, 25: 833-839.
Not in PICO
- Naef, M., Buhlmann, M. & Baer, H. U. (1999) Small bowel tumors: diagnosis, therapy and prognostic factors. *Langenbecks Archives of Surgery*, 384: 176-180.
Not in PICO
- Nagorni, A., Bjelakovic, G. & Petrovic, B. (2012) Narrow band imaging versus conventional white light colonoscopy for the detection of colorectal polyps. *Cochrane.Database.of.Systematic.Reviews.* (Outcomes) not in PICO
- Namkung, J., Kim, S. J., Kim, J. H., Kim, J. & Hur, S. Y. (2011) Rectal endometriosis with invasion into lymph nodes. *Journal of Obstetrics & Gynaecology Research*, 37: 1117-1121.
Not in PICO
- Napolitano, L., de, N. P., Di, B. N., Aceto, L., Liddo, G., Angelucci, D. & Innocenti, P. (2005) [A case of perforated small bowel adenocarcinoma as first symptom of Crohn's disease]. [Italian]. *Giornale di Chirurgia*, 26: 212-214.
Not in PICO
- Ndukwe, N., Jenkins, K., Branagan, G. & King, L. (2010) The experiences of patients referred for colorectal symptoms on a rapid referral 'two week rule' - An examination of quantitative and qualitative data from two hospitals. *Psycho-Oncology*, 19: S171-S172.
Not in PICO
- Nelson, R. L., Persky, V. & Turyk, M. (1999) Determination of factors responsible for the declining incidence of colorectal cancer. *Diseases of the Colon & Rectum*, 42: 741-752.
Not in PICO
- Newman, C. M., Nash, G. F., Armstrong, T. & Darcy, K. (2006) Colorectal cancer and rectal bleeding in primary care: rectal bleeding needs attention in primary care. *BMJ*, 333: 201.
Comment

- Niederle, M. B. & Niederle, B. (2011) Diagnosis and treatment of gastroenteropancreatic neuroendocrine tumors: current data on a prospectively collected, retrospectively analyzed clinical multicenter investigation. *The Oncologist*, 16: 602-613.
Not in PICO
- Nielsen, T. N., Hansen, R. P. & Vedsted, P. (2010) [Symptom presentation in cancer patients in general practice]. [Danish]. *Ugeskrift for Laeger*, 172: 2827-2831.
Not in PICO
- Nilsson, E., Bolin, S. & Sjudahl, R. (1982) Carcinoma of the colon and rectum. Delay in diagnosis. *Acta Chirurgica Scandinavica*, 148: 617-622.
Not in PICO
- Nittka, S., Bohm, C., Zentgraf, H. & Neumaier, M. (2008) The CEACAM1-mediated apoptosis pathway is activated by CEA and triggers dual cleavage of CEACAM1. *Oncogene*, 27: 3721-3728.
Not in PICO
- Nomura, H., Wada, H., Mizuno, T., Yamashita, Y., Saito, K., Kitano, S., Katayama, N., Yamada, N., Sugiyama, T., Sudo, A., Usui, M., Isaji, S. & Nobori, T. (2010) Elevated fibrin-related markers in patients with malignant diseases suspected of having thrombotic disorders. *Clinical & Applied Thrombosis/Hemostasis*, 16: 266-272.
Not in PICO
- Nordkild, P. & Kjaergard, H. (1986) Primary tumours of the small intestine--the diagnostic problem. *Annales Chirurgiae et Gynaecologiae*, 75: 31-36.
Not in PICO
- Norrelund, N. & Norrelund, H. (1998) [Rectal hemorrhage. Colorectal cancer and polyps in patients aged 40 and over seeking consultation]. [Danish]. *Ugeskrift for Laeger*, 160: 434-436.
Danish publication of same data as Noerrelund & Noerrelund already included in Astin et al.
- Notman, F., Porteous, T., Bond, C. & Murchie, P. (2013) Understanding patients' selfmanagement of early cancer symptoms and exploring the potential role of community pharmacy in earlier diagnosis. *International Journal of Pharmacy Practice*, 21: 24.
Not in PICO
- NOWAK, J. (1953) [Symptomatic anemia in neoplasms of the colon]. [Undetermined]. *Revue Medicale de Liege*, 8: 98-100.
Pre-1980
- Nowak, W., Tobiasz-Adamczyk, B., Brzyski, P., Salowka, J., Kulis, D. & Richter, P. (2011) Adaptation of quality of life module EORTC QLQ-CR29 for Polish patients with rectal cancer: initial assessment of validity and reliability. *Polski Przegląd Chirurgiczny*, 83: 502-510.
Not in PICO
- Numans, M. E., van der Graaf, Y., de Wit, N. J. & de Melker, R. A. (2001) How useful is selection based on alarm symptoms in requesting gastroscopy? An evaluation of diagnostic determinants for gastro-oesophageal malignancy. *Scandinavian Journal of Gastroenterology*, 36: 437-443.
Not in PICO (referred population)
- Oberle, E., Brunner, K. & Rhyner, K. (1993) [Gastrointestinal hemorrhage: how much evaluation is necessary?]. [German]. *Schweizerische Rundschau fur Medizin Praxis*, 82: 1244-1252.
Not in PICO (secondary care setting)
- Olde, B. M., McCowan, C., Falk, G. A., Teljeur, C., Van de Laar, F. A. & Fahey, T. (2010) Diagnostic accuracy systematic review of rectal bleeding in combination with other symptoms, signs and tests in relation to colorectal cancer. [Review] [47 refs]. *British Journal of Cancer*, 102: 48-58.
Duplicate
- Olokoba, A. B., Obateru, O. A., Bojuwoye, M. O., Olatoke, S. A., Bolarinwa, O. A. & Olokoba, L. B. (2013) Indications and findings at colonoscopy in Ilorin, Nigeria. *Nigerian Medical Journal*, 54: 111-114.
Not in PICO

- Olsson, C. A., Deckers, P. J., Williams, L. & Mozden, P. J. (1976) New look at pelvic exenteration. *Urology*, 7: 355-361.
Pre-1980
- Olsson, H., Attner, B., Noreen, D. & Lithman, T. (2009) Comorbidity prior to diagnosis in patients with common cancer diagnoses. *Journal of Clinical Oncology*, 27: e22180.
Not in PICO
- Olynyk, J. K., Aquilia, S., Platell, C. F., Fletcher, D. R., Henderson, S. & Dickinson, J. A. (1998) Colorectal cancer screening by general practitioners: comparison with national guidelines. *Medical Journal of Australia*, 168: 331-334.
Not in PICO
- Orbell, J. & West, N. J. (2002) Improving detection of colorectal cancer. *The Practitioner*, 254: 17-213.
Narrative review
- Osoha, D., Hsu, M. A., Copley-Merriman, C., Coombs, J., Johnson, F. R., Hauber, B., Manjunath, R. & Pyles, A. (2006) Stated preferences of patients with cancer for health-related quality-of-life (HRQOL) domains during treatment. *Quality of Life Research*, 15: 273-283.
Not in PICO
- Ostergaard, I. (2002) Early diagnosis of cancer. [Danish]. *Ugeskrift for Laeger*, 164: 2897-2901.
Narrative review
- Otto, S., Czalbert, J. H., Papp, I. & Eckhardt, S. (1990) Early detection of colorectal cancer. Preliminary report on the prospective value of a combined screening method for occult rectal bleeding. *Oncology*, 47: 209-214.
Not in PICO
- Padwick, R. T., Bajwa, A. A., Shaw, A., Leung, E., Francombe, J. & Stellakis, M. L. (2013) The Two-Week Referral System for colorectal cancer - Not fit for purpose. *International Journal of Colorectal Disease*, 28: 1531-1534.
Not in PICO
- Panagiotopoulou, I. G., Fitzrol, D., Parker, R. A., Kuzhively, J., Luscombe, N., Wells, A. D., Menon, M., Bajwa, F. M. & Watson, M. A. (2014) - The yield of colorectal cancer among fast track patients with normocytic and microcytic anaemia. - *Annals of the Royal College of Surgeons of England*, 96: 289-293.
Not in PICO
- Paneesha, S., McManus, A., Arya, R., Scriven, N., Farren, T., Nokes, T., Bacon, S., Nieland, A., Cooper, D., Smith, H., O'Shaughnessy, D., Rose, P. & VERITY, I. (2010) Frequency, demographics and risk (according to tumour type or site) of cancer-associated thrombosis among patients seen at outpatient DVT clinics. *Thrombosis & Haemostasis*, 103: 338-343.
Not in PICO
- Panter, S. J., Bramble, M. G., O'Flanagan, H. & Hungin, A. P. (2004) Urgent cancer referral guidelines: a retrospective cohort study of referrals for upper gastrointestinal adenocarcinoma. *British Journal of General Practice*, 54: 611-613.
Not in PICO
- Park, J. S., Park, D. I., Park, S. K., Choi, J. S., Kim, Y. H., Chang, D. K., Son, H. J., Kim, J. E., Kim, J. O., Lee, S. H., Kim, H. S., Sin, J. E., Lee, S. G., Lee, S. Y., Park, S. J., Park, C. H., Baek, I. H., Jang, B. I., Jeon, Y. T. & Huh, K. C. (2009) Endoscopic evaluation of significant gastrointestinal lesions in patients with iron deficiency with and without anaemia: a Korean Association for the Study of Intestinal Disease study. *Internal Medicine Journal*, 39: 441-446.
Not in PICO
- Parramore, J. B., Wei, J. P. & Yeh, K. A. (567) Colorectal cancer in patients under forty: presentation and outcome. *American Surgeon*, 64: 563-567.
Not relevant; cancer patients not symptomatic patients

- Patterson, R. N. & Johnston, S. D. (2003) Iron deficiency anaemia: are the British Society of Gastroenterology guidelines being adhered to? *Postgraduate Medical Journal*, 79: 226-228.
Not in PICO
- Pedersen, A. F., Hansen, R. P. & Vedsted, P. (2013) Patient Delay in Colorectal Cancer Patients: Associations with Rectal Bleeding and Thoughts about Cancer. *PLoS ONE*, 8.
Not in PICO
- Pedersen, J. W., Gentry-Maharaj, A., Fourkala, E.-O., Dawnay, A., Burnell, M., Zaikin, A., Pedersen, A. E., Jacobs, I., Menon, U. & Wandall, H. H. (2013) Early detection of cancer in the general population: A blinded case-control study of p53 autoantibodies in colorectal cancer. *British Journal of Cancer*, 108: 107-114.
Not in PICO
- Peschl, L. & Munda, W. (1987) [Early clinical diagnosis of stomach and large intestine cancer]. [German]. *ZFA - Zeitschrift fur Alternsforschung*, 42: 155-164.
Narrative review
- Pfenninger, J. L. & Zainea, G. G. (2001) Common anorectal conditions: Part I. Symptoms and complaints. *American Family Physician*, 63: 2391-2398.
Narrative review
- Pieczyrak, R., Kotulska, A. & Kucharz, E. (2010) Neoplasia in patients with symptoms of inflammatory connective tissue diseases. *Internal Medicine Journal*, 40: 150.
Not in PICO
- Piramanayagam, B., Mackay, B., Fidler, L., Farmer, M. & Lengyel, J. (2010) Is it true that screen detected colorectal cancer (CRC) patients are asymptomatic? Results from north staffordshire bowel cancer screening unit. *Colorectal Disease*, 12: 13.
Not in PICO
- Pisanu, A., Ravarino, A., Nieddu, R. & Uccheddu, A. (2007) Synchronous isolated splenic metastasis from colon carcinoma and concomitant splenic abscess: a case report and review of the literature. [Review] [31 refs]. *World Journal of Gastroenterology*, 13: 5516-5520.
Not in PICO
- Pistevou-Gombaki, K., Eleftheriadis, N., Plataniotis, G. A., Sofroniadis, I. & Kouloulis, V. E. (2003) Octreotide for palliative treatment of hepatic metastases from non-neuroendocrine primary tumours: evaluation of quality of life using the EORTC QLQ-C30 questionnaire. *Palliative Medicine*, 17: 257-262.
Not in PICO
- Pitiakoudis, M., Tsaroucha, A. K., Mimidis, K., Polychronidis, A., Minopoulos, G. & Simopoulos, C. (2004) Mucocele of the appendix: a report of five cases. *Techniques in Coloproctology*, 8: 109-112.
Not in PICO
- Pitluk, H. & Poticha, S. M. (1983) Carcinoma of the colon and rectum in patients less than 40 years of age. *Surgery, Gynecology & Obstetrics*, 157: 335-337.
Not in PICO
- Poddar, N., Raza, S., Sharma, B., Liu, M., Gohari, A. & Kalavar, M. (2011) Small bowel adenocarcinoma presenting with refractory iron deficiency anemia - case report and review of literature. *Case Reports Oncology*, 4: 458-463.
Not in PICO
- Popovits, J. & Rosta, I. (2003) [Focus on colorectal adenomas--therapeutic possibilities in precancerous changes and conditions of the colon and rectum in our daily practice]]. [Hungarian]. *Orvosi Hetilap*, 144: 1707-1711.
Not in PICO
- Poston, G. J., Tait, D., O'Connell, S., Bennett, A. & Berendse, S. (2011) Diagnosis and management of colorectal cancer: Summary of NICE guidance. *BMJ (Online)*, 343: 1010-1012.
Guideline

- Powsner, E., Grosowoy, G. & Wolloch, Y. (265) [Rectosigmoid carcinoma in an adolescent girl]. [Hebrew]. *Harefuah*, 123: 169-170.
Case report
- Pra, D., Rech Franke, S. I., Pegas Henriques, J. A. & Fenech, M. (2009) A possible link between iron deficiency and gastrointestinal carcinogenesis. [Review] [129 refs]. *Nutrition & Cancer*, 61: 415-426.
Narrative review
- Pribic, S., Trtica-Majnaric, L., Gmajnic, R., Lukic, M. & Prlic, N. (2011) Colorectal cancer early detection program integrated in practice of family physicians. *Medicinski Glasnik*, 8: 31-38.
Not in PICO
- Prichard, P. J. & Tjandra, J. J. (1998) Colorectal cancer. [Review] [46 refs]. *Medical Journal of Australia*, 169: 493-498.
Narrative review
- Provenzale, D., Ofman, J., Gralnek, I., Rabeneck, L., Koff, R. & McCrory, D. (2003) Gastroenterologist specialist care and care provided by generalists--an evaluation of effectiveness and efficiency. [Review] [33 refs]. *American Journal of Gastroenterology*, 98: 21-28.
Not in PICO
- Przybylowski, J., Podolecki, A. & Bresler, M. (1980) [Thrombophlebitis as an early symptom of cancer]. [Polish]. *Wiadomosci Lekarskie*, 33: 821-823.
Not in PICO
- Pullens, H. J., Laheij, R. J., Vleggaar, F. P., van Oijen, M. G. & Siersema, P. D. (2013) Symptoms associated with finding colorectal cancer during colonoscopy. *European Journal of Gastroenterology & Hepatology*, 25: 1295-1299.
Not in PICO
- Pullens, H. J. M., Joosten, M., Siersema, P. D. & Brink, M. A. (2014) Open-access flexible sigmoidoscopy frequently leads to additional colonoscopy in symptomatic patients over 50 years. *Journal of Gastrointestinal and Liver Diseases*, 23: 153-159.
Not in PICO (S&S: population; Tests: outcomes)
- Pullyblank, A. M., Cawthorn, S. J. & Dixon, A. R. (2002) Knowledge of cancer symptoms among patients attending one-stop breast and rectal bleeding clinics. *European Journal of Surgical Oncology*, 28: 511-515.
Not in PICO
- Purkayastha, S. & Darzi, A. (2006) Colorectal cancer and rectal bleeding in primary care: urban or rural myth? *BMJ*, 333: 201-202.
Comment
- Purysko, A. S., Coppa, C. P., Kalady, M. F., Pai, R. K., Leao Filho, H. M., Thupili, C. R. & Remer, E. M. (2014) - Benign and malignant tumors of the rectum and perirectal region. - *Abdominal Imaging*, 39: 824-852.
Narrative review
- Qasim, A., Muldoon, C. & McKiernan, S. (2009) Colonic adenoma patients have higher incidence of hyperplastic polyps on surveillance colonoscopy. *European Journal of Gastroenterology & Hepatology*, 21: 877-881.
Not in PICO
- Quach, D. & Nguyen, O. (2011) The clinical, endoscopic and pathological characteristics of early-onset colorectal cancer in Vietnamese population. *Journal of Gastroenterology and Hepatology*, 26: 108.
Not in PICO
- Quintas-Cardama, A., Lazar, A. J., Woodman, S. E., Kim, K., Ross, M. & Hwu, P. (2008) Complete response of stage IV anal mucosal melanoma expressing KIT Val560Asp to the multikinase inhibitor sorafenib. *Nature Clinical Practice Oncology*, 5: 737-740.
Not in PICO

- Quintas, L. P., Dacal, R. A., Gonzalez, M. F., Cubiella, F. J., Lopez, S. L., Garcia Garcia, M. J. & Fernandez, S. J. (2011) [Referrals to a gastroenterology outpatient clinic from primary care: evaluation of two programs]. [Spanish]. *Gaceta Sanitaria*, 25: 468-473.
Not in PICO
- Rai, S. & Hemingway, D. (2005) Iron deficiency anaemia--useful diagnostic tool for right sided colon cancers? *Colorectal Disease*, 7: 588-590.
Not in PICO
- Raje, D., Mukhtar, H., Oshowo, A. & Ingham, C. C. (2007) What proportion of patients referred to secondary care with iron deficiency anemia have colon cancer? *Diseases of the Colon & Rectum*, 50: 1211-1214.
Not in PICO
- Raje, D., Scott, M., Irvine, T., Walshe, M., Mukhtar, H., Oshowo, A. & Ingham, C. C. (2007) Telephonic management of rectal bleeding in young adults: a prospective randomized controlled trial. *Colorectal Disease*, 9: 86-89.
Not in PICO
- Ramsay, G., MacKay, C., Nanthakumaran, S., Craig, W. L., Mcadam, T. K. & Loudon, M. A. (2012) Urgency of referral and its impact on outcome in patients with colorectal cancer. *Colorectal Disease*, 14: E375-E377.
Not in PICO
- Ramsay, J. A., Rose, T. H. & Ross, T. (1996) Colonic carcinoma presenting as an appendiceal abscess in a young woman. *Canadian Journal of Surgery*, 39: 53-56.
Not in PICO
- Rao, S. K., Schilling, T. F. & Sequist, T. D. (2009) Challenges in the management of positive fecal occult blood tests. *Journal of General Internal Medicine*, 24: 356-360.
Not in PICO
- Raphael, C., Lydia, O., Eric, B., Stefan, C., Jean-Francois, B., Gilles, G., Daniel, S., Bernard, G. & Anne, B. (2011) Clinical and diagnosis outcome of above 65-years old iron deficiency anemic patients after a non-diagnostic standardized endoscopic procedure: Multicentric retrospective study. *European Journal of Internal Medicine*, 22: S21.
Not in PICO
- Rigor, B. M., Sr. (2000) Pelvic cancer pain. [Review] [46 refs]. *Journal of Surgical Oncology*, 75: 280-300.
Narrative review
- Riss, S., Weiser, F. A., Schwameis, K., Mittlbock, M. & Stift, A. (2011) Haemorrhoids, constipation and faecal incontinence: is there any relationship? *Colorectal Disease*, 13: e227-e233.
Not in PICO
- Ristvedt, S. L., Birnbaum, E. H., Dietz, D. W., Fleshman, J. W., Kodner, I. J. & Read, T. E. (2005) Delayed treatment for rectal cancer. *Diseases of the Colon & Rectum*, 48: 1736-1741.
Not in PICO
- Ritchie, M. C., Clifford, G. M., Dempsey, N., Painter, J. E., Nylander, D., Singh, J., Henry, J. A., Bowes, J. & Rees, C. (2010) It's normal is n't it? An audit of pre existing symptoms & subsequent behaviour in bowel cancers screening participants. *Gastroenterology*, 138: S192.
Not in PICO
- Rivero, M. M., Murie Carrillo De, A. M. & Hernandez, P. R. (1998) [Symptomatic recurrent or episodic fever of unknown origin in adenocarcinoma of the colon]. [Spanish]. *Gastroenterologia y Hepatologia*, 21: 261.
Not in PICO
- Rizzo, D., Arlotta, A., Maurizi, P., Ruggiero, A., Attina, G. & Riccardi, R. (2011) Gastric adenocarcinoma presenting as thrombotic microangiopathy in a 14-year-old girl. *Journal of Pediatric Hematology/Oncology*, 33: e213-e215.
Not in PICO

- Robertson, R., Campbell, N. C., Smith, S., Donnan, P. T., Sullivan, F., Duffy, R., Ritchie, L. D., Millar, D., Cassidy, J. & Munro, A. (2004) Factors influencing time from presentation to treatment of colorectal and breast cancer in urban and rural areas. *British Journal of Cancer*, 90: 1479-1485.
Not in PICO
- Rosenberg, J. M. & Welch, J. P. (1985) Carcinoid tumors of the colon. A study of 72 patients. *American Journal of Surgery*, 149: 775-779.
Not in PICO
- Rubin, G. & Hamilton, W. (2009) Alarm features of colorectal cancer. *Gut*., 58: 1026.
Comment/letter
- Ruffolo, C., Scarpa, M., Polese, L., D'Amico, F. E., Boetto, R., Pozza, A., D'Inca, R., Checchin, D., Sturniolo, G. C., Bassi, N. & Angriman, I. (2010) Clinical presentation and diagnosis of intestinal adenocarcinoma in Crohn's disease. *Gastroenterology*, 138: S883.
Not in PICO
- Ruiz-Torrejón, A., Ramos-Monserrat, M. & Llobera-Canaves, J. (2006) Family practice and diagnosis of cancer. [Spanish]. *Atencion Primaria*, 37: 16-21.
Not in PICO
- Ryan, J. & Murkies, A. (2006) Diagnosis of upper gastrointestinal malignancy. [Review] [3 refs]. *Australian Family Physician*, 35: 200-201.
Narrative review
- Saif, M. W. (2005) Management of colorectal cancer in pregnancy: a multimodality approach. [Review] [84 refs]. *Clinical Colorectal Cancer*, 5: 247-256.
Not in PICO
- Saint-Blancard, P., Hervouet, M. & Chapuis, O. (2010) [Poorly differentiated endocrine carcinoma of the colon]. [French]. *Revue de Medecine Interne*, 31: e10-e12.
Not in PICO
- Sakellariadis, T., Mathioulakis, S. & Antiochos, C. (2005) Synchronous early primary adenocarcinoma of both rectum and gallbladder. Report of a case. *International Seminars in Surgical Oncology*, 2: 19.
Not in PICO
- Salas-Valverde, S., Lizano, A., Gamboa, Y., Vega, S., Barrantes, M., Santamaria, S. & Zamora, J. B. (2009) Colon carcinoma in children and adolescents: prognostic factors and outcome-a review of 11 cases. *Pediatric Surgery International*, 25: 1073-1076.
Not in PICO
- Saldanha, J. D., Moug, S. J., Linton, K. & Diament, R. H. (2013) Symptoms do not predict colorectal cancer in an FOB screened population. *Scottish Medical Journal*, 58: 95-98.
Not in PICO
- Salzman, B. E., Lamb, K., Olszewski, R. F., Tully, A. & Studdiford, J. (2009) Diagnosing Cancer in the Symptomatic Patient. *Primary Care - Clinics in Office Practice*, 36: 651-670.
Narrative review
- Samaritan, G. & Pearlman, R. A. (2007) Underdiagnosed and undertreated colorectal cancer tops liability list. *Journal of the Medical Association of Georgia*, 96: 48.
Not in PICO
- Sanchez, A., Munoz, C., Bujanda, L., Iriando, C., Gil-Molet, A., Cosme, A., Sarasqueta, C. & Echenique-Elizondo, M. (2012) The value of colonoscopy to assess rectal bleeding in patients referred from Primary Care Units. *Revista Espanola de Enfermedades Digestivas*, 97: 870-876.
Not in PICO (referred patients)
- Sascha, D. R., Brown, V. S. F., Loukogeorgakis, S. P., Kallis, G. & Meleagros, L. (2009) The two-week rule in colorectal cancer. Can it deliver its promise? *International Journal Of Surgery*, 7: 521-525.
Not in PICO
- Schiff, G. D., Hasan, O., Kim, S., Abrams, R., Cosby, K., Lambert, B. L., Elstein, A. S., Hasler, S., Kabongo, M. L., Krosnjak, N., Odwazny, R., Wisniewski, M. F. & McNutt, R. A. (2009) Diagnostic

- error in medicine: Analysis of 583 physician-reported errors. *Archives of Internal Medicine*, 169: 1881-1887.
Not in PICO
- Schiff, G. D. (2014) Diagnosis and diagnostic errors: Time for a new paradigm. *BMJ Quality and Safety*, 23: 1-3.
Not in PICO
- Schillaci, F., Stagnitti, F., Iurato, C., Mongardini, M., Dall'olio, D., Salvi, P. F., Cazzaniga, M., Bresadola, L., Schultze, W. & Natalini, E. (1998) [Deep venous thrombosis and neoplastic pathology: our experience in emergencies]. [Italian]. *Giornale di Chirurgia*, 19: 293-300.
Not in PICO
- Schonberg, M. A., York, M., Basu, N., Olveczky, D. & Marcantonio, E. R. (2008) Preventive health care among older women in an academic primary care practice. *Womens Health Issues*, 18: 249-256.
Not in PICO
- Schroder, J., Wesner, F. & Kremer, B. (2000) Diagnostic procedures in patients with the principal sign of weight loss. [German]. *Chirurgische Gastroenterologie Interdisziplinär*, 16: 61-64.
Narrative review
- Schroeder, K. (2002) Rectal bleeding: history is key. [Review] [7 refs]. *Practitioner*, 246: 604-607.
Narrative review
- Schwenter, F., Gradinger, A., Berk, T., Pollett, A., Gryfe, R., Gallinger, S., Faughnan, M. E. & Durno, C. (2011) Juvenile polyposis and early onset colorectal cancer in patients with hereditary hemorrhagic telangiectasia syndrome and SMAD4 mutation. *Familial Cancer*, 10: S59-S60.
Not in PICO
- Scott, M. A., Knight, A., Brown, K. & Novell, J. R. (2006) A single common urgent pathway for all colorectal referrals reduces time to diagnosis and treatment. *Colorectal Disease*, 8: 766-771.
Not in PICO
- SCOTT, W. G. (1950) Significance of rectal bleeding and the importance of diagnosing early cancer of the colon. *Journal of the National Medical Association*, 42: 352-353.
Pre-1980
- Segal, W. N., Greenberg, P. D., Rockey, D. C., Cello, J. P. & McQuaid, K. R. (1998) The outpatient evaluation of hematochezia. *American Journal of Gastroenterology*, 93: 179-182.
Not in PICO
- Selvachandran, S. N., Hodder, R. J., Ballal, M. S., Jones, P. & Cade, D. (2002) Prediction of colorectal cancer by a patient consultation questionnaire and scoring system: a prospective study. *Lancet*, 360: 278-283.
Not in PICO
- Sewitch, M., Waschke, K., Stein, D. & Arthurs, E. (2009) Time intervals from initial symptom report to colonoscopy and histologic diagnosis in rectal cancer patients. *Canadian Journal of Gastroenterology*, 23.
Not in PICO
- Shah, J., Valdes, M. & Rockey, D. C. (2009) Incidence and clinical characteristics of colorectal cancer in a safety-net hospital system: Implications for U.S. national healthcare policy. *Gastroenterology*, 136: A333-A334.
Not in PICO
- Shah, S., Dowell, J. & Greene, S. (2006) Evaluation of clinical pharmacy services in a hematology/oncology outpatient setting. *Annals of Pharmacotherapy*, 40: 1527-1533.
Not in PICO
- Shapley, M., Mansell, G., Jordan, J. L. & Jordan, K. P. (2010) Positive predictive values of $\geq 5\%$ in primary care for cancer: systematic review. [Review]. *British Journal of General Practice*, 60: e366-e377.
Systematic review, but current review updates it

- Sharma, M., Mallows, K., West, S., Hodges, G. & Budhoo, M. (2010) Bowel symptoms don't predict cancer in bowel cancer screening. *Colorectal Disease*, 12: 15.
Not in PICO
- Sharma, R., Zucknick, M., London, R., Kacevska, M., Liddle, C. & Clarke, S. J. (2008) Systemic inflammatory response predicts prognosis in patients with advanced-stage colorectal cancer. *Clinical Colorectal Cancer*, 7: 331-337.
Not in PICO
- Shaw, A. G., Simpson, J., Tierney, G., Goddard, A. F., Reynolds, J. R. & Lund, J. N. (2008) Referral of patients with iron deficiency anaemia under the lower gastrointestinal two-week wait rule. *Colorectal Disease*, 10: 294-297.
Not in PICO
- Shaw, A. G., Lund, J. N., Longman, C., Tierney, G. M. & Goddard, A. F. (2009) The misuse of the faecal occult blood test under the lower gastrointestinal two week wait rule. *Colorectal Disease*, 11: 94-96.
Not in PICO
- Sherwood, L. A., Knowles, G., Wilson, R. G. & Potter, M. A. (2006) Retrospective review of laser therapy for palliation of colorectal tumours. *European Journal of Oncology Nursing*, 10: 30-38.
Not in PICO
- Shields, H. M., Stoffel, E. M., Chung, D. C., Sequist, T. D., Li, J. W., Pelletier, S. R., Spencer, J., Silk, J. M., Austin, B. L., Diguette, S., Furbish, J. E., Lederman, R. & Weingart, S. N. (2014) - Disparities in evaluation of patients with rectal bleeding 40 years and older. - *Clinical Gastroenterology & Hepatology*, 12: 669-675.
Not in PICO
- Shima, Y., Ohtsu, A., Shirao, K. & Sasaki, Y. (2008) Clinical efficacy and safety of octreotide (SMS201-995) in terminally ill Japanese cancer patients with malignant bowel obstruction. *Japanese Journal of Clinical Oncology*, 38: 354-359.
Not in PICO
- Shinagare, A. B., Giardino, A. A., Jagannathan, J. P., Van Den Abbeele, A. D. & Ramaiya, N. H. (2011) Hereditary cancer syndromes: A radiologist's perspective. *American Journal of Roentgenology*, 197: W1001-W1007.
Not in PICO
- Shyung, L. R., Lin, S. C., Shih, S. C., Chang, W. H., Chu, C. H. & Wang, T. E. (2009) Proposed scoring system to determine small bowel mass lesions using capsule endoscopy. *Journal of the Formosan Medical Association*, 108: 533-538.
Not in PICO
- Sidhu, R., Wilson, P., Foye, L., McAlindon, M. E., Morley, S., Lobo, A. J. & Sanders, D. S. (2009) The use of faecal lactoferrin as a non-invasive marker in the diagnosis of colorectal diseases: Pilot data. *Gut*, 58: A132-A133.
Not in PICO
- Sigstad, H. & Fugelli, P. (1982) [Diarrhea and constipation in general practice]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 102: 1585-1587.
Narrative review
- Silverman, A. L., Desai, T. K., Dhar, R., Ehrinpreis, M. N., Kinzie, J. L. & Luk, G. D. (1988) Clinical features, evaluation, and detection of colorectal cancer. [Review] [57 refs]. *Gastroenterology Clinics of North America*, 17: 713-725.
Narrative review
- Simons, P. C., Van Steenberghe, L. N., De Witte, M. T. & Janssen-Heijnen, M. L. (2013) Miss rate of colorectal cancer at CT colonography in average-risk symptomatic patients. *European Radiology*, 23: 908-913.
Not in PICO

- Singhal, S., Mathur, S., Basi, P. S., Butt, A. S., Singh, M., Sonpal, N., Momeni, M. & Anand, S. (2010) Screening of Symptomatic (SOS) approach for colorectal cancer screening above age 75 in African Americans, Hispanics and Asian Americans. *Gastrointestinal Endoscopy*, 71: AB357.
Not in PICO
- Singhal, S., Verma, A. & Anand, K. (2011) Colonoscopy for colorectal cancer screening above age 75: outcomes in symptomatic african american and Hispanic adults. *Journal of Gastrointestinal Cancer*, 42: 212-216.
Not in PICO
- Sirtori, C. (1974) Current possibilities in the early diagnosis of tumors of the digestive system. Introduction. [Italian]. *Minerva Medica*, 65: 2923-2926.
Pre-1980
- Sladden, M. J. & Thomson, A. N. (1998) How do general practitioners manage rectal bleeding? *Australian Family Physician*, 27: 78-82.
Not in PICO
- Sladden, M. J., Thomson, A. N. & Lombard, C. J. (1999) Rectal bleeding in general practice patients. *Australian Family Physician*, 28: 750-754.
Not in PICO
- Sleiman, W. H., Asfahani, Z., Taher, A. T., Al, R. D. & Khalil, I. (2005) Venous thromboembolism in cancer patients referred to the American University of Beirut - Medical Center secondary to deep vein thrombosis; occurrence and risk factors. *Journal of Thrombosis and Thrombolysis*, 20: 179-182.
Not in PICO
- Smith, D., Ballal, M., Hodder, R., Soin, G., Selvachandran, S. N. & Cade, D. (2006) Symptomatic presentation of early colorectal cancer. *Annals of the Royal College of Surgeons of England*, 88: 185-190.
Not in PICO
- Smith, G. F. & Toonen, T. R. (2007) Primary care of the patient with cancer. *American Family Physician*, 75: 1207-1214.
Not in PICO
- Solem, C. A., Harmsen, W. S., Zinsmeister, A. R. & Loftus, E. V., Jr. (2004) Small intestinal adenocarcinoma in Crohn's disease: a case-control study. *Inflammatory Bowel Diseases*, 10: 32-35.
Not in PICO
- Soler, S., Delgado, C., Ballaz, A., Cisneros, E., Maly, R., Babalis, D. & Monreal, M. (2012) PL-03 unsuspected pulmonary embolism in patients with cancer. *Thrombosis Research*, 129: S16-S19.
Not in PICO
- Soncini, M., Rondonotti, E., Girelli, C. M. & De, F. R. (2012) Diagnostic yield, practical issues and safety of small bowel capsule endoscopy in clinical practice: Prospective data from a regional registry. *Gastrointestinal Endoscopy*, 75: AB253.
Not in PICO
- Sonoo, H., Kameyama, M., Inatugi, N., Nonomura, A. & Enomoto, Y. (2009) Pedunculated polyp of early sigmoid colon cancer with invasive micropapillary carcinoma. *Japanese Journal of Clinical Oncology*, 39: 523-527.
Not in PICO
- Spelsberg, F. & Schmidtler, F. (1980) Primary malignant tumours in the small bowel. (A report about 43 of our own cases and 1134 cases from literature). *Acta Chirurgica Iugoslavica*, 27: 39-46.
Not in PICO
- Spruce, L. R. & Sanford, J. T. (2012) An intervention to change the approach to colorectal cancer screening in primary care. *Journal of the American Academy of Nurse Practitioners*, 24: 167-174.
Not in PICO

- Spyckerelle, Y., Piette, F., Steinmetz, J., Fournier, B., Bussy, C., Giordanella, J.-P. & Boulange, M. (2000) Iron deficiency in over 60-year old population: Study in health screening centers. [French]. *Gastroenterologie Clinique et Biologique*, 24: 709-713.
Not in PICO
- Staniland, J. R., Ditchburn, J. & de Dombal, F. T. (1976) Clinical presentation of diseases of the large bowel. A detailed study of 642 patients. *Gastroenterology*, 70: 22-28.
Pre-1980
- Stapley, S., Peters, T. J., Sharp, D. & Hamilton, W. (2006) The mortality of colorectal cancer in relation to the initial symptom at presentation to primary care and to the duration of symptoms: a cohort study using medical records. *British Journal of Cancer*, 95: 1321-1325.
Not in PICO
- Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M. & Hamilton, W. (2013) The risk of oesophago-gastric cancer in symptomatic patients in primary care: a large case-control study using electronic records. *British Journal of Cancer*, 108: 25-31.
Not in PICO
- Stebbing, J. F. & Nash, A. G. (1995) Avoidable delay in the management of carcinoma of the right colon. *Annals of the Royal College of Surgeons of England*, 77: 21-23.
Not in PICO
- Stephen, F. O. & Rossaro, L. (2008) 12th Update in Gastroenterology and Hepatology for the Primary Care Practitioner. *Expert review of gastroenterology & hepatology*, 2: 635-637.
Not in PICO
- Studd, C., Mollison, L. & Nicholson, R. (2010) An approach to the patient with bloody diarrhoea. *Medicine Today*, 11: 43-48.
Narrative review
- Surgeon, C. M., Duffy, M. J., Stenman, U. H., Lilja, H., Brunner, N., Chan, D. W., Babaian, R., Bast, R. C., Jr., Dowell, B., Esteva, F. J., Haglund, C., Harbeck, N., Hayes, D. F., Holten-Andersen, M., Klee, G. G., Lamerz, R., Looijenga, L. H., Molina, R., Nielsen, H. J., Rittenhouse, H., Semjonow, A., Shih, I., Sibley, P., Soletormos, G., Stephan, C., Sokoll, L., Hoffman, B. R., Diamandis, E. P. & National Academy of Clinical Biochemistry (2008) National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers. *Clinical Chemistry*, 54: e11-e79.
Not in PICO
- Sugiura, M., Tsuji, H., Sato, A., Haruki, N., Kurehara, H., Maeda, Y., Yamakawa, Y., Tatematsu, T., Ando, N., Maeda, Y. & Yamakawa, Y. (2009) [A case of double cancer of sigmoid colon cancer with lung metastases, peritoneal dissemination and early gastric cancer responding to S-1]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 36: 1175-1178.
Not in PICO
- Sule, A. Z. & Mandong, B. M. (1999) Malignant colorectal tumours in patients 30 years and below: a review of 35 cases. *Central African Journal of Medicine*, 45: 209-212.
Not in PICO
- Summers, A. & Khan, Z. (2009) Managing dyspepsia in primary care. *Practitioner*, 253: 23-27.
Narrative review
- Summerton, N. & Paes, R. (2000) The clinical assessment of patients with large bowel symptoms by general practitioners. *European Journal of General Practice*, 6: 43-47.
Not in PICO
- Summerton, N., Mann, S., Sutton, J., Rigby, A., Theakston, A., Clark, J., Williams-Hardy, H. & Summerton, A. (2003) Developing clinically relevant and reproducible symptom-defined populations for cancer diagnostic research in general practice using a community survey. *Family Practice*, 20: 340-346.
Not in PICO

- Svendsen, R. P., Stovring, H., Hansen, B. L., Kragstrup, J., Sondergaard, J. & Jarbol, D. E. (2010) Prevalence of cancer alarm symptoms: A population-based cross-sectional study. *Scandinavian Journal of Primary Health Care*, 28: 132-137.
Not in PICO
- Swensen, R. E., Garcia, R. L. & Goff, B. A. (2004) Ovarian metastasis from gastrointestinal tract cancer: A review. *CME Journal of Gynecologic Oncology*, 9: 115-124.
Not in PICO
- Syed, A. A., Silwadi, M. F. & Khatoon, B. A. (2002) Detection and diagnosis of blood in feces and urine: an overview. [Review] [125 refs]. *Clinica Chimica Acta*, 318: 1-17.
Narrative review
- Tadros, M. B. & Chauhan, K. (2011) Lower extremity edema, Could it be cancer? *Journal of General Internal Medicine*, 26: S548.
Not in PICO
- Taggarshe, D., Rehil, N., Sharma, S., Flynn, J. C. & Damadi, A. (316) Colorectal cancer: are the "young" being overlooked? *American Journal of Surgery*, 205: 312-316.
Not in PICO
- Talley, N. J. & Jones, M. (1998) Self-reported rectal bleeding in a united states community: Prevalence, risk factors, and health care seeking. *American Journal of Gastroenterology*, 93: 2179-2183.
Not in PICO
- Tan, S. P., Liau, S. S., Habeeb, S. M. & O'riordan, D. (2007) Synchronous colonic carcinomas presenting as an inguinoscrotal hernial mass: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 1: 36.
Not in PICO
- Tang, E., Davis, J. & Silberman, H. (836) Bowel obstruction in cancer patients. *Archives of Surgery*, 130: 832-836.
Not relevant; cancer patients not symptomatic patients
- Taskila, T., Wilson, S., Damery, S., Roalfe, A., Redman, V., Ismail, T. & Hobbs, R. (2009) Factors affecting attitudes toward colorectal cancer screening in the primary care population. *British Journal of Cancer*, 101: 250-255.
Not in PICO
- Taucher, S., Salat, A., Gnant, M., Kwasny, W., Mlineritsch, B., Menzel, R. C., Schmid, M., Smola, M. G., Stierer, M., Tausch, C., Galid, A., Steger, G., Jakesz, R. & Austrian Breast and Colorectal Cancer Study Group (2003) Impact of pretreatment thrombocytosis on survival in primary breast cancer. *Thrombosis & Haemostasis*, 89: 1098-1106.
Not in PICO
- Taylor, E., Campbell, J., Donnelly, M. & Hebden, J. (2014) A specialist iron deficiency anaemia clinic significantly reduces the need for secondary care follow up. *Gut*, 63: A222-A223.
Not in PICO
- Taylor, K. M., Powell, N., Foxton, M. R. & McNair, A. (2010) Follow-up of patients with iron deficiency anemia subsequent to negative upper and lower gastrointestinal investigations. *Gastroenterology*, 138: S636.
Not in PICO
- Teoh, W.-C., Digiusto, E. & McDonald, J. (2009) Too many patients are unaware of and unenthusiastic about bowel cancer screening. *Journal of Gastroenterology and Hepatology*, 24: A237.
Not in PICO
- Terhaar sive Droste, J. S., Oort, F. A., van der Hulst, R. W. M., Coupe, V. M. H., Craanen, M. E., Meijer, G. A., Morsink, L. M., Visser, O., van Wanrooij, R. L. J. & Mulder, C. J. J. (2010) Does delay in diagnosing colorectal cancer in symptomatic patients affect tumor stage and survival? A

- population-based observational study. *Bmc Cancer*, 10.
Not in PICO
- Terrazas Hontanon, J. M., Buelta-Carrillo, L. & Val-Bernal, J. F. (1988) [Colorectal carcinoma: symptomatology and semiology]. [Spanish]. *Revista Espanola de Las Enfermedades del Aparato Digestivo*, 73: t-9.
Not in PICO
- Thomas, P. D., Forbes, A., Green, J., Howdle, P., Long, R., Playford, R., Sheridan, M., Stevens, R., Valori, R., Walters, J., Addison, G. M., Hill, P. & Brydon, G. (2003) Guidelines for the investigation of chronic diarrhoea, 2nd edition. *Gut*, 52: v1-v15.
Guideline
- Thompson, M. & Prytherch, D. (1996) Rectal bleeding: when is it right to refer?. [Review] [9 refs]. *Practitioner*, 240: 198-200.
Narrative review
- Thompson, M. R. (2002) Referral guidelines for colorectal cancer. *Colorectal Disease*, 4: 287-297.
Guideline
- Thompson, M. R., Flashman, K. G., Wooldrage, K., Rogers, P. A., Senapati, A., O'Leary, D. P. & Atkin, W. (2008) Flexible sigmoidoscopy and whole colonic imaging in the diagnosis of cancer in patients with colorectal symptoms. *British Journal of Surgery*, 95: 1140-1146.
Not in PICO
- Thompson, M. R., Asiimwe, A., Flashman, K. & Tsavellas, G. (2011) Is earlier referral and investigation of bowel cancer patients presenting with rectal bleeding associated with better survival? *Colorectal Disease*, 13: 1242-1248.
Not in PICO
- Thompson, M. R., Flashman, K. G., Asiimwe, A., Tsavellas, G., Parvaiz, A., Senapati, A. & O'Leary, D. P. (2012) How does bowel cancer present? Implications for DOH plans to achieve earlier diagnosis. *Colorectal Disease*, 14: 15.
Not in PICO
- Tolwinka, A., Kisielewski, R. & Laudanski, P. (2012) Chronic pelvic pain in menopausal women. *Przegląd Menopauzalny*, 16: 187-191.
Narrative review
- Tomlinson, C., Wong, C., Au, H. J. & Schiller, D. (2012) Factors associated with delays to medical assessment and diagnosis for patients with colorectal cancer. *Canadian Family Physician*, 58: e495-e501.
Not in PICO
- Tong, G. X., Chai, J., Cheng, J., Xia, Y., Feng, R., Zhang, L. & Wang, D. B. (2014) Diagnostic Value of Rectal Bleeding in Predicting Colorectal Cancer: a Systematic Review. *Asian Pacific Journal of Cancer Prevention*, 15: 1015-1021.
Systematic review, checked for relevant studies (Brenna 1990 [patients referred for colonoscopy, but not a diagnostic test accuracy study, i.e., outcomes not in PICO for tests and cannot be calculated], Farrands 1985 [referred patients], Zarchy 1991 [patients referred for barium enema, but not a diagnostic test accuracy study, i.e., outcomes not in PICO for tests])
- Tong, S., Hughes, K., Oldenburg, B. B. & Mar, C. D. (2006) Colorectal cancer screening with faecal occult blood testing: community intention, knowledge, beliefs and behaviour. *Asia-Pacific Journal of Public Health*, 18: 16-23.
Not in PICO
- Torrance, A., Patel, A. & Singh, J. (2012) Urgent referrals for colorectal cancer: Can patients go 'straight-to-test'? *Colorectal Disease*, 14: 14.
Not in PICO
- Treasure, W. (2013) Symptoms and risk factors to identify people with suspected cancer in primary care. *British Journal of General Practice*, 63: 125.
Comment

- Trimbath, J. D., Petersen, G. M., Erdman, S. H., Ferre, M., Luce, M. C. & Giardiello, F. M. (2001) Cafe-au-lait spots and early onset colorectal neoplasia: a variant of HNPCC? *Familial Cancer*, 1: 101-105.
Not in PICO
- Trueman, P., Haynes, S. M., Felicity, L. G., Louise, M. E., McQuigg, M. S., Mongia, S., Noble, P. A., Quinn, M. F., Ross, H. M., Thompson, F., Broom, J. I., Laws, R. A., Reckless, J. P., Kumar, S., Lean, M. E., Frost, G. S., Finer, N., Haslam, D. W., Morrison, D., Sloan, B. & Counterweight Project Team (2010) Long-term cost-effectiveness of weight management in primary care. *International Journal of Clinical Practice*, 64: 775-783.
Not in PICO
- Trujillo-Santos, J., Prandoni, P., Rivron-Guillot, K., Roman, P., Sanchez, R., Tiberio, G. & Monreal, M. (2008) Clinical outcome in patients with venous thromboembolism and hidden cancer: Findings from the RIETE Registry. *Journal of Thrombosis and Haemostasis*, 6: 251-255.
Not in PICO
- Turi, S., Rockelein, G., Dobroschke, J. & Wiedmann, K. H. (2004) [Lipoma of the small bowel]. [German]. *Zeitschrift fur Gastroenterologie*, 42: 147-151.
Not in PICO
- Turkoglu, M. A., Elpek, G. O., Dogru, V., Calis, H., Ucar, A. & Arici, C. (2014) - An unusual case of primary colonic dedifferentiated liposarcoma. - *International Journal of Surgery Case Reports*, 5: 8-11.
Not in PICO
- Turunen, M. J. & Peltokallio, P. (1982) Delay in the diagnosis of colorectal cancer. *Annales Chirurgiae et Gynaecologiae*, 71: 277-282.
Not in PICO
- Uchino, R., Kusano, S., Hanada, N., Ohara, C., Okino, T. & Yamaguchi, K. (2011) [Clinical efficacy of octreotide acetate in cancer patients with malignant bowel symptoms depend on terminal stage]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 38: 255-257.
Not in PICO
- Ukarapol, N., Wongsawasdi, L. & Singhavejsakul, J. (2000) Colonic carcinoma: a case report in a child and review literature. [Review] [12 refs]. *Journal of the Medical Association of Thailand*, 83: 204-207.
Not in PICO
- Unek, I. T., Celtik, A., Alacacioglu, A., Cokmert, S., Yavuzsen, T., Dogan, N. S., Oztop, I., Demirkan, B. & Yilmaz, U. (2007) Gastric carcinoma during pregnancy: report of a case. *Turkish Journal of Gastroenterology*, 18: 41-43.
Not in PICO
- Vakil, N., Halling, K., Ohlsson, L. & Wernersson, B. (2013) Symptom overlap between postprandial distress and epigastric pain syndromes of the Rome III dyspepsia classification. *American Journal of Gastroenterology*, 108: 767-774.
Not in PICO
- Valdovinos Diaz, M. A., Guerrero, C., Nava, A. A., Jacobo, J. & Villalobos, J. J. (1991) [The biological behavior of colorectal carcinoma in young patients]. [Spanish]. *Revista de Gastroenterologia de Mexico*, 56: 55-60.
Not in PICO
- Van Hout, A. M., de Wit, N. J., Rutten, F. H. & Peeters, P. H. (2011) Determinants of patient's and doctor's delay in diagnosis and treatment of colorectal cancer. *European Journal of Gastroenterology & Hepatology*, 23: 1056-1063.
Not in PICO
- van, P. B., Kurver, M. J., Damoiseaux, R. A., Boukes, F. S. & Goudswaard, A. N. (2009) [Summary of Dutch College of General Practitioners guidelines on "Rectal bleeding"]. [Review] [1 refs] [Dutch].

- Nederlands Tijdschrift Voor Geneeskunde*, 153: A121.
Guideline
- Vaughan-Shaw, P. G., Cutting, J., Borley, N., Brooklyn, T. & Wheeler, J. M. D. (2014) Two-week wait symptoms are prevalent in screened patients with a positive faecal occult blood test but do not predict cancer. *Colorectal Disease*, 16: 40-47.
Not in PICO
- Vaughan-Shaw, P. G., Cutting, J., Borley, N., Brooklyn, T. & Wheeler, J. M. D. (2014) Two-week wait symptoms are prevalent in screened patients with a positive faecal occult blood test but do not predict cancer. *Colorectal Disease*, 16: 40-47.
Not in PICO
- Velstra, B., Mesker, W. E., Tollenaar, R. A. E. M. & De Groot, C. J. M. (2011) Primary breast and colon cancer: Is hypertension/preeclampsia during pregnancy an independent marker for individual risk stratification? *Angiogenesis*, 14: 113.
Not in PICO
- Venara, A., Thibaudeau, E., Lebdai, S., Mucci, S., Ridereau-Zins, C., Azzouzi, R. & Hamy, A. (2010) Rectal metastasis of prostate cancer: about a case. *Journal of Clinical Medicine Research*, 2: 137-139.
Not in PICO
- Vilbergsson, E., Isaksson, H. J. & Moller, P. H. (2010) [Case report: facial skin metastasis from rectal adenocarcinoma]. [Icelandic]. *Laeknabladid*, 96: 109-110.
Not in PICO
- Voutilainen, M., Mantynen, T., Kunnamo, I., Juhola, M., Mecklin, J. P. & Farkkila, M. (2003) Impact of clinical symptoms and referral volume on endoscopy for detecting peptic ulcer and gastric neoplasms. *Scandinavian Journal of Gastroenterology*, 38: 109-113.
Not in PICO
- Vukobrat-Bijedic, Z., Husic-Selimovic, A., Bijedic, N., Mujkic, A., Sofic, A., Gogov, B., Mehmedovic, A., Bjelogrljic, I., Glavas, S. & Djuran, A. (2014) Sensitivity of symptomatology Versus diagnostic procedures and concentration of CEA and CA19-9 in the early detection of colorectal cancer. *Acta Informatica Medica*, 22: 89-93.
Not in PICO
- Vukobrat-Bijedic, Z., Husic-Selimovic, A., Bijedic, N., Mujkic, A., Sofic, A., Gogov, B., Mehmedovic, A., Bjelogrljic, I., Glavas, S. & Djuran, A. (2014) - Sensitivity of Symptomatology Versus Diagnostic Procedures and Concentration of CEA and CA19-9 in the Early Detection of Colorectal Cancer. - *Acta Informatica Medica*, 22: 89-93.
Duplicate
- Wahlberg, H., Valle, P. C., Malm, S. & Broderstad, A. R. (2013) Practical health co-operation - the impact of a referral template on quality of care and health care co-operation: study protocol for a cluster randomized controlled trial. *Trials [Electronic Resource]*, 14: 7.
Not in PICO
- Wahls, T. L. & Peleg, I. (2009) Patient- and system-related barriers for the earlier diagnosis of colorectal cancer. *Bmc Family Practice*, 10.
Not in PICO
- Wauters, H. (2001) Erratum: Rectal bleeding and colorectal cancer in general practice: Diagnostic study (British Medical Journal (October 21, 2000) (998-999)). *British Medical Journal*, 322: 488.
Erratum to Wauters et al 2000 already included
- Wayte, N., Da, S. L., Chenevix-Trench, G. & Lakhani, S. R. (2008) What's in a cancer syndrome? Genes, phenotype and pathology. *Pathology*, 40: 247-259.
Narrative review
- Weaver, P., Harrison, B., Eskander, G., Jahan, M. S., Tanzo, V., Williams, W., Weaver, W. L., Walker, C. R., Turner, E. & Hoover, E. L. (1991) Colon cancer in blacks: a disease with a worsening

- prognosis. *Journal of the National Medical Association*, 83: 133-136.
Not in PICO
- Wedding, U., Hoffken, K., Friedrich, C. & Pientka, L. (2007) [Health services research and geriatrics: deficits and research approaches using the example of colorectal carcinoma and anaemia]. [German]. *Zeitschrift für Ärztliche Fortbildung und Qualitätssicherung*, 101: 587-592.
Narrative review
- Weinrich, S. P., Blesch, K. S., Dickson, G. W., Nussbaum, J. S. & Watson, E. J. (1989) Timely detection of colorectal cancer in the elderly. Implications of the aging process. *Cancer Nursing*, 12: 170-176.
Narrative review
- Weiser, M. A., Cabanillas, M., Vu, K., Tamm, E. P., Wallace, M. J., Escalante, C. P. & Bresalier, R. S. (2005) Diagnostic evaluation of patients with a high suspicion of malignancy: Comorbidities and clinical predictors of cancer. *American Journal of the Medical Sciences*, 330: 11-18.
Not in PICO
- Weller, D. (2010) Diagnosing colorectal cancer in primary care. *BMJ (Online)*, 340: 769.
Editorial
- Wender, R. C. (2007) Preserving primary care: The front line in the war against cancer. *Ca-A Cancer Journal for Clinicians*, 57: 4-5.
Not in PICO
- Werner, J. C., Zock, M., Khalil, P. N., Hoffmann, J., Kanz, K. G. & Jauch, K. W. (2013) [Evidence for the digital rectal examination in the emergency assessment of acute abdominal pain]. [German]. *Zentralblatt für Chirurgie*, 138: 669-676.
Narrative review
- Whitehead, W. E., Bassotti, G., Palsson, O., Taub, E., Cook, E. C., III & Drossman, D. A. (2003) Factor analysis of bowel symptoms in US and Italian populations. *Digestive & Liver Disease*, 35: 774-783.
Not in PICO
- Whittemore, A. S., Paffenbarger, R. S., Jr., Anderson, K. & Lee, J. E. (1985) Early precursors of site-specific cancers in college men and women. *Journal of the National Cancer Institute*, 74: 43-51.
Not in PICO
- Whynes, D. K. & Neilson, A. R. (1997) Symptoms before and after surgery for colorectal cancer. *Quality of Life Research*, 6: 61-66.
Not in PICO
- WIANCKO, K. B. & MACKENZIE, W. C. (1963) Primary tumours of the small bowel and its mesentery. *Canadian Medical Association Journal*, 88: 1225-1230.
Pre-1980
- Wiener, Y., Gold, R., Zehavy, S., Sandbank, J. & Halevy, A. (116) [Primary gastrointestinal stromal tumors]. [Hebrew]. *Harefuah*, 140: 377-380.
Not relevant; cancer patients not symptomatic patients
- Wireko, M. B., Subramanian, V. & Rangunath, K. (2011) The two week wait (2WW) referral for upper gastrointestinal cancer: Predictors and prevalence of non-upper gastrointestinal cancers in those with negative gastroscopy. *Gut*, 60: A47-A48.
Not in PICO
- Wong, H., Chan, P. & Yau, T. (2012) Colon cancer in a patient with underlying aplastic anemia: A clinical challenge. *World Journal of Clinical Oncology*, 3: 29-31.
Not in PICO
- Woods, R., Larkin, J. O., Muldoon, C., Kennedy, M. J., Mehigan, B. & McCormick, P. (2012) Metastatic paediatric colorectal carcinoma. *Irish Medical Journal*, 105: 88-89.
Not in PICO
- Wou, C., Chaston, N. & Doughan, S. (2014) - Mistaken identity: endometrial or rectal cancer? - *BMJ Case Reports*, 2014, 2014..
Not in PICO

- Wright, W. F. (2012) Clostridium septicum myonecrosis presenting as an acute painful foot. *American Journal of Emergency Medicine*, 30: 253-255.
Not in PICO
- Yabroff, K. R., Klabunde, C. N., Yuan, G. G., Mcneel, T. S., Brown, M. L., Casciotti, D., Buckman, D. W. & Taplin, S. (2011) Are Physicians' Recommendations For Colorectal Cancer Screening Guideline-Consistent? *Journal of General Internal Medicine*, 26: 177-184.
Not in PICO
- Yakan, S., Caliskan, C., Makay, O., Denecli, A. G. & Korkut, M. A. (2009) Intussusception in adults: clinical characteristics, diagnosis and operative strategies. *World Journal of Gastroenterology*, 15: 1985-1989.
Not in PICO
- Yang, Y. S., Huang, Q. Y., Wang, W. F., Sun, G. & Peng, L. H. (2003) Primary jejunoileal neoplasmas: a review of 60 cases. *World Journal of Gastroenterology*, 9: 862-864.
Not in PICO
- Yildiz, C., Karadayi, K., Sarkis, C. & Cetin, A. (2011) Huge cystic lymphangioma mimicking ovarian malignancy: a case report. *Turkish Journal of Gastroenterology*, 22: 344-346.
Not in PICO
- Yoon, S. N., Yu, C. S., Shin, U. S., Kim, C. W., Lim, S. B. & Kim, J. C. (2010) Clinicopathological characteristics of rectal carcinoids. *International Journal of Colorectal Disease*, 25: 1087-1092.
Not in PICO
- Yoshida, M., Matsuda, H. & Furuya, K. (2009) Successful treatment of gastric cancer in pregnancy. *Taiwanese Journal of Obstetrics & Gynecology*, 48: 282-285.
Not in PICO
- Yun, G. W., Yang, Y. J., Song, I. C., Park, K. U., Baek, S. W., Yun, H. J., Kim, S., Jo, D. Y. & Lee, H. J. (2011) A prospective evaluation of adult men with iron-deficiency anemia in Korea. *Internal Medicine*, 50: 1371-1375.
Not in PICO
- Yusuf, T. E., Levy, M. J. & Wiersema, M. J. (2005) EUS features of recurrent transitional cell bladder cancer metastatic to the GI tract. *Gastrointestinal Endoscopy*, 61: 314-316.
Not in PICO
- Zafar, A., Mak, T., Whinnie, S. & Chapman, M. A. S. (2012) The 2-week wait referral system does not improve 5-year colorectal cancer survival. *Colorectal Disease*, 14: E177-E180.
Not in PICO
- Zdravkovic, D., Bilanovic, D., Randelovic, T., Zdravkovic, M. & Toskovic, B. (2009) [Implication of late diagnosis for survival of patients with colorectal carcinoma]. [Serbian]. *Vojnosanitetski Pregled*, 66: 135-140.
Not in PICO
- Zhang, H., Hammad, T. A., Giovannuci, E., Kang, E. & Christiani, D. C. (2010) Validation of cancer diagnoses recorded in the general practice research database. *Pharmacoepidemiology and Drug Safety*, 19: S11-S12.
Not in PICO
- Zheng, S., Ouyang, Q., Li, G., Xu, H., Jiang, M., Cui, D., Xue, L. & Li, J. (2012) Primary intestinal NK/T cell lymphoma: a clinicopathologic study of 25 Chinese cases. *Archives of Iranian Medicine*, 15: 36-42.
Not relevant; cancer patients, not symptomatic primary care patients
- Zondervan, K. T., Yudkin, P. L., Vessey, M. P., Dawes, M. G., Barlow, D. H. & Kennedy, S. H. (1999) Prevalence and incidence of chronic pelvic pain in primary care: evidence from a national general practice database. *British Journal of Obstetrics & Gynaecology*, 106: 1149-1155.
Not in PICO

Zou, J., Bao, Z., Zheng, S., Yang, J., Ji, D. & Xiang, P. (2010) Multiple regression analysis of factors in diagnosis of colorectal cancer. [Chinese]. *Chinese Journal of Gastroenterology*, 15: 355-357.
Not in PICO

Zucca, A. C., Boyes, A. W., Linden, W. & Girgis, A. (2012) All's well that ends well? Quality of life and physical symptom clusters in long-term cancer survivors across cancer types. *Journal of Pain & Symptom Management*, 43: 720-731.
Not relevant; cancer patients, not symptomatic primary care patients

Review question:

Which investigations of symptoms of suspected colorectal cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

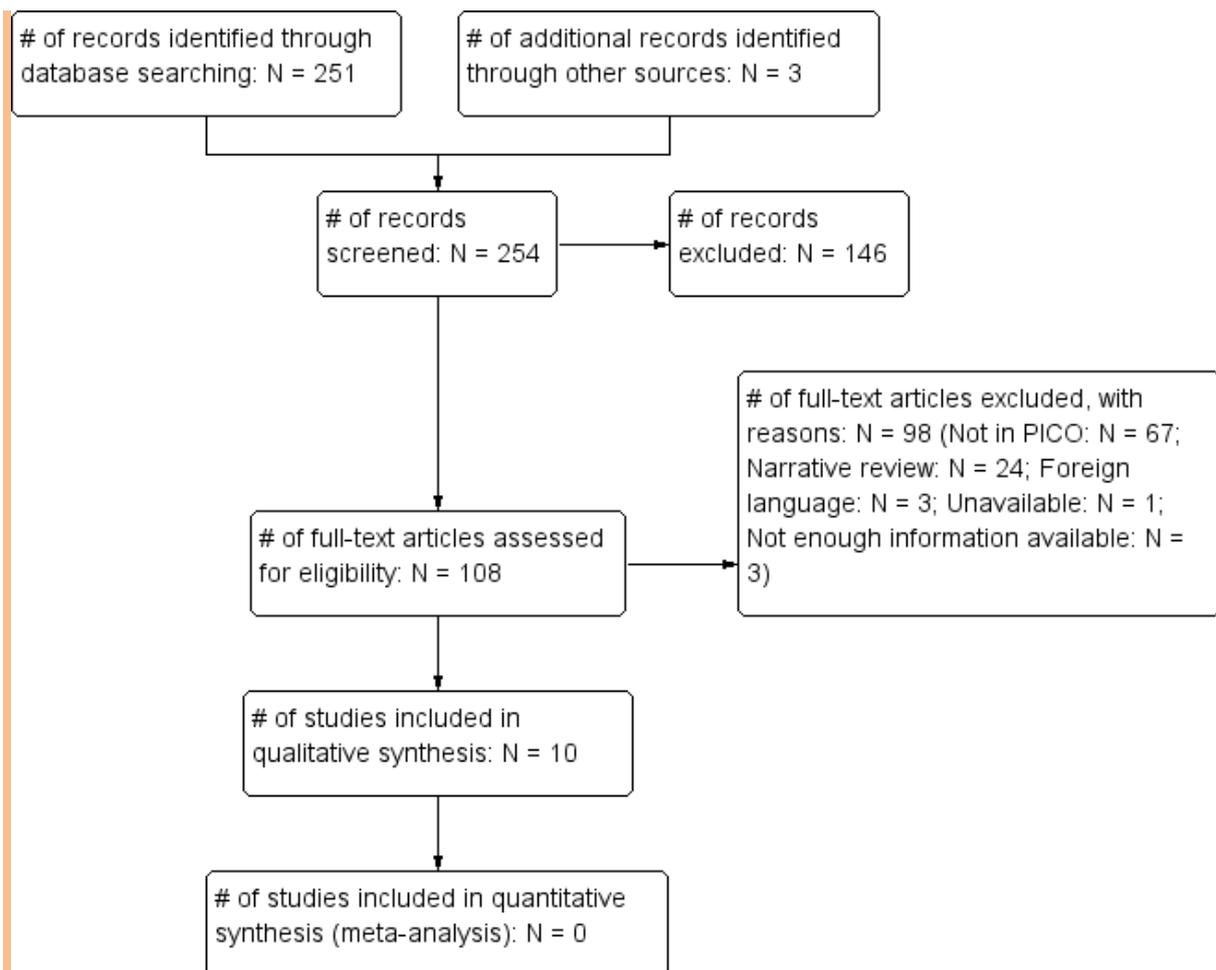
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	1321	136	10/01/2013
<i>Premedline</i>	1980-2013	35	4	14/01/2013
<i>Embase</i>	1980-2013	896	132	14/01/2013
<i>Cochrane Library</i>	1980-2013	116	3	14/01/2013
<i>Psychinfo</i>	1980-2013	4	1	14/01/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	79	21	14/01/2013
<i>Biomed Central</i>	1980-2013	68	0	14/01/2013

Total References retrieved (after de-duplication): 226

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-13/08/2014	48	9	13/08/2014
<i>Premedline</i>	2013-13/08/2014	37	4	13/08/2014
<i>Embase</i>	2013-13/08/2014	131	26	13/08/2014
<i>Cochrane Library</i>	2013-13/08/2014	15	1	13/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-13/08/2014	118	1	13/08/2014

Total References retrieved (after de-duplication): 25



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The studies were associated with a number of bias and validity issues. Two of the main issues to note relate to the patient selection methods employed and study settings, some of which were not clearly consecutive or random (and may therefore bias the results) or clearly transferable to UK-based primary care. Other issues of concern relate to missing data (and the concern that this may not be missing at random) and sub-optimal reference standards, which may both influence the results to an unknown extent.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Fijten (1995)	+	+	+	-	?	+	+
Gillberg (2012)	+	+	+	+	?	+	+
Glaser (1989)	?	+	-	-	-	+	-
Jensen (1993)	+	+	?	+	?	+	+
Kalra (1988)	+	+	-	-	?	+	-
Kok (2012)	?	+	?	?	?	+	?
Leicester (1984)	?	+	-	-	+	+	-
Niv (1992)	+	+	-	-	?	+	+
Steine (1993)	+	+	+	+	?	+	+
Stellon (1997)_BE	+	+	+	-	+	+	+
Stellon (1997)_FOB	+	+	+	-	+	+	+
Stellon (1997)_FS	+	+	+	+	+	+	+

 High	 Unclear	 Low
--	---	---

Study results

Table 1: Colorectal cancer: Faecal occult blood

Study	Test	Prevalence	Sensitivity	Specificity	Other results (95% CI)
Fijten (1995)	Faecal occult blood (Haemoccult)	5/225	50%	82%	Positive predictive value = 5% Negative predictive value = 99% False negativity rate = 50% 95% CI cannot be calculated as 2-by2 table could not be extracted
Gillberg (2012)	Faecal occult blood (Haemoccult II)	161/8928	75%	87%	TP = 120 FN = 41 TN = 7585 FP = 1182 Positive predictive value = 9.2% (7.7-11) False negativity rate = 25%
Jensen (1993)	Faecal occult blood	5/149	60%	79%	TP = 3 FN = 2 TN = 114 FP = 30

	(Hemoccult II)				Positive predictive value = 9.1% (2.4-25.5) False negativity rate = 40%
Kok (2012)	Faecal occult blood (Clearview One Step immune-chemical)	19/386	84%	76%	Data only available for N = 376 TP = 16 FN = 3 TN = 270 FP = 87 Positive predictive value = 15.5% (9.4-24.3) False negativity rate = 16%
Leicester (1984)	Faecal occult blood (Haemoccult)	4 cancers in 25 positive results out of 161 tests	56%	Not reported	Positive predictive value = 16% False negativity rate = 44% 95% CI cannot be calculated as 2-by-2 table could not be extracted
Stellon (1997)	Faecal occult blood (Haemoccult)	1/22	0%	76%	TP = 0 FN = 1 TN = 16 FP = 5 Positive predictive value = 0% (0-54) False negativity rate = 100%

The data were not meta-analysed due to concerns about excessive heterogeneity (see forest plots below), differences in the tests employed and missing data. TP = true positives, FP = false positives, TN = true negatives, FN = false negatives. See forest plots below for the 95% CI for sensitivity and specificity.

Table 2: Colorectal cancer: Sigmoidoscopy

Study	Test	Prevalence	Sensitivity (95% CI)	Specificity (95% CI)	Other results (95% CI)
Glaser (1989)	Rigid sigmoidoscopy	7/351	37.5% (10.2-74.1)	100% (98.6-100)	TP = 3 FN = 5 TN = 343 FP = 0 Positive predictive value = 100% (31-100) False negativity rate = 62.5%
Jensen (1993)	Rectosigmoidoscopy	5/149	40% (7.3-83)	100% (96.8-100)	TP = 2 FN = 3 TN = 144 FP = 0 Positive predictive value = 100% (19.8-100) False negativity rate = 60%
Kalra (1988)	Fibre-sigmoidoscopy	64 cancers in 216 abnormal findings in 541 patients	Not reported	Not reported	- Fibresigmoidoscopy unsuccessful in 31/541 patients - 4 cancers missed by fibresigmoidoscopy Positive predictive value = 29.6% 95% CI cannot be calculated as 2-by-2 table could not be extracted
Niv (1992)	Flexible sigmoidoscopy	5/255	Not reported	Not reported	TP = 4 FN = ≥ 1 TN = ? FP = 0 Positive predictive value = 100% (39.6-100) False negativity rate = cannot be ascertained as negative cases did not

					appear to be followed up
Stellon (1997)	Flexible sigmoidoscopy	2/26	0% (0-80.2)	100% (82.8-100)	TP = 0 FN = 2 TN = 24 FP = 0 Positive predictive value = 0% False negativity rate = 100%

The data were not meta-analysed due to concerns about differences in the tests employed and missing data. TP = true positives, FP = false positives, TN = true negatives, FN = false negatives.

Table 3: Colorectal cancer: Double-contrast barium enema

Study	Test	Prevalence	Sensitivity	Specificity	Other results
Jensen (1993)	Double-contrast barium enema	5/149	60%	100%	TP = 3 FN = 2 TN = 144 FP = 0 Positive predictive value = 100% (31-100) False negativity rate = 40%
Steine (1993)	Double-contrast barium enema	8/189	100%	98%	TP = 8 FN = 0 TN = 177 FP = 4 False negativity rate = 0% Positive predictive value = 66.7% (35.4-88.7) 1 patient with anal cancer was not examined
Stellon (1997)	Double-contrast barium enema	2/22	50%	100%	TP = 1 FN = 1 TN = 20 FP = 0 Positive predictive value = 100% (54.6-100) False negativity rate = 50%

The data were not meta-analysed due to concerns about excessive heterogeneity (see forest plot below). TP = true positives, FP = false positives, TN = true negatives, FN = false negatives. See forest plots below for the 95% CI for sensitivity and specificity.

Forests plots

Faecal occult blood

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gillberg (2012)	120	1182	41	7585	0.75 [0.67, 0.81]	0.87 [0.86, 0.87]		
Jensen (1993)	3	30	2	114	0.60 [0.15, 0.95]	0.79 [0.72, 0.85]		
Kok (2012)	16	87	3	270	0.84 [0.60, 0.97]	0.76 [0.71, 0.80]		
Stellon (1997)_FOB	0	5	1	16	0.00 [0.00, 0.97]	0.76 [0.53, 0.92]		

Double-contrast barium enema

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Jensen (1993)	3	0	2	144	0.60 [0.15, 0.95]	1.00 [0.97, 1.00]		
Steine (1993)	8	4	0	177	1.00 [0.63, 1.00]	0.98 [0.94, 0.99]		
Stellon (1997)_BE	1	0	1	20	0.50 [0.01, 0.99]	1.00 [0.83, 1.00]		

No evidence was found for colonoscopy, CT-colonoscopy/colonography, CT, and CEA.

Evidence statement(s):

Faecal occult blood (6 studies, N = 9871) conducted in symptomatic patients presenting in a primary care setting is associated with sensitivities that ranged from 0-84%, specificities that ranged from 76-87%, positive predictive values that ranged from 0-16%, and false negativity rates that ranged from 16-100% for colorectal cancer. All the studies were associated with 1-5 bias or applicability concerns (see also Table 1).

Sigmoidoscopy (5 studies, N = 1322) conducted in symptomatic patients presenting in a primary care setting is associated with sensitivities that ranged from 0-40%, specificities of up to 100%, positive predictive values that ranged from 0-100%, and false negativity rates that ranged from 60-100% for colorectal cancer. All the studies were associated with 0-5 bias or applicability concerns (see also Table 2).

Double-contrast barium enema (3 studies, N = 360) conducted in symptomatic patients presenting in a primary care setting is associated with sensitivities that ranged from 50-100%, specificities that ranged from 98-100%, positive predictive values that ranged from 66.7-100%, and false negativity rates that ranged from 0-50% for colorectal cancer. All the studies were associated with ≤ 2 bias or applicability concerns (see also Table 3).

Evidence tables

Fijten (1995)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive patient series
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 269 (118 males/151 females), mean (SD, range) age = 42 (15, 18-75). Mean (SD) follow up time = 20 (5) months. For 51% rectal bleeding was the main reason for the encounter, and 49% had another reason (e.g., abdominal complaints), but blood loss per rectum was seen and mentioned by the patients. N = 8 used anticoagulants.</p> <p><u>Inclusion criteria:</u> From September 1988 to April 1990, patients with rectal bleeding were recruited by 83 GPs in Limburg, with an average duration of participation of 11 months per doctor. Patients were included when overt rectal bleeding was the reason for encounter or when there was a history of recent (within the previous three months) rectal blood loss visible for the patient.</p> <p><u>Exclusion criteria:</u> Aged below 18 or above 75 years, pregnancy, urgent admission to hospital (for, e.g., a massive bleeding or acute abdominal pain), and if follow-up data were not available.</p> <p><u>Clinical setting:</u> Primary care, Netherlands</p>

Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Faecal occult blood (Haemoccult test, 3 X, with a diet low of peroxidase and free of red meat); ≥ 1 positive out of 3 regarded as a positive result
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up for min 1 year.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 290 patients were recruited, however 21/290 were excluded as they were lost to follow-up (moved to an unknown destination) and the haeoccult test data were available for 225/269 included patients. 5/225 patients had cancer (9/269 patients had cancer in the whole included sample) which means that almost half of the cancer patients were not included in the test data calculations.
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	2-by-2 table cannot be extracted
Gillberg (2012)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Database study covering 20 public primary care centres and a few private centres in Sörmland County (population 265000), Sweden.
Was a consecutive or random sample of patients enrolled?	Yes

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 8928 (3481 males/5447 females), age groups: 0-10: N = 100; 11-20: N = 304; 21-30: N = 619; 31-40: N = 820; 41-50: N = 1103; 51-60: N = 1458; 61-70: N = 1550; 71-80: N = 1876; 81-90: N = 1006; 90+: N = 92. <u>Inclusion criteria:</u> All patients who between 2000-2005 had undergone faecal occult blood testing in one of the participating primary care centres. <u>Exclusion criteria:</u> Repeat faecal occult blood testing for the same individual. <u>Clinical setting:</u> Primary care, Sweden.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Faecal occult blood (Haemocult II test, 3 X; samples not rehydrated; read at the GP centre); ≥ 1 positive out of 3 regarded as a positive result
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up using the Swedish Cancer Registry; diagnosis of cancer within 2 years of faecal occult blood test
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 9048 patients were recruited, however 104 patients were excluded as they had adenoma (984), colorectal cancer diagnosis > 2 years after faecal occult blood test (19), or refused further investigation (1), which leaves 8944 patients as opposed to the 8928 included in the study. It is unclear what happened to the missing 16 patients.
Was there an appropriate interval between index test and reference standard?	Yes

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Low risk
NOTES	
Glaser (1989)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series from a private family practice
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 351; 149 males, 202 females; mean age = 57.9 years. <u>Inclusion criteria:</u> Patients who received a diagnostic sigmoidoscopy for a variety of clinical problems (e.g., rectal bleeding, abdominal pain or cramps, anaemia, change in bowel habits, hernia, constipation, proctalgia, weight loss, diarrhoea, pruritis ani, positive results of faecal occult blood test, rectal mass, palpable abdominal mass, condyloma, unusual flatulence, other) in which colorectal cancer or other significant disease was suspected in the author's private family practice between 1977 and 1986. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Canadian private family practice
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	Rigid sigmoidoscopy
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Barium enema or colonoscopy
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	High concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	High risk
NOTES	
Jensen (1993)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective? consecutive patient series from the Department of Radiology at Varberg Hospital, Sweden.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 149; 63 males, 86 females; mean age (range) = 64 (52-74) years. <u>Inclusion criteria:</u> All patients referred with symptoms of colorectal disease by general practitioners to the Department of Radiology, Varberg Hospital, Sweden, for a double-contrast enema. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Swedish department of radiology.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Faecal occult blood on 3 separate samples using the Hemoccult II test (≥ 1 positive test indicate a positive result); 60-cm rectosigmoidoscopy; double-contrast barium enema
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	

Reference standard(s)	3-5 year follow up in the local cancer register.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
<u>A. risk of bias</u>	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis? All test	Yes
Could the patient flow have introduced bias? All tests	Low risk
NOTES	
Kalra (1988)	
PATIENT SELECTION	
<u>A. risk of bias</u>	
Patient sampling	Retrospective consecutive patients who were referred for open access fibresigmoidoscopy in the UK.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Patient characteristics and setting	N = 541; male:female ratio = 35:65. Abdominal pain was the commonest cause of open access referral followed by diarrhoea, rectal bleeding and constipation. <u>Inclusion criteria:</u> All patients referred for fibresigmoidoscopy for the first time during 1982-6. Open access referrals were defined as patients seen for the first time during the procedure and in whom no examination or investigations had previously been undertaken. <u>Exclusion criteria:</u> Hospital inpatients, patients attending the outpatient department for colorectal symptoms in whom results of other investigations were available. <u>Clinical setting:</u> UK open access fibresigmoidoscopy clinic
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	

A. Risk of bias	
Index test	Fibresigmoidoscopy (examination was deemed as a failure if in the absence of disease the rectosigmoid junction could not be negotiated).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up and some barium enema/colonoscopy studies
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	High concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk
NOTES	2-by-2 cannot be extracted.
Kok (2012)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Data from the CEDAR (Cost-effectiveness of a decision rule for abdominal complaints in primary care) study, an ongoing, prospective, cross-sectional, diagnostic study in 170 general practices in 2 regions (central and south) of Holland.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient	N = 8928 (3481 males/5447 females), age groups: 0-10: N = 100; 11-20: N =

characteristics and setting	304; 21-30: N = 619; 31-40: N = 820; 41-50: N = 1103; 51-60: N = 1458; 61-70: N = 1550; 71-80: N = 1876; 81-90: N = 1006; 90+: N = 92. <u>Inclusion criteria:</u> Patients who between July 2009 – January 2011 consulted their GP for persistent (≥ 2 weeks) lower-abdomen complaints who also experienced ≥ 1 of the following: Rectal bleeding, altered defecation pattern, abdominal pain, fever, diarrhoea, weight loss, sudden onset in the elderly, or findings at physical examination suggestive of organic bowel disease (palpable abdominal or rectal mass). <u>Exclusion criteria:</u> Patients aged < 18 years, unable to give informed consent, previously diagnosed with organic bowel disease, or positive on triple faeces test (testing for intestinal parasites) not requiring endoscopy. <u>Clinical setting:</u> Primary care, Holland.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Faecal occult blood test (Clearview One Step immunochemical point of care test).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Colonoscopy (N = 351)/sigmoidoscopy (N = 21; other bowel examinations in N = 10)) with biopsies if required according to routine clinical practice + 3 month follow-up for all patients with an inconclusive colonoscopy/sigmoidoscopy.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	Data only available for 376/386 included patients.
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No

Could the patient flow have introduced bias?		Unclear risk
NOTES		
Leicester (1984)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective random selection of consecutive? patients from UK general practice.	
Was a consecutive or random sample of patients enrolled?	Yes probably	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?		Unclear risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 315; 121 males, 194 females; mean age (SD) = 58.2 (13.9) years, who were then randomly allocated to haemoccult testing or control. 161 patients (99.4%) in the haemoccult group complied with the testing and 24 tested positive.</p> <p><u>Inclusion criteria:</u> Patients aged > 40 years presenting in general practice with any abdominal or bowel complaints.</p> <p><u>Exclusion criteria:</u> None listed.</p> <p><u>Clinical setting:</u> UK GP</p>	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	Haemoccult testing	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	<p>Patients with a negative haemoccult test were managed conventionally by their GP including specialist referral, if appropriate. Patients with a positive haemoccult test underwent flexible sigmoidoscopy and double-contrast barium enema at the earliest opportunity, followed by urgent outpatient appointment and colonoscopy where indicated.</p>	
Is the reference standard likely to correctly classify the target condition?	Unclear	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk

B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		High concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing		
Was there an appropriate interval between index test and reference standard?		Unclear
Did all patients receive the same reference standard?		No
Were all patients included in the analysis?		Unclear
Could the patient flow have introduced bias?		High risk
NOTES	Published as abstract only. 2-by-2 table cannot be extracted	
Niv (1992)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective consecutive patient series from an open-access flexible sigmoidoscopy outpatient clinic in Israel.	
Was a consecutive or random sample of patients enrolled?		Yes
Was a case-control design avoided?		Yes
Did the study avoid inappropriate exclusions?		Yes
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 255; 123 males, 132 females; mean age (range) = 54 (10-90) years. The patients were referred with the following indications: Change in bowel habit (N = 103), rectal bleeding (N = 107), abdominal pain (N = 45), anaemia (3%), weight loss (N = 15), Fx colon cancer (N = 26), positive faecal occult blood test (N = 26), "post polyp." (N = 11).</p> <p><u>Inclusion criteria:</u> All patients referred for open-access flexible sigmoidoscopy by general practitioners.</p> <p><u>Exclusion criteria:</u> Bad state of health, referral error.</p> <p><u>Clinical setting:</u> Israeli open-access flexible sigmoidoscopy outpatient clinic.</p>	
Are there concerns that the included patients and setting do not match the review question?		Unclear concern
INDEX TEST		
A. Risk of bias		
Index test	Flexible sigmoidoscopy	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		

Reference standard(s)	When a polyp or cancer was found, the patient was referred for total colonoscopy. Negative results did not appear to be followed up.	
Is the reference standard likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk	
<u>B. Concerns regarding applicability</u>		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
<u>A. risk of bias</u>		
Flow and timing	As the negative results did not appear to be followed up, the false negative rate cannot be ascertained	
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	No	
Were all patients included in the analysis?	No	
Could the patient flow have introduced bias? All tests	High risk	
NOTES		
Steine (1993)		
PATIENT SELECTION		
<u>A. risk of bias</u>		
Patient sampling	Retrospective randomly selected patient series from the Central Roentgen Institute in Oslo, Norway.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
<u>B. Concerns regarding applicability</u>		
Patient characteristics and setting	N = 190; age range = 45-79 years. <u>Inclusion criteria:</u> Random sample (9%) of patients referred by GPs for double-contrast barium enema at the Central Roentgen Institute. <u>Exclusion criteria:</u> Patients not aged 45-79. <u>Clinical setting:</u> Norwegian roentgen institute.	
Are there concerns that the included patients and setting do not match the review question?	Unclear concern	
INDEX TEST		
<u>A. Risk of bias</u>		
Index test	Double-contrast barium enema	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test	Low risk	

have introduced bias?	
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Colonoscopy (with histology)
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias? All tests	Low risk
NOTES	One patient with anal cancer was not examined

Stellon (1997)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective? consecutive patient series from semi-rural UK general practice with a patient list between 2400-3400 during the study period.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 26; 5 males, 21 females; age range = 51-87 years. <u>Inclusion criteria:</u> All patients aged > 50 years found to have iron deficiency anaemia (< 12 g/dl haemoglobin and/or mean corpuscular volume < 80 fl with ferritin ≤ 16 ng/l) between January 1989 and March 1994. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> UK GP
Are there concerns that the included patients and setting	Low concern

do not match the review question?		
INDEX TEST		
A. Risk of bias		
Index test	Faecal occult blood on 3 separate samples using the haemocult test; flexible sigmoidoscopy; double-contrast barium enema	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up during 5 year study period.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	22/26 patients received the faecal occult blood test (FOB); 22/26 patients received double contrast barium enema (BE); 26/26 patients received the flexible sigmoidoscopy (FS).	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis? FOB	No	
Were all patients included in the analysis? BE	No	
Were all patients included in the analysis? FS	Yes	
Could the patient flow have introduced bias? FOB	High risk	
Could the patient flow have introduced bias? BE	High risk	
Could the patient flow have introduced bias? FS	Low risk	
NOTES		

References

Included studies

Fijten, G. H., Starmans, R., Muris, J. W., Schouten, H. J., Blijham, G. H., and Knottnerus, J. A. Predictive value of signs and symptoms for colorectal cancer in patients with rectal bleeding in general practice. *Family Practice* 12[3], 279-286. 1995.

- Gillberg, A., Ericsson, E., Granstrom, F., and Olsson, L. I. A population-based audit of the clinical use of faecal occult blood testing in primary care for colorectal cancer. *Colorectal Disease* 14[9], e539-e546. 2012.
- Glaser, S. R. Sigmoidoscopy in general practice. *Canadian Family Physician* 35, 2243-2246. 1989.
- Jensen, J., Kewenter, J., and Swedenborg, J. The correlation of symptoms, occult blood tests, and neoplasms in patients referred for double-contrast barium enema. [Review] [15 refs]. *Scandinavian Journal of Gastroenterology* 28[10], 911-914. 1993.
- Kalra, L., Price, W. R., Jones, B. J., and Hamlyn, A. N. Open access fibresigmoidoscopy: a comparative audit of efficacy. *British Medical Journal Clinical Research Ed.* 296[6629], 1095-1096. 16-4-1988.
- Kok, L., Elias, S. G., Witteman, B. J. M., Goedhard, J. G., Muris, J. W. M., Moons, K. G. M., and De Wit, N. J. Diagnostic accuracy of point-of-care fecal calprotectin and immunochemical occult blood tests for diagnosis of organic bowel disease in primary care: The cost-effectiveness of a decision rule for abdominal complaints in primary care (CEDAR) study. *Clinical Chemistry* 58[6], 989-998. 2012.
- Leicester, R. J., Colin-Jones, D. G., Hunt, R. H., Millar, J., and Leicester, R. J. Haemoccult testing in general practice for early diagnosis of colorectal cancer. *Gut* 25[5], A561. 1984.
- Niv, Y. and Asaf, V. Open-access, flexible, fiberoptic sigmoidoscopy in a regional primary-care clinic. [Review] [9 refs]. *Journal of Clinical Gastroenterology* 15[3], 218-221. 1992.
- Steine, S., Stordahl, A., Lunde, O. C., Loken, K., and Laerum, E. Double-contrast barium enema versus colonoscopy in the diagnosis of neoplastic disorders: aspects of decision-making in general practice. *Family Practice* 10[3], 288-291. 1993.
- Stellon, A. J. and Kenwright, S. E. Iron deficiency anaemia in general practice: Presentations and investigations. *British Journal of Clinical Practice* 51[2], 78-80. 1997.

Excluded studies (with excl reason)

- (1935) New test provides ease in detecting colon cancer. *Dentistry Today*, 19: 32.
Narrative review
- (2005) Summaries for patients. What is the best way to test for colorectal cancer?. [Original report in *Ann Intern Med.* 2005 Jan 18;142(2):81-5; PMID: 15657155]. *Annals of Internal Medicine*, 142: 123.
Not in PICO
- (2009) The Dutch College of General Practitioners guideline for rectal bleeding. [Dutch]. *Huisarts en Wetenschap*, 52: 23-38.
Guideline
- (2011) Colorectal carcinoma - The acceptance of early diagnosis with CT colonography increases?. [German]. *RoFo Fortschritte auf dem Gebiet der Rontgenstrahlen und der Bildgebenden Verfahren*, 183: 330.
Not in PICO
- (2013) EUS-guided deep biopsy and EMR in the early diagnosis and treatment of rectal carcinoid tumors. *Journal of Gastroenterology and Hepatology*, 28: 718-719.
Not in PICO
- (2014) If you want to avoid colonoscopy, you still have effective options. Colonoscopy is best for early colorectal cancer prevention, but stool testing also works pretty well if you have it every year. *Harvard men's health watch*, 18: 4-5.
Narrative review
- (2014) - If you want to avoid colonoscopy, you still have effective options. Colonoscopy is best for early colorectal cancer prevention, but stool testing also works pretty well if you have it every year. - *Harvard Mens Health Watch*, 18: 4-5.
Duplicate

- Abdel Razek, A. A., Abu Zeid, M. M., Bilal, M. & Abdel Wahab, N. M. (2005) Virtual CT colonoscopy versus conventional colonoscopy: a prospective study. *Hepato-Gastroenterology*, 52: 1698-1702.
Not in PICO
- Acher, P. L., Al-Mishlab, T., Rahman, M. & Bates, T. (2003) Iron-deficiency anaemia and delay in the diagnosis of colorectal cancer. *Colorectal Disease*, 5: 145-148.
Not in PICO
- Adelstein, B. A., Macaskill, P., Chan, S. F., Katelaris, P. H. & Irwig, L. (2011) Most bowel cancer symptoms do not indicate colorectal cancer and polyps: a systematic review. [Review]. *BMC Gastroenterology*, 11: 65.
Not in PICO
- Ahnen, D. J., Wade, S. W., Jones, W. F., Sifri, R., Mendoza, S. J., Greenamyre, J., Guiffre, S., Axilbund, J., Spiegel, A. & You, Y. N. (2014) The increasing incidence of young-onset colorectal cancer: a call to action. *Mayo Clinic Proceedings*, 89: 216-224.
Narrative review
- Akhtar, M., Boshnaq, M., Creamer, A., Doughan, S. & Marzouk, D. (2013) Assessment of efficiency of tissue biopsy process in the diagnosis of rectal cancer; current practice and the outcome. *Colorectal Disease*, 15: 66.
Not in PICO
- Aljarabah, M. M., Borley, N. R., Goodman, A. J. & Wheeler, J. M. (2009) Referral letters for 2-week wait suspected colorectal cancer do not allow a 'straight-to-test' pathway. *Annals of the Royal College of Surgeons of England*, 91: 106-109.
Not in PICO
- Allen, J. I. (2010) Maximizing the value of colonoscopy in community practice. [Review]. *Gastrointestinal Endoscopy Clinics of North America*, 20: 771-781.
Narrative review
- Alonso-Abreu, I., Alarcon-Fernandez, O., Gonzalez-Mendez, Y., Jimenez-Sosa, A. & Quintero, E. (2010) Diagnostic predictive value of indications for prompt referral colonoscopy. *Gastroenterology*, 138: S285-S286.
Not in PICO
- An, J. W., Cheung, D. Y., Seo, M. W., Lee, H. J., Lee, I. K., Kim, T. J., Kim, J. I. & Kim, J. K. (2013) [A case of spindle cell carcinoma of the stomach presenting with hematochezia and weight loss due to fistulous tract formation with colon]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 62: 126-130.
Not in PICO
- Ang, C. W., Dawson, R., Hall, C. & Farmer, M. (2008) The diagnostic value of digital rectal examination in primary care for palpable rectal tumour. *Colorectal Disease*, 10: 789-792.
Not in PICO
- Ares, D. M., Barrenechea, I. M. G., Souto-Ruzo, J., Lopez, J. Y., Peral, A. P. & Vazquez-Iglesias, J. L. (2005) The value of abdominal ultrasound in the diagnosis of colon cancer. [Spanish, English]. *Revista Espanola de Enfermedades Digestivas*, 97: 877-886.
Not in PICO
- Ares, D. M., Aguirre, P. A. A., Barrenechea, I. M. G., Gomez, L. C. & Peral, A. P. (2008) Usefulness of ultrasonography in diagnosing patients suspect for digestive tract neoplasms. *Revista Espanola de Enfermedades Digestivas*, 100: 545-551.
Not in PICO
- Arumugam, P. J., Rao, G. N., West, J., Foster, M. E. & Haray, P. N. (2000) The impact of open access flexible sigmoidoscopy: a comparison of two services. *Journal of the Royal College of Surgeons of Edinburgh*, 45: 366-368.
Not in PICO

- Ata, R. M. (2013) Clinical and histopathologic profile of patients with early & late-onset colorectal cancer. *Journal of Gastroenterology and Hepatology*, 28: 110.
Not in PICO
- Atkin, W., Dadswell, E., Wooldrage, K., Kralj-Hans, I., von, W. C., Edwards, R., Yao, G., Kay, C., Burling, D., Faiz, O., Teare, J., Lilford, R. J., Morton, D., Wardle, J., Halligan, S. & SIGGAR, i. (2013) Computed tomographic colonography versus colonoscopy for investigation of patients with symptoms suggestive of colorectal cancer (SIGGAR): a multicentre randomised trial. *Lancet*, 381: 1194-1202.
Same as Halligan 2013
- Bacigalupo, L. & Paparo, F. (2014) Imaging for suspected colorectal cancer in frail and elderly patients. *Techniques in Coloproctology*, 18: 125-127.
Narrative review
- Badger, S. A., Gilliland, R. & Neilly, P. J. D. (2005) The effectiveness of flexible sigmoidoscopy as the primary method for investigating colorectal symptoms in low-risk patients. *Surgical Endoscopy and Other Interventional Techniques*, 19: 1349-1352.
Not in PICO
- Badiani, S., Hernandez, S. T., Karandikar, S. & Roy-Choudhury, S. (2011) CT Colonography to exclude colorectal cancer in symptomatic patients. *European Radiology*, 21: 2029-2038.
Not in PICO
- Badiani, S., Desai, A. & Chapman, M. A. (2012) Is whole colonic imaging necessary for symptoms of change in bowel habit and/or rectal bleeding? *Colorectal Disease*, 14: 1197-1200.
Not in PICO
- Bafandeh, Y., Khoshbaten, M., Eftekhari-Sadat, A. T. & Farhang, S. (2007) Colorectal neoplasms in symptomatic patients without evidence of bleeding: a prospective study in an Iranian population. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 8: 485-488.
Not in PICO
- Barosi, G., Marchetti, M., Dazzi, L. & Quaglini, S. (1997) Testing for occult cancer in patients with idiopathic deep vein thrombosis--a decision analysis. *Thrombosis & Haemostasis*, 78: 1319-1326.
Not in PICO
- Barrett, J., Jiwa, M., Rose, P. & Hamilton, W. (2006) Pathways to the diagnosis of colorectal cancer: an observational study in three UK cities. *Family Practice*, 23: 15-19.
Not in PICO
- Beggs, A. D., Bhate, R. D., Irukulla, S., Achiek, M. & Abulafi, A. M. (2011) Straight to colonoscopy: the ideal patient pathway for the 2-week suspected cancer referrals? *Annals of the Royal College of Surgeons of England*, 93: 114-119.
Not in PICO
- Bekkink, M. O., McCowan, C., Falk, G. A., Teljeur, C., Van de Laar, F. A. & Fahey, T. (2010) Diagnostic accuracy systematic review of rectal bleeding in combination with other symptoms, signs and tests in relation to colorectal cancer. *British Journal of Cancer*, 102: 48-58.
Presents no data in PICO
- Bellentani, S., Baldoni, P., Petrella, S., Tata, C., Armocida, C., Marchegiano, P., Saccoccio, G. & Manenti, F. (1990) A simple score for the identification of patients at high risk of organic diseases of the colon in the family doctor consulting room. The Local IBS Study Group. *Family Practice*, 7: 307-312.
Not in PICO
- Berger, M., De, W. N., Vogelenzang, R., Wetzels, R., Van Rijn-Van, K. N. & Opstelten, W. (2011) The NHG guideline diverticulitis. [Dutch]. *Huisarts en Wetenschap*, 54: 492-499.
Not in PICO
- Bhangu, A., Khan, M., Roberts, L., Reynolds, A., Desai, A. & Mathew, G. (2011) Detection and survival of colorectal cancer from a 2 week wait service. *Surgeon Journal of the Royal Colleges of Surgeons*

- of *Edinburgh & Ireland*, 9: 78-82.
Not in PICO
- Bhargava, A., Aldameh, A., Stewart, J. & Hill, A. G. (2007) Prioritization of patients with rectal bleeding for urgent outpatient colonoscopy--a pilot study. *New Zealand Medical Journal*, 120: U2637.
Not in PICO
- Biswas, S., Willington, A. & Ellis, A. J. (2013) Impact of primary care education on the two week wait referral process for GI cancers. *Gastroenterology*, 144: S581-S582.
Not in PICO
- Bjerregaard, N. C., Tottrup, A., Sorensen, H. T. & Laurberg, S. (2009) Detection of colorectal cancer in symptomatic outpatients without visible rectal bleeding: Validity of the fecal occult blood test. *Clinical Epidemiology*, 1: 119-124.
Not in PICO
- Blaylock, B., Hay, J. & Zarchy, T. (2012) The cost-effectiveness of diagnostic sigmoidoscopy before colonoscopy in 40 to 49-year-old symptomatic patients. *Value in Health*, 15: A67.
Not in PICO
- Boellaard, T. N., De Haan, M. C., Venema, H. W. & Stoker, J. (2013) Colon distension and scan protocol for CT-colonography: An overview. *European Journal of Radiology*, 82: 1144-1158.
Narrative review
- Boffa, C., Wright, H., Nickinson, A., Barker, T., Lamparelli, M. & Lewis, M. (2012) The effect of the bowel cancer symptoms pilot media campaign on colorectal referrals to a district general hospital. *Colorectal Disease*, 14: 37-38.
Not in PICO
- Bolton-Obubi, R., Itobi, E., Shata, M., Miles, A. J. G. & Gore, D. M. (2010) A one-stop flexible sigmoidoscopy clinic significantly reduces time to definitive treatment decision in patients with distal bowel cancer. *Colorectal Disease*, 12: 16.
Not in PICO
- Bond, J. H. (2000) Is referral for colonoscopy underutilized by primary care physicians? *Gastrointestinal Endoscopy*, 52: 693-696.
Editorial/narrative review
- Borhan-Manesh, F. (2009) "Low caliber stool" and "pencil thin stool" are not signs of colo-rectal cancer. [Review] [30 refs]. *Digestive Diseases & Sciences*, 54: 208-211.
Narrative review
- Borjeson, S., Starkhammar, H., Unosson, M. & Bertero, C. (2012) Common Symptoms and Distress Experienced Among Patients with Colorectal Cancer: A Qualitative part of Mixed Method Design. *The Open Nursing Journal*, 6: 100-107.
Not in PICO
- Boulos, P. B., Cowin, A. P., Karamanolis, D. G. & Clark, C. G. (1985) Diverticula, neoplasia, or both? Early detection of carcinoma in sigmoid diverticular disease. *Annals of Surgery*, 202: 607-609.
Not in PICO
- Brown, J. S. (1984) Sigmoidoscopy in general practice. *Practitioner*, 228: 837-839.
Not in PICO (no reference test)
- Budzynski, J., Manerowski, M. & Swiatkowski, M. (2007) The neoplasms of digestive tract in patients referred with abdominal tumor suspicion by family doctors to gastroenterology department in 2006. [Polish]. *Family Medicine and Primary Care Review*, 9: 378-380.
Not in PICO
- Bull-Henry, K. & Al-Kawas, F. H. (2013) Evaluation of occult gastrointestinal bleeding. *American Family Physician*, 87: 430-436.
Narrative review

- Bulow, S. & Christensen, I. J. (2001) Flexible sigmoidoscopy as the primary examination in patients with bowel symptoms. [Danish]. *Ugeskrift for Laeger*, 163: 6573-6576.
Not in PICO (referred patients)
- Butt, S. K., Jaggs, K., Warren, S., Francis, D., Ward, M., Klein, M., Van, S. N. & Besherdas, K. (2009) How accurate is an endoscopist's hunch for cancer? Correlation with histology. *Gut*, 58: A92.
Not in PICO
- Butt, S. K. & Besherdas, K. (2014) How rewarding is gastroscopy in diagnosis of cancer in isolated iron deficiency anaemia? *Gut*, 63: A59-A60.
Published as abstract only. Not enough information can be extracted to ascertain final relevance, but it appears to be not in PICO
- Cabrera-Abreu, J. C., Smellie, W. S. A., Bowley, R. & Shaw, N. (2012) Best practice in primary care pathology: review 13. *Journal of Clinical Pathology*, 65: 97-100.
Not in PICO
- Cappell, M. S. (2003) Colon cancer during pregnancy. [Review] [323 refs]. *Gastroenterology Clinics of North America*, 32: 341-383.
Not in PICO
- Cash, B. D., Riddle, M. S., Bhattacharya, I., Barlow, D., Jensen, D., del Pino, N. M. & Pickhardt, P. J. (2012) CT colonography of a Medicare-aged population: outcomes observed in an analysis of more than 1400 patients. *AJR.American Journal of Roentgenology*, 199: W27-W34.
Not in PICO
- Castiglione, G., Pacini, F., Palli, D., Fucini, C., Ciani, P., D'Albasio, G. & Falorni, P. (1987) Haemocult test and a self-administered questionnaire in the early diagnosis of colorectal cancer. *Italian Journal of Gastroenterology*, 19: 83-86.
Mixed symptomatic/asymptomatic population; cannot extract the information for symptomatic patients only; large number did not receive reference standard
- Chan, T. H. & Goh, K. L. (2006) Appropriateness of colonoscopy using the ASGE guidelines: experience in a large Asian hospital. *Chinese Journal of Digestive Diseases*, 7: 24-32.
Not in PICO
- Chatt, C., Khalid, S., Budhoo, M., Roy-Choudhury, S. & Karandikar, S. (2010) What is the ideal investigation for patients referred via rapid access with suspected colorectal cancer? *Colorectal Disease*, 12: 16.
Not in PICO
- Chiao, H., Tsai, F. & Strum, W. (2013) Risks for advanced adenomas in patients with a positive family history of sporadic colorectal cancer have a bimodal age distribution. *American Journal of Gastroenterology*, 108: S171.
Not in PICO
- Choi, Y., Choi, H. S., Jeon, W. K., Kim, B. I., Park, D. I., Cho, Y. K., Kim, H. J., Park, J. H. & Sohn, C. I. (2012) Optimal number of endoscopic biopsies in diagnosis of advanced gastric and colorectal cancer. *Journal of Korean Medical Science*, 27: 36-39.
Not in PICO
- Clark, K., Smith, J. M. & Currow, D. C. (2012) The prevalence of bowel problems reported in a palliative care population. *Journal of Pain & Symptom Management*, 43: 993-1000.
Not in PICO
- Courtney, R. J., Paul, C. L., Sanson-Fisher, R. W., Macrae, F. A., Attia, J. & McEvoy, M. (2012) Factors associated with consultation behaviour for primary symptoms potentially indicating colorectal cancer: a cross-sectional study on response to symptoms. *BMC Gastroenterology*, 12: 100.
Not in PICO
- Crespi, M. (2001) [Diagnostic strategies for the early detection of colorectal tumors: a critical analysis]. [Italian]. *Tumori*, 87: Suppl-Feb.
Narrative review

- Cubiella, J., Salve, M., Diaz-Ondina, M., Vega, P., Alves, M. T., Iglesias, F., Sanchez, E., Macia, P., Blanco, I., Bujanda, L. & Fernandez-Seara, J. (2014) Diagnostic accuracy of the faecal immunochemical test for colorectal cancer in symptomatic patients: Comparison with NICE and SIGN referral criteria. *Colorectal Disease*, 16: O273-O282.
Not in PICO (only 17.5% primary care patients)
- Cubiella, J., Salve, M., Diaz-Ondina, M., Vega, P., Alves, M. T., Iglesias, F., Sanchez, E., Macia, P., Blanco, I., Bujanda, L. & Fernandez-Seara, J. (2014) - Diagnostic accuracy of the faecal immunochemical test for colorectal cancer in symptomatic patients: comparison with NICE and SIGN referral criteria. - *Colorectal Disease*, 16: O273-O282.
Duplicate
- De Boer, E. M., Pincock, D. & Van Zanten, S. V. (2012) The 'natural history' of declined outpatient gastroenterology referrals. *Canadian Journal of Gastroenterology*, 26: 785-790.
Not in PICO
- de, B., V, Froehlich, F., Rey, J. P., Thorens, J., Schneider, C., Wietlisbach, V., Vader, J. P., Burnand, B., Muhlhaupt, B., Fried, M. & Gonvers, J. J. (2002) Do explicit appropriateness criteria enhance the diagnostic yield of colonoscopy? *Endoscopy*, 34: 360-368.
Not in PICO
- de, J. E., Numans, M. E., de Wit, N. J., Heemstra-Borst, C. G., Geijer, R. M. & Burgers, J. S. (2013) [Summary of the Dutch College of General Practitioners' (NHG) practice guideline 'Gastric symptoms']. [Review] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 157: A6101.
Narrative review/guideline
- Demers, R. Y., Neale, A. V., Budev, H. & Schade, W. J. (1990) Pathologist agreement in the interpretation of colorectal polyps. *American Journal of Gastroenterology*, 85: 417-421.
Not in PICO
- Deng, S. X., An, W., Gao, J., Yin, J., Cai, Q. C., Yang, M., Hong, S. Y., Fu, X. X., Yu, E. D., Xu, X. D., Zhu, W. & Li, Z. S. (2012) Factors influencing diagnosis of colorectal cancer: a hospital-based survey in China. *Journal of Digestive Diseases*, 13: 517-524.
Not in PICO
- Diaz, O. M., Blanco Vila, M. I., Ceballos, O. S., Salve, B. M., Macia, C. P. & Cubiella, F. J. (2014) Clinical or analytical criteria for colorectal cancer (CRC) detection in symptomatic patients? A diagnostic tests study. *Clinical Chemistry and Laboratory Medicine*, 52: S384.
Published as abstract only. Not enough information can be extracted to ascertain final relevance, but it appears to be not in PICO
- Dominguez-Ayala, M., Diez-Vallejo, J. & Comas-Fuentes, A. (2012) Missed opportunities in early diagnosis of symptomatic colorectal cancer. *Revista Espanola de Enfermedades Digestivas*, 104: 343-349.
Not in PICO
- Donald, I. P., Fitzgerald Frazer, J. S. & Wilkinson, S. P. (1985) Sigmoidoscopy/proctoscopy service with open access to general practitioners. *British Medical Journal Clinical Research Ed.*, 290: 759-761.
Not in PICO
- Dozois, E. J., Boardman, L. A., Suwanthanma, W., Limburg, P. J., Cima, R. R., Bakken, J. L., Vierkant, R. A., Aakre, J. A. & Larson, D. W. (2008) Young-onset colorectal cancer in patients with no known genetic predisposition: can we increase early recognition and improve outcome? *Medicine*, 87: 259-263.
Not in PICO
- Dregan, A., Moller, H., Charlton, J. & Gulliford, M. C. (2013) Are alarm symptoms predictive of cancer survival? Population-based cohort study. *British Journal of General Practice*, 63: e807-e812.
Not in PICO

- du, T. J. (1916) Assessing patients for risk of colorectal cancer in primary care. [Review] [27 refs]. *Practitioner*, 250: 6-8.
Narrative review
- Dua, R. S., Brown, V. S., Loukogeorgakis, S. P., Kallis, G. & Meleagros, L. (2009) The two-week rule in colorectal cancer. Can it deliver its promise? *International Journal Of Surgery*, 7: 521-525.
Not in PICO
- Duff, S. E., Murray, D., Rate, A. J., Richards, D. M. & Kumar, N. A. (2006) Computed tomographic colonography (CTC) performance: one-year clinical follow-up. *Clinical Radiology*, 61: 932-936.
Not in PICO
- Eickhoff, A., Maar, C., Birkner, B. & Riemann, J. F. (2003) [Colorectal cancer in Germany. Means for prevention and early detection: implications for laity and physicians]. [German]. *Internist*, 44: 278-6.
Not in PICO
- Eickhoff, A., Bechtler, M. & Riemann, J. F. (2009) Early diagnosis of colorectal cancer - Current procedures: Colonoscopy, feces test, radiology. [German]. *Best Practice Onkologie*, 4: 4-14.
Narrative review
- Eladawy, M., Dominguez, S. R., Anderson, M. S. & Glode, M. P. (2013) Kawasaki disease and the pediatric gastroenterologist: a diagnostic challenge. *Journal of Pediatric Gastroenterology & Nutrition*, 56: 297-299.
Not in PICO
- Elliot, M. S., Levenstein, J. H. & Wright, J. P. (1984) Faecal occult blood testing in the detection of colorectal cancer. *British Journal of Surgery*, 71: 785-786.
Not in PICO (asymptomatic)
- Ellis, B. G. & Thompson, M. R. (2005) Factors identifying higher risk rectal bleeding in general practice. *British Journal of General Practice*, 55: 949-955.
Not in PICO
- Elmi, A., Hedgire, S. S., Pargaonkar, V., Cao, K., McDermott, S. & Harisinghani, M. (2013) Is early colonoscopy beneficial in patients with CT-diagnosed diverticulitis? *AJR.American Journal of Roentgenology*, 200: 1269-1274.
Not in PICO
- Encinas, S. A., Zufia, G. J. & Cano Lopez, J. M. (1994) [Colorectal cancer. A current perspective from the primary care viewpoint]. [Spanish]. *Atencion Primaria*, 13: 324-330.
Not in PICO
- Eskaros, S., Ghevariya, V., Diamond, I. & Anand, S. (2009) Correlation of incidental colorectal wall thickening at CT compared to colonoscopy. *Emergency Radiology*, 16: 473-476.
Not in PICO
- Esteva, M., Leiva, A., Ramos, M., Pita-Fernandez, S., Gonzalez-Lujan, L., Casamitjana, M., Sanchez, M. A., Pertega-Diaz, S., Ruiz, A., Gonzalez-Santamaria, P., Martin-Rabadan, M., Costa-Alcaraz, A. M., Espi, A., Macia, F., Segura, J. M., Lafita, S., Arnal-Monreal, F., Amengual, I., Bosca-Watts, M. M., Hospital, A., Manzano, H., Magallon, R. & DECCIRE GROUP (2013) Factors related with symptom duration until diagnosis and treatment of symptomatic colorectal cancer. *BMC Cancer*, 13: 87.
Not in PICO
- Evans, P. W. (1987) A sigmoidoscope in the practice. *Practitioner*, 231: 189-195.
Narrative review
- Ferguson, H. J. M., Mak, T., Royle, T. J., Simpson, J. & Bhalerao, S. (2010) The RADAR one-stop clinic for suspected colorectal cancer: An analysis of 1690 patients. *Colorectal Disease*, 12: 17.
Not in PICO
- Fisch, M. J., Zhao, F., O'Mara, A. M., Wang, X. S., Cella, D. & Cleeland, C. S. (2014) Predictors of significant worsening of patient-reported fatigue over a 1-month timeframe in ambulatory patients with common solid tumors. *Cancer*, 120: 442-450.
Not in PICO

- Ford, A. C., van Zanten, S. J. O. V., Rodgers, C. C., Talley, N. J., Vakil, N. B. & Moayyedi, P. (2008) Diagnostic utility of alarm features for colorectal cancer: systematic review and meta-analysis. *Gut*, 57: 1545-1552.
Not in PICO
- Ford, A. C. & Moayyedi, P. (2013) Dyspepsia. *BMJ (Online)*, 347.
Narrative review
- Fotiadis, C., Genetzakis, M., Tsekouras, D. K. & Zografos, G. (2005) Synchronous colorectal carcinoma. A review article. [Greek]. *Archives of Hellenic Medicine*, 22: 571-574.
Not in PICO
- Gardner, H. J. (1986) Flexible sigmoidoscopy in the primary care setting. *Primary Care; Clinics in Office Practice*, 13: 543-547.
Narrative review
- Ghafoor, A., Jan, M. A. & Bokhari, H. (1998) Clinical presentation and diagnosis of colorectal cancer. *Journal of the College of Physicians and Surgeons Pakistan*, 8: 126-128.
Not in PICO
- Glancy, D. G., Card, M., Sylvester, P. A., Thomas, M. G., Durdey, P., Callaway, M. & Virjee, J. (2005) Fast-track barium enema: meeting the two-week wait rule for patients with suspected colorectal cancer. *Colorectal Disease*, 7: 241-244.
Not in PICO
- Goulston, K. J., Cook, I. & Dent, O. F. (1986) How important is rectal bleeding in the diagnosis of bowel cancer and polyps? *Lancet*, 2: 261-265.
Not in PICO
- Graffner, H., Hallin, E., Stridbeck, H. & Nilsson, J. (1986) The frequency of digital and endoscopic examination of the rectum before radiological barium enema. *Scandinavian Journal of Primary Health Care*, 4: 249-251.
Not in PICO
- Grassini, M., Verna, C., Niola, P., Navino, M., Battaglia, E. & Bassotti, G. (2007) Appropriateness of colonoscopy: Diagnostic yield and safety in guidelines. *World Journal of Gastroenterology*, 13: 1816-1819.
Not in PICO
- Griggs, R., Cork, T. & Robertson, C. (2013) Rigid sigmoidoscopy: A dinosaur diagnostic tool? *International Journal of Surgery*, 11: 626.
Abstract only, not enough information can be extracted to ascertain relevance, but I think it is not in PICO.
- Grzebieniak, Z., Agrawal, A. K., Kielan, W., Winowski, J., Marek, G. & Grzebieniak, T. (2008) The role of primary health care physician in diagnosis and treatment of colorectal cancer. [Polish]. *Family Medicine and Primary Care Review*, 10: 839-841.
Narrative review
- Grzebieniak, Z., Kielan, W., Winowski, J., Agrawal, A. K., Marek, G., Duda, L. & Niepokoj, A. (2010) Primary health care physician's tasks in dealing with the most common diseases of anus. [Polish]. *Family Medicine and Primary Care Review*, 12: 347-350.
Narrative review
- Guillem, J. G., Forde, K. A., Treat, M. R., Neugut, A. I. & Bodian, C. A. (1987) The impact of colonoscopy on the early detection of colonic neoplasms in patients with rectal bleeding. *Annals of Surgery*, 206: 606-611.
Not in PICO
- Gunnarsson, J. & Simren, M. (2008) Efficient diagnosis of suspected functional bowel disorders. *Nature Clinical Practice Gastroenterology & Hepatology*, 5: 498-507.
Narrative review
- Ha, T. H., Jeon, T. J., Park, J. Y., Jang, Y. H., Kim, D. H., Ryu, M. J., Sinn, D. H. & Oh, T. H. (2013) [A case of basaloid squamous cell carcinoma of rectosigmoid colon]. [Korean]. *Korean Journal of*

Gastroenterology/Taehan Sohwagi Hakhoe Chi, 62: 375-378.

Not in PICO

Halligan, S., Altman, D. G., Taylor, S. A., Mallett, S., Deeks, J. J., Bartram, C. I. & Atkin, W. (2005) CT colonography in the detection of colorectal polyps and cancer: systematic review, meta-analysis, and proposed minimum data set for study level reporting. [Review] [83 refs]. *Radiology*, 237: 893-904.

Not in PICO

Halligan, S., Lilford, R. J., Wardle, J., Morton, D., Rogers, P., Wooldrage, K., Edwards, R., Kanani, R., Shah, U. & Atkin, W. (2007) Design of a multicentre randomized trial to evaluate CT colonography versus colonoscopy or barium enema for diagnosis of colonic cancer in older symptomatic patients: The SIGGAR study. *Trials*, 8.

Protocol

Halligan, S., Wooldrage, K., Dadswell, E., Kralj-Hans, I., von, W. C., Edwards, R., Yao, G., Kay, C., Burling, D., Faiz, O., Teare, J., Lilford, R. J., Morton, D., Wardle, J., Atkin, W. & SIGGAR, i. (2013) Computed tomographic colonography versus barium enema for diagnosis of colorectal cancer or large polyps in symptomatic patients (SIGGAR): a multicentre randomised trial. *Lancet*, 381: 1185-1193.

Not in PICO (referred population)

Halligan, S. (2013) CT colonography for investigation of patients with symptoms potentially suggestive of colorectal cancer: a review of the UK SIGGAR trials. [Review]. *British Journal of Radiology*, 86: 20130137.

Narrative review

Halligan, S. & Atkin, W. S. (2013) CT colonography for diagnosis of symptomatic colorectal cancer: The SIGGAR trials and their implication for service delivery. *Clinical Radiology*, 68: 643-645.

Same as Halligan 2013

Hardcastle, J. D. & Vellacott, K. D. (1982) Colorectal cancer. Early diagnosis and detection. *Recent Results in Cancer Research*, 83: 86-100.

Narrative review

Haykir, R., Karakose, S., Karabacakoglu, A., Kayacetin, E. & Sahin, M. (2006) Detection of colonic masses with MR colonography. *Turkish Journal of Gastroenterology*, 17: 191-197.

Test not in PICO

Heap, T. (1996) Managing diarrhoea. Current thinking. [Review] [11 refs]. *Australian Family Physician*, 25: 38-45.

Narrative review

Hewett, D. G. & Rex, D. K. (2011) Colonoscopy and diminutive polyps: hot or cold biopsy or snare? Do I send to pathology? *Clinical Gastroenterology & Hepatology*, 9: 102-105.

Narrative review

Hodder, R. J., Ballal, M., Selvachandran, S. N. & Cade, D. (2005) Variations in the evaluation of colorectal cancer risk. *Colorectal Disease*, 7: 254-262.

Not in PICO

Hogberg, C., Karling, P., Rutegard, J., Lilja, M. & Ljung, T. (2013) Immunochemical faecal occult blood tests in primary care and the risk of delay in the diagnosis of colorectal cancer. *Scandinavian Journal of Primary Health Care*, 31: 209-214.

Not in PICO

Hovendal, C. P., Kronborg, O., Hem, J., Grinsted, P. & Fenger, C. (1990) Rectoscopy and Hemoccult II in irritable colon. A prospective study. [Danish]. *Ugeskrift for Laeger*, 152: 2732-2734.

Not in PICO

Hsiang, J. C., Bai, W. & Lal, D. (2013) Symptom presentations and other characteristics of colorectal cancer patients and the diagnostic performance of the Auckland Regional Grading Criteria for Suspected Colorectal Cancer in the South Auckland population. *New Zealand Medical Journal*,

126: 95-107.

Not in PICO

Humphries, A., Clarke, J., Bhatnagar, G., Jenkins, I., Burling, D. & Thomas-Gibson, S. (2013) A new lower gastrointestinal 2-week wait -direct to test' pathway results in earlier diagnosis of cancer. *Gut*, 62: A262.

Not in PICO

Iseli, A. (1999) Sigmoidoscopy. Is it a general practice procedure? *Australian Family Physician*, 28: 61-64.

Narrative review

Ivanova, A., Iarumov, N., Toshev, S., Adzharov, D., Krustev, Z., Angelov, K., Sokolov, M. & Gribnev, P. (2007) Pilot study on M2-PK-- a new non-invasive parameter for early diagnosis of colorectal carcinoma. [Bulgarian]. *Khirurgiia*, 5-7.

Not in PICO

Jacob, B. J., Moineddin, R., Sutradhar, R., Baxter, N. N. & Urbach, D. R. (2012) Effect of colonoscopy on colorectal cancer incidence and mortality: an instrumental variable analysis. *Gastrointestinal Endoscopy*, 76: 355-364.

Not in PICO

Janda, M., Hughes, K., Tong, S., Stanton, W. R., Aitken, J., Clavarino, A., Short, L., Del, M. C., Leggett, B. & Newman, B. (2002) Faecal occult blood test: current practice in a rural Queensland community. *Australian Journal of Rural Health*, 10: 57-64.

Not in PICO

Jellema, P., Windt, D. A., Bruinvels, D. J., Mallen, C. D., Weyenberg, S. J., Mulder, C. J. & Vet, H. C. (2010) Value of symptoms and additional diagnostic tests for colorectal cancer in primary care: systematic review and meta-analysis (DARE structured abstract). *BMJ*, 340:c1269.

SR, but no meta-analysis. The relevant included studies will be assessed separately.

Jiang, X., Yuan, Y. P., Xu, D. T., Zhang, B. & Liu, Y. L. (2011) [Influences of diagnostic modes on an early diagnosis of colorectal cancer]. [Chinese]. *Chung-Hua i Hsueh Tsa Chih [Chinese Medical Journal]*, 91: 2886-2890.

Not in PICO

Jin, P., Wu, Z., Meng, M., Wang, X., Gong, L., Yu, D., Xie, H., Li, A., Li, S., Yen, L., Rao, J. & Sheng, J. (2012) Combined fecal transferrin test and immuno fecal occult blood test for detecting colorectal cancer and advanced adenoma in asymptomatic and symptomatic populations. *Journal of Cancer Science and Therapy*, 4: 243-248.

Not in PICO (think referred population)

Jiwa, M., Gordon, M., Skinner, P., Coker, A. O., Colwell, B., Kenny, R., Shaw, L. & Campbell, M. (2007) Which symptomatic patients merit urgent referral for colonoscopy? A UK general practice perspective. *Quality in Primary Care*, 15: 21-25.

Not in PICO

John, S. K. P., George, S., Howell, R. D., Primrose, J. N. & Fozard, B. J. (2008) Validation of the Lower Gastrointestinal Electronic Referral Protocol. *British Journal of Surgery*, 95: 506-514.

Not in PICO

Johnson, R. A., Rodney, W. M. & Quan, M. (1982) Outcomes of flexible sigmoidoscopy in a family practice residency. *Journal of Family Practice*, 15: 785-789.

Not in PICO

Johnson, R. A., Quan, M. & MacMillan, R. W. (1984) Continued assessment of flexible sigmoidoscopy in a family practice residency. *Journal of Family Practice*, 18: 723-727.

Not in PICO

Jonsson, J. S., Jonasson, A. & Leppert, J. (1990) Proctosigmoidoscopy in primary health care. *Scandinavian Journal of Primary Health Care*, 8: 183-186.

Not in PICO

- Joosten, E., Meeuwissen, J., Vandewinckele, H. & Hiele, M. (2008) Iron status and colorectal cancer in symptomatic elderly patients. *American Journal of Medicine*, 121: 1072-1077.
Not in PICO
- Jordan, K. P., Hayward, R. A., Blagojevic-Bucknall, M. & Croft, P. (2013) Incidence of prostate, breast, lung and colorectal cancer following new consultation for musculoskeletal pain: a cohort study among UK primary care patients. *International Journal of Cancer*, 133: 713-720.
Cannot extract outcome in PICO (PPVs) as cancer data only reported in total for 10-year follow up
- Kalra, L. & Hamlyn, A. N. (1988) Comparative evaluation of investigations for colorectal carcinoma in symptomatic patients. *Postgraduate Medical Journal*, 64: 666-668.
Not in PICO
- Kaul, A., Shah, A., Magill, F. H., Hawkins, S. A. & Skaife, P. (2013) Immunological faecal occult blood testing: a discriminatory test to identify colorectal cancer in symptomatic patients. *International Journal Of Surgery*, 11: 329-331.
Not in PICO
- Kazama, S. & Watanabe, T. (2014) [Diagnosis of colorectal cancer by measurement of tumor markers]. [Japanese]. *Nihon rinsho*, Japanese: 71-76.
Narrative review
- Keane, M. G. & Johnson, G. J. (2002) Early diagnosis improves survival in colorectal cancer. *Practitioner*, 256: 15-18.
Not in PICO
- Kemppainen, M., Raiha, I., Rajala, T. & Sourander, L. (1993) Delay in diagnosis of colorectal cancer in elderly patients. *Age & Ageing*, 22: 260-264.
Not in PICO
- Kennington, E., Carter, S., Dear, M., Allen, B. & Patel, N. (2012) Bowel cancer symptom presentation in community pharmacy-an opportunity for early detection? *International Journal of Pharmacy Practice*, 20: 19-20.
Not in PICO
- Khan, R., Davis, T., Wilson, L., Daci, K., Gould, M., El-Serag, H. & Singh, H. (2010) Measuring and improving the timeliness of colorectal cancer diagnosis: A mixed-methods approach. *Gastroenterology*, 138: S326.
Not in PICO
- Ko, C., Hyman, N. H. & Standards Committee of The American Society of Colon and Rectal Surgeons (2006) Practice parameter for the detection of colorectal neoplasms: an interim report (revised). *Diseases of the Colon & Rectum*, 49: 299-301.
Not in PICO
- Ko, C. W., Dominitz, J. A., Green, P., Kreuter, W. & Baldwin, L. M. (2010) Utilization and predictors of early repeat colonoscopy in Medicare beneficiaries. *American Journal of Gastroenterology*, 105: 2670-2679.
Not in PICO
- Koo, B. C., Ng, C. S., King-Im, J., Prevost, A. T. & Freeman, A. H. (2006) Minimal preparation CT for the diagnosis of suspected colorectal cancer in the frail and elderly patient. [Review] [60 refs]. *Clinical Radiology*, 61: 127-139.
Narrative review
- Kumar, R. R., King, J., Holt, A., Huynh, R., Mittal, R., Deen, R. & Kim, J. (2007) Prevalence of left-sided colorectal cancer and benefit of flexible sigmoidoscopy: a county hospital experience. *American Surgeon*, 73: 994-997.
Not in PICO
- Kyle, G. & Prynne, P. (2004) Guidelines for patients undergoing faecal occult blood testing. [Review] [7 refs]. *Nursing Times*, 100: 62-64.
Narrative review

- Lacatena, M., Comes, P., Argese, A. V. & Colucci, G. (1989) CEA (carcinoembryonic antigen): its value as an early indicator of recurrence of neoplastic disease in carcinoma of the colon and rectum. [Italian]. *Minerva Chirurgica*, 44: 1597-1599.
Not in PICO
- Ladabaum, U., Fioritto, A., Mitani, A., Desai, M., Kim, J. P., Rex, D. K., Imperiale, T. & Gunaratnam, N. (2013) Real-time optical biopsy of colon polyps with narrow band imaging in community practice does not yet meet key thresholds for clinical decisions. *Gastroenterology*, 144: 81-91.
Not in PICO
- Lahr, C. J., Griffith, J., Subramony, C., Halley, L., Adams, K., Paine, E. R., Schmiege, R., Islam, S., Salameh, J., Spree, D., Kothari, T., Kedar, A., Nikitina, Y. & Abell, T. (2013) Gastric electrical stimulation for abdominal pain in patients with symptoms of gastroparesis. *American Surgeon*, 79: 457-464.
Not in PICO
- Lao, I. H., Chao, H., Wang, Y. J., Mak, C. W., Tzeng, W. S., Wu, R. H., Chang, S. T. & Fang, J. L. (2013) Computed tomography has low sensitivity for the diagnosis of early colon cancer. *Colorectal Disease*, 15: 807-811.
Not in PICO
- Lauenstein, T., Holtmann, G., Schoenfelder, D., Bosk, S., Ruehm, S. G. & Debatin, J. F. (2001) MR colonography without colonic cleansing: a new strategy to improve patient acceptance. *AJR.American Journal of Roentgenology*, 177: 823-827.
N = 6 (and these 6 likely to be referred patients)
- Lecoules, S., Carmoi, T., Klotz, C., Rapp, C., Perrot, G., Galeano, C. & Algayres, J. P. (2013) [Fever as the presenting manifestation of colon cancer: a case series of 11 patients]. [French]. *Revue de Medecine Interne*, 34: 136-140.
Not in PICO
- Lee, J. S., Cho, J. H., Kim, K. O., Lee, S. H. & Jang, B. I. (2012) [Clinical significance of the large intestinal wall thickening detected by abdominal computed tomography]. [Korean]. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi*, 60: 300-305.
Not in PICO
- Lee, M. G., Martin, A. & Terry, S. I. (1989) Colonoscopy in Jamaica--a 12-year experience. *West Indian Medical Journal*, 38: 213-216.
Not in PICO
- Leicester, R. J., Hawley, P. R., Pollett, W. G. & Nicholls, R. J. (1982) Flexible fiberoptic sigmoidoscopy as an outpatient procedure. *Lancet*, 1: 34-35.
Not in PICO
- Levin, B. & Murphy, G. P. (1992) Revision in American Cancer Society recommendations for the early detection of colorectal cancer. *CA: A Cancer Journal for Clinicians*, 42: 296-299.
Guideline
- Lim, C. S., McGeever, L., Grey, J. H., Krishna, A., Jabbar, A. A. & Hendry, W. S. (2009) How important is it to investigate the whole of the colon after initial assessment at a rapid access colorectal clinic? *International Journal of Colorectal Disease*, 24: 1341-1345.
Not in PICO
- Lin, G. A., Halley, M., Rendle, K. A., Tietbohl, C., May, S. G., Trujillo, L. & Frosch, D. L. (2013) An effort to spread decision aids in five California primary care practices yielded low distribution, highlighting hurdles. *Health Affairs*, 32: 311-320.
Not in PICO
- Lindgren, S. (2005) [CT colonography instead of coloscopy. A new computer tomographic method in suspected colonic polyps or malignant tumors]. [Swedish]. *Lakartidningen*, 102: 1705-1706.
Narrative review
- Liu, M. & Barnetson, R. (2008) Cutaneous signs of malignant disease. *Medicine Today*, 9: 29-36.
Not in PICO

- Loftus, W. K., Metreweli, C., Sung, J. J., Yang, W. T., Leung, V. K. & Set, P. A. (1999) Ultrasound, CT and colonoscopy of colonic cancer. *British Journal of Radiology*, 72: 144-148.
Not in PICO
- Lorinczi, K., Denheyer, V., Pickard, A., Lee, A. & Mager, D. R. (2012) Referral criteria for assessment and treatment in an ambulatory dysphagia clinic. *Canadian Journal of Dietetic Practice & Research*, 73: 189-194.
Not in PICO
- Lu, Y.-Y., Chen, J.-H., Chien, C.-R., Chen, W. T. L., Tsai, S.-C., Lin, W.-Y. & Kao, C.-H. (2013) Use of FDG-PET or PET/CT to detect recurrent colorectal cancer in patients with elevated CEA: A systematic review and meta-analysis. *International Journal of Colorectal Disease*, 28: 1039-1047.
Not in PICO
- Luman, W. & Ng, K. L. (2003) Audit of Investigations in Patients with Iron Deficiency Anaemia. *Singapore Medical Journal*, 44: 504-510.
Not in PICO
- Lung, P. F., Burling, D., Kallarackel, L., Muckian, J., Ilangoan, R., Gupta, A., Marshall, M., Shorvon, P., Halligan, S., Bhatnagar, G., Bassett, P. & Taylor, S. A. (2014) - Implementation of a new CT colonography service: 5 year experience. - *Clinical Radiology*, 69: 597-605.
Not in PICO (secondary care, emailed author and confirmed with Willie)
- Lupaltsov, V. & Shalkov, Y. (2013) Colorectal cancer: Factors of the early recognition. *Colorectal Disease*, 15: 111.
Abstarct only, not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Lynch, B. M., Youlden, D., Fritschi, L., Newman, B., Pakenham, K. I., Leggett, B., Owen, N. & Aitken, J. F. (2008) Self-reported information on the diagnosis of colorectal cancer was reliable but not necessarily valid. *Journal of Clinical Epidemiology*, 61: 498-504.
Not in PICO
- Lynch, H. T., Smyrk, T. C., Lanspa, S. J., Jenkins, J. X., Cavalieri, J. & Lynch, J. F. (1993) Cancer control problems in the Lynch syndromes. *Diseases of the Colon & Rectum*, 36: 254-260.
Narrative review
- MacMillan, R. W. & Felmer, E. (1984) Why flexible sigmoidoscopy instead of rigid sigmoidoscopy? *Journal of Family Practice*, 19: 471-476.
Narrative review
- Makino, S., Okada, K., Wada, Y., Kato, R., Takeoka, T., Yanagisawa, T., Okamura, S., Fukuchi, N., Ebisui, C., Murata, K., Yokouchi, H., Kinuta, M., Nakagomi, N. & Tamai, M. (2013) [A case of jejunum cancer diagnosed by anemia]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 40: 1720-1722.
Not in PICO
- Manerowski, M., Budzynski, J. & Swiatkowski, M. (2007) Alarm symptoms in patients with colorectal cancer referred by family doctors to the chair of gastroenterology in 2006. [Polish]. *Family Medicine and Primary Care Review*, 9: 516-518.
Not in PICO
- Manning-Dimmitt, L. L., Dimmitt, S. G. & Wilson, G. R. (2005) Diagnosis of gastrointestinal bleeding in adults. *American Family Physician*, 71: 1339-1346.
Narrative review
- Mansson, J., Bjorkelund, C. & Hultborn, R. (1999) Symptom pattern and diagnostic work-up of malignancy at first symptom presentation as related to level of care. A retrospective study from the primary health care centre area of Kungsholmen, Sweden. *Neoplasma*, 46: 93-99.
Not in PICO
- Mansson, J., Marklund, B. & Hultborn, R. (2001) The diagnosis of cancer in the "roar" of potential cancer symptoms of patients in primary health care - Research by means of the computerised

- journal. *Scandinavian Journal of Primary Health Care*, 19: 83-89.
Not in PICO
- Manzotti, L. N., Bolino, M. C., Braner, M., Cerisoli, C. & Caro, L. E. (2013) Prevalence of rectosigmoid adenomas and adenocarcinomas in patients younger than 50 years old referred for proctorrhagia. *Acta Gastroenterologica Latinoamericana*, 43: 279-283.
Not in PICO
- Martinez-Ares, D., Martin-Granizo, B., I, Souto-Ruzo, J., Yanez, L. J., Pallares, P. A. & Vazquez-Iglesias, J. L. (2005) The value of abdominal ultrasound in the diagnosis of colon cancer. *Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva*, 97: 877-886.
Not in PICO
- Maruthachalam, K., Stoker, E., Chaudhri, S., Noblett, S. & Horgan, A. F. (2005) Evolution of the two-week rule pathway--direct access colonoscopy vs outpatient appointments: one year's experience and patient satisfaction survey. *Colorectal Disease*, 7: 480-485.
Not in PICO
- Maruthachalam, K., Stoker, E., Nicholson, G. & Horgan, A. F. (2006) Nurse led flexible sigmoidoscopy in primary care--the first thousand patients. *Colorectal Disease*, 8: 557-562.
Not in PICO
- Maruthachalam, K., Stoker, E., Nicholson, G. & Horgan, A. F. (2006) The two week rule for colorectal cancer: Experience of a nurse led flexible sigmoidoscopy clinic in primary care. *Gut*, 55: A95.
Not in PICO
- Matsukawa, M. (1998) An accuracy of detecting a colorectal early cancer by barium enema. [Japanese]. *Stomach and Intestine*, 33: 705-711.
Not in PICO
- McArdle, C. S. (2002) Faecal occult blood testing for colorectal cancer. *Annals of Oncology*, 13: 35-39.
Not in PICO
- McCallum, R. W., Meyer, C. T. & Marignani, P. (1984) Flexible sigmoidoscopy: Diagnostic yield in 1015 patients. *American Journal of Gastroenterology*, 79: 433-437.
Not in PICO (Mixed population, results not reported for relevant patient group, not really DTA study)
- McIntyre, A. S. & Long, R. G. (1993) Prospective survey of investigations in outpatients referred with iron deficiency anaemia. *Gut*, 34: 1102-1107.
Not in PICO
- Michel, P. (1992) What is the role of rectosigmoidoscopy in the early diagnosis of colorectal cancer?. [French]. *Gastroenterologie Clinique et Biologique*, 16: 728-730.
Narrative review
- Million, R., Howarth, J., Turnberg, E. & Turnberg, L. A. (1982) Faecal occult blood testing for colorectal cancer in general practice. *Practitioner*, 226: 659-663.
Not in PICO
- Miyake, K. K., Nakamoto, Y. & Togashi, K. (2012) Dual-time-point 18F-FDG PET/CT in patients with colorectal cancer: clinical value of early delayed scanning. *Annals of Nuclear Medicine*, 26: 492-500.
Not in PICO
- Modiri, A., Makipour, K., Gomez, J. & Friedenberg, F. (2013) Predictors of colorectal cancer testing using the California Health Inventory Survey. *World Journal of Gastroenterology*, 19: 1247-1255.
Not in PICO
- Moiseenko, S. I. & Blinov, N. N. (1993) A retrospective comparative study of colonoscopy and irrigoscopy application for primary examination of large bowel cancer suspects. [Russian]. *Voprosy Onkologii*, 39: 80-84.
In Russian. Not enough relevant information can be extracted to determine relevance, but on the basis of what can be extracted, it is unlikely to be in PICO.

- Monreal, M., Lafoz, E., Casals, A., Inaraja, L., Montserrat, E., Callejas, J. M. & Martorell, A. (1991) Occult cancer in patients with deep venous thrombosis. A systematic approach. *Cancer*, 67: 541-545.
Not in PICO
- Moore, H. & Dodd, N. (2013) Computed tomographic colonography (CTC); Colorectal cancer diagnosis with CTC in an Auckland population. *Journal of Medical Imaging and Radiation Oncology*, 57: 572-575.
Not in PICO
- Morrow, T. (2012) Biomarker panel for colon cancer rivals fecal occult blood test. *Managed Care*, 21: 51-52.
Narrative review
- Nagasako, K. (1981) Merit and demerit of colonoscopy in the early diagnosis of colorectal cancer. [Japanese]. *Gastroenterological Endoscopy*, 23: 1618-1620.
Not in PICO
- Nagorni, A. (1998) Characteristics of synchronous colorectal tumors in symptomatic patients. *Archives of Gastroenterohepatology*, 17: 101-109.
Not in PICO
- Nagorni, A., Bjelakovic, G. & Petrovic, B. (2012) Narrow band imaging versus conventional white light colonoscopy for the detection of colorectal polyps. *Cochrane.Database.of Systematic.Reviews.. (Outcomes)* not in PICO
- Naumov, I. & Fenjvesi, A. (2012) [Pilot programme--detection of colon tumour in subjects living in the district of northern Banat]. [Serbian]. *Medicinski Pregled*, 65: 285-288.
In Serbian, N = 300 that I think are all referred patients, i.e., Not in PICO
- Ng, D. P., Mayberry, J. F., McIntyre, A. S. & Long, R. G. (1991) The practice of rectal examination. *Postgraduate Medical Journal*, 67: 904-906.
Not in PICO
- Ngwenya, S. (2006) General practitioner's pathology case 8. *SADJ*, 61: 360.
Not in PICO
- Niv, Y., Brenner, B., Fireman, Z., Fraser, G., Gal, E. & Levy, Z. (2006) [Colonoscopy for early detection of colorectal cancer in average-risk population]. [Review] [22 refs] [Hebrew]. *Harefuah*, 145: 841-842.
Not available from the British library. Have emailed author for the paper, but not received a response so far.
- Notman, F., Porteous, T., Bond, C. & Murchie, P. (2013) Understanding patients' selfmanagement of early cancer symptoms and exploring the potential role of community pharmacy in earlier diagnosis. *International Journal of Pharmacy Practice*, 21: 24.
Not in PICO
- Ogutu, E. O., Okoth, F. A. & Lule, G. N. (1998) Colonoscopic findings in Kenyan African patients. *East African Medical Journal*, 75: 540-543.
Not in PICO
- Olde, B. M., McCowan, C., Falk, G. A., Teljeur, C., Van de Laar, F. A. & Fahey, T. (2010) Diagnostic accuracy systematic review of rectal bleeding in combination with other symptoms, signs and tests in relation to colorectal cancer. [Review] [47 refs]. *British Journal of Cancer*, 102: 48-58.
Same as Bekkink
- Olokoba, A. B., Obateru, O. A., Bojuwoye, M. O., Olatoke, S. A., Bolarinwa, O. A. & Olokoba, L. B. (2013) Indications and findings at colonoscopy in Ilorin, Nigeria. *Nigerian Medical Journal*, 54: 111-114.
Not in PICO
- Olsson, L., Loof, L. & Ekblom, A. (2004) A population-based audit for diagnosing colorectal cancer. *Scandinavian Journal of Gastroenterology*, 39: 158-163.
Not in PICO

- Ozsunar, Y., Coskun, G., Delibas, N., Uz, B. & Yukselen, V. (2009) Diagnostic accuracy and tolerability of contrast enhanced CT colonoscopy in symptomatic patients with increased risk for colorectal cancer. *European Journal of Radiology*, 71: 513-518.
Not in PICO
- Padwick, R. T., Bajwa, A. A., Shaw, A., Leung, E., Francombe, J. & Stellakis, M. L. (2013) The Two-Week Referral System for colorectal cancer - Not fit for purpose. *International Journal of Colorectal Disease*, 28: 1531-1534.
Not in PICO
- Park, D. I., Kim, Y. H., Kim, H. S., Kim, W. H., Kim, T. I., Kim, H. J., Yang, S. K., Byeon, J. S., Lee, M. S., Jung, I. K., Chung, M. K., Jung, S. A., Jeon, Y. T., Choi, J. H., Choi, H., Han, D. S. & Song, J. S. (2006) Diagnostic yield of advanced colorectal neoplasia at colonoscopy, according to indications: An investigation from the Korean Association for the Study of Intestinal Diseases (KASID). *Endoscopy*, 38: 449-455.
Not in PICO
- Patel, A., Mastrianni, D. & Bartholomew, C. (2012) A rare case of metastatic adenocarcinoma with signet ring cells of unknown primary diagnosed on a myocardial biopsy. *American Journal of Gastroenterology*, 107: S254-S255.
Not in PICO
- Patterson, R. N. & Johnston, S. D. (2003) Iron deficiency anaemia: are the British Society of Gastroenterology guidelines being adhered to? *Postgraduate Medical Journal*, 79: 226-228.
Not in PICO
- Pedersen, A. F., Hansen, R. P. & Vedsted, P. (2013) Patient Delay in Colorectal Cancer Patients: Associations with Rectal Bleeding and Thoughts about Cancer. *PLoS ONE*, 8.
Not in PICO
- Pedersen, B. G., Achiam, M. P. & Arnesen, R. B. (2005) [Virtual colonoscopy is now reality]. [Danish]. *Ugeskrift for Laeger*, 167: 4175-4179.
Narrative review
- Pedersen, J. W., Gentry-Maharaj, A., Fourkala, E.-O., Dawnay, A., Burnell, M., Zaikin, A., Pedersen, A. E., Jacobs, I., Menon, U. & Wandall, H. H. (2013) Early detection of cancer in the general population: A blinded case-control study of p53 autoantibodies in colorectal cancer. *British Journal of Cancer*, 108: 107-114.
Not in PICO
- Petruzzello, L., Hassan, C., Alvaro, D., Kohn, A., Rossi, Z., Zullo, A., Cesaro, P., Annibale, B., Barca, A., Di, G. E., Giorgi, R. P., Grasso, E., Ridola, L., Spada, C., Costamagna, G. & Lazio Appropriateness Group (2012) Appropriateness of the indication for colonoscopy: is the endoscopist the 'gold standard'? *Journal of Clinical Gastroenterology*, 46: 590-594.
Not in PICO
- Peulen, J. J., De Witte, M. T., Friederich, P., Dirix, H. L., de Visser, D. C., van, L. H. & Simons, P. C. (2010) [CT colonography as first-line diagnostic procedure in patients with bowel symptoms]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 154: A1681.
Not in PICO
- Peytremann-Bridevaux, I., Arditi, C., Froehlich, F., O'Malley, J., Fairclough, P., Le Moine, O., Dubois, R. W., Gonvers, J. J., Fillietaz, S. S., Vader, J. P., Juillerat, P., Pittet, V. & Burnand, B. (2009) Iron-deficiency anemia and hematochezia. *Endoscopy*, 41: 227-233.
Review of guidelines
- Pickhardt, P. J., Hassan, C., Halligan, S. & Marmo, R. (2011) Colorectal cancer: CT colonography and colonoscopy for detection--systematic review and meta-analysis. [Review]. *Radiology*, 259: 393-405.
Not in PICO

- Pierzchajlo, R. P., Ackermann, R. J. & Vogel, R. L. (1997) Colonoscopy performed by a family physician. A case series of 751 procedures. *Journal of Family Practice*, 44: 473-480.
Not in PICO (not diagnostic test accuracy study)
- Piramanayagam, B., Mittapalli, D., Cutler, K., Church, R., Muscroft, T. & Odogwu, S. (2009) Colitis in patients with low risk colorectal cancer symptoms: A black country experience. *Colorectal Disease*, 11: 31.
Not in PICO
- Poston, G. J., Tait, D., O'Connell, S., Bennett, A., Berendse, S. & Guideline Development Group (2011) Diagnosis and management of colorectal cancer: summary of NICE guidance. *BMJ*, 343: d6751.
Guideline
- Pricolo, V. E. (2011) Rectal cancer: the good, the bad, and the ugly. *Archives of Surgery*, 146: 544.
Comment
- Prilepskaia, S. I., Baryshnikov, E. N., Kosacheva, T. A., Parfenov, A. I. & Lazebnik, L. B. (2011) [Prevalence of diverticulosis and colon tumors among adult population of Moscow with constipation and symptoms of anxiety (according to population-based study MUSA)]. [Russian]. *Ekspierimental'Naia i Klinicheskaia Gastroenterologija*.(2):22-6, 2011., 22-26.
Not in PICO
- Pullens, H. J., Laheij, R. J., Vleggaar, F. P., van Oijen, M. G. & Siersema, P. D. (2013) Symptoms associated with finding colorectal cancer during colonoscopy. *European Journal of Gastroenterology & Hepatology*, 25: 1295-1299.
Not in PICO
- Pye, G., Marks, C. G., Martin, S., Marks, V., Jackson, J. & Hardcastle, J. D. (1989) An evaluation of Fecatwin/Feca EIA; a faecal occult blood test for detecting colonic neoplasia. *European Journal of Surgical Oncology*, 15: 446-448.
Not in PICO
- Qi, Z. T., Deng, L. L., Huang, H., Zhao, J. H. & Zhou, G. H. (2010) [Advances in early diagnosis of colorectal cancer based on detection of RNAs in stool.]. [Review] [Chinese]. *Yi Chuan*, 32: 994-1002.
Narrative review
- Ransohoff, D. F. (2005) Have we oversold colonoscopy? *Gastroenterology*, 129: 1815.
Narrative review
- Rao, V. S. R., Ahmad, N., Al-Mukhtar, A., Stojkovic, S., Moore, P. J. & Ahmad, S. M. (2005) Comparison of rigid vs flexible sigmoidoscopy in detection of significant anorectal lesions. *Colorectal Disease*, 7: 61-64.
Not in PICO
- Rees, C. J., Rajasekhar, P. T., Rutter, M. D. & Dekker, E. (2014) Quality in colonoscopy: European perspectives and practice. *Expert Review of Gastroenterology and Hepatology*, 8: 29-47.
Narrative review
- Robertson, R., Campbell, C., Weller, D. P., Elton, R., Mant, D., Primrose, J., Nugent, K., Macleod, U. & Sharma, R. (2006) Predicting colorectal cancer risk in patients with rectal bleeding. *British Journal of General Practice*, 56: 763-767.
Not in PICO
- Robinson, C., Halligan, S., Iinuma, G., Topping, W., Punwani, S., Honeyfield, L. & Taylor, S. A. (2011) CT colonography: computer-assisted detection of colorectal cancer. *British Journal of Radiology*, 84: 435-440.
Not in PICO
- Rodney, W. M. & Felmar, E. (1984) Why flexible sigmoidoscopy instead of rigid sigmoidoscopy? *Journal of Family Practice*, 19: 471-476.
Duplicate, same as MacMillan 1984

- Rodney, W. M. (1988) Procedural skills in flexible sigmoidoscopy and colonoscopy for the family physician. [Review] [34 refs]. *Primary Care; Clinics in Office Practice*, 15: 79-91.
Narrative review
- Rogalla, P., Janka, R., Baum, U., Feuerbach, S., Helmberger, H., Rieber-Brambs, A., Brambs, H. J. & Aschoff, A. (2008) [CT colography: guideline of the Gastrointestinal Diagnostics Team of the German Radiological Society regarding the indication and technical implementation of endoluminal colon diagnostics using computed tomography (known as virtual colonoscopy)]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 180: 466-469.
Guideline
- Royle, T. J., Ferguson, H. J. M., Mak, T. W. C., Simpson, J. A., Thumbe, V. & Bhalerao, S. (2014) Same-day assessment and management of urgent (2-week wait) colorectal referrals: An analysis of the outcome of 1606 patients attending an endoscopy unit-based colorectal clinic. *Colorectal Disease*, 16: O176-O181.
Not in PICO
- Sakamoto, T., Saito, Y., Nakajima, T. & Matsuda, T. (2011) [Essence of endoscopic diagnosis for the depth of early colorectal cancer]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 69: Suppl-63.
Unavailable from British Library, in Japanese, and don't think in PICO
- Salazar, A. G., Prieto, S. A., Ortega, C. A., Cabrera Martin, M. N., Gonzalez, R. C., Ortiz Zapata, J. J., Cardona, A. J., Lapena, G. L. & Carreras Delgado, J. L. (2012) Clinical relevance of incidental finding of focal uptakes in the colon during 18F-FDG PET/CT studies in oncology patients without known colorectal carcinoma and evaluation of the impact on management. *Revista Espanola de Medicina Nuclear e Imagen Molecular*, 31: 15-21.
Not in PICO
- Saldanha, J. D., Moug, S. J., Linton, K. & Diament, R. H. (2013) Symptoms do not predict colorectal cancer in an FOB screened population. *Scottish Medical Journal*, 58: 95-98.
Not in PICO
- Sanchez, A., Munoz, C., Bujanda, L., Iriando, C., Gil-Molet, A., Cosme, A., Sarasqueta, C. & Echenique-Elizondo, M. (2005) The value of colonoscopy to assess rectal bleeding in patients referred from Primary Care Units. *Revista Espanola de Enfermedades Digestivas*, 97: 870-876.
Not in PICO (not a diagnostic test accuracy study)
- Sardinha, T. C., Nogueiras, J. J., Ehrenpreis, E. D., Zeitman, D., Estevez, V., Weiss, E. G. & Wexner, S. D. (1999) Colonoscopy in octogenarians: a review of 428 cases. *International Journal of Colorectal Disease*, 14: 172-176.
Not in PICO
- Schiff, G. D. (2014) Diagnosis and diagnostic errors: Time for a new paradigm. *BMJ Quality and Safety*, 23: 1-3.
Not in PICO
- Schmidt, C. (2012) Colonoscopy vs sigmoidoscopy: new studies fuel ongoing debate. *Journal of the National Cancer Institute*, 104: 1350-1351.
Narrative review
- Schoenfeld, P. (2009) Is this diagnostic test useful? *American Journal of Gastroenterology*, 104: 2139-2142.
Not in PICO
- Schroder, J., Wesner, F. & Kremer, B. (2000) Diagnostic procedures in patients with the principal sign of weight loss. [German]. *Chirurgische Gastroenterologie Interdisziplinär*, 16: 61-64.
Narrative review
- Schusdziarra, V. (1993) [Are there still indications for sigmoidoscopy?]. [German]. *Bildgebung*, 60: Suppl-4.
Narrative review

- Scott, M., Allen, S., Bamford, A., Walshe, M. & Clark, C. I. (2002) Influence of a nurse practitioner on non-attendance rate for barium enema. *Journal of the Royal Society of Medicine*, 95: 448-449.
Not in PICO
- Scott, M. A., Knight, A., Brown, K. & Novell, J. R. (2006) A single common urgent pathway for all colorectal referrals reduces time to diagnosis and treatment. *Colorectal Disease*, 8: 766-771.
Not in PICO
- Sehgal, V., Krishnan, B. & Besherdas, K. (2012) How many biopsies at colonoscopy are required to confirm the diagnosis histologically in suspected colorectal cancer? *Gastrointestinal Endoscopy*, 75: AB294.
Not in PICO
- Selinger, R. R. E., Norman, S. & Dominitz, J. A. (2003) Failure of health care professionals to interpret fecal occult blood tests accurately. *American Journal of Medicine*, 114: 64-67.
Not in PICO
- Sequist, T. D. (2006) Is referral for colonoscopy overutilized by primary care physicians? *Journal of Clinical Outcomes Management*, 13: 678-680.
Not in PICO
- Sewitch, M., Waschke, K., Stein, D. & Arthurs, E. (2009) Time intervals from initial symptom report to colonoscopy and histologic diagnosis in rectal cancer patients. *Canadian Journal of Gastroenterology*, 23.
Not in PICO
- Shakil, A. O., Ellis, A., Faizallah, R. & Cochrane, A. M. (1995) Sigmoidoscopy service in a district general hospital: open-access versus hospital-referred. *British Journal of Clinical Practice*, 49: 25-27.
Not in PICO
- Shapley, M., Mansell, G., Jordan, J. L. & Jordan, K. P. (2010) Positive predictive values of $\geq 5\%$ in primary care for cancer: systematic review. *British Journal of General Practice*, 60: 681-688.
Systematic review: Any relevant data will be reported per study
- Shaw, A. G., Lund, J. N., Longman, C., Tierney, G. M. & Goddard, A. F. (2009) The misuse of the faecal occult blood test under the lower gastrointestinal two week wait rule. *Colorectal Disease*, 11: 94-96.
Not in PICO
- Shimano, T., Okuda, H., Monden, T., Morimoto, H., Tamaki, Y., Shimizu, M., Inaji, H., Saito, M. & Mori, T. (1988) Colonic cancer; problems of early diagnosis. 3. Neoplasm makers. [Japanese]. *Nippon rinsho*, Japanese: 387-391.
Narrative review
- Siegel, C. A., Schwartz, L. M., Woloshin, S., Cole, E. B., Rubin, D. T., Vay, T., Baars, J. & Sands, B. E. (2010) When should ulcerative colitis patients undergo colectomy for dysplasia? Mismatch between patient preferences and physician recommendations. *Inflammatory Bowel Diseases*, 16: 1658-1662.
Not in PICO
- Simons, P. C., Van Steenberghe, L. N., De Witte, M. T. & Janssen-Heijnen, M. L. (2013) Miss rate of colorectal cancer at CT colonography in average-risk symptomatic patients. *European Radiology*, 23: 908-913.
Not in PICO
- Singh, H., Daci, K., Petersen, L. A., Collins, C., Petersen, N. J., Shethia, A. & El-Serag, H. B. (2009) Missed opportunities to initiate endoscopic evaluation for colorectal cancer diagnosis. *American Journal of Gastroenterology*, 104: 2543-2554.
Not in PICO
- Singh, H., Nugent, Z., Demers, A. A. & Bernstein, C. N. (2010) Rate and predictors of early/missed colorectal cancers after colonoscopy in Manitoba: a population-based study. *American Journal of*

- Gastroenterology*, 105: 2588-2596.
Not in PICO
- Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M. & Hamilton, W. (2013) The risk of oesophago-gastric cancer in symptomatic patients in primary care: a large case-control study using electronic records. *British Journal of Cancer*, 108: 25-31.
Not in PICO
- Steine, S. & Laerum, E. (1994) Referrals for radiological examination of the large bowel. Pre-radiological examinations, tests and referral letters. *Family Practice*, 11: 21-25.
Not in PICO
- Steine, S., Stordahl, A., Laerum, F. & Laerum, E. (1994) Referrals for double-contrast barium examination. Factors influencing the probability of finding polyps or cancer. *Scandinavian Journal of Gastroenterology*, 29: 260-264.
Not in PICO
- Stermer, E., Lavy, A., Rainis, T., Goldstein, O., Keren, D. & Zeina, A. R. (2008) Incidental colorectal computed tomography abnormalities: would you send every patient for a colonoscopy? *Canadian Journal of Gastroenterology*, 22: 758-760.
Not in PICO
- Stermer, E., Tamir, A., Goldstein, O., Keren, D., Rainis, T., Paster, E. & Lavy, A. (2022) [Open access colonoscopy: do primary care physicians use it properly?]. [Hebrew]. *Harefuah*, 145: 803-806.
Not in PICO
- Summerton, N. & Paes, R. (2000) The clinical assessment of patients with large bowel symptoms by general practitioners. *European Journal of General Practice*, 6: 43-47.
Not in PICO
- Tada, M. (1981) Merits and demerits of sigmoidoscopy for the early diagnosis of colo-rectal cancer. [Japanese]. *Gastroenterological Endoscopy*, 23: 1616-1618.
Not in PICO
- Tada, M., Shimizu, S., Ogawa, M., Inatomi, I. & Kawai, K. (1988) Colonic cancer; problems of early diagnosis. 1. Early diagnosis and the fecal occult blood test. [Japanese]. *Nippon rinsho*, Japanese: 375-381.
Narrative review
- Taggarshe, D., Rehil, N., Sharma, S., Flynn, J. C. & Damadi, A. (316) Colorectal cancer: are the "young" being overlooked? *American Journal of Surgery*, 205: 312-316.
Not in PICO
- Takemoto, T. & Matsuura, S. (1988) Colonic cancer; problems of early diagnosis. 2. Radiographic and endoscopic diagnosis. [Japanese]. *Nippon rinsho*, Japanese: 382-386.
Narrative review
- Tan, L. C., Senapati, A. & Thompson, M. R. (2000) Early flexible sigmoidoscopy in the evaluation of acute left iliac fossa pain. *Colorectal Disease*, 2: 84-87.
Not in PICO
- Tang, T., Lim, P. B. & Miller, R. (2005) An approach to haemorrhoids. *Colorectal Disease*, 7: 143-147.
Not in PICO
- Tate, J. J. & Royle, G. T. (1988) Open access colonoscopy for suspected colonic neoplasia. *Gut*, 29: 1322-1325.
Not in PICO (not diagnostic study)
- Taylor, S. A., Halligan, S., Saunders, B. P., Morley, S., Riesewyk, C., Atkin, W. & Bartram, C. I. (2003) Use of multidetector-row CT colonography for detection of colorectal neoplasia in patients referred via the Department of Health "2-Week-wait" initiative. *Clinical Radiology*, 58: 855-861.
Not in PICO
- Teng, C.-L., Yu, J.-T., Chen, Y.-H., Lin, C.-H. & Hwang, W.-L. (2014) Early colonoscopy confers survival benefits on colon cancer patients with pre-existing iron deficiency anemia: A nationwide

- population-based study. *PLoS ONE*, 9.
Not in PICO
- Thapar, A., Rodney, S., Haboubi, D., Wilson, J., Bhan, C., Walshe, M., Haddow, J., Oshowo, A. & Mukhtar, H. (2014) Nurse telephone triaged straight to test colonoscopy. *Gut*, 63: A239-A240.
Not in PICO
- Thoeni, R. F. & Petras, A. (1982) Detection of rectal and rectosigmoid lesions by double-contrast barium enema examination and sigmoidoscopy. Accuracy of technique and efficacy of standard overhead views. *Radiology*, 142: 59-62.
Not in PICO
- Thompson, M. R., Flashman, K. G., Wooldrage, K., Rogers, P. A., Senapati, A., O'Leary, D. P. & Atkin, W. (2008) Flexible sigmoidoscopy and whole colonic imaging in the diagnosis of cancer in patients with colorectal symptoms. *British Journal of Surgery*, 95: 1140-1146.
Not in PICO
- Thompson, M. R., Flashman, K. G., Asiimwe, A., Tsavellas, G., Parvaiz, A., Senapati, A. & O'Leary, D. P. (2012) How does bowel cancer present? Implications for DOH plans to achieve earlier diagnosis. *Colorectal Disease*, 14: 15.
Not in PICO
- Todd, J. A., Zubir, M. A., Goudie, B. M. & Johnston, D. A. (2000) Response to open access endoscopy findings by general practitioners guidelines need education for implementation. *Scottish Medical Journal*, 45: 49-50.
Not in PICO
- Tolan, D. J., Armstrong, E. M. & Chapman, A. H. (2007) Replacing barium enema with CT colonography in patients older than 70 years: the importance of detecting extracolonic abnormalities. *AJR.American Journal of Roentgenology*, 189: 1104-1111.
Outcome not in PICO. Referred population?
- Tolwinka, A., Kisielewski, R. & Laudanski, P. (2012) Chronic pelvic pain in menopausal women. *Przegląd Menopauzalny*, 16: 187-191.
Narrative review
- Tomlinson, C., Wong, C., Au, H. J. & Schiller, D. (2012) Factors associated with delays to medical assessment and diagnosis for patients with colorectal cancer. *Canadian Family Physician*, 58: e495-e501.
Not in PICO
- Toomey, P., Asimakopoulos, G., Zbar, A. & Kmiot, W. (1998) 'One-stop' rectal bleeding clinics without routine flexible sigmoidoscopy are unsafe. *Annals of the Royal College of Surgeons of England*, 80: 131-133.
Not in PICO
- Torrance, A., Patel, A. & Singh, J. (2012) Urgent referrals for colorectal cancer: Can patients go 'straight-to-test'? *Colorectal Disease*, 14: 14.
Not in PICO
- Ugalde, F. C., Moneva, F. A., Tapia, A. G., Domingo, J. I., Serrano, E. L. & Saenz, F. Z. (1992) Colorectal-Cancer - Detection with the Guaiac Test in A Primary Care Center. *Medicina Clinica*, 98: 325-328.
Not in PICO (screening)
- Vakil, N., Halling, K., Ohlsson, L. & Wernersson, B. (2013) Symptom overlap between postprandial distress and epigastric pain syndromes of the Rome III dyspepsia classification. *American Journal of Gastroenterology*, 108: 767-774.
Not in PICO
- van, P. B., Kurver, M. J., Damoiseaux, R. A., Boukes, F. S. & Goudswaard, A. N. (2009) [Summary of Dutch College of General Practitioners guidelines on "Rectal bleeding"]. [Review] [1 refs] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 153: A121.
Guideline

- Vaughan-Shaw, P. G., Cutting, J., Borley, N., Brooklyn, T. & Wheeler, J. M. D. (2014) Two-week wait symptoms are prevalent in screened patients with a positive faecal occult blood test but do not predict cancer. *Colorectal Disease*, 16: 40-47.
Not in PICO
- Veit, P., Kuhle, C., Beyer, T., Kuehl, H., Herborn, C. U., Borsch, G., Stergar, H., Barkhausen, J., Bockisch, A. & Antoch, G. (2006) Whole body positron emission tomography/computed tomography (PET/CT) tumour staging with integrated PET/CT colonography: Technical feasibility and first experiences in patients with colorectal cancer. *Gut*, 55: 68-73.
Not in PICO
- Verma, S. & Giaffer, M. H. (2001) Open-access versus hospital-initiated flexible sigmoidoscopy: a comparative audit of efficacy. *European Journal of Gastroenterology & Hepatology*, 13: 655-658.
Not in PICO
- Viiiala, C. H., Tang, K. W., Lawrance, I. C., Murray, K. & Olynyk, J. K. (2007) Waiting times for colonoscopy and colorectal cancer diagnosis. *Medical Journal of Australia*, 186: 282-285.
Not in PICO
- Vipond, M. N. & Moshakis, V. (1996) Four-year evaluation of a direct-access fiberoptic sigmoidoscopy service. *Annals of the Royal College of Surgeons of England*, 78: 23-26.
Not in PICO
- Vironen, J., Kellokumpu, S., Andersson, L. C. & Kellokumpu, I. (2004) Comparison of a peanut agglutinin test and an immunochemical faecal occult blood test in detecting colorectal neoplasia in symptomatic patients. *Scandinavian Journal of Clinical & Laboratory Investigation*, 64: 140-145.
Not in PICO (think referred population)
- Voelker, R. (2009) Colonoscopy: Prime time for primary care? *JAMA - Journal of the American Medical Association*, 301: 921-922.
Narrative review
- Wahlberg, H., Valle, P. C., Malm, S. & Broderstad, A. R. (2013) Practical health co-operation - the impact of a referral template on quality of care and health care co-operation: study protocol for a cluster randomized controlled trial. *Trials [Electronic Resource]*, 14: 7.
Not in PICO
- Wang, Y., Gong, S.-G., Zhang, W.-G., Chen, J.-H., Zhang, L.-Y. & Chen, J.-P. (2004) Sensitivity and specificity of pneumocolon CT in detecting colorectal neoplasms. [Chinese]. *World Chinese Journal of Digestology*, 12: 359-362.
In Chinese, but thinks it's referred patients, so not in PICO
- Weiser, M. A., Cabanillas, M., Vu, K., Tamm, E. P., Wallace, M. J., Escalante, C. P. & Bresalier, R. S. (2005) Diagnostic evaluation of patients with a high suspicion of malignancy: Comorbidities and clinical predictors of cancer. *American Journal of the Medical Sciences*, 330: 11-18.
Not in PICO
- Weiss, B. D. (2005) Sigmoidoscopy versus colonoscopy: ask yourself. *Family Medicine*, 37: 743-744.
Comment
- Werner, J. C., Zock, M., Khalil, P. N., Hoffmann, J., Kanz, K. G. & Jauch, K. W. (2013) [Evidence for the digital rectal examination in the emergency assessment of acute abdominal pain]. [German]. *Zentralblatt fur Chirurgie*, 138: 669-676.
Narrative review
- Winawer, S. J. & Fleisher, M. (1982) Sensitivity and specificity of the fecal occult blood test for colorectal neoplasia. *Gastroenterology*, 82: t-91.
Narrative review
- Wright, H. L. (2012) A colorectal telephone assessment service (CTAS) for the initial assessment of colorectal referrals: Our first 3 years' experience. *Colorectal Disease*, 14: 10.
Not in PICO

Wu, R. S., Chan, S. S., Cheung, N. K., Graham, C. A. & Rainer, T. H. (2011) Open-access colonoscopy: outcomes of referrals from the emergency department. *Colorectal Disease*, 13: 826-828.

Not in PICO

Yoshii, Y., Kobayashi, S., Kuroda, T. & Kasugai, T. (1981) Early carcinoma and adenoma of the large intestine; Usefulness of fecal occult blood testing for detection and factors relating to bleeding. [Japanese]. *Journal of the Japan Society of Colo-Proctology*, 34: 220-289.

Not in PICO

Yun, G. W., Yang, Y. J., Song, I. C., Park, K. U., Baek, S.-W., Yun, H. J., Kim, S., Jo, D. Y. & Lee, H. J. (2011) A prospective evaluation of adult men with iron-deficiency anemia in Korea. *Internal Medicine*, 50: 1371-1375.

Not in PICO

Zervos, E. E., Badgwell, B. D., Burak, W. E., Jr., Arnold, M. W. & Martin, E. W. (643)

Fluorodeoxyglucose positron emission tomography as an adjunct to carcinoembryonic antigen in the management of patients with presumed recurrent colorectal cancer and nondiagnostic radiologic workup. *Surgery*, 130: 636-643.

Not in PICO

Zycinska, K., Wardyn, K. A., Krupa, R., Zycinski, Z. & Nitsch-Osuch, A. (2007) Lower GI tract endoscopy - The usefulness and the accuracy of GP's referrals. [Polish]. *Family Medicine and Primary Care Review*, 9: 650-654.

Not in PICO

ANAL CANCER

Review question:

What is the risk of anal cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

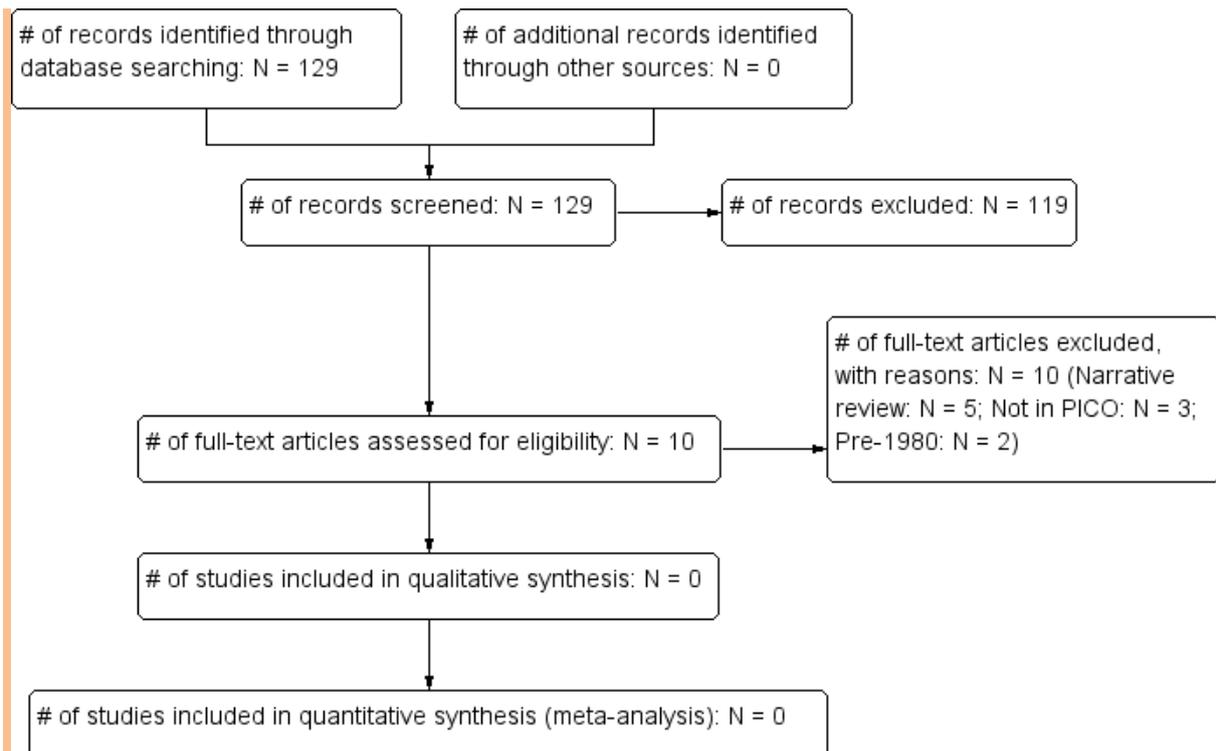
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	217	99	04/09/2012
<i>Premedline</i>	All-2012	8	1	04/09/2012
<i>Embase</i>	All-2012	264	61	04/09/2012
<i>Cochrane Library</i>	All-2012	132	2	12/09/2012
<i>Psychinfo</i>	All-2012	6	0	12/09/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	85	11	12/09/2012
<i>Biomed Central</i>	All-2012	2	0	12/09/2012

Total References retrieved (after de-duplication): 128

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	9/2012-26/08/2014	7	0	26/08/2014
<i>Premedline</i>	9/2012-26/08/2014	38	0	26/08/2014
<i>Embase</i>	9/2012-26/08/2014	61	1	26/08/2014
<i>Cochrane Library</i>	9/2012-26/08/2014	58	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	9/2012-26/08/2014	27	0	26/08/2014

Total References retrieved (after de-duplication): 1



References

Study results

No evidence was found.

Included studies

None

Excluded studies (with excl reason)

The Dutch College of General Practitioners guideline for rectal bleeding. [Dutch]. Huisarts en Wetenschap 52[1], 23-38. 2009.

Excl reason: Guideline

-Medical-Advisory-SecretariatOntario-Ministry-of-Health-and-Long-Term-Care-. Anal dysplasia screening: an evidence-based analysis (Structured abstract). Toronto.: Medical Advisory Secretariat., Ontario.Ministry.of Health and Long Term Care , 45. 2007.

Excl reason: Not in PICO

Abbas, A., Yang, G., and Fakih, M. Management of anal cancer in 2010. Part 2: current treatment standards and future directions. Oncology (Williston Park, N 24[5], 417-424. 30-4-2010.

Excl reason: Not in PICO

Abboud, B., Ingea, H., Tayar, C., and Abadjian, G. [Epidermoid carcinoma developing in a chronic anal fistula]. [French]. Presse Medicale 29[14], 786-787. 15-4-2000.

Excl reason: Not in PICO

Achauer, B. M. and Vander Kam, V. M. Ulcerated anogenital hemangioma of infancy. Plastic & Reconstructive Surgery 87[5], 861-866. 867.

Excl reason: Not in PICO

Anand, B. S., Verstovsek, G., and Cole, G. Tubulovillous adenoma of anal canal: a case report. *World Journal of Gastroenterology* 12[11], 1780-1781. 21-3-2006.
Excl reason: Not in PICO

Basso, L. and Pescatori, M. Sources of clinical referrals to an urban coloproctology unit in Italy. *Techniques in Coloproctology* 5[2], 67-71. 2001.
Excl reason: Not in PICO

Bean, S. M. and Chhieng, D. C. Anal-rectal cytology: The other pap test. *Laboratory Medicine* 41[3], 168-171. 2010.
Excl reason: Not in PICO

Berndt, H. and Neumann, P. Early diagnosis of malignant tumors of the digestive organs. 2. [German]. *Zeitschrift fur Arztliche Fortbildung* 77[3], 100-102. 1983.
Excl reason: Narrative review

Berry, J. M., Palefsky, J. M., and Welton, M. L. Anal cancer and its precursors in HIV-positive patients: perspectives and management. [Review] [45 refs]. *Surgical Oncology Clinics of North America* 13[2], 355-373. 2004.
Excl reason: Not in PICO

Billingham, R. P. Anorectal miscellany: pilonidal disease, anal cancer, Bowen's and Paget's diseases, foreign bodies, and hidradenitis suppurativa. [Review] [29 refs]. *Primary Care; Clinics in Office Practice* 26[1], 171-177. 1999.
Excl reason: Narrative review

Bolanca, A. On early detection of neoplastic processes of the rectum (author's transl). [Serbian]. *Lijecnicki Vjesnik* 99[3], 153-157. 1977.
Excl reason: Pre-1980

Briccoli, A., Farinetti, A., Ricchi, E., Rizzente, A. G., Morganti, I., and Guernelli, N. Anal cancer. Analysis of surgical experience. [Italian]. *Minerva Chirurgica* 54[5], 289-293. 1999.
Excl reason: Not in PICO

Briccoli, A., Farinetti, A., Ricchi, E., Rizzente, A. G., Morganti, I., and Guernelli, N. [Cancer of the anus. Analysis of our surgical experience]. [Italian]. *Minerva Chirurgica* 54[5], 289-293. 1999.
Excl reason: Not in PICO

Chou, Y. P., Saito, Y., Matsuda, T., Nakajima, T., Mashimo, Y., Moriya, Y., and Shimoda, T. Novel diagnostic methods for early-stage squamous cell carcinoma of the anal canal successfully resected by endoscopic submucosal dissection. *Endoscopy* 41, Suppl-5. 2009.
Excl reason: Not in PICO

Cohen, M. G., Greenwald, M. L., Garbus, J. E., and Zager, J. S. Granular cell tumor--a unique neoplasm of the internal anal sphincter: report of a case. *Diseases of the Colon & Rectum* 43[10], 1444-1446. 20-11-1447.
Excl reason: Not in PICO

Couetil, J. P., McGoldrick, J. P., Wallwork, J., and English, T. A. Malignant tumors after heart transplantation. *Journal of Heart Transplantation* 9[6], 622-626. 1990.
Excl reason: Not in PICO

Crooms, J. W. and Kovalcik, P. J. Anal lesions. When to suspect carcinoma. *Postgraduate Medicine* 77[5], 85-90. 1985.
Excl reason: Narrative review

Cuffy, M., Abir, F., and Longo, W. E. Management of less common tumors of the colon, rectum, and anus. *Clinical Colorectal Cancer* 5[5], 327-337. 2006.
Excl reason: Narrative review

D'Souza, G., Cook, R. L., Ostrow, D., Johnson-Hill, L. M., Wiley, D., and Silvestre, T. Anal cancer screening behaviors and intentions in men who have sex with men. *Journal of General Internal Medicine* 23[9], 1452-1457. 2008.
Excl reason: Not in PICO

da Costa e Silva, Gimenez, F. S., Guimaraes, R. A., Camelo, R. T., Melo, M. N., de Barros, F. S., Daumas, A., Cabral, C. R., and Guimaraes, E. L. Anal cytology as a screening method for early detection of anal cancer: are hydrophilic cotton smears really unsatisfactory?. [Portuguese]. *Acta cirurgica brasileira / Sociedade Brasileira para Desenvolvimento Pesquisa em Cirurgia* 20[1], 109-114. 2005.
Excl reason: Not in PICO

Dahl, O. and Fluge, O. Anal cancer. [Norwegian]. *Tidsskrift for Den Norske Laegeforening* 128[2], 198-200. 17-1-2008.
Excl reason: Narrative review

Damin, D. C., Rosito, M. A., Gus, P., Spiro, B. L., Amaral, B. B., Meurer, L., Cartel, A., and Schwartzmann, G. Sentinel lymph node procedure in patients with epidermoid carcinoma of the anal canal: early experience. *Diseases of the Colon & Rectum* 46[8], 1032-1037. 2003.
Excl reason: Not in PICO

Daniel, W. J. Anorectal pain, bleeding and lumps. *Australian Family Physician* 39[6], 376-381. 2010.
Excl reason: Narrative review

deSouza, N. M., Hall, A. S., Puni, R., Gilderdale, D. J., Young, I. R., and Kmiot, W. A. High resolution magnetic resonance imaging of the anal sphincter using a dedicated endoanal coil. Comparison of magnetic resonance imaging with surgical findings. *Diseases of the Colon & Rectum* 39[8], 926-934. 1996.
Excl reason: Not in PICO

Devaraj, B. and Cosman, B. C. Expectant management of anal squamous dysplasia in patients with HIV. *Diseases of the Colon & Rectum* 49[1], 36-40. 2006.
Excl reason: Not in PICO

Di, Comite A. and De, Vita L. [Congenital telangiectasic (pyogenic) granuloma of the anus: a rare location of a benign neonatal tumor]. [Italian]. *Minerva Pediatrica* 41[9], 481-483. 1989.
Excl reason: Narrative review

Dietrich, K. F. [Proctology in daily medical practice]. [German]. *Medizinische Klinik* 63[15], 596-601. 12-4-1968.
Excl reason: Not in PICO

Dietz, C. A. and Nyberg, C. R. Genital, oral, and anal human papillomavirus infection in men who have sex with men. [Review]. *Journal of the American Osteopathic Association* 111[3:Suppl 2], Suppl-25. 2011.
Excl reason: Not in PICO

Dindo, D., Nocito, A., Schettle, M., Clavien, P. A., and Hahnloser, D. What should we do about anal condyloma and anal intraepithelial neoplasia? Results of a survey. *Colorectal Disease* 13[7], 796-801. 2011.
Excl reason: Not in PICO

Fargo, M. V. and Latimer, K. M. Evaluation and Management of Common Anorectal Conditions. *American Family Physician* 85[6], 624-630. 2012.
Excl reason: Narrative review

Ferrandiz-Pulido, C. [Early detection of anal intraepithelial neoplasia in high-risk patients]. [Spanish]. *Actas Dermo-Sifiliograficas* 102[10], 754-756. 2011.
Excl reason: Narrative review

Ferron, P., Young, S., Doyle, F., Symes, S., Powell, A., Diaz-Mendez, N., and Rosa-Cunha, I. A case illustration about the importance of integrating women's anal health in an HIV primary care clinic. *Journal of the Association of Nurses in AIDS Care* 22[6], 489-493. 2011.
Excl reason: Not in PICO

Ficari, F., Fazi, M., Garcea, A., Nesi, G., and Tonelli, F. Anal carcinoma occurring in Crohn's disease patients with chronic anal fistula. *I supplementi di Tumori : official journal of Societa italiana di cancerologia* [et3], S31-Jun. 11-11-1111.
Excl reason: Not in PICO

- Fonio de, Gijon T., Amarillo, H., and Japaze, H. Epithelial changes in the anal canal associated with hemorrhoids, fissures and fistulas. [Spanish]. *Acta Gastroenterologica Latinoamericana* 14[2], 155-159. 1984.
Excl reason: Not in PICO (surgical specimens)
- Forti, R. L., Medwell, S. J., Aboulafia, D. M., Surawicz, C. M., and Spach, D. H. Clinical presentation of minimally invasive and in situ squamous cell carcinoma of the anus in homosexual men. *Clinical Infectious Diseases* 21[3], 603-607. 1995.
Excl reason: Not in PICO
- Fox, P. Anal cancer screening in men who have sex with men. [Review] [25 refs]. *Current Opinion in HIV & AIDS* 4[1], 64-67. 2009.
Excl reason: Not in PICO
- Gaertner, W. B., Hagerman, G. F., Finne, C. O., Alavi, K., Jessurun, J., Rothenberger, D. A., and Madoff, R. D. Fistula-associated anal adenocarcinoma: Good results with aggressive therapy. *Diseases of the Colon and Rectum* 51[7], 1061-1067. 2008.
Excl reason: Not in PICO
- Gee, R. Primary care health issues among men who have sex with men. [Review] [61 refs]. *Journal of the American Academy of Nurse Practitioners* 18[4], 144-153. 2006.
Excl reason: Narrative review
- Gervaz, P., Buchs, N., and Morel, P. Diagnosis and management of anal cancer. *Current gastroenterology reports* 10[5], 502-506. 2008.
Excl reason: Narrative review
- Gilbert, J. M., Mann, C. V., Scholefield, J., and Domizio, P. The aetiology and surgery of carcinoma of the anus, rectum and sigmoid colon in Crohn's disease. Negative correlation with human papillomavirus type 16 (HPV 16). *European Journal of Surgical Oncology* 17[5], 507-513. 1991.
Excl reason: Not in PICO
- Goldstone, S. E., Winkler, B., Ufford, L. J., Alt, E., and Palefsky, J. M. High prevalence of anal squamous intraepithelial lesions and squamous-cell carcinoma in men who have sex with men as seen in a surgical practice. *Diseases of the Colon & Rectum* 44[5], 690-698. 2001.
Excl reason: Not in PICO
- Greene, M. D. Diagnosis and management of HPV-related anal dysplasia. [Review] [65 refs]. *Nurse Practitioner* 34[5], 45-51. 2009.
Excl reason: Narrative review
- Gretschel, S., Warnick, P., Bembenek, A., Dresel, S., Koswig, S., String, A., Hunerbein, M., and Schlag, P. M. Lymphatic mapping and sentinel lymph node biopsy in epidermoid carcinoma of the anal canal. *European Journal of Surgical Oncology* 34[8], 890-894. 2008.
Excl reason: Not in PICO
- Grosse, G., Dumke, K., Scheffzek, M., and Niedobitek, F. [Diagnostic problems of virus-induced atypical squamous cell proliferations in the area of the anus and genitalia. A case report on Bowenoid papulosis]. [German]. *Geburtshilfe und Frauenheilkunde* 45[4], 232-237. 1985.
Excl reason: Not in PICO
- Grover, D.; Johnson, M.; Smith, C.; Fine, C.; Ogunbiyi, O. Anal intraepithelial neoplasia: Single centre experience. *HIV Medicine*, 13, 33. 2012
Excl reason: Not in PICO
- Gupta, P. J. Common anorectal conditions. *Turkish Journal of Medical Sciences* 34[5], 285-293. 2004.
Excl reason: Not in PICO
- Gupta, P. J. A review of proctological disorders. *European Review for Medical and Pharmacological Sciences* 10[6], 327-335. 2006.
Excl reason: Narrative review
- Gupta, P. J. Family practice in ano-rectal diseases. *Pakistan Journal of Medical Sciences* 22[1], 85-90. 2006.
Excl reason: Narrative review

- Gutierrez, C., Hernansanz, S., Rubiales, A. S., Del Valle, M. L., Cuadrillero, Rodriguez F., Flores, L. A., and Garcia, C. Clinical manifestations and care in tumors with pelvic involvement: Is there a pelvic syndrome in Palliative Care?. [Spanish]. *Medicina Paliativa* 13[1], 32-36. 2006.
Excl reason: Not in PICO
- Handa, Y., Watanabe, O., Adachi, A., and Yamanaka, N. Squamous cell carcinoma of the anal margin with pruritus ani of long duration. *Dermatologic Surgery* 29[1], 108-110. 2003.
Excl reason: Not in PICO
- Handa, Y., Yamanaka, N., Inagaki, H., and Tomita, Y. Large ulcerated perianal hidradenoma papilliferum in a young female. *Dermatologic Surgery* 29[7], 790-792. 2003.
Excl reason: Not in PICO
- Higes, Pascual F., Rubio, Esteban G., Garcia, Guijo C., Pascual Martin-Gamero, M. L., and Liano, Martinez H. [Leptomeningeal carcinomatosis as a form of presentation of anorectal melanoma]. [Spanish]. *Revista Espanola de Enfermedades Digestivas* 81[1], 49-51. 1992.
Excl reason: Not in PICO
- Ho, K. S. and Cranston, R. D. Anal cytology screening in HIV-positive men who have sex with men: What's new and what's now? *Current Opinion in Infectious Diseases* 23[1], 21-25. 2010.
Excl reason: Not in PICO
- Hou, J., Smotkin, D., Isani, S., Smith, H., Ben-David, O., Goldberg, G., and Einstein, M. High incidence of anal disease diagnosed from screening HIV-infected women with anal cytology and triage to high-resolution anoscopy. *Gynecologic Oncology* 120, S122. 2011. Academic Press Inc.
Excl reason: Not in PICO
- Jay, N. Elements of an anal dysplasia screening program. *Journal of the Association of Nurses in AIDS Care* 22[6], 465-477. 2011.
Excl reason: v
- John, Daniel W. Anorectal pain, bleeding and lumps. *Australian Family Physician* 39[6], 376-381. 2010.
Excl reason: Narrative review
- Karandikar, S. S., Borley, A., Crosby, T., Williams, G., Reynolds, S., and Radcliffe, A. G. A five-year audit of anal cancer in Wales. *Colorectal Disease* 8[4], 266-272. 2006.
Excl reason: Not in PICO
- Khatri, V. P. and Chopra, S. Clinical presentation, imaging, and staging of anal cancer. *Surgical Oncology Clinics of North America* 13[2], 295-308. 2004.
Excl reason: Narrative review
- Kim, T., Chae, G., Chung, S. S., Sands, D. R., Speranza, J. R., Weiss, E. G., Noguerras, J. J., and Wexner, S. D. Faecal incontinence in male patients. *Colorectal Disease* 10[2], 124-130. 2008.
Excl reason: Not in PICO
- Kimura, T., Yamagishi, H., and Ichikawa, K. Introduction of the general rules for clinical and pathological studies on cancer of the colon, rectum and anus: Evaluation of invasion distance and budding appearance in early colorectal cancer. *Dokkyo Journal of Medical Sciences* 36[1], 71-74. 2009.
Excl reason: Not in PICO
- Knysh, V. I. and Timofeev, I. M. Malignant tumors of the anal canal. [Russian]. *Voprosy Onkologii* 38[5], 610-615. 1992.
Excl reason: Not in PICO
- Kratzer, G. L. What the family physician should know about proctology. *GP* 38[5], 126-132. 1968.
Excl reason: Pre-1980
- Kreuter, A., Wieland, U., and Brockmeyer, N. [Anal carcinoma and anal intraepithelial neoplasia in HIV-infections]. [German]. *Journal der Deutschen Dermatologischen Gesellschaft* 4[7], 611-612. 2006.
Excl reason: Not in PICO

- Kreuter, A., Brockmeyer, N. H., and Wieland, U. Anal intraepithelial neoplasia and anal carcinoma: An increasing problem in HIV patients. [German]. *Hautarzt* 61[1], 21-26. 2010.
Excl reason: Not in PICO
- Kriz, M., Hegyi, J., Ruzicka, T., and Berking, C. Fluorescence diagnostics as a guide for demarcation and biopsy of suspected anal cancer. *International Journal of Dermatology* 51[1], 31-34. 2012.
Excl reason: Not in PICO
- Kwong, J. J., Cook, P., and Bradley-Springer, L. Improving anal cancer screening in an ambulatory HIV clinic: Experience from a quality improvement initiative. *Aids Patient Care and STDS* 25[2], 73-78. 1-2-2011.
Excl reason: Not in PICO
- Larghero, G. C., Scarpettini, S., Pavero, R., Costanzo, A., Cariati, A., Berti, S., Maritato, F., and Zoli, S. [Adenocarcinoma of the anal glands. Description of a clinical case and review of the literature]. [Italian]. *Minerva Chirurgica* 51[7-8], 573-576. 1996.
Excl reason: Not in PICO
- Lee, J. S., Rieger, N. A., Stephens, J. H., Hewett, P. J., Rodda, D. J., and Lawrence, M. J. Six-year prospective analysis of the rectal bleeding clinic at the Queen Elizabeth Hospital, Adelaide, South Australia. *ANZ Journal of Surgery* 77[7], 553-556. 2007.
Excl reason: Not in PICO (secondary care setting)
- Leiman, G. Anal screening cytology. *CytoJournal* 2. 16-2-2005.
Excl reason: Not in PICO
- Lindsey, K., Decristofaro, C., and James, J. Anal pap smears: Should we be doing them? *Journal of the American Academy of Nurse Practitioners* 21[8], 437-443. 2009.
Excl reason: Not in PICO
- Lopez, M. J., Bliss, Jr, Kraybill, W. G., and Soybel, D. I. Carcinoma of the anal region. *Current Problems in Surgery* 26[8], 525-600. 1989.
Excl reason: Not in PICO
- Marco, V., Autonell, J., Farre, J., Fernandez-Layos, M., and Doncel, F. Retrorectal cyst-hamartomas. Report of two cases with adenocarcinoma developing in one. *American Journal of Surgical Pathology* 6[8], 707-714. 1982.
Excl reason: Not in PICO
- Markos, A. R. The presentation of anogenital cancers as sexually transmissible infection: a case for vigilance. *Sexual Health* 4[1], 79-80. 2007.
Excl reason: Narrative review
- May, C., Brunialti, M., Glaser, K. S., and Stanek, C. Retrospective 10 year analysis of 37 patients with anal carcinoma - Outlook and recommendations for a standardized treatment. *European Surgery - Acta Chirurgica Austriaca* 43, 113. 2011. Springer Wien.
Excl reason: Not in PICO
- McCloskey, J. C., Metcalf, C., French, M. A., Flexman, J. P., Burke, V., and Beilin, L. J. The frequency of high-grade intraepithelial neoplasia in anal/perianal warts is higher than previously recognized. *International journal of STD & AIDS* 18[8], 538-542. 2007.
Excl reason: Not in PICO
- Meyer, J., Willett, C., and Czito, B. Current and emerging treatment strategies for anal cancer. [Review] [30 refs]. *Current Oncology Reports* 12[3], 168-174. 2010.
Excl reason: Not in PICO
- Mlakar, B. Proctoscopy should be mandatory in men that have sex with men with external anogenital warts. *Acta Dermatovenerologica Alpina, Pannonica et Adriatica* 18[1], 7-11. 2009.
Excl reason: Not in PICO
- Nathan, M., Sheaff, M., Fox, P., Goon, P., Gilson, R., and Lacey, C. Early treatment of anal intraepithelial neoplasia. *BMJ* 343, d7717. 2011.
Excl reason: Not in PICO

- Nikias, G., Eisner, T., Katz, S., Levin, L., Eskries, D., Urmacher, C., and McKinley, M. Crohn's disease and colorectal carcinoma: rectal cancer complicating longstanding active perianal disease. *American Journal of Gastroenterology* 90[2], 216-219. 1995.
Excl reason: Not in PICO
- Ojima, Y., Nakatsuka, H., Haneji, H., Kurihara, T., Sadamoto, S., Ohmoto, T., Katayama, N., and Taniyama, K. Primary anorectal malignant melanoma: report of a case. *Surgery Today* 29[2], 170-173. 1999.
Excl reason: Not in PICO
- Ong, J., Jit-Fong, L., Ming-Hian, K., Boon-Swee, O., Kok-Sun, H., and Eu, K. W. Perianal mucinous adenocarcinoma arising from chronic anorectal fistulae: a review from a single institution. *Techniques in Coloproctology* 11[1], 34-38. 2007.
Excl reason: Not in PICO
- Ortholan, C., Ramaioli, A., Peiffert, D., Lusinchi, A., Romestaing, P., Chauveinc, L., Touboul, E., Peignaux, K., Bruna, A., de La, Roche G., Lagrange, J. L., Alzieu, C., and Gerard, J. P. Anal canal carcinoma: early-stage tumors < or =10 mm (T1 or Tis): therapeutic options and original pattern of local failure after radiotherapy. *International Journal of Radiation Oncology, Biology, Physics* 62[2], 479-485. 1-6-2005.
Excl reason: Not in PICO
- Ortholan, C., Resbeut, M., Hannoun-Levi, J.-M., Teissier, E., Gerard, J.-P., Ronchin, P., Zaccariotto, A., Minsat, M., Benezery, K., Francois, E., Salem, N., Ellis, S., Azria, D., Champetier, C., Gross, E., and Cowen, D. Anal canal cancer: Management of inguinal nodes and benefit of prophylactic inguinal irradiation (CORS-03 study). *International Journal of Radiation Oncology Biology Physics* 82[5], 1988-1995. 1-4-2012.
Excl reason: Not in PICO
- Ott, J. J., Ullrich, A., and Miller, A. B. The importance of early symptom recognition in the context of early detection and cancer survival. *European Journal of Cancer* 45[16], 2743-2748. 2009.
Excl reason: Narrative review
- Pardela, M. [Early form of anal cancer in an 11-year-old boy]. [Polish]. *Wiadomosci Lekarskie* 37[7], 555-556. 1-4-1984.
Excl reason: Not in PICO
- Pfenninger, J. L. and Zainea, G. G. Common anorectal conditions: Part II. Lesions. *American Family Physician* 64[1], 77-88. 1-7-2001.
Excl reason: Narrative review
- Pfenninger, J. L. and Zainea, G. G. Common anorectal conditions: Part I. Symptoms and complaints. *American Family Physician* 63[12], 2391-2398. 15-6-2001.
Excl reason: Narrative review
- Pfenninger, J. L. and Zainea, G. G. Common anorectal conditions. *Obstetrics and Gynecology* 98[6], 1130-1139. 2001.
Excl reason: Narrative review
- Pietri, P., Terranova, O., Gabrielli, F., and Rebuffat, C. [Clinical aspects and therapy of malignant neoplasms of the anal margin and canal]. [Italian]. *Minerva Medica* 71[10], 751-762. 17-3-1980.
Excl reason: Not in PICO
- Pocard, M. and Sabourin, J. C. [Sentinel lymph node biopsy in gastro-intestinal surgery: facts and future implications]. [Review] [99 refs] [French]. *Journal de Chirurgie* 145, Spec-12S20. 2008.
Excl reason: Not in PICO
- Pollastri, E., Brosutti, O., Montenovo, A., Bergero, A., and Moroni, J. [Adenocarcinoma of anal canal. Report of a case and review of the literature]. [Review] [34 refs] [Spanish]. *Acta Gastroenterologica Latinoamericana* 24[4], 239-244. 1994.
Excl reason: Not in PICO
- Prieto, Reyes M. and Vazquez, Marquez L. [Anal epidermoid carcinoma: a rare incidence or a rare diagnosis?]. [Review] [53 refs] [Spanish]. *Revista Espanola de Enfermedades Digestivas* 89[2],

128-132. 1997.

Excl reason: Not in PICO

Quintas-Cardama, A., Lazar, A. J., Woodman, S. E., Kim, K., Ross, M., and Hwu, P. Complete response of stage IV anal mucosal melanoma expressing KIT Val560Asp to the multikinase inhibitor sorafenib. *Nature Clinical Practice Oncology* 5[12], 737-740. 2008.

Excl reason: Not in PICO

Reshef, R., Libner, E., Rennert, H. S., Cohen, I., Shiler, M., Shkolnik, T., and Rennert, G. A community hospital experience with colonoscopic polypectomies. *Israel Journal of Medical Sciences* 33[10], 666-673. 1997.

Excl reason: Not in PICO

Rosa-Cunha, I., Degennaro, V. A., Hartmann, R., Milikowski, C., Irizarry, A., Heitman, B., Gomez-Marin, O., and Dickinson, G. M. Description of a pilot anal pap smear screening program among individuals attending a veteran's affairs HIV clinic. *Aids Patient Care and STDS* 25[4], 213-219. 1-4-2011.

Excl reason: Not in PICO

Sato, M., Ogawa, H., Shibata, C., Miura, K., Ando, T., Saijo, F., Haneda, S., Kakyo, M., Kinouchi, M., Fukushima, K., Funayama, Y., Takahashi, K., and Sasaki, I. [A case of anal cancer with rapidly rising CEA in longstanding perianal Crohn disease after infliximab administration]. [Japanese]. *Nippon Shokakibyo Gakkai Zasshi - Japanese Journal of Gastroenterology* 107[6], 885-892. 2010.

Excl reason: Not in PICO

Scarpini, C., White, V., Muralidhar, B., Patterson, A., Hickey, N., Singh, N., Mullerat, J., Winslet, M., Davies, R. J., Phillips, M.-L., Stacey, P., Laskey, R. A., Miller, R., Nathan, M., and Coleman, N. Improved screening for anal neoplasia by immunocytochemical detection of minichromosome maintenance proteins. *Cancer Epidemiology Biomarkers and Prevention* 17[10], 2855-2864. 2008.

Excl reason: Not in PICO

Sendagorta, E., Herranz, P., Guadalajara, H., and Zamora, F. X. Early detection of anal intraepithelial neoplasia in high-risk patients. [Spanish]. *Actas Dermo-Sifiliograficas* 102[10], 757-765. 2011.

Excl reason: Narrative review

Shepherd, N. A. Anal Intraepithelial Neoplasia and Other Neoplastic Precursor Lesions of the Anal Canal and Perianal Region. *Gastroenterology Clinics of North America* 36[4], 969-987. 2007.

Excl reason: Narrative review

Shlebak, A. A. and Smith, D. B. Incidence of objectively diagnosed thromboembolic disease in cancer patients undergoing cytotoxic chemotherapy and/or hormonal therapy. *Cancer Chemotherapy & Pharmacology* 39[5], 462-466. 1997.

Excl reason: Not in PICO

Siekas, L. and Aboulafia, D. M. Establishing an anal dysplasia clinic for hiv-infected men: initial experience. *AIDS Reader* 19[5], 178-182+183. 2009.

Excl reason: Not in PICO

Simpson, J. A. D. and Scholefield, J. H. Diagnosis and management of anal intraepithelial neoplasia and anal cancer. *BMJ (Online)* 343[7831], 1004-1009. 12-11-2011.

Excl reason: Narrative review

Sonnex, C., Scholefield, J. H., Kocjan, G., Kelly, G., Whatrup, C., Mindel, A., and Northover, J. M. A. Anal human papillomavirus infection: A comparative study of cytology, colposcopy and DNA hybridisation as methods of detection. *Genitourinary Medicine* 67[1], 21-25. 1991.

Excl reason: Not in PICO

Sugita, A., Koganei, K., Tatsumi, K., Yamada, K., Futatsuki, R., Kuroki, H., Arai, K., Kimura, H., Kitoh, F., and Fukushima, T. Optimal diagnosis for fistula-associated anal cancer with Crohn's disease. [Japanese]. *Gastroenterological Endoscopy* 54[1], 66-72. 2012.

Excl reason: Narrative review

- Takashima, S., Fukunaga, J., Kushibiki, K., and Kinami, Y. [A case of carcinoma arising from an anal fistula]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics* 33[11], 1391-1396. 1987.
Excl reason: Not in PICO
- Tanum, G. Diagnosis and treatment of anal carcinoma. *Acta Oncologica* 31[5], 513-518. 1992.
Excl reason: Narrative review
- Tarazi, R. and Nelson, R. L. Anal adenocarcinoma: A comprehensive review. *Seminars in Surgical Oncology* 10[3], 235-240. 1994.
Excl reason: Narrative review
- Thang, N. N., Cochet, S., George, A. C., Betz, M., and Roth, A. [Management of anal canal carcinoma]. [French]. *Revue Medicale Suisse* 7[296], 1144-1148. 25-5-2011.
Excl reason: Narrative review
- Tjandra, J. J., Antoniuk, P. M., Webb, B., Petras, R. E., and Fazio, V. W. Leiomyosarcoma of the rectum and anal canal. *Australian and New Zealand Journal of Surgery* 63[9], 703-709. 1993.
Excl reason: Not in PICO
- Tran, Thang N. N., Cochet, S., George, A.-C., Betz, M., and Roth, A. Management of anal canal carcinoma. [French]. *Revue Medicale Suisse* 7[296], 1144-1148. 25-5-2011.
Excl reason: Narrative review
- Trovato, C., Sonzogni, A., Fiori, G., Ravizza, D., De, Roberto G., Tamayo, D., De, Leone A., and Crosta, C. Detection of anal intraepithelial neoplasia and anal carcinoma in-vivo using confocal laser endomicroscopy. *Gastroenterology* 138[5 SUPPL. 1], S95-S96. 2010. W.B. Saunders.
Excl reason: Not in PICO
- Turk, P. S., Belliveau, J. F., Darnowski, J. W., Weinberg, M. C., Leenen, L., and Wanebo, H. J. Isolated pelvic perfusion for unresectable cancer using a balloon occlusion technique. *Archives of Surgery* 128[5], 533-538. 538.
Excl reason: Not in PICO
- Tyerman, Z. and Aboulafia, D. M. Review of screening guidelines for non-AIDS-defining malignancies: evolving issues in the era of highly active antiretroviral therapy. [Review]. *AIDS Reviews* 14[1], 3-16. 2012.
Excl reason: Not in PICO
- van Zeeburg, H. J., Snijders, P. J., Wu, T., Gluckman, E., Soulier, J., Surralles, J., Castella, M., van der Wal, J. E., Wennerberg, J., Califano, J., Velleuer, E., Dietrich, R., Ebell, W., Bloemena, E., Joenje, H., Leemans, C. R., and Brakenhoff, R. H. Clinical and molecular characteristics of squamous cell carcinomas from Fanconi anemia patients. *Journal of the National Cancer Institute* 100[22], 1649-1653. 19-11-2008.
Excl reason: Not in PICO
- Varnai, A. D., Bollmann, M., Griefingholt, H., Speich, N., Schmitt, C., Bollmann, R., and Decker, D. HPV in anal squamous cell carcinoma and anal intraepithelial neoplasia (AIN). Impact of HPV analysis of anal lesions on diagnosis and prognosis. *International Journal of Colorectal Disease* 21[2], 135-142. 2006.
Excl reason: Not in PICO
- Venclauskas, L., Saladzinskas, Z., Tamelis, A., Pranys, D., and Pavalkis, D. Mucinous adenocarcinoma arising in an anorectal fistula. *Medicina (Kaunas, Lithuania)* 45[4], 286-290. 2009.
Excl reason: Not in PICO
- Verardino, G. C., Silva, R. S., Obadia, D. L., Gripp, A. C., and Alves, Mde F. Rare cutaneous metastasis from a probable basaloid carcinoma of the colon mimicking pyogenic granuloma. *Anais Brasileiros de Dermatologia* 86[3], 537-540. 2011.
Excl reason: Not in PICO
- Weis, S. E., Vecino, I., Pogoda, J. M., Susa, J. S., Nevoit, J., Radaford, D., McNeely, P., Colquitt, C. A., and Adams, E. Prevalence of anal intraepithelial neoplasia defined by anal cytology screening and high-resolution anoscopy in a primary care population of HIV-infected men and women.

Diseases of the Colon and Rectum 54[4], 433-441. 2011.

Excl reason: Not in PICO (screening)

Wienert, V. Perianal squamous cell carcinoma. [Review] [20 refs]. Journal der Deutschen Dermatologischen Gesellschaft 4[11], 984-985. 2006.

Excl reason: Narrative review

Wietfeldt, E. D. and Thiele, J. Malignancies of the anal margin and perianal skin. Clinics in Colon & Rectal Surgery 22[2], 127-135. 2009.

Excl reason: Narrative review

Williams, G. R. and Talbot, I. C. Anal carcinoma - A histological review. Histopathology 25[6], 507-516. 1994.

Excl reason: Narrative review

Williams, V. M., Metcalf, C., French, M. A., and McCloskey, J. C. Audit of paired anal cytology and histopathology outcomes in patients referred to a public sexual health clinic. Sexual Health 7[3], 346-351. 2010.

Excl reason: Not in PICO

Winder, D. M., Ball, S. L., Vaughan, K., Hanna, N., Woo, Y. L., Franzer, J. T., Sterling, J. C., Stanley, M. A., Sudhoff, H., and Goon, P. K. Sensitive HPV detection in oropharyngeal cancers. BMC cancer 9, 440. 2009.

Excl reason: Not in PICO

Wong, A. Y., Rahilly, M. A., Adams, W., and Lee, C. S. Mucinous anal gland carcinoma with perianal Pagetoid spread. Pathology 30[1], 1-3. 1998.

Excl reason: Not in PICO

Yabe, N., Murai, S., Shimizu, H., Fukushima, H., Minagawa, T., Ishida, T., Shoji, T., Amemiya, T., Hasegawa, H., and Kitagawa, Y. [Treatment of early rectal carcinoma by transanal resection-a case report]. [Japanese]. Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy] 38[12], 1972-1974. 2011.

Excl reason: Not in PICO

Yang, B. L., Shao, W. J., Sun, G. D., Chen, Y. Q., and Huang, J. C. Perianal mucinous adenocarcinoma arising from chronic anorectal fistulae: a review from single institution. International Journal of Colorectal Disease 24[9], 1001-1006. 2009.

Excl reason: Not in PICO

Yokoyama, Y., Nishimura, Y., Yatsuoka, T., Sakamoto, H., Tanaka, Y., Nishimura, Y., and Kurosumi, M. [A case of anal metastasis from sigmoid colon cancer in a long-term survivor who had repeated local excisions]. [Japanese]. Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy] 37[12], 2585-2587. 2010.

Excl reason: Not in PICO

Zachary, T. and Aboulafia, D. M. Review of screening guidelines for non-AIDS-defining malignancies: Evolving issues in the era of highly active antiretroviral therapy. AIDS Reviews 14[1], 3-16. 2012.

Excl reason: Not in PICO

Review question:

Which investigations of symptoms of suspected anal cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references	No of references	Finish date of
---------------	---------------	------------------	------------------	----------------

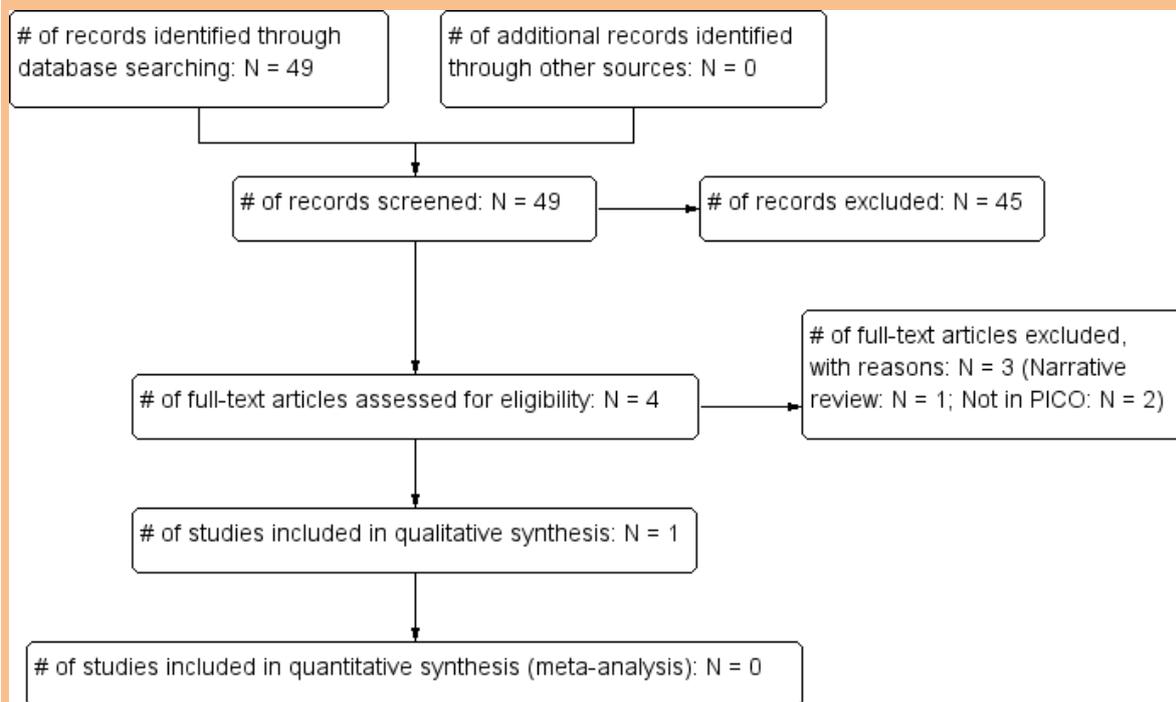
		found	retrieved	search
<i>Medline</i>	1980-2013	146	19	11/06/2013
<i>Premedline</i>	1980-2013	19	2	11/06/2013
<i>Embase</i>	1980-2013	196	29	12/06/2013
<i>Cochrane Library</i>	1980-2013	57	0	12/06/2013
<i>Psychinfo</i>	1980-2013	5	0	11/06/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	93	9	13/06/2013

Total References retrieved (after de-duplication): 44

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	6/2013-26/08/2014	5	0	26/08/2014
<i>Premedline</i>	6/2013-26/08/2014	13	1	26/08/2014
<i>Embase</i>	6/2013-26/08/2014	38	4	26/08/2014
<i>Cochrane Library</i>	6/2013-26/08/2014	12	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	6/2013-26/08/2014	12	0	26/08/2014

Total References retrieved (after de-duplication): 5



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The only included study was associated with a number of bias and validity issues, with the main concerns

relating to whether the results are representative of those of UK-based primary care practice and the fact that negative sigmoidoscopy results were not verified or followed up.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Niv (1992)	+	+	-	-	?	+	+

 High	 Unclear	 Low
--	---	---

Study results

Table 1: Anal cancer: Sigmoidoscopy

Study	Test	Prevalence	Sensitivity (95% CI)	Specificity (95% CI)	Other results (95% CI)
Niv (1992)	Flexible sigmoidoscopy	5/255	Not reported	Not reported	TP = 4 FN = ≥ 1 TN = ? FP = 0 Positive predictive value = 100% (39.6-100) False negativity rate = cannot be ascertained as negative cases did not appear to be followed up

TP = true positives, FP = false positives, TN = true negatives, FN = false negatives.

No evidence was found for proctoscopy.

Evidence statement(s):

Sigmoidoscopy (1 study, N = 255) conducted in symptomatic patients presenting in a primary care setting is associated with a positive predictive values of 100%. The included study was associated with 3 bias/applicability concerns (see also Table 1).

Evidence tables

Niv (1992)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective consecutive patient series from an open-access flexible sigmoidoscopy outpatient clinic in Israel.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes

Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 255; 123 males, 132 females; mean age (range) = 54 (10-90) years. The patients were referred with the following indications: Change in bowel habit (N = 103), rectal bleeding (N = 107), abdominal pain (N = 45), anaemia (3%), weight loss (N = 15), Fx colon cancer (N = 26), positive faecal occult blood test (N = 26), "post polyp." (N = 11). <u>Inclusion criteria:</u> All patients referred for open-access flexible sigmoidoscopy by general practitioners. <u>Exclusion criteria:</u> Bad state of health, referral error. <u>Clinical setting:</u> Israeli open-access flexible sigmoidoscopy outpatient clinic.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Flexible sigmoidoscopy
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	When a polyp or cancer was found, the patient was referred for total colonoscopy. Negative results did not appear to be followed up.
Is the reference standard likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	As the negative results did not appear to be followed up, the false negative rate cannot be ascertained
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	No
Could the patient flow have introduced bias? All tests	High risk

References

Included studies

Niv, Y. and Asaf, V. Open-access, flexible, fiberoptic sigmoidoscopy in a regional primary-care clinic. *Journal of Clinical Gastroenterology* 15[3], 218-221. 1992.

Excluded studies (with excl reason)

(2009) The Dutch College of General Practitioners guideline for rectal bleeding. [Dutch]. *Huisarts en Wetenschap*, 52: 23-38.

Guideline

Abbas, A., Yang, G. & Fakih, M. (2010) Management of Anal Cancer in 2010 Part 1: Overview, Screening, and Diagnosis. *Oncology-New York*, 24: 364-369.

Narrative review

Beart, R. W., Jr. (1990) Colon, rectum, and anus. [Review] [32 refs]. *Cancer*, 65: Suppl-8.

Narrative review

Berndt, H. & Neumann, P. (1983) [Early diagnosis of malignant tumors of the digestive organs. 2]. [Review] [0 refs] [German]. *Zeitschrift fur Arztliche Fortbildung (Jena)*, 77: 100-102.

Narrative review

Billingham, R. P. (1999) Anorectal miscellany: pilonidal disease, anal cancer, Bowen's and Paget's diseases, foreign bodies, and hidradenitis suppurativa. [Review] [29 refs]. *Primary Care; Clinics in Office Practice*, 26: 171-177.

Narrative review

Crooms, J. W. & Kovalcik, P. J. (1990) Anal lesions. When to suspect carcinoma. *Postgraduate Medicine*, 77: 85-88.

Narrative review

Dahl, O. & Fluge, O. (2008) Anal cancer. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 128: 198-200.

Narrative review

De, P., V, Bouillet, T., Parisot, C. & Atienza, P. (1998) The role of endosonography in anal cancer. [French]. *Acta Endoscopica*, 28: 359-365.

Narrative review

Gervaz, P., Buchs, N. & Morel, P. (2008) Diagnosis and management of anal cancer. [Review] [45 refs]. *Current Gastroenterology Reports*, 10: 502-506.

Narrative review

Goldstone, S. E., Winkler, B., Ufford, L. J., Alt, E. & Palefsky, J. M. (2001) High prevalence of anal squamous intraepithelial lesions and squamous-cell carcinoma in men who have sex with men as seen in a surgical practice. *Diseases of the Colon and Rectum*, 44: 690-698.

Not in PICO

Greene, M. D. (2009) Diagnosis and management of HPV-related anal dysplasia. [Review] [65 refs]. *Nurse Practitioner*, 34: 45-51.

Narrative review

Gross, G. (2014) - Genitoanal human papillomavirus infection and associated neoplasias. - *Current Problems in Dermatology*, 45: 98-122.

Narrative review

Grover, D., Johnson, M., Smith, C., Fine, C. & Ogunbiyi, O. (2012) Anal intraepithelial neoplasia: Single centre experience. *HIV Medicine*, 13: 33.

Not in PICO

- Gupta, P. J. (2006) A review of proctological disorders. *European Review for Medical and Pharmacological Sciences*, 10: 327-335.
Narrative review
- Hillman, R. J., van Leeuwen, M. T., Vajdic, C. M., McHugh, L., Prestage, G. P., Botes, L. P., Zablotska, I., Medley, G., Tabrizi, S. N., Grulich, A. E. & Jin, F. (2012) Prevalence and predictors of high-grade anal intraepithelial neoplasia in a community-based sample of homosexual men. *Sexual Health*, 9: 574-579.
Not in PICO
- John, D. W. (2010) Anorectal pain, bleeding and lumps. *Australian Family Physician*, 39: 376-381.
Narrative review
- Karandikar, S. S., Borley, A., Crosby, T., Williams, G., Reynolds, S. & Radcliffe, A. G. (2006) A five-year audit of anal cancer in Wales. *Colorectal Disease*, 8: 266-272.
Not in PICO
- Kaul, A., Shah, A., Magill, F. H., Hawkins, S. A. & Skaife, P. (2013) Immunological faecal occult blood testing: a discriminatory test to identify colorectal cancer in symptomatic patients. *International Journal Of Surgery*, 11: 329-331.
Not in PICO
- Khatri, V. P. & Chopra, S. (2004) Clinical presentation, imaging, and staging of anal cancer. *Surgical Oncology Clinics of North America*, 13: 295-308.
Narrative review
- Knysh, V. I. & Timofeev, I. (1992) [Malignant tumors of the anal canal]. [Russian]. *Voprosy Onkologii*, 38: 610-615.
Not in PICO
- Kreuter, A., Brockmeyer, N. H. & Wieland, U. (2010) Anal intraepithelial neoplasia and anal carcinoma: An increasing problem in HIV patients. [German]. *Hautarzt*, 61: 21-26.
Narrative review
- Lee, J. S. J., Rieger, N. A., Stephens, J. H., Hewett, P. J., Rodda, D. J. & Lawrence, M. J. (2007) Six-year prospective analysis of the rectal bleeding clinic at the Queen Elizabeth Hospital, Adelaide, South Australia. *ANZ Journal of Surgery*, 77: 553-556.
Not in PICO
- Lindsey, K., DeCristofaro, C. & James, J. (2009) Anal Pap smears: Should we be doing them?. [Review] [26 refs]. *Journal of the American Academy of Nurse Practitioners*, 21: 437-443.
Narrative review
- Lopez, M. J., Bliss, D. P., Jr., Kraybill, W. G. & Soybel, D. I. (1989) Carcinoma of the anal region. [Review] [172 refs]. *Current Problems in Surgery*, 26: 525-600.
Narrative review
- Martinez-Ramos, D., Nomdedeu-Guinot, J., Artero-Sempere, R., Escrig-Sos, J., Gibert-Gerez, J., Alcalde-Sanchez, M. & Salvador-Sanchis, J. L. (2009) Prospective study to evaluate diagnostic accuracy in benign anal diseases in primary care. *Atencion Primaria*, 41: 207-212.
Not in PICO
- Mathews, W. C., Cachay, E. R., Caperna, J., Sitapati, A., Cosman, B. & Abramson, I. (2010) Estimating the accuracy of anal cytology in the presence of an imperfect reference standard. *PLoS ONE [Electronic Resource]*, 5: e12284.
Not in PICO
- Mehta, R. & Khurana, K. K. (2014) Anal cytology as a predictor of anal intraepithelial neoplasia; an institutional experience. *Laboratory Investigation*, 94: 113A.
Not in PICO
- Mlakar, B. (2009) Proctoscopy should be mandatory in men that have sex with men with external anogenital warts. *Acta Dermatovenerologica Alpina, Panonica et Adriatica*, 18: 7-11.
Not in PICO

- Pietri, P., Terranova, O., Gabrielli, F. & Rebuffat, C. (1980) [Clinical aspects and therapy of malignant neoplasms of the anal margin and canal]. [Italian]. *Minerva Medica*, 71: 751-762.
Not in PICO
- Roberts, J. M. & Ekman, D. (2012) The reporting of anal cytology and histology samples: establishing terminology and criteria. *Sexual Health*, 9: 562-567.
Narrative review
- Sakamoto, T., Konishi, F., Yoshida, T., Yoshinaga, Y., Izumo, T. & Lefor, A. (2014) Adenocarcinoma arising from an anal gland - Report of a case. *International Journal of Surgery Case Reports*, 5: 234-236.
Not in PICO
- Sendagorta, E., Herranz, P., Guadalajara, H. & Zamora, F. X. (2011) Early detection of anal intraepithelial neoplasia in high-risk patients. [Spanish]. *Actas Dermo-Sifiliograficas*, 102: 757-765.
Narrative review
- Serra, F. & Naves, A. (2014) Anal cancer: Precursor lesions and early cancer. considerations on terminology, diagnosis and treatment. *Revista Medica de Rosario*, 80: 21-32.
Narrative review
- Simpson, J. A. D. & Scholefield, J. H. (2011) Diagnosis and management of anal intraepithelial neoplasia and anal cancer. *BMJ (Online)*, 343: 1004-1009.
Narrative review
- Sonnex, C., Scholefield, J. H., Kocjan, G., Kelly, G., Whatrup, C., Mindel, A. & Northover, J. M. A. (1991) Anal human papillomavirus infection: A comparative study of cytology, colposcopy and DNA hybridisation as methods of detection. *Genitourinary Medicine*, 67: 21-25.
Not in PICO
- Sugita, A., Koganei, K., Tatsumi, K., Yamada, K., Futatsuki, R., Kuroki, H., Arai, K., Kimura, H., Kitoh, F. & Fukushima, T. (2012) Optimal diagnosis for fistula-associated anal cancer with Crohn's disease. [Japanese]. *Gastroenterological Endoscopy*, 54: 66-72.
Narrative review
- Tanum, G., Tveit, K. & Karlsen, K. O. (1991) Diagnosis of Anal Carcinoma - Doctors Finger Still the Best. *Oncology*, 48: 383-386.
Not in PICO
- Tanum, G. (1992) Diagnosis and treatment of anal carcinoma. *Acta Oncologica*, 31: 513-518.
Narrative review
- Tarazi, R. & Nelson, R. L. (1994) Anal adenocarcinoma: a comprehensive review. [Review] [26 refs]. *Seminars in Surgical Oncology*, 10: 235-240.
Narrative review
- Thang, N. N., Cochet, S., George, A. C., Betz, M. & Roth, A. (2011) [Management of anal canal carcinoma]. [French]. *Revue Medicale Suisse*, 7: 1144-1148.
Narrative review
- Trovato, C., Sonzogni, A., Fiori, G., Ravizza, D., De, R. G., Tamayo, D., De, L. A. & Crosta, C. (2010) Detection of anal intraepithelial neoplasia and anal carcinoma in-vivo using confocal laser endomicroscopy. *Gastroenterology*, 138: S95-S96.
Not in PICO
- Uronis, H. E. & Bendell, J. C. (2007) Anal cancer: An overview. *The Oncologist*, 12: 524-534.
Narrative review
- van Dalen, R. M. & Hershman, M. J. (1997) How to do it in surgery: transanal endoscopic microsurgery. [Review] [13 refs]. *British Journal of Hospital Medicine*, 58: 498-500.
Narrative review
- Varnai, A. D., Bollmann, M., Griefingholt, H., Speich, N., Schmitt, C., Bollmann, R. & Decker, D. (2006) HPV in anal squamous cell carcinoma and anal intraepithelial neoplasia (AIN). Impact of HPV analysis of anal lesions on diagnosis and prognosis. *International Journal of Colorectal Disease*,

21: 135-142.

Not in PICO

Vijayaraghavan, M., Kharbanda, K. & Mathur, M. (1992) S-100 staining for the diagnosis of melanoma of the anal canal. *Indian Journal of Pathology & Microbiology*, 35: 113-117.

Not in PICO

Wietfeldt, E. D. & Thiele, J. (2009) Malignancies of the anal margin and perianal skin. *Clinics in Colon & Rectal Surgery*, 22: 127-135.

Narrative review

Zefelippo, A., Botti, F., Oreggia, B., Carrara, A. & Contessini-Avesani, E. (2014) Perianal crohn's disease and fistulaassociated carcinoma: A case series. *Techniques in Coloproctology*, 18: 105.

Not in PICO

Zhi-Ming, X. & Shi-Xin, L. (1997) Analysis of 60 cases of rare malignant tumors in the anorectal region. [Chinese]. *Chinese Journal of Clinical Oncology*, 24: 347-350.

Not in PICO

BREAST CANCER

Review question:

What is the risk of breast cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

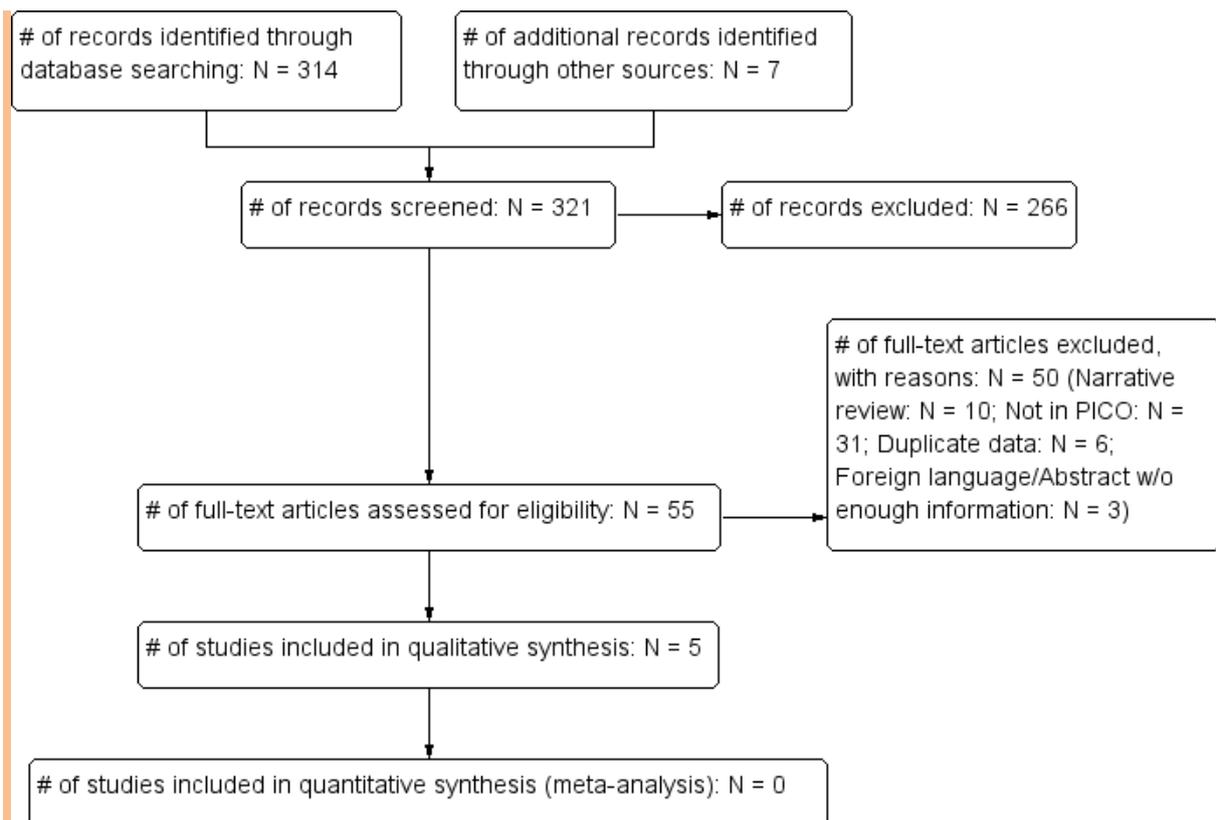
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-4/2013	1361	122	22/04/2013
<i>Premedline</i>	1980-4/2013	275	24	23/04/2013
<i>Embase</i>	1980-4/2013	1776	151	25/04/2013
<i>Cochrane Library</i>	1980-4/2013	426	4	25/04/2013
<i>Psychinfo</i>	1980-4/2013	385	23	23/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-4/2013	1541	84	26/04/2013

Total References retrieved (after de-duplication): 284

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-12/08/2014	145	9	12/08/2014
<i>Premedline</i>	4/2013-12/08/2014	172	11	12/08/2014
<i>Embase</i>	4/2013-12/08/2014	578	13	12/08/2014
<i>Cochrane Library</i>	4/2013-12/08/2014	138	0	12/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	4/2013-12/08/2014	95	2	12/08/2014

Total References retrieved (after de-duplication): 30



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issues to note is that 3/5 studies employed samples of patients that are not directly representative of an unselected symptomatic population of patients presenting to the UK-based GP and a fourth study employed a case-control design which has been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors may have gone some way in counteracting this influence. Two of the studies also employed reference standards that are subject to an unclear risk of bias, one study only reported episode-(not patient)based analyses, which seems to result in overestimation of the PPVs, and one study had a large amount of missing data; all of which must be born in mind when evaluating the evidence contributed by these studies.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Barton (1999)	+	+	?	+	?	+	+
Eberl (2008)	+	+	?	+	?	+	+
McCowan (2011)	+	+	+	-	+	+	+
Oudega (2006)	+	+	+	+	?	+	+
Walker (2014)	-	+	+	+	+	+	+

- High ? Unclear + Low

Study results

Table 1: Breast cancer: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)% Prevalence
Barton (1999) <i>Episode-based analysis</i>	Breast pain	Women aged 40-79 years	1.8 (0.6-4.9) 4/221 episodes in 372 women
Eberl (2008)	Breast pain	Women aged <25 – 75+ years	0.9 (0.5-1.7) 11/1191
McCowan (2011)	Breast pain	Women aged 25- >80 years	5.9 (1-21.1) 2/34
Walker (2014)	Breast pain	Women aged 40-49 years	0.17 (0.16-0.17)
Walker (2014)	Breast pain	Women aged 50-59 years	0.8 (0.52-1.2)
Walker (2014)	Breast pain	Women aged 60-69 years	1.2 (0.73-2)
Walker (2014)	Breast pain	Women aged 70+ years	2.8 (1.4-5.4)
Barton (1999) <i>Episode-based analysis</i>	Breast mass	Women aged 40-79 years	10.7 (6.9-16.1) 21/196 episodes in 372 women
Eberl (2008)	Breast lump/mass	Women aged <25 – 75+ years	8.1 (6.3-10.4) 60/741
Walker (2014)	Breast lump	Women aged 40-49 years	4.8 (3.6-5.4)
Walker (2014)	Breast lump	Women aged 50-59 years	8.5 (6.7-11)
Walker (2014)	Breast lump	Women aged 60-69 years	25 (17-36)

Walker (2014)	Breast lump	Women aged 70+ years	48 (35-61)
McCowan (2011)	Discrete breast lump	Women aged 25- >80 years	10 (3.7-22.6) 5/50
McCowan (2011)	Discrete breast lump < 2 cm	Women aged 25- >80 years	7.7 (0.4-37.9) 1/13
McCowan (2011)	Discrete breast lump ≥ 2 cm	Women aged 25- >80 years	14.3 (2.5-43.8) 2/14
McCowan (2011)	Discrete breast lump: Round, oblong mass	Women aged 25- >80 years	25 (4.5-64.4) 2/8
McCowan (2011)	Discrete breast lump: Irregular in shape	Women aged 25- >80 years	0 (0-69) 0/3
McCowan (2011)	Discrete breast lump: Mobile	Women aged 25- >80 years	12.5 (2.2-40) 2/16
McCowan (2011)	Discrete breast lump: Tethered to skin or chest wall	Women aged 25- >80 years	40 (7.3-83) 2/5
McCowan (2011)	Discrete breast lump: Smooth texture	Women aged 25- >80 years	18.2 (3.2-52.2) 2/11
McCowan (2011)	Discrete breast lump: Irregular texture	Women aged 25- >80 years	33.3 (6-75.9) 2/6
McCowan (2011)	Discrete breast lump: Spongy texture	Women aged 25- >80 years	0 (0-94.5) 0/1
Walker (2014)	Nipple discharge	Women aged 40-49 years	1.2 (NR)
Walker (2014)	Nipple discharge	Women aged 50-59 years	2.1 (0.81-5.1)
Walker (2014)	Nipple discharge	Women aged 60-69 years	2.3 (NR)
Walker (2014)	Nipple discharge	Women aged 70+ years	23 (NR)
McCowan (2011)	Nipple discharge	Women aged 25- >80 years	0 (0-37.1) 0/9
McCowan (2011)	Nipple discharge: Bloodstained	Women aged 25- >80 years	0 (0-53.7) 0/5
McCowan (2011)	Nipple discharge: Persistent	Women aged 25- >80 years	0 (0-43.9) 0/7
Barton (1999) <i>Episode-based analysis</i>	Skin or nipple change	Women aged 40-79 years	3 (0.5-11.3) 2/67 episodes in 372 women
Eberl (2008)	Nipple complaint	Women aged <25 – 75+ years	1.9 (0.6-5.1) 4/210
McCowan (2011)	Nipple eczema	Women aged 25- >80 years	0 (0-94.3) 0/1
McCowan (2011)	Nipple retraction	Women aged 25- >80 years	0 (0-53.7) 0/5
Walker (2014)	Nipple retraction	Women aged 40-49 years	NR (NR) 4 cases, 0 controls
Walker (2014)	Nipple retraction	Women aged 50-59 years	2.6 (NR)
Walker (2014)	Nipple retraction	Women aged 60-69 years	3.4 (NR)

Walker (2014)	Nipple retraction	Women aged 70+ years	12 (NR)
Barton (1999) <i>Episode-based analysis</i>	Breast lumpiness	Women aged 40-79 years	2.6 (0.1-15.4) 1/38 episodes in 372 women
McCowan (2011)	Breast thickening	Women aged 25- >80 years	11.1 (0.6-49.3) 1/9
McCowan (2011)	Breast abscess	Women aged 25- >80 years	0 (0-94.3) 0/1
Barton (1999) <i>Episode-based analysis</i>	Other breast symptom	Women aged 40-79 years	0 (0-43.9) 0/7 episodes in 372 women
Eberl (2008)	Other breast complaint	Women aged <25 – 75+ years	1.7 (0.7-3.8) 6/361
McCowan (2011)	Other breast symptom (skin nodules, general nodularity)	Women aged 25- >80 years	25 (1.3-78.1) 1/4
McCowan (2011)	Lymphadenopathy	Women aged 25- >80 years	40 (7.3-83) 2/5
Oudega (2006)	Deep vein thrombosis	All patients	0.93 (0.3-2.53) 4/430

CI = Confidence interval. Please note the calculations of the positive predictive values differ between the studies with Barton (1999), Eberl (2008), McCowan (2011) and Oudega (2006) using (TP)/(TP+FP) and Walker (2014) using Bayesian statistics due to the case-control design of this study. No meta-analyses were performed as there were not enough studies for this analysis to be performed with both Barton (1999) and Walker (2014) being ineligible for inclusion due to the episode-based analysis and case-control design, respectively.

Table 2: Breast cancer: Symptom combinations

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)%
Barton (1999) <i>Episode-based analysis</i>	Breast pain (reported twice in an episode??)	Women aged 40-79 years	1.2 (0.2-4.7)* 2/169 episodes in 372 women
Barton (1999) <i>Episode-based analysis</i>	Breast mass (reported twice in an episode??)	Women aged 40-79 years	10.7 (6.5-16.8)* 17/159 episodes in 372 women
Barton (1999) <i>Episode-based analysis</i>	Skin or nipple change (reported twice in an episode??)	Women aged 40-79 years	2 (0.1-11.8)* 1/51 episodes in 372 women
Barton (1999) <i>Episode-based analysis</i>	Breast lumpiness (reported twice in an episode??)	Women aged 40-79 years	4 (0.2-22.3)* 1/25 episodes in 372 women
Barton (1999) <i>Episode-based analysis</i>	Breast pain and breast mass	Women aged 40-79 years	6.5 (1.1-22.8) 2/31 episodes in 372 women
Walker (2014)	Breast lump and breast pain	Women aged 40-49 years	4.9 (NR)
Walker (2014)	Breast lump and breast pain	Women aged 50-59 years	5.7 (NR)
Walker (2014)	Breast lump and breast	Women aged 60-69 years	6.5 (NR)

	pain	years	
Walker (2014)	Breast lump and breast pain	Women aged 70+ years	> 5 (NR)
Barton (1999) <i>Episode-based analysis</i>	Breast pain and skin or nipple change	Women aged 40-79 years	0 (0-26.8) 0/14 episodes in 372 women
Barton (1999) <i>Episode-based analysis</i>	Breast pain and breast lumpiness	Women aged 40-79 years	0 (0-43.9) 0/7 episodes in 372 women
Barton (1999) <i>Episode-based analysis</i>	Breast mass and skin or nipple change	Women aged 40-79 years	100 (5.5-100) 1/1 episodes in 372 women
Barton (1999) <i>Episode-based analysis</i>	Breast mass and breast lumpiness	Women aged 40-79 years	20 (10.5-70.1) 1/5 episodes in 372 women
Barton (1999) <i>Episode-based analysis</i>	Skin or nipple change and breast lumpiness	Women aged 40-79 years	0 (0-94.5) 0/1 episodes in 372 women

CI = Confidence interval. Please note the calculations of the positive predictive values differ between the studies with Barton (1999) using (TP)/(TP+FP) and Walker (2014) using Bayesian statistics due to the case-control design of this study. * These results are presented in a table (Table 5) entitled "Breast Cancer Diagnosis According to Combinations of Symptoms", it is however unclear what they reflect: Since they are similar, but not identical to those presented as single symptoms, they cannot be that; also, since only 56 women had 2 episodes and 35 women had 3 or more episodes, these results cannot represent a repeat presentation of the same symptom across episodes; which leaves repeat presentations of these symptoms within episodes as an option. However, that is not clearly reported either in the paper, so it cannot be confirmed what exactly these results reflect.

Evidence statement(s):

The positive predictive values for breast cancer of single symptoms presenting in a primary care setting ranged from 0% (for an 'irregularly shaped discrete breast lump', a 'breast lump with a spongy texture', nipple discharge, nipple eczema, nipple retraction, breast abscess, 'other breast symptom') to 48% (for breast lump in women aged 70+ years; 5 studies, N = 24269), but these extreme PPVs were based on small patient/episode numbers. The studies were subject to 1-2 bias or applicability concerns (see also Table 1).

The positive predictive values for breast cancer of symptom pairs presenting in a primary care setting ranged from 0% (for breast lumpiness with 'skin or nipple change' or breast pain, and for breast pain with 'skin or nipple change') to 100% (for breast mass and 'skin or nipple change'; 2 studies, N = 21239), but these extreme PPVs were based on small patient/episode numbers. The studies were subject to 1-2 bias/applicability concerns (see also Table 2).

Evidence tables

Barton (1999)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective cohort study at a large health maintenance organisation (HMO).

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>372 women presented with breast symptoms in 539 separate episodes; although most women had only 1 breast-symptom episode, 56 women presented twice and 35 women presented three or more times. Total number of episodes = 539, consisting of 221 for pain, 196 for mass, 67 for skin or nipple change, 38 for lumpiness, 7 for other, and 69 episodes where no specific symptom was documented. 23/372 women had breast cancer. 24/539 episodes lead to a diagnosis of breast cancer.</p> <p><u>Inclusion criteria:</u> "Female HMO members with automated medical records were eligible. We selected a cohort of 2400 women who were continuously enrolled in the HMO from 1 July 1983 through 30 June 1995. Women 40 to 69 years of age as of 1 July 1983 were sampled in a random, age-stratified manner to include 1200 women in the age group 40 to 49, 600 women in the age group 50 to 59 years, and 600 women in the age group 60 to 69 years." "Information on all breast-related encounters between 1 July 1983 and 30 June 1993 was collected from a computerized medical record". "The reason for each visit was determined to be screening (unrelated to any previously recognized breast abnormality or symptom) or diagnostic (to investigate an abnormality noted by the patient, by the clinician at an earlier examination or on previous mammography). This study reports on diagnostic visits related to patient symptoms."</p> <p><u>Exclusion criteria:</u> Women with insurance coverage in addition to that of the HMO during the study period (N = 1), had breast cancer before 1 July 1983 (N = 4), or had reduction mammoplasty or prophylactic mastectomy before or during the study period (N = 11).</p> <p><u>Clinical setting:</u> Health maintenance organisation, USA.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	<p>Patient symptoms were classified as follows:</p> <ol style="list-style-type: none"> 1) Mass (a single lump or nodule) 2) Pain (a report of pain or tenderness in either breast or bilaterally) 3) Skin or nipple change (including nipple discharge) 4) Multiple lumps or nodules (often described by patients as "lumpiness" and by clinicians as "fibrocystic" or "diffuse cystic change") 5) Other symptoms (such as increasing size of breast) <p>Physical examination findings were recorded by using the same five categories. More than one symptom/finding could be documented.</p> <p>"We defined a breast-symptom episode as the initial patient visit and all subsequent related visits and evaluations; a woman could have more than one episode during the 10-year study. We defined a new episode as beginning with a breast-symptom visit more than 6 months after the end of any previous episode. We considered a breast-symptom visit within 6</p>

	months of a previous episode to be the beginning of a new episode when the symptom was in the contralateral breast.”	
Were the index test results interpreted without knowledge of the results of the reference standard?		Unclear
Could the conduct or interpretation of the index test have introduced bias?		Low risk
<u>B. Concerns regarding applicability</u>		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
<u>A. risk of bias</u>		
Reference standard(s)	<p>“Breast cancer outcomes were determined for all women from 1 July 1983 to 30 June 1994 to ensure adequate time for follow-up of all breast-symptom episodes. To determine outcomes, we reviewed the computerized medical records and the HMO’s tumor registry for diagnoses of breast cancer.”</p> <p>Given that the time between symptom and diagnosis could be 10 years according to the study methodology, cancer may not always be the cause of the symptom, and the authors only report that the median (range) time to diagnosis from the <i>last</i> breast-symptom episode was 36 days (1-155) days, but not the corresponding data for the first symptom, which, I believe is still included in the analyses.</p>	
Is the reference standard likely to correctly classify the target condition?		Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?		No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
<u>B. Concerns regarding applicability</u>		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
<u>A. risk of bias</u>		
Flow and timing	It appears that all patients are accounted for, but the results reported are not patient-based, but rather episode-based.	
Was there an appropriate interval between index test and reference standard?		Yes (probably)
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		Yes
Could the patient flow have introduced bias?		Low risk
NOTES	<p>The episode-based analysis undertaken in this paper makes the results less comparable with other results presented for this guideline than would otherwise have been the case, and the net result of this type of analysis may be an underestimation of the PPVs.</p> <p>It is unclear whether the patients included span the ages of 40-69 years or 40-79 years, as reported in the inclusion criteria and discussion, and in Table 1, respectively.</p>	

Eberl (2008)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the Transition Project database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 2503 females, aged from below 25 to above 65 years who had the following breast-related symptoms: Breast lump/mass (N = 741), breast pain (N = 1191), nipple complaint (N = 210), and other breast complaint (N = 361). 81/2503 patients had breast cancer.</p> <p><u>Inclusion criteria:</u> Patients with breast-related encounters in the Transition Project “Between 1985 and 2003, the Transition Project in the Netherlands comprehensively and prospectively coded office visits to family physicians based on the <i>International Classification of Primary Care (ICPC)</i>. The term <i>encounter</i> is synonymous with an office visit in the United States. For the Transition Project, 58 Dutch family physicians routinely coded data on reasons for encounter, diagnoses, and interventions for all episodes of care they provided between 1985 and 2003. Given that each patient in the Netherlands must register with a family practice office, clinic-based participation is reflective of the broader population-based health care system. Only visits to physicians participating in the Dutch Transition project are contained in the study database; visits to nurse-practitioners and physician’s assistants were not included.”</p> <p><u>Exclusion criteria:</u> None reported.</p> <p><u>Clinical setting:</u> Dutch primary care.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	“Breast symptoms include specific complaints, such as breast lump/mass, breast pain or tenderness, and nipple discharge; however, it is clear that women also come to physicians with fear of breast cancer and anxiety regarding their family history and risk of cancer. Fear of breast cancer is considered a unique reason for encounter in the Transition Project.”
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	“A final diagnosis of benign (absence of neoplasm) vs malignant (including ductal carcinoma in situ, lobular carcinoma in situ, and histologic atypical)

	disease was assigned to each breast-related reason for encounter,” “Participating family physicians completed all coding for their patients; no cancer registry match was performed.”
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Although it does not explicitly stated that women with pre-existing breast cancer were excluded, even if they consulted with a breast-related episode, it appears that they were.
McCowan (2011)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 11 UK-based general practices.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	97 women, aged: 25-39 years: N = 28; 40-49 years: N = 31; 50-59 years: N = 14; 60-69 years: N = 11; 70-79 years: N = 10; ≥ 80 years: N = 3; Past history: Any breast problems: N = 60; previous clinic attendance: N = 43; breast cancer: N = 3; breast lump: N = 37; breast abscess: N = 9; breast pain: N = 41. <u>Inclusion criteria:</u> “11 participating general practices in the region agreed to recruit all women who attended for an initial consultation regarding symptomatic breast problems between January 2006 and June 2007.” <u>Exclusion criteria:</u> “Patients were excluded if the consultation was related to issues around cosmetic surgery or breastfeeding problems.” <u>Clinical setting:</u> Primary care, UK
Are there concerns that the included patients and setting do not match the review question?	Low concern

INDEX TEST	
A. Risk of bias	
Index test	Symptomatic breast problems
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	"All patients in the two cohorts were traced for a diagnosis of breast cancer using the regional prospective cancer audit in the year following their initial consultation. This audit identifies all diagnosed breast cancers to allow reporting on the standards of care against national targets and is the basis of cancer registry returns."
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appears to be accounted for, but only 97/202 eligible patients took part (mainly due to lack of telephone contact details being available/correct; 16/118 contacted patients declined participation and 5/118 contact patients failed to return the written consent).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk (missing data as per above)
NOTES	
Oudega (2006)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective study of all primary care physicians (N = 50) within a catchment area (ca 130000 inhabitants) of a non-teaching hospital in Holland.
Was a consecutive or random sample of patients enrolled?	Yes

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 430; 162 males, 268 females; mean age (SD) = 60.7 (18.2) years. <u>Inclusion criteria:</u> Consecutive patients who consulted their GP between January 1996 and July 2002 and who, after investigation (not referral) was confirmed to have deep vein thrombosis. <u>Exclusion criteria:</u> Patients with a known malignancy or a malignancy detected within 2 weeks of deep vein thrombosis diagnosis. <u>Clinical setting:</u> Primary care, Holland.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Deep vein thrombosis (suspicion based on painful swollen leg \leq 30 days). Patients were classified as having secondary deep vein thrombosis if \geq 1 of the following risk factors for deep vein thrombosis were present: Recent surgery, prolonged immobilisation, use of oral contraceptives or hormonal replacement therapy. If no risk factors were present patients were classified as having idiopathic deep vein thrombosis.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2 years follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 19 had cancer: 3 colorectal, 5 urogenital (not further subgrouped), 4 breast, 3 lung and 4 other. The urogenital data is added to the renal cancer evidence review.
Walker (2014)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Matched case-control study using patients in the UK's Clinical Practice Research Database (CPRD).
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> 3994 women, median age at diagnosis = 63 (IQR = 55-74) years; median number of consultations: in the year before index = 9 (IQR = 5-15), in 6 months before index = 9 (IOR = 4-16); UK.</p> <p><u>Controls:</u> 16873 women; median number of consultations: in the year before index = 7 (IQR = 4-13), in 6 months before index = 6 (IOR = 2-12); UK.</p> <p><u>Inclusion criteria:</u> Cases: Women aged ≥ 40 years with one of 56 identified breast tumour diagnostic codes in the CPRD between 1 January 2000 and 31 December 2009, with min. 1 year of data before diagnosis. The first instance of a breast cancer code was assigned the data of diagnosis/index date. Controls: 5 randomly selected controls matched on sex, general practice, and to 1 year of age of the case. The index date was the index date of the matched case.</p> <p><u>Exclusion criteria:</u> Males diagnosed with breast cancer, ill-defined medcodes giving multiple sites of cancer; skin cancer of the breast; cases with a mastectomy, chemotherapy or radiotherapy medcode > 90 days before the index date (as this strongly suggested that the index date was wrong); controls diagnosed with breast cancer (or having a mastectomy) before the index date; and women with no consultations in the year before diagnosis.</p> <p><u>Clinical setting:</u> UK primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	

A. Risk of bias	
Index test	All symptoms, signs or abnormal investigations previously recorded in the breast cancer literature and cancer charity websites were studied. "The CPRD stores clinical information in just over 100,000 medcodes, each describing a facet of primary care, such as a symptom. There are several codes for each symptom, differing usually in a qualifier such as duration or severity, so generally containing more information than a specific Read code. All the codes pertaining to individual symptoms were collated into single symptom libraries." "Occurrences of symptoms in the year before the index date were identified. Features were only retained in the study if they occurred in $\geq 1\%$ of the cases or controls (this was invariably cases). We assembled a list of plausible laboratory abnormalities <i>a priori</i> using the literature and our clinical knowledge (WH, CH). We also identified all abnormal laboratory results in the year before the index date, using the local laboratory's normal range, which is supplied with the data. We considered women without a test to be equivalent to those with a normal result. Some abnormal tests were grouped: abnormal liver function was defined as the presence of any liver enzyme above the normal range. The variable 'raised inflammatory markers' was defined as a raised erythrocyte sedimentation rate, C-reactive protein or plasma viscosity. These simplifications were necessary as different localities in the UK contributing to the CPRD have different tests available."
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	One of 56 identified breast tumour diagnostic codes in the CPRD.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 26162 women were identified, 21755 controls and 4407 cases. Of the controls the following exclusions were applied: Mastectomy medcode before index date of case (N = 564), breast cancer before the index date of

	the case (N = 380), no GP consultations in the year before the index date of the case (N = 2238), and controls of excluded cases (N = 1700). Of the cases the following exclusions were applied: Males (N = 51), ill-defined codes giving multiple sites of cancer (N = 52), skin cancers in breast (N = 18), cancers in sites other than breast (N = 2), medcodes > 3 months pre-index of mastectomy (N = 150) or chemotherapy./radiotherapy (N = 45), no GP consultations in the year before the index date of case (N = 89), and no controls (N = 6).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	23 symptoms and 22 abnormal test results were considered initially. The proportion of patients with a recorded fracture did not differ between cases (1.8%) and controls (1.6%).

References

Included studies

- Barton, M. B., Elmore, J. G. & Fletcher, S. W. (1999) Breast symptoms among women enrolled in a health maintenance organization: Frequency, evaluation, and outcome. *Annals of Internal Medicine*, 130: 651.
- Eberl, M. M., Phillips, R. L., Jr., Lamberts, H., Okkes, I. & Mahoney, M. C. (2008) Characterizing breast symptoms in family practice. *Annals of Family Medicine*, 6: 528-533.
- McCowan, C., Donnan, P. T., Dewar, J., Thompson, A. & Fahey, T. (2011) Identifying suspected breast cancer: development and validation of a clinical prediction rule. *British Journal of General Practice*, 61: e205-e214.
- Oudega, R., Moons, K. G. M., Nieuwenhuis, H. K., van Nierop, F. L. & Hoes, A. W. (2006) Deep vein thrombosis in primary care: Possible malignancy? *British Journal of General Practice*, 56: September.
- Walker, S., Hamilton, W., Hyde, C. (2014). Risk of breast cancer in symptomatic women in primary care: Case-control study using electronic records. *Under review*

Excluded studies (with excl reason)

- (1111) What's new in early-stage breast cancer. *American Journal of Hematology/ Oncology*, 8: August.
Not in PICO
- (2013) Technology assessment No. 9: Digital breast tomosynthesis. *Obstetrics & Gynecology*, 121: 1415-1417.
Narrative review
- Abdel-Fattah, M. M., Anwar, M. A., Mari, E., El-Shazly, M. K., Zaki, A. A., Bedwani, R. N. & Nicolucci, A. (1999) Patient- and system-related diagnostic delay in breast cancer - Evidence from Alexandria, Egypt. *European Journal of Public Health*, 9: 15-19.
Not in PICO
- Abdelhadi, M. S. (2006) Breast cancer awareness campaign: will it make a difference? *Journal of Family and Community Medicine*, 13: 115-118.
Not in PICO
- Abdolmohammadi, A., Sears, W., Rai, S., Pan, J., Alexander, J. & Kloecker, G. (2014) - Survey of primary care physicians on therapeutic approaches to lung and breast cancers. - *Southern*

- Medical Journal*, 107: 437-442.
Not in PICO
- Aboserea, M., Abdelgawad, M. & Wafik, W. (2011) Early Detection of Breast Cancer among Females at Fakous District, Sharqia Governorate, Egypt. *Life Science Journal-Acta Zhengzhou University Overseas Edition*, 8: 196-203.
Population not in PICO
- Agaba, A. E., Bagul, A., Adenugba, J. B. & Kenogbon, J. I. (2002) Audit of patient's waiting time to see their family doctor prior to referral to a fast-access breast clinic in the era of a guaranteed 2-week wait. *Breast*, 11: 430-433.
Not in PICO
- Akbari, A., Mayhew, A., Al-Alawi, M. A., Grimshaw, J., Winkens, R., Glidewell, E., Pritchard, C., Thomas, R. & Fraser, C. (2008) Interventions to improve outpatient referrals from primary care to secondary care. *Cochrane Database of Systematic Reviews*.
Not in PICO
- Al-Amri, A. M. (2011) Breast carcinoma in pregnancy and lactation: A diagnostic and therapeutic dilemma. *International Journal of Collaborative Research on Internal Medicine and Public Health*, 3: July.
Not in PICO
- Allgar, V. L. & Neal, R. D. (2005) General practitioners' management of cancer in England: secondary analysis of data from the National Survey of NHS Patients-Cancer. *European Journal of Cancer Care*, 14: 409-416.
Not in PICO
- Allgar, V. L. & Neal, R. D. (2005) Delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS Patients: Cancer. *British Journal of Cancer*, 92: 1959-1970.
Not in PICO
- Andersen, M. R. Symptoms of breast cancer in an age of technologic screening. [References]. *Journal of Women's Health* 20[8], 1129-1131. 2011.
Not in PICO
- Andersen, T. & Ruland, C. M. (2009) Cancer patients' questions and concerns expressed in an online nurse-delivered mail service: preliminary results. *Studies in Health Technology & Informatics*, 146: 149-153.
Not in PICO
- Ando, N., Iwamitsu, Y., Kuranami, M., Okazaki, S., Wada, M., Yamamoto, K., Todoroki, K., Watanabe, M. & Miyaoka, H. (2009) Psychological characteristics and subjective symptoms as determinants of psychological distress in patients prior to breast cancer diagnosis. *Supportive Care in Cancer*, 17: 1361-1370.
Not in PICO
- Arrangoiz, R., Papavasiliou, P., Dushkin, H. & Farma, J. M. (2011) Case report and literature review: Metastatic lobular carcinoma of the breast an unusual presentation. *International Journal of Surgery Case Reports*, 2: 301-305.
Not in PICO
- Atkins, L. A., Forbes, L. J. L., Austoker, J., Bankhead, C., Martin, F., Robb, K., Wardle, J. & Ramirez, A. J. (2010) Interventions to increase cancer awareness and promote early presentation: A systematic review. *Psycho-Oncology. Conference: British Psychosocial Oncology Society 2009 Conference Cardiff United Kingdom. Conference Start: 20091203 Conference End: 20091204. Conference Publication: (var.pagings)*, 19: May.
Not in PICO
- Austoker, J., Bankhead, C., Forbes, L. J., Atkins, L., Martin, F., Robb, K., Wardle, J. & Ramirez, A. J. (2009) Interventions to promote cancer awareness and early presentation: systematic review. [Review] [38 refs]. *British Journal of Cancer*, 101: Suppl-9.
Not in PICO

- Banks, A. L., Titus, R. & Melnik, M. (2013) Detection of new or additional significant breast disease by MRI compared to standard imaging in "high-risk" and "non-high-risk" patients. *Journal of Clinical Oncology*, 31.
Not in PICO
- Bansal, S., Sahoo, B., Agarwal, P., Garg, V. & Rao, S. (2013) A rare presentation of mammary Paget's disease involving the entire breast in the absence of any underlying ductal malignancy. *Indian Journal of Dermatology, Venereology and Leprology*, 79: 518-521.
Not in PICO
- Barber, M. D., Jack, W. & Dixon, J. M. (2004) Diagnostic delay in breast cancer. *British Journal of Surgery*, 91: 49-53.
Not in PICO
- Barnes, N. L., Dimopoulos, N., Williams, K. E., Howe, M. & Bundred, N. J. (2014) - The frequency of presentation and clinico-pathological characteristics of symptomatic versus screen detected ductal carcinoma in situ of the breast. - *European Journal of Surgical Oncology*, 40: 249-254.
Not in PICO
- Barosi, G., Marchetti, M., Dazzi, L. & Quaglini, S. (1997) Testing for occult cancer in patients with idiopathic deep vein thrombosis - A decision analysis. *Thrombosis and Haemostasis*, 78: November.
Not in PICO
- Bassett, A. A. (1999) Guide for the management of breast lumps: Litigious aspects. *Canadian Journal of Surgery*, 42: 1999.
Narrative review
- Baughan, P., O'Neill, B. & Fletcher, E. (2009) Auditing the diagnosis of cancer in primary care: the experience in Scotland. *British Journal of Cancer*, 101: S87-S91.
Not in PICO
- Bays, J. K. (1992) Physical and mammographic diagnosis of breast cancer and initial work-up. *Journal of the American Medical Womens Association*, 47: 158-160.
Narrative review
- Bazovsky, P. (1983) [Cytology of nipple secretions in the early diagnosis of carcinoma of the breast]. [Slovak]. *Bratislavské Lekárske Listy*, 79: 606-613.
In Slovak. Don't think it is in PICO (cytologic examinations of the nipple secretions of N = 904)
- Beattie, A. (2009) Detecting breast cancer in a general practice Like finding needles in a haystack? *Australian Family Physician*, 38: 1003-1006.
Not in PICO
- Berna-Serna, J. D., Torres-Ales, C., Berna-Mestre, J. D., Sola-Perez, J. & Canteras-Jordana, M. (2010) Galactography: an application of the Galactogram Imaging Classification System (GICS). *Acta radiologica (Stockholm, Sweden : 1987)*, 51: Mar.
Not in PICO
- Bick, U., Engelken, F., Diederichs, G., Dzyuballa, R., Ortmann, M. & Fallenberg, E. M. (2013) MRI of the breast as part of the assessment in population-based mammography screening. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 185: 849-856.
Not in PICO
- Bish, A., Ramirez, A., Burgess, C. & Hunter, M. (2005) Understanding why women delay in seeking help for breast cancer symptoms. *Journal of Psychosomatic Research*, 58: 321-326.
Not in PICO
- Bland, K. I. & Love, N. (101) Evaluation of common breast masses. *Postgraduate Medicine*, 92: 95-97.
Narrative review
- Bleyer, A. (2009) CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology*, 36: June.
Narrative review

- Blichert-Toft, M., Dyreborg, U. & Andersen, J. (1988) Diagnostic strategy in the management of patients with breast symptoms. A recommended design and present experience. *Acta Oncologica*, 27: 597-600.
Not in PICO
- Bock, K., Duda, V. F., Hadji, P., Ramaswamy, A., Schulz-Wendtland, R., Klose, K.-J. & Wagner, U. (2005) Pathologic breast conditions in childhood and adolescence: Evaluation by sonographic diagnosis. *Journal of Ultrasound in Medicine*, 24: October.
Not in PICO
- Borneman, T., Koczywas, M., Sun, V. C.-Y., Piper, B. F., Uman, G. & Ferrell, B. Reducing patient barriers to pain and fatigue management. [References]. *Journal of Pain and Symptom Management* 39[3], 486-501. 2010.
Not in PICO
- Brennan, M., Houssami, N. & French, J. (2005) Management of benign breast conditions. Part 3-- Other breast problems. *Australian Family Physician*, 34: May.
Narrative review
- Brennan, M. E. & Houssami, N. (2006) Image-detected 'probably benign' breast lesions: A significant reason for referral from primary care. *Breast*, 15: 683-686.
Not in PICO
- Bridge Study Group (2002) Responses of primary health care professionals to UK national guidelines on the management and referral of women with breast conditions. *Journal of Evaluation in Clinical Practice*, 8: 319-325.
Not in PICO
- Bright, K., Barghash, M., Donach, M., de la Barrera, M. G., Schneider, R. J. & Formenti, S. C. (2011) The role of health system factors in delaying final diagnosis and treatment of breast cancer in Mexico City, Mexico. *Breast*, 20: S54-S59.
Not in PICO
- Bullough, B. (1947) Discovery of the first signs and symptoms of breast cancer. *Nurse Practitioner*, 5: 31-32.
Not in PICO
- Burgess, C., Hunter, M. S. & Ramirez, A. J. (2001) A qualitative study of delay among women reporting symptoms of breast cancer. *British Journal of General Practice*, 51: 967-971.
Not in PICO
- Burgess, C. C., Ramirez, A. J., Richards, M. A. & Love, S. B. (1998) Who and what influences delayed presentation in breast cancer? *British Journal of Cancer*, 77: 1343-1348.
Not in PICO
- Burgess, C. C., Ramirez, A. J., Smith, P. & Richards, M. A. (2000) Do adverse life events and mood disorders influence delayed presentation of breast cancer? *Journal of Psychosomatic Research*, 48: 171-175.
Not in PICO
- Burgess, C. C., Potts, H. W., Hamed, H., Bish, A. M., Hunter, M. S., Richards, M. A. & Ramirez, A. J. (2006) Why do older women delay presentation with breast cancer symptoms? *Psycho-Oncology*, 15: 962-968.
Not in PICO
- Burgess, C. C., Bish, A. M., Hunter, H. S., Salkovskis, P., Michell, M., Whelehan, P. & Ramirez, A. J. Promoting early presentation of breast cancer: Development of a psycho-educational intervention. [References]. *Chronic Illness* 4[1], 13-27. 2008.
Not in PICO
- Burgess, C. C., Linsell, L., Kapari, M., Omar, L., Michell, M., Whelehan, P., Richards, M. A. & Ramirez, A. J. (2009) Promoting early presentation of breast cancer by older women: A preliminary evaluation of a one-to-one health professional-delivered intervention. *Journal of Psychosomatic*

- Research*, 67: 377-387.
Not in PICO
- Cady, B., Steele, G. D., Morrow, M., Gardner, B., Smith, B. L., Lee, N. C., Lawson, H. W. & Winchester, D. P. (1998) Evaluation of common breast problems: Guidance for primary care providers. *Ca-A Cancer Journal for Clinicians*, 48: 49-+.
Narrative review
- Cai, L. S., Zhang, J. X., Song, G. H., Chen, L. & Dai, J. L. (2013) [Value of contrast-enhanced sonography in early diagnosis of breast cancer]. [Chinese]. *Nan Fang Yi Ke Da Xue Xue Bao = Journal of Southern Medical University*, 33: 1801-1805.
Not in PICO
- Campbell, C., Durning, P., Cheema, I. & Naisby, G. (2004) A simple tool for rapid access to a symptomatic breast clinic. *European Journal of Surgical Oncology*, 30: 248-251.
Not in PICO
- Cant, P. J. & Yu, D. S. (2000) Impact of the '2 week wait' directive for suspected cancer on service provision in a symptomatic breast clinic. *British Journal of Surgery*, 87: 1082-1086.
Not in PICO
- Caplan, L. S. (1995) Patient delay in seeking help for potential breast cancer. *Public Health Reviews*, 23: 263-274.
Not in PICO
- Carcoforo, P., Raiji, M., Langan, R., Lanzara, S., Portinari, M., Maestroni, U., Palini, G., Zanzi, M., Bonazza, S., Pedriali, M., Feo, C., Stojadinovic, A. & Avital, I. (2012) Infiltrating lobular carcinoma of the breast presenting as gastrointestinal obstruction: a mini review. *Journal of Cancer*, 3: 328-332.
Not in PICO
- Carlsson, L., Hakansson, A. & Nordenskjold, B. (2001) Common cancer-related symptoms among GP patients - Opportunistic screening in primary health care. *Scandinavian Journal of Primary Health Care*, 19: 199-203.
Not in PICO (does not go into detail about symptoms, only report "comon cancer related symptoms by cancer", 275/379 reported symptoms already investigated, not broken down by investigation/symptom and cancer status
- Carney, P. A., Steiner, E., Goodrich, M. E., Dietrich, A. J., Kasales, C. J., Weiss, J. E. & MacKenzie, T. (2006) Discovery of breast cancers within 1 year of a normal screening mammogram: How are they found? *Annals of Family Medicine*, 4: 512-518.
Not in PICO
- Carney, P. A., Parikh, J., Sickles, E. A., Feig, S. A., Monsees, B., Bassett, L. W., Smith, R. A., Rosenberg, R., Ichikawa, L., Wallace, J., Tran, K. & Miglioretti, D. L. (2013) Diagnostic mammography: identifying minimally acceptable interpretive performance criteria. *Radiology*, 267: 359-367.
Not in PICO
- Carrasco, R. M., Benito, M. A. & del Campo, E. R. (2013) Value of mammography and breast ultrasound in male patients with nipple discharge. *European Journal of Radiology*, 82: 478-484.
Not in PICO
- Chen, C.-Y., Fu, J.-M., Yuan, Y., Yu, R., Jiang, H.-B. & Li, S.-L. (2013) Analysis of image features of breast mucinous carcinoma. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 29: 411-414.
Not in PICO
- Cheung, W. Y., Le, L. W. & Zimmermann, C. (2009) Symptom clusters in patients with advanced cancers. *Supportive Care in Cancer*, 17: September.
Not in PICO
- Cho, J., Han, W., Ko, E., Lee, J. W., Jung, S. Y., Kim, E. K., Lee, H. C., Park, I. A., Oh, S. K., Youn, Y. K., Kim, S. W., Hwang, K. T. & Noh, D. Y. (2007) The clinical and histopathological characteristics of

- male breast cancer patients. *Journal of Breast Cancer*, 10: 211-216.
Not in PICO
- Christmas, P. & Nichols, S. (1982) 'Don't take a chance': a public campaign to encourage the early reporting of breast symptoms. *Health Education Journal*, 41: 61-68.
Not in PICO
- Chuwa, E. W. L., Yeo, A. W. Y., Koong, H. N., Wong, C. Y., Yong, W. S., Tan, P. H., Ho, J. T. S., Wong, J. S. L. & Ho, G. H. (2009) Early Detection of Breast Cancer through Population-Based Mammographic Screening in Asian Women: A Comparison Study between Screen-Detected and Symptomatic Breast Cancers. *Breast Journal*, 15: 133-139.
Not in PICO
- Cid, J. A., Rampaul, R. S., Ellis, I. O., Wilson, A. R. M., Burrell, H. C., Evans, A. J., Blamey, R. W. & MacMillan, R. D. (2004) Woman feels breast lump - Surgeon cannot: The role of ultrasound in arbitration. *European Journal of Cancer*, 40: September.
Not in PICO
- Clegg-Lamprey, J. N., Aduful, H. K., Yarney, J., Adu-Aryee, N. A., Vanderpuye, V., Kyereh, M., Nkansah, A. & Edwin, A. (2009) Profile of breast diseases at a self-referral clinic in Ghana. *West African Journal of Medicine*, 28: 114-117.
Not in PICO (breast cancer cases cannot be linked to specific symptoms)
- Cochrane, R. A., Singhal, H., Monypenny, I. J., Webster, D. J. T., Lyons, K. & Mansel, R. E. (1997) Evaluation of general practitioner referrals to a specialist breast clinic according to the UK national guidelines. *European Journal of Surgical Oncology*, 23: 198-201.
Not in PICO
- Cochrane, R. A., Davies, E. L., Singhal, H., Sweetland, H. M., Webster, D. J. T., Monypenny, I. J., Lyons, K. & Mansel, R. E. (1999) The National Breast Referral Guidelines have cut down inappropriate referrals in the under 50s. *European Journal of Surgical Oncology*, 25: 251-254.
Not in PICO
- Cockburn, J., Pit, S., Zorbas, H. & Redman, S. (2001) Investigating breast symptoms in primary care: enhancing concordance with current best advice. *Cancer Detection & Prevention*, 25: 407-413.
Not in PICO
- Cornford, C. S., Harley, J. & Oswald, N. (2004) The '2-week rule' for suspected breast carcinoma: a qualitative study of the views of patients and professionals. *British Journal of General Practice*, 54: 584-588.
Not in PICO
- Coroneos, C. J. & Hamm, C. (2010) Ductal carcinoma in situ in a 25-year-old man presenting with apparent unilateral gynecomastia. *Current Oncology*, 17: 133-137.
Not in PICO
- Crea, P. (1995) Breast cancer: A GP's guide to detection and treatment options. *Modern Medicine of Australia*, 38.
Narrative review
- Cuhaci, N., Polat, S. B., Evranos, B., Ersoy, R. & Cakir, B. (2014) - Gynecomastia: Clinical evaluation and management. [Review]. - *Indian Journal of Endocrinology and Metabolism*, 18: 150-158.
Narrative review
- Culver, J. O., Bowen, D. J., Reynolds, S. E., Pinsky, L. E., Press, N. & Burke, W. (2009) Breast cancer risk communication: assessment of primary care physicians by standardized patients. *Genetics in Medicine*, 11: 735-741.
Not in PICO
- Cusack, L. & Brennan, M. (2011) Lactational mastitis and breast abscess Diagnosis and management in general practice. *Australian Family Physician*, 40: 976-979.
Not in PICO
- Davis, C. Breast Cancer. [References]. 214-225. 2005.
Narrative review

- Day, P. J. & O'Rourke, M. G. E. (1990) The diagnosis of breast cancer: A clinical and mammographic comparison. *Medical Journal of Australia*, 152.
Not in PICO
- De Waal, J. C., Baltzer, J. & Muthmann-Nagy, C. (1987) Value of palpation and mammography in primary breast cancer. A retrospective study of the years 1973-1982. [German]. *Geburtshilfe und Frauenheilkunde*, 47: 1987.
Not in PICO
- Dinkel, H.-P. (1111) Features of benign and malignant breast disease in galactography. *Radiologist*, 7: November.
Narrative review
- Dixon, J. M. (488) Managing breast pain. [Review] [9 refs]. *Practitioner*, 243: 484-486.
Narrative review
- Dixon, J. M. & Mansel, R. E. (1994) ABC of breast diseases. Symptoms assessment and guidelines for referral. [Review] [0 refs]. *BMJ*, 309: 722-726.
Narrative review
- Dolan, R. T., Butler, J. S., Kell, M. R., Gorey, T. F. & Stokes, M. A. (2010) Nipple discharge and the efficacy of duct cytology in evaluating breast cancer risk. *Surgeon-Journal of the Royal Colleges of Surgeons of Edinburgh and Ireland*, 8: 252-258.
Not in PICO
- Donegan, W. L., Redlich, P. N., Lang, P. J. & Gall, M. T. (1998) Carcinoma of the breast in males - A multiinstitutional survey. *Cancer*, 83: 498-509.
Not in PICO
- Donnelly, J. (2010) Breast lump detection: who is more accurate, patients or their GPs? *International Journal of Clinical Practice*, 64: 439-441.
Not in PICO
- Duijm, L. E. M., Guit, G. L., Hendriks, J. H. C. L., Zaat, J. O. M. & Mali, W. P. T. M. (1998) Value of breast imaging in women with painful breasts: observational follow up study. *British Medical Journal*, 317: 1492-1495.
Not in PICO
- Dye, T. D., Bogale, S., Hobden, C., Tilahun, Y., Deressa, T. & Reeler, A. (2012) Experience of initial symptoms of breast cancer and triggers for action in ethiopia. *International Journal of Breast Cancer*, 2012: 908547.
Not in PICO
- Edwards, A. G. K., Robling, M. R., Wilkinson, C., Matthews, S. J., Pill, R. M., Stott, N. C. H., Austoker, J., Cohen, D., McKell-Redwood, D., Mansel, R., Russell, I. T. & Thapar, A. (1999) The presentation and management of breast symptoms in general practice in South Wales. *British Journal of General Practice*, 49.
Not in PICO
- Emery, J., Walter, F. M., Gray, V., Sinclair, C., Bulsara, C., Bulsara, M., Auret, K., Nowak, A., Saunders, C. & Holman, D. (2012) Diagnosing cancer in the bush: A mixed methods study of diagnostic intervals in people with cancer from rural Western Australia. *Asia-Pacific Journal of Clinical Oncology.Conference: COSA 39th Annual Scientific Meeting and IPOS 14th World Congress of Psycho-Oncology Brisbane, QLD Australia.Conference Start: 20121111 Conference End: 20121115.Conference Publication: (var.pagings)*, 8: November.
Not in PICO
- Emery, J. D., Walter, F. M., Gray, V., Sinclair, C., Howting, D., Bulsara, M., Bulsara, C., Webster, A., Auret, K., Saunders, C., Nowak, A. & Holman, D. (2013) Diagnosing cancer in the bush: a mixed methods study of GP and specialist diagnostic intervals in rural Western Australia. *Family Practice*, 30: 541-550.
Not in PICO

- Ermiah, E., Abdalla, F., Buhmeida, A., Larbesh, E., Pyrhonen, S. & Collan, Y. (2012) Diagnosis delay in Libyan female breast cancer. *BMC Research Notes*, 5: 452.
Not in PICO
- Evans, W. P. (1995) Breast masses. Appropriate evaluation. [Review] [87 refs]. *Radiologic Clinics of North America*, 33: 1085-1108.
Narrative review
- Ezeome, E. R. (2010) Delays in Presentation and Treatment of Breast Cancer in Enugu, Nigeria. *Nigerian Journal of Clinical Practice*, 13: 311-316.
Not in PICO
- Facione, N. C. & Giancarlo, C. A. (1998) Narratives of breast symptom discovery and cancer diagnosis: Psychologic risk for advanced cancer at diagnosis. *Cancer Nursing*, 21: 430-440.
Not in PICO
- Facione, N. C., Miaskowski, C., Dodd, M. J. & Paul, S. M. (2002) The self-reported likelihood of patient delay in breast cancer: new thoughts for early detection. *Preventive Medicine*, 34: 397-407.
Not in PICO
- Facione, N. C. & Facione, P. A. (2006) The cognitive structuring of patient delay in breast cancer. *Social Science & Medicine*, 63: 3137-3149.
Not in PICO
- Farooq, A. & Horgan, K. (2011) Male breast cancer presenting as nipple discharge. *Case Reports in Surgery*, 2011: 804843.
Not in PICO
- Farrokh, D. (2014) Pregnancy-Associated Breast Cancer: Significance of Early Detection and Imaging Appearance. *Iranian Journal of Radiology*, 11: S17-S18.
Not in PICO
- Flobbe, K., Bosch, A. M., Kessels, A. G., Beets, G. L., Nelemans, P. J. & et al. (2003) The additional diagnostic value of ultrasonography in the diagnosis of breast cancer. *Arch Intern Med*, 163: 1194-1199.
Not in PICO. From National Breast Cancer Centre Sydney Australia SR.
- Flobbe, K., Kessels, A. G., Severens, J. L., Beets, G. L., Koning, H. J., Meyenfeldt, M. F. & Engelshoven, J. M. (2004) Costs and effects of ultrasonography in the evaluation of palpable breast masses (Structured abstract). *International Journal of Technology Assessment in Health Care*, 20: 440-448.
Not in PICO
- Forbes, L. J., Atkins, L., Thurnham, A., Layburn, J., Haste, F. & Ramirez, A. J. (2011) Breast cancer awareness and barriers to symptomatic presentation among women from different ethnic groups in East London. *British Journal of Cancer*, 105: 1474-1479.
Not in PICO
- Forbes, L. J., Forster, A. S., Dodd, R. H., Tucker, L., Laming, R., Sellars, S., Patnick, J. & Ramirez, A. J. (2012) Promoting early presentation of breast cancer in older women: implementing an evidence-based intervention in routine clinical practice. *Journal of Cancer Epidemiology and Prevention*, 2012: 835167.
Not in PICO
- Forbes, L. J., Warburton, F., Richards, M. A. & Ramirez, A. J. (2014) - Risk factors for delay in symptomatic presentation: a survey of cancer patients. - *British Journal of Cancer*, 111: 581-588.
Not in PICO
- Foulkes, R. E., Heard, G., Boyce, T., Skyrme, R., Holland, P. A. & Gateley, C. A. (2011) Duct Excision is Still Necessary to Rule out Breast Cancer in Patients Presenting with Spontaneous Bloodstained Nipple Discharge. *International Journal of Breast Cancer*, 2011: 495315.
Not in PICO
- Friedman, L. C., Kalidas, M., Elledge, R., Dulay, M. F., Romero, C., Chang, J. & Liscum, K. R. (2006) Medical and psychosocial predictors of delay in seeking medical consultation for breast

- symptoms in women in a public sector setting. *Journal of Behavioral Medicine*, 29: 327-334.
Not in PICO
- Froman, J., Landercasper, J., Ellis, R., De, M. B. & Theede, L. (2011) Red breast as a presenting complaint at a breast center: An institutional review. *Surgery*, 149: June.
Not in PICO
- Gallagher, T. H., Greene, S., Roblin, D., Calvi, J., Horner, K., Prouty, C., Firreno, C., Lemay, C., Lo, C. & Mazor, K. (2010) Patients' views on delayed diagnosis in cancer. *Journal of Clinical Oncology. Conference: 2010 Annual Meeting of the American Society of Clinical Oncology, ASCO Chicago, IL United States. Conference Start: 20100604 Conference End: 20100608. Conference Publication: (var.pagings)*, 28: 20.
Not in PICO
- Ganesan, K., Acharya, R. U., Chua, C. K., Min, L. C., Mathew, B. & Thomas, A. K. (2013) Decision support system for breast cancer detection using mammograms. *Proceedings of the Institution of Mechanical Engineers. Part H - Journal of Engineering in Medicine*, 227: 721-732.
Not in PICO
- Gencturk, N. (2013) The status of knowledge and practice of early diagnosis methods for breast cancer by women healthcare professionals. *Meme Sagligi Dergisi / Journal of Breast Health*, 9: 5-9.
Not in PICO
- Ghimire, B., Khan, M. I., Bibhusal, T., Singh, Y. & Sayami, P. (2008) Accuracy of Triple Test Score in The Diagnosis of Palpable Breast Lump. *Journal of Nepal Medical Association*, 47: 189-192.
Not in PICO
- Ghosh, K. & Ghosh, A. K. (2006) Clinical approach to breast disorders: A primer for internists. *Journal of Association of Physicians of India*, 54: May.
Narrative review
- Giese-Davis, J., Tamagawa, R., Yutsis, M., Twirbutt, S., Piemme, K., Neri, E., Taylor, C. B. & Spiegel, D. (2014) Which symptoms matter? Self-report and observer discrepancies in repressors and high-anxious women with metastatic breast cancer. *Journal of Behavioral Medicine*, 37: 22-36.
Not in PICO
- Goedendorp, M. M., Gielissen, M. F., Verhagen, C. A., Peters, M. E. & Bleijenberg, G. (2008) Severe fatigue and related factors in cancer patients before the initiation of treatment. *British Journal of Cancer*, 99: 1408-1414.
Not in PICO
- Gonzalez-Perez, B., Salas-Flores, R., Sosa-Lopez, M. L., Barrientos-Guerrero, C. E., Hernandez-Aguilar, C. M., Gomez-Contreras, D. E. & Sanchez-Garza, J. A. (2013) Female breast symptoms in patients attended in the family medicine practice. *Revista Medica del Instituto Mexicano del Seguro Social*, 51: 558-561.
Outcomes not in PICO and cannot be calculated from the presented data. Setting is unclear
- Gorman, D. R., Mackinnon, H., Storrie, M., Wilson, G. S. & Parker, S. (2000) The general practice perspective on cancer services in Lothian. *Family Practice*, 17: 323-328.
Not in PICO
- Grady, D., Hodgkins, M. L. & Goodson, W. H., III (1988) The lumpy breast. [Review] [8 refs]. *Western Journal of Medicine*, 149: 226-229.
Narrative review
- Granek, L., Fitzgerald, B., Fergus, K., Clemons, M. & Heisey, R. (2012) Travelling on parallel tracks: patient and physician perspectives on why women delay seeking care for breast cancer symptoms. *Canadian Oncology Nursing Journal*, 22: 101-113.
Not in PICO
- Grimshaw, J. M., Winkens, R. A. G., Shirran, L., Cunningham, C., Mayhew, A., Thomas, R. & Fraser, C. (2005) Interventions to improve outpatient referrals from primary care to secondary care.

Cochrane Database of Systematic Reviews.

Not in PICO

Grunfeld, E. A., Hunter, M. S., Ramirez, A. J. & Richards, M. A. (2003) Perceptions of breast cancer across the lifespan. *Journal of Psychosomatic Research*, 54: 141-146.

Not in PICO

Haghighat, S., Yunesian, M., Akbari, M. E., Ansari, M. & Montazeri, A. (2007) Telephone and face-to-face consultation in breast cancer diagnosis: a comparative study. *Patient Education & Counseling*, 67: 39-43.

Not in PICO

Hamilton, W. (2010) Cancer diagnosis in primary care. *British Journal of General Practice*, 60: 121-128.

Narrative review

Heimans, J. J., Taphoorn, M. J. & van, K. B. (1993) [Neurologic consultation in cancer patients]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 137: 2705-2709.

Not in PICO

Heins, M. J., Korevaar, J. C., Rijken, P. M. & Schellevis, F. G. (2013) For which health problems do cancer survivors visit their General Practitioner? *European Journal of Cancer*, 49: 211-218.

Not in PICO

Heisey, R., Clemons, M., Granek, L., Fergus, K., Hum, S., Lord, B., McCready, D. R. & Fitzgerald, B. (2011) Health care strategies to promote earlier presentation of symptomatic breast cancer: perspectives of women and family physicians. *Current Oncology*, 18: e227-e237.

Not in PICO

Heisey, R. E. & McCready, D. R. (2010) Office management of a palpable breast lump with aspiration. *CMAJ Canadian Medical Association Journal*, 182: 693-696.

Not in PICO

Hider, P. & Nicholas, B. (1999) The early detection and diagnosis of breast cancer: a literature review. An update (Structured abstract). *Database of Abstracts of Reviews of Effects.*, 150. Systematic review without meta-analysis. Included studies checked for relevance.

Hieken, T. J., Trull, B. C., Boughey, J. C., Jones, K. N., Reynolds, C. A., Shah, S. S. & Glazebrook, K. N. (838) Preoperative axillary imaging with percutaneous lymph node biopsy is valuable in the contemporary management of patients with breast cancer. *Surgery*, 154: 831-838.

Not in PICO

Hines, S. L., Tan, W. W., Yasrebi, M., DePeri, E. R. & Perez, E. A. (2007) The role of mammography in male patients with breast symptoms. *Mayo Clinic Proceedings*, 82: 297-300.

Not in PICO

Hirst, C. (126) Managing the breast lump. Solving the dilemma--reassurance versus investigation. *Australian Family Physician*, 18: 121-123.

Narrative review

Hoffmann, J. (11111) The influence of the referring doctor's clinical evaluation on the waiting time guarantee for breast cancer. [Danish]. *Ugeskrift for Laeger*, 167: 30.

Not in PICO

Holzmann, J., Lawn, A. & Kothari, M. (2013) Do mammograms aid the diagnosis of breast cancer in symptomatic young women? *European Journal of Surgical Oncology*, 39: 482.

Abstract only, not enough information to ascertain relevance.

Hou, M. F., Tsai, K. B., Ou-Yang, F., Lin, H. J., Liu, C. S. & et al. (2002) Is a one-step operation for breast cancer patients presenting nipple discharge without palpable mass feasible? *Breast*, 11: 402-407.

From National Breast Cancer Centre Sydney Australia SR. Not in PICO

Houssami, N., Irwig, L., Simpson, J. M., McKessar, M., Blome, S. & et al. (2003) Sydney Breast Imaging Accuracy Study: Comparative sensitivity and specificity of mammography and sonography in

- young women with symptoms. *AJR Am J Roentgenol*, 180: 935-940.
From National Breast Cancer Centre Sydney Australia SR. Not in PICO
- Houssami, N., Ciatto, S., Martinelli, F., Bonardi, R. & Duffy, S. W. (2009) Early detection of second breast cancers improves prognosis in breast cancer survivors. *Annals of Oncology*, 20: 2009.
Not in PICO
- Howard, M. B., Battaglia, T., Prout, M. & Freund, K. (2012) The effect of imaging on the clinical management of breast pain. *Journal of General Internal Medicine*, 27: 817-824.
Not in PICO
- Hung, W.-K., Chan, S. W. W., Suen, D. T. K., Chan, M. C. M., Lau, Y. & Yip, A. W. C. (2006) Triaging referral to a specialist breast clinic. *ANZ Journal of Surgery*, 76: May.
Not in PICO
- Hunter, M. S., Grunfeld, E. A. & Ramirez, A. J. (2003) Help-seeking intentions for breast-cancer symptoms: a comparison of the self-regulation model and the theory of planned behaviour. *British Journal of Health Psychology*, 8: 3-33.
Not in PICO
- Hussain, A., Naheed, K. & Imran, A. (11111) Frequency of benign and malignant diseases of the breast lump in females. *Medical Forum Monthly*, 22: February.
Full text unavailable. Don't think it is in PICO (breast cancer prevalence = 12%)
- Inaji, H., Yayoi, E., Maeura, Y., Matsuura, N., Tominaga, S., Koyama, H., Takatsuka, Y. & Mori, T. (1987) Carcinoembryonic antigen estimation in nipple discharge as an adjunctive tool in the diagnosis of early breast cancer. *Cancer*, 60: 3008-3013.
Not in PICO
- Inaji, H., Koyama, H., Motomura, K., Noguchi, S., Mori, Y., Kimura, Y., Sugano, K. & Ohkura, H. (1993) ErbB-2 protein levels in nipple discharge: Role in diagnosis of early breast cancer. *Tumor Biology*, 14: 1993.
Not in PICO
- Iniesta, M. D., Mooney, C. J. & Merajver, S. D. (2009) Inflammatory breast cancer: what are the treatment options?. [Review] [71 refs]. *Expert Opinion on Pharmacotherapy*, 10: 2987-2997.
Not in PICO
- Innos, K., Padrik, P., Valvere, V., Eelma, E., Kutner, R., Lehtsaar, J. & Tekkel, M. (2013) Identifying women at risk for delayed presentation of breast cancer: a cross-sectional study in Estonia. *BMC Public Health*, 13: 947.
Not in PICO
- Irwig, L., Macaskill, P. & Houssami, N. (2002) Evidence relevant to the investigation of breast symptoms: the triple test. *Breast*, 11: 215-220.
Narrative review
- Isaacs, J. H. (1989) Physician breast examination and breast self-examination. *Clinical Obstetrics & Gynecology*, 32: 761-767.
Narrative review
- Isley, L. M., Leddy, R. J., Rumboldt, T. & Bernard, J. M. (2012) Asymptomatic Incidental Ductal Carcinoma in situ in a Male Breast Presenting with Contralateral Gynecomastia. *Journal of Clinical Imaging Science*, 2: 9.
Not in PICO
- Jalalian, A., Mashohor, S. B., Mahmud, H. R., Sariapan, M. I., Ramli, A. R. & Karasfi, B. (2013) Computer-aided detection/diagnosis of breast cancer in mammography and ultrasound: a review. [Review]. *Clinical Imaging*, 37: 420-426.
Narrative review
- Johnson, T. L. & Kini, S. R. (1991) Cytologic and clinicopathologic features of abnormal nipple secretions: 225 cases. *Diagnostic Cytopathology*, 7: 17-22.
Not in PICO

- Jones, R. V. & Dudgeon, T. A. (1992) Time between presentation and treatment of six common cancers: a study in Devon. *British Journal of General Practice*, 42: 419-422.
Not in PICO
- Jones, S. C. & Johnson, K. (2012) Women's awareness of cancer symptoms: a review of the literature. [Review]. *Women's health*, 8: 579-591.
Narrative review
- Jordan, K. P. & Croft, P. (2010) Mortality and cancer in patients with new musculoskeletal episodes: A cohort study. *British Journal of General Practice*, 60: e150-112.
Outcomes not in PICO. Presented data only for cancer as a whole, not by individual cancers.
- Jordan, K. P., Hayward, R. A., Blagojevic-Bucknall, M. & Croft, P. (2013) Incidence of prostate, breast, lung and colorectal cancer following new consultation for musculoskeletal pain: a cohort study among UK primary care patients. *International Journal of Cancer*, 133: 713-720.
Cannot extract outcome in PICO (PPVs) as cancer data only reported in total for 10-year follow up
- Kalles, V., Zografos, G. C., Provatopoulou, X., Koulocheri, D. & Gounaris, A. (2013) The current status of positron emission mammography in breast cancer diagnosis. [Review]. *Breast Cancer*, 20: 123-130.
Narrative review
- Kapdi, C. C. & Parekh, N. J. (1983) The male breast. *Radiologic Clinics of North America*, 21: 137-148.
Narrative review
- Kashgari, R. H. & Ibrahim, A. M. (1996) Breast cancer: attitude, knowledge and practice of breast self examination of 157 saudi women. *Journal of Family and Community Medicine*, 3: 10-13.
Not in PICO
- Kashiwagi, S., Onoda, N., Asano, Y., Noda, S., Kawajiri, H., Takashima, T., Ohsawa, M., Kitagawa, S. & Hirakawa, K. (2013) Adjunctive imprint cytology of core needle biopsy specimens improved diagnostic accuracy for breast cancer. *Springerplus*, 2: 372.
Not in PICO
- Katz, S. J., Hislop, T. G., Thomas, D. B. & Larson, E. B. (1993) Delay from symptom to diagnosis and treatment of breast cancer in Washington State and British Columbia. *Medical Care*, 31: 264-268.
Not in PICO
- Kawamoto, M. (1994) Breast cancer diagnosis by lactate dehydrogenase isozymes in nipple discharge. *Cancer*, 73: 1836-1841.
Not in PICO
- Kawasaki, T., Mochizuki, K., Yamauchi, H., Yagata, H., Kondo, T., Tsunoda, H., Nakamura, S., Oishi, N., Nakazawa, T., Yamane, T., Inoue, A., Maruyama, T., Inoue, M., Inoue, S., Fujii, H. & Katoh, R. (2012) High prevalence of neuroendocrine carcinoma in breast lesions detected by the clinical symptom of bloody nipple discharge. *Breast*, 21: 652-656.
Not in PICO
- Keeble, S., Abel, G. A., Saunders, C. L., McPhail, S., Walter, F. M., Neal, R. D., Rubin, G. P. & Lyratzopoulos, G. (2014) Variation in promptness of presentation among 10,297 patients subsequently diagnosed with one of 18 cancers: Evidence from a National Audit of Cancer Diagnosis in Primary Care. *International Journal of Cancer*, 135: 1220-1228.
Not in PICO
- Keeble, S., Abel, G. A., Saunders, C. L., McPhail, S., Walter, F. M., Neal, R. D., Rubin, G. P. & Lyratzopoulos, G. (2014) Variation in promptness of presentation among 10,297 patients subsequently diagnosed with one of 18 cancers: Evidence from a National Audit of Cancer Diagnosis in Primary Care. *International Journal of Cancer*, 135: 1220-1228.
Duplicate
- Keinan, G., Carmil, D. & Rieck, M. (1991) Predicting women's delay in seeking medical care after discovery of a lump in the breast: the role of personality and behavior patterns. *Behavioral Medicine*, 17: 177-183.
Not in PICO

- Kerlikowske, K., Smith-Bindman, R., Ljung, B. M. & Grady, D. (2003) Evaluation of abnormal mammography results and palpable breast abnormalities. *Annals of Internal Medicine*, 139: 274-284.
Narrative review
- Kern, K. A. (2001) The delayed diagnosis of breast cancer: Medicolegal implications and risk prevention for surgeons. *Breast Disease*, 12.
Not in PICO
- Kim, S. J., Ha, S. Y., Choi, B. M., Lee, M. Y., Jin, J. Y., Yeom, S. J., Kim, T. W., Kim, Y. M. & Lee, K. (2013) The prevalence and clinical characteristics of cancer among anemia patients treated at an outpatient clinic. *Blood Research*, 48: 46-50.
Not in PICO
- Kollias, J., Bochner, M. A., Gill, P. G., Malycha, P. & Coventry, B. J. (2001) Quality assurance in a multidisciplinary symptomatic breast assessment clinic. *Australian and New Zealand Journal of Surgery*, 71: 271-273.
Not in PICO
- Kopp, W., Fotter, R. & Schneider, G. (1986) Roentgen symptoms of early cancer of the breast. [German]. *Der Radiologe*, 26: Oct.
Not in PICO
- Kosir, M. A., Chism, L., Bland, K., Choi, L., Gorski, D. & Simon, M. S. (1916) Common breast symptoms: when to refer to a breast surgeon. *Advance for NPs & PAs*, 4: 12-15.
Narrative review
- Kostopoulou, O., Delaney, B. C. & Munro, C. W. (2008) Diagnostic difficulty and error in primary care - A systematic review. *Family Practice*, 25: 2008.
Not in PICO
- Krajcar, N., Mascitti, A. & Simons, K. (2011) Improving primary to acute referrals: the role of the cancer clinical network in developing consistent information for general practitioners. *Asia-Pacific Journal of Clinical Oncology. Conference: 38th Annual Scientific Meeting of the Clinical Oncological Society of Australia, COSA 2011 Perth, WA Australia. Conference Start: 20111115 Conference End: 20111117. Conference Publication: (var.paging, 7: November.*
Not in PICO
- Krishnaiah, G., Sher-Ahmed, A., Ugwu-Dike, M., Regan, P., Singer, J., Totoonchie, A., Spiegler, E. & Sardi, A. (2003) Technetium-99m sestamibi scintimammography complements mammography in the detection of breast cancer. *Breast Journal*, 9: July/August.
Not in PICO
- Kroman, N. T., Grinsted, P. & Nielsen, N. S. (2007) [Symptoms and diagnostic work-up in breast cancer]. [Danish]. *Ugeskrift for Laeger*, 169: 2980-2981.
Narrative review
- Kubiak, T. (2013) Correlation between iron metabolism and development of breast cancer in pre-and postmenopausal women. [Polish]. *Przegląd Menopauzalny*, 17: 339-342.
Narrative review
- Kurtz, M. E., Kurtz, J. C., Given, C. W. & Given, B. A. (2005) Utilization of services among elderly cancer patients--relationship to age, symptoms, physical functioning, comorbidity, and survival status. *Ethnicity & Disease*, 15: Suppl-22.
Not in PICO
- Kwak, H. Y., Chae, B. J., Bae, J. S., Kim, E. J., Chang, E. Y., Kim, S. H., Jung, S. S. & Song, B. J. (2013) Feasibility of sentinel lymph node biopsy in breast cancer patients clinically suspected of axillary lymph node metastasis on preoperative imaging. *World Journal of Surgical Oncology*, 11: 104.
Not in PICO
- Lam, W. W., Fielding, R., Chan, M. & Or, A. (2009) Factors influencing delayed presentation with symptomatic breast cancer in Hong Kong Chinese women. *Hong Kong Medical Journal*, 15: Suppl-

7.

Not in PICO

Lam, W. W. M., Chan, C. P., Chan, C. F., Mak, C. C. C., Chan, C. F., Chong, K. W. H., Leung, M. H. J. & Tang, M. H. (2008) Factors affecting the palpability of breast lesion by self-examination. *Singapore Medical Journal*, 49: 228-232.

Not in PICO

Lam, W. W. T., Tsuchiya, M., Chan, M., Chan, S. W. W., Or, A. & Fielding, R. (2009) Help-seeking patterns in Chinese women with symptoms of breast disease: a qualitative study. *Journal of Public Health*, 31: 59-68.

Not in PICO

Lambert, P. A., Kolm, P. & Perry, R. R. (2000) Parameters that predict nipple involvement in breast cancer. *Journal of the American College of Surgeons*, 191: 354-359.

Not in PICO

Lauver, D. & Angerame, M. (1993) Women's expectations about seeking care for breast cancer symptoms. [Review] [43 refs]. *Oncology Nursing Forum*, 20: 519-525.

Not in PICO

Lennard, T. W. & Harvey, J. R. (2004) FAQs: breast pain and fibroadenosis. *The Practitioner*, 248: Oct. Narrative review

Leung, J. W. T., Kornguth, P. J. & Gotway, M. B. (2002) Utility of targeted sonography in the evaluation of focal breast pain. *Journal of Ultrasound in Medicine*, 21.

Not in PICO

Lewis, C. L., Kinsinger, L. S., Harris, R. P. & Schwartz, R. J. (2004) Breast cancer risk in primary care: implications for chemoprevention. *Archives of Internal Medicine*, 164: 1897-1903.

Not in PICO

Li, W., Ray, R. M., Lampe, J. W., Lin, M.-G., Gao, D. L., Wu, C., Nelson, Z. C., Fitzgibbons, E. D., Horner, N., Hu, Y. W., Shannon, J., Satia, J. A., Patterson, R. E., Stalsberg, H. & Thomas, D. B. (2005) Dietary and other risk factors in women having fibrocystic breast conditions with and without concurrent breast cancer: A nested case-control study in Shanghai, China. *International Journal of Cancer*, 115: 20.

Not in PICO

Linsell, L., Burgess, C. C. & Ramirez, A. J. (2008) Breast cancer awareness among older women. *British Journal of Cancer*, 99: 1221-1225.

Not in PICO

Liukkonen, S., Saarto, T., Maenpaa, H. & Sjostrom-Mattson, J. (2010) Male breast cancer: A survey at the Helsinki University Central Hospital during 1981-2006. *Acta Oncologica*, 49: 322-327.

Not in PICO

Lord, B., Howell, D., McCreedy, D. & Escallon, J. (2009) Rapid diagnostic assessment for a suspicious breast abnormality: Impact on uncertainty, stress and anxiety. *Supportive Care in Cancer. Conference: 2009 International MASCC/ISOO Symposium Rome Italy. Conference Start: 20090625 Conference End: 20090627. Conference Publication: (var.pagings)*, 17: July.

Ongoing study

Loutfi, A. (1998) Recommended management for breast lumps. *Canadian Journal of Surgery*, 41.

Not in PICO

Love, N. (155) Why patients delay seeking care for cancer symptoms. What you can do about it. [Review] [27 refs]. *Postgraduate Medicine*, 89: 151-152.

Narrative review

Loveland-Jones, C. E., Wang, F., Bankhead, R. R., Huang, Y. & Reilly, K. J. (2010) Squamous cell carcinoma of the nipple following radiation therapy for ductal carcinoma in situ: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 4: 186.

Not in PICO

- Lyon, D., Knowles, J., Slater, B. & Kennedy, R. (2009) Improving the early presentation of cancer symptoms in disadvantaged communities: Putting local people in control. *British Journal of Cancer*, 101: December.
Not in PICO
- Lyratzopoulos, G., Neal, R. D., Barbiere, J. M., Rubin, G. P. & Abel, G. A. (2012) Variation in number of general practitioner consultations before hospital referral for cancer: Findings from the 2010 National Cancer Patient Experience Survey in England. *The Lancet Oncology*, 13: April.
Not in PICO
- Lyratzopoulos, G. & Abel, G. (2013) Earlier diagnosis of breast cancer: focusing on symptomatic women. *Nature Reviews Clinical Oncology*, 10: 2013.
Narrative review
- Lyratzopoulos, G., Abel, G. A., McPhail, S., Neal, R. D. & Rubin, G. P. (2013) Measures of promptness of cancer diagnosis in primary care: secondary analysis of national audit data on patients with 18 common and rarer cancers. *British Journal of Cancer*, 108: 686-690.
Not in PICO
- MacArthur, C. & Smith, A. (1981) Delay in breast cancer and the nature of presenting symptoms. *Lancet*, 1: t-3.
Not in PICO
- Macleod, U., Mitchell, E. D., Burgess, C., Macdonald, S. & Ramirez, A. J. (2009) Risk factors for delayed presentation and referral of symptomatic cancer: evidence for common cancers. *British Journal of Cancer*, 101: Suppl-S101.
Not in PICO
- Madeya, S. & Borsch, G. (1992) Upper intestinal endoscopy in 188 bronchial cancer patients and 118 breast cancer patients with abdominal symptoms. The GI Metastases Study Group. [German]. *Medizinische Klinik (Munich, Germany : 1983)*, 87: 15.
Not in PICO
- Mahoney, M. C. & Newell, M. S. (2013) Breast intervention: how I do it. [Review]. *Radiology*, 268: 12-24.
Narrative review
- Mak, C. & Pokorny, C. S. (2010) Investigating a woman with a breast lump. *Medicine Today*, 11: June.
Narrative review
- Malik, A. (2009) Pattern of presentation and management of Ca breast in the developing countries. There is a lot to do. *Maturitas.Conference: 8th European Congress on Menopause, EMAS London United Kingdom.Conference Start: 20090516 Conference End: 20090520 Sponsor: PANTARHEI BIOSCIENCE, FSDeducation.eu.Conference Publication: (var.pagings)*, 63: May.
Not in PICO
- Malik, A. M., Pathan, R., Shaikh, N. A., Qureshi, J. N. & Talpur, K. A. H. (2010) Pattern of presentation and management of Ca breast in developing countries. There is a lot to do. *Journal of the Pakistan Medical Association*, 60: 718-721.
Not in PICO
- Mamoon, N., Hassan, U. & Mushtaq, S. (2009) Breast carcinoma in young women aged 30 or less in Northern Pakistan - the Armed Forces Institute of Pathology experience. *Asian Pacific journal of cancer prevention : APJCP*, 10.
Not in PICO
- Mansson, J. & Bengtsson, C. (1992) The diagnosis of breast cancer--experiences from the community of Kungsbacka, Sweden. *Neoplasma*, 39: 305-308.
Not in PICO
- Mansson, J., Bjorkelund, C. & Hultborn, R. (1999) Symptom pattern and diagnostic work-up of malignancy at first symptom presentation as related to level of care. A retrospective study from the primary health care centre area of Kungsbacka, Sweden. *Neoplasma*, 46: 93-99.
Not in PICO

- Mansson, J., Marklund, B. & Hultborn, R. (2001) The diagnosis of cancer in the "roar" of potential cancer symptoms of patients in primary health care. Research by means of the computerised journal. *Scandinavian Journal of Primary Health Care*, 19: 83-89.
Symptoms not linked with cancers; analysis based on number of codes, not patients.
- Mansson, J., Marklund, B. & Carlsson, P. (2006) Costs in primary care of investigating symptoms suspicious of cancer in a defined population. *Scandinavian Journal of Primary Health Care*, 24: 243-250.
Symptoms not linked with cancers; analysis based on number of codes, not patients.
- Marchant, D. J. (1998) Controversies in benign breast disease. *Surgical Oncology Clinics of North America*, 7.
Narrative review
- Marchant, D. J. (2002) Inflammation of the breast. [Review] [46 refs]. *Obstetrics & Gynecology Clinics of North America*, 29: 89-102.
Narrative review
- Marlow, L. A., McGregor, L. M., Nazroo, J. Y. & Wardle, J. (2014) - Facilitators and barriers to help-seeking for breast and cervical cancer symptoms: a qualitative study with an ethnically diverse sample in London. - *Psycho-Oncology*, 23: 749-757.
Not in PICO
- Mason, T. A., Thompson, W. W., Allen, D., Rogers, D., Gabram-Mendola, S. & Arriola, K. R. (2013) Evaluation of the Avon Foundation community education and outreach initiative Community Patient Navigation Program. *Health Promotion Practice*, 14: 105-112.
Not in PICO
- Matsunaga, T., Kawakami, Y., Namba, K. & Fujii, M. (2004) Intraductal biopsy for diagnosis and treatment of intraductal lesions of the breast. *Cancer*, 101: 15.
Not in PICO
- Mawhinney, A. C., McClements, J., Kennedy, R. J., Newell, J. & Kirk, S. J. (2014) Patient perceptions of the breast clinic. *European Journal of Cancer*, 50: S173-S174.
Not in PICO
- Mcavoy, B. R. (2007) General practitioners and cancer control. *Medical Journal of Australia*, 187: 115-117.
Narrative review
- McCain, S., Newell, J., Badger, S., Kennedy, R. & Kirk, S. (2011) Referral patterns, clinical examination and the two-week-rule for breast cancer: a cohort study. *Ulster Medical Journal*, 80: 68-71.
Not in PICO
- Meehan, G., Collins, J. & Petrie, K. (2002) Delay in seeking medical care for self-detected breast symptoms in New Zealand women. *New Zealand Medical Journal*, 115: U257.
Not in PICO
- Meehan, G., Collins, J. & Petrie, K. J. (2003) The relationship of symptoms and psychological factors to delay in seeking medical care for breast symptoms. *Preventive Medicine*, 36: 374-378.
Not in PICO
- Mehrotra, P., Townend, A. & Lunt, L. (2011) Incidental breast cancers identified in the one-stop symptomatic breast clinic. *Journal of Breast Cancer*, 14: 28-32.
Not in PICO
- Melnikow, J., Tancredi, D. J., Yang, Z., Ritley, D., Jiang, Y., Slee, C., Popova, S., Rylett, P., Knutson, K. & Smalley, S. (2013) Program-specific cost-effectiveness analysis: breast cancer screening policies for a safety-net program. *Value in Health*, 16: 932-941.
Not in PICO
- Mikulin, T. & Blamey, R. W. (1988) The problems referred to a breast clinic. *Practitioner*, 232.
Not in PICO

- Millet, A. V. & Dirbas, F. M. (2002) Clinical management of breast pain: a review. [Review] [93 refs]. *Obstetrical & Gynecological Survey*, 57: 451-461.
Narrative review
- Miranda, B. H., Malahias, M., El-Said, T. F. & Fahmy, F. S. (2014) - Axillary skin malignancy: a rare breast cancer presentation. - *Annals of Plastic Surgery*, 72: 513-514.
Not in PICO
- Molassiotis, A., Wilson, B., Brunton, L. & Chandler, C. (2010) Mapping patients' experiences from initial change in health to cancer diagnosis: a qualitative exploration of patient and system factors mediating this process. *European Journal of Cancer Care*, 19: 98-109.
Not in PICO
- Molckovsky, A., Fitzgerald, B., Freedman, O., Heisey, R. & Clemons, M. (2009) Approach to inflammatory breast cancer. *Canadian Family Physician*, 55: January.
Not in PICO
- Mon, M. M., Mon, M. & Than, K. K. (2009) Women's awareness, knowledge and perceived magnitude regarding common female cancers in Yangon, Myanmar. *Asian Pacific journal of cancer prevention : APJCP*, 10.
Not in PICO
- Montazeri, A., Vahdaninia, M., Harirchi, I., Harirchi, A. M., Sajadian, A., Khaleghi, F., Ebrahimi, M., Haghghat, S. & Jarvandi, S. (2008) Breast cancer in Iran: need for greater women awareness of warning signs and effective screening methods. *Asia Pacific Family Medicine*, 7: 6.
Not in PICO
- Morio, S., Kawahara, S., Okamoto, N., Suzuki, T., Okamoto, T., Harada, M. & Shimizu, A. (1989) An expert system for early detection of cancer of the breast. *Computers in Biology & Medicine*, 19: 295-305.
Not in PICO
- Morris, K. T., Pommier, R. F., Morris, A., Schmidt, W. A., Beagle, G., Alexander, P. W., Toth-Fejel, S., Schmidt, J. & Vetto, J. T. (2001) Usefulness of the triple test score for palpable breast masses. *Archives of Surgery*, 136: 1008-1012.
Not in PICO
- Morrison, C. (1998) The significance of nipple discharge: diagnosis and treatment regimes. [Review] [36 refs]. *Lippincott's Primary Care Practice*, 2: 129-140.
Narrative review
- Morrison, J. H. The relationship of sex-type, self-esteem, and coping strategies on delay in seeking medical treatment for breast cancer. Dissertation Abstracts International: Section B: The Sciences and Engineering 56[6-B], 3123. 1995.
Not in PICO
- Mousa, S. M., Seifeldin, I. A., Hablas, A., Elbana, E. S. & Soliman, A. S. (2011) Patterns of seeking medical care among Egyptian breast cancer patients: Relationship to late-stage presentation. *Breast*, 20: 555-561.
Not in PICO
- Mouton, W., Kienle, Y., Muggli, B., Naef, M. & Wagner, H. (2010) Tumors associated with superficial thrombophlebitis. *Vasa - Journal of Vascular Diseases.Conference: 15.Dreilandertagung der Deutschen, Osterreichischen und Schweizerischen Gesellschaft fur Angiologie Basel Switzerland.Conference Start: 20100909 Conference End: 20100912.Conference Publication: (var.pagi, 39.*
Not in PICO, I think. Setting seems to be surgery department
- Munoz, C. R., Alvarez, B. M. & Rivin del, C. E. (2013) Value of mammography and breast ultrasound in male patients with nipple discharge. *European Journal of Radiology*, 82: 478-484.
Not in PICO
- Murphy, I. G., Dillon, M. F., Doherty, A. O., McDermott, E. W., Kelly, G., O'Higgins, N. & Hill, A. D. (2007) Analysis of patients with false negative mammography and symptomatic breast

- carcinoma. *Journal of Surgical Oncology*, 96: 457-463.
Not in PICO
- Murtagh, J. (823) Mastalgia. *Australian Family Physician*, 20: 818-819.
Narrative review
- Muthoni, A. & Miller, A. N. An exploration of rural and urban Kenyan women's knowledge and attitudes regarding breast cancer and breast cancer early detection measures. [References]. *Health Care for Women International* 31[9], 801-816. 2010.
Not in PICO
- National Breast Cancer Centre, S. A. (1998) *The value of ultrasound in the detection of cancers in women presenting with breast lumps or asymmetrical prominence.*
<http://www.nbcc.org.au/pages/info/resource/nbccpubs/brcasymp/sec3.htm>.
From Hider HTA. Systematic review without meta-analysis. Checked for relevant studies.
- Neal, C. H., Coletti, M. C., Joe, A., Jeffries, D. O. & Helvie, M. A. (2013) Does digital mammography increase detection of high-risk breast lesions presenting as calcifications? *AJR.American Journal of Roentgenology*, 201: 1148-1154.
Not in PICO
- Neal, R. D., Din, N. U., Hamilton, W., GBroumune, O. C., Carter, B., Stapley, S. & Rubin, G. (2014) Comparison of cancer diagnostic intervals before and after implementation of NICE guidelines: Analysis of data from the GBR General Practice Research Database. *British Journal of Cancer*, 110: 584-592.
Not in PICO
- Neary, M., Lowery, A. J., O'Conghaile, A., Pervaz, M., Kerin, M. J. & Sweeney, K. J. (2011) NCCP breast cancer referral guidelines--are breast cancer patients prioritised? *Irish Medical Journal*, 104: 39-41.
Not in PICO
- Nekhlyudov, L., Nicola, M., Jung, I. & Buechler, E. (2008) Clinicians' knowledge and attitudes about breast symptom management: is there a use for clinical guidelines? *Journal of Women's Health*, 17: 57-65.
Not in PICO
- Nekhlyudov, L. & Latosinsky, S. (2010) The interface of primary and oncology specialty care: From symptoms to diagnosis. *Journal of the National Cancer Institute - Monographs*.(40) (pp 11-17), 2010.Date of Publication: 2010..
Narrative review
- Newton, P., Hannay, D. R. & Laver, R. (1999) The presentation and management of female breast symptoms in general practice in Sheffield. *Family Practice*, 16: 360-365.
Not in PICO
- Nichols, S., Waters, W. E., Fraser, J. D., Wheeler, M. J. & Ingham, S. K. (1981) Delay in the presentation of breast symptoms for consultant investigation. *Community Medicine*, 3: 217-225.
Not in PICO
- Nielsen, T. N., Hansen, R. P. & Vedsted, P. (2010) [Symptom presentation in cancer patients in general practice]. [Danish]. *Ugeskrift for Laeger*, 172: 2827-2831.
Not in PICO
- Niikura, N., Odisio, B. C., Tokuda, Y., Symmans, F. W., Hortobagyi, G. N. & Ueno, N. T. (2013) Latest biopsy approach for suspected metastases in patients with breast cancer. *Nature Reviews Clinical Oncology*, 10: 711-719.
Not in PICO
- Nikolaev, K. S. (2013) [Clinical and morphological features of breast cancer in men]. [Russian]. *Voprosy Onkologii*, 59: 358-362.
Narrative review
- Nishiguchi, T., Hishimoto, T., Funahashi, S., Takatsuka, Y. & Kawahara, T. (1992) [Clinical usefulness of carcinoembryonic antigen measurement in nipple discharge as an adjunctive tool for diagnosis

- of breast cancer]. [Japanese]. *Rinsho Byori - Japanese Journal of Clinical Pathology*, 40: 67-72.
Not in PICO
- Noh, K. T., Oh, B., Sung, S. H., Lee, R. A., Chung, S. S., Moon, B. I. & Kim, K. H. (2011) Metastasis to the breast from colonic adenocarcinoma. *Journal of The Korean Surgical Society*, 81: Suppl-6.
Not in PICO
- Norsa'adah, B., Rampal, K. G., Rahmah, M. A., Naing, N. N. & Biswal, B. M. (2011) Diagnosis delay of breast cancer and its associated factors in Malaysian women. *BMC Cancer*, 11: 141.
Not in PICO
- Nosarti, C., Crayford, T., Roberts, J. V., Elias, E., McKenzie, K. & David, A. S. (2000) Delay in presentation of symptomatic referrals to a breast clinic: patient and system factors. *British Journal of Cancer*, 82: 742-748.
Not in PICO
- O'Mahony, M. & Hegarty, J. (2009) Factors influencing women in seeking help from a health care professional on self discovery of a breast symptom, in an Irish context. *Journal of Clinical Nursing*, 18: 2020-2029.
Not in PICO
- O'Mahony, M., Hegarty, J. & McCarthy, G. (2011) Women's help seeking behaviour for self discovered breast cancer symptoms. *European Journal of Oncology Nursing*, 15: 410-418.
Not in PICO
- Ohanlon, D. M., Kent, P., Kerin, M. J. & Given, H. F. (1995) Unilateral Breast Masses in Men Over 40 - A Diagnostic Dilemma. *American Journal of Surgery*, 170: 24-26.
Not in PICO
- Osborn, G. D., Gahir, J. K., Preece, K., Vaughan-Williams, E. & Gower-Thomas, K. (2006) Is general practitioner access to breast imaging safe? *Clinical Radiology*, 61: 431-435.
Not in PICO
- Osborn, G. D., Jones, M., Gower-Thomas, K. & Vaughan-Williams, E. (2010) Breast disease diagnostic ability of nurse practitioners and surgeons. *Journal of Advanced Nursing*, 66: 1452-1458.
Not in PICO
- Osuch, J. R. & Bonham, V. L. (1994) The Timely Diagnosis of Breast-Cancer - Principles of Risk Management for Primary-Care Providers and Surgeons. *Cancer*, 74: 271-278.
Narrative review
- Osuch, J. R., Bonham, V. L. & Morris, L. L. (1998) Primary care guide to managing a breast mass: step-by-step workup. *Medscape Womens Health*, 3: 4.
Narrative review
- Osuch, J. R., Bonham, V. L. & Morris, L. L. (1998) Primary care guide to managing a breast mass: a legal perspective on risk management. *Medscape Womens Health*, 3: 3.
Narrative review
- Otieno, E. S., Micheni, J. N., Kimende, S. K. & Mutai, K. K. (2010) Delayed presentation of breast cancer patients. *East African Medical Journal*, 87: 147-150.
Not in PICO
- Ott, J. J., Ullrich, A. & Miller, A. B. (2009) The importance of early symptom recognition in the context of early detection and cancer survival. *European Journal of Cancer*, 45: 2743-2748.
Narrative review
- Padden, D. L. (2000) Mastalgia: evaluation and management. [Review] [11 refs]. *Nurse Practitioner Forum*, 11: 213-218.
Narrative review
- Pan, S., Liu, W., Jin, K., Liu, Y. & Zhou, Y. (2014) Ultrasound-guided vacuum-assisted breast biopsy using Mammotome biopsy system for detection of breast cancer: results from two high volume hospitals. *International journal of clinical and experimental medicine*, 7: 239-246.
Not in PICO

- Park, C. S., Jung, N. Y., Kim, K., Jung, H. S., Sohn, K. M. & Oh, S. J. (2013) Detection of breast cancer in asymptomatic and symptomatic groups using computer-aided detection with full-field digital mammography. *Journal of Breast Cancer*, 16: 322-328.
Not in PICO
- Park, S., Kim, J. H., Koo, A., Park, B. W. & Lee, K. S. (2008) Clinicopathological Characteristics of Male Breast Cancer. *Yonsei Medical Journal*, 49: 978-986.
Not in PICO
- Parker, A., Schroen, A. T. & Brenin, D. R. (2013) MRI utilization in newly diagnosed breast cancer: a survey of practicing surgeons. *Annals of Surgical Oncology*, 20: 2600-2606.
Not in PICO
- Parkyn, R. (1993) Discovering a breast lump. Management plans and pitfalls. *Australian Family Physician*, 22: 43-46.
Narrative review
- Parthasarathy, V. & Rathnam, U. (2012) Nipple discharge: an early warning sign of breast cancer. *International Journal of Preventive Medicine*, 3: 810-814.
Not in PICO
- Patel, R. S., Smith, D. C. & Reid, I. (2000) One stop breast clinics--victims of their own success? A prospective audit of referrals to a specialist breast clinic. *European Journal of Surgical Oncology*, 26: 452-454.
Not in PICO
- Pill, R., Wood, F. C., Renold, E., Robling, M., Edwards, A., Wilkinson, C. & Bridge Study Group (2003) Welsh women's comments about breast problems and the care given: a qualitative study in the community. *European Journal of Cancer Care*, 12: 240-248.
Not in PICO
- Pineros, M., Sanchez, R., Cendales, R., Perry, F. & Ocampo, R. (2009) Patient delay among Colombian women with breast cancer. *Salud Publica de Mexico*, 51: 372-380.
Not in PICO
- Polyzoidis, K. S., Miliaras, G. & Pavlidis, N. (2005) Brain metastasis of unknown primary: A diagnostic and therapeutic dilemma. *Cancer Treatment Reviews*, 31: June.
Not in PICO
- Poum, A., Promthet, S., Duffy, S. W. & Parkin, D. M. (2014) - Factors associated with delayed diagnosis of breast cancer in northeast Thailand. - *Journal of Epidemiology*, 24: 102-108.
Not in PICO
- Psyrris, A. & Burtness, B. (2005) Pregnancy-associated breast cancer. *Cancer journal (Sudbury, Mass.)*, 11: -2Apr.
Not in PICO
- Pullyblank, A. M., Cawthorn, S. J. & Dixon, A. R. (2002) Knowledge of cancer symptoms among patients attending one-stop breast and rectal bleeding clinics. *European Journal of Surgical Oncology*, 28: 511-515.
Not in PICO
- Quigley, M. R., Fukui, O., Chew, B., Bhatia, S. & Karlovits, S. (2013) The shifting landscape of metastatic breast cancer to the CNS. *Neurosurgical Review*, 36: 377-382.
Not in PICO
- Ramirez, A. J., Westcombe, A. M., Burgess, C. C., Sutton, S., Littlejohns, P. & Richards, M. A. (1999) Factors predicting delayed presentation of symptomatic breast cancer: a systematic review. [Review] [34 refs]. *Lancet*, 353: 1127-1131.
Not in PICO
- Raneta, O., Bella, V., Bellova, L. & Zamecnikova, E. (2013) The use of electrical impedance tomography to the differential diagnosis of pathological mammographic/sonographic findings. *Neoplasma*, 60: 647-654.
Not in PICO

- Redman, S., Henrikus, D., Clover, K. & Sanson-Fisher, R. Responses of women and their doctors to the occurrence of a breast symptom: A community study. *Health Promotion International* 8[3], 177-187. 1993.
Not in PICO
- Rezende, M. C. R., Koch, H. A., Figueiredo, J. A. & Thuler, L. C. S. (2009) Factors leading to delay in obtaining definitive diagnosis of suspicious lesions for breast cancer in a dedicated health unit in Rio de Janeiro. [Portuguese]. *Revista Brasileira de Ginecologia e Obstetricia*, 31: February.
Not in PICO
- Rissanen, T., Suvanto-Luukkonen, E., Nieminen, E. & Apaja-Sarkkinen, M. (1904) [Examination and therapy of a painful breast]. [Review] [31 refs] [Finnish]. *Duodecim*, 117: 1897-1904.
Narrative review
- Roberts, J. C. & Rainsbury, R. M. (1994) 'Tactile sensation': a new clinical sign during fine needle aspiration of breast lumps. *Annals of the Royal College of Surgeons of England*, 76: 136-138.
Not in PICO
- Robertson, R., Campbell, N. C., Smith, S., Donnan, P. T., Sullivan, F., Duffy, R., Ritchie, L. D., Millar, D., Cassidy, J. & Munro, A. (2004) Factors influencing time from presentation to treatment of colorectal and breast cancer in urban and rural areas. *British Journal of Cancer*, 90: 1479-1485.
Not in PICO
- Robling, M., Matthews, S. J., Hood, K., Russell, I. T., Holloway, R., Wilkinson, C., Edwards, A. G. K., Austoker, J., Cohen, D., Mansel, R., Pill, R. M., Stott, N. C. H. & Thapar, A. The development of a new site-specific measure of quality of life for breast problems: The Cardiff breast scales. [References]. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation* 11[4], 339-348. 2002.
Not in PICO
- Rodden, A. M. (2009) Common breast concerns. [Review] [45 refs]. *Primary Care; Clinics in Office Practice*, 36: 103-113.
Narrative review
- Rogulski, L. & Binczyk, J. (2013) Estimated breast cancer risk and screening outcomes among premenopausal women with non-cyclic mastalgia. *Ginekologia Polska*, 84: 754-757.
Not in PICO (secondary care)
- Roorda, C., Berendsen, A. J., Haverkamp, M., Van Der Meer, K. & De Bock, G. H. (2013) Discharge of breast cancer patients to primary care at the end of hospital follow-up: A cross-sectional survey. *European Journal of Cancer*, 49: 1836-1844.
Not in PICO
- RoshanLall, C., Leinster, S., Mitchell, S. & Holcombe, C. (2000) Current patterns of referral in breast disease. *Breast*, 9: 334-337.
Not in PICO
- Rubin, M., Horiuchi, K., Joy, N. W., Read, R., Ratzer, E. & Fenoglio, M. (1997) Use of fine needle aspiration for solid breast lesions is accurate and cost effective. *American Journal of Surgery*, 174: 694-698.
From Hider HTA. Not in PICO
- Ruiz-Torrejon, A., Ramos-Monserrat, M. & Llobera-Canaves, J. (2006) Family practice and diagnosis of cancer. [Spanish]. *Atencion Primaria*, 37: January.
Not in PICO
- Ruston, A. Risk, anxiety and defensive action: General practitioner's referral decisions for women presenting with breast problems. [References]. *Health, Risk & Society* 6[1], 25-38. 2004.
Not in PICO
- Saidin, N., Mat Sakim, H. A., Ngah, U. K. & Shuaib, I. L. (2013) Computer aided detection of breast density and mass, and visualization of other breast anatomical regions on mammograms using graph cuts. *Computational & Mathematical Methods in Medicine*, 2013: 205384.
Not in PICO

- Sainsbury, R., Johnston, C. & Haward, B. (1999) Effect on survival of delays in referral of patients with breast-cancer symptoms: a retrospective analysis. *Lancet*, 353: 1132-1135.
Not in PICO
- Salzman, B., Fleegle, S. & Tully, A. S. (2012) Common breast problems. [Review]. *American Family Physician*, 86: 343-349.
Narrative review
- Salzman, B. E., Lamb, K., Olszewski, R. F., Tully, A. & Studdiford, J. (2009) Diagnosing Cancer in the Symptomatic Patient. *Primary Care*, 36: 651-+.
Narrative review
- Samaila, M. & Waziri, G. D. (2012) Tuberculosis of the breast masquerading as cancer. *Journal of Pathology.Conference: 201st Scientific Meeting of the Pathological Society of Great Britain and Ireland London United Kingdom.Conference Start: 20120105 Conference End: 20120106.Conference Publication: (var.pagings)*, 226: March.
Not in PICO
- Samers, J. M., Galetakis, S., Scott, C. J., Drummond, R., Neil, S., Waters, L., Woolf, S. & Rodger, A. (2004) Breast cancer management: the perspective of general practitioners in inner and eastern Melbourne.[Erratum appears in *Breast*. 2005 Aug;14(4):335]. *Breast*, 13: 468-475.
Not in PICO
- Sauven, P. (2002) Impact of the '2 week wait' on referrals to breast units in the UK. *Breast*, 11: 262-264.
Not in PICO
- Scanlon, E. F. (1981) The early diagnosis of breast cancer. *Cancer*, 48: Suppl-6.
Narrative review
- Schairer, C., Soliman, A. S., Omar, S., Khaled, H., Eissa, S., Ayed, F. B., Khalafallah, S., Ayoub, W. B., Kantor, E. D., Merajver, S., Swain, S. M., Gail, M. & Brown, L. M. (2013) Assessment of diagnosis of inflammatory breast cancer cases at two cancer centers in Egypt and Tunisia. *Cancer Medicine*, 2: 178-184.
Not in PICO
- Schlesselman, J. J., Stadel, B. V., Korper, M., Yu, W. & Wingo, P. A. (1992) Breast cancer detection in relation to oral contraception. *Journal of Clinical Epidemiology*, 45: 449-459.
Not in PICO
- Schulz, K. D., Kreienberg, R., Fischer, R., Albert, U. S., Deutsche Gesellschaft, f. S., Deutsche, K. & Deutsche Krebshilfe und die Mitglieder der Plangungskommission (2003) [Stage 3 recommendations--the early recognition of breast cancer in Germany. Abridged version for medical practitioners]. [German]. *Radiologe*, 43: 495-502.
Guideline
- Schulz, K. D., Koller, M., Lorenz, W., Kreienberg, R., Fischer, R., Albert, U. S. & Mitglieder der Planungskommission und Leiter der Arbeitsgruppen (2004) [Short version of the guideline "Early Detection of Breast Cancer in Germany"]. [German]. *Zeitschrift für Ärztliche Fortbildung und Qualitätssicherung*, 98: 361-373.
Guideline
- Shankpal, P. D. (2010) Supportive care in breast cancer patients: The role of non-government organizations [NGOs] in resource-poor developing nations. *Annals of Oncology.Conference: IMPAKT 2010 Breast Cancer Conference Brussels Belgium.Conference Start: 20100506 Conference End: 20100508.Conference Publication: (var.pagings)*, 21.
Not in PICO
- Shapley, M., Mansell, G., Jordan, J. L. & Jordan, K. P. (2010) Positive predictive values of $\geq 5\%$ in primary care for cancer: Systematic review. *British Journal of General Practice*, 60: September.
Systematic review. Checked for relevant studies (which have been included separately).
- Sheahan, S. L. (1984) Management of breast lumps. *Nurse Practitioner*, 9: 19-22.
Narrative review

- Shetty, M. K., Shah, Y. P. & Sharman, R. S. (2003) Prospective evaluation of the value of combined mammographic and sonographic assessment in patients with palpable abnormalities of the breast. *J Ultrasound Med*, 22: 263-268 (quiz 9-70).
From National Breast Cancer Centre Sydney Australia SR. Not in PICO
- Shetty, M. K. & Longatto-Filho, A. (2011) Early detection of breast, cervical, ovarian and endometrial cancers in low resource countries: an integrated approach. *Indian Journal of Surgical Oncology*, 2: 165-171.
Narrative review
- Siddiqui, I., Bhally, H. S., Niaz, Q. & Burney, I. A. (2002) Tumor-induced hypercalcemia: predictors of early mortality. *JPMA - Journal of the Pakistan Medical Association*, 52: 361-364.
Not in PICO
- Sidiropoulos, K. P., Kostopoulos, S. A., Glotsos, D. T., Athanasiadis, E. I., Dimitropoulos, N. D., Stonham, J. T. & Cavouras, D. A. (2013) Multimodality GPU-based computer-assisted diagnosis of breast cancer using ultrasound and digital mammography images. *International Journal of Computer Assisted Radiology & Surgery*, 8: 547-560.
Not in PICO
- Simo, C. E., Urena Tapia, M. M., Vernet, V. M., Sender Palacios, M. J., Larrossa, S. P. & Jovell, F. E. (2000) [Intervention of the family physician in the diagnosis of cancer]. [Spanish]. *Atencion Primaria*, 26: 104-106.
Not in PICO
- Skaane, P., Karesen, R., Jacobsen, U., Amlie, E., Sauer, T. & Skjorten, F. (1995) Investigation of palpable breast tumours. Patient flow and quality assessment of the tripple diagnostic procedure. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 115: 20.
Narrative review
- Smallwood, J. A., Kye, D. A. & Taylor, I. (1986) Mastalgia; is this commonly associated with operable breast cancer? *Annals of the Royal College of Surgeons of England*, 68: 262-263.
Not in PICO
- Smith-Bindman, R. (1111) Diagnostic imaging in the differential diagnosis of vaginal bleeding and breast mass. *Advanced Studies in Medicine*, 4: October.
Narrative review
- Stiefel, F. Understanding why women delay in seeking help for breast cancer symptoms. [References]. *Journal of Psychosomatic Research* 60[3], 309-310. 2006.
Not in PICO
- Stravodimou, A. & Voutsadakis, I. A. (2013) Pretreatment thrombocytosis as a prognostic factor in metastatic breast cancer. *International Journal of Breast Cancer*, 2013.
Not in PICO
- Suehiro, S., Inai, K., Tokuoka, S., Hamada, Y., Toi, M., Niimoto, M. & Hattori, T. (1989) Involvement of the nipple in early carcinoma of the breast. *Surgery, Gynecology & Obstetrics*, 168: 244-248.
Not in PICO
- Svensden, R. P., Stovring, H., Hansen, B. L., Kragstrup, J., Sondergaard, J. & Jarbol, D. E. (2010) Prevalence of cancer alarm symptoms: A population-based cross-sectional study. *Scandinavian Journal of Primary Health Care*, 28: 132-137.
Not in PICO
- Szrajda, M., Szyca, R., Jasinski, A., Gryz, M. & Leksowski, K. (2011) A case of a giant phyllodes tumour of the breast. *Wspolczesna Onkologia-Contemporary Oncology*, 15: 44-46.
Not in PICO
- Taib, N. A., Yip, C. H. & Low, W. Y. (2011) Recognising Symptoms of Breast Cancer as a Reason for Delayed Presentation in Asian Women - The Psycho-sociocultural Model for Breast Symptom Appraisal: Opportunities for Intervention. *Asian Pacific Journal of Cancer Prevention*, 12: 1601-1608.
Not in PICO

- Talpur, A. A., Surahio, A. R., Ansari, A. & Ghumro, A. A. (2011) Late presentation of breast cancer: a dilemma. *JPMA - Journal of the Pakistan Medical Association*, 61: 662-666.
Not in PICO
- Taylor, K., Ames, V. & Wallis, M. (2013) The diagnostic value of clinical examination and imaging used as part of an age-related protocol when diagnosing male breast disease: An audit of 1141 cases from a single centre. *Breast*, 22: 268-272.
Not in PICO (secondary care)
- Taylor, R. & Taguchi, K. (2005) Tamoxifen for breast cancer chemoprevention: Low uptake by high-risk women after evaluation of a breast lump. *Annals of Family Medicine*, 3: 242-247.
Not in PICO
- Tesfamariam, A., Gebremichael, A. & Mufunda, J. (2013) Breast cancer clinicopathological presentation, gravity and challenges in Eritrea, East Africa: management practice in a resource-poor setting. *South African Medical Journal.Suid-Afrikaanse Tydskrif Vir Geneeskunde*, 103: 526-528.
Not in PICO
- Thomas, E. (1939) Original Research: Men's awareness and knowledge of male breast cancer. *American Journal of Nursing*, 110: 32-37.
Not in PICO
- Thulesius, H. O., Lindgren, A. C., Olsson, H. L. & Hakansson, A. (2004) Diagnosis and prognosis of breast and ovarian cancer--a population-based study of 234 women. *Acta Oncologica*, 43: 175-181.
Not in PICO
- Timko, C. (1987) Seeking medical care for a breast cancer symptom: determinants of intentions to engage in prompt or delay behavior. *Health Psychology*, 6: 305-328.
Not in PICO
- Toomey, D. P., Cahill, R. A., Birido, N., Jeffers, M., Loftus, B., McInerney, D., Rothwell, J. & Geraghty, J. G. (2006) Rapid assessment breast clinics--evolution through audit. *European Journal of Cancer*, 42: 2961-2967.
Not in PICO
- Torrington, M. L., Frydenberg, M., Hansen, R. P., Olesen, F. & Vedsted, P. (2013) Evidence of increasing mortality with longer diagnostic intervals for five common cancers: A cohort study in primary care. *European Journal of Cancer*, 49: 2187-2198.
Not in PICO
- Townsend, C. M., Jr. (1980) Breast lumps. [Review] [11 refs]. *Clinical Symposia*, 32: 1-32.
Narrative review
- Trygonis, S., Akritidis, Z., Trygonis, C., Tsiaousi, E. & Mikrou, I. (1111) Pyloric obstruction as the initial manifestation of metastatic lobular breast cancer. [Greek]. *Surgical Chronicles*, 11: April/June.
Not in PICO
- Ueno, E., Tohno, E., Tsunoda-Shimizu, H., Aiyoshi, Y., Morishima, I., Ishikawa, T., Fukasawa, M., Yazawa, T. & Yashiro, T. (1994) Clinical diagnosis of early breast cancer. [Japanese]. *Gan to kagaku ryoho.Cancer & chemotherapy*, 21: Jun.
Not in PICO
- Ukwenya, A. Y., Yusufu, L. M., Nmadu, P. T., Garba, E. S. & Ahmed, A. (2008) Delayed treatment of symptomatic breast cancer: the experience from Kaduna, Nigeria. *South African Journal of Surgery*, 46: 106-110.
Not in PICO
- Unger-Saldana, K. & Infante-Castaneda, C. (2009) Delay of medical care for symptomatic breast cancer: a literature review. *Salud Publica de Mexico*, 51.
Not in PICO

- van Beelen, K. J. & Welvaart, K. (11111) Nipple discharge: A problem for the general practitioner?. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 135: 1991.
Duplicate of van Beelen
- van Beelen, K. J. & Welvaart, K. (1991) [Nipple secretion: a concern for the family physician?]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 135: 2171-2173.
Narrative review
- van, B. S., V, Nederend, J., Voogd, A. C., Coebergh, J. W., van, B. M., Jansen, F. H., Louwman, W. J. & Duijm, L. E. (2013) Trends in breast biopsies for abnormalities detected at screening mammography: a population-based study in the Netherlands. *British Journal of Cancer*, 109: 242-248.
Not in PICO
- VanderWalde, A. & Hurria, A. (2012) Early Breast Cancer in the Older Woman. *Clinics in Geriatric Medicine*, 28: February.
Narrative review
- Varga, L., Botos, A. & Minik, K. (1997) Difficulties in early diagnosis and treatment of uncommon breast tumours. *Acta Chirurgica Hungarica*, 36: 375-377.
Not in PICO
- Vetto, J., Jun, S.-Y., Padduch, D., Eppich, H. & Shih, R. (1999) Stages at presentation, prognostic factors, and outcome of breast cancer in males. *American Journal of Surgery*, 177: May.
Not in PICO
- Viswanathan, S. & Ramaswamy, B. (2011) Pregnancy-associated Breast Cancer. *Clinical Obstetrics and Gynecology*, 54: 546-555.
Narrative review
- Wall, P., Moore, C., El-Tamer, M. & Reilly, J. J. (1998) Diagnostic delay in breast disease - A system analysis of a public urban hospital. *Archives of Surgery*, 133: 662-666.
Not in PICO
- Wang, L. C., Sullivan, M., Du, H., Feldman, M. I. & Mendelson, E. B. (2013) US appearance of ductal carcinoma in situ. [Review]. *Radiographics*, 33: 213-228.
Narrative review
- Wang, S. Y., Peng, D. F., Cai, Z. G., Zhang, R. Z., Yao, T. J., Zhang, H., Yang, M. & Dong, H. M. (2008) [Clinicopathologic analysis of the nipple-areolar complex occult involvement in early stage breast carcinoma]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 30: 203-206.
Not in PICO
- West, K. W., Rescorla, F. J., Scherer, L. R. & Grosfeld, J. L. (1995) Diagnosis and Treatment of Symptomatic Breast Masses in the Pediatric Population. *Journal of Pediatric Surgery*, 30: 182-187.
Not in PICO
- Wu, Y. H., Chen, F. Y., Ouyang, H. Y. & Wang, S. M. (2008) [Clinical diagnosis of breast cancer with nonpalpable tumor]. [Chinese]. *Zhong Nan da Xue Xue Bao. Yi Xue Ban = Journal of Central South University. Medical Sciences*, 33: 861-864.
Not in PICO
- Xiao, C., Polomano, R. & Bruner, D. W. (2013) Comparison between patient-reported and clinician-observed symptoms in oncology. *Cancer Nursing*, 36: E1-E16.
Not in PICO
- Xin, Z., Wu, B. & Liu, H. (11111) The correlation between precancerous lesions of the breast and the early-stage breast cancer. [Chinese]. *Chinese Journal of Clinical Oncology*, 33: January.
In Chinese, and almost certainly not primary care
- Yin, J., Carter, J. V., Hunt, R., Burd, E., El-Abbar, M., Price, R. & Gill, J. (2011) One UK breast unit's experience of GP 2 week wait referrals to breast care clinic - Are they appropriate? *Breast. Conference: 1st Consensus Conference on Advanced Breast Cancer, ABC1 Lisbon Portugal. Conference Start: 20111103 Conference End: 20111105. Conference Publication:*

(var.pagings), 20: October.

Not in PICO

Zheng, W., Wen, M. & Kang, H. (1998) [The diagnosis and treatment of nipple discharge in 253 cases]. [Chinese]. *Bulletin of Hunan Medical University*, 23: 311-313.

In Chinese, and almost certainly not primary care

Review question:

Which investigations of symptoms of suspected breast cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

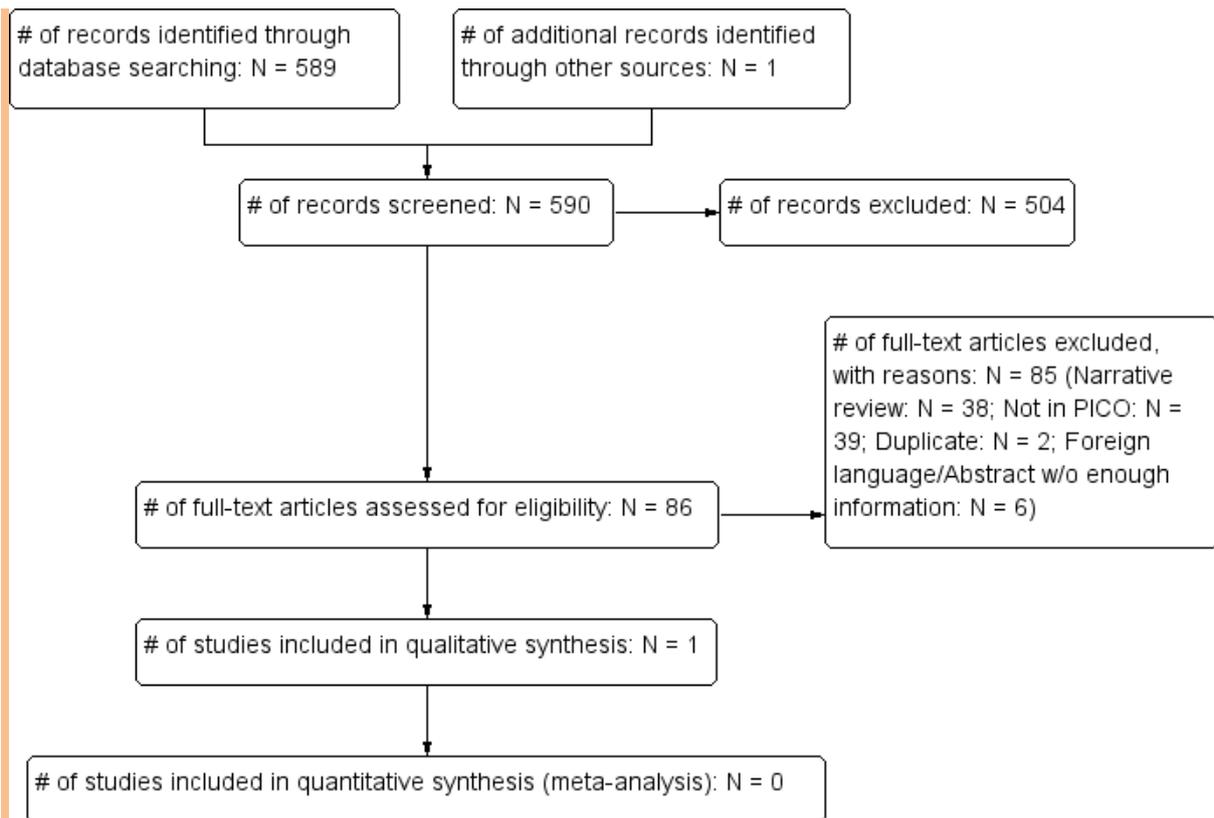
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-4/2013	1663	326	24/04/2013
<i>Premedline</i>	1980-4/2013	350	45	24/04/2013
<i>Embase</i>	1980-4/2013	1509	290	25/04/2013
<i>Cochrane Library</i>	1980-4/2013	274	22	25/04/2013
<i>Psychinfo</i>	1980-4/2013	67	4	24/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-4/2013	164	14	25/04/2013

Total References retrieved (after de-duplication): 553

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-12/08/014	349	17	12/08/014
<i>Premedline</i>	4/2013-12/08/014	180	11	12/08/014
<i>Embase</i>	4/2013-12/08/014	137	11	12/08/014
<i>Cochrane Library</i>	4/2013-12/08/014	77	0	12/08/014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	4/2013-12/08/014	16	0	12/08/014

Total References retrieved (after de-duplication): 36



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included study in the figure below. The study was associated with a number of bias and validity issues. The following issues compromise the validity and applicability of this study, (1) only about half of the patient population were patients relevant to the current question, to the extent that Dutch primary care is comparable to UK-based primary care, and no subgroup analyses were presented for this group of patients, (2) the results of the ultrasound scan was interpreted non-blinded to the results of the mammography and clinical examination, which biases the accuracy of the outcome measures study, most likely upwards, and (3) the time span between the index test and reference standard is unclear and the results are therefore compromised to an unknown extent.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Flobbe (2003)	+	?	+	?	-	?	+
	- High		? Unclear		+ Low		

Study results

Table 1: Breast cancer: Study results

Study	Test	Prevalence	Sensitivity (95% CI) %	Specificity (95% CI) %	Other results (95% CI)
Flobbe (2003)	Mammography	129/3835 breasts 127/2020 patients	82.9 (75.1-88.8)	91.9 (90.9-92.7)	TP = 107 FN = 22 TN = 3405 FP = 301 Positive predictive value = 26.2 (22.1-30.8)% Negative predictive value = 99.4 (99-99.6)% False negativity rate = 17.1%
Flobbe (2003)	Ultrasound	129/3835 breasts 127/2020 patients	87.6 (80.4-92.5)%	95.5 (94.8-96.1)%	TP = 113 FN = 16 <i>TN = 3556 FP = 167 These values from the paper are wrong as the total of negatives should be 3706 and not 3723 as is the case here. This means that apart from the sensitivity and false negativity rate, the remaining results for ultrasound should be interpreted with extreme caution.</i> Positive predictive value = 40.4 (34.6-46.4) % Negative predictive value = 99.6 (99.3-99.7)% False negativity rate = 12.4%

TP = true positives, FP = false positives, TN = true negatives, FN = false negatives.

No evidence was found for FNA.

Evidence statement(s):

Mammography (1 study, N = 2020 patients/ 3835 breasts) is associated with a sensitivity of 82.9%, a specificity of 91.9%, a positive predictive value of 26.2%, and a false negativity rate of 17.1% for breast cancer. Ultrasound (1 study, N = 2020 patients/ 3835 breasts) is associated with a sensitivity of 87.6%, a specificity of 95.5%, a positive predictive value of 40.4%, and a false negativity rate of 12.4% for breast cancer. The study was associated with 4 bias or applicability concerns (see also Table 1).

Evidence tables

Flobbe (2003)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospectiveconsecutive patient series
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 2020 (20 males/2000 females), mean (range) age = 50.2 (16.8-90.3) years; Referred by: GP (N = 1044), surgeons (N = 712), other specialists (N = 264); Indications for referral: Palpable breast lump (N = 470), other breast symptoms, such as pain or skin or nipple abnormalities (N = 486), follow up of prior breast malignancy(N = 438), follow up of prior benign breast disease (N = 152), mammography abnormalities detected at screening (N = 144), family history of breast cancer (N = 234), patient anxiety (N = 13), other asymptomatic reasons (N = 83).</p> <p><i>The results are only reported for breasts as the unit of analysis, not patients: There were 3835 breasts examined in 2020 patients, with 129 malignancies found in 127 patients (2 bilateral breast cancers).</i></p> <p><u>Inclusion criteria:</u> "Between October 1, 1999, and August 1, 2000, all consecutive patients referred to our radiology department for diagnostic breast imaging underwent additional US after a CE [clinical examination] and MAM [mammography]" .</p> <p><u>Exclusion criteria:</u> When ultrasound could not be performed because of logistic reasons or when no informed consent was given.</p> <p><u>Clinical setting:</u> Unclear, the Netherlands</p>
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	Bilateral clinical performed while the patient was in standing and sitting positions, followed by mammography (standard craniocaudal and mediolateral oblique examination; Siemens Mammomat-2 unit/Kodak Min-R film screen combination) followed by whole-breast ultrasound (model ATL5000, 12.5-MHz linear array transducer; Philips Medical Systems, Best, the Netherlands) both scored on a scale from 1-5 with increasing suggestion of malignancy (1 and 2 defined as negative results and 3-5 defined as positive results). All examinations were performed and interpreted with full knowledge of prior test results.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Pathologic results of core needle biopsy, excision biopsy and other surgical interventions during a follow up of 12 months. An additional 2 months were added, accounting for administrative routing of test results at the end of the follow up period. Pathologic results were retrieved from the hospital pathology department and the Dutch Network and National Database for Pathology, to which all Dutch hospital pathology departments are linked. Breast cancer status was considered negative when non pathologic condition was reported in either system.

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	Of the 2720 scheduled imaging examinations, 112 were cancelled and 84 were excluded from the study due to earlier inclusion. 279 did not receive the additional ultrasound for logistical reasons, and 255 refused consent. The patients excluded from the study had a comparable prevalence of breast cancer, age distribution, reason for referral, and imaging interpretation.
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk
NOTES	

References

Included studies

Flobbe, K., Bosch, A. M., Kessels, A. G. H., Beets, G. L., Nelemans, P. J., Meyenfeldt, M. F. v. & Engelshoven, J. M. A. v. (2003) The additional diagnostic value of ultrasonography in the diagnosis of breast cancer. *Archives of Internal Medicine*, 163: 1194-1199.

Excluded studies (with excl reason)

(1983) New data may alter lymph node biopsy practices in early breast cancer. *Oncology (Williston Park, N, 17: 74, 83.*

Not in PICO

(1996) The management of primary breast cancer (Structured abstract). *Health Technology Assessment.Database.*, 16.

Not in PICO

(1998) Questions and answers on breast cancer. A guide for women and their physicians. Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. *CMAJ Canadian Medical Association Journal*, 158: Suppl-31.

Not in PICO

(1999) The early detection and diagnosis of breast cancer: a literature review - an update (Structured abstract). *Health Technology Assessment.Database.*

Duplicate of Hider (1999)

(1999) Directional, vacuum-assisted breast biopsy (Structured abstract). *Health Technology Assessment.Database.*, 18.

Not in PICO

- (2001) Advanced breast biopsy instrumentation (ABBI) system for non-palpable breast lesions (Structured abstract). *Health Technology Assessment.Database.*, 54.
Not in PICO
- (2003) Mammography can detect breast cancer early and save women's lives. *Ethnicity & Disease*, 13: 298.
Narrative review
- (2006) Sentinel lymph node biopsy in breast cancer (Structured abstract). *Health Technology Assessment.Database.*, 132.
Not in PICO
- (2010) [Third revision of the National Consensus on Diagnosis and Treatment of Breast Cancer (first of three parts)]. [Spanish]. *Ginecologia y Obstetricia de Mexico*, 78: 72-82.
Consensus guideline
- (2011) The breast density--breast cancer connection. Women whose breasts appear dense on mammograms have a higher risk for some aggressive breast cancers. *Harvard Women's Health Watch*, 19: 1-2.
Narrative review
- (2013) Technology assessment No. 9: Digital breast tomosynthesis. *Obstetrics & Gynecology*, 121: 1415-1417.
Narrative review
- Abbruzzese, J. L., Abbruzzese, M. C., Lenzi, R., Hess, K. R. & Raber, M. N. (1995) Analysis of a diagnostic strategy for patients with suspected tumors of unknown origin. *Journal of Clinical Oncology*, 13: 2094-2103.
Not in PICO
- Abdel-Fattah, M. M., Anwar, M. A., Mari, E., El-Shazly, M. K., Zaki, A. A., Bedwani, R. N. & Nicolucci, A. (1999) Patient- and system-related diagnostic delay in breast cancer: Evidence from Alexandria, Egypt. *European Journal of Public Health*, 9: 15-19.
Not in PICO
- Adler, D. D. (2012) Breast cancer: evaluating mammography in early diagnosis. [Review] [22 refs]. *Geriatrics*, 43: 51-55.
Narrative review
- Ahern, C. H. & Shen, Y. (2009) Cost-effectiveness analysis of mammography and clinical breast examination strategies: a comparison with current guidelines (Structured abstract). *Cancer Epidemiology, Biomarkers and Prevention.*, 18: 718-725.
Not in PICO (screening)
- Al, S. W., Salhab, M. & Mokbel, K. (2006) Does mammary ductoscopy have a role in clinical practice? *International Seminars in Surgical Oncology*, 3: 16.
Not in PICO
- Albert, U.-S. & Schulz, K.-D. (2004) Short version of the guideline: Early detection of breast cancer in Germany - An evidence-, consensus-, and outcome-based guideline according to the German association of the scientific medical societies (AWMF) and the German agency for quality in medicine (AeZQ). *Journal of Cancer Research and Clinical Oncology*, 130: 527-536.
Guideline
- Albert, U.-S., Altland, H., Duda, V., Engel, J., Geraedts, M., Heywang-Kobrunner, S., Holzel, D., Kalbheim, E., Koller, M., Konig, K., Kreienberg, R., Kuhn, T., Lebeau, A., Nass-Griegoleit, I., Schlake, W., Schmutzler, R., Schreer, I., Schulte, H., Schulz-Wendtland, R., Wagner, U. & Kopp, I. (2008) Summary of the updated stage 3 guideline for early detection of breast cancer in Germany 2008. [German]. *RoFo Fortschritte auf dem Gebiet der Rontgenstrahlen und der Bildgebenden Verfahren*, 180: 455-465.
Guideline
- Allgayer, B., Lukas, P., Loos, W. & Muhlbauer, K. (1991) [The accuracy of MRI diagnosis for the early detection of breast cancer in mammographic and clinically unclear cases. The diagnostic problem

- case]. [German]. *Rontgenpraxis*, 44: 368-371.
Not in PICO
- Alonso, J. C., Soriano, A., Zarca, M. A., Guerra, P., Alcazar, R. & Molino, C. (1997) Breast cancer detection with sestamibi-Tc-99m and Tl-201 radionuclides in patients with non conclusive mammography. *Anticancer Research*, 17: 1661-1665.
Not in PICO
- Amri, A., Saidane, A. & Pulko, S. (2011) Thermal analysis of a three-dimensional breast model with embedded tumour using the transmission line matrix (TLM) method. *Computers in Biology & Medicine*, 41: 76-86.
Not in PICO
- Andersen, M. R., Urban, N. & Etzioni, R. (1999) Community attitudes and mammography use: does it really matter what other people think? *Women & Health*, 29: 83-95.
Not in PICO
- Andreou, D. & Tunn, P. U. (2009) Sentinel node biopsy in soft tissue sarcoma. [Review] [65 refs]. *Recent Results in Cancer Research*, 179: 25-36.
Not in PICO
- Armstrong, A. C. & Evans, G. D. (2014) - Management of women at high risk of breast cancer. [Review]. - *BMJ*, 348: g2756.
Narrative review
- Aubry, C., Martin, E., Fournier, B., Guillemin, F., Longis, M. J., Monneau, J. P. & Deschamps, J. P. (1991) Early detection of breast cancer remains insufficient. A study of breast surveillance in women aged over 50 in the Lorraine-Champagne region. [French]. *Journal de Gynecologie Obstetrique et Biologie de la Reproduction*, 20: 775-782.
Not in PICO
- Auguste, P., Barton, P., Hyde, C. & Roberts, T. E. (2001) An economic evaluation of positron emission tomography (PET) and positron emission tomography/computed tomography (PET/CT) for the diagnosis of breast cancer recurrence. [Review]. *Health Technology Assessment (Winchester, England)*, 15: iii-iv.
Not in PICO
- Bach, K., Strandberg, C., Bitsch, K. & Brunner, S. (1990) Why and by whom are patients referred for mammography? *Recent Results in Cancer Research*, 119: 122-126.
Not in PICO
- Badowski, A., Zaras, T. & Stawiarczyk, S. (1989) [Early (minimal) breast cancer and possibilities of its detection]. [Polish]. *Wiadomosci Lekarskie*, 42: 622-631.
Narrative review
- Baek, S. E., Kim, M. J., Kim, E. K., Youk, J. H., Lee, H. J. & Son, E. J. (2009) Effect of clinical information on diagnostic performance in breast sonography. *Journal of Ultrasound in Medicine*, 28: 1349-1356.
Not in PICO
- Banks, A. L., Titus, R. & Melnik, M. (2013) Detection of new or additional significant breast disease by MRI compared to standard imaging in "high-risk" and "non-high-risk" patients. *Journal of Clinical Oncology*, 31.
Not in PICO
- Bansal, S., Sahoo, B., Agarwal, P., Garg, V. & Rao, S. (2013) A rare presentation of mammary Paget's disease involving the entire breast in the absence of any underlying ductal malignancy. *Indian Journal of Dermatology, Venereology and Leprology*, 79: 518-521.
Not in PICO
- Barentsz, M. W., Wessels, H., Van Diest, P. J., Pijnappel, R. M., Van Der Pol, C. C., Witkamp, A. J., Van Den Bosch, M. A. A. J. & Verkooijen, H. M. (2014) Same-day diagnosis based on histology for women suspected of breast cancer: High diagnostic accuracy and favorable impact on the

patient. *PLoS ONE*, 9.

Not in PICO

Barentsz, M. W., Wessels, H., Van Diest, P. J., Pijnappel, R. M., Van Der Pol, C. C., Witkamp, A. J., van den Bosch, M. A. & Verkooijen, H. M. (2014) - Same-day diagnosis based on histology for women suspected of breast cancer: high diagnostic accuracy and favorable impact on the patient. - *PLoS ONE [Electronic Resource]*, 9: e103105.

Duplicate

Barnes, N. L., Dimopoulos, N., Williams, K. E., Howe, M. & Bundred, N. J. (2014) - The frequency of presentation and clinico-pathological characteristics of symptomatic versus screen detected ductal carcinoma in situ of the breast. - *European Journal of Surgical Oncology*, 40: 249-254.

Not in PICO

Barreto, V., Hamed, H., Griffiths, A. B., Hanby, A., Chaudary, M. A. & Fentiman, I. S. (1991) Automatic needle biopsy in the diagnosis of early breast cancer. *European Journal of Surgical Oncology*, 17: 237-239.

Not in PICO

Barton, M. B., Harris, R. & Fletcher, S. W. (1999) Does this patient have breast cancer? The screening clinical breast examination: should it be done? How? (DARE structured abstract). *JAMA*, 282: 1270-1280.

Not in PICO

Bassett, A. A. (1999) Guide for the management of breast lumps: Litigious aspects. *Canadian Journal of Surgery*, 42: 166.

Narrative review

Bastani, R., Mojica, C. M., Berman, B. A. & Ganz, P. A. (2010) Low-income women with abnormal breast findings: results of a randomized trial to increase rates of diagnostic resolution. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*, 19: 1927-1936.

Not in PICO

Bays, J. K. (1992) Physical and mammographic diagnosis of breast cancer and initial work-up. *Journal of the American Medical Womens Association*, 47: 158-160.

Narrative review

Bazhutova, G. A., Iagel'skij, V. P., Anan'eva, N. A., Kishkineva, T. S., Tamrazova, L. I., Martynova, N. V. & Miroshnichenko, I. V. (2004) A cytological study as a part of integrated examinations of patients with the mammary gland pathologies in the ambulatory and clinical settings. [Russian]. *Klinicheskaja Laboratornaia Diagnostika*, 37-38.

Not in PICO (secondary care)

Bazhutova, G. A., Efimenko, I., Kishkineva, T. S., Martynova, N. V. & Zorenko, E. A. (2005) [Nonpalpable breast masses: outpatient diagnostic methods]. [Russian]. *Klinicheskaja Laboratornaia Diagnostika*.(11):15-6, 2005 Nov., 15-16.

In Russian, not enough information can be extracted to ascertain relevance, but I think it is not in PICO

Bellucci, M. C. & Panzarola, P. (1990) [Preoperative localization using a bidimensional mammographic technique of non-palpable lesions of the breast]. [Italian]. *Radiologia Medica*, 80: 89-92.

Not in PICO

Beran, L., Liang, W., Nims, T., Paquelet, J. & Sickle-Santanello, B. (2005) Correlation of targeted ultrasound with magnetic resonance imaging abnormalities of the breast. *American Journal of Surgery*, 190: 592-594.

Not in PICO

Berg, W. A., Blume, J. D., Cormack, J. B. & Mendelson, E. B. (2012) Training the ACRIN 6666 Investigators and effects of feedback on breast ultrasound interpretive performance and agreement in BI-RADS ultrasound feature analysis. *AJR.American Journal of Roentgenology*, 199:

- 224-235.
Not in PICO
- Berghammer, P., Obwegeser, R. & Sinzinger, H. (2001) Nuclear medicine and breast cancer: a review of current strategies and novel therapies. *Breast*, 10: 184-197.
Narrative review
- Berlin, L. (2011) Should a radiologist be a referring physician? *AJR.American Journal of Roentgenology*, 196: W349.
Not in PICO
- Bick, U., Engelken, F., Diederichs, G., Dzyuballa, R., Ortmann, M. & Fallenberg, E. M. (2013) MRI of the breast as part of the assessment in population-based mammography screening. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 185: 849-856.
Not in PICO
- Bilali, M., Lagoudianakis, E. E., Peitsidis, P., Grosomanidis, D., Papadima, A., Koronakis, N., Chrysikos, J., Tsekouras, D., Nakos, S., Katergiannakis, V. & Manouras, A. (2009) The role of sonography in the diagnosis of cystic lesions of the breast. *European Journal of Gynaecological Oncology*, 30: 506-508.
Not in PICO (secondary care)
- Bilous, M., Brennan, M., French, J. & Boyages, J. (2005) Making sense of breast pathology. *Australian Family Physician*, 34: 581-586.
Narrative review
- Bland, K. I. & Love, N. (101) Evaluation of common breast masses. *Postgraduate Medicine*, 92: 95-97.
Narrative review
- Blichert-Toft, M., Dyreborg, U., Bogh, L. & Kiaer, H. (1982) Nonpalpable breast lesions: Mammographic wire-guided biopsy and radiologic-histologic correlation. *World Journal of Surgery*, 6: 119-125.
Not in PICO
- Blichert-Toft, M., Dyreborg, U. & Andersen, J. (1988) Diagnostic strategy in the management of patients with breast symptoms. A recommended design and present experience. *Acta Oncologica*, 27: 597-600.
Not in PICO
- Bliznakova, K. (2012) Application of synchrotron radiation in Mammography. *Recent Patents on Medical Imaging*, 2: 94-110.
Narrative review
- Boba, M., Koltun, U., Bobek-Billewicz, B., Chmielik, E., Eksner, B. & Olejnik, T. (2011) False-negative results of breast core needle biopsies - retrospective analysis of 988 biopsies. *Polish Journal of Radiology*, 76: 25-29.
Not in PICO
- Bock, K., Hadji, P., Duda, V. F., Jackisch, C. & Wagner, U. (2005) [Mammographic breast density and breast cancer risk during HRT]. [Review] [33 refs] [German]. *Zentralblatt fur Gynakologie*, 127: 217-221.
Narrative review
- Boisserie-Lacroix, M., Dos, S. E., Bouzgarrou, M., El-Ferzli, J., Nivault, C., Cangini, A., Kerioui, N., Belleannee, G. & Trillaud, H. (2001) Contribution of imaging and management of inflammatory breast cancer. [French]. *Sein*, 11: 107-117.
Narrative review
- Boisserie-Lacroix, M., Mac, G. G., Debled, M., Ferron, S., Asad-Syed, M., Brouste, V., Mathoulin-Pelissier, S. & Hurtevent-Labrot, G. (2012) Radiological features of triple-negative breast cancers (73 cases). *Diagnostic and Interventional Imaging*, 93: 183-190.
Not in PICO
- Bonazzi, G., Cistaro, A., Bello, M., Bessone, M., Tetti, M., Villata, E., Coluccia, C., Ardine, M., Moz, G., Massaioli, N. & Bisi, G. (2001) Breast cancer cellular proliferation indexes and 99mTc-sesta Mibi

- capture: what correlation? *Journal of Experimental & Clinical Cancer Research*, 20: 91-94.
Not in PICO
- Borchard-Tuch, C. (2007) Early detection of cancer: Effectiveness of current tests. [German]. *Pharmazeutische Zeitung*, 152: 18-25.
Narrative review
- Brandon, C. J. & Mullan, P. B. (2011) Patients' perception of care during image-guided breast biopsy in a rural community breast center: communication matters. *Journal of Cancer Education*, 26: 156-160.
Not in PICO
- Braverman, A. S. (2010) The Role of the Primary Care Physician in the Prevention, Diagnosis and Treatment of Breast Cancer: Contemporary Knowledge and Controversies. *Southern Medical Journal*, 103: 287-288.
Narrative review
- Britton, P. & Sinnatamby, R. (2007) Investigation of suspected breast cancer. [Review] [9 refs]. *BMJ*, 335: 347-348.
Narrative review
- Britton, P., Duffy, S. W., Sinnatamby, R., Wallis, M. G., Barter, S., Gaskarth, M., O'Neill, A., Caldas, C., Brenton, J. D., Forouhi, P. & Wishart, G. C. (2009) One-stop diagnostic breast clinics: How often are breast cancers missed. *British Journal of Cancer*, 100: 1873-1878.
Not in PICO
- Brown, H. G. (1991) The messages primary care physicians should convey to their patients about mammography. *Womens Health Issues*, 1: 74-77.
Narrative review
- Bruening, W., Fontanarosa, J., Tipton, K., Treadwell, J. R., Launder, J. & Schoelles, K. (2009) Systematic review: comparative effectiveness of core-needle and open surgical biopsy to diagnose breast lesions (DARE structured abstract). *Annals of Internal Medicine*, 152: 238-246.
Not in PICO
- Bukharin, D. G., Velichko, S. A., Slonimskaja, E. M., Frolova, I. G., Luneva, S. V., Garbukov, E. I. & Doroshenko, A. V. (2011) [Specific features of mammographic visualization of "small" breast tumors developing on the background of fibrocystic disease]. [Russian]. *Voprosy Onkologii*, 57: 664-667.
Not in PICO
- Burack, R. C., Gimotty, P. A., Stengle, W., Warbasse, L. & Moncrease, A. Patterns of use of mammography among inner-city Detroit women: Contrasts between a health department, HMO, and private hospital. *Medical Care* 31[4], 322-334. 1993.
Not in PICO
- Buscombe, J., Paganelli, G., Burak, Z. E., Waddington, W., Maublant, J., Prats, E., Palmedo, H., Schillaci, O., Maffioli, L., Lassmann, M., Chiesa, C., Bombardieri, E., Chiti, A. & European Association of Nuclear Medicine Oncology Committee and Dosimetry Committee (2007) Sentinel node in breast cancer procedural guidelines. *European Journal of Nuclear Medicine & Molecular Imaging*, 34: 2154-2159.
Not in PICO
- Cady, B., Steele, G. D., Morrow, M., Gardner, B., Smith, B. L., Lee, N. C., Lawson, H. W. & Winchester, D. P. (1998) Evaluation of common breast problems: Guidance for primary care providers. *Ca-A Cancer Journal for Clinicians*, 48: 49-+.
Narrative review
- Cai, L. S., Zhang, J. X., Song, G. H., Chen, L. & Dai, J. L. (2013) [Value of contrast-enhanced sonography in early diagnosis of breast cancer]. [Chinese]. *Nan Fang Yi Ke Da Xue Xue Bao = Journal of Southern Medical University*, 33: 1801-1805.
Not in PICO

- Caldarella, C., Treglia, G. & Giordano, A. (2014) Diagnostic performance of dedicated positron emission mammography using fluorine-18-fluorodeoxyglucose in women with suspicious breast lesions: A meta-analysis. *Clinical Breast Cancer*, 14: 241-248.
Not in PICO
- Calvo-Plaza, I., Ugidos, L., Miro, C., Quevedo, P., Parras, M., Marquez, C., de la Cruz, J. J., Suarez-Gauthier, A., Perez, F. J., Herrero, M., Marcos, M., Garcia-Aranda, M., Hidalgo, M. & Estevez, L. G. (2013) Retrospective study assessing the role of MRI in the diagnostic procedures for early breast carcinoma: a correlation of new foci in the MRI with tumor pathological features. *Clinical & Translational Oncology: Official Publication of the Federation of Spanish Oncology Societies & of the National Cancer Institute of Mexico*, 15: 205-210.
Not in PICO
- Capasso, I., Esposito, E., Montella, M., Crispo, A., Grimaldi, M., D'Aiuto, M., Beneduce, G., Esposito, G. & D'Aiuto, G. (2009) Gail's model as first step for early diagnosis: National Cancer Institute of Naples experience. *Breast Cancer Research*, 11: S10.
Abstract only. Not enough information can be extracted to ascertain relevance, but I think it is not in PICO.
- Carney, P. A., Parikh, J., Sickles, E. A., Feig, S. A., Monsees, B., Bassett, L. W., Smith, R. A., Rosenberg, R., Ichikawa, L., Wallace, J., Tran, K. & Miglioretti, D. L. (2013) Diagnostic mammography: identifying minimally acceptable interpretive performance criteria. *Radiology*, 267: 359-367.
Not in PICO
- Carter, T. I. & Reilly, J. J. (2012) Missed opportunities: clinical antecedents in the diagnosis of advanced breast cancer. *Annals of Surgical Oncology*, 19: 2782-2785.
Not in PICO
- Carvalho, S. M. T., Netto, M. M., Lima, E. N. P., Pimentel, A. M., Makdissi, F. B., Osorio, C. A. B. T., Maciel, M. S., Iyeyasu, H., Collins, J. B., Fontes, C. M., Perina, A. L. & Soares, F. A. Sentinel node biopsy in breast cancer: Results in a large series. [References]. *Brazilian Journal of Medical and Biological Research* 43[6], 593-599. 2010.
Not in PICO
- Caseldine, J. (1988) The radiographer's role in an early detection programme for breast cancer. *Radiography Today*, 54: 36-37.
Narrative review
- Cederblom, S. (1988) [Mammography is the supreme method for early diagnosis of breast cancer]. [Swedish]. *Lakartidningen*, 85: 3928.
Narrative review
- Celi, S., Di, P. F. & Forte, P. (2011) Advances in finite element simulations of elastosonography for breast lesion detection. *Journal of Biomechanical Engineering*, 133: 081006.
Narrative review
- Chae, E. Y., Cha, J. H., Kim, H. H., Shin, H. J., Kim, H. J., Oh, H. Y., Koh, Y. H. & Moon, D. H. (2012) Analysis of incidental focal hypermetabolic uptake in the breast as detected by 18F-FDG PET/CT: clinical significance and differential diagnosis. *Acta Radiologica*, 53: 530-535.
Not in PICO
- Chalabian, J. & Dunnington, G. (1998) Do our current assessments assure competency in clinical breast evaluation skills? *American Journal of Surgery*, 175: 497-502.
Not in PICO
- Challa, V. R., Seenu, V., Srivastava, A., Kumar, R., Dhar, A., Chumber, S., Parshad, R. & Misra, M. C. (2010) Sentinel lymph node mapping in early breast cancer - Our experience. *Indian Journal of Surgical Oncology*, 1: 52-58.
Not in PICO
- Chapman, C., Murray, A., Chakrabarti, J., Thorpe, A., Woolston, C., Sahin, U., Barnes, A. & Robertson, J. (2007) Autoantibodies in breast cancer: their use as an aid to early diagnosis. *Annals of*

- Oncology*, 18: 868-873.
Not in PICO
- Chapman, D., Cox, E., Britton, P. D. & Wishart, G. C. (2009) Patient-led breast cancer follow up. *Breast*, 18: 100-102.
Not in PICO
- Chargari, C., Kirova, Y., Bollet, M., Sigal-Zafrani, B., Dendale, R., Rizand, P., de la Rochefordiere, A., Fourquet, A. & Campana, F. (2008) [Shared responsibility for follow-up of breast cancer patients. Experience of the Institut Curie]. [French]. *Bulletin du Cancer*, 95: 1047-1051.
Not in PICO
- Chen, C.-Y., Fu, J.-M., Yuan, Y., Yu, R., Jiang, H.-B. & Li, S.-L. (2013) Analysis of image features of breast mucinous carcinoma. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 29: 411-414.
Not in PICO
- Chen, M., Palleschi, S., Khoynezhad, A., Gecelter, G., Marini, C. P. & Simms, H. H. (2002) Role of primary breast cancer characteristics in predicting positive sentinel lymph node biopsy results - A multivariate analysis. *Archives of Surgery*, 137: 606-609.
Not in PICO
- Chen, Q., Wang, W. & Zhou, L. (2008) Value of diffuse optical imaging with ultrasound localization in distinguishing benign breast lesions from malignant ones. [Chinese]. *Chinese Journal of Clinical Oncology*, 35: 1223-1225.
Not in PICO
- Chen, S. H., Ma, Q. H., Li, Z. J. & Hu, C. W. (2007) [Diagnosis of breast diseases by mammography in combination with MRI]. [Chinese]. *Zhongguo Yiliao Qixie Zazhi*, 31: 216-218.
Not in PICO
- Cheng, Y. S., Zhou, Z. R., Yang, W. T., Peng, W. J. & Chen, J. (2012) [Neuroendocrine carcinoma of the breast: mammographic features correlated with sonography and histopathological findings]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 34: 917-922.
Not in PICO
- Cheung, K. L., Wong, A. W. S., Parker, H., Li, V. W. Y., Winterbottom, L., Morgan, D. A. L. & Ellis, I. O. (2008) Pathological features of primary breast cancer in the elderly based on needle core biopsies-A large series from a single centre. *Critical Reviews in Oncology/Hematology*, 67: 263-267.
Not in PICO
- Choi, Y. D., Gong, G. Y., Kim, M. J., Lee, J. S., Nam, J. H., Juhng, S. W. & Choi, C. (2006) Clinical and cytologic features of papillary neoplasms of the breast. *Acta Cytologica*, 50: 35-40.
Not in PICO
- Chow, H. T., Tran, K., Millar, E. K., Lynch, J. & Murrell, D. F. (2012) Diverse presentations of carcinoma erysipelatoides from a teaching hospital in australia. *Case Reports in Dermatological Medicine*, 2012: 134938.
Not in PICO
- Chuo, C. B. & Corder, A. P. (2003) Core biopsy vs fine needle aspiration cytology in a symptomatic breast clinic. *European Journal of Surgical Oncology*, 29: 374-378.
Not in PICO
- Ciatto, S., Rosselli Del, T. M. & Bravetti, P. (1989) Nonpalpable breast lesions: stereotaxic fine-needle aspiration cytology. *Radiology*, 173: 57-59.
Not in PICO
- Ciatto, S. & Brancato, B. (2005) Role of multimodal diagnosis of breast cancer in women below 36 year of age. *Radiologia Medica*, 109: 321-329.
Not in PICO
- Cid, J. A., Rampaul, R. S., Ellis, I. O., Wilson, A. R. M., Burrell, H. C., Evans, A. J., Blamey, R. W. & MacMillan, R. D. (2004) Woman feels breast lump - Surgeon cannot: The role of ultrasound in

- arbitration. *European Journal of Cancer*, 40: 2053-2055.
Not in PICO
- Clarke, D., Sudhakaran, N. & Gateley, C. A. (2001) Replace fine needle aspiration cytology with automated core biopsy in the triple assessment of breast cancer. *Annals of the Royal College of Surgeons of England*, 83: 110-112.
Not in PICO
- Cole, K., Tabernero, M. & Anderson, K. S. (2010) Biologic characteristics of premalignant breast disease. *Cancer Biomarkers: Section A of Disease Markers*, 9: 177-192.
Narrative review
- Colin, C. (1996) Hierarchy of breast examinations after twenty years experience. [French]. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction*, 25: 439-444.
Not in PICO
- Collins, C. D. (2008) The sentinel node in breast cancer. *Cancer Imaging*, 8: S10-S18.
Not in PICO
- Conrad, C. & Vejborg, I. (2007) [Diagnostic imaging of breast cancer]. [Review] [10 refs] [Danish]. *Ugeskrift for Laeger*, 169: 2982-2985.
Narrative review
- Corsetti, V., Ferrari, A., Ghirardi, M., Bergonzini, R., Bellarosa, S., Angelini, O., Bani, C. & Ciatto, S. (2006) Role of ultrasonography in detecting mammographically occult breast carcinoma in women with dense breasts (Structured abstract). *Radiologia Medica*, 111: 440-448.
Not in PICO
- Corsetti, V., Houssami, N., Ferrari, A., Ghirardi, M., Bellarosa, S., Angelini, O., Bani, C., Sardo, P., Remida, G., Galligioni, E. & Ciatto, S. (2008) Breast screening with ultrasound in women with mammography-negative dense breasts: evidence on incremental cancer detection and false positives, and associated cost (Structured abstract). *European Journal of Cancer*, 44: 539-544.
Not in PICO
- Costantini, M., Cipriani, A., Belli, P., Bufi, E., Fubelli, R., Visconti, G., Salgarello, M. & Bonomo, L. (2013) Radiological findings in mammary autologous fat injections: a multi-technique evaluation. *Clinical Radiology*, 68: 27-33.
Not in PICO
- Cregan, P. C., Parer, J. G. & Power, A. R. (2010) Accuracy of mammography in an Australian community setting. *Medical Journal of Australia*, 193: 408.
Not in PICO
- Cressa, C., Gozzi, G., Tonutti, M., Macorig, D. & Tessa, I. (1994) [The diagnostic contribution of direct radiographic enlargement and of echography in the study of breast neoplasms]. [Italian]. *Radiologia Medica*, 87: 405-411.
Not in PICO
- Crivello, M. L., Ruth, K., Sigurdson, E. R., Egleston, B. L., Wong, Y., Boraas, M. & Bleicher, R. J. (2012) Advanced imaging modalities in early stage breast cancer: Preoperative use in the united states medicare patient. *Annals of Surgical Oncology*, 19: S12-S13.
Not in PICO
- Cuk, M., Gajanin, R., Malis, M., Eric, D., Lalovic, N. & Maric, H. (2013) [The importance of cytology in diagnosing rare breast carcinoma--two case reports]. [Serbian]. *Medicinski Pregled*, 66: 86-91.
Not in PICO
- Cwikla, J. B., Buscombe, J. R., Parbhoo, S. P., Kelleher, S. M., Thakrar, D. S., Hinton, J., Crow, J., Deery, A. & Hilson, A. J. (1998) Use of ⁹⁹Tcm-MIBI in the assessment of patients with suspected recurrent breast cancer. *Nuclear Medicine Communications*, 19: 649-655.
Not in PICO
- Cwikla, J. B., Buscombe, J. R. & Hilson, A. J. (2000) Detection of DCIS using ^{99m}Tc-MIBI scintimammography in patients with suspected primary breast cancer, comparison with

- conventional mammography. *Nuclear Medicine Review*, 3: 41-45.
Not in PICO
- D'Orsi, C. J. (1991) Early detection of breast cancer: mammography. [Review] [16 refs]. *Breast Cancer Research & Treatment*, 18: Suppl-9.
Narrative review
- Dambrosio, F. (1989) [The problem: early clinical diagnosis of cancer of the breast]. [Review] [70 refs] [Italian]. *Annali di Ostetricia, Ginecologia, Medicina Perinatale.Spec No:1-16, 1989.*, 1-16.
Narrative review
- Das, B. K., Biswal, B. M. & Bhavaraju, M. (2006) Role of scintimammography in the diagnosis of breast cancer. *The Malaysian Journal of Medical Science*, 13: 52-57.
Narrative review
- Dawson, C., Lancashire, M. J., Reece-Smith, H. & Faber, R. G. (1993) Breast disease and the general surgeon. 1. Referral of patients with breast problems. *Annals of the Royal College of Surgeons of England*, 75: 79-82.
Not in PICO
- de Waal, J. C., Baltzer, J., Muthmann-Nagy, C., Schmid, M. & Zander, J. (1987) [Value of palpation and mammography in primary breast cancer. A retrospective study 1973-1982]. [German]. *Geburtshilfe und Frauenheilkunde*, 47: 93-95.
Not in PICO
- Debnath, D., Taribagil, S., Al-Janabi, K. J. & Inwang, R. (2012) A large epidermoid cyst of breast mimicking carcinoma: A case report and review of literature. *International Journal of Surgery Case Reports*, 3: 437-440.
Not in PICO
- Deck, W. (2006) Vacuum-assisted breast biopsy (Structured abstract). *Health Technology Assessment.Database.*, 38.
Not in PICO
- Degrell, I. (1982) Aspiration cytology of breast carcinoma. *Acta Morphologica Academiae Scientiarum Hungaricae*, 30: 277-288.
Narrative review
- Deibl, A. K. (1982) The most efficient method for early detection of mammary carcinoma. [German]. *Monatskurse fur die Arztliche Fortbildung*, 32: 13-29.
Narrative review
- Demidov, V. P., Bazhenova, A. P., Ostrovstev, L. D., Barvitenko, P. G. & Kas'ianova, I. V. (1983) [Methods of early detection of breast cancer]. [Russian]. *Sovetskaia Meditsina.(12):14-8, 1983.*, 14-18.
Not in PICO (screening)
- den Outer, A. J., Pauwels, E. K., Zwaveling, A., Puylaert, J. B., Hermans, J. & De Lange, E. E. (1986) Breast scintigraphy with ^{99m}Tc-diethylene triamine penta-acetic acid for the detection of malignant disease. *British Journal of Surgery*, 73: 613-614.
Not in PICO
- Dey, P., Bundred, N., Gibbs, A., Hopwood, P., Baildam, A., Boggis, C., James, M., Knox, F., Leidecker, V. & Woodman, C. (2002) Costs and benefits of a one stop clinic compared with a dedicated breast clinic: randomised controlled trial. *BMJ*, 324: 507.
Not in PICO
- Dhawan, A. P., Buelloni, G. & Gordon, R. (1986) Enhancement of mammographic features by optimal adaptive neighborhood image processing. *IEEE Transactions on Medical Imaging*, 5: 8-15.
Not in PICO
- Dheeba, J. & Selvi, S. T. (2012) A swarm optimized neural network system for classification of microcalcification in mammograms. *Journal of Medical Systems*, 36: 3051-3061.
Not in PICO

- Di, M. C., La, G. M., Pescarini, L., Attanazio, A. & Lattanzio, E. (1995) A good use of cytology and needle core-biopsy of breast diseases in current medical practice: Lesions characterized by mammographic mixed signal. [French]. *Sein*, 5: 155-158.
Narrative review
- Dingari, N. C., Barman, I., Saha, A., McGee, S., Galindo, L. H., Liu, W., Plecha, D., Klein, N., Dasari, R. R. & Fitzmaurice, M. (2013) Development and comparative assessment of Raman spectroscopic classification algorithms for lesion discrimination in stereotactic breast biopsies with microcalcifications. *Journal of Biophotonics*, 6: 371-381.
Not in PICO
- Dinkelspiel, E., Chu, P. & Smith-Bindman, R. (2008) Access to diagnostic mammography in the San Francisco bay area. *Journal of Women's Health*, 17: 893-899.
Not in PICO
- Dixon, J. M. & Mansel, R. E. (1994) ABC of breast diseases. Symptoms assessment and guidelines for referral. [Review] [0 refs]. *BMJ*, 309: 722-726.
Narrative review
- Dodd, L. G. & Layfield, L. J. (1996) Fine-needle aspiration of inflammatory carcinoma of the breast. *Diagnostic Cytopathology*, 15: 363-366.
Not in PICO
- Donovan, A. J. (1990) Bilateral breast cancer. [Review] [14 refs]. *Surgical Clinics of North America*, 70: 1141-1149.
Narrative review
- Dorrius, M. D., Pijnappel, R. M. & Oudkerk, M. (2009) Breast magnetic resonance imaging as a problem-solving modality? *Imaging Decisions MRI*, 13: 126-129.
Narrative review
- dos Santos, G. D. & Chubaci, R. Y. (2011) [Awareness about breast cancer and mammography in elderly women who frequent Daycare Centers in Sao Paulo (SP, Brazil)]. [Portuguese]. *Ciencia & Saude Coletiva*, 16: 2533-2540.
Not in PICO
- Doubeni, C. A., Field, T. S., Yood, M. U., Rolnick, S. J., Quessenberry, C. P., Fouayzi, H., Gurwitz, J. H. & Wei, F. (2006) Patterns and predictors of mammography utilization among breast cancer survivors. *Cancer*, 106: 2482-2488.
Not in PICO
- Doyle, A. J., King, A. R., Miller, M. V. & Collins, J. P. (1998) Implementation of image-guided large-core needle biopsy of the breast on a limited budget. *Australasian Radiology*, 42: 199-203.
Not in PICO
- Doyle, S., Messiou, C., Rutherford, J. M. & Dineen, R. A. (2009) Cancer presenting during pregnancy: radiological perspectives. [Review] [109 refs]. *Clinical Radiology*, 64: 857-871.
Narrative review
- Drukteinis, J. S., Gombos, E. C., Raza, S., Chikarmane, S. A., Swami, A. & Birdwell, R. L. (2012) MR imaging assessment of the breast after breast conservation therapy: distinguishing benign from malignant lesions. *Radiographics*, 32: 219-234.
Not in PICO
- Du Toit, R. S., Locker, A. P., Ellis, I. O., Elston, C. W. & Blamey, R. W. (1990) Evaluation of the prognostic value of triple node biopsy in early breast cancer. *British Journal of Surgery*, 77: 163-167.
Not in PICO
- Duijm, L., Guit, G. L., Zaat, J. O. M., Koomen, A. R. & Willebrand, D. (1997) Sensitivity, specificity and predictive values of breast imaging in the detection of cancer. *British Journal of Cancer*, 76: 377-381.
N = 3014, of whom 1931 received mammography only, 996 received mammography + US, and 87

- received US only, but results only reported for them all irrespective of which test they received, thus results cannot be split by test.
- Durante, E. (1980) [Early diagnosis of breast tumors:/is echography conclusive?]. [Italian]. *Minerva Chirurgica*, 35: 989-992.
Narrative review
- Dymarskii, L. I., Chernomordikova, M. F., Semiglazov, V. F. & Popova, R. T. (1983) [Early diagnosis of breast carcinoma by mammographic demonstration of nonpalpable tumors]. [German]. *Radiologia Diagnostica*, 24: 181-187.
Not in PICO
- Ekeh, A. P., Alleyne, R. S. & Duncan, A. O. (2000) Role of mammography in diagnosis of breast cancer in an inner-city hospital. *Journal of the National Medical Association*, 92: 372-374.
Not in PICO
- Eklund, G. W. & Cardenosa, G. (1992) The art of mammographic positioning. [Review] [18 refs]. *Radiologic Clinics of North America*, 30: 21-53.
Narrative review
- el-Kwae, E. A., Fishman, J. E., Bianchi, M. J., Pattany, P. M. & Kabuka, M. R. (1998) Detection of suspected malignant patterns in three-dimensional magnetic resonance breast images. *Journal of Digital Imaging*, 11: 83-93.
Not in PICO
- El-Zaart, A. (2010) Expectation-maximization technique for fibro-glandular discs detection in mammography images. *Computers in Biology and Medicine*, 40: 392-401.
Not in PICO
- Ell, K., Vourlekis, B., Lee, P. J. & Xie, B. (2007) Patient navigation and case management following an abnormal mammogram: a randomized clinical trial. *Preventive Medicine*, 44: 26-33.
Not in PICO
- Eltahir, A., Jibril, J. A., Squair, J., Heys, S. D., Ah-See, A. K., Needham, G., Gilbert, F. J., Deans, H. E., Mckean, M. E., Smart, L. M. & Eremin, O. (1999) The accuracy of 'one-stop' diagnosis for 1110 patients presenting to a symptomatic breast clinic. *Journal of the Royal College of Surgeons of Edinburgh*, 44: 226-230.
Not in PICO
- Endo, T. (1996) Mammographic diagnosis of breast cancer. [Review] [10 refs]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 23: Suppl-13.
Narrative review
- Engel, J., Baumert, J., Dirschedl, P., Sauer, H. & Holzel, D. (2000) Effectiveness of self-examination, palpation, and mammography for the early detection of breast cancer: First results of the Munich Field Study. [German]. *Geburtshilfe und Frauenheilkunde*, 60: 155-164.
Not in PICO
- English, R., Li, J., Parker, A. J. C., Roskell, D., Adams, R. F., Parulekar, V., Baldwin, J., Chi, Y. & Noble, J. A. (2011) A pilot study to evaluate assisted freehand ultrasound elasticity imaging in the sizing of early breast cancer: A comparison of B-mode and AFUSON elasticity ultrasound with histopathology measurements. *British Journal of Radiology*, 84: 1011-1019.
Not in PICO
- Ermilov, S. A., Khamapirad, T., Conjusteau, A., Leonard, M. H., Lacewell, R., Mehta, K., Miller, T. & Oraevsky, A. A. (2009) Laser optoacoustic imaging system for detection of breast cancer. *Journal of Biomedical Optics*, 14: 024007-024Apr.
Not in PICO
- Esber, H. J., Ceccacci, L. & Rosenkrantz, H. (1985) Comparative usefulness of cytology and peroxidase activity in conjunction with carcinoembryonic antigen levels for the diagnosis of mammary cancer. *Life Sciences*, 36: 1445-1449.
Not in PICO

- Eulenburg, R. & Lauth, G. (1986) [Improvement in the early detection of breast cancer by thermography]. [German]. *Rontgen-Blatter*, 39: 60-62.
Narrative review
- Eulenburg, R. & Lauth, G. (1986) Improved early detection of cancer of the breast via mammography. [German]. *Rontgen-Blatter*, 39: 60-62.
Narrative review
- Evans, W. P. (1995) Breast masses: Appropriate evaluation. *Radiologic Clinics of North America*, 33: 1085-1108.
Narrative review
- Evers, D. J., Nachabe, R., Vranken Peeters, M. J., van der Hage, J. A., Oldenburg, H. S., Rutgers, E. J., Lucassen, G. W., Hendriks, B. H., Wesseling, J. & Ruers, T. J. (2013) Diffuse reflectance spectroscopy: towards clinical application in breast cancer. *Breast Cancer Research & Treatment*, 137: 155-165.
Not in PICO
- Fayanju, O. M., Jeffe, D. B., Elmore, L., Ksiazek, D. N. & Margenthaler, J. A. (2013) Patient and process factors associated with late-stage breast cancer diagnosis in Safety-Net patients: a pilot prospective study. *Annals of Surgical Oncology*, 20: 723-732.
Not in PICO
- Feig, S. A. (1992) Breast masses. Mammographic and sonographic evaluation. [Review] [85 refs]. *Radiologic Clinics of North America*, 30: 67-92.
Narrative review
- Ferchichi, I., Sassi, H. S., Baccar, A., Marrakchi, T. R., Cremet, J. Y., Ben, R. K., Prigent, C. & Ben Ammar El, G. A. (2013) Assessment of Aurora A kinase expression in breast cancer: A tool for early diagnosis? *Disease Markers*, 34: 63-69.
Not in PICO
- Ferrari, G., Pazzaglia, M., Preite, M., Veronese, E. & Meneghelli, R. (1987) [Malignant tumors of the breast: instrumental diagnosis]. [Review] [7 refs] [Italian]. *Chirurgia Italiana*, 39: 423-428.
Narrative review
- Fischer, U. (798) [X-ray mammography : calcifications, masses and architectural distortions]. [Review] [8 refs] [German]. *Radiologe*, 48: 785-797.
Narrative review
- Fischer, U. & Liersch, T. (2002) Update ranking of X-ray mammography, sonography, and MR mammography in the detection of pre-invasive/invasive malignomas of the female breast. [German]. *Viszeralchirurgie*, 37: 99-105.
Narrative review
- Fisher, T., Redman, S. & Bollen, M. (1994) The role of general practitioners in the control of breast cancer. [Review] [19 refs]. *Australian Family Physician*, 23: 1733-1737.
Narrative review
- Flatley, R., Ardeshtna, K., D'Sa, S., Percy, L. & Basu, S. (2010) A new approach to long term follow up of lymphoma patients: Transfer to the primary care setting. *Haematologica*, 95: 369.
Not in PICO
- Flatten, G. (1982) More examination of the breast in general practice. [German]. *Monatskurse fur die Arztliche Fortbildung*, 32: 15-16+32.
Narrative review
- Flatten, G. (1982) Mammary carcinoma: Ambulatory early detection and definitive elucidation. [German]. *Monatskurse fur die Arztliche Fortbildung*, 32: 32-39.
Narrative review
- Fletcher, M. E., Sharma, N. & Dall, B. G. (2011) Should general practitioner access to breast imaging and 2WW co-exist? *Breast Cancer Research*, 13: S11.
Not in PICO

- Flobbe, K., Kessels, A. G., Severens, J. L., Beets, G. L., de Koning, H. J., von Meyenfeld, M. F. & van Engelshoven, J. M. (2004) Costs and effects of ultrasonography in the evaluation of palpable breast masses. *International Journal of Technology Assessment in Health Care*, 20: 440-448.
Not in PICO
- Fotou, M., Oikonomou, V., Zagouri, F., Sergentanis, T. N., Nonni, A., Athanassiadou, P., Drouveli, T., Atsouris, E., Kotzia, E. & Zografos, G. C. (2007) Imprint cytology on microcalcifications excised by Vacuum-Assisted Breast Biopsy: A rapid preliminary diagnosis. *World Journal of Surgical Oncology*, 5.
Not in PICO
- Frable, W. J. (1984) Needle aspiration of the breast. *Cancer*, 53: Suppl-6.
Not in PICO
- Franceschi, D., Crowe, J. P., Lie, S., Duchesneau, R., Zollinger, R., Shenk, R., Stefanek, G. & Shuck, J. M. (1970) Not all nonpalpable breast cancers are alike. *Archives of Surgery*, 126: 967-970.
Not in PICO
- Franceschi, D., Crowe, J., Zollinger, R., Duchesneau, R., Shenk, R., Stefanek, G. & Shuck, J. M. (1990) Biopsy of the breast for mammographically detected lesions. *Surgery, Gynecology & Obstetrics*, 171: 449-455.
Not in PICO
- Franceschi, D., Crowe, J., Zollinger, R., Duchesneau, R., Shenk, R., Stefanek, G. & Shuck, J. M. (1990) Breast biopsy for calcifications in nonpalpable breast lesions. A prospective study. *Archives of Surgery*, 125: 170-173.
Not in PICO
- Frayne, J. R. (1987) Early breast cancer. Mammography--the state of the art 1986. *Australasian Radiology*, 31: 108-112.
Narrative review
- Freeman, S. (1111) One-stop clinic can diagnose suspect lesions in a day. *Oncology Report*, 14+15-October.
Not in PICO
- French, R. & Kurup, V. (2012) Targetted Axillary node sampling- Is there a role in the era of sentinal node biopsy? *European Journal of Surgical Oncology*, 38: 426.
Not in PICO
- Friedrich, M. & Semmler, W. (1987) [MR tomography of the breast. Supplemental information in select cases]. [German]. *Radiologe*, 27: 165-177.
Not in PICO
- Friis, M., Dahl, C., Christensen, A. H. & Rordam, P. (1989) [Non-palpable tumors of the breast demonstrated by mammography]. [Danish]. *Ugeskrift for Laeger*, 151: 988-989.
Not in PICO
- Froman, J., Landercasper, J., Ellis, R., De, M. B. & Theede, L. (2011) Red breast as a presenting complaint at a breast center: An institutional review. *Surgery*, 149: 813-819.
Not in PICO
- Frykberg, E. R., Masood, S., Copeland III, E. M. & Bland, K. I. (1993) Ductal carcinoma in situ of the breast. *Surgery Gynecology and Obstetrics*, 177: 425-435.
Narrative review
- Furukawa, M., Taira, N., Iha, S., Nogami, T., Shien, T., Omori, M. & Doihara, H. (2012) A radial sclerosing lesion mimicking breast cancer on mammography in a young woman. *Case Reports Oncology*, 5: 99-103.
Not in PICO
- Fysh, T., Short, M., Godden, A., Cameron, D. & Dunn, J. (2012) The role of triple assessment in benign breast disease. *European Journal of Surgical Oncology*, 38: 461.
Not in PICO

- Galea, M. & Blamey, R. W. (1991) Diagnosis by team work: an approach to conservatism. *British Medical Bulletin*, 47: 295-304.
Narrative review/Not in PICO
- Ganesan, K., Acharya, R. U., Chua, C. K., Min, L. C., Mathew, B. & Thomas, A. K. (2013) Decision support system for breast cancer detection using mammograms. *Proceedings of the Institution of Mechanical Engineers.Part H - Journal of Engineering in Medicine*, 227: 721-732.
Not in PICO
- Gantenbein, H. & Spieler, P. (1986) [Fine-needle aspiration biopsy of the breast. Frequency, indication and accuracy, studied on material from the Cytological Laboratory of the Pathology Institute, St. Gallen Canton Hospital, 1981-1984]. [German]. *Schweizerische Medizinische Wochenschrift.Journal Suisse de Medecine*, 116: 1513-1518.
Not in PICO (only 377/1376 received reference standard)
- Gao, T. X., Fan, X. F., Xuan, L. X., Zhang, B. N., Li, X. & Bai, J. (2008) [The clinical detection of breast cancer by spectrum method]. [Chinese]. *Guang Pu Xue Yu Guang Pu Fen Xi/Spectroscopy & Spectral Analysis*, 28: 2531-2535.
Not in PICO
- Garbay, J. R., Guinebretiere, J. M., Mathieu, M. C. & Rochard, F. (2002) Sentinel node biopsy in breast cancer. Will this lead to the end of lymphadenectomy for small tumors without suspected axillary adenopathy?. [French]. *Gynecologie, Obstetrique & Fertilité*, 30: 514-522.
Not in PICO
- Gautherie, M. (1983) Thermobiological assessment of benign and malignant breast diseases. *American Journal of Obstetrics & Gynecology*, 147: 861-869.
Narrative review
- Geiser, W. R., Haygood, T. M., Santiago, L., Stephens, T., Thames, D. & Whitman, G. J. (2011) Challenges in mammography: part 1, artifacts in digital mammography. [Review]. *AJR.American Journal of Roentgenology*, 197: W1023-W1030.
Narrative review
- Geller, B. M., Oppenheimer, R. G., Worden, J. K. & Ashley, J. A. (1999) Referral patterns for the evaluation of non-palpable breast abnormalities. *Southern Medical Journal*, 92: 886-892.
Not in PICO
- Gencturk, N. (2013) The status of knowledge and practice of early diagnosis methods for breast cancer by women healthcare professionals. *Meme Sagligi Dergisi / Journal of Breast Health*, 9: 5-9.
Not in PICO
- Ghys, R. (1983) The early diagnosis of breast tumours. *Journal of Nuclear Medicine and Allied Sciences*, 27: 317-325.
Narrative review
- Gibbs, P., Liney, G. P., Lowry, M., Kneeshaw, P. J. & Turnbull, L. W. (2004) Differentiation of benign and malignant sub-1 cm breast lesions using dynamic contrast enhanced MRI. *Breast*, 13: 115-121.
Not in PICO
- Giese-Davis, J., Tamagawa, R., Yutsis, M., Twirbutt, S., Piemme, K., Neri, E., Taylor, C. B. & Spiegel, D. (2014) Which symptoms matter? Self-report and observer discrepancies in repressors and high-anxious women with metastatic breast cancer. *Journal of Behavioral Medicine*, 37: 22-36.
Not in PICO
- Gil Martinez, E. M. & Moya, G. F. (2004) FDG-PET in breast cancer. [Spanish]. *Ciencia Ginecologica*, 8: 81-86.
Not in PICO
- Giuseppetti, G. M., Rizzato, G., Gozzi, G. & Ercolani, P. (1989) [Role of ultrasonics in the diagnosis of subclinical carcinoma of the breast]. [Italian]. *Radiologia Medica*, 78: 339-342.

Not in PICO (only US or mammography-positive patients received reference standard, so not possible to establish the number of true negatives and false negatives)

Goepel, E. & Pahnke, V. G. (1991) [Successful therapy of nonpuerperal mastitis--already routine or still a rarity?]. [German]. *Geburtshilfe und Frauenheilkunde*, 51: 109-116.
Not in PICO

Goerres, G. W., Michel, S. C., Fehr, M. K., Kaim, A. H., Steinert, H. C., Seifert, B., von Schulthess, G. K. & Kubik-Huch, R. A. (2003) Follow-up of women with breast cancer: comparison between MRI and FDG PET. *European Radiology*, 13: 1635-1644.
Not in PICO

Gonzalez-Perez, B., Salas-Flores, R., Sosa-Lopez, M. L., Barrientos-Guerrero, C. E., Hernandez-Aguilar, C. M., Gomez-Contreras, D. E. & Sanchez-Garza, J. A. (2013) Female breast symptoms in patients attended in the family medicine practice. *Revista Medica del Instituto Mexicano del Seguro Social*, 51: 558-561.
Outcomes not in PICO and cannot be calculated from the presented data. Setting is unclear

Gorgel, P., Sertbas, A. & Ucan, O. N. (2010) A wavelet-based mammographic image denoising and enhancement with homomorphic filtering. *Journal of Medical Systems*, 34: 993-1002.
Narrative review/Not in PICO

Gorisek, B. (1984) [The role of clinical examination in the diagnosis of breast cancer]. [Croatian]. *Jugoslavenska Ginekologija i Opstetricija*, 24: 34-36.
Not in PICO (S&S: "The Center for the diagnosis of breast disease in Maribor", so think secondary care, and no symptoms linked to breast cancer; test: no relevant outcomes)

Gosein, M. A., Pinto Pereira, S. M., Narinesingh, D. & Ameer, A. (2014) - Breast cancer and mammography: knowledge, attitudes, practices and patient satisfaction post-mammography at the San Fernando General Hospital, Trinidad. - *Journal of Health Care for the Poor & Underserved*, 25: 142-160.
Not in PICO

Gostout, B. S. & Brewer, M. A. (2006) Guidelines for referral of the patient with an adnexal mass. [Review] [43 refs]. *Clinical Obstetrics & Gynecology*, 49: 448-458.
Not in PICO

Grady, K. E., Lemkau, J. P., Mcvay, J. M., Carlson, S., Lee, N., Minchella, M. & Caddell, C. (1996) Clinical decision-making and mammography referral. *Preventive Medicine*, 25: 327-338.
Not in PICO

Graham, N. L. & Bauer, T. L. (1988) Early detection of occult breast cancer: the York experience with 678 needle localization biopsies. *American Surgeon*, 54: 234-239.
Not in PICO

Greene, L. R. & George, R. F. (2012) Radiologist views of positron emission mammography. [Review]. *Radiologic Technology*, 84: 18-30.
Not in PICO

Griffen, M. M. & Welling, R. E. (1990) Needle-localized biopsy of the breast. *Surgery, Gynecology & Obstetrics*, 170: 145-148.
Not in PICO

Groenewoud, J. H., Otten, J. D., Fracheboud, J., Draisma, G., Ineveld, B. M., Holland, R., Verbeek, A. L. & Koning, H. J. (2007) Cost-effectiveness of different reading and referral strategies in mammography screening in the Netherlands (Provisional abstract). *Breast Cancer Research and Treatment*, 102: 211-218.
Not in PICO

Grosfeld, S., Veenendaal, L., Toonen, H. & Ernst, M. (2014) Breast cancer: Fast diagnosis. *European Journal of Cancer*, 50: S67.
Not in PICO

- Grossman, E., Phillips, R. S. & Weingart, S. N. (2010) Performance of a fail-safe system to follow up abnormal mammograms in primary care. *Journal of patient safety*, 6: 172-179.
Not in PICO
- Gumus, H., Gumus, M., Mills, P., Fish, D., Devalia, H., Jones, S. E., Jones, P. A. & Sever, A. R. (2012) Clinically palpable breast abnormalities with normal imaging: is clinically guided biopsy still required? *Clinical Radiology*, 67: 437-440.
Not in PICO
- Habegger, D. & Ellerhorst-Ryan, J. M. (1988) Needle localization for nonpalpable breast lesions. *Oncology Nursing Forum*, 15: 192-194.
Narrative review
- Hall, F. M. (1990) Mammographic second opinions prior to biopsy of nonpalpable breast lesions. *Archives of Surgery*, 125: 298-299.
Narrative review
- Hamed, H., De, F., Jr., Rasbridge, S., Fisher, C., Chaudary, M. A. & Fentiman, I. S. (1995) A prospective randomized study of two gauges of Biopsy-cut needle in diagnosis of early breast cancer. *Breast*, 4: 135-136.
Not in PICO
- Hamy, A. S., Giacchetti, S., Albitar, M., de, B. C., Cuvier, C., Perret, F., Bonfils, S., Charveriat, P., Hocini, H., de, R. A. & Espie, M. (2012) BI-RADS categorisation of 2,708 consecutive nonpalpable breast lesions in patients referred to a dedicated breast care unit. *European Radiology*, 22: 9-17.
Not in PICO
- Han, X. J., Ren, J. H., Ma, N., Tan, Q. T. & Wang, S. Y. (2012) [The study in detection of microcalcification in early breast cancer by ultrasound and its correlation with pathohistology]. [Chinese]. *Chung-Hua i Hsueh Tsa Chih [Chinese Medical Journal]*, 92: 2349-2352.
Not in PICO
- Hanavadi, S., Monypenny, I. J. & Mansel, R. E. (2006) Is mammography overused in male patients? *Breast*, 15: 123-126.
Not in PICO
- Handel, N. & Silverstein, M. J. (2004) Breast Cancer Detection in Women with Implants. *Seminars in Breast Disease*, 7: 172-181.
Not in PICO
- Harada, S., Mick, R., Roses, R. E., Graves, H., Niu, H., Sharma, A., Schueller, J. E., Nisenbaum, H., Czerniecki, B. J. & Zhang, P. J. (2011) The significance of HER-2/neu receptor positivity and immunophenotype in ductal carcinoma in situ with early invasive disease. *Journal of Surgical Oncology*, 104: 458-465.
Not in PICO
- Harnan, S. E., Cooper, K. L., Meng, Y., Ward, S. E., Fitzgerald, P., Papaioannou, D., Ingram, C., Lorenz, E., Wilkinson, I. D. & Wyld, L. (2011) Magnetic resonance for assessment of axillary lymph node status in early breast cancer: a systematic review and meta-analysis. [Review]. *European Journal of Surgical Oncology*, 37: 928-936.
Not in PICO
- Hasert, V. (1990) [Diagnostic imaging of the breast--a survey]. [Review] [57 refs] [German]. *Radiologia Diagnostica*, 31: 425-432.
Narrative review
- Hassan, A. M. & El-Shenawee, M. (2011) Review of electromagnetic techniques for breast cancer detection. [Review]. *IEEE Reviews in Biomedical Engineering*, 4: 103-118.
Narrative review
- Heidenreich, W. (1983) [Tasks of the general practitioner in the diagnosis and therapy of breast cancer]. [German]. *ZFA - Zeitschrift fur Allgemeinmedizin*, 59: 541-545.
Narrative review

- Heinig, J., Witteler, R., Schmitz, R., Kiesel, L. & Steinhard, J. (2008) Accuracy of classification of breast ultrasound findings based on criteria used for BI-RADS. *Ultrasound in Obstetrics & Gynecology*, 32: 573-578.
Not in PICO
- Heins, M. J., Korevaar, J. C., Rijken, P. M. & Schellevis, F. G. (2013) For which health problems do cancer survivors visit their General Practitioner? *European Journal of Cancer*, 49: 211-218.
Not in PICO
- Heinzerling, J. (1988) Mammography and early recognition of breast cancer. [German]. *Medizintechnik*, 108: 210-212.
Narrative review
- Helvie, M. A. (2010) Digital Mammography Imaging: Breast Tomosynthesis and Advanced Applications. *Radiologic Clinics of North America*, 48: 917-929.
Narrative review
- Henderson, M. A., Cawson, J. M. & Bilous, M. (498) Breast cancer: Getting the diagnosis right. *Medical Journal of Australia*, 163: 494-499.
Narrative review
- Hendrick, R. E. (1991) What primary care physicians should know about radiation exposure, image quality, and accreditation of mammography providers. *Womens Health Issues*, 1: 79-85.
Not in PICO
- Herreria, J. (2003) Community Hospitals Indianapolis creates breast cancer awareness. The hospital joins a partnership with local ABC affiliate. *Profiles in Healthcare Marketing*, 15: 24-27.
Not in PICO
- Heywang-Kobrunner, S. & Schreer, I. (1999) Tissue removal in suspected breast cancer: Needle replaces scalpel. [German]. *Onkologe*, 5: 744-746.
Not in PICO
- Heywang, S. H., Dritschilo, A. & Cigtay, O. (1985) [Calcifications after tylectomy and irradiation for breast cancer. Their symptomatic picture and diagnostic value]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 142: 457-460.
Not in PICO
- Hider, P. & Nicholas, B. (1999) The early detection and diagnosis of breast cancer: a literature review. An update (DARE structured abstract). *Database of Abstracts of Reviews of Effects.*, 150. Systematic review without meta-analysis. Included studies checked for relevance.
- Hieken, T. J., Trull, B. C., Boughey, J. C., Jones, K. N., Reynolds, C. A., Shah, S. S. & Glazebrook, K. N. (838) Preoperative axillary imaging with percutaneous lymph node biopsy is valuable in the contemporary management of patients with breast cancer. *Surgery*, 154: 831-838.
Not in PICO
- Hines, S. L., Tan, W. W., Yasrebi, M., DePeri, E. R. & Perez, E. A. (2007) The role of mammography in male patients with breast symptoms. *Mayo Clinic Proceedings*, 82: 297-300.
Not in PICO
- Hirst, C., Furnival, C. M., Fielding, G. D. & Porter, A. J. (1987) The detection of early breast cancer: Three-year results from a diagnostic breast clinic. *Medical Journal of Australia*, 147: 328-330.
Not in PICO
- Hoe, A. L., Mullee, M. A., Royle, G. T., Guyer, P. B. & Taylor, I. (1993) Breast size and prognosis in early breast cancer. *Annals of the Royal College of Surgeons of England*, 75: 18-22.
Not in PICO
- Hoehn, J. L., Hardacre, J. M., Swanson, M. K., Williams, G. H. & Kuehner, M. E. (104) Early breast cancer detected by mammography. Marshfield Clinic experience. *Postgraduate Medicine*, 79: 99-101.
Narrative review

- Holland, K. (2012) Taking a breast center one step further: implementing breast tomosynthesis. *Radiology Management*, 34: 40-42.
Not in PICO
- Holzmann, J., Lawn, A. & Kothari, M. (2013) Do mammograms aid the diagnosis of breast cancer in symptomatic young women? *European Journal of Surgical Oncology*, 39: 482.
Abstract only, not enough information to ascertain relevance.
- Homer, M. J., Smith, T. J. & Marchant, D. J. (1984) Outpatient needle localization and biopsy for nonpalpable breast lesions. *JAMA*, 252: 2452-2454.
Not in PICO
- Homer, M. J., Schmidt-Ullrich, R., Safaii, H., Pile-Spellman, E. R., Marchant, D. J., Smith, T. J., Kelly, K. & Robert, N. J. (1989) Residual breast carcinoma after biopsy: role of mammography in evaluation. *Radiology*, 170: t-7.
Not in PICO
- Hoorntje, L. E., Peeters, P. H., Mali, W. P. & Borel Rinke, I. H. (2003) [Stereotactic large core needle biopsy for the diagnosis of nonpalpable breast lesions: reliable without additional excision biopsy]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 147: 868-873.
Not in PICO
- Houssami, N., Ciatto, S., Martinelli, F., Bonardi, R. & Duffy, S. W. (2009) Early detection of second breast cancers improves prognosis in breast cancer survivors. *Annals of Oncology*, 20: 1505-1510.
Not in PICO
- Howard, M. B., Battaglia, T., Prout, M. & Freund, K. (2012) The effect of imaging on the clinical management of breast pain. *Journal of General Internal Medicine*, 27: 817-824.
Not in PICO
- Howe, H. L., Lehnerr, M. & Katterhagen, J. G. (1994) Education of rural physicians about breast cancer through an oncology outreach program. *Public Health Reports*, 109: 804-808.
Not in PICO
- Howell, A. (2010) The emerging breast cancer epidemic: early diagnosis and treatment. *Breast Cancer Research*, 12: Suppl.
Narrative review
- Hsu, H. H., Yu, J. C., Lee, H. S., Lin, W. C., Chang, W. C., Tung, H. J., Huang, G. S. & Hsu, G. C. (2011) Complex cystic lesions of the breast on ultrasonography: feature analysis and BI-RADS assessment. *European Journal of Radiology*, 79: 73-79.
Not in PICO
- Hu, W. & Gong, S. (2012) Diagnosis of breast calcifications under ultrasonography. *Academic Journal of Second Military Medical University*, 33: 900-902.
Narrative review
- Huber, J. C., Fischl, F., Kubista, E. & Reinold, E. (1982) [Real time ultrasound in routine breast diagnosis]. [German]. *Ultraschall in der Medizin*, 3: 137-139.
Narrative review
- Hunt, K. K. & Ross, M. I. (1997) Changing trends in the diagnosis and treatment of early breast cancer. *Cancer Treatment and Research*, 90: 171-201.
Narrative review
- Iima, M., Nakamoto, Y., Kanao, S., Sugie, T., Ueno, T., Kawada, M., Mikami, Y., Toi, M. & Togashi, K. (2012) Clinical performance of 2 dedicated PET scanners for breast imaging: initial evaluation. *Journal of Nuclear Medicine*, 53: 1534-1542.
Not in PICO
- Ikeda, D. M., Birdwell, R. L. & Daniel, B. L. (2001) Potential role of magnetic resonance imaging and other modalities in ductal carcinoma in situ detection. [Review] [96 refs]. *Magnetic Resonance Imaging Clinics of North America*, 9: 345-356.
Narrative review

- Ilic, N., Frleta, I. N., Juricic, B., Banovic, J. & Krnic, D. (2012) Comparison of intraoperative ultrasound guided and radio guided biopsy of non-palpable breast cancer lesions. *European Journal of Surgical Oncology*, 38: 815-816.
Not in PICO
- Imamoto, H., Takatsuka, Y., Kawahara, T., Tokunaga, K. & Morimoto, K. (1983) [Ultrasonographic diagnosis of early breast cancer]. [Japanese]. *Nippon Gan Chiryō Gakkai Shi - Journal of Japan Society for Cancer Therapy*, 18: 1998-2003.
Not in PICO
- Imbriaco, M., Caprio, M. G., Limite, G., Pace, L., De, F. T., Capuano, E. & Salvatore, M. (2008) Dual-time-point 18F-FDG PET/CT versus dynamic breast MRI of suspicious breast lesions. *AJR.American Journal of Roentgenology*, 191: 1323-1330.
Not in PICO
- Innos, K., Padrik, P., Valvere, V., Eelma, E., Kutner, R., Lehtsaar, J. & Tekkel, M. (2013) Identifying women at risk for delayed presentation of breast cancer: a cross-sectional study in Estonia. *BMC Public Health*, 13: 947.
Not in PICO
- Inoue, M., Sano, T., Watai, R., Ashikaga, R., Ueda, K., Watatani, M. & Nishimura, Y. (2003) Dynamic multidetector CT of breast tumors: diagnostic features and comparison with conventional techniques. *AJR.American Journal of Roentgenology*, 181: 679-686.
Not in PICO
- Iwashita, T., Yasuda, I., Doi, S., Nakashima, M., Tsurumi, H., Hirose, Y., Takami, T., Enya, M., Mukai, T., Ohnishi, T., Iwata, K., Tomita, E. & Moriwaki, H. (2009) Endoscopic ultrasound-guided fine-needle aspiration in patients with lymphadenopathy suspected of recurrent malignancy after curative treatment. *Journal of Gastroenterology*, 44: 190-196.
Not in PICO
- Izzo, L., Stasolla, A., Basso, L., Caputo, M., Kharrub, Z., Marini, M., Mingazzini, P., Fiori, E., Galati, G., D'Aprile, M. R., Mele, L. L. & Marini, M. (2005) Characterization of tumoral lesions of the breast: preliminary experience with multislice spiral CT. *Journal of Experimental & Clinical Cancer Research*, 24: 209-215.
Not in PICO
- Jacobs, I. A., Chevinsky, A. H., Diehl, W. & Smith, T. J. (2001) Advanced breast biopsy instrumentation (ABBI) and management of nonpalpable breast abnormalities: a community hospital experience. *Breast*, 10: 421-426.
Not in PICO
- Jaka, R. C., Zaveri, S. S., Somashekhar, S. P., Sureshchandra & Parameswaran, R. V. (2010) Value of frozen section and primary tumor factors in determining sentinel lymph node spread in early breast carcinoma. *Indian Journal of Surgical Oncology*, 1: 27-36.
Not in PICO
- Jalalian, A., Mashohor, S. B., Mahmud, H. R., Saripan, M. I., Ramli, A. R. & Karasfi, B. (2013) Computer-aided detection/diagnosis of breast cancer in mammography and ultrasound: a review. [Review]. *Clinical Imaging*, 37: 420-426.
Narrative review
- Jalalian, A., Mashohor, S. B., Mahmud, H. R., Saripan, M. I., Ramli, A. R. & Karasfi, B. (2013) Computer-aided detection/diagnosis of breast cancer in mammography and ultrasound: a review. *Clinical Imaging*, 37: 420-426.
Narrative review
- Jan, W. A., Zada, N., Samieullah, A. & Israr, M. (2002) Comparison of FNAC and core biopsy for evaluating breast lumps. *Journal of the College of Physicians and Surgeons Pakistan*, 12: 686-688.
Not in PICO
- Jansen, S. A., Fan, X., Medved, M., Abe, H., Shimauchi, A., Yang, C., Zamora, M., Foxley, S., Olopade, O. I., Karczmar, G. S. & Newstead, G. M. (2010) Characterizing early contrast uptake of ductal

- carcinoma in situ with high temporal resolution dynamic contrast-enhanced MRI of the breast: a pilot study. *Physics in Medicine & Biology*, 55: N473-N485.
Not in PICO
- Jeanmart, L. & Crevecoeur, M. (1985) [Evolution of the strategy for the early diagnosis of breast cancer]. [French]. *Bulletin et Memoires de l'Academie Royale de Medecine de Belgique*, 140: 238-254.
Narrative review
- Jenner, D. C., Middleton, A., Webb, W. M., Oommen, R. & Bates, T. (2000) In-hospital delay in the diagnosis of breast cancer. *British Journal of Surgery*, 87: 914-919.
Not in PICO
- Jeter, D. D., Vest, G. R. & Buday, S. J. (1991) Mammographic guidewire localization of nonpalpable breast lesions. *American Surgeon*, 57: 431-433.
Not in PICO
- Jin, Z. & Shu-Ling, L. (1996) Study of tumor markers in nipple discharge for early detection of breast carcinoma - I. [Chinese]. *Chinese Journal of Clinical Oncology*, 23: 457-460.
In Chinese, not enough information can be extracted to ascertain relevance, but I think it is not in PICO.
- Jiwa, M., Thompson, J., Coleman, R. & Reed, M. (2006) Breast cancer follow-up: Could primary care be the right venue? *Current Medical Research and Opinion*, 22: 625-630.
Not in PICO
- Johnson, P. (2003) Inflammatory breast cancer in primary care. *The Nurse practitioner*, 28: 58-59.
Narrative review
- Johnson, T. L. & Kini, S. R. (1991) Cytologic and clinicopathologic features of abnormal nipple secretions: 225 cases. *Diagnostic Cytopathology*, 7: 17-22.
Not in PICO
- Jones III, R. F. (1994) Mammography in the obstetrician-gynecologist's office: Early detection of breast cancer. *Clinical Obstetrics and Gynecology*, 37: 944-947.
Not in PICO
- Jong, R. A., Yaffe, M. J., Skarpathiotakis, M., Shumak, R. S., Danjoux, N. M., Gunsekara, A. & Plewes, D. B. (2003) Contrast-enhanced digital mammography: initial clinical experience. *Radiology*, 228: 842-850.
Not in PICO
- Jordan, K. P. & Croft, P. (2010) Mortality and cancer in patients with new musculoskeletal episodes: A cohort study. *British Journal of General Practice*, 60: e150-112.
Outcomes not in PICO. Presented data only for cancer as a whole, not by individual cancers.
- Jordan, K. P., Hayward, R. A., Blagojevic-Bucknall, M. & Croft, P. (2013) Incidence of prostate, breast, lung and colorectal cancer following new consultation for musculoskeletal pain: a cohort study among UK primary care patients. *International Journal of Cancer*, 133: 713-720.
Cannot extract outcome in PICO (PPVs) as cancer data only reported in total for 10-year follow up
- Kaiser, W. A. (1991) MR mammography (MRM). *Medicamundi*, 36: 168-182.
Narrative review
- Kaiser, W. A., Diedrich, K., Reiser, M. & Krebs, D. (1993) [Modern diagnostics of the breast]. [Review] [150 refs] [German]. *Geburtshilfe und Frauenheilkunde*, 53: 1-14.
Narrative review
- Kaiser, W. A. (1993) Magnetic resonance mammography. [German]. *Radiologe*, 33: 292-299.
Not in PICO
- Kalles, V., Zografos, G. C., Provatopoulou, X., Kalogera, E., Liakou, P., Georgiou, G., Sagkriotis, A., Nonni, A. & Gounaris, A. (2012) Circulating levels of endothelin-1 (ET-1) and its precursor (Big ET-1) in breast cancer early diagnosis. *Tumour Biology*, 33: 1231-1236.
Not in PICO

- Kalles, V., Zografos, G. C., Provatopoulou, X., Koulocheri, D. & Gounaris, A. (2013) The current status of positron emission mammography in breast cancer diagnosis. [Review]. *Breast Cancer*, 20: 123-130.
Narrative review
- Kamal, R. M., Abdel Razek, N. M., Hassan, M. A. & Shaalan, M. A. (2007) Missed breast carcinoma; why and how to avoid? *Journal of Egyptian National Cancer Institute*, 19: 178-194.
Not in PICO
- Kanbour-Shakir, A., Harris, K. M., Johnson, R. R. & Kanbour, A. I. (1997) Breast care consultation center: role of the pathologist in a multidisciplinary center. *Diagnostic Cytopathology*, 17: 191-196.
Not in PICO
- Kane, K. Y., Lindbloom, E. J. & Stevermer, J. J. (2000) Does mammography add any benefit to a thorough clinical breast examination (CBE)? *The Journal of family practice.*, 49: 1078.
Not in PICO
- Kanwal, S. & Hussain, R. (2005) Sentinel lymph node biopsy in early carcinoma breast with blue dye. *Journal of the College of Physicians and Surgeons Pakistan*, 15: 515-516.
Not in PICO
- Kapdi, C. C. & Parekh, N. J. (1983) The male breast. *Radiologic Clinics of North America*, 21: 137-148.
Narrative review
- Kappadath, S. C. & Shaw, C. C. (2003) Dual-energy digital mammography: calibration and inverse-mapping techniques to estimate calcification thickness and glandular-tissue ratio. *Medical Physics*, 30: 1110-1117.
Not in PICO
- Kashiwagi, S., Onoda, N., Asano, Y., Noda, S., Kawajiri, H., Takashima, T., Ohsawa, M., Kitagawa, S. & Hirakawa, K. (2013) Adjunctive imprint cytology of core needle biopsy specimens improved diagnostic accuracy for breast cancer. *Springerplus*, 2: 372.
Not in PICO
- Kataoka, T., Nishiki, M., Yamane, M., Kushiro, J., Fujii, Y., Matsuyama, T. & Dohi, K. (1986) Improvement in early detection of breast cancer by combining aspiration biopsy cytology and xeromammography. *Hiroshima Journal of Medical Sciences*, 35: 245-251.
Not in PICO
- Katz, S. J., Hislop, T. G., Thomas, D. B. & Larson, E. B. (1993) Delay from symptom to diagnosis and treatment of breast cancer in Washington State and British Columbia. *Medical Care*, 31: 264-268.
Not in PICO
- Kawaguchi, Y., Nawa, M., Takahashi, T., Yamaguchi, K., Osada, S., Yoshida, K., Morimitsu, K., Futamura, M. & Hirose, Y. (2012) [Sentinel lymph node biopsy under local anaesthesia for outpatient]. [Japanese]. *Nihon rinsho*, Japanese: 354-359.
Not in PICO
- Keating, N. L., Landrum, M. B., Ayanian, J. Z., Winer, E. P. & Guadagnoli, E. (2005) The association of ambulatory care with breast cancer stage at diagnosis among medicare beneficiaries. *Journal of General Internal Medicine*, 20: 38-44.
Not in PICO
- Kelly, P. & Winslow, E. H. (1996) Needle wire localization for nonpalpable breast lesions: sensations, anxiety levels, and informational needs. *Oncology Nursing Forum*, 23: 639-645.
Not in PICO
- Kern, K. A. (546) Causes of breast cancer malpractice litigation. A 20-year civil court review. *Archives of Surgery*, 127: 542-546.
Not in PICO
- Khalkhali, I. & Vargas, H. I. (2001) The role of nuclear medicine in breast cancer detection: functional breast imaging. [Review] [68 refs]. *Radiologic Clinics of North America*, 39: 1053-1068.
Narrative review

- Khalkhali, I. & Itti, E. (2002) Functional breast imaging using the single photon technique. *Nuclear Medicine Communications*, 23: 609-611.
Narrative review
- Kibil, W., Hodorowicz-Zaniewska, D., Popiela, T. J. & Kulig, J. (2013) Vacuum-assisted core biopsy in diagnosis and treatment of intraductal papillomas. *Clinical Breast Cancer*, 13: 129-132.
Not in PICO
- Kim, A. C., Ying, D., Sheth, P. & Park, J. M. (2011) Diffusion-weighted magnetic resonance imaging in patients with known or suspected breast malignancy: Correlation between apparent diffusion coefficient and histopathologic diagnoses. *Journal of Clinical Oncology*, 29.
Not in PICO
- Kim, I. J., Kim, S. J. & Kim, Y. K. (2008) Comparison of double phase Tc-99m MIBI and Tc-99m tetrofosmin scintimammography for characterization of breast lesions: Visual and quantitative analyses. *Neoplasma*, 55: 526-531.
Not in PICO
- Kim, J., Han, W., Moon, H. G., Ahn, S. K., Shin, H. C., You, J. M., Chang, J. M., Cho, N., Moon, W. K., Park, I. A. & Noh, D. Y. (2014) - Low rates of additional cancer detection by magnetic resonance imaging in newly diagnosed breast cancer patients who undergo preoperative mammography and ultrasonography. - *Journal of Breast Cancer*, 17: 167-173.
Not in PICO
- Kim, M. J., Kim, J. Y., Yoon, J. H., Youk, J. H., Moon, H. J., Son, E. J., Kwak, J. Y. & Kim, E. K. (2011) How to find an isoechoic lesion with breast US. [Review]. *Radiographics*, 31: 663-676.
Narrative review
- Koizumi, M., Nomura, E., Yamada, Y., Takiguchi, T., Ishii, M., Yamashita, T., Tada, K., Nishimura, S., Takahashi, K., Makita, M., Iwase, T., Yoshimoto, M. & Kasumi, F. (2004) Improved detection of axillary hot nodes in lymphoscintigraphy in breast cancer located in the upper lateral quadrant with additional projection imaging. *Annals of Nuclear Medicine*, 18: 707-710.
Not in PICO
- Konforte, D. & Diamandis, E. P. (2013) Is early detection of cancer with circulating biomarkers feasible? *Clinical Chemistry*, 59: 35-37.
Not in PICO
- Kopp, W., Fotter, R. & Schneider, G. (1986) [Roentgen symptoms of early cancer of the breast]. [German]. *Radiologe*, 26: 498-502.
Not in PICO
- Kosir, M. A., Chism, L., Bland, K., Choi, L., Gorski, D. & Simon, M. S. (1916) Common breast symptoms: when to refer to a breast surgeon. *Advance for NPs & PAs*, 4: 12-15.
Narrative review
- Kriedemann, E. & Noffke, E. (1981) [The role of mammography in the early detection of breast cancer (author's transl)]. [German]. *Archiv fur Geschwulstforschung*, 51: 691-703.
Not in PICO
- Krishnaiah, G., Sher-Ahmed, A., Ugwu-Dike, M., Regan, P., Singer, J., Totoonchie, A., Spiegler, E. & Sardi, A. (2003) Technetium-99m sestamibi scintimammography complements mammography in the detection of breast cancer. *Breast Journal*, 9: 288-294.
Not in PICO
- Kroman, N. T., Grinsted, P. & Nielsen, N. S. (2007) [Symptoms and diagnostic work-up in breast cancer]. [Danish]. *Ugeskrift for Laeger*, 169: 2980-2981.
Narrative review
- Kubiak, T. (2013) Correlation between iron metabolism and development of breast cancer in pre-and postmenopausal women. [Polish]. *Przegląd Menopauzalny*, 17: 339-342.
Narrative review

- Kuhn, T. & Kreienberg, R. (2006) Certified breast centers - Current state from the point of view of physicians. [German]. *Geburtshilfe und Frauenheilkunde*, 66: 902-906.
Not in PICO
- Kwak, H. Y., Chae, B. J., Bae, J. S., Kim, E. J., Chang, E. Y., Kim, S. H., Jung, S. S. & Song, B. J. (2013) Feasibility of sentinel lymph node biopsy in breast cancer patients clinically suspected of axillary lymph node metastasis on preoperative imaging. *World Journal of Surgical Oncology*, 11: 104.
Not in PICO
- Lang, N. P., Talbert, G. E., Shewmake, K. B., Diner, W. C., Weiss, D., Bivins, F. G. & Westbrook, K. C. (1987) The current evaluation of nonpalpable breast lesions. *Archives of Surgery*, 122: 1389-1391.
Not in PICO
- Langer, M. (2004) [Early detection of breast cancer. Is digital mammography more sensitive? (interview by Dr. Thomas Meissner)]. [German]. *MMW Fortschritte der Medizin*, 146: 12.
Narrative review
- Lasser, J. L. & Lasser, S. (1994) Improving the yield of positive breast biopsies: a statistical analysis of mammographic patterns in a private practice. *Rhode Island Medicine*, 77: 41-44.
Not in PICO
- Lattanzio, E. (1997) Mammography and ultrasound in early detection of breast cancer. *FORUM - Trends in Experimental and Clinical Medicine*, 7: 79-81.
Narrative review
- Lay, S. F., Crump, J. M., Frykberg, E. R., Goedde, T. A. & Copeland, E. M., III (1990) Breast biopsy. Changing patterns during a five-year period. *American Surgeon*, 56: 79-85.
Not in PICO
- Lee, J. H., Seong, Y. K., Chang, C. H., Park, J., Park, M., Woo, K. G. & Ko, E. Y. (2012) Fourier-based shape feature extraction technique for computer-aided B-Mode ultrasound diagnosis of breast tumor. *Conference Proceedings: ...Annual International Conference of the IEEE Engineering in Medicine & Biology Society*, 2012: 6551-6554.
Not in PICO
- Lee, S. J. & Zelen, M. (2003) Modelling the early detection of breast cancer. *Annals of Oncology*, 14: 1199-1202.
Not in PICO
- Lefranc, J. P. & Blondon, J. (1984) Mammography in the early diagnosis of breast cancer. [French]. *Gynecologie*, 35: 23-30.
Narrative review
- Legg, J. S. (2002) The clinical breast exam: opportunities for R.T.s. *Radiologic Technology*, 74: 111-122.
Not in PICO
- Lerner, B. H. (1998) Fighting the war on breast cancer: debates over early detection, 1945 to the present. [Review] [94 refs]. *Annals of Internal Medicine*, 129: 74-78.
Narrative review
- Li, G., Liu, H. & Cheng, J. (2011) [Computer aided diagnosis of calcifications in mammograms]. [Review] [Chinese]. *Shengwu Yixue Gongchengxue Zazhi/Journal of Biomedical Engineering*, 28: 170-174.
Narrative review
- Li, L., Wu, Z., Salem, A., Chen, Z., Chen, L., George, F., Kallergi, M. & Berman, C. (2006) Computerized analysis of tissue density effect on missed cancer detection in digital mammography. *Computerized Medical Imaging & Graphics*, 30: 291-297.
Not in PICO
- Li, S. (1984) The value of selected excisional biopsy of locally thickened breast tissue in the diagnosis of early breast cancer. [Chinese]. *Clinical Oncology*, 11: 211-213.
Not in PICO

- Liberman, M., Sampalis, F., Mulder, D. S. & Sampalis, J. S. (2003) Breast cancer diagnosis by scintimammography: a meta-analysis and review of the literature (DARE structured abstract). *Breast Cancer Research and Treatment.*, 80: 115-126.
Not in PICO
- Lin, Z. C. & Effken, J. A. (2010) Effects of a tailored web-based educational intervention on women's perceptions of and intentions to obtain mammography. *Journal of Clinical Nursing*, 19: 1261-1269.
Not in PICO
- Lindfors, K. K., O'Connor, J., Acredolo, C. R. & Liston, S. E. (1998) Short-interval follow-up mammography versus immediate core biopsy of benign breast lesions: Assessment of patient stress. *American Journal of Roentgenology*, 171: 55-58.
Not in PICO
- Linguraru, M. G., Marias, K., English, R. & Brady, M. (2006) A biologically inspired algorithm for microcalcification cluster detection. *Medical Image Analysis*, 10: 850-862.
Not in PICO
- Lisboa, F. C., Viana, S. M., Silva, G. M., Diener, L. S., Oliveira, W. B., Fonseca, P. G., Morais, L. C. & Andrade, G. (2012) The validity of the use of fine needle aspiration cytology (FNAC) ultrasound-guided in the diagnosis and guidance of the practice in breast lumps. *International Journal of Gynecology and Obstetrics*, 119: S739.
Abstract only. Not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Liu, J., Chen, J., Liu, X., Chun, L., Tang, J. & Deng, Y. (2011) Mass segmentation using a combined method for cancer detection. *BMC Systems Biology*, 5: Suppl.
Not in PICO
- Liu, W., Fernando, P. D. & Alasio, T. M. (2009) Primary Small Cell Carcinoma of the Lung Initially Presenting as a Breast Mass: A Fine-Needle Aspiration Diagnosis. *Diagnostic Cytopathology*, 37: 208-212.
Not in PICO
- Locker, A. P., Horrocks, C., Gilmour, A. S., Ellis, I. O., Dowle, C. S., Elston, C. W. & Blamey, R. W. (1990) Flow cytometric and histological analysis of ductal carcinoma in situ of the breast. *British Journal of Surgery*, 77: 564-567.
Not in PICO
- Lohbeck, H. U. (1987) [Possibilities and limits of the early detection of breast cancer by mammography and other methods]. [German]. *Archives of Gynecology & Obstetrics*, 242: 276-280.
Narrative review
- Lopez-Narvaez, R. A., Garza-Montemayor, M. L., Garza-Garcia, N. L., Ojeda-Mendez, E. E., Rangel-Nava, H., Mendez-Lozano, D. & Morales-Caballero, F. G. (2012) [Detection of invasive breast lobular carcinoma by image analysis: comparison between mammography and ultrasound]. [Spanish]. *Ginecologia y Obstetricia de Mexico*, 80: 320-326.
Not in PICO
- Lopez-Narvaez, R. A., Garza-Montemayor, M. L., Garza-Garcia, N. L., Ojeda-Mendez, E. E., Rangel-Nava, H., Mendez-Lozano, D. & Morales-Caballero, F. G. (2012) Evaluation for image on the detection of invasive lobular carcinoma breast: Comparison of mammography and ultrasound. *Ginecologia y Obstetricia de Mexico*, 80: 320-326.
Not in PICO
- Lord, S. J., Lei, W., Craft, P., Cawson, J. N., Morris, I., Walleiser, S., Griffiths, A., Parker, S. & Houssami, N. (2007) A systematic review of the effectiveness of magnetic resonance imaging (MRI) as an addition to mammography and ultrasound in screening young women at high risk of breast cancer (DARE structured abstract). *European Journal of Cancer*, 43: 1905-1917.
Not in PICO

- Loutfi, A. (1998) Recommended management for breast lumps. *Canadian Journal of Surgery*, 41: 421.
Not in PICO
- Lu, W. L., Jansen, L., Post, W. J., Bonnema, J., Van de Velde, J. C. & De Bock, G. H. (2009) Impact on survival of early detection of isolated breast recurrences after the primary treatment for breast cancer: a meta-analysis. *Breast Cancer Research & Treatment*, 114: 403-412.
Not in PICO
- Lucas, J. H. & Cone, D. L. (2003) Breast Cyst Aspiration. *American Family Physician*, 68: 1983-1986+1989.
Narrative review
- Luedders, D. W., von Tengg-Kobligk, H., Hornemann, A., Thill, M., Franke, F. E., Muenstedt, K. & Bohlmann, M. K. (2011) Current diagnostic modalities and clinical pitfalls in malignant secondary breast tumours. [Review]. *Archives of Gynecology & Obstetrics*, 284: 687-694.
Not in PICO
- Lumachi, F., Ferretti, G., Povolato, M., Marzola, M. C., Zucchetta, P., Geatti, O., Brandes, A. A. & Bui, F. (2001) Accuracy of technetium-99m sestamibi scintimammography and X-ray mammography in premenopausal women with suspected breast cancer. *European Journal of Nuclear Medicine*, 28: 1776-1780.
Not in PICO
- Lyratzopoulos, G. & Abel, G. (2013) Earlier diagnosis of breast cancer: focusing on symptomatic women. *Nature Reviews Clinical Oncology*, 10: 2013.
Narrative review
- Ma, J., Xu, J.-M., Du, M., Zhou, Y.-Y., Zang, D., Yang, Z., Zhou, D.-X. & Mai, P.-C. (2008) The histological underestimation of stereotactic core needle biopsy in breast lesions. [Chinese]. *Chinese Journal of Radiology*, 42: 597-600.
Not in PICO
- Macaskill, E. J., Purdie, C. A., Jordan, L. B., Mclean, D., Whelehan, P., Brown, D. C. & Evans, A. (2012) Axillary lymph node core biopsy for breast cancer metastases -- how many needle passes are enough? *Clinical Radiology*, 67: 417-419.
Not in PICO
- Macura, K. J., Ouwerkerk, R., Jacobs, M. A. & Bluemke, D. A. (2011) Patterns of enhancement on breast MR images: interpretation and imaging pitfalls. [Review] [35 refs]. *Radiographics*, 26: 1719-1734.
Narrative review
- Mahmood, S., Sabih, Z. & Sabih, D. (2011) Lymphoma presenting as gynaecomastia. *Biomedical Imaging & Intervention Journal*, 7: e10.
Not in PICO
- Mahoney, M. C. & Newell, M. S. (2013) Breast intervention: how I do it. [Review]. *Radiology*, 268: 12-24.
Narrative review
- Mak, C. & Pokorny, C. S. (2010) Investigating a woman with a breast lump. *Medicine Today*, 11: 34-39.
Narrative review
- Makanjuola, D. (1998) A clinico-radiological correlation of breast diseases during lactation and the significance of unilateral failure of lactation. *West African Journal of Medicine*, 17: 217-223.
Not in PICO
- Malar, E., Kandaswamy, A., Chakravarthy, D. & Giri, D. A. (2012) A novel approach for detection and classification of mammographic microcalcifications using wavelet analysis and extreme learning machine. *Computers in Biology & Medicine*, 42: 898-905.
Not in PICO

- Malhaire, C., El, K. C., Thibault, F., Athanasiou, A., Petrow, P., Ollivier, L. & Tardivon, A. (2010) Vacuum-assisted biopsies under MR guidance: results of 72 procedures. *European Radiology*, 20: 1554-1562.
Not in PICO
- Malhotra, G. K., Zhao, X., Band, H. & Band, V. (2010) Histological, molecular and functional subtypes of breast cancers. [Review]. *Cancer Biology & Therapy*, 10: 955-960.
Not in PICO
- Malich, A., Fritsch, T., Mauch, C., Boehm, T., Freesmeyer, M., Fleck, M., Anderson, R. & Kaiser, W. A. (2001) Electrical impedance scanning: a new technique in the diagnosis of lymph nodes in which malignancy is suspected on ultrasound. *British Journal of Radiology*, 74: 42-47.
Not in PICO
- Mann, B. D., Giuliano, A. E., Bassett, L. W., Barber, M. S., Hallauer, W. & Morton, D. L. (1983) Delayed diagnosis of breast cancer as a result of normal mammograms. *Archives of Surgery*, 118: 23-24.
Not in PICO
- Marchant, D. J. (1998) Controversies in benign breast disease. *Surgical Oncology Clinics of North America*, 7: 285-298.
Narrative review
- Marchant, D. J. (2002) The diagnostic evaluation. [Review] [4 refs]. *Obstetrics & Gynecology Clinics of North America*, 29: 31-41.
Narrative review
- Marcus, V. L. (1988) Mammography in the early detection of breast cancer. *Nebraska Medical Journal*, 73: 355-357.
Narrative review
- Margari, N., Palis, L., Boutou, S., Kampitsis, K., Gavriil, M., Stylianidou, A. & Margari, C. (2012) The significance of ultrasound-guided FNAC in non-palpable breast lumps. *Cytopathology*, 23: 91-92.
Not in PICO
- Margolin, F. R. & Lagios, M. D. (1986) Mammographic detection of early breast cancer. Ten years' experience in a community hospital. *Western Journal of Medicine*, 144: 46-48.
Not in PICO
- Margolin, F. R. (1989) Detecting early breast cancer. Experience in a community hospital. *Cancer*, 64: Suppl-5.
Not in PICO
- Margolin, F. R. (1992) Needle localization guided excisional biopsy for mammographically identified nonpalpable breast lesions. *Pathology (Philadelphia, Pa)*, 1: 1-10.
Not in PICO
- Marinello, G., Calitchi, E., Le Bourgeois, J. P. & Pierquin, B. (1991) Improvement of the method used at Creteil for early breast cancer: 1970-1990. *Radiotherapy & Oncology*, 22: 266-268.
Narrative review
- Markopoulos, C., Kakisis, J., Kouskos, S., Kontzoglou, K., Koufopoulos, K. & Gogas, J. (1999) Management of nonpalpable, mammographically detectable breast lesions. *World Journal of Surgery*, 23: 434-438.
Not in PICO
- Marquet, K. L., Funk, A., Fendel, H. & Handt, S. (1993) [The echo-dense edge and hyper-reflective spikes: sensitive criteria for malignant processes in breast ultrasound]. [German]. *Geburtshilfe und Frauenheilkunde*, 53: 20-23.
Not in PICO
- Martinez, A. M., Medina, C. J., Bustos, C. & Hernandez, J. A. (2003) Assessment of breast lesions using Doppler with contrast agents. *European Journal of Gynaecological Oncology*, 24: 527-530.
Not in PICO
- Mason, T. A., Thompson, W. W., Allen, D., Rogers, D., Gabram-Mendola, S. & Arriola, K. R. (2013) Evaluation of the Avon Foundation community education and outreach initiative Community

- Patient Navigation Program. *Health Promotion Practice*, 14: 105-112.
Not in PICO
- Mastboom, W. J. B., Wobbes, T., Van Der Sluis, R. F. & Van, A., V (1988) The role of aspiration cytology in clinically and radiologically suspected mammary tumours. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 132: 206-208.
Not in PICO
- Matousek, P. & Stone, N. (1111) Prospects for the diagnosis of breast cancer by noninvasive probing of calcifications using transmission Raman spectroscopy. *Journal of Biomedical Optics*, 12: 024008-024Apr.
Not in PICO
- Matsunaga, T., Kawakami, Y., Namba, K. & Fujii, M. (2004) Intraductal biopsy for diagnosis and treatment of intraductal lesions of the breast. *Cancer*, 101: 2164-2169.
Not in PICO
- Matthai, P. (1995) [Does use of mammography and fine-needle biopsy help in early detection of breast carcinoma?]. [Polish]. *Ginekologia Polska*, 66: 179-184.
Not in PICO
- Maxim, R. B. (2000) A resource for the primary care physician. *Medicine and Health, Rhode Island*, 83: 116-118.
Narrative review
- McCann, S., MacAuley, D. & Barnett, Y. (2005) Genetic consultations in primary care: GPs' responses to three scenarios. *Scandinavian Journal of Primary Health Care*, 23: 109-114.
Not in PICO
- McCarthy, E. P., Burns, R. B., Freund, K. M., Ash, A. S., Shwartz, M., Marwill, S. L. & Moskowitz, M. A. Mammography use, breast cancer stage at diagnosis, and survival among older women. *Journal of the American Geriatrics Society* 48[10], 1226-1233. 2000.
Not in PICO
- McCormick, R. S., Wilson, M. S. J., Aspinall, S. R., Goulbourne, I. A., Kasaraneni, R., Serra, P. & Carr, W. (2012) Should we be using ultrasound guidance for all fine needle aspiration cytology and core biopsies in symptomatic breast patients? *European Journal of Surgical Oncology*, 38: 436.
Not in PICO
- Medeiros, L. R., Duarte, C. S., Rosa, D. D., Edelweiss, M. I., Edelweiss, M., Silva, F. R., Winnikow, E. P., Pires, P. D. & Rosa, M. I. (2011) Accuracy of magnetic resonance in suspicious breast lesions: a systematic quantitative review and meta-analysis (DARE structured abstract). *Breast Cancer Research and Treatment.*, 126: 273-285.
Not in PICO
- Medina-Franco, H., Abarca-Perez, L., Cortes-Gonzalez, R., Soto-Germes, S., Ulloa, J. A. & Uribe, N. (2005) Fine needle aspiration biopsy of breast lesions: Institutional experience. [Spanish]. *Revista de Investigacion Clinica*, 57: 394-398.
Not in PICO
- Melnikow, J., Tancredi, D. J., Yang, Z., Ritley, D., Jiang, Y., Slee, C., Popova, S., Rylett, P., Knutson, K. & Smalley, S. (2013) Program-specific cost-effectiveness analysis: breast cancer screening policies for a safety-net program. *Value in Health*, 16: 932-941.
Not in PICO
- Mendelson, E. B., Harris, K. M., Doshi, N. & Tobon, H. (1989) Infiltrating lobular carcinoma: mammographic patterns with pathologic correlation. *AJR.American Journal of Roentgenology*, 153: 265-271.
Not in PICO
- Merkle, E., Muller, M., Vogel, J., Klatt, S., Gorich, J., Beger, H. G. & Brambs, H. J. (1996) [Clinical relevance of mammography in men]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 164: 7-12.
Not in PICO

- Merkle, E., Muller, M., Vogel, J., Klatt, S., Gorich, J., Beger, H.-G. & Brambs, H.-J. (1996) The clinical use of mammography in the male. [German]. *RoFo Fortschritte auf dem Gebiete der Rontgenstrahlen und der Neuen Bildgebenden Verfahren*, 164: 7-12.
Not in PICO
- Merrill, J. T. & Oh, Y. S. (2011) Diagnosis of metastatic breast cancer to an intraabdominal lymph node by endoscopic ultrasound. *Case Reports Gastroenterology*, 5: 189-191.
Not in PICO
- Meyer, J. E. & Kopans, D. B. (1983) Breast physical examination by the mammographer. An aid to improved diagnostic accuracy. *Applied Radiology*, 12: 103-106.
Not in PICO
- Mikula, C. (1972) Mammography and biopsy. An overview for primary care providers. [Review] [2 refs]. *Advance for Nurse Practitioners*, 15: 69-70.
Narrative review
- Mikulin, T. & Blamey, R. W. (1988) The problems referred to a breast clinic. *Practitioner*, 232: 606-610.
Not in PICO
- Mistry, S. G., Barnes, N. & Ooi, J. (2013) Will adherence to new guidance lead to missed cancer diagnoses? Evaluation of limiting symptomatic mammograms to over forties. *Breast Journal*, 19: 142-148.
Not in PICO
- Mitchell, G. W., Jr. & Homer, M. J. (1982) Outpatient breast biopsies on a gynecologic service. *American Journal of Obstetrics & Gynecology*, 144: 127-130.
Not in PICO
- Mizuno, S., Isaji, S., Ogawa, T., Tabata, M., Yamagiwa, K., Yokoi, H. & Uemoto, S. (2005) Approach to fine-needle aspiration cytology-negative cases of breast cancer. *Asian Journal of Surgery*, 28: 13-17.
Not in PICO
- Montoro, A. F. & Monteiro, D. M. (1982) The importance of early diagnosis of Paget's carcinoma of the breast. *Breast, Diseases*: 17-21.
Not in PICO
- Morris, A. M., Flowers, C. R., Morris, K. T., Schmidt, W. A., Pommier, R. F. & Vetto, J. T. (2003) Comparing the cost-effectiveness of the triple test score to traditional methods for evaluating palpable breast masses (Structured abstract). *Medical.Care*, 41: 962-971.
Not in PICO
- Morris, P. G., Lynch, C., Feeney, J. N., Patil, S., Howard, J., Larson, S. M., Dickler, M., Hudis, C. A., Jochelson, M. & McArthur, H. L. (2010) Integrated positron emission tomography/computed tomography may render bone scintigraphy unnecessary to investigate suspected metastatic breast cancer. *Journal of Clinical Oncology*, 28: 3154-3159.
Not in PICO
- Moseson, D. (1992) Audit of mammography in a community setting. *American Journal of Surgery*, 163: 544-546.
Not in PICO
- Moyle, P., Sonoda, L., Britton, P. & Sinnatamby, R. (2010) Incidental breast lesions detected on CT: What is their significance? *British Journal of Radiology*, 83: 233-240.
Not in PICO
- Muller-Schimpfle, M., Stern, W., Stoll, P., Kaiser, J. W. & Claussen, C. D. (1997) [Mammography and mammary ultrasonography: which examination sequence is preferable?]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 167: 348-354.
Not in PICO

- Munoz, C. R., Alvarez, B. M. & Rivin del, C. E. (2013) Value of mammography and breast ultrasound in male patients with nipple discharge. *European Journal of Radiology*, 82: 478-484.
Not in PICO
- Muralidhar, G. S., Haygood, T. M., Stephens, T. W., Whitman, G. J., Bovik, A. C. & Markey, M. K. (2008) Computer-aided detection of breast cancer - have all bases been covered? *Breast Cancer*, 2: 5-9.
Narrative review
- Murphy, I. G., Dillon, M. F., Doherty, A. O., McDermott, E. W., Kelly, G., O'Higgins, N. & Hill, A. D. (2007) Analysis of patients with false negative mammography and symptomatic breast carcinoma. *Journal of Surgical Oncology*, 96: 457-463.
Not in PICO
- Nakano, S., Sakamoto, H., Ohtsuka, M., Mibu, A., Karikomi, M., Sakata, H. & Yamamoto, M. (2011) Successful use of multi-detector row computed tomography for detecting contralateral breast cancer. *Journal of Computer Assisted Tomography*, 35: 148-152.
Not in PICO
- Nakayama, R., Uchiyama, Y., Yamamoto, K., Watanabe, R. & Namba, K. (2006) Computer-aided diagnosis scheme using a filter bank for detection of microcalcification clusters in mammograms. *IEEE Transactions on Biomedical Engineering*, 53: 273-283.
Not in PICO
- Nasser, S. M. (2009) Flat epithelial atypia of the breast. [Review] [46 refs]. *Journal Medical Libanais - Lebanese Medical Journal*, 57: 105-109.
Narrative review
- Neal, C. H., Coletti, M. C., Joe, A., Jeffries, D. O. & Helvie, M. A. (2013) Does digital mammography increase detection of high-risk breast lesions presenting as calcifications? *AJR.American Journal of Roentgenology*, 201: 1148-1154.
Not in PICO
- Neary, M., Lowery, A. J., Conghaile, A. O., Pervaz, M., Kerin, M. J. & Sweeney, K. J. (2011) NCCP breast cancer referral guidelines are breast cancer patients Prioritised? *Irish Medical Journal*, 104.
Not in PICO
- Nelson, T. R., Tran, A., Fakourfar, H. & Nebeker, J. (2012) Positional calibration of an ultrasound image-guided robotic breast biopsy system. *Journal of Ultrasound in Medicine*, 31: 351-359.
Not in PICO
- Neumayer, L., Meterissian, S., McMasters, K. & Evidence Based Reviews in Surgery Group (2007) Canadian Association of General Surgeons and American College of Surgeons Evidence Based Reviews in Surgery. 23. ASCO recommended guidelines for sentinel lymph node biopsy for early-stage breast cancer. Evidence-based medicine. A new approach to teaching the practice of medicine. *Canadian Journal of Surgery*, 50: 482-484.
Not in PICO
- Newman, J. (1997) Early detection techniques in breast cancer management. *Radiologic Technology*, 68: 309-324.
Narrative review
- Niikura, N., Odisio, B. C., Tokuda, Y., Symmans, F. W., Hortobagyi, G. N. & Ueno, N. T. (2013) Latest biopsy approach for suspected metastases in patients with breast cancer. *Nature Reviews Clinical Oncology*, 10: 711-719.
Not in PICO
- Nikolaev, K. S. (2013) [Clinical and morphological features of breast cancer in men]. [Russian]. *Voprosy Onkologii*, 59: 358-362.
Narrative review
- Nishizawa, Y., Koyama, H., Wada, T., Terasawa, T., Wada, A., Nangumo, S. & Matsuda, M. (1983) Early diagnosis of breast cancer by needle aspiration. [Japanese]. *Nippon Gan Chiryō Gakkai shi*,

18: 661-665.

Duplicate of Nishizawa (1983)

Nishizawa, Y., Koyama, H. & Wada, T. (1983) Needle aspiration cytology in early diagnosis of breast cancer. [Japanese]. *Journal of Japan Society for Cancer Therapy*, 18: 661-665.

Not in PICO

Noguchi, S., Tsukamoto, F., Miyoshi, Y., Inaji, H., Watatani, M., Sasa, M., Inazawa, J. & Takami, S. (1999) Detection of numerical aberrations in chromosomes by fluorescence in situ hybridization in fine needle aspirates in the preoperative diagnosis of cancer. [Japanese]. *Gan to Kagaku Ryoho, Cancer*: 2127-2130.

Not in PICO

Norsa'adah, B., Rampal, K. G., Rahmah, M. A., Naing, N. N. & Biswal, B. M. (2011) Diagnosis delay of breast cancer and its associated factors in Malaysian women. *BMC Cancer*, 11: 141.

Not in PICO

Nussbaum, H. & O'Connell, T. X. (1980) Minimal breast cancer. Is excisional biopsy alone adequate treatment?. [Review] [22 refs]. *Cancer Clinical Trials*, 3: 19-22.

Narrative review

Nyirjesy, I. & Billingsley, F. S. (1992) Management of breast problems in gynecologic office practice using sonography and fine-needle aspiration. *Obstetrics & Gynecology*, 79: t-702.

Not in PICO

Ohi, J., Kitamura, K., Sato, M., Furuta, M., Nakamoto, Y., Kanao, S., Ishizu, K., Miyake, K. K. & Togashi, K. (2010) First clinical trials of dedicated breast PET scanners. *Molecular Imaging and Biology*, 12: S536.

Not in PICO

Ohlinger, R., Klein, G. M. & Kohler, G. (2004) Ultrasound of the breast - value of sonographic criteria for the differential diagnosis of solid lesions. *Ultraschall in der Medizin*, 25: 48-53.

Not in PICO

Ojeda-Fournier, H. & Nguyen, J. Q. (2009) How to improve your breast cancer program: Standardized reporting using the new American College of Radiology Breast Imaging-Reporting and Data System. *Indian Journal of Radiology & Imaging*, 19: 266-277.

Not in PICO

Opielinski, K. J. & Gudra, T. (2006) Multi-parameter ultrasound transmission tomography of biological media. *Ultrasonics*, 44: e295-e302.

Not in PICO

Opstal-van Winden, A. W., Krop, E. J., Karedal, M. H., Gast, M. C., Lindh, C. H., Jeppsson, M. C., Jonsson, B. A., Grobbee, D. E., Peeters, P. H., Beijnen, J. H., van Gils, C. H. & Vermeulen, R. C. (2011) Searching for early breast cancer biomarkers by serum protein profiling of pre-diagnostic serum; a nested case-control study. *BMC Cancer*, 11: 381.

Not in PICO

Orel, S. G. & Schnall, M. D. (2001) MR imaging of the breast for the detection, diagnosis, and staging of breast cancer. *Radiology*, 220: 13-30.

Not in PICO

Osborn, G. D., Gahir, J. K., Preece, K., Vaughan-Williams, E. & Gower-Thomas, K. (2006) Is general practitioner access to breast imaging safe? *Clinical Radiology*, 61: 431-435.

Not in PICO

Ostrow, L. B., DuBois, J. J., Hoefler, R. A., Jr. & Brant, W. E. (1987) Needle-localized biopsy of occult breast lesions. *Southern Medical Journal*, 80: 29-32.

Not in PICO

Osuch, J. R., Bonham, V. L. & Morris, L. L. (1998) Primary care guide to managing a breast mass: step-by-step workup. *Medscape Womens Health*, 3: 4.

Narrative review

- Palma, L. D. & Longo, R. (1997) New frontiers in diagnostic imaging of breast cancer. *FORUM - Trends in Experimental and Clinical Medicine*, 7: 82-86.
Narrative review
- Palmedo, H., Schomburg, A., Grunwald, F., Mallmann, P., Krebs, D. & Biersack, H. J. (1996) Technetium-99m-MIBI scintimammography for suspicious breast lesions. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine*, 37: 626-630.
Not in PICO
- Palmer, M. L. & Tsangaris, T. N. (1993) Breast biopsy in women 30 years old or less. *American Journal of Surgery*, 165: 708-712.
Not in PICO
- Palomar, M. A., Garcia Vicente, A. M., Talavera Rubio, M. P., Pilkington Woll, J. P., Poblete Garcia, V. M., Bellon Guardia, M. E., Leon, M. A., Cordero Garcia, J. M. & Soriano, C. A. (2010) [Diagnostic and therapeutic impact of 18F-FDG-PET/CT in patients with suspected breast cancer recurrence]. [Spanish]. *Revista Espanola de Medicina Nuclear*, 29: 100-108.
Not in PICO
- Pan, S., Liu, W., Jin, K., Liu, Y. & Zhou, Y. (2014) - Ultrasound-guided vacuum-assisted breast biopsy using Mammotome biopsy system for detection of breast cancer: results from two high volume hospitals. - *International journal of clinical and experimental medicine*, 7: 239-246.
Not in PICO
- Pan, S., Liu, W., Jin, K., Liu, Y. & Zhou, Y. (2014) Ultrasound-guided vacuum-assisted breast biopsy using Mammotome biopsy system for detection of breast cancer: results from two high volume hospitals. *International journal of clinical and experimental medicine*, 7: 239-246.
Not in PICO
- Panageas, K. S., Sima, C. S., Liberman, L. & Schrag, D. (2012) Use of high technology imaging for surveillance of early stage breast cancer. *Breast Cancer Research & Treatment*, 131: 663-670.
Not in PICO
- Pandya, S. & Moore, R. G. (2011) Breast development and anatomy. *Clinical Obstetrics & Gynecology*, 54: 91-95.
Narrative review
- Panu, N. & Morris, E. (2011) Establishing a comprehensive breast magnetic resonance imaging service in a community hospital. *Canadian Association of Radiologists Journal*, 62: 22-30.
Not in PICO
- Pappo, I., Horne, T. & Orda, R. (1998) Tc-99m-sestamibi scintimammography for the diagnosis of breast malignancies. *Breast Journal*, 4: 441-446.
Not in PICO
- Paramagul, C. P., Helvie, M. A., Roubidoux, M. A., Kleer, C. G. & Newman, L. A. (2005) Lobular Carcinoma in Situ (LCIS): Clinical and mammography findings of subsequent breast cancers. *Journal of Women's Imaging*, 7: 181-189.
Not in PICO
- Park, C. S., Jung, N. Y., Kim, K., Jung, H. S., Sohn, K. M. & Oh, S. J. (2013) Detection of breast cancer in asymptomatic and symptomatic groups using computer-aided detection with full-field digital mammography. *Journal of Breast Cancer*, 16: 322-328.
Not in PICO
- Parker, A., Schroen, A. T. & Brenin, D. R. (2013) MRI utilization in newly diagnosed breast cancer: a survey of practicing surgeons. *Annals of Surgical Oncology*, 20: 2600-2606.
Not in PICO
- Parkyn, R. (1993) Discovering a breast lump. Management plans and pitfalls. *Australian Family Physician*, 22: 43-46.
Narrative review

- Parthasarathy, V. & Rathnam, U. (2012) Nipple discharge: an early warning sign of breast cancer. *International Journal of Preventive Medicine*, 3: 810-814.
Not in PICO
- Patel, M. R. & Whitman, G. J. (1998) Negative mammograms in symptomatic patients with breast cancer. *Academic Radiology*, 5: 26-33.
Not in PICO
- Paul, L., Iribar, M., Vilarrasa, A., Lopez, M. A., Hernandez, R. & Carrasco, A. (1995) Localization of occult breast lesions: Mammographic findings in noninfiltrating carcinoma. [Spanish]. *Radiologia*, 37: 283-289.
Not in PICO
- Paz, A., Melloul, M., Cytron, S., Koren, R., Ohana, G., Michalevich, D., Gal, R. & Wolloch, Y. (2000) The value of early and double phase ⁹⁹Tcm-sestamibi scintimammography in the diagnosis of breast cancer. *Nuclear Medicine Communications*, 21: 341-348.
Not in PICO
- Pedersen, L., Balslev, I., Guldhammer, B. & Rose, C. (1988) Repeated fine needle aspirations in the diagnosis of soft tissue metastases in breast cancer. *European Journal of Cancer and Clinical Oncology*, 24: 1039-1040.
Not in PICO
- Percudani, M., Baratta, V., Palli, D. & Dell'Anna, B. (1985) Ultrasonography and mammography in diagnosis of breast tumors. [Italian]. *Giornale Italiano di Senologia*, 6: 47-50.
Not in PICO
- Peters, M. V. (1984) "Local" treatment of early breast cancer. *Surgical Clinics of North America*, 64: 1151-1154.
Not in PICO
- Petrillo, R., Balzarini, L., Bargellini, A., Bartoli, C., Ceglia, E., Coopmans de, Y. G., Greco, M., Tess, J. D. & Musumeci, R. (1989) The role of magnetic resonance imaging in the evaluation of neoplastic lesions of the breast. *Tumori*, 75: 14-17.
Not in PICO
- Pfanzelter, R., Wulfing, U., Boedeker, B. & Heywang-Kobrunner, S. (2010) [Diagnostic image quality of mammograms in german outpatient medical care]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 182: 993-1000.
Not in PICO
- Pilz, U., Rosenkranz, G., Grosche, N. & Tellkamp, H. (1990) [Computed tomographic measurements of breast density]. [German]. *Radiologia Diagnostica*, 31: 455-458.
Not in PICO
- Pinkney, T. D., Raman, S., Piramanayagam, B. & Corder, A. P. (2007) The results of a structured diagnostic pathway designed to minimise the chance of breast cancer misdiagnosis. *European Journal of Surgical Oncology*, 33: 551-555.
Not in PICO
- Poellinger, A., Burock, S., Grosenick, D., Hagen, A., Ludemann, L., Diekmann, F., Engelken, F., Macdonald, R., Rinneberg, H. & Schlag, P. M. (2011) Breast cancer: early- and late-fluorescence near-infrared imaging with indocyanine green--a preliminary study. *Radiology*, 258: 409-416.
Not in PICO
- Poole, K. & Lyne, P. A. (2000) The 'cues' to diagnosis: describing the monitoring activities of women undergoing diagnostic investigations for breast disease. *Journal of Advanced Nursing*, 31: 752-758.
Not in PICO
- Porok, J. J., Trostle, D. R., Scarlato, M. & Rachman, R. (1983) Excisional breast biopsy and roentgenographic examination for mammographically detected microcalcification. *American Journal of Surgery*, 145: 684-686.
Not in PICO

- Prats, E., Abos, M., Aisa, F., Villavieja, L., Asenjo, M., Garcia-Lopez, F., Tomas, A., Sainz, J., Razola, P. & Banzo, J. (1998) [Gammagraphy using Tc 99m MIBI in patients with suspected breast cancer. Proposed diagnostic protocol]. [Spanish]. *Revista Espanola de Medicina Nuclear*, 17: 73-81.
Not in PICO
- Prats, E., Abos, M. D., Aisa, F., Villavieja, L., Asenjo, M. J., Garcia-Lopez, F., Tomas, A., Sainz, J. M., Razola, P. & Banzo, J. (1998) Radioisotopic scan with MIBI-(99m)Tc in patients with suspected breast cancer. Proposed diagnostic protocol. [Spanish]. *Revista Espanola de Medicina Nuclear*, 17: 73-81.
Not in PICO
- Prats, E., Aisa, F., Abos, M. D., Villavieja, L., Garcia-Lopez, F., Asenjo, M. J., Razola, P. & Banzo, J. (1999) Mammography and 99mTc-MIBI scintimammography in suspected breast cancer. *Journal of Nuclear Medicine*, 40: 296-301.
Not in PICO
- Prats, E., Banzo, J., Merono, E., Herranz, R., Carril, J. M. & SMCSTMS (2001) 99mTc-MIBI scintimammography as a complement of the mammography in patients with suspected breast cancer. A multicentre experience. *Breast*, 10: 109-116.
Not in PICO
- Preece, P. E. (1989) Sclerosing adenosis. *World Journal of Surgery*, 13: 721-725.
Not in PICO
- Prorok, J. J., Trostle, D. R., Scarlato, M. & Rachman, R. (1983) Excisional breast biopsy and roentgenographic examination for mammographically detected microcalcification. *American Journal of Surgery*, 145: 684-686.
Not in PICO
- Qiu, Y., Sridhar, M., Tsou, J. K., Lindfors, K. K. & Insana, M. F. (2008) Ultrasonic Viscoelasticity Imaging of Nonpalpable Breast Tumors. Preliminary Results. *Academic Radiology*, 15: 1526-1533.
Not in PICO
- Quigley, M. R., Fukui, O., Chew, B., Bhatia, S. & Karlovits, S. (2013) The shifting landscape of metastatic breast cancer to the CNS. *Neurosurgical Review*, 36: 377-382.
Not in PICO
- Rahbar, H., Partridge, S. C., Eby, P. R., Demartini, W. B., Gutierrez, R. L., Peacock, S. & Lehman, C. D. (2011) Characterization of ductal carcinoma in situ on diffusion weighted breast MRI. *European Radiology*, 21: 2011-2019.
Not in PICO
- Rajentheran, R., Rao, C. M., Lim, E. & Lennard, T. W. (2001) Palpable breast cancer which is mammographically invisible. *Breast*, 10: 416-420.
Not in PICO
- Raneta, O., Bella, V., Bellova, L. & Zamecnikova, E. (2013) The use of electrical impedance tomography to the differential diagnosis of pathological mammographic/sonographic findings. *Neoplasma*, 60: 647-654.
Not in PICO
- Renaud, R., Gairard, B. & Sussmann, M. (1985) The role of the general practitioner in the detection of breast cancer. [French]. *Journal de Medecine de Strasbourg*, 16: 255-259.
Narrative review
- Reyes, C., Gomez-Fernandez, C. & Nadji, M. (2012) Metaplastic and medullary mammary carcinomas do not express mammaglobin. *American Journal of Clinical Pathology*, 137: 747-752.
Not in PICO
- Rezende, M. C. R., Koch, H. A., Figueiredo, J. A. & Thuler, L. C. S. (2009) Factors leading to delay in obtaining definitive diagnosis of suspicious lesions for breast cancer in a dedicated health unit in Rio de Janeiro. [Portuguese]. *Revista Brasileira de Ginecologia e Obstetricia*, 31: 75-81.
Not in PICO

- Rissanen, T., Pamilo, M. & Suramo, I. (1998) Ultrasonography as a guidance method in the evaluation of mammographically detected nonpalpable breast lesions of suspected malignancy. *Acta Radiologica*, 39: 292-297.
Not in PICO
- Robertson, C., Ragupathy, S. K. A., Boachie, C., Fraser, C., Heys, S. D., MacLennan, G., Mowatt, G., Thomas, R. E. & Gilbert, F. J. (2011) Surveillance mammography for detecting ipsilateral breast tumour recurrence and metachronous contralateral breast cancer: A systematic review. *European Radiology*, 21: 2484-2491.
Not in PICO
- Rodrigues, P. S., Giraldo, G. A., Provenzano, M., Faria, M. D., Chang, R. F. & Suri, J. S. (2006) A new methodology based on q-entropy for breast lesion classification in 3-D ultrasound images. *Conference Proceedings: ...Annual International Conference of the IEEE Engineering in Medicine & Biology Society*, 1: 1048-1051.
Not in PICO
- Roetzheim, R. G., Ferrante, J. M., Lee, J. H., Chen, R., Love-Jackson, K. M., Gonzalez, E. C., Fisher, K. J. & McCarthy, E. P. (2012) Influence of primary care on breast cancer outcomes among Medicare beneficiaries. *Annals of Family Medicine*, 10: 401-411.
Not in PICO
- Rogulski, L. & Binczyk, J. (2013) Estimated breast cancer risk and screening outcomes among premenopausal women with non-cyclic mastalgia. *Ginekologia Polska*, 84: 754-757.
Not in PICO (secondary care)
- Rojas, M. P., Telaro, E., Russo, A., Moschetti, I., Coe, L., Fossati, R., Palli, D., del Roselli, T. M. & Liberati, A. (2005) Follow-up strategies for women treated for early breast cancer. *Cochrane database of systematic reviews (Online)*, CD001768.
Not in PICO
- Roorda, C., Berendsen, A. J., Haverkamp, M., Van Der Meer, K. & De Bock, G. H. (2013) Discharge of breast cancer patients to primary care at the end of hospital follow-up: A cross-sectional survey. *European Journal of Cancer*, 49: 1836-1844.
Not in PICO
- Rosselli Del, T. M., Ciatto, S., Bravetti, P. & Pacini, P. (1986) The significance of mammographic calcifications in early breast cancer detection. *Radiologia Medica*, 72: 7-12.
Not in PICO
- Rowan, T. (1991) Breast cancer: pathologic and prognostic evaluation. *Wisconsin Medical Journal*, 90: 679-684.
Narrative review
- Rubin, G. & Zammit, C. (2010) Breast cancer in 35 to 39 year olds and imaging: Is changing to ultrasound without mammography going to be safe? What are the workload implications? *Breast Cancer Research*, 12: S15-S16.
Not in PICO
- Ruhland, F., Heinrich, J., Budner, M. & Jeschke, A. (2000) Diagnostic value of mammography and breast ultrasound for clinically occult lesions of the breast. [German]. *Geburtshilfe und Frauenheilkunde*, 60: 104-110.
Not in PICO
- Ruhlmann, J., Oehr, P., Bender, H., Kozak, B., Willkomm, P., Schrader, M. & Biersack, H. J. (1997) [PET scan in general practice for diagnosis of breast carcinoma]. [German]. *Acta Medica Austriaca*, 24: 63-67.
Not in PICO
- Rustamadji, P. (2012) NM23HI as marker of metastasis in invasive ductal breast cancer. *Acta Medica Indonesiana*, 44: 40-46.
Not in PICO

- Sadaf, A., Crystal, P., Scaranelo, A. & Helbich, T. (2011) Performance of computer-aided detection applied to full-field digital mammography in detection of breast cancers. *European Journal of Radiology*, 77: 457-461.
Not in PICO
- Safir, J., Zito, J. L., Gershwind, M. E., Faegenburg, D., Tobin, C. E., Cayea, P. D., Wortman, W. J., Sclafani, L. M. & Maurer, V. E. (1998) Contrast-enhanced breast MRI for cancer detection using a commercially available system--a perspective. [Review] [56 refs]. *Clinical Imaging*, 22: 162-179.
Narrative review
- Saha, A., Barman, I., Dingari, N. C., McGee, S., Volynskaya, Z., Galindo, L. H., Liu, W., Plecha, D., Klein, N., Dasari, R. R. & Fitzmaurice, M. (2011) Raman spectroscopy: a real-time tool for identifying microcalcifications during stereotactic breast core needle biopsies. *Biomedical Optics Express*, 2: 2792-2803.
Not in PICO
- Saha, A., Barman, I., Dingari, N. C., Galindo, L. H., Sattar, A., Liu, W., Plecha, D., Klein, N., Dasari, R. R. & Fitzmaurice, M. (2012) Precision of Raman spectroscopy measurements in detection of microcalcifications in breast needle biopsies. *Analytical Chemistry*, 84: 6715-6722.
Not in PICO
- Saidin, N., Mat Sakim, H. A., Ngah, U. K. & Shuaib, I. L. (2013) Computer aided detection of breast density and mass, and visualization of other breast anatomical regions on mammograms using graph cuts. *Computational & Mathematical Methods in Medicine*, 2013: 205384.
Not in PICO
- Sakka, E., Prentza, A. & Koutsouris, D. (2006) Classification algorithms for microcalcifications in mammograms (Review). [Review] [28 refs]. *Oncology Reports*, 15: Spec-55.
Narrative review
- Salih, A., Webb, W. M. & Bates, T. (1999) Does open-access mammography and ultrasound delay the diagnosis of breast cancer? *Breast*, 8: 129-132.
Not in PICO
- Salzman, B., Fleegle, S. & Tully, A. S. (2012) Common breast problems. [Review]. *American Family Physician*, 86: 343-349.
Narrative review
- Samphao, S., Wheeler, A. J., Rafferty, E., Michaelson, J. S., Specht, M. C., Gadd, M. A., Hughes, K. S. & Smith, B. L. (2009) Diagnosis of breast cancer in women age 40 and younger: delays in diagnosis result from underuse of genetic testing and breast imaging. *American Journal of Surgery*, 198: 538-543.
Not in PICO
- Samuels, T. H. (1992) Mammography: Unravelling the mystery. *Canadian Family Physician*, 38: 132-140.
Narrative review
- Sankar, D. & Thomas, T. (2010) A new fast fractal modeling approach for the detection of microcalcifications in mammograms. *Journal of Digital Imaging*, 23: 538-546.
Not in PICO
- Scanlon, E. F. (1981) The early diagnosis of breast cancer. *Cancer*, 48: Suppl-6.
Narrative review
- Schairer, C., Soliman, A. S., Omar, S., Khaled, H., Eissa, S., Ayed, F. B., Khalafallah, S., Ayoub, W. B., Kantor, E. D., Merajver, S., Swain, S. M., Gail, M. & Brown, L. M. (2013) Assessment of diagnosis of inflammatory breast cancer cases at two cancer centers in Egypt and Tunisia. *Cancer Medicine*, 2: 178-184.
Not in PICO
- Schillaci, O. (2005) Is there a clinical role for scintimammography in breast cancer diagnosis? *Journal of Nuclear Medicine*, 46: 1571-1573.
Not in PICO

- Schilling, R. B., Cox, J. D. & Sharma, S. R. (1998) Advanced digital mammography. [Review] [2 refs]. *Journal of Digital Imaging*, 11: Suppl-5.
Narrative review
- Schulz-Wendtland, R., Bock, K., Aichinger, U., de, W. J., Bader, W., Albert, U. S. & Duda, V. F. (2005) [Ultrasound examination of the breast with 7.5 MHz and 13 MHz-transducers: scope for improving diagnostic accuracy in complementary breast diagnostics?]. [German]. *Ultraschall in der Medizin*, 26: 209-215.
Not in PICO
- Schulz, K.-D., Duda, V., Schreer, I. & Heywang-Kobrunner, S. H. (1997) Possibilities of early diagnosis of breast cancer. [German]. *Gynakologe*, 30: 631-636.
Narrative review
- Schulz, K.-D., Kreienberg, R., Fischer, R. & Albert, U.-S. (2003) Stage 3 recommendations - The early recognition of breast cancer in Germany. Abridged version for medical practitioners. [German]. *Radiologe*, 43: 495-502.
Guideline
- Schulz, K.-D., Koller, M., Lorenz, W., Kreienberg, R., Fischer, R., Albert, U.-S., Altland, H., Berg, D., Dietel, M., Engel, J., Fischer, J., Geraedts, M., Heywang-Kobrunner, S., Holzel, D., Kalbheim, E., Kaufmann, M., Lebeau, A., Madjar, H., Modder, U., Nass-Griegoleit, I., Prechtel, K., Schlake, W., Schreer, I., Schulz-Wendtland, R., Schumacher, G. & Steiner, M. (2004) Short version of the guideline "Early Detection of Breast Cancer in Germany". [German]. *Zeitschrift für Ärztliche Fortbildung und Qualitätssicherung*, 98: 361-373.
Guideline
- Schunemann, H., Langecker, P. J., Ellgas, W., Leonhardt, A. & Merkl, H. (1990) Value of bone scanning in the follow-up of breast cancer patients. A study of 1000 cases. *Journal of Cancer Research & Clinical Oncology*, 116: 486-491.
Not in PICO
- Scielzo, G. & Maggi, S. (1993) [Physics, dosimetry, and quality control in mammography]. [Italian]. *Radiologia Medica*, 86: 687-694.
Not in PICO
- Seyednoori, T., Pakseresht, S. & Roushan, Z. (2012) Risk of developing breast cancer by utilizing Gail model. *Women & Health*, 52: 391-402.
Not in PICO
- Shah, S. K., Shah, S. K. & Greatrex, K. V. (2005) Current role of magnetic resonance imaging in breast imaging: a primer for the primary care physician. [Review] [60 refs]. *Journal of the American Board of Family Practice*, 18: 478-490.
Not in PICO
- Shahmammadov, N. S. (2007) Possibilities of mammography in diagnostics of breast tumors. [Azerbaijani]. *Azerbaijan Medical Journal*, 141-143.
Not in PICO
- Shao, Z. M., Liu, Y. & Nguyen, M. (2001) The role of the breast ductal system in the diagnosis of cancer (review). [Review] [33 refs]. *Oncology Reports*, 8: 153-156.
Narrative review
- Shen, S.-J., Sun, Q., Xu, Y.-L., Zhou, Y.-D., Guan, J.-H., Mao, F., Lin, Y., Wang, X.-J. & Han, S.-M. (2012) Comparative analysis of early diagnostic tools for breast cancer. [Chinese]. *Chinese Journal of Oncology*, 34: 877-880.
Not in PICO
- Sheppard, D. G., Whitman, G. J., Huynh, P. T., Sahin, A. A., Fornage, B. D. & Stelling, C. B. (2000) Tubular carcinoma of the breast: mammographic and sonographic features. *AJR.American Journal of Roentgenology*, 174: 253-257.
Not in PICO

- Shkumat, N. A., Springer, A., Walker, C. M., Rohren, E. M., Yang, W. T., Adrada, B. E., Arribas, E., Carkaci, S., Chuang, H. H., Santiago, L. & Mawlawi, O. R. (2011) Investigating the limit of detectability of a positron emission mammography device: a phantom study. *Medical Physics*, 38: 5176-5185.
Not in PICO
- Sickle-Santanello, B. J., O'Dwyer, P. J., McCabe, D. P., Farrar, W. B., Minton, J. P. & James, A. G. (1987) Needle localization of mammographically detected lesions in perspective. *American Journal of Surgery*, 154: 279-282.
Not in PICO
- Sickles, E. A. (1984) Mammographic features of "early" breast cancer. *AJR.American Journal of Roentgenology*, 143: 461-464.
Narrative review
- Sickles, E. A. (1986) Mammographic features of 300 consecutive nonpalpable breast cancers. *AJR.American Journal of Roentgenology*, 146: 661-663.
Not in PICO
- Sidiropoulos, K. P., Kostopoulos, S. A., Glotsos, D. T., Athanasiadis, E. I., Dimitropoulos, N. D., Stonham, J. T. & Cavouras, D. A. (2013) Multimodality GPU-based computer-assisted diagnosis of breast cancer using ultrasound and digital mammography images. *International Journal of Computer Assisted Radiology & Surgery*, 8: 547-560.
Not in PICO
- Silliman, R. A. (2009) When cancer in older adults is undermanaged: the breast cancer story. *Journal of the American Geriatrics Society*, 57: Suppl-61.
Not in PICO
- Silverstein, M. J. (1997) Recent advances. Diagnosis and treatment of early breast cancer. [Review] [37 refs]. *BMJ*, 314: 1736-1739.
Narrative review
- Singh-Ranger, G. & Mokbel, K. (2004) The sentinel node biopsy is a new standard of care for patients with early breast cancer. *International journal of fertility and women's medicine*, 49: 225-227.
Not in PICO
- Sivaramakrishna, R. (2005) Foreword: Imaging techniques alternative to mammography for early detection of breast cancer. *Technology in Cancer Research and Treatment*, 4: 1-3.
Narrative review
- Sizilio, G. R., Leite, C. R., Guerreiro, A. M. & Neto, A. D. (2012) Fuzzy method for pre-diagnosis of breast cancer from the Fine Needle Aspirate analysis. *Biomedical Engineering Online*, 11: 83.
Not in PICO
- Sziopikou, K. P., Jokich, P. & Cobleigh, M. (2011) Pathologic findings in MRI-guided needle core biopsies of the breast in patients with newly diagnosed breast cancer. *International Journal of Breast Cancer*, 1.
Not in PICO
- Skaane, P., Karesen, R., Jacobsen, U., Amlie, E., Sauer, T. & Skjorten, F. (1995) [Investigation of palpable breast tumours. Patient flow and quality assessment of the tripple diagnostic procedure]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 115: 1965-1969.
Narrative review
- Slubowski, T., Slubowska, M. & Wojciechowski, A. (2007) [Diagnostic techniques in breast cancer detection. Part III. The new cytobiological methods]. [Review] [33 refs] [Polish]. *Ginekologia Polska*, 78: 554-559.
Narrative review
- Slubowski, T., Slubowska, M. & Wojciechowski, A. (2007) [Diagnostic techniques in breast cancer detection. Part II: Physical and biopsy methods]. [Review] [37 refs] [Polish]. *Ginekologia Polska*, 78: 479-483.
Narrative review

- Slubowski, T., Slubowska, M. & Wojciechowski, A. (2007) [Diagnostic techniques in breast cancer detection. Part I: imaging methods and their modifications]. [Review] [35 refs] [Polish]. *Ginekologia Polska*, 78: 388-392.
Narrative review
- Smetherman, D., Dydynski, P. & Jackson, P. (2007) Effect of breast core needle biopsy technique on detection of lobular intraepithelial neoplasia. *Ochsner Journal*, 7: 121-124.
Not in PICO
- Smith-Behn, J. & Ghani, A. (1987) Non-palpable breast lesions: out-patient needle localization and biopsy. *Postgraduate Medical Journal*, 63: 17-18.
Not in PICO
- Smith-Bindman, R. (2004) Diagnostic imaging in the differential diagnosis of vaginal bleeding and breast mass. *Advanced Studies in Medicine*, 4: 476-482.
Narrative review
- Smith, J. L., Hawver, M., Crabtree, B., Falk, R., Davis, C. & Paulman, A. (1996) Nebraska family physician approaches to mammograms. *The Nebraska medical journal*, 81: 58-62.
Not in PICO
- Smith, M. J., Heffron, C. C., Rothwell, J. R., Loftus, B. M., Jeffers, M. & Geraghty, J. G. (2012) Fine needle aspiration cytology in symptomatic breast lesions: still an important diagnostic modality? *Breast Journal*, 18: 103-110.
Not in PICO
- Snell, M. J., Ostrow, L. B., DuBois, J. J., Boyle, L. M. & Calfee, L. W. (1992) Needle-localized biopsy of occult breast lesions: an update. *Military Medicine*, 157: 61-64.
Not in PICO
- Sohns, C., Angic, B., Sossalla, S., Konietschke, F. & Obenauer, S. (2010) Computer-assisted diagnosis in full-field digital mammography--results in dependence of readers experiences. *Breast Journal*, 16: 490-497.
Not in PICO
- Solin, L. J., Fowble, B. & Martz, K. (1986) Results of re-excisional biopsy of the primary tumor in preparation for definitive irradiation of patients with early stage breast cancer. *International Journal of Radiation Oncology Biology Physics*, 12: 721-725.
Not in PICO
- Sterns, E. E. (1996) Relation between clinical and mammographic diagnosis of breast problems and the cancer/biopsy rate. *Canadian Journal of Surgery*, 39: 128-132.
Not in PICO
- Stoekelhuber, B. M. & Fischer, D. (2006) Current guidelines for interventional procedures in breast biopsy. [German]. *Gynakologe*, 39: 533-537.
Guideline
- Stomper, P. C., Davis, S. P., Weidner, N. & Meyer, J. E. (1988) Clinically occult, noncalcified breast cancer: serial radiologic-pathologic correlation in 27 cases. *Radiology*, 169: 621-626.
Not in PICO
- Stomper, P. C., Nava, M. E., Budnick, R. M. & Stewart, C. C. (1997) Specimen mammography-guided fine-needle aspirates of clinically occult benign and malignant lesions. Analysis of cell number and type. *Investigative Radiology*, 32: 277-281.
Not in PICO
- Stone, N., Baker, R., Rogers, K., Parker, A. W. & Matousek, P. (2007) Subsurface probing of calcifications with spatially offset Raman spectroscopy (SORS): future possibilities for the diagnosis of breast cancer. *Analyst*, 132: 899-905.
Not in PICO
- Stravodimou, A. & Voutsadakis, I. A. (2013) Pretreatment thrombocytosis as a prognostic factor in metastatic breast cancer. *International Journal of Breast Cancer*, 2013.
Not in PICO

- Stuver, S. O., Zhu, J., Simchowitz, B., Hassett, M. J., Shulman, L. N. & Weingart, S. N. (2011) Identifying women at risk of delayed breast cancer diagnosis. *Joint Commission Journal on Quality & Patient Safety*, 37: 568-575.
Not in PICO
- Sun, Z., Liang, H. & Xu, H. (2005) Relationship between the full-field digital mammographic features and clinicopathologic characteristics in 178 cases with breast cancer. [Chinese]. *Chinese Journal of Clinical Oncology*, 32: 928-931.
Not in PICO
- Sutton, S. M. & Doner, L. D. (1992) Insights into the physician's role in mammography utilization among older women. *Womens Health Issues*, 2: 175-179.
Narrative review
- Szabo-Moskal, J., Lasek, W., Kozłowska, R., Sir, J. & Serafin, Z. (2005) The role of preoperative hooked-wire localization of occult lesions for early detection of breast cancer. [Polish]. *Ginekologia Polska*, 76: 15-19.
Not in PICO
- Szynglarewicz, B., Kasprzak, P., Kornafel, J., Forgacz, J., Pudelko, M., Majewski, A. & Matkowski, R. (2011) Duration time of vacuum-assisted biopsy for nonpalpable breast masses: comparison between stereotactic and ultrasound-guided procedure. *Tumori*, 97: 517-521.
Not in PICO
- Tadin, T. (2006) Breast diseases in general practice - Challenges of the future. *Proceedings of the XIV World Congress on Breast Diseases*, 15-19.
Narrative review
- Taggart, F., Donnelly, P. & Dunn, J. (2012) Options for early breast cancer follow-up in primary and secondary care - a systematic review. *BMC Cancer*, 12: 238.
Not in PICO
- Taibi, A. (2009) Generalized subtraction methods in digital mammography. [Review] [46 refs]. *European Journal of Radiology*, 72: 447-453.
Narrative review
- Takasaki, T., Akiba, S., Sagara, Y. & Yoshida, H. (1998) Histological and biological characteristics of microinvasion in mammary carcinomas ≤ 2 cm in diameter. *Pathology International*, 48: 800-805.
Not in PICO
- Takatsuka, Y., Imamoto, H. & Kawahara, T. (1983) Usefulness of ultrasonography for the diagnosis of early breast cancer. [Japanese]. *IRYO - Japanese Journal of National Medical Services*, 37: 1170-1173+1152.
Not in PICO
- Tang, J., Rangayyan, R. M., Xu, J., El, N., I & Yang, Y. (2009) Computer-aided detection and diagnosis of breast cancer with mammography: recent advances. [Review] [154 refs]. *IEEE Transactions on Information Technology in Biomedicine*, 13: 236-251.
Narrative review
- Taylor, K., Ames, V. & Wallis, M. (2013) The diagnostic value of clinical examination and imaging used as part of an age-related protocol when diagnosing male breast disease: An audit of 1141 cases from a single centre. *Breast*, 22: 268-272.
Not in PICO (secondary care)
- Tesfamariam, A., Gebremichael, A. & Mufunda, J. (2013) Breast cancer clinicopathological presentation, gravity and challenges in Eritrea, East Africa: management practice in a resource-poor setting. *South African Medical Journal.Suid-Afrikaanse Tydskrif Vir Geneeskunde*, 103: 526-528.
Not in PICO
- Tian, J.-W., Chen, Y. & Liu, Y.-J. (2006) Diagnostic value of high frequency ultrasound combined with mammography for early breast cancer. [Chinese]. *Chinese Journal of Medical Imaging*

- Technology*, 22: 557-559.
In Chinese. Not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Tillman, G. F., Orel, S. G., Schnall, M. D., Schultz, D. J., Tan, J. E. & Solin, L. J. (2002) Effect of breast magnetic resonance imaging on the clinical management of women with early-stage breast carcinoma. *Journal of Clinical Oncology*, 20: 3413-3423.
Not in PICO
- Torrington, M. L., Frydenberg, M., Hansen, R. P., Olesen, F. & Vedsted, P. (2013) Evidence of increasing mortality with longer diagnostic intervals for five common cancers: A cohort study in primary care. *European Journal of Cancer*, 49: 2187-2198.
Not in PICO
- Townsend, C. M., Jr. (1980) Breast lumps. [Review] [11 refs]. *Clinical Symposia*, 32: 1-32.
Narrative review
- Trecate, G., Tess, J. D., Vergnaghi, D., Bergonzi, S., Mariani, G., Ferraris, C. & Musumeci, R. (2001) Lobular breast cancer: how useful is breast magnetic resonance imaging? *Tumori*, 87: 232-238.
Not in PICO
- Trufelli, D. C., Miranda, V. C., Santos, M. B., Fraile, N. M., Pecoroni, P. G., Gonzaga, S. F., Riechelmann, R., Kaliks, R. & Del, G. A. (2008) [Analysis of delays in diagnosis and treatment of breast cancer patients at a public hospital]. [Portuguese]. *Revista da Associação Médica Brasileira*, 54: 72-76.
Not in PICO
- Tsoi, D., Holloway, C., Bordeleau, L., Brezden-Masley, C., Causer, P. & Warner, E. (2011) Willingness of breast cancer survivors to participate in a randomized controlled trial of digital mammography with or without MRI as breast cancer surveillance: a feasibility study. *Breast*, 20: 96-98.
Not in PICO
- Tsouskas, L. I., Rankin, S. & Fentiman, I. S. (1991) The role of mammography in the diagnosis of breast cancer in women aged 35-40. *Breast Disease*, 4: 193-196.
Not in PICO
- Tukel, S. & Ozcan, H. (1996) Mammography in men with breast cancer: Review of the mammographic findings in five cases. *Australasian Radiology*, 40: 387-390.
Not in PICO
- Twelves, D., Nerurkar, A., Osin, P., Ward, A., Isacke, C. M. & Gui, G. P. (2012) The anatomy of fluid-yielding ducts in breast cancer. *Breast Cancer Research & Treatment*, 132: 555-564.
Not in PICO
- Twomey, M., Hayes, S., Browne, T. J., Duddy, L. & Smiddy, P. (2011) Assessment of the axilla in primary operable breast carcinoma. *Breast Cancer Research*, 13: S13.
Not in PICO
- Ueno, E., Tohno, E., Tsunoda-Shimizu, H., Aiyoshi, Y., Morishima, I., Ishikawa, T., Fukasawa, M., Yazawa, T. & Yashiro, T. (1994) [Clinical diagnosis of early breast cancer]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 21: Suppl-7.
Not in PICO
- Ukwenya, A. Y., Yusufu, L. M., Nmadu, P. T., Garba, E. S. & Ahmed, A. (2008) Delayed treatment of symptomatic breast cancer: the experience from Kaduna, Nigeria. *South African Journal of Surgery*, 46: 106-110.
Not in PICO
- Ulery, M., Carter, L., McFarlin, B. L. & Giurgescu, C. (2009) Pregnancy-associated breast cancer: significance of early detection. *Journal of Midwifery & Women's Health*, 54: 357-363.
Narrative review
- Uriarte, I., Carril, J. M., Quirce, R., Gutierrez-Mendiguchia, C., Blanco, I., Banzo, I., Vega, A. & Hernandez, A. (1998) Optimization of X-ray mammography and technetium-99m methoxyisobutylisonitrile scintimammography in the diagnosis of non-palpable breast lesions.

- European Journal of Nuclear Medicine*, 25: 491-496.
Not in PICO
- Usmani, S., Khan, H. A., Javed, A., Al, M. S., Al Huda, F. A. & Al, S., I (2008) Functional breast imaging with Tc 99m Mibi for detection of primary breast lesion and axillary lymph node metastases. *The gulf journal of oncology*.(4):52-7, 2008 Jul., 52-57.
Not in PICO
- Vachon, C. M., van Gils, C. H., Sellers, T. A., Ghosh, K., Pruthi, S., Brandt, K. R. & Pankratz, V. S. (2007) Mammographic density, breast cancer risk and risk prediction. *Breast Cancer Research*, 9.
Narrative review
- Van Den Bosch, H., Seynaeve, P., Kockx, M. M. & Storms, J. L. (1990) Radiological guidelines for the detection of early breast cancer: A review. *Journal Belge de Radiologie*, 73: 339-356.
Narrative review
- van, B. S., V, Nederend, J., Voogd, A. C., Coebergh, J. W., van, B. M., Jansen, F. H., Louwman, W. J. & Duijm, L. E. (2013) Trends in breast biopsies for abnormalities detected at screening mammography: a population-based study in the Netherlands. *British Journal of Cancer*, 109: 242-248.
Not in PICO
- van, H. M., Elske, v. d. A., van de Velde, C. J. H., Scholten, A. N. & Hille, E. T. M. (2012) Costs of different follow-up strategies in early breast cancer: A review of the literature. *Breast*, 21: 693-700.
Not in PICO
- Van, S. A. & Van, O. C. (1995) [Mammographic symptomatology of malignant breast lesions]. [Dutch]. *Journal Belge de Radiologie*, 78: 18-23.
Narrative review
- Vanovcanova, L., Lehotska, V. & Rauova, K. (2010) Digital mammography--a new trend in breast carcinoma diagnostics. *Bratislavske Lekarske Listy*, 111: 510-513.
Not in PICO (screening)
- Vennin, P., Belkacemi, Y. & Chauvet, M. P. (2008) [Follow-up of patients treated for localized invasive breast carcinoma]. [Review] [38 refs] [French]. *Gynecologie, Obstetrique & Fertilité*, 36: 183-189.
Not in PICO
- Vercauteren, L. D., Kessels, A. G., van der Weijden, T., Severens, J. L., van Engelshoven, J. M. & Flobbe, K. (2010) Association between guideline adherence and clinical outcome for patients referred for diagnostic breast imaging. *Quality & Safety in Health Care*, 19: 503-508.
Not in PICO
- Vetshev, P. S., Shkrob, O. S., Kuznetsov, N. S., Lotov, A. N., Kulezneva, I. & Beltsevich, D. G. (1995) [Ultrasound diagnosis of breast nodules]. [Russian]. *Khirurgiia*.(1):8-11, 1995 Jan., 8-11.
Not in PICO
- Vetshev, P. S., Shkrob, O. S., Kuznetsov, N. S., Lotov, A. N., Kulezneva, Y. & Beltsevich, D. G. (1995) Ultrasonic diagnosis of nodular new growths in the breast. [Russian]. *Khirurgiya*, 71: 8-11.
Not in PICO
- Villanueva-Meyer, J., Leonard, J., Briscoe, E., Cesani, F., Ali, S. A., Rhoden, S., Hove, M. & Cowan, D. (1996) Mammoscintigraphy with technetium-99m-sestamibi in suspected breast cancer. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine*, 37: 926-930.
Not in PICO
- Volcy, J. (2003) Breast cancer: diagnosis and treatment. *Ethnicity & Disease*, 13: Suppl-41.
Narrative review
- von, L. G., Duda, V., Eulenburg, R., Hackeloer, B. J. & Huneke, B. (1984) [Possibilities and limits of the early diagnosis of breast cancer using ultrasound mammography]. [German]. *Rontgenpraxis*, 37: 62-65.
Narrative review

- Vural, G., Atasever, T., Ozdemir, A., Oznur, I., Karabacak, N. I., Gokcora, N., Isik, S. & Unlu, M. (1997) 201Tl scintigraphy in the evaluation of palpable and nonpalpable breast lesions: correlation with mammography and ultrasonography. *Nuclear-Medizin*, 36: 282-288.
Not in PICO
- Vural, G., Unlu, M., Atasever, T., Ozur, I., Ozdemir, A. & Gokcora, N. (1997) Comparison of indium-111 octreotide and thallium-201 scintigraphy in patients mammographically suspected of having breast cancer: preliminary results. *European Journal of Nuclear Medicine*, 24: 312-315.
Not in PICO
- Walker, E. (1987) Mammography. Linking the referring physician. *Administrative Radiology*, 6: 16-18.
Narrative review
- Walker, R. A., Dearing, S. J. & Brown, L. A. (1999) Comparison of pathological and biological features of symptomatic and mammographically detected ductal carcinoma in situ of the breast. *Human Pathology*, 30: 943-948.
Not in PICO
- Wallis, M. G., Walsh, M. T. & Lee, J. R. (1991) A review of false negative mammography in a symptomatic population. *Clinical Radiology*, 44: 13-15.
Not in PICO
- Wang, J., Wang, X., Liang, J. W., Gao, J. D. & Bai, X. F. (2007) [Clinical application of localized biopsy on breast microcalcification]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]*, 45: 881-882.
Not in PICO
- Wang, L. C., Sullivan, M., Du, H., Feldman, M. I. & Mendelson, E. B. (2013) US appearance of ductal carcinoma in situ. [Review]. *Radiographics*, 33: 213-228.
Narrative review
- Wang, L. C., Sullivan, M., Du, H., Feldman, M. I. & Mendelson, E. B. (2013) US appearance of ductal carcinoma in situ. *Radiographics*, 33: 213-228.
Narrative review
- Wang, X., Chao, L., Chen, L., Ma, G., Jin, G., Hua, M. & Zhou, G. (2010) The mammographic correlations with Basal-like phenotype of invasive breast cancer. *Academic Radiology*, 17: 333-339.
Not in PICO
- Wang, Y. (2010) [A new approach to mammogram detection by using morphological and laplacian-of-a-gaussian filter]. [Chinese]. *Shengwu Yixue Gongchengxue Zazhi/Journal of Biomedical Engineering*, 27: 907-911.
Not in PICO
- Watanabe, S. (1988) [Mammographic detection of early breast cancer]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1378-1387.
Narrative review
- Wauters, C. A., Sanders-Eras, M. C., de Kievit-van der Heijden IM, Wesseling, P., Venderink, D. J., van Dijk, A. R., van den Wildenberg, F., Kooistra, B. W. & Strobbe, L. J. (2010) Modified core wash cytology (CWC), an asset in the diagnostic work-up of breast lesions. *European Journal of Surgical Oncology*, 36: 957-962.
Not in PICO
- Waxman, A. D. (1997) The role of (99m)Tc methoxyisobutylisonitrile in imaging breast cancer. [Review] [75 refs]. *Seminars in Nuclear Medicine*, 27: 40-54.
Narrative review
- Weinstock, C., Bigenwald, R., Hochman, T., Sun, P., Narod, S. A. & Warner, E. (2012) Outcomes of surveillance for contralateral breast cancer in patients less than age 60 at the time of initial diagnosis. *Current Oncology*, 19: e160-e164.
Not in PICO

- Weiss, M., Meyer, M., Siegert, S., Bartenstein, P. & Pfluger, T. (2013) [Metastases in patients with breast cancer despite of negative sentinel lymph node. Has the concept to be changed?]. [German]. *Nuclear-Medizin*, 52: 14-20.
Not in PICO
- Welch, S. T., Babcock, D. S. & Ballard, E. T. (2004) Sonography of pediatric male breast masses: Gynecomastia and beyond. *Pediatric Radiology*, 34: 952-957.
Not in PICO
- Wiener, J. I., Schilling, K. J., Adami, C. & Obuchowski, N. A. (2005) Assessment of suspected breast cancer by MRI: a prospective clinical trial using a combined kinetic and morphologic analysis. *AJR.American Journal of Roentgenology*, 184: 878-886.
Not in PICO
- Wilczek, B., Aspelin, P., Bone, B., Pegerfalk, A., Frisell, J. & Danielsson, R. (2003) Complementary use of scintimammography with 99m-Tc-MIBI to triple diagnostic procedure in palpable and non-palpable breast lesions. *Acta Radiologica*, 44: 288-293.
Not in PICO
- Wilhelm, M. C., Edge, S. B., Cole, D. D., DeParedes, E. & Frierson, J. (1991) Nonpalpable invasive breast cancer. *Annals of Surgery*, 213: 600-605.
Not in PICO
- Winslet, M. C. & Obeid, M. L. (1994) Submammary approach for the excision of mammographically localised lesions of the breast. *European Journal of Surgery*, 160: 209-211.
Not in PICO
- Wu, Y.-H., Chen, F.-Y., Ouyang, H.-Y. & Wang, S.-M. (2008) Clinical diagnosis of breast cancer with nonpalpable tumor. [Chinese]. *Journal of Central South University (Medical Sciences)*, 33: 861-864.
Not in PICO
- Wu, Y. P., Cai, P. Q., Zhang, W. Z., Tang, J., Gu, Y. K., Li, L., Ouyang, Y., He, J. H. & Lin, H. G. (2004) [Clinical evaluation of three methods of fine-needle aspiration, large-core needle biopsy and frozen section biopsy with focus staining for non-palpable breast disease]. [Chinese]. *Aizheng*, 23: 346-349.
Not in PICO
- Xiao, C., Polomano, R. & Bruner, D. W. (2013) Comparison between patient-reported and clinician-observed symptoms in oncology. *Cancer Nursing*, 36: E1-E16.
Not in PICO
- Xie, Y., Guo, B., Xu, L., Li, J. & Stoica, P. (2006) Multistatic adaptive microwave imaging for early breast cancer detection. *IEEE Transactions on Biomedical Engineering*, 53: 1647-1657.
Not in PICO
- Yamaguchi, R., Tsuchiya, S. I., Koshikawa, T., Ishihara, A., Masuda, S., Maeda, I., Takimoto, M., Kawamoto, M., Satoh, H., Narita, M., Itoh, H., Kitamura, T., Tsuda, Y., Ogane, N., Abe, E., Ikeda, K., Nakamura, T., Kamaguchi, H. & Tokoro, Y. (2012) Diagnostic accuracy of fine-needle aspiration cytology of the breast in Japan: report from the Working Group on the Accuracy of Breast Fine-Needle Aspiration Cytology of the Japanese Society of Clinical Cytology. *Oncology Reports*, 28: 1606-1612.
Not in PICO
- Yang, W. T. & Tse, G. M. (2004) Sonographic, mammographic, and histopathologic correlation of symptomatic ductal carcinoma in situ. *AJR.American Journal of Roentgenology*, 182: 101-110.
Not in PICO
- Yong, W. S., Chia, K. H., Poh, W. T. & Wong, C. Y. (1999) A comparison of trucut biopsy with fine needle aspiration cytology in the diagnosis of breast cancer. *Singapore Medical Journal*, 40: 587-589.
Not in PICO

Youk, J. H., Jung, I., Kim, E. K., Kim, M. J., Son, E. J., Moon, H. J. & Kwak, J. Y. (2012) US follow-up protocol in concordant benign result after US-guided 14-gauge core needle breast biopsy. *Breast Cancer Research & Treatment*, 132: 1089-1097.

Not in PICO

Zadelis, S. & Houssami, N. (2003) Mammographic features of breast cancer in young symptomatic women. *Australasian Radiology*, 47: 404-408.

Not in PICO

Zerm, C. (2004) A plea for individual care of patients with breast cancer - Point of view of the general practitioner. [German]. *Deutsche Zeitschrift für Onkologie*, 36: 31-34.

Not in PICO

Zhang, F., Kaufman, H. L., Deng, Y. & Drabier, R. (2013) Recursive SVM biomarker selection for early detection of breast cancer in peripheral blood. *BMC Medical Genomics [Electronic Resource]*, 6: Suppl.

Not in PICO

Zhao, J.-Q., He, J. & Zhang, J.-Q. (2009) Multi-mode ultrasound analysis of male breast cancer. [Chinese]. *Academic Journal of Second Military Medical University*, 30: 917-920.

Not in PICO

Zhu, Q., Huang, M., Chen, N., Zarfos, K., Jagjivan, B., Kane, M., Hedge, P. & Kurtzman, S. H. (2003) Ultrasound-guided optical tomographic imaging of malignant and benign breast lesions: initial clinical results of 19 cases. *Neoplasia (New York)*, 5: 379-388.

Not in PICO

Zylka-Menhorn, V. (2007) Increase of diagnostic accuracy rate with MRI for early forms of breast cancer. [German]. *Deutsches Arzteblatt*, 104: A2326-A2327.

Narrative review/Not in PICO

GYNAECOLOGICAL CANCERS

ENDOMETRIAL CANCER

Review question:

What is the risk of endometrial cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

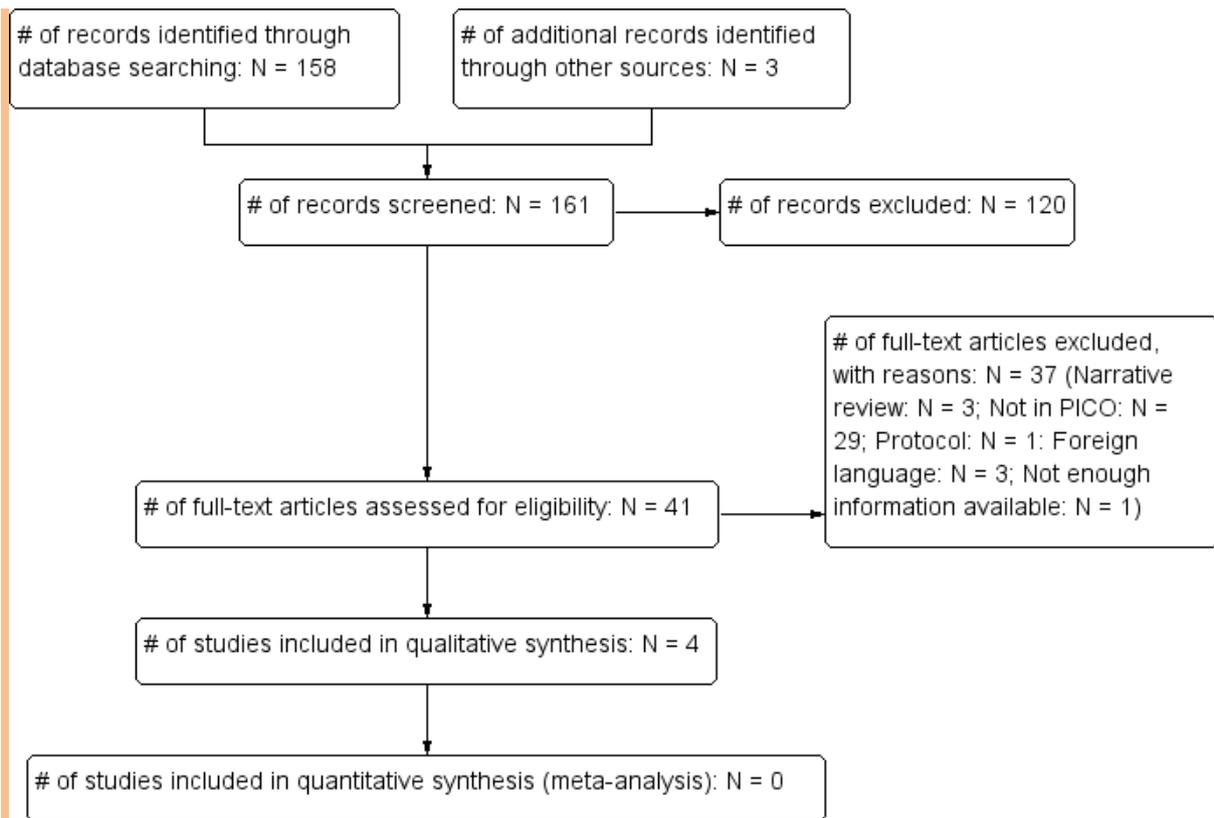
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	849	63	12/04/2013
<i>Premedline</i>	All-2012	24	3	12/04/2013
<i>Embase</i>	All-2012	2855	111	15/04/2013
<i>Cochrane Library</i>	All-2012	565	3	15/04/2013
<i>Psychinfo</i>	All-2012	5	0	12/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	259	9	16/04/2013

Total References retrieved (after de-duplication): 144

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-13/08/2014	41	2	13/08/2014
<i>Premedline</i>	4/2013-13/08/2014	32	7	13/08/2014
<i>Embase</i>	4/2013-13/08/2014	196	6	13/08/2014
<i>Cochrane Library</i>	4/2013-13/08/2014	81	0	13/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	4/2013-13/08/2014	14	1	13/08/2014

Total References retrieved (after de-duplication): 14



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included studies in the figure below. The main issues to note are that one of the studies was conducted in a Dutch primary care setting, which may limit the applicability of the result to UK primary care and this study may also not have accounted for all the patients. Moreover, another study employed a case-control design which has been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors of the study may have gone some way in counteracting this influence. Finally, the population in one of the studies comprises a mix of 'old' and 'new' investigated or uninvestigated symptoms, and it is unclear how directly applicable this sample is to the current question.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Droogendijk (2011)	+	+	+	?	?	+	+
Hallissey (1990)	+	+	+	+	?	+	+
Parker (2007)	+	+	+	+	+	+	+
Walker (2013)	-	+	+	+	+	+	+

● -	High	● ?	Unclear	● +	Low
-----	------	-----	---------	-----	-----

Study results

Table 1: Endometrial cancer: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI)
Walker (2013)	Abdominal pain (first presentation to GP)	Women ≥ 55 years	0.1 (0.1-0.1)
Walker (2013)	Abdominal pain (repeated symptom)	Women ≥ 55 years	0.2 (0.1-0.1) <i>As reported, but CI is not correct</i>
Hallissey (1990)	Dyspepsia	All patients	0.04 (0.002-0.25) 1/2585
Walker (2013)	Haematuria (first presentation to GP)	Women ≥ 55 years	0.7 (0.5-1)
Walker (2013)	Vaginal discharge (first presentation to GP)	Women ≥ 55 years	1.1 (0.8-1.5)
Parker (2007)	Post-menopausal bleeding	All women	1.7 (1.4-2) 170/10122
		Women 40-44 years	0 (0-5.9) 0/77
		Women 45-54 years	0.3 (0.2-0.7) 10/2896
		Women 55-64 years	1.1 (0.9-1.5) 49/4278
		Women 65-74 years	3.1 (2.4-4.1) 54/1718
		Women 75-84 years	5.4 (4-7.2) 46/856
		Women ≥ 85 years	3.7 (2-6.7) 11/297
Walker (2013)	Post-menopausal bleeding (first presentation to GP)	Women ≥ 55 years	4 (3.2-5.2)
Walker (2013)	Post-menopausal bleeding (repeated symptom)	Women ≥ 55 years	9.6 (6.2-17.8)
Droogendijk	Anaemia	All women	0.63 (0.03-4.01) 1/158
Walker (2013)	Low haemoglobin (test)	Women ≥ 55 years	0.1 (0.1-0.1)
Walker (2013)	High platelets (test)	Women ≥ 55 years	0.1 (0.1-0.1)
Walker (2013)	High glucose (test)	Women ≥ 55 years	0.1 (0.1-0.2)

Walker (2013) calculated the positive predictive values using Bayesian statistics.

Table 2: Endometrial cancer: Symptom combinations

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI)
Walker (2013)	Post-menopausal bleeding + haematuria	Women ≥ 55 years	9.1 (NR)

Walker (2013)	Post-menopausal bleeding + vaginal discharge	Women ≥ 55 years	8.3 (NR)
Walker (2013)	Post-menopausal bleeding + abdominal pain	Women ≥ 55 years	2.9 (1.6-5.7)
Walker (2013)	Post-menopausal bleeding + low haemoglobin (test)	Women ≥ 55 years	6.4 (NR)
Walker (2013)	Post-menopausal bleeding + high platelets (test)	Women ≥ 55 years	5.4 (3.1-10.2)
Walker (2013)	Post-menopausal bleeding + high glucose (test)	Women ≥ 55 years	3.4 (1.3-9.5)
Walker (2013)	Abdominal pain + haematuria	Women ≥ 55 years	0.7 (NR)
Walker (2013)	Abdominal pain + vaginal discharge	Women ≥ 55 years	0.5 (0.2-1.3)
Walker (2013)	Abdominal pain + low haemoglobin (test)	Women ≥ 55 years	0.2 (0.1-0.4)
Walker (2013)	Abdominal pain + high platelets (test)	Women ≥ 55 years	0.1 (0.1-0.2)
Walker (2013)	Abdominal pain + high glucose (test)	Women ≥ 55 years	0.3 (0.1-0.5)
Walker (2013)	Vaginal discharge + haematuria	Women ≥ 55 years	2.2 (NR)
Walker (2013)	Vaginal discharge + low haemoglobin (test)	Women ≥ 55 years	0.6 (NR)
Walker (2013)	Vaginal discharge + high platelets (test)	Women ≥ 55 years	1.4 (NR)
Walker (2013)	Vaginal discharge + high glucose (test)	Women ≥ 55 years	0.6 (NR)
Walker (2013)	Haematuria + low haemoglobin (test)	Women ≥ 55 years	2.7 (NR)
Walker (2013)	Haematuria + high platelets (test)	Women ≥ 55 years	1.9 (NR)
Walker (2013)	Haematuria + high glucose (test)	Women ≥ 55 years	1.1 (NR)
Walker (2013)	Low haemoglobin (test) + high glucose (test)	Women ≥ 55 years	0.2 (0.1-0.2)
Walker (2013)	Low haemoglobin (test) + high platelets (test)	Women ≥ 55 years	0.1 (0.1-0.2)
Walker (2013)	High platelets (test) + high glucose (test)	Women ≥ 55 years	0.1 (0.1-0.2)

Walker (2013) calculated the positive predictive values using Bayesian statistics. NR = not reported.

Evidence statement(s):

For uterine cancer the positive predictive values of single symptoms (4 studies, N = 25134) presenting in primary care ranged from 0% (for post-menopausal bleeding in women aged 40-44

years) to 9.6% (for repeated post-menopausal bleeding). The included studies were associated with 0-2 bias/applicability concerns (see also Table 1).

For uterine cancer the positive predictive values of symptom combinations (1 study, N = 12269) presenting in primary care ranged from 0.1% (for high platelets in combination with either abdominal pain, low haemoglobin or high glucose) to 9.1% (for post-menopausal bleeding combined with haematuria). The included study was associated with 1 bias concern (see also Table 2).

Evidence tables

Droogendijk (2011)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective peripheral hospital laboratory database study serving 265 GPs in Dordrecht (Holland).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 287; 129 men, 158 women; median (range) age = 70 (19-87) years. <u>Inclusion criteria:</u> All women aged > 50 years and all men aged ≥ 18 years who between January 2004 and December 2005 were diagnosed with iron-deficiency anaemia (haemoglobin < 13.7 g/dl in men and < 12.1 g/dl in women, and a serum ferritin level < 25 µg/l for men and < 20 µg/l for women). <u>Exclusion criteria:</u> Patients with a known history of iron-deficiency anaemia in the previous 2 years, a history of gastrointestinal malignancy or congenital haemoglobinopathy. <u>Clinical setting:</u> GPs in Holland
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	New onset iron-deficiency anaemia (haemoglobin < 13.7 g/dl in men and < 12.1 g/dl in women, and a serum ferritin level < 25 µg/l for men and < 20 µg/l for women).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy and 12-month follow up.

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	It is unclear if all patients are accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Unclear
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk
NOTES	In addition to the 24 patients with colorectal cancer, 3 patients had gastric cancer, 1 patient had oesophageal cancer and 1 patient had locally invasive endometrial cancer.
Hallissey (1990)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive patient series from a group of 10 general practices in England.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia. <u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, England.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia of any degree
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes

Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	2659 patients were seen and 2585 attended for investigation
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), carcinomatosis of unknown primary (7).

Parker (2007)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	Rectal bleeding: N = 29007 (13931, males, 15076 females); median age (inter-quartile range) = 54 (40-69) years. Post-menopausal bleeding: N = 10122 (10122 females); median age (inter-quartile range) = 58 (54-67) years.

	<p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system before 1 April 1998 and had complete data up to 1 April 2005. Patients were included if they were registered with an eligible practice at any time between 1 April 1998 and 31 March 2003, had been registered with the practice for ≥ 12 months and had a first-ever consultation for rectal bleeding and were aged ≥ 25 years, or post-menopausal bleeding and were aged ≥ 40 years, between 1 April 1998 and 31 March 2003.</p> <p><u>Exclusion criteria:</u> Previous record of colorectal cancer (for patients presenting with rectal bleeding) and endometrial cancer (for patients presenting with post-menopausal bleeding)</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	First ever presentation of rectal bleeding, first ever presentation of post-menopausal bleeding.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up (relevant cancer for rectal bleeding was colorectal cancer; relevant cancer for post-menopausal bleeding was endometrial cancer).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

NOTES	
Walker (2013)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Matched case-control study using patients in the UK's General Practice Research Database (GPRD).
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> N = 2732; median number of consultations in the year before the index date = 14 (IQR = 9-21); median number of consultations in the 6 months before the index date = 9 (IQR = 6-14); median age at diagnosis = 67 (IQR = 59-75); UK.</p> <p><u>Controls:</u> N = 9537; median number of consultations in the year before the index date = 8 (IQR = 4-14); median number of consultations in the 6 months before the index date = 4 (IQR = 2-8); UK.</p> <p><u>Inclusion criteria:</u> Cases: A list of 30 uterine tumour diagnostic codes was collated from the GPRD master code library, all mapping to Read Codes within the B43..00 tree for uterine cancer. Codes relating to cervical cancer were omitted. All women aged ≥40 years with one of these codes, diagnosed between 1 January 2000 and 31 December 2009, were identified. The date of the first cancer code in the records was taken to be the date of diagnosis; this was labelled the index date. Controls: For each case, five controls, matched to the case by year of birth, sex, and practice, were randomly selected, using a computer-generated sequence. The matched controls were assigned the index date of their case.</p> <p><u>Exclusion criteria:</u> The following exclusion criteria were applied: Cases with <1 year of data meeting GPRD quality standards before the first diagnostic code; leiomyosarcoma (the GPRD had ascribed all leiomyosarcomas to uterine origin: as there are several possible sites for leiomyosarcomas, all were excluded); diagnosis before 1 January 2000; controls diagnosed with uterine cancer before the index date; metastatic cancer from a non-uterine primary cancer; women with a recorded hysterectomy before the index date; and women with no consultations in the year before the index date. Women with a hysterectomy recorded >3 months before their first uterine cancer</p>

	code were also excluded, as the date of diagnosis was unreliable; if the discrepancy was <3 months, the index date was taken to be the date of the hysterectomy. <u>Clinical setting</u> : Primary care UK
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	All symptoms, signs or abnormal investigations previously recorded in the uterine cancer literature and cancer charity websites were studied. Libraries of codes relating to these were collated. All codes for fractures were also identified, as a test for any recording bias between cases and controls (making the assumption that the fracture rate would be approximately equal). Occurrences of these features in the year before the index date were identified. Features were only retained for further study if they occurred in $\geq 2\%$ of cases or controls. A list of plausible laboratory abnormalities was assembled a priori, using the literature and the authors' clinical knowledge. All abnormal laboratory results in the year before the index date were also identified, using the local laboratory's normal range, which is supplied with the data. Women without a test were considered to be equivalent to those with a normal result. Some abnormal tests were grouped: abnormal liver function was defined as the presence of any liver enzyme above the normal range. The variable 'raised inflammatory markers' was defined as a raised erythrocyte sedimentation rate, C-reactive protein, or plasma viscosity. These simplifications were necessary, as different localities in the UK contributing to the GPRD have different tests available.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Uterine cancer code in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined	Low concern

by the reference standard does not match the question?		
FLOW AND TIMING		
A. risk of bias		
Flow and timing	A total of 18841 patients were identified, 15675 controls and 3166 cases. Of the controls the following exclusions were applied: Uterine cancer before index date of case (N = 41), hysterectomy before index date of case (N = 2732), case excluded (N = 2074) and no data in year pre-index date (N = 1291). Of the cases the following exclusions were applied: No controls (N = 13), sarcoma (N = 251), metastatic cancer (N = 3), and hysterectomy recorded > 3 months prior to cancer index date (N = 167).	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	One subgroup analysis examined women aged ≥55 years, as a proxy for being postmenopausal, and for this analysis all abnormal menstrual bleeding variables were categorised as postmenopausal bleeding.	

References

Included studies

- Droogendijk, J., Beukers, R., Berendes, P. B., Tax, M. G. H. M., Sonneveld, P., and Levin, M. D. Screening for gastrointestinal malignancy in patients with iron deficiency anemia by general practitioners: An observational study. *Scandinavian Journal of Gastroenterology* 46[9], 1105-1110. 2011.
- Hallissey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.
- Parker, C., Hippisley-Cox, J., Coupland, C., and Vinogradova, Y. Rectal and postmenopausal bleeding: consultation and referral of patients with and without severe mental health problems. *British Journal of General Practice* 57[538], 371-376. 2007.
- Walker, S., Hyde, C. & Hamilton, W. (2013) Risk of uterine cancer in symptomatic women in primary care: case-control study using electronic records. *British Journal of General Practice*, 63: 643-648.

Excluded studies (with reason)

- (1111) Standard of the Dutch College of General Practitioners on vaginal bleeding: Second revision. [Dutch]. *Huisarts en Wetenschap*, 51: March. Narrative review
- (2004) Endometrial cancer. Better odds with early detection. *Mayo Clinic Health Letter*, 22: 4-5. Narrative review
- Achillarre, M. T., Ceci, O., Mangiatordi, G., Pinto, L., Laera, A., Chiarulli, E. & Bettocchi, S. (2010) Is Office Hysteroscopy always necessary after endometrial ultrasound evaluation in postmenopausal women? *Journal of Minimally Invasive Gynecology*. Conference: 39th Global Congress of Minimally Invasive Gynecology, AAGL 2010 Las Vegas, NV United States. Conference Start: 20101108 Conference End: 20101112. Conference Publication: (var.pagings), 17: November-December. Not in PICO
- Aedo, O. (2012) New techniques for the diagnosis of endometrial and ovarian pathology. *Cytopathology*. Conference: 37th European Congress of Cytopathology Dubrovnik-Cavtat Croatia. Conference Start: 20120930 Conference End: 20121003. Conference Publication:

- (var.pagings), 23: October.
Narrative review
- Ajao, M., Vachon, T. & Snyder, P. (2013) Ovarian dysgerminoma: a case report and literature review. *Military Medicine*, 178: e954-e955.
Not in PICO
- Al-Kadri, H. M., Al-Awami, S. H. & Madkhali, A. M. (2004) Assessment of risk factors of uterine cancer in Saudi patients with postmenopausal bleeding. *Saudi Medical Journal*, 25: 857-861.
Not in PICO
- Albers, J. R., Hull, S. K. & Wesley, R. M. (2004) Abnormal uterine bleeding. [Review] [45 refs]. *American Family Physician*, 69: 1915-1926.
Narrative review
- Alexopoulos, E. D., Fay, T. N. & Simonis, C. D. (1999) A review of 2581 out-patient diagnostic hysteroscopies in the management of abnormal uterine bleeding. *Gynaecological Endoscopy*, 8.
Not in PICO (secondary care)
- Apgar, B. S. & Newkirk, G. R. (1997) Office procedures. Endometrial biopsy. *Primary care*, 24: Jun.
Narrative review
- Aslam, N., Oniah, M., Gaber, M. & Hollingworth, J. (2012) An audit of one stop post menopausal bleeding (PMB) clinic, do we need to change the endometrial thickness (ET) cut-off of 4MM? *International Journal of Gynecology and Obstetrics.Conference: 20th FIGO World Congress of Gynecology and Obstetrics Rome Italy.Conference Start: 20121007 Conference End: 20121012.Conference Publication: (var.pagings)*, 119: October.
Not in PICO
- Atiomo, W. U., Shrestha, R. & Falconer, A. D. (1998) Evaluation of a one-stop clinic for the rapid assessment of post-menopausal bleeding. *Journal of Obstetrics and Gynaecology*, 18.
Not in PICO
- Bachet, W., Brunner, P., Dodenhoft, J. D. J. & Strobel, E. (1983) The diagnostic accuracy of endometrial cytology with prevical. [German]. *Geburtshilfe und Frauenheilkunde*, 43.
Not in PICO
- Bachmann, L. M., Ter, R. G., Clark, T. J., Gupta, J. K. & Khan, K. S. (2003) Probability analysis for diagnosis of endometrial hyperplasia and cancer in postmenopausal bleeding: An approach for a rational diagnostic workup. *Acta Obstetrica et Gynecologica Scandinavica*, 82: 01.
Not in PICO (secondary care)
- Baiocchi, G. & Gilardi, G. (1997) Endometrial carcinoma: an increasing neoplasm. Screening and early diagnosis: proposal for a protocol. [Italian]. *Minerva Ginecologica*, 49: Apr.
Protocol
- Barwick, T. D., Rockall, A. G., Barton, D. P. & Sohaib, S. A. (2006) Imaging of endometrial adenocarcinoma. *Clinical Radiology*, 61: July.
Narrative review
- Bennett, G. L., Andreotti, R. F., Lee, S. I., Dejesus Allison, S. O., Brown, D. L., Dubinsky, T., Glanc, P., Mitchell, D. G., Podrasky, A. E., Shipp, T. D., Siegel, C. L., Wong-You-Cheong, J. J. & Zelop, C. M. (2011) ACR appropriateness criteria() on abnormal vaginal bleeding. *Journal of the American College of Radiology*, 8: 460-468.
Narrative review
- Boukes, F. S., Meijer, L. J., Flikweert, S., Assendelft, W. J. & Nederlands, H. G. (2002) [Summary of the standard "Vaginal bleeding" (first revision) of the Dutch College of General Practitioners]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 146: 2179-2183.
Narrative review
- Boukes, F. S., Meijer, L. J., Flikweert, S. & Assendelft, W. J. J. (2002) Summary of the Dutch College of General Practitioners' practice guideline 'Vaginal bleeding' (first revised version). [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 146: 16.
Narrative review

- Boukes, F. S., Beijderwellen, L., van der Does, F. E. & Assendelft, W. J. (2004) [Summary of the practice guideline 'Hormonal contraception' (second revision) from the Dutch College of General Practitioners]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 148: 1285-1289.
Narrative review
- Broggi, E., Tambouret, R. & Bell, D. A. (2002) Classification of benign endometrial glandular cells in cervical smears from postmenopausal women. *Cancer*, 96: 25.
Not in PICO
- Brooks, S. E. (1997) A review of screening and early detection of endometrial cancer and use of risk assessment. *Journal of the Association for Academic Minority Physicians : the official publication of the Association for Academic Minority Physicians*, 8.
Narrative review
- Broso, P. R. & Giradi, F. (1995) Is it possible to screen for endometrial carcinoma? Incidence and risk factors. [Italian]. *Minerva Ginecologica*, 47: Dec.
Narrative review
- Burbos, N., Musonda, P. & Rufford, B. (2011) Diagnostic performance of urgent referrals for suspected gynaecological malignancies. *Archives of Gynecology & Obstetrics*, 284: 1495-1500.
Not in PICO
- Burbos, N., Musonda, P., Duncan, T. J., Crocker, S. G., Morris, E. P. & Nieto, J. J. (2011) Estimating the risk of endometrial cancer in symptomatic postmenopausal women: a novel clinical prediction model based on patients' characteristics. *International Journal of Gynecological Cancer*, 21: 500-506.
Not in PICO
- Burke, T. W., Tortolero-Luna, G., Malpica, A., Baker, V. V., Whittaker, L., Johnson, E. & Mitchell, M. F. (1996) Endometrial hyperplasia and endometrial cancer. *Obstetrics and Gynecology Clinics of North America*, 23.
Narrative review
- Cao, Z. Y. (1990) Endometrial carcinoma in young women. [Chinese]. *Zhonghua fu chan ke za zhi*, 25: Mar.
Not in PICO
- Casey, P. & Allensworth, S. (2012) Endometrial malignancy & premalignancy in women with benign endometrial cells on cervical cytology: Risk and outcomes. *Journal of Lower Genital Tract Disease. Conference: 2012 American Society for Colposcopy and Cervical Pathology, ASCCP Biennial Scientific Meeting San Francisco, CA United States. Conference Start: 20120314 Conference End: 20120317. Conference Publication*, 16: April.
Not in PICO
- Clark, T. J., Voit, D., Gupta, J. K., Hyde, C., Song, F., Khan, K. S. & Mol, B. W. (1111) Hysteroscopy is an accurate diagnostic test for endometrial cancer in women with abnormal uterine bleeding - Meta-analysis. *Evidence-based Obstetrics and Gynecology*, 5: June.
Not in PICO as not reported separately for primary care, if indeed any studies are where primary care retains the clinical responsibility
- Clark, T. J., Mann, C. H., Shah, N., Khan, K. S., Song, F. & Gupta, J. K. (2002) Accuracy of outpatient endometrial biopsy in the diagnosis of endometrial cancer: a systematic quantitative review. [Review] [70 refs][Summary for patients in *J Fam Pract*. 2002 Jul;51(7):601; PMID: 12160494], [Summary for patients in *J Fam Pract*. 2002 Jul;51(7):600; PMID: 12160493]. *BJOG: An International Journal of Obstetrics & Gynaecology*, 109: 313-321.
Not in PICO as not reported separately for primary care, if indeed any studies are where primary care retains the clinical responsibility
- Clark, T. J., Barton, P. M., Coomarasamy, A., Gupta, J. K. & Khan, K. S. (2006) Investigating postmenopausal bleeding for endometrial cancer: cost-effectiveness of initial diagnostic strategies. *BJOG: An International Journal of Obstetrics & Gynaecology*, 113: 502-510.
Not in PICO

- Clark, T. J. (2006) Hysteroscopy and ultrasonography in the diagnosis of endometrial cancer. [Review] [60 refs]. *Gynakologisch-Geburtshilfliche Rundschau*, 46: 3-12.
Narrative review
- Clocuh, Y. P. A. & Peters-Welte, C. (1982) Results of the cytological examinations of cells from the uterine cavity. [German]. *Geburtshilfe und Frauenheilkunde*, 42.
In German. It is "Not in PICO" for signs nad symptoms and I also think it is secondary care, so "Not in PICO" for tests.
- Costa, C., Melo, A. & Martinho, M. (1111) Office hysteroscopy in the diagnosis of postmenopausal bleeding. *Gynecological Surgery.Conference: 19th Annual Congress of the European Society for Gynaecological Endoscopy, ESGE Barcelona Spain.Conference Start: 20100929 Conference End: 20101002.Conference Publication: (var.pagings)*, 7: October.
Not in PICO
- Costa, C., Melo, A. & Martinho, M. (2010) Office hysteroscopy: Clinical and histopatologic characterization of endometrial polyps identified over a year in a tertiary care unit. *Gynecological Surgery.Conference: 19th Annual Congress of the European Society for Gynaecological Endoscopy, ESGE Barcelona Spain.Conference Start: 20100929 Conference End: 20101002.Conference Publication: (var.pagings)*, 7: October.
Not in PICO
- Crispi, C. P., Vanin, C. M., Dibi, R. P., Kato, S. K. & Pessini, S. A. (2011) Postmenopausal bleeding: Findings and accuracy of hysteroscopy and histopathologic in the diagnosis of endometrial cancer. *Journal of Minimally Invasive Gynecology.Conference: 40th Global Congress of Minimally Invasive Gynecology, AAGL 2011 Hollywood, FL United States.Conference Start: 20111106 Conference End: 20111110.Conference Publication: (var.pagings)*, 18: November-December.
Not in PICO (secondary care)
- Critchley, H. O. D., Warner, P., Lee, A. J., Brechin, S., Guise, J. & Graham, B. (2004) Evaluation of abnormal uterine bleeding: Comparison of three outpatient procedures within cohorts defined by age and menopausal status. *Health Technology Assessment*, 8: September.
Not in PICO
- Curcic, A., Durdevic, S., Mladenovic-Segedi, L., Grujic, Z. & Visnjevac, N. (2009) [Ultrasound in screening of endometrial carcinoma in asymptomatic postmenopausal women]. [Serbian]. *Medicinski Pregled*, 62: 263-267.
Not in PICO
- Damle, R. P., Dravid, N. V., Suryawanshi, K. H., Gadre, A. S., Bagale, P. S. & Ahire, N. (2013) Clinicopathological spectrum of endometrial changes in peri-menopausal and post-menopausal abnormal uterine bleeding: A 2 years study. *Journal of Clinical and Diagnostic Research*, 7: 2774-2776.
Not in PICO
- Daniele, A., Ferrero, A., Maggiorotto, F., Perrini, G., Volpi, E. & Sismondi, P. (2013) Suspecting malignancy in endometrial polyps: Value of hysteroscopy. *Tumori*, 99: 204-209.
Not in PICO
- de, A. D., Rocca, G. & Miliffi, L. (1986) Cyto-histologic evaluation of the endometrium in climacteric women at risk for endometrial carcinoma. *Tumori*, 72: 431-437.
Not in PICO
- De, C. F., Valenzano, A., Rossiello, F., Trecca, P., Cinque, B., Mango, D. & Dell'Acqua, S. (1111) Medroxy-progesterone acetate test (MPA-test) for screening of endometrial adenocarcinoma in asymptomatic post-menopausal women. *Acta Medica Romana*, 32: 1994.
Not in PICO
- Degenhardt, F., Bohmer, S., Frisch, K. & Schneider, J. (1111) Assessment of endometrium in postmenopausal women via vaginal sonography. [German]. *Ultraschall in der Medizin*, 12: 1991.
Not in PICO

- Degenhardt, F., Bohmer, S., Frisch, K. & Schneider, J. (1991) [Transvaginal ultrasonic assessment of the endometrium in menopause]. [German]. *Ultraschall in der Medizin*, 12: 119-123.
Narrative review
- Deligdisch, L. (2007) Stage I ovarian carcinoma: two distinct malignancies?. [French]. *Bulletin de l'Academie nationale de medecine*, 191: Nov.
Narrative review
- Deruelle, P. & Leroy, J.-L. (2001) Diagnosis of endometrial cancer. [French]. *Revue du Praticien*, 51: 01.
Narrative review
- Diesing, D., Cordes, T., Finas, D., Loning, M., Mayer, K., Diedrich, K. & Friedrich, M. (2006) Endometrial stromal sarcomas--a retrospective analysis of 11 patients. *Anticancer Research*, 26: 655-661.
Not in PICO
- El Agouza, I. M. A. & El Nashar, D. E. (2011) Serum taurine as a marker of endometrial cancer. *Open Women's Health Journal*, 5.
Not in PICO
- Elit, L. (2000) Endometrial cancer. Prevention, detection, management, and follow up. [Review] [17 refs]. *Canadian Family Physician*, 46: 887-892.
Narrative review
- Elliott, J., Connor, M. E. & Lashen, H. (2003) The value of outpatient hysteroscopy in diagnosing endometrial pathology in postmenopausal women with and without hormone replacement therapy. *Acta Obstetrica et Gynecologica Scandinavica*, 82: 1112-1119.
Not in PICO (secondary care)
- Eze, J. N., Emeka-Irem, E. N. & Edegebe, F. O. (2013) A six-year study of the clinical presentation of cervical cancer and the management challenges encountered at a state teaching hospital in southeast Nigeria. *Clinical Medicine Insights.Oncology*, 7: 151-158.
Not in PICO
- Feldman, S., Cook, E. F. & Harlow, B. L. (1995) Predicting Endometrial Cancer Among Older Women Who Present with Abnormal Vaginal Bleeding. *Gynecologic Oncology*, 56: 376-381.
Not in PICO
- Franceschi, S., La, V. C., Gallus, G., Decarli, A., Colombo, E., Mangioni, C. & Tognoni, G. (1983) Delayed diagnosis of endometrial cancer in Italy. *Cancer*, 51: 1176-1178.
Not in PICO
- Gan, D. E., Jawan, R. A. & Moy, F. M. (2013) Concordance between hysteroscopic impression and endometrial histopathological diagnosis. *Preventive Medicine*, 57: Suppl-3.
Not in PICO (secondary care)
- Gaolebale, P. A. & Burke, C. (2011) Review of management of postmenopausal bleeding. *Irish Journal of Medical Science.Conference: Insitute of Obstetricians and Gynaecologists, RCPI Four Provinces Meeting, Junior Obstetrics and Gynaecology Society Annual Scientific Meeting, Royal Academy of Medicine in Ireland, Dublin Maternity Hospitals*, 180: April.
Not in PICO
- Gerber, B., Krause, A., Muller, H., Reimer, T., Kulz, T., Kundt, G. & Friese, K. (2001) Ultrasonographic detection of asymptomatic endometrial cancer in postmenopausal patients offers no prognostic advantage over symptomatic disease discovered by uterine bleeding (Structured abstract). *European Journal of Cancer*, 37: 64-71.
Not in PICO
- Giannella, L., Mfuta, K., Setti, T., Cerami, L. B., Bergamini, E. & Boselli, F. (2014) - A Risk-Scoring Model for the Prediction of Endometrial Cancer among Symptomatic Postmenopausal Women with Endometrial Thickness > 4mm. - *BioMed Research International*, 2014: 130569.
Not in PICO (setting, confirmed by Willie)

- Gordon, S. J. & Westgate, J. (1999) The incidence and management of failed pipelle sampling in a general outpatient clinic. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 39.
Not in PICO
- Grigoriadis, C., Zygouris, D., Derdelis, G., Apostolou, G., Papakonstantinou, E. & Terzakis, E. (2010) *Gynecological Surgery.Conference: 19th Annual Congress of the European Society for Gynaecological Endoscopy, ESGE Barcelona Spain.Conference Start: 20100929 Conference End: 20101002.Conference Publication: (var.pagings)*, 7: October.
Not in PICO
- Gruboeck, K., Jurkovic, D., Lawton, F., Savvas, M., Tailor, A. & Campbell, S. (1996) The diagnostic value of endometrial thickness and volume measurements by three-dimensional ultrasound in patients with postmenopausal bleeding. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology*, 8: Oct.
Not in PICO
- Guida, M., Bramante, S., Lavitola, G., Acunzo, G., Sparice, S., Cirillo, P. & Nappi, C. (2003) [Hysteroscopy in suspected endometrial carcinoma: a comparison among cavity-distention media]. [Italian]. *Tumori*, 89: Suppl-2.
Not in PICO
- Gupta, J. K., Chien, P. F., Voit, D., Clark, T. J. & Khan, K. S. (2002) Ultrasonographic endometrial thickness for diagnosing endometrial pathology in women with postmenopausal bleeding: a meta-analysis (Structured abstract). *Acta Obstetricia et Gynecologica Scandinavica*, 81: 799-816.
Think it's not in PICO for endometrial as cancer prevalence = 14%, and not reported separately for primary care, if indeed any studies are primary care
- Guralp, O., Sheridan, S. M., Harter, J., Hinshaw, J. L., Seo, S., Hartenbach, E. M., Lindheim, S., Stewart, S. & Kushner, D. M. (2013) A new diagnostic test for endometrial cancer?: Cytology analysis of sonohysterography distention media. *International Journal of Gynecological Cancer*, 23: 1252-1257.
Not in PICO
- Hansen, P. K., Junge, J. & Roed, H. (1986) Endoscann cell sampling for cytological assessment of endometrial pathology. *Acta Obstetricia et Gynecologica Scandinavica*, 65.
Not in PICO
- Hou, D. M., Xie, Y. & He, W. (2009) Early diagnosis of endometrial disorder in women with postmenopausal bleeding by three-dimensional transvaginal sonography and hysterosonography. [Chinese]. *Zhonghua yi xue za zhi*, 89: 4.
In Chinese, not enough information can be extracted to ascertain eligibility status, but I think it is "Not in PICO"
- Issat, T., Beta, J., Nowicka, M. A. & Jakimiuk, A. J. (2014) - Accuracy and diagnostic value of outpatient hysteroscopy for malign and benign disease. - *European Journal of Gynaecological Oncology*, 35: 52-55.
Not in PICO
- Istatkov, M., Mirkov, K., Krutilin, S., Ivanova, K. & Karag'ozova, Z. (1986) Current possibilities for the early diagnosis of endometrial cancer. [Bulgarian]. *Akusherstvo i Ginekologija*, 25.
In Bulgarian. Not enough information can be extracted, but I think it is "Not in PICO"
- Jaber, R. (1988) Detection of and screening for endometrial cancer. *Journal of Family Practice*, 26.
Narrative review
- Jimenez-Ayala, M., Jimenez-Ayala, P. B., Iglesias, E. & Vallejo, M. R. (1111) Endometrial adenocarcinoma: prevention and early diagnosis. *Monographs in Clinical Cytology*, 17: 2008.
Narrative review
- Jimenez-Ayala, M. (2012) Current status and future of prevention and early diagnosis of endometrial adenocarcinoma. *Cytopathology.Conference: 37th European Congress of Cytopathology Dubrovnik-Cavtat Croatia.Conference Start: 20120930 Conference End: 20121003.Conference*

- Publication: (var.pagings), 23: October.*
Narrative review
- Johann, S. & Mueller, M. D. (2008) [Follow-up after malignant tumours of the uterus (cancer of the uterine corpus / cervical cancer)]. [German]. *Therapeutische Umschau*, 65: 341-346.
Not in PICO
- Johnson, N., Miles, T., Bailey, D., Tylko-Hill, K., Das, N., Ahson, G., Waring, K., Acheson, N., Voss, M., Gordon, J., Keates-Porter, S., Hughes, G., Golby, S., Fort, E., Newton, L., Nallaswamy, V., Murdoch, J. & Anderson, R. (2011) Delays in treating endometrial cancer in the South West of England. *British Journal of Cancer*, 104: 1836-1839.
Not in PICO
- Kellas-Slecza, S., Wojcieszek, P. & Bialas, B. (2012) Adjuvant vaginal brachytherapy as a part of management in early endometrial cancer. *Journal of Contemporary Brachytherapy*, 4: 247-252.
Not in PICO
- Keskin, U., Ozturk, M., Ercan, M., Dede, M., Yenen, M. C. & Ergun, A. (2013) Narrow-band imaging endoscopy for diagnosis of endometrial neoplasia, pilot study. *European Surgical Research*, 50: 146.
Abstract only, not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Kingery, J. E. & Noble, W. G. (2012) Endometrial biopsy. *Osteopathic Family Physician*, 4: September.
Narrative review
- Koonings, P. P. & Grimes, D. A. (1989) Endometrial sampling techniques for the office. *American Family Physician*, 40.
Narrative review
- Kurlov, T., Diankova, T., Kurlov, A., Katerinski, K. & Ivanov, S. (1998) The evaluation of the transvaginal ultrasonography of endometrial thickness in women with postmenopausal bleeding and suspected endometrial carcinoma. [Bulgarian]. *Akusherstvo i Ginekologija*, 37.
Not in PICO
- Le, T., Bentley, J., Farrell, S., Fortier, M. P., Giede, C., Kupets, R., Plante, M., Power, P., Renaud, M. C., Schepansky, A., Senikas, V., Kwon, J., Prefontaine, M., Germain, I., Pearcey, R., D'Souza, D., Senterman, M., Hoskins, P. & SOGC-GOC-SCC Policy and Practice Guidelines Committee (2013) Epidemiology and investigations for suspected endometrial cancer. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC*, 35: 380-383.
Narrative review/guideline
- Liberis, V., Tsikouras, P., Christos, Z., Ammari, A., Dislian, V., Koutlaki, N., Liberis, A. & Maroulis, G. (2010) The contribution of hysteroscopy to the detection malignancy in symptomatic postmenopausal women. *Minimally Invasive Therapy & Allied Technologies: Mitat*, 19: 83-93.
Not in PICO
- Lim, Y. K., Padma, R., Foo, L., Chia, Y. N., Yam, P., Chia, J., Khoo-Tan, H., Yap, S. P. & Yeo, R. (2011) Survival outcome of women with synchronous cancers of endometrium and ovary: a 10 year retrospective cohort study. *Journal of Gynecologic Oncology*, 22: 239-243.
Not in PICO
- Litta, P., Merlin, F., Saccardi, C., Pozzan, C., Sacco, G., Fracas, M., Capobianco, G. & Dessole, S. (2005) Role of hysteroscopy with endometrial biopsy to rule out endometrial cancer in postmenopausal women with abnormal uterine bleeding. *Maturitas*, 50: 117-123.
Not in PICO
- Lotfallah, H., Farag, K., Hassan, I. & Watson, R. (2005) One-stop hysteroscopy clinic for postmenopausal bleeding. *Journal of Reproductive Medicine*, 50: 101-107.
Not in PICO

- Low, E. L., Simon, A. E., Waller, J., Wardle, J. & Menon, U. (2013) Experience of symptoms indicative of gynaecological cancers in UK women. *British Journal of Cancer*, 109: 882-887.
Not in PICO
- Mais, V., Cirronis, M. G., Piras, B., Silvetti, E., Cossu, E. & Melis, G. B. (2011) Intraoperative lymphatic mapping techniques for endometrial cancer. [Review]. *Expert Review of Anticancer Therapy*, 11: 83-93.
Not in PICO
- Mallmann, P. (2014) Early recognition of endometrial cancer. [German]. *Gynakologe*, 47: 340-345.
Narrative review
- Mazhar, S., Masood, M. S. & Malik, K. M. (1111) Diagnostic value of endometrial sampling with pipelle suction curettage in patients with abnormal uterine bleeding and postmenopausal bleeding. *Medical Forum Monthly*, 16: June.
Not in PICO
- Melnikow, J. & Nuovo, J. (1997) Cancer prevention and screening in women. *Primary Care - Clinics in Office Practice*, 24.
Narrative review
- Mencaglia, L., Valle, R. F., Perino, A. & Keith, L. G. (1988) Early detection of endometrial carcinoma and its precursors. *Current Problems in Obstetrics, Gynecology and Fertility*, 11.
Narrative review
- Mencaglia, L., Valle, R. F., Perino, A. & Gilardi, G. (1990) Endometrial carcinoma and its precursors: early detection and treatment. [Review] [23 refs]. *International Journal of Gynaecology & Obstetrics*, 31: 107-116.
Narrative review
- Mencaglia, L. (1995) Hysteroscopy and adenocarcinoma. [Review] [30 refs]. *Obstetrics & Gynecology Clinics of North America*, 22: 573-579.
Narrative review
- Miklos, P., Klacko, M., Babala, P., Masak, L., Ondrus, D. & Waczulikova, I. (2014) Transvaginal ultrasound examination of myometrial infiltration by endometrial cancer. *Bratislavske Lekarske Listy*, 115: 14-18.
Not in PICO
- Miller, J. & Holman, J. R. (2005) Abnormal uterine bleeding: A primary care primer. *Consultant*, 45.
Narrative review
- Montgomery, B. E., Daum, G. S. & Dunton, C. J. (2004) Endometrial hyperplasia: a review. [Review] [75 refs]. *Obstetrical & Gynecological Survey*, 59: 368-378.
Narrative review
- Morelli, M., Di, C. A., Venturella, R., Mocciaro, R., D'Alessandro, P. & Zullo, F. (2013) Efficacy of the levonorgestrel intrauterine system (LNG-IUS) in the prevention of the atypical endometrial hyperplasia and endometrial cancer: retrospective data from selected obese menopausal symptomatic women. *Gynecological Endocrinology*, 29: 156-159.
Not in PICO
- Mossa, B., Ebano, V. & Marziani, R. (2010) Reliability of outpatient endometrial brush cytology vs biopsy in postmenopausal symptomatic women. *European Journal of Gynaecological Oncology*, 31: 621-626.
Not in PICO
- Murthy, N., Moncreiffe, L. & Seif, M. W. (2012) The role of expectant management of incidental thickened endometrium in asymptomatic postmenopausal women. *BJOG: An International Journal of Obstetrics and Gynaecology. Conference: 10th International Scientific Congress of the Royal College of Obstetricians and Gynaecologists, RCOG 2012 Kuching, Sarawak Malaysia. Conference Start: 20120605 Conference End: 2012*, 119: June.
Not in PICO

- Musonda, P., Burbos, N., Duncan, T. J., Crocker, S. G., Morris, E. P. & Nieto, J. J. (2011) Comparing the performance of two clinical models in estimating the risk of endometrial cancer in symptomatic postmenopausal women. *European Journal of Obstetrics, Gynecology, & Reproductive Biology*, 159: 433-438.
Not in PICO
- Myriokefalitaki, E., D'Costa, D., Smith, M. & Ahmed, A. S. (2013) Primary bone metastasis as initial presentation of endometrial cancer (stage IVb). *Archives of Gynecology & Obstetrics*, 288: 739-746.
Not in PICO
- Nagase, E., Yasuda, M., Kajiwara, H., Osamura, R. Y., Yoshitake, T., Hirasawa, T., Muramatsu, T., Miyamoto, T., Murakami, M., Makino, T. & Ogawa, T. (2004) Uterine body cancer mass screening at Tokai University Hospital. *Tokai Journal of Experimental & Clinical Medicine*, 29: 43-48.
Not in PICO
- Nguyen, T. N., Bourdeau, J.-L., Ferenczy, A. & Franco, E. L. (1998) Clinical significance of histiocytes in the detection of endometrial adenocarcinoma and hyperplasia. *Diagnostic Cytopathology*, 19: August.
Not in PICO
- Nieto, D. A., Solano Calvo, J. A., Tacuri, C. C. & Cortes, P. J. (2002) Endometrial cancer in the 90s. Analysis of 126 cases. [Spanish]. *Oncologia*, 25.
Not in PICO
- Okadome, M., Saito, T., Tsukamoto, N., Nishi, K., Nishiyama, N. & Nagata, E. (2006) Endometrial scraping cytology in women with extragenital malignancies. *Acta Cytologica*, 50: 158-163.
Not in PICO
- Oliver, A. & Overton, C. (2002) Detecting ovarian disorders in primary care. *The Practitioner*, 258: 15-19, 2.
Duplicate
- Oliver, A. & Overton, C. (2002) - Detecting ovarian disorders in primary care. - *Practitioner*, 258: 15-19.
Narrative review
- Oriel, K. A. & Schrager, S. (1981) Abnormal uterine bleeding. *American Family Physician*, 60: 1371-1380.
Narrative review
- Osmers, R., Volksen, M. & Schauer, A. (1990) Vaginosonography for early detection of endometrial carcinoma? *Lancet*, 335: 1569-1571.
Not in PICO
- Pace, S., Grassi, A., Ferrero, S., Figliolini, N., Catania, R., Labi, F. L., Pachi, A. & Figliolini, M. (1995) Diagnostic methods of early detection of endometrial hyperplasia and cancer. *European Journal of Gynaecological Oncology*, 16: 373-381.
Narrative review
- Panda, J. K. (2002) One-stop clinic for postmenopausal bleeding. *Journal of Reproductive Medicine*, 47: 761-766.
Not in PICO
- Persadie, R. J. (2002) Ultrasonographic assessment of endometrial thickness: a review. [Review] [49 refs]. *Journal of Obstetrics & Gynaecology Canada: JOGC*, 24: 131-136.
Narrative review
- Pinar, G., Algier, L., Dogan, N. & Kaya, N. (2008) Determination of the risk factors in individuals with gynecological cancer. [Turkish]. *UHOD - Uluslararası Hematoloji-Onkoloji Dergisi*, 18.
Not in PICO
- Pinzauti, S., Altomare, A., Perrone, A. M., Bocchi, C., Gabbanini, M., Franchini, M., Litta, P., Pelusi, G., Petraglia, F. & Florio, P. (2009) Serum activin a testing in the early diagnosis of endometrial cancer. *Gynecological Surgery.Conference: 18th Annual Congress of the European Society for*

Gynaecological Endoscopy, ESGE Florence Italy. Conference Start: 20091028 Conference End: 20091031. Conference Publication: (var.pagings), 6.

Not in PICO

Poppendiek, G. & Bayer, K.-H. (1981) The cytology of endometrium by aspiration - a method for the early detection of endometrial carcinoma. [German]. *Geburtshilfe und Frauenheilkunde*, 41.

Not in PICO (prevalence 26%)

Proca, D., Keyhani-Rofagha, S., Copeland, L. J. & Hameed, A. (1998) Exfoliative cytology of neuroendocrine small cell carcinoma of the endometrium: A report of two cases. *Acta Cytologica*, 42.

Not in PICO

Redman, C. W. (2000) An audit of the management of uterine malignancy within the West Midlands. West Midlands Gynaecological Oncology Group. *BJOG: An International Journal of Obstetrics & Gynaecology*, 107: 552-555.

Not in PICO

Rivkine, E., Jakubowicz, D., Marciano, L., Polliand, C., Poncelet, C., Ziol, M. & Barrat, C. (2013) Hepatic endometrioma: a case report and review of the literature: report of a case. *Surgery Today*, 43: 1188-1193.

Not in PICO

Robertson, G. (2003) Screening for endometrial cancer. [Review] [11 refs]. *Medical Journal of Australia*, 178: 657-659.

Narrative review

Rohr, G. & Kragstrup, J. (1997) General practitioners' choice of treatment for young women with metrorrhagia as evaluated by vignettes. [Danish]. *Ugeskrift for Laeger*, 159: 3.

Not in PICO

Ronghe, R. & Gaudoin, M. (2010) Women with recurrent postmenopausal bleeding should be re-investigated but are not more likely to have endometrial cancer. *Menopause International*, 16: March.

Not in PICO

Rosen, K. A. & Pritzker, J. (1998) Transvaginal sonography and sonohysterography as screening tools for postmenopausal bleeding. *Primary Care Update for Ob/Gyns*, 5: January/February.

Not in PICO

Rosenthal, A. N., Panoskaltis, T., Smith, T. & Soutter, W. P. (2001) The frequency of significant pathology in women attending a general gynaecological service for postcoital bleeding. *British Journal of Obstetrics and Gynaecology*, 108: 103-106.

Not in PICO

Salani, R., Nagel, C. I., Drennen, E. & Bristow, R. E. (2011) Recurrence patterns and surveillance for patients with early stage endometrial cancer. *Gynecologic Oncology*, 123: 205-207.

Not in PICO

Saso, S., Chatterjee, J., Georgiou, E., Ditri, A. M., Smith, J. R. & Ghaem-Maghani, S. (2011) Endometrial cancer. *BMJ*, 343: 09.

Narrative review

Schneider, L. G. (1983) Causes of abnormal vaginal bleeding in a Family Practice Center. *Journal of Family Practice*, 16: 281-283.

Not in PICO

Seamark, C. J. (1998) Endometrial sampling in general practice. *British Journal of General Practice*, 48: 1597-1598.

Not in PICO

Seebacher, V., Schmid, M., Polterauer, S., Hefler-Frischmuth, K., Leipold, H., Concin, N., Reinthaller, A. & Hefler, L. (2009) The presence of postmenopausal bleeding as prognostic parameter in patients with endometrial cancer: a retrospective multi-center study. *BMC Cancer*, 9: 460.

Not in PICO

- Selo-Ojeme, D. O., Dayoub, N., Patel, A. & Metha, M. (2004) A clinico-pathological study of postcoital bleeding. *Archives of Gynecology and Obstetrics*, 270: July.
Not in PICO
- Shapley, M. & Redman, C. W. E. (1997) Endometrial sampling and general practice. *British Journal of General Practice*, 47: 387-391.
Narrative review
- Shapley, M., Mansell, G., Jordan, J. L. & Jordan, K. P. (2010) Positive predictive values of $\geq 5\%$ in primary care for cancer: Systematic review. *British Journal of General Practice*, 60: September.
Systematic review, relevant papers added separately
- Sivvas, T., Giagloglou, K., Savvidis, A. & Tsikouras, P. (2010) Transvaginal sonography as a prognostic value to detect endometrial pathology in postmenopausal symptomatic women without hormone replacement therapy. *Archives of Gynecology and Obstetrics. Conference: 58th Congress of the German Society for Gynecology and Obstetrics (Deutsche Gesellschaft für Gynäkologie und Geburtshilfe, DGGG) Munich Germany. Conference Start: 20101005 Conference End: 20101008. Confer*, 282: October.
Not in PICO
- Skaarland, E. (1986) New concept in diagnostic endometrial cytology: diagnostic criteria based on composition and architecture of large tissue fragments in smears. *Journal of Clinical Pathology*, 39: 36-43.
Not in PICO (secondary/tertiary care)
- Smith-Bindman, R., Weiss, E. & Feldstein, V. (2004) How thick is too thick? When endometrial thickness should prompt biopsy in postmenopausal women without vaginal bleeding. *Ultrasound in Obstetrics & Gynecology*, 24: 558-565.
Not in PICO
- Smith, E. M. & Anderson, B. (1987) Symptomatology, delay, and stage of disease in endometrial cancer. *Cancer Detection & Prevention*, 10: 247-254.
Not in PICO
- Soliman, P. T., Slomovitz, B. M., Broaddus, R. R., Sun, C. C., Oh, J. C., Eifel, P. J., Gershenson, D. M. & Lu, K. H. (2004) Synchronous primary cancers of the endometrium and ovary: a single institution review of 84 cases. [Review] [20 refs]. *Gynecologic Oncology*, 94: 456-462.
Not in PICO
- Sonoda, Y. & Barakat, R. R. (2006) Screening and the prevention of gynecologic cancer: endometrial cancer. [Review] [69 refs]. *Best Practice & Research in Clinical Obstetrics & Gynaecology*, 20: 363-377.
Narrative review
- Spiewankiewicz, B., Stelmachow, J., Sawicki, W. & Kietlinska, Z. (1995) Hysteroscopy with selective endometrial sampling after unsuccessful dilatation and curettage in diagnosis of symptomatic endometrial cancer and endometrial hyperplasias. *European Journal of Gynaecological Oncology*, 16: 26-29.
Not in PICO
- Srinivasan, M. & Bakour, S. (2012) Prevalence of endometrial cancer in symptomatic post menopausal women with thickened endometrium. *Maturitas. Conference: 9th European Congress on Menopause and Andropause Athens Greece. Conference Start: 20120328 Conference End: 20120331. Conference Publication: (var.pagings)*, 71: March.
Not in PICO
- Studzinski, Z. & Branicka, D. (1999) [The coexistence of endometrial cancer with second primary malignant neoplasms]. [Polish]. *Ginekologia Polska*, 70: 186-192.
Not in PICO
- Sugita, K., Takada, S., Yamamoto, T., Aleemuzzaman, S. & Nemoto, N. (2011) A case of double cancer that was difficult to diagnose by cancer screening. *International Journal of Gynecological Cancer. Conference: 17th International Meeting of the European Society of Gynaecological*

Oncology, ESGO 2011 Milan Italy. Conference Start: 20110911 Conference End: 20110914. Conference Publication: (var.pagings), 21: October.

Not in PICO

Surkont, G., Wlazlak, E., Bitner, A., Stetkiewicz, T., Topczewska-Tylinska, K., Suzin, J. & Baranowski, W. (1111) Endometrial aspiration biopsy (EAB) as diagnostic tool of ultrasound suspicious endometrial lesions in women without abnormal bleeding. [Polish]. *Przegląd Menopauzalny*, 5: 2006.

In Polish. I don't think it is in PICO

Sweet, M. G., Schmidt-Dalton, T. A., Weiss, P. M. & Madsen, K. P. (2012) Evaluation and management of abnormal uterine bleeding in premenopausal women. [Review][Summary for patients in Am Fam Physician. 2012 Jan 1;85(1):44; PMID: 22230307]. *American Family Physician*, 85: 35-43.

Narrative review

Tarrazo Millet, M. P., Canete San, P. P., Ferrer, P. M., Izquierdo, P. D. & Cano, S. A. (2011) Endometrial cancer: Symptoms and diagnosis. *International Journal of Gynecological Cancer. Conference: 17th International Meeting of the European Society of Gynaecological Oncology, ESGO 2011 Milan Italy. Conference Start: 20110911 Conference End: 20110914. Conference Publication: (var.pagings), 21: October.*

Not in PICO

Taylor, E., Campbell, J., Donnelly, M. & Hebden, J. (2014) A specialist iron deficiency anaemia clinic significantly reduces the need for secondary care follow up. *Gut*, 63: A222-A223.

Not in PICO

Tiffen, J. M. & Mahon, S. M. (2006) Educating women regarding the early detection of endometrial cancer--what is the evidence?. [Review] [25 refs]. *Clinical Journal of Oncology Nursing*, 10: 102-104.

Narrative review

Tinelli, R., Tinelli, F. G., Cicinelli, E., Malvasi, A. & Tinelli, A. (2008) The role of hysteroscopy with eye-directed biopsy in postmenopausal women with uterine bleeding and endometrial atrophy. *Menopause*, 15: July/August.

Not in PICO

Tripodi, A., De Salvo, C., Ermio, C., Manuzio, D., Romeo, G. & Vadala, P. (2011) Importance of office hysteroscopy screening to diagnose endometrial carcinoma in menopausal women. *European Journal of Gynaecological Oncology*, 32: 303-306.

Narrative review

Tsikouras, P., Liberis, V., Galazios, G., Grapsas, X., Kantari, P., Papageorgiou, S. & Maroulis, G. (2008) TV sonographic assessment in postmenopausal women with bleeding. *European Journal of Gynaecological Oncology*, 29: 67-71.

Not in PICO

Ueda, Y., Enomoto, T., Egawa-Takata, T., Miyatake, T., Yoshino, K., Fujita, M., Matsuzaki, S., Yokoyama, T., Miyoshi, Y. & Kimura, T. (2010) Endometrial carcinoma: better prognosis for asymptomatic recurrences than for symptomatic cases found by routine follow-up. *International Journal of Clinical Oncology*, 15: 406-412.

Not in PICO

Uhiara, J. E., Dwarakanath, L. S. & Newton, J. R. (1999) Audit of a new one-stop menstrual disorder service. *Gynaecological Endoscopy*, 8: 1999.

Not in PICO

van Doorn, H. C., Opmeer, B. C., Burger, C. W., Duk, M. J., Kooi, G. S., Mol, B. W. & Dutch Study in Postmenopausal Bleeding (DUPOMEB) (2007) Inadequate office endometrial sample requires further evaluation in women with postmenopausal bleeding and abnormal ultrasound results. *International Journal of Gynaecology & Obstetrics*, 99: 100-104.

Not in PICO

- van Os, W. A. (1999) The intrauterine device and its dynamics. [Review] [19 refs]. *Advances in Contraception*, 15: 119-132.
Narrative review
- van, T. M., Wieser, F. & Nagele, F. (2000) Diagnostic hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal patients. *Contributions to Gynecology & Obstetrics*, 20: 21-26.
Not in PICO
- Vandborg, M. P., Christensen, R. D., Kragstrup, J., Edwards, K., Vedsted, P., Hansen, D. G. & Mogensen, O. (2011) Reasons for diagnostic delay in gynecological malignancies. *International Journal of Gynecological Cancer*, 21: 967-974.
Not in PICO
- Vilos, G. A., Edris, F., Abu-Rafea, B., Hollett-Caines, J., Ettler, H. C. & Al-Mubarak, A. (2009) Miscellaneous uterine malignant neoplasms detected during hysteroscopic surgery. *Journal of Minimally Invasive Gynecology*, 16: 318-325.
Not in PICO
- Von Gruenigen, V. E. & Karlen, J. R. (1995) Carcinoma of the endometrium. *American Family Physician*, 51.
Narrative review
- Washington, D. L., Danz, M. & Cordasco, K. M. (2014) Development of quality indicators for the care of women with abnormal uterine bleeding. *Journal of General Internal Medicine*, 29: S68-S69.
Not in PICO
- Wathen, P. I., Henderson, M. C. & Witz, C. A. (1995) Abnormal uterine bleeding. [Review] [27 refs]. *Medical Clinics of North America*, 79: 329-344.
Narrative review
- Wentzensen, N., Bakkum-Gamez, J. N., Killian, J. K., Sampson, J., Guido, R., Glass, A., Adams, L., Luhn, P., Brinton, L. A., Rush, B., d'Ambrosio, L., Gunja, M., Yang, H. P., Garcia-Closas, M., Lacey, J. V., Jr., Lissowska, J., Podratz, K., Meltzer, P., Shridhar, V. & Sherman, M. E. (2014) - Discovery and validation of methylation markers for endometrial cancer. - *International Journal of Cancer*, 135: 1860-1868.
Not in PICO
- Wethington, S., Herzog, T., Burke, W., Sun, X., Lewin, S. & Wright, J. (2010) Low risk of malignancy in endometrial polyps. *Gynecologic Oncology.Conference: 41st Annual Meeting of the Society of Gynecologic Oncologists, SGO San Francisco, CA United States.Conference Start: 20100314 Conference End: 20100317.Conference Publication: (var.pagings)*, 116: March.
Not in PICO
- Wethington, S. L., Herzog, T. J., Burke, W. M., Sun, X., Lerner, J. P., Lewin, S. N. & Wright, J. D. (2011) Risk and predictors of malignancy in women with endometrial polyps. *Annals of Surgical Oncology*, 18: 3819-3823.
Not in PICO
- Wierzbowski, T., Gottwald, L., Bienkiewicz, A. & Suzin, J. (2003) [Hysteroscopic evaluation of the uterine cavity in postmenopausal women with uterine bleeding]. [Polish]. *Ginekologia Polska*, 74: 892-896.
Not in PICO
- Wieser, F., Albrecht, A., Kurz, C., Wenzl, R. & Nagele, F. (1999) [Ambulatory hysteroscopy in evaluation of postmenopausal bleeding]. [German]. *Wiener Klinische Wochenschrift*, 111: 289-293.
Not in PICO (secondary care)
- Williams, S. C., Lopez, C., Yoong, A. & McHugo, J. M. (2007) Developing a robust and efficient pathway for the referral and investigation of women with post-menopausal bleeding using a cut-off of < or =4 mm for normal thickness. *British Journal of Radiology*, 80: 719-723.
Not in PICO

Yakasai, A., Allam, M. & Thompson, A. J. (2011) Incidence of bladder cancer in a one-stop clinic.
Annals of African Medicine, 10: 112-114.
 Not in PICO

Review question:

Which investigations of symptoms of suspected endometrial cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

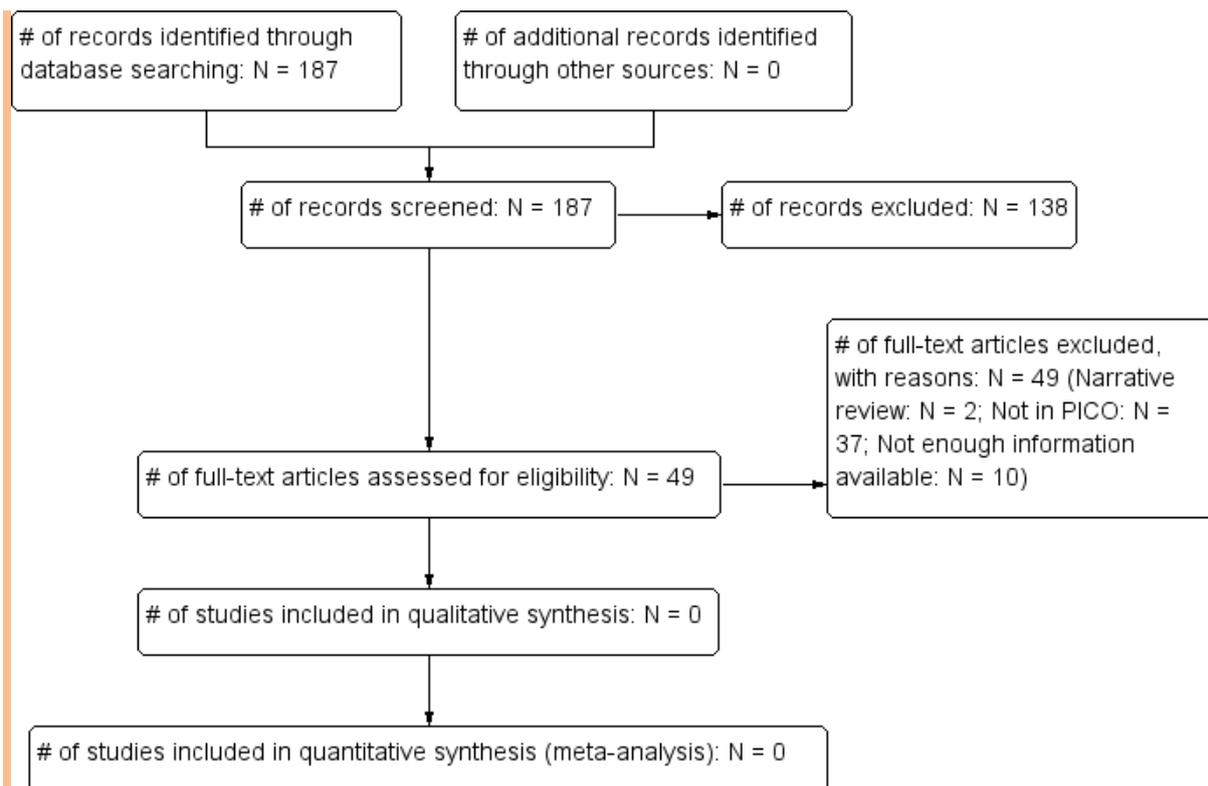
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	1107	80	19/06/2013
<i>Premedline</i>	1980-2013	66	6	19/06/2013
<i>Embase</i>	1980-2013	2720	101	20/06/2013
<i>Cochrane Library</i>	1980-2013	145	8	20/06/2013
<i>Psychinfo</i>	1980-2013	3	1	19/06/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	57	16	20/06/2013

Total References retrieved (after de-duplication): 181

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	6/2013-13/08/2014	10	1	13/08/2014
<i>Premedline</i>	6/2013-13/08/2014	51	4	13/08/2014
<i>Embase</i>	6/2013-13/08/2014	45	4	13/08/2014
<i>Cochrane Library</i>	6/2013-13/08/2014	78	0	13/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	6/2013-13/08/2014	7	0	13/08/2014

Total References retrieved (after de-duplication): 6



Study results

No evidence was identified pertaining to the diagnostic accuracy of transvaginal/abdominal ultrasound, pipelle sampling, CA125 or hysteroscopy in patients with suspected endometrial cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

(2001) American cancer society guidelines for the early detection of cancer. *Ca-A Cancer Journal for Clinicians*, 51: 87-88.

Guideline

Abu, H. F., Bilek, K., Baier, D., Nuwayhid, M. & Kade, R. (1992) [Ultrasound assessment of the endometrium in early detection of endometrial cancer in high risk patients]. [German]. *Zentralblatt fur Gynakologie*, 114: 455-458.

Not in PICO

Abu, H. F., Bilek, K., Baier, D., Nuwayhid, M. & Kade, R. (1992) [Ultrasound image of endometrial cancer]. [German]. *Ultraschall in der Medizin*, 13: 178-182.

In German. Not enough information can be extracted, but I think it is secondary care and not in PICO

Abu, H. F., Bilek, K., Baier, D., Nuwayhid, M. & Kade, R. (1992) The sonographic picture of endometrial cancer. [German]. *Ultraschall in der Medizin*, 13: 178-182.

Duplicate

Abu, H. F., Bilek, K., Baier, D., Nuwayhid, M. & Kade, R. (1992) Sonography of endometrium for early detection of endometrial cancer in risk patients. [German]. *Zentralblatt fur Gynakologie*, 114:

455-458.

Duplicate

Ahson, G. Z., Iftikhar, M. & Newton, L. (2009) Feasibility and patient acceptance of outpatient hysteroscopy: Review of one stop PMB clinic. *Gynecological Surgery*, 6: S163.

Not in PICO

Ajao, M., Vachon, T. & Snyder, P. (2013) Ovarian dysgerminoma: a case report and literature review. *Military Medicine*, 178: e954-e955.

Not in PICO

Al-Kadri, H. M., Al-Awami, S. H. & Madkhali, A. M. (2004) Assessment of risk factors of uterine cancer in Saudi patients with postmenopausal bleeding. *Saudi Medical Journal*, 25: 857-861.

Not in PICO

Al, K. A., Lim, P., Aquino-Parsons, C. & Gilks, C. B. (2002) Markers of proliferative activity are predictors of patient outcome for low-grade endometrioid adenocarcinoma but not papillary serous carcinoma of endometrium. *Modern Pathology*, 15: 365-371.

Not in PICO

Albers, J. R., Hull, S. K. & Wesley, R. M. (2004) Abnormal uterine bleeding. *American Family Physician*, 69: 1915-1926.

Narrative review

Alomari, A., Abi-Raad, R., Buza, N. & Hui, P. (2013) Correlation of K-ras mutation with histological subtypes of endometrial mucinous lesions: Implications for biological progression and molecular diagnosis. *Laboratory Investigation*, 93: 264A.

Not in PICO

Altuncu, N., Kal, U., Benhabib, M. & Nurluoglu, M. (1992) Vaginosonographic measurements of the postmenopausal endometrial thickness for the early detection of endometrial carcinoma. [Turkish]. *Istanbul Tip Fakultesi Mecmuasi*, 55: 445-449.

In Turkish, not enough information can be extracted, but I think it is secondary care and "not in PICO"

Anastasiadis, P., von, L. M., Ruhl, F. & Bowry, A. M. (1981) [Aspiration cytology of the endometrium for the early diagnosis of carcinoma of the endometrium in its precursors (author's transl)]. [German]. *Geburtshilfe und Frauenheilkunde*, 41: 136-140.

Not in PICO

Apgar, B. S. & Newkirk, G. R. (1997) Office procedures. Endometrial biopsy. [Review] [61 refs]. *Primary Care; Clinics in Office Practice*, 24: 303-326.

Narrative review

Bachmann, L. M., Ter, R. G., Clark, T. J., Gupta, J. K. & Khan, K. S. (2003) Probability analysis for diagnosis of endometrial hyperplasia and cancer in postmenopausal bleeding: An approach for a rational diagnostic workup. *Acta Obstetrica et Gynecologica Scandinavica*, 82: 564-569.

Not in PICO (secondary care)

Bachmeyer, H., Gusek, W. & Gnann, G. (1984) [Endometrial cytology using the new Abradul instrument]. [German]. *Geburtshilfe und Frauenheilkunde*, 44: 25-31.

In German. Not enough information can be extracted, but I think it is secondary care and not in PICO

Bakos, O., Smith, P. & Heimer, G. (1994) Transvaginal ultrasonography for identifying endometrial pathology in postmenopausal women. *Maturitas*, 20: 181-189.

Not in PICO (secondary care)

Bakour, S. H., Jones, S. E. & O'Donovan, P. (2006) Ambulatory hysteroscopy: evidence-based guide to diagnosis and therapy. *Best Practice & Research in Clinical Obstetrics & Gynaecology*, 20: 953-975.

Narrative review

- Barney, S. P., Muller, C. Y. & Bradshaw, K. D. (2008) Pelvic Masses. *Medical Clinics of North America*, 92: 1143-1161.
Narrative review
- Barranger, E., Delpach, Y., Coutant, C., Dubernard, G., Uzan, S. & Darai, E. (2009) Laparoscopic sentinel node mapping using combined detection for endometrial cancer: a study of 33 cases--is it a promising technique? *American Journal of Surgery*, 197: 1-7.
Not in PICO
- Bartolazzi, A., Mottolese, M., Vocaturo, A., Bigotti, A., Vocaturo, G., Atlante, G., Prat, M. & Natali, P. G. (1991) Expression of CAR-3 and TAG-72 macromolecules in normal and transformed endometrium: potential diagnostic application in postmenopausal patients. *Cancer Research*, 51: 3001-3005.
Not in PICO
- Beck, E. P., Wagner, M., Anselmino, L., Xu, F., Bast, R. C., Jr. & Jaeger, W. (1997) Is OVX1 a suitable marker for endometrial cancer? *Gynecologic Oncology*, 65: 291-296.
Not in PICO
- Beukenholdt, R. & Guerrero, K. (2003) An audit of a specialist registrar-run outpatient diagnostic hysteroscopy service in a district general hospital. *Journal of Obstetrics & Gynaecology*, 23: 294-296.
Not in PICO
- Birnholz, J. & Hrozencik, D. (1988) Technical improvement for ultrasonic study of the endometrium. *International Journal of Fertility*, 33: 194-200.
Narrative review
- Bocanera, A. R., Roncoroni, E. C., Schlaen, I., Ben, J., Monteverde, R., Gonzalez, G. M., Puche, R. C. & Tozzini, R. (1994) An articulated rotating brush for office endometrial evaluation of climacteric outpatients. *Maturitas*, 19: 67-76.
Not in PICO
- Bostwick, D. G., Hossain, D., Turbat-Herrera, E. & Schlosshauer, P. (2013) Diagnostic clinical application of multi-target fluorescence in situ hybridization in endometrial biopsies: Prospective study of 282 cases. *Laboratory Investigation*, 93: 267A.
Not in PICO
- Bourne, T. H. (1995) Evaluating the endometrium of postmenopausal women with transvaginal ultrasonography. [Review] [44 refs]. *Ultrasound in Obstetrics & Gynecology*, 6: 75-80.
Narrative review
- Bremond, A., Bataillard, A., Thomas, L., Achard, J. L., Fervers, A., Fondrinier, E., Lansac, J., Bailly, C., Hoffstetter, S., Basuyau, J. P., D'Anjou, J., Descamps, P., Farsi, F., Guastalla, J. P., Laffargue, F., Rodier, J. F., Vincent, P. & Pigneux, J. (2002) Standards, options and recommendations 2000: non metastatic endometrial cancer. *Bulletin du Cancer*, 89: 697-706.
Not in PICO
- Brown, J. J., Thurnher, S. & Hricak, H. (1990) MR imaging of the uterus: low-signal-intensity abnormalities of the endometrium and endometrial cavity. *Magnetic Resonance Imaging*, 8: 309-313.
Not in PICO
- Butureanu, S., Pricop, F., Stratan, E., Radulescu, D., Patras, C., Dragomir, D., Dumitrache, F., Gheorghita, V., Popovici, C. & Popovici, R. (1990) THE role of biopsy in the early diagnosis of cancer of the cervix uteri. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 94: 129-131.
In Rumanian. I think it is secondary care, so not in PICO
- Cavanagh, D. & Roberts, W. S. (1985) Early detection of uterine cancer. *Journal of the Florida Medical Association*, 72: 36-40.
Narrative review

- Clark, J., Barton, P., Gupta, J. & Khan, K. (2002) Outpatient diagnosis of endometrial cancer in women with first episode of postmenopausal bleeding (Structured abstract). *Health Technology Assessment Database.*, 154.
Not in PICO as not reported separately for primary care, if indeed any studies are where primary care retains the clinical responsibility
- Clark, T. J., Mann, C. H., Shah, N., Khan, K. S., Song, F. & Gupta, J. K. (2002) Accuracy of outpatient endometrial biopsy in the diagnosis of endometrial cancer: a systematic quantitative review. [Review] [70 refs][Summary for patients in *J Fam Pract.* 2002 Jul;51(7):601; PMID: 12160494], [Summary for patients in *J Fam Pract.* 2002 Jul;51(7):600; PMID: 12160493]. *BJOG: An International Journal of Obstetrics & Gynaecology*, 109: 313-321.
Not in PICO as not reported separately for primary care, if indeed any studies are where primary care retains the clinical responsibility
- Clark, T. J., Godwin, J., Khan, K. S. & Gupta, J. K. (2002) Ambulatory endoscopic treatment of symptomatic benign endometrial polyps: A feasibility study. *Gynaecological Endoscopy*, 11: 91-97.
Not in PICO
- Clark, T. J., Voit, D., Gupta, J. K., Hyde, C., Song, F. & Khan, K. S. (2002) Accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia: a systematic quantitative review (DARE structured abstract). *JAMA*, 288: 1610-1621.
Not in PICO as not reported separately for primary care, if indeed any studies are where primary care retains the clinical responsibility
- Clark, T. J., Voit, D., Gupta, J. K., Hyde, C., Song, F., Khan, K. S. & Mol, B. W. (2003) Hysteroscopy is an accurate diagnostic test for endometrial cancer in women with abnormal uterine bleeding - Meta-analysis. *Evidence-based Obstetrics and Gynecology*, 5: 94-95.
Not in PICO as not reported separately for primary care, if indeed any studies are primary care
- Clark, T. J., Barton, P. M., Coomarasamy, A., Gupta, J. K. & Khan, K. S. (2006) Investigating postmenopausal bleeding for endometrial cancer: cost-effectiveness of initial diagnostic strategies. *BJOG: An International Journal of Obstetrics & Gynaecology*, 113: 502-510.
Not in PICO
- Clark, T. J. (2006) Hysteroscopy and ultrasonography in the diagnosis of endometrial cancer. *Gynakologisch-Geburtshilfliche Rundschau*, 46: 3-12.
Narrative review
- Clark, T. J., Barton, P. M., Coomarasamy, A., Gupta, J. K. & Khan, K. S. (2006) Investigating postmenopausal bleeding for endometrial cancer: cost-effectiveness of initial diagnostic strategies (Structured abstract). *BJOG. An International Journal of Obstetrics and Gynaecology*, 113: 502-510.
Not in PICO
- Coppola, C., Di Spiezio, S. A., Spinelli, M., Zizolfi, B., Mansueto, G. & Nappi, C. (2009) Hysteroscopic diagnosis of stromomyoma. *Gynecological Surgery*, 6: S43-S44.
Not in PICO
- Costa, C., Melo, A. & Martinho, M. (2010) Office hysteroscopy in the diagnosis of postmenopausal bleeding. *Gynecological Surgery*, 7: S182-S183.
Not in PICO
- Costa, S., Guerra, B., Diana, M. R. & Antonini, P. (1980) [Pistolet-aspiration method for the early diagnosis of pre-neoplastic and neoplastic lesions of the endometrium]. [Italian]. *Rivista Italiana di Ginecologia*, 59: 213-221.
In Italian. I think it is secondary care, so not in PICO
- Crescini, C., Artuso, A., Comerio, D., Idi, G., Repetti, F., Reale, D. & Pezzica, E. (1991) [Ambulatory hysteroscopic diagnosis. Analysis of 425 cases]. [Review] [33 refs] [Italian]. *Minerva Ginecologica*, 43: 449-456.
Not in PICO (secondary care)

- Crispi, C. P., Vanin, C. M., Dibi, R. P., Kato, S. K. & Pessini, S. A. (2011) Postmenopausal bleeding: Findings and accuracy of hysteroscopy and histopathologic in the diagnosis of endometrial cancer. *Journal of Minimally Invasive Gynecology*, 18: S83-December.
Not in PICO
- Critchley, H. O. D., Warner, P., Lee, A. J., Brechin, S., Guise, J. & Graham, B. (2004) Evaluation of abnormal uterine bleeding: Comparison of three outpatient procedures within cohorts defined by age and menopausal status. *Health Technology Assessment*, 8: iii-77.
Not in PICO
- Crum, C. P., Hornstein, M. D., Nucci, M. R. & Mutter, G. L. (2003) Hertig and beyond: A systematic and practical approach to the endometrial biopsy. *Advances in Anatomic Pathology*, 10: 301-318.
Narrative review
- Damle, R. P., Dravid, N. V., Suryawanshi, K. H., Gadre, A. S., Bagale, P. S. & Ahire, N. (2013) Clinicopathological spectrum of endometrial changes in peri-menopausal and post-menopausal abnormal uterine bleeding: A 2 years study. *Journal of Clinical and Diagnostic Research*, 7: 2774-2776.
Not in PICO
- Dane, C., Tatar, Z., Dane, B., Erqinbas, M. & Cetin, A. (2009) A single horn endometrial carcinoma of a uterus bicornis unicollis. *Journal of Gynecologic Oncology*, 20: 195-197.
Not in PICO
- Daniele, A., Ferrero, A., Maggiorotto, F., Perrini, G., Volpi, E. & Sismondi, P. (2013) Suspecting malignancy in endometrial polyps: Value of hysteroscopy. *Tumori*, 99: 204-209.
Not in PICO
- Daniele, A., Ferrero, A., Maggiorotto, F., Perrini, G., Volpi, E. & Sismondi, P. (2013) Suspecting malignancy in endometrial polyps: value of hysteroscopy. *Tumori*, 99: 204-209.
Not in PICO
- de Wit, A. C., Vleugels, M. P. & de Kruif, J. H. (2003) Diagnostic hysteroscopy: a valuable diagnostic tool in the diagnosis of structural intra-cavitary pathology and endometrial hyperplasia or carcinoma?. Six years of experience with non-clinical diagnostic hysteroscopy. *European Journal of Obstetrics, Gynecology, & Reproductive Biology*, 110: 79-82.
Not in PICO
- De, C. E., Fabrizio, L. & Polidoro, M. (1985) Early diagnosis of endometrial carcinoma. The use of hysteroscopy. [Italian]. *Minerva Ginecologica*, 37: 93-97.
Not in PICO
- Degenhardt, F., Bohmer, S., Frisch, K. & Schneider, J. (1991) [Transvaginal ultrasonic assessment of the endometrium in menopause]. [German]. *Ultraschall in der Medizin*, 12: 119-123.
Narrative review
- Degenhardt, F., Bohmer, S., Frisch, K. & Schneider, J. (1991) Assessment of endometrium in postmenopausal women via vaginal sonography. [German]. *Ultraschall in der Medizin*, 12: 119-123.
Not in PICO
- Deichert, U., Van de Sandt, M., Lauth, G. & Daume, E. (1988) The transvaginal hystero-contrast-sonography (CoSy)- A new diagnostic procedure to differentiate intrauterine and myometrial findings. [German]. *Geburtshilfe und Frauenheilkunde*, 48: 835-844.
Not in PICO
- Di, L. A. & Schmitt, F. (2013) Molecular alterations in endometrial cytology. *Acta Cytologica*, 57: 102.
Not in PICO
- Dietl, J. & Stoll, P. (1985) [Value of the early detection of endometrial cancer by intra-uterine cell sampling with the Mi-Mark spiral]. [German]. *Geburtshilfe und Frauenheilkunde*, 45: 299-301.
Not in PICO
- Dijkhuizen, F. P., Mol, B. W., Brolmann, H. A. & Heintz, A. P. (2000) The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia: a meta-

- analysis (DARE structured abstract). *Cancer*, 89: 1765-1772.
Not in PICO as not reported separately for primary care, if indeed any studies are where primary care retains the clinical responsibility
- Dotto, J. E., Lema, B., Dotto, J. E., Jr. & Hamou, J. (2003) Classification of microhysteroscopic images and their correlation with histologic diagnoses. *Journal of the American Association of Gynecologic Laparoscopists*, 10: 233-246.
Not in PICO
- Eddowes, H. A., Read, M. D. & Codling, B. W. (1990) Pipelle: a more acceptable technique for outpatient endometrial biopsy. *British Journal of Obstetrics & Gynaecology*, 97: 961-962.
Not in PICO
- El-Ahmady, O., Gad, M., El-Sheimy, R., Halim, A.-B., Eissa, S., Hassan, F. & Walker, R. (1996) Comparative study between sonography, pathology and UGP in women with perimenopausal bleeding. *Anticancer Research*, 16: 2309-2313.
Not in PICO
- El Agouza, I. M. A. & El Nashar, D. E. (2011) Serum taurine as a marker of endometrial cancer. *Open Women's Health Journal*, 5: 1-6.
Not in PICO
- Elit, L. (2000) Endometrial cancer - Prevention, detection, management, and follow up. *Canadian Family Physician*, 46: 887-892.
Narrative review
- Ely, J. W., Kennedy, C. M., Clark, E. C. & Bowdler, N. C. (2006) Abnormal uterine bleeding: A management algorithm. *Journal of the American Board of Family Medicine*, 19: 590-602.
Not in PICO
- Emanuel, M. H., Verdel, M. J. C., Stas, H., Wamsteker, K. & Lammes, F. B. (1995) An audit of true prevalence of intra-uterine pathology: The hysteroscopic findings controlled for patient selection in 1202 patients with abnormal uterine bleeding. *Gynaecological Endoscopy*, 4: 237-241.
Not in PICO
- Eze, J. N., Emeka-Irem, E. N. & Edegebe, F. O. (2013) A six-year study of the clinical presentation of cervical cancer and the management challenges encountered at a state teaching hospital in southeast Nigeria. *Clinical Medicine Insights.Oncology*, 7: 151-158.
Not in PICO
- Fambrini, M., Buccoliero, A. M., Pieralli, A., Andersson, K. L., Mattei, A., Scarselli, G., Taddei, G. & Marchionni, M. (2011) Tamoxifen, endometrial cancer risk and liquid based cytology. A paradigmatic case report. [Italian]. *Minerva Ginecologica*, 63: 465-470.
Narrative review
- Franceschi, S., La, V. C., Gallus, G., Decarli, A., Colombo, E., Mangioni, C. & Tognoni, G. (1983) Delayed diagnosis of endometrial cancer in Italy. *Cancer*, 51: 1176-1178.
Not in PICO
- Fung Kee, F. M., Burnett, M. & Faught, W. (1997) Does persistent postmenopausal bleeding justify hysterectomy? *European Journal of Gynaecological Oncology*, 18: 26-28.
Not in PICO
- Gan, D. E., Jawan, R. A. & Moy, F. M. (2013) Concordance between hysteroscopic impression and endometrial histopathological diagnosis. *Preventive Medicine*, 57: Suppl-3.
Not in PICO (secondary care)
- Gao, Q. L., Ye, F., Li, J., Xing, H., Lu, Y. P. & Ma, D. (2003) [PTEN coding product: a marker for tumorigenesis and progression of endometrial carcinoma]. [Chinese]. *Aizheng*, 22: 640-644.
Not in PICO
- Gaolebale, P. A. & Burke, C. (2011) Review of management of postmenopausal bleeding. *Irish Journal of Medical Science*, 180: S121.
Not in PICO

- Gerber, B., Krause, A., Muller, H., Reimer, T., Kulz, T., Kundt, G. & Friese, K. (2001) Ultrasonographic detection of asymptomatic endometrial cancer in postmenopausal patients offers no prognostic advantage over symptomatic disease discovered by uterine bleeding (Structured abstract). *European Journal of Cancer*, 37: 64-71.
Not in PICO
- Ghirardini, G., Montanari, R. & Gualerzi, C. (1991) Vaginosonography in primary prevention of endometrial oncological pathology. *Clinical & Experimental Obstetrics & Gynecology*, 18: 149-151.
Not in PICO
- Gine, L., Sabria, E., Ponce, J., Sanchez, A. & Fernandez, M. (2009) Clinic and diagnosis of uterine myomas. Current situation. [Spanish]. *Ginecologia y Obstetricia Clinica*, 10: 15-20.
Narrative review
- Gordon, S. J. & Westgate, J. (1999) The incidence and management of failed pipelle sampling in a general outpatient clinic. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 39: 115-118.
Not in PICO
- Gorlero, F., Nicoletti, L., Lijoi, D., Ferrero, S., Pulle, A. & Ragni, N. (2008) Endometrial directed biopsy during sonohysterography using the NiGo device: prospective study in women with abnormal uterine bleeding. *Fertility and Sterility*, 89: 984-990.
Not in PICO
- Griffin, K. W., Ellis, M. R., Wilder, L. & DeArmond, L. (460) Clinical inquiries. What is the appropriate diagnostic evaluation of fibroids?. [Review] [12 refs]. *Journal of Family Practice*, 54: 458.
Not in PICO
- Guillen, C., Munoz, L., Marqueta, L., Perez, C., Tejerizo, A., Munoz, J. L., Jimenez, J. S. & Hernandez, J. M. (2009) Ambulatory hysteroscopy in postmenopausal women. Diagnostic accuracy by the presence of symptoms. *Maturitas*, 63: S109.
Abstract, not enough information can be extracted, but think it is "Not in PICO"
- Gupta, J. K., Chien, P. F., Voit, D., Clark, T. J. & Khan, K. S. (2002) Ultrasonographic endometrial thickness for diagnosing endometrial pathology in women with postmenopausal bleeding: a meta-analysis (DARE structured abstract). *Acta Obstetrica et Gynecologica Scandinavica*, 81: 799-816.
Think it's not in PICO for endometrial as cancer prevalence = 14%, and not reported separately for primary care, if indeed any studies are primary care
- Guralp, O., Sheridan, S. M., Harter, J., Hinshaw, J. L., Seo, S., Hartenbach, E. M., Lindheim, S., Stewart, S. & Kushner, D. M. (2013) A new diagnostic test for endometrial cancer?: Cytology analysis of sonohysterography distention media. *International Journal of Gynecological Cancer*, 23: 1252-1257.
Not in PICO
- Hurskainen, R., Grenman, S., Komi, I., Kujansuu, E., Luoto, R., Orrainen, M., Patja, K., Penttinen, J., Silventoinen, S., Tapanainen, J. & Toivonen, J. (2007) Diagnosis and treatment of menorrhagia. *Acta Obstetrica et Gynecologica Scandinavica*, 86: 749-757.
Narrative review
- Hurt, W. G. & Hall, D. J. (1980) Outpatient endometrial sampling. *The Journal of family practice*, 10: 115-118.
Narrative review
- Issat, T., Beta, J., Nowicka, M. A. & Jakimiuk, A. J. (2014) - Accuracy and diagnostic value of outpatient hysteroscopy for malign and benign disease. - *European Journal of Gynaecological Oncology*, 35: 52-55.
Not in PICO (secondary care)
- Istatkov, M., Mirkov, K., Krutilin, S., Ivanova, K. & Karag'ozova, Z. (1986) [Current possibilities for the early diagnosis of endometrial cancer]. [Bulgarian]. *Akusherstvo i Ginekologija*, 25: 56-58.
In Bulgarian. Not enough information can be extracted, but I think it is "Not in PICO"

Ivanov, S., Katerinski, K., Zervoudis, S. & Ivanov, S. (2004) [Study of neovascularisation in endometrial cancer and hyperplasia using angio-Doppler technique]. [Bulgarian]. *Akusherstvo i Ginekologija*, 43: 41-43.

In Bulgarian, not enough information can be extracted to ascertain eligibility status, but I think it is "Not in PICO"

Jaffe, J. S. Use of outpatient endometrial biopsy in a population with intellectual disability. [References]. *Journal of Applied Research in Intellectual Disabilities* 21[2], 194-197. 2008.

Ref Type: Generic

Ref ID: 87

Reprint: Not in File

Abstract: Background: To demonstrate the feasibility of outpatient endometrial sampling to evaluate abnormal uterine bleeding in a population of women with intellectual disability. Method: Retrospective chart review was completed of all endometrial biopsies performed on women attending a dedicated gynaecology clinic for women with intellectual disability over an 8-year period. A fine calibre disposable suction curette was utilized. Results: Of the 64 women sampled, adequate tissue for pathological diagnosis was obtained in 84%. Of the 35 with post-menopausal bleeding, a pathological diagnosis was reported in 86% including one endometrial adenocarcinoma. Intravenous sedation was necessary in 12 cases. Conclusions: Endometrial sampling can be successfully performed on an outpatient basis in women with intellectual disability. Most were performed without sedation in a clinic setting suggesting that this technique is generally applicable in this population. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

Notes: DB - PsycINFO

AN - Peer Reviewed Journal: 2008-01714-011

MA - Jaffe, Joshua S.: jjaffe@snet.net

SO - *Journal of Applied Research in Intellectual Disabilities*. Vol.21(2), Mar 2008, pp. 194-197

Jimenez-Ayala, M., Jimenez-Ayala, P. B., Iglesias, E. & Vallejo, M. R. (2008) Endometrial adenocarcinoma: prevention and early diagnosis. [Review] [233 refs]. *Monographs in Clinical Cytology*, 17: 1-91.

Narrative review

jr, J. C. & Marine, C. S. (1989) Early detection of gynecologic malignancies. *Seminars in Surgical Oncology*, 5: 176-178.

Narrative review

Kalilic, J., Bakotin, J. & Bokun, R. (1987) The role of aspiration in the early detection of the endometrial carcinoma and its precursors. [Serbian]. *Medicinski Anali*, 13: 55-62.

Not in PICO (133/169 included women were asymptomatic)

Kang, S., Yoo, H. J., Hwang, J. H., Lim, M. C., Seo, S. S. & Park, S. Y. (2011) Sentinel lymph node biopsy in endometrial cancer: meta-analysis of 26 studies (DARE structured abstract). *Gynecologic Oncology*, 123: 522-527.

Not in PICO

Kassab, A., Trotter, P. & Fox, R. (2008) Risk of cancer in symptomatic postmenopausal women with endometrial polyps at scan. *Journal of Obstetrics & Gynaecology*, 28: 522-525.

Not in PICO

Keskin, U., Ozturk, M., Ercan, M., Dede, M., Yenen, M. C. & Ergun, A. (2013) Narrow-band imaging endoscopy for diagnosis of endometrial neoplasia, pilot study. *European Surgical Research*, 50: 146.

Abstract only, not enough information can be extracted to ascertain relevance, but I think it is not in PICO

Kisu, I., Banno, K., Kobayashi, Y., Ono, A., Masuda, K., Ueki, A., Nomura, H., Hirasawa, A., Abe, T., Kouyama, K., Susumu, N. & Aoki, D. (2011) Narrow band imaging hysteroscopy: A comparative

- study using randomized video images. *International Journal of Oncology*, 39: 1057-1062.
Not in PICO
- Koonings, P. P. & Grimes, D. A. (1989) Endometrial sampling techniques for the office. *American Family Physician*, 40: 207-210.
Narrative review
- Kozbagarova, R. G., Shibanova, A. I. & Patrusheva, A. S. (1989) Cytologic study of the endometrium and detection of groups at increased risk of developing cancer. [Russian]. *Laboratornoe Delo*, 43-47.
Not in PICO
- Kramer, S. C., Volkmer, B., Mattes, R., Brandle, E., Gorich, J. & Gottfried, H. W. (1999) [3D endosonography to clarify distal ureteral processes]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 170: 470-473.
Not in PICO
- Kudela, M., Pilka, R., Hejtmanek, P., Dzvincuk, P. & Ondrova, D. (2008) [The importance of sonography and hysteroscopy at suspected findings on endometrium of menopausal women]. [Czech]. *Ceska Gynekologie*, 73: 104-108.
Not in PICO
- Lahousen, M., Pickel, H., Tscherne, G. & Zierler, H. (1982) Early detection of endometrial cancer. [German]. *Wiener Medizinische Wochenschrift*, 132: 391-393.
Not in PICO (asymptomatic women)
- Laughead, M. K. & Stones, L. M. (1997) Clinical utility of saline solution infusion sonohysterography in a primary care obstetric-gynecologic practice. *American Journal of Obstetrics and Gynecology*, 176: 1313-1316.
Not in PICO
- Lazarov, L., Mang'rova, S. & Lazarov, N. (2001) [Hysteroscopic diagnosis of endometrial carcinoma]. [Bulgarian]. *Akusherstvo i Ginekologija*, 41: Suppl-7.
In Bulgarian, not enough information can be extracted to ascertain eligibility status, but I think it is a narrative review
- Le, T., Bentley, J., Farrell, S., Fortier, M. P., Giede, C., Kupets, R., Plante, M., Power, P., Renaud, M. C., Schepansky, A., Senikas, V., Kwon, J., Prefontaine, M., Germain, I., Pearcey, R., D'Souza, D., Senterman, M., Hoskins, P. & SOGC-GOC-SCC Policy and Practice Guidelines Committee (2013) Epidemiology and investigations for suspected endometrial cancer. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC*, 35: 380-383.
Narrative review/guideline
- Leroy-Brasme, T., Leroy, J. L. & Delecour, M. (1988) [Early diagnosis of cancer of the endometrium and its precursors: clinical and imaging aspects]. [Review] [42 refs] [French]. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction*, 17: 727-732.
Narrative review
- Liberis, V., Tsikouras, P., Christos, Z., Ammari, A., Dislian, V., Koutlaki, N., Liberis, A. & Maroulis, G. (2010) The contribution of hysteroscopy to the detection malignancy in symptomatic postmenopausal women. *Minimally Invasive Therapy and Allied Technologies*, 19: 83-93.
Not in PICO (secondary care, confirmed by Willie)
- Lickrish, G. M., Colgan, T. J. & Wright, V. C. (1993) Colposcopy of adenocarcinoma in situ and invasive adenocarcinoma of the cervix. *Obstetrics and Gynecology Clinics of North America*, 20: 111-122.
Narrative review
- Linden, M. & Roger, V. (1982) Diagnosis of endometrial carcinoma using the Mi-Marker helix sampling technique. *Acta Obstetrica et Gynecologica Scandinavica*, 61: 227-232.
Not in PICO

- Loh, J. S. (2011) An audit on the management of heavy menstrual bleeding in NHS primary and secondary care. *Journal of Obstetrics and Gynaecology*, 31: 783-784.
Not in PICO
- Lotfallah, H., Farag, K., Hassan, I. & Watson, R. (2005) One-stop hysteroscopy clinic for postmenopausal bleeding. *Journal of Reproductive Medicine*, 50: 101-107.
Not in PICO
- Loverro, G., Greco, P., Vimercati, A. & Selvaggi, L. (1998) [Angiogenesis and endometrial carcinoma. Correlations with blood flow analysis by transvaginal color Doppler ultrasonography]. [Review] [21 refs] [Italian]. *Minerva Ginecologica*, 50: 83-87.
Narrative review
- Lyngø, E. (1982) [Vaginal cytological examinations in Denmark]. [Danish]. *Ugeskrift for Læger*, 144: 124-129.
Not in PICO
- Mahoney, S., Parker, C., Potlog-Nahari, C. & Armstrong, A. (2006) Abnormal uterine bleeding: A primary care primer. *Consultant*, 46: 225-232.
Narrative review
- Mancini, F., Regnani, G., Persico, N., de, A. D. & Battaglia, C. (2002) Sonohysterography in the evaluation of endometrial abnormalities. *Italian Journal of Gynaecology and Obstetrics*, 14: 69-72.
Not in PICO
- Marchetti, M., Litta, P., Lanza, P., Lauri, F. & Pozzan, C. (2002) The role of hysteroscopy in early diagnosis of endometrial cancer. *European Journal of Gynaecological Oncology*, 23: 151-153.
Not in PICO
- Marret, H., Fauconnier, A., Chabbert-Buffet, N., Cravello, L., Golfier, F., Gondry, J., Agostini, A., Bazot, M., Brailly-Tabard, S., Brun, J. L., De Raucourt, E., Gervaise, A., Gompel, A., Graesslin, O., Huchon, C., Lucot, J. P., Plu-Bureau, Roman, H. & Fernandez, H. (2010) Clinical practice guidelines on menorrhagia: management of abnormal uterine bleeding before menopause. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 152: 133-137.
Narrative review
- Massoni, E. A. & Hajdu, S. I. (1984) Cytology of primary and metastatic uterine sarcomas. *Acta Cytologica*, 28: 93-100.
Not in PICO
- Mazhar, S., Masood, M. S. & Malik, K. M. (2005) Diagnostic value of endometrial sampling with pipelle suction curettage in patients with abnormal uterine bleeding and postmenopausal bleeding. *Medical Forum Monthly*, 16: 8-14.
Not in PICO
- Mazzon, I., Scotto, V., Guidi, M. L., Vittori, G., Ricci, G., Crisci, G. & Pignanelli, A. (1988) Outpatient hysteroscopy in the diagnosis of neoplastic and preneoplastic lesions of the endometrium. *European Journal of Gynaecological Oncology*, 9: 261-264.
Not in PICO
- Mencaglia, L., Valle, R. F., Perino, A. & Keith, L. G. (1988) Early detection of endometrial carcinoma and its precursors. *Current Problems in Obstetrics, Gynecology and Fertility*, 11: 173-176.
Narrative review
- Mencaglia, L., Valle, R. F., Perino, A. & Gilardi, G. (1990) Endometrial carcinoma and its precursors: Early detection and treatment. *International Journal of Gynecology and Obstetrics*, 31: 107-116.
Narrative review
- Mencaglia, L. (1995) Hysteroscopy and adenocarcinoma. [Review] [30 refs]. *Obstetrics & Gynecology Clinics of North America*, 22: 573-579.
Narrative review
- Mencarelli, R., Mainenti, M., Ottaviani, A., Righetti, G., Gilioli, E., Faccioli, G. & Cestaro, A. (1992) [Hysteroscopy in the early diagnosis of endometrial neoplasia. Personal experience with 200

- consecutive cases]. [Italian]. *Minerva Ginecologica*, 44: 429-432.
Not in PICO (secondary care)
- Mestwerdt, W. & Kranzfelder, D. (1983) [Current diagnostic possibilities in endometrial carcinoma and its precursors]. [German]. *Gynakologe*, 16: 87-92.
Narrative review
- Miklos, P., Klacko, M., Babala, P., Masak, L., Ondrus, D. & Waczulikova, I. (2014) Transvaginal ultrasound examination of myometrial infiltration by endometrial cancer. *Bratislavske Lekarske Listy*, 115: 14-18.
Not in PICO
- Mills, A. M. & Longacre, T. A. (2010) Endometrial hyperplasia. [Review]. *Seminars in Diagnostic Pathology*, 27: 199-214.
Narrative review
- Mkrtchian, B. B. & Tokhunts, K. A. (2007) [Transvaginal ultra sonography in atypical hyperplasia and early cancer of endometrium (diagnostic significance and prognostic evaluation)]. [Russian]. *Georgian Medical News*.(145):12-6, 2007 Apr., 12-16.
In Russian. Not enough information can be extracted, but I think it is "Not in PICO"
- Mohan, S., Page, L. M. & Higham, J. M. (2007) Diagnosis of abnormal uterine bleeding. *Best Practice and Research in Clinical Obstetrics and Gynaecology*, 21: 891-903.
Narrative review
- Morantz, C. (2004) ACS Guidelines for Early Detection of Cancer. *American Family Physician*, 69: 2013.
Guideline
- Murthy, N., Moncreiffe, L. & Seif, M. W. (2012) The role of expectant management of incidental thickened endometrium in asymptomatic postmenopausal women. *BJOG: An International Journal of Obstetrics and Gynaecology*, 119: 171.
Not in PICO
- Mutter, G. L., Lin, M. C., Fitzgerald, J. T., Kum, J. B., Baak, J. P., Lees, J. A., Weng, L. P. & Eng, C. (2000) Altered PTEN expression as a diagnostic marker for the earliest endometrial precancers. *Journal of the National Cancer Institute*, 92: 924-930.
Not in PICO
- Myriokefalitaki, E., D'Costa, D., Smith, M. & Ahmed, A. S. (2013) Primary bone metastasis as initial presentation of endometrial cancer (stage IVb). *Archives of Gynecology & Obstetrics*, 288: 739-746.
Not in PICO
- Neis, K. J. & Brandner, P. (2003) Early detection of endometrial cancer - Chances and limitations. [German]. *Onkologe*, 9: 1202-1210.
Narrative review
- Nocun, A., Pitynski, K., Wiechec, M., Ludwin, A., Jach, R., Knafel, A. & Pietrus, M. (2012) [The value of three-dimensional multiplanar (MPV) and volume contrast imaging (VCI) in the ultrasound evaluation of endometrial pathology]. [Polish]. *Przegląd Lekarski*, 69: 1271-1275.
Not in PICO
- Noda, K. (1984) Early diagnosis of uterine cancer. *Asian Medical Journal*, 27: 624-630.
Narrative review
- Nykjaer, H., Sorensen, E., Thorsen, N., Hansen, K. & Hagerup, L. (1980) [Vaginal cytology examination in general practice. a retrospective study]. [Danish]. *Ugeskrift for Laeger*, 142: 3233-3235.
Not in PICO
- Okadome, M., Saito, T., Tsukamoto, N., Nishi, K., Nishiyama, N. & Nagata, E. (2006) Endometrial scraping cytology in women with extragenital malignancies. *Acta Cytologica*, 50: 158-163.
Not in PICO
- Okeahialam, M. G., Jones, S. E. & O'Donovan, P. J. (2001) Outcome of outpatient micro-hysteroscopy performed for abnormal bleeding while on hormone replacement therapy. *Journal of Obstetrics*

- & *Gynaecology*, 21: 277-279.
Not in PICO
- Oriel, K. A. & Schrager, S. (1999) Abnormal uterine bleeding. *American Family Physician*, 60: 1371-1382.
Narrative review
- Paschopoulos, M., Paraskevaïdis, E., Stefanidis, K., Kofinas, G. & Lolis, D. (1997) Vaginoscopic approach to outpatient hysteroscopy. *Journal of the American Association of Gynecologic Laparoscopists*, 4: 465-467.
Not in PICO
- Penney, G., Vale, L., Souter, V. & Templeton, A. (1997) Endometrial assessment procedures: an audit of current practice in Scotland. *Human Reproduction*, 12: 2041-2045.
Not in PICO
- Persadie, R. J. (2002) Ultrasonographic assessment of endometrial thickness: a review. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC*, 24: 131-136.
Narrative review
- Poppendiek, G. & Bayer, K. H. (1981) [The cytology of endometrium by aspiration-a method for the early detection of endometrial carcinoma (author's transl)]. [German]. *Geburtshilfe und Frauenheilkunde*, 41: 188-191.
Not in PICO
- Prislin, M. D., Dinh, T. & Giglio, M. (1997) On-site colposcopy services in a family practice residency clinic: impact on physician test-ordering behavior, patient compliance, and practice revenue generation. *Journal of the American Board of Family Practice*, 10: 259-264.
Not in PICO
- Protheroe, J. (2004) Modern management of menorrhagia. *Journal of Family Planning and Reproductive Health Care*, 30: 118-122.
Narrative review
- Qian, J., Weber, D., Cochran, R., Hossain, D. & Bostwick, D. G. (2010) Detection of chromosomal anomalies in endometrial atypical hyperplasia and carcinoma by using fluorescence in situ hybridization. *Cancer Cytopathology*, 118: 97-104.
Not in PICO
- Renaud, M. C., Le, T., Le, T., Bentley, J., Farrell, S., Fortier, M. P., Giede, C., Kupets, R., Plante, M., Power, P., Renaud, M. C., Schepansky, A., Senikas, V., Kwon, J., Prefontaine, M., Germain, I., Pearcey, R., D'Souza, D., Senterman, M., Hoskins, P. & SOGC-GOC-SCC Policy and Practice Guidelines Committee (2013) Epidemiology and investigations for suspected endometrial cancer. *Journal of Obstetrics & Gynaecology Canada: JOGC*, 35: 380-383.
Not in PICO
- Rivkine, E., Jakubowicz, D., Marciano, L., Polliand, C., Poncelet, C., Zioli, M. & Barrat, C. (2013) Hepatic endometrioma: a case report and review of the literature: report of a case. *Surgery Today*, 43: 1188-1193.
Not in PICO
- Rudelstorfer, R., Schieder, K. & Bernaschek, G. (1988) Vaginosonographic measurement of endometrial thickness for early detection of carcinoma of the endometrium. *Journal d'Echographie et de Medecine Ultrasonore*, 9: 244-246.
Not in PICO
- Rudigoz, R. C., Sergeant, P., Isoard, L. & Salle, B. (1997) [Early ultrasonographic detection of endometrial cancer]. [Review] [49 refs] [French]. *Fertilite Contraception Sexualite*, 25: 21-26.
Narrative review
- Saccucci, P., Rigon, G., Provenza, C., Mastrone, M., Are, P., Pisani, G. & Bartolelli, C. (1996) [Hysteroscopic features in postmenopausal uterine bleeding]. [Italian]. *Minerva Ginecologica*, 48:

- 401-404.
Not in PICO (secondary care)
- Saso, S., Chatterjee, J., Georgiou, E., Ditri, A. M., Smith, J. R. & Ghaem-Maghami, S. (2011) Endometrial cancer. *BMJ*, 343.
Narrative review
- Schmidt, T., Rein, D. T., Romer, T., Straube, W. & Mallmann, P. (1999) The role of hysteroscopy in the management of asymptomatic postmenopausal patients with suspicious ultrasound findings of the uterine endometrium - Correlation with sonographic and histologic findings. [German]. *Geburtshilfe und Frauenheilkunde*, 59: 163-166.
Not in PICO
- Schneider, A. (2011) Detection rate and diagnostic accuracy of sentinel-node biopsy in early stage endometrial cancer: A prospective multicentre study (SENTI-ENDO). [German]. *Onkologe*, 17: 725-726.
Not in PICO
- Seamark, C. J. (1998) Endometrial sampling in general practice. *British Journal of General Practice*, 48: 1597-1598.
Not in PICO
- Sempowski, I. P., Rungi, A. A. & Seguin, R. (2006) A cross sectional survey of urban Canadian family physicians' provision of minor office procedures. *BMC Family Practice*, 7: 18.
Not in PICO
- Shafi, M. I. (1994) Management of women with mild dyskaryosis. Cytological surveillance avoids overtreatment. *BMJ*, 309: 590-591.
Not in PICO
- Shapley, M. & Redman, C. W. (1997) Endometrial sampling and general practice. *British Journal of General Practice*, 47: 387-391.
Narrative review
- Shun-Jiao, Z. (1990) Value of multiple punch biopsy plus endocervical curettage in early diagnosis of cancer of the cervix uteri. [Chinese]. *Chinese Journal of Clinical Oncology*, 17: 3-5.
Not in PICO
- Siristatidis, C., Chrelias, C., Salamalekis, G. & Kassanos, D. (2010) Office hysteroscopy: Current trends and potential applications: A critical review. *Archives of Gynecology and Obstetrics*, 282: 383-388.
Narrative review
- Sivvas, T., Giagloglou, K., Savvidis, A. & Tsikouras, P. (2010) Transvaginal sonography as a prognostic value to detect endometrial pathology in postmenopausal symptomatic women without hormone replacement therapy. *Archives of Gynecology and Obstetrics*, 282: S118.
Not in PICO
- Smith-Bindman, R., Weiss, E. & Feldstein, V. (2004) How thick is too thick? When endometrial thickness should prompt biopsy in postmenopausal women without vaginal bleeding. *Ultrasound in Obstetrics and Gynecology*, 24: 558-565.
Not in PICO
- Smith, E. M. & Anderson, B. (1987) Symptomatology, delay, and stage of disease in endometrial cancer. *Cancer Detection and Prevention*, 10: 247-254.
Not in PICO
- Socolov, D., Socolov, R. V., Butureanu, S., Flaiser, C., Amalinei, C. & Balan, R. (2005) [The use of hysteroscopy in the diagnostic on perimenopausal metrorrhagia. A study of 35 cases]. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 109: 813-816.
Not in PICO
- Soutter, W. P. (1994) Management of women with mild dyskaryosis. Immediate referral to colposcopy is safer. *BMJ*, 309: 591-592.
Not in PICO

- Spagnolo, A., Torrini, V., Cavallari, L. & Patella, A. (1985) Uterine cervix: Colposcopic, cytologic, histologic correlations in 5602 women observed. [Italian]. *Giornale Italiano di Oncologia*, 5: 295-300.
In Italian, limited information provided about patients, but I believe it is "Not in PICO"
- Spiewankiewicz, B., Stelmachow, J., Sawicki, W. & Kietlinska, Z. (1995) Hysteroscopy with selective endometrial sampling after unsuccessful dilatation and curettage in diagnosis of symptomatic endometrial cancer and endometrial hyperplasias. *European Journal of Gynaecological Oncology*, 16: 26-29.
Not in PICO
- Stock, R. J. & Gallup, D. G. (1987) Hysterography in patients with suspected uterine cancer: radiographic and histologic correlations and clinical implications. *Obstetrics & Gynecology*, 69: 872-878.
Not in PICO
- Sudoma, I. A., Iatskovskaia, N. L. & Kokhanevich, E. V. (1990) [Hysteroscopic semeiotics of cancer of the uterine body]. [Russian]. *Voprosy Onkologii*, 36: 351-355.
Not in PICO
- Surico, N., Ragonesi, G. & Porcelli, A. (1985) Hysteroscopic diagnosis during metrorrhagia. [Italian]. *Minerva Ginecologica*, 37: 519-521.
Not in PICO (secondary care)
- Sweet, M. G., Schmidt-Dalton, T. A., Weiss, P. M. & Madsen, K. P. (2012) Evaluation and management of abnormal uterine bleeding in premenopausal women. *American Family Physician*, 85: 35-43.
Narrative review
- Tahir, M. M., Bigrigg, M. A., Browning, J. J., Brookes, S. T. & Smith, P. A. (1999) A randomised controlled trial comparing transvaginal ultrasound, outpatient hysteroscopy and endometrial biopsy with inpatient hysteroscopy and curettage. *British Journal of Obstetrics & Gynaecology*, 106: 1259-1264.
Not in PICO
- Takashima, E. (1985) Usefulness of hysteroscopy for detection of cancer in the endocervical canal. *Nippon Sanka Fujinka Gakkai Zasshi - Acta Obstetrica et Gynaecologica Japonica*, 37: 2401-2409.
Not in PICO
- Teter, J. & Szamborski, J. (1984) [Ambulatory endometrial biopsy as a method of detection of high-risk conditions and cancer of the uterus]. [Polish]. *Ginekologia Polska*, 55: 435-443.
Not in PICO (87.9% women were asymptomatic)
- Tinelli, R., Tinelli, F. G., Cicinelli, E., Malvasi, A. & Tinelli, A. (2008) The role of hysteroscopy with eye-directed biopsy in postmenopausal women with uterine bleeding and endometrial atrophy. *Menopause*, 15: 737-742.
Not in PICO
- Trichot, C., Barthier, S., Rivain, A. L., Prevot, S., Demoulin, G., Kai, G. S., Thubert, T. & Deffieux, X. (1994) [Diagnosis for uterine cervix and endometrial cancer]. [French]. - *Revue du Praticien*, 64: 789-791.
Guideline
- Tsai, M. C. & Goldstein, S. R. (2012) Office Diagnosis and Management of Abnormal Uterine Bleeding. *Clinical Obstetrics and Gynecology*, 55: 635-650.
Narrative review
- van Doorn, H. C., Opmeer, B. C., Burger, C. W., Duk, M. J., Kooi, G. S., Mol, B. W. & Dutch Study in Postmenopausal Bleeding (DUPOMEB) (2007) Inadequate office endometrial sample requires further evaluation in women with postmenopausal bleeding and abnormal ultrasound results. *International Journal of Gynaecology & Obstetrics*, 99: 100-104.
Not in PICO

- van Hanegem, N., Breijer, M. C., Khan, K. S., Clark, T. J., Burger, M. P. M., Mol, B. W. J. & Timmermans, A. (2011) Diagnostic evaluation of the endometrium in postmenopausal bleeding: An evidence-based approach. *Maturitas*, 68: 155-164.
Narrative review
- van, T. M., Wieser, F. & Nagele, F. (2000) Diagnostic hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal patients. *Contributions to Gynecology and Obstetrics*, 20: 21-26.
Not in PICO
- Vercellini, P., Cortesi, I., Oldani, S., Moschetta, M., De, G. O. & Crosignani, P. G. (1997) The role of transvaginal ultrasonography and outpatient diagnostic hysteroscopy in the evaluation of patients with menorrhagia. *Human Reproduction*, 12: 1768-1771.
Not in PICO
- Walker, S., Hyde, C. & Hamilton, W. (2013) Risk of uterine cancer in symptomatic women in primary care: case-control study using electronic records. *British Journal of General Practice*, 63: e643-e648.
Already included
- Wang, Z. Q., Yang, X. Q., Wang, J. L., Xie, J. L., Shen, D. H. & Wei, L. H. (2011) [An analysis on the clinicopathological characteristics of 79 cases atypical endometrial hyperplasia]. [Chinese]. *Chung-Hua Fu Chan Ko Tsa Chih [Chinese Journal of Obstetrics & Gynecology]*, 46: 19-23.
Not in PICO
- Weed, J. C., Jr. & Marine, C. S. (1989) Early detection of gynecologic malignancies. [Review] [9 refs]. *Seminars in Surgical Oncology*, 5: 176-178.
Narrative review
- Woo, M. M., Alkushi, A., Verhage, H. G., Magliocco, A. M., Leung, P. C., Gilks, C. B. & Auersperg, N. (2004) Gain of OGP, an estrogen-regulated oviduct-specific glycoprotein, is associated with the development of endometrial hyperplasia and endometrial cancer. *Clinical Cancer Research*, 10: 7958-7964.
Not in PICO
- Woodard, T. L., Awonuga, A. O. & Puscheck, E. (2012) Malignant transformation of endometrioma in a woman with a history of ovulation induction and in vitro fertilization. *Case Reports in Medicine*, 2012: 497362.
Not in PICO
- Wu, H. H. J., Casto, B. D. & Elsheikh, T. M. (2003) Endometrial brush biopsy: An accurate outpatient method of detecting endometrial malignancy. *Journal of Reproductive Medicine for the Obstetrician and Gynecologist*, 48: 41-45.
Not in PICO
- Xiong, Y., Xiong, Y. Y. & Zhou, Y. F. (2009) [Expression of beta-catenin, Glut-1, PTEN proteins in uterine endometrioid adenocarcinoma and its precursor lesions]. [Chinese]. *Chung-Hua Ping Li Hsueh Tsa Chih - Chinese Journal of Pathology*, 38: 594-599.
Not in PICO
- Yakasai, A., Allam, M. & Thompson, A. J. (2011) Incidence of bladder cancer in a one-stop clinic. *Annals of African Medicine*, 10: 112-114.
Not in PICO
- Yamashita, Y., Mizutani, H., Torashima, M., Takahashi, M., Miyazaki, K., Okamura, H., Ushijima, H., Ohtake, H. & Tokunaga, T. (1993) Assessment of myometrial invasion by endometrial carcinoma: transvaginal sonography vs contrast-enhanced MR imaging. *AJR.American Journal of Roentgenology*, 161: 595-599.
Not in PICO
- Yang, G. C. H. & Wan, L. S. (2000) Endometrial biopsy using the Tao Brush (R) method - A study of 50 women in a general gynecologic practice. *Journal of Reproductive Medicine*, 45: 109-114.
Not in PICO

Yela, D. A., Hidalgo, S. R., Pereira, K. C., Gabiatti, J. R. & Monteiro, I. M. (2011) [Comparative study of transvaginal sonography and outpatient hysteroscopy for the detection of intrauterine diseases]. [Portuguese]. *Acta Medica Portuguesa*, 24: Suppl-70.

Not in PICO

Zarcone, R., D'Apuzzo, N., Sansone, A., Vullo, G. & Monarca, M. (1997) [Early diagnosis of adenocarcinoma by endometrial cytologic samples]. [Italian]. *Minerva Ginecologica*, 49: 421-423.

Not in PICO (secondary care)

Zehavi, S., Schneider, D., Bukovsky, I. & Halperin, R. (2003) Pathological findings in early-stage endometrial cancer. *European Journal of Gynaecological Oncology*, 24: 18-20.

Not in PICO

Zhou, J., Tomashefski, J. F., Jr. & Khiyami, A. (2007) ThinPrep Pap tests in patients with endometrial cancer: a histo-cytological correlation. *Diagnostic Cytopathology*, 35: 448-453.

Not in PICO

Zivanovic, O., Houry-Collado, F., Abu-Rustum, N. R. & Gemignani, M. L. (2009) Sentinel Lymph Node Biopsy in the Management of Vulvar Carcinoma, Cervical Cancer, and Endometrial Cancer. *The Oncologist*, 14: 695-705.

Not in PICO

Zlatkov, V., Kostova, P., Barzakov, G., Tcholakova, A., Milochev, V., Velinov, E., Radeva, V. & Mihova, A. (2007) Flexible hysteroscopy in irregular uterine bleeding. *Journal of B.U.On.*, 12: 53-56.

Not in PICO

CERVICAL CANCER

Review question:

What is the risk of cervical cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

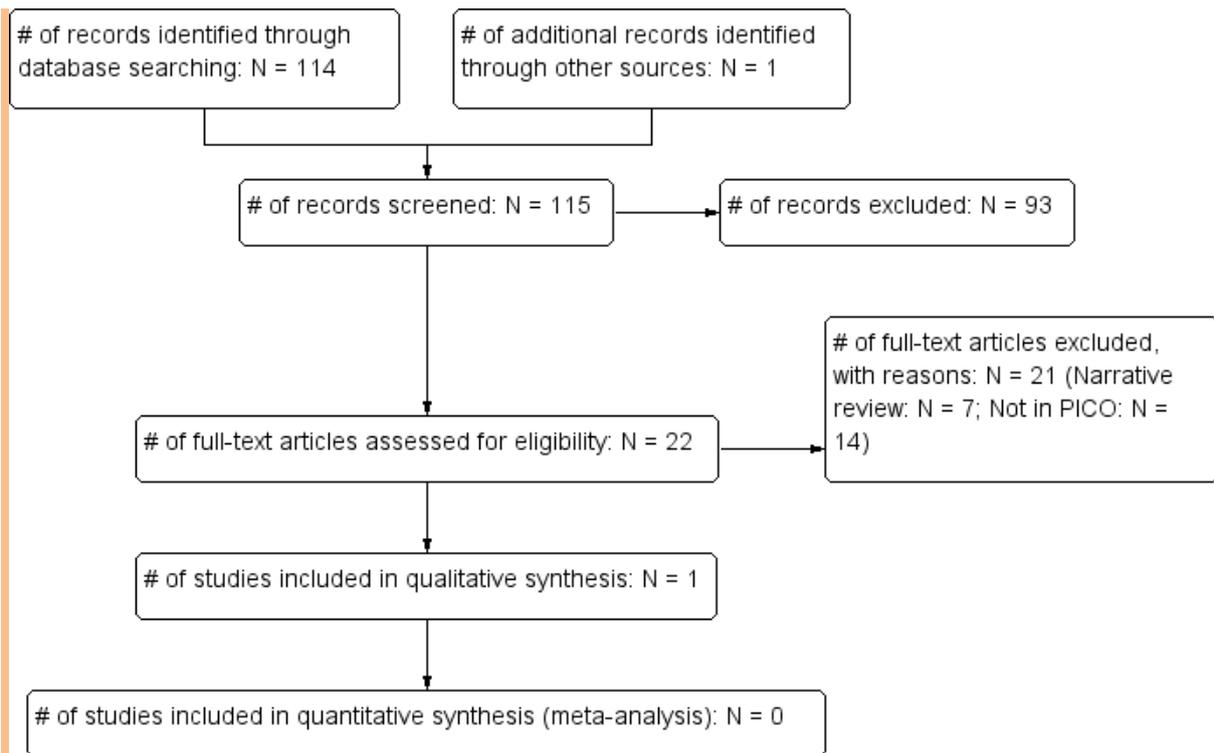
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	1076	34	17/04/2013
<i>Premedline</i>	All-2012	42	5	18/04/2013
<i>Embase</i>	All-2012	1532	44	18/04/2013
<i>Cochrane Library</i>	All-2012	529	3	19/04/2013
<i>Psychinfo</i>	All-2012	31	2	18/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	539	16	19/04/2013

Total References retrieved (after de-duplication): 96

Update Search

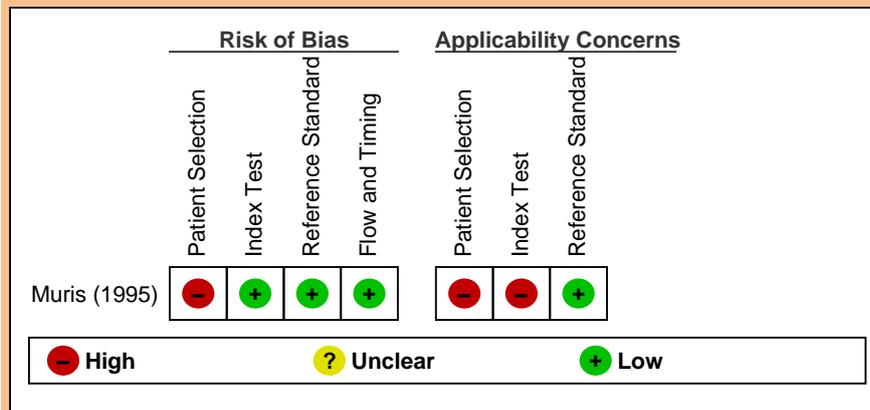
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-13/08/2014	166	4	13/08/2014
<i>Premedline</i>	4/2013-13/08/2014	56	5	13/08/2014
<i>Embase</i>	4/2013-13/08/2014	315	9	13/08/2014
<i>Cochrane Library</i>	4/2013-13/08/2014	99	0	13/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	4/2013-13/08/2014	20	2	13/08/2014

Total References retrieved (after de-duplication): 18



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included study in the figure below. The main issues to note are that the study results are compromised by both the non-consecutive/non-random patient selection as well as by the under-specification of the symptom under investigation and the setting, which may not be directly applicable to UK-based primary care.



Study results

Table 1: Cervical cancer: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI)
Muris (1995)	Non-acute abdominal complaints	All women	0.5 (0.1-1.6) 3/598: 1 cervix, 2 other cancer of the female genital

Evidence statement(s):

Non-acute abdominal complaints presenting in primary care do not appear to be associated with an increased risk of cervical cancer (PPV = 0.5%; 1 study, N = 598). The included study was associated with 3 bias/applicability concerns (see also Table 1).

Evidence tables**Muris (1995)**

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 80/460 general practitioners in Limburg (Holland)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 933; 335 males, 598 females; age range = 18-75, aged > 30 years: N = 712, aged > 40 years: N = 517, aged > 60 years: N = 171. <u>Inclusion criteria:</u> Patients who in 1989 consulted one of the participating GPs for new abdominal complaints lasting ≥ 2 weeks and with whom the GPs had a diagnostic problem. <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> GPs in Holland
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	New abdominal complaints lasting ≥ 2 weeks. Not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up for ≥ 12 months (mean = 18 months).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No

Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Other cancers diagnosed in these patients were: Stomach (2/933), pancreas (2/933), trachea/bronchus/lung (2/933), kidney (1/933), colorectal (4/933), and other and unspecified sites (2/933).

References

Included studies

Muris, J. W., Starmans, R., Fijten, G. H., Crebolder, H. F., Schouten, H. J., and Knottnerus, J. A. Non-acute abdominal complaints in general practice: diagnostic value of signs and symptoms. *British Journal of General Practice* 45[395], 313-316. 1995.

Excluded studies (with reason)

(2002) Patient pages. Early detection of cervical cancer. *CA: A Cancer Journal for Clinicians*, 52: 375-376.

Not in PICO

(2012) Observational study of cervical cancer. *Indian Journal of Medical Ethics*, 9: 50-51.

Narrative review

Abu, J., Davies, Q. & Ireland, D. (2006) Should women with postcoital bleeding be referred for colposcopy? *Journal of Obstetrics & Gynaecology*, 26: 45-47.

Not in PICO

Adanu, R. M., Seffah, J. D., Duda, R., Darko, R., Hill, A. & Anarfi, J. (2010) Clinic visits and cervical cancer screening in accra. *Ghana Medical Journal*, 44: 59-63.

Not in PICO

Aktas, A., Walsh, D., Rybicki, L. & Schleckman, E. (2011) Cancer symptom clusters by primary site (414-A). *Journal of Pain and Symptom Management. Conference: Annual Assembly of American Academy of Hospice and Palliative Medicine and Hospice and Palliative Nurses Association Vancouver, BC Canada. Conference Start: 20110216 Conference End: 20110219. Conference*, 41: January.

Not in PICO

Al-Kadri, H. M., Al-Awami, S. H. & Madkhali, A. M. (2004) Assessment of risk factors of uterine cancer in Saudi patients with postmenopausal bleeding. *Saudi Medical Journal*, 25: 857-861.

Not in PICO

Albers, J. R., Hull, S. K. & Wesley, R. M. (2004) Abnormal uterine bleeding. *American Family Physician*, 69: 1915-1926.

Narrative review

- Alleyne, G. (1996) Early detection of cervical cancer. *Bulletin of the Pan American Health Organization*, 30: 283-284.
Narrative review
- Anorlu, R. I., Orakwue, C. O., Oyeneyin, L. & Abudu, O. O. (2004) Late presentation of patients with cervical cancer to a tertiary hospital in Lagos: what is responsible? *European Journal of Gynaecological Oncology*, 25: 729-732.
Not in PICO
- Apgar, B. S., Kaufman, A. J., Bettcher, C. & Parker-Featherstone, E. (2013) Gynecologic procedures: colposcopy, treatments for cervical intraepithelial neoplasia and endometrial assessment. [Review]. *American Family Physician*, 87: 836-843.
Narrative review
- Bakos, O., Smith, P. & Heimer, G. (1994) Transvaginal ultrasonography for identifying endometrial pathology in postmenopausal women. *Maturitas*, 20: 181-189.
Ordered for endometrial tests
- Benedet, J. L., Anderson, G. H. & Maticic, J. P. (1992) A comprehensive program for cervical cancer detection and management. *American Journal of Obstetrics & Gynecology*, 166: 1254-1259.
Not in PICO
- Boissel, J. P., Collet, J. P., Alborini, A., Cordel, J. C., Filsnoel, J., Gillet, J., Nemoz, C., Brémond, A., Bernhard, G. & Bourdin, J. F. (1995) Education program for general practitioners on breast and cervical cancer screening: a randomized trial. PRE.SA.GF Collaborative Group. *Revue d'épidémiologie.et de santé.publique.*, 43: 541-547.
Not in PICO
- Boon, M. E., Duineveld, S. M., Ouwerkerk-Noordam, E. & Dias, D. (2007) Preneoplastic and neoplastic cervical lesions as detected in Cytoblock sections: the importance of sampling women with bleeding symptoms. *European Journal of Gynaecological Oncology*, 28: 282-286.
Not in PICO
- Buchsbaum, G., Doyle, P., Glantz, J. C., Sato, H. & Thomas, S. (2012) Prevalence of pelvic floor disorders in various gynecologic cancers. *Neurourology and Urodynamics.Conference: 42nd Annual Meeting of the International Continence Society, ICS 2012 Beijing China.Conference Start: 20121015 Conference End: 20121019.Conference Publication: (var.pagings)*, 31: August.
Not in PICO
- Burbos, N., Musonda, P. & Rufford, B. (2011) Diagnostic performance of urgent referrals for suspected gynaecological malignancies. *Archives of Gynecology & Obstetrics*, 284: 1495-1500.
Not in PICO
- Casey, C., Chen, L.-M. & Rabow, M. W. (2011) Symptom management in gynecologic malignancies. *Expert Review of Anticancer Therapy*, 11: July.
Narrative review
- Cavanagh, D. & Roberts, W. S. (1985) Early detection of uterine cancer. *Journal of the Florida Medical Association*, 72: 36-40.
Narrative review
- Chhabra, S., Bhavani, M. & Deshpande, A. (2014) Trends of vulvar cancer. *Journal of Obstetrics & Gynaecology*, 34: 165-168.
Not in PICO
- Cooper, C. P., Polonec, L. & Gelb, C. A. (11111) Women's knowledge and awareness of gynecologic cancer: A multisite qualitative study in the United States. *Journal of Women's Health*, 20: 01.
Not in PICO
- Cooper, C. P., Polonec, L., Stewart, S. L. & Gelb, C. A. (2013) Gynaecologic cancer symptom awareness, concern and care seeking among US women: A multi-site qualitative study. *Family Practice*, 30: February.
Not in PICO

- Crowder, S. & Tuller, E. (2007) Small Cell Carcinoma of the Female Genital Tract. *Seminars in Oncology*, 34: February.
Narrative review
- Deshields, T. L., Potter, P., Olsen, S., Liu, J. & Dye, L. (2011) Documenting the symptom experience of cancer patients. *Journal of Supportive Oncology*, 9: November.
Not in PICO
- Digumarti, L. & Katamreddy, B. (2011) Gynaecologic malignancies in post-menopausal women-an observational study. *International Journal of Gynecological Cancer.Conference: International Gynecologic Cancer Society Regional Meeting on Gynecologic Cancers, IGCS 2011 New Delhi India.Conference Start: 20110402 Conference End: 20110403.Conference Publication: (var.pagin*, 21: May.
Not in PICO
- Ding, S. L., Yin, C. S., Ger, L. P., Chen, A. & Kao, S. J. (1991) [A clinical study on 268 patients with cervical carcinoma]. [Chinese]. *Chung Hua i Hsueh Tsa Chih - Chinese Medical Journal*, 48: 439-444.
Not in PICO
- Dubuisson, J., Boukrid, M. & Petignat, P. (1936) [Management of post-coital bleeding: should all women be referred?]. [French]. *Revue Medicale Suisse*, 9: 1933-1934.
Narrative review
- Ebeling, K. (1986) [Practical points of reference for the prevention and early detection of cervical cancer]. [German]. *Zeitschrift fur Arztliche Fortbildung (Jena)*, 80: 306-310.
Narrative review
- Ebeling, K. (1987) [Early diagnosis of cervical cancer]. [German]. *Zeitschrift fur Arztliche Fortbildung (Jena)*, 81: 763-769.
Narrative review
- Elit, L. (2000) Endometrial cancer - Prevention, detection, management, and follow up. *Canadian Family Physician*, 46: 887-892.
Not in PICO
- Emery, J. D., Shaw, K., Williams, B., Mazza, D., Fallon-Ferguson, J., Varlow, M. & Trevena, L. J. (2014) The role of primary care in early detection and follow-up of cancer. *Nature Reviews Clinical Oncology*, 11: 38-48.
Narrative review
- Evans, R. J. & Watson, C. P. The hot foot syndrome: Evans' sign and the old way. [References]. *Pain Research & Management* 17[1], 31-34. 2012.
Not in PICO
- Eze, J. N., Emeka-Irem, E. N. & Edegbe, F. O. (2013) A six-year study of the clinical presentation of cervical cancer and the management challenges encountered at a state teaching hospital in southeast Nigeria. *Clinical Medicine Insights.Oncology*, 7: 151-158.
Not in PICO
- Falcone, T. & Parker, W. H. (2013) Surgical management of leiomyomas for fertility or uterine preservation. [Review]. *Obstetrics & Gynecology*, 121: 856-868.
Narrative review
- Feldman, S. (2003) How often should we screen for cervical cancer? *New England Journal of Medicine*, 349: 1495-1496.
Not in PICO
- Fowler, J. M., Carpenter, K. M., Gupta, P., Golden-Kreutz, D. M. & Andersen, B. L. (2004) The gynecologic oncology consult: Symptom presentation and concurrent symptoms of depression and anxiety. *Obstetrics and Gynecology*, 103: June.
Not in PICO
- Gale, A. & Dey, P. (2009) Postmenopausal bleeding. *Menopause International*, 15: December.
Narrative review

- Giannella, L., Mfuta, K., Setti, T., Cerami, L. B., Bergamini, E. & Boselli, F. (2014) A risk-scoring model for the prediction of endometrial cancer among symptomatic postmenopausal women with endometrial thickness > 4 mm. *BioMed Research International*, 2014.
Not in PICO
- Goh, C. & Chia, Y. N. (2012) Clear cell carcinoma of the cervix - The KKH experience from 2000-2010. *International Journal of Gynecology and Obstetrics.Conference: 20th FIGO World Congress of Gynecology and Obstetrics Rome Italy.Conference Start: 20121007 Conference End: 20121012.Conference Publication: (var.pagings)*, 119: October.
Not in PICO
- Golan, A., Cohen-Sahar, B., Keidar, R., Condrea, A., Ginath, S. & Sagiv, R. (2010) Endometrial polyps: Symptomatology, menopausal status and malignancy. *Gynecologic and Obstetric Investigation*, 70: August.
Not in PICO
- Gupta, J. K., Wilson, S., Desai, P. & Hau, C. (1996) How should we investigate women with postmenopausal bleeding? *Acta Obstetrica et Gynecologica Scandinavica*, 75: 475-479.
Not in PICO
- Gupta, J. K., Chien, P. F., Voit, D., Clark, T. J. & Khan, K. S. (2002) Ultrasonographic endometrial thickness for diagnosing endometrial pathology in women with postmenopausal bleeding: a meta-analysis (Structured abstract). *Acta Obstetrica et Gynecologica Scandinavica*, 81: 799-816.
Not in PICO
- Haroon, S. & Cui, M. (2012) Role of Pap smear in early diagnosis of cervical cancer- A Case Study of women in Saudi Arabia. *Life Science Journal-Acta Zhengzhou University Overseas Edition*, 9: 1027-1036.
Not in PICO
- Hasumi, K. (1988) [Differential diagnosis of early carcinoma of the uterus]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1416-1420.
Narrative review
- Hertel, H. & Hillemanns, P. (1111) Pre-menopausal vaginal bleeding in cases of gynaecological malignancy. [German]. *Gynakologische Endokrinologie*, 5: May.
Narrative review
- Hippisley-Cox, J. & Coupland, C. (2013) Symptoms and risk factors to identify women with suspected cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice*, 63: 11-21.
Not in PICO
- Huang, Y. W., Fan, Y. H., Lin, A. T. & Chen, K. K. (2012) The clinical characteristics of uterine tumor-related bladder outlet obstruction. *International Urogynecology Journal*, 23: 105-110.
Not in PICO
- Ikechebelu, J. I., Onyiaorah, I. V., Ugboaja, J. O., Anyiam, D. C. D. & Eleje, G. U. (2010) Clinicopathological analysis of cervical cancer seen in a tertiary health facility in Nnewi, south-east Nigeria. *Journal of Obstetrics and Gynaecology*, 30: April.
Not in PICO
- Issah, F., Maree, J. E. & Mwinituo, P. P. (2011) Expressions of cervical cancer-related signs and symptoms. *European Journal of Oncology Nursing*, 15: 67-72.
Not in PICO
- Jiwa, M., Walters, S. & Cooper, C. (2002) Quality of referrals to gynaecologists: Towards consensus. *Journal of Clinical Governance*, 10: 2002.
Not in PICO
- Johnson, J. K., John, R., Humera, A., Kukreja, S., Found, M. & Lindow, S. W. (2007) The prevalence of emotional abuse in gynaecology patients and its association with gynaecological symptoms. *European Journal of Obstetrics Gynecology and Reproductive Biology*, 133: July.
Not in PICO

- Jones, S. C. & Johnson, K. (2012) Womens awareness of cancer symptoms: A review of the literature. *Women's Health*, 8: September.
Narrative review
- Kalish, G. M., Patel, M. D., Gunn, M. L. D. & Dubinsky, T. J. (2007) Computed tomographic and magnetic resonance features of gynecologic abnormalities in women presenting with acute or chronic abdominal pain. *Ultrasound Quarterly*, 23: September.
Narrative review
- Khattab, A. F., Ewies, A. A., Appleby, D. & Cruickshank, D. J. (2005) The outcome of referral with postcoital bleeding (PCB). *Journal of Obstetrics & Gynaecology*, 25: 279-282.
Not in PICO
- Kim, S. J., Ha, S. Y., Choi, B. M., Lee, M. Y., Jin, J. Y., Yeom, S. J., Kim, T. W., Kim, Y. M. & Lee, K. (2013) The prevalence and clinical characteristics of cancer among anemia patients treated at an outpatient clinic. *Blood Research*, 48: 46-50.
Not in PICO (secondary care)
- Kostova, P. & Zlatkov, V. (2013) [Pregnancy and malignant diseases. Part V. Some rare gynecological tumors during pregnancy]. [Bulgarian]. *Akusherstvo i ginekologii*{combining double inverted breve}a, 52: 48-50.
Narrative review
- Lahousen, M., Pickel, H., Tscherne, G. & Zierler, H. (1982) [Early diagnosis of uterine carcinoma]. [German]. *Wiener Medizinische Wochenschrift*, 132: 391-394.
Not in PICO
- Lal, M., Raheja, S., Kale, S., Das, N., Gogia, A. R. & Bhowmik, K. T. (2012) An experience with 156 patients attending a newly organized pain and palliative care clinic in a tertiary hospital. *Indian Journal of Cancer*, 49: 293-297.
Not in PICO
- Leeson, S. C., Edmondson, R. J., Heatley, M. K., Nunns, D., Rollason, T., Reynolds, K., Seddon, D., Whitaker, R. & Kehoe, S. (2006) Guidelines for gynecological cancer - An audit of current network documents in England and Wales. *International Journal of Gynecological Cancer*, 16: March/April.
Not in PICO
- Lentz, S. S. & Homesley, H. D. (1998) Gynecologic problems in older women. *Clinics in Geriatric Medicine*, 14.
Narrative review
- Liberis, V., Tsikouras, P., Christos, Z., Ammari, A., Dislian, V., Koutlaki, N., Liberis, A. & Maroulis, G. (2010) The contribution of hysteroscopy to the detection malignancy in symptomatic postmenopausal women. *Minimally Invasive Therapy & Allied Technologies: Mitat*, 19: 83-93.
Not in PICO (secondary care, confirmed by Willie)
- Llanos, A. A. & Salas, M. M. (2009) Evaluation of the "Early detection and opportune attention of cervicouterine cancer" program. *Atencion Primaria*, 41: 300-305.
Not in PICO
- Lopez, V., Copp, G., Brunton, L. & Molassiotis, A. (2011) Symptom experience in patients with gynecological cancers: The development of symptom clusters through patient narratives. *Journal of Supportive Oncology*, 9: March-April.
Not in PICO
- Low, E. L., Simon, A. E., Waller, J., Wardle, J. & Menon, U. (2013) Experience of symptoms indicative of gynaecological cancers in UK women. *British Journal of Cancer*, 109: 882-887.
Duplicate
- Low, E. L., Simon, A. E., Waller, J., Wardle, J. & Menon, U. (2013) Experience of symptoms indicative of gynaecological cancers in UK women. *British Journal of Cancer*, 109: 882-887.
Not in PICO
- MacCio, A., Madeddu, C., Gramignano, G., Mulas, C., Floris, C., Sanna, E., Cau, M. C., Panzone, F. & Mantovani, G. (2012) A randomized phase III clinical trial of a combined treatment for cachexia in

- patients with gynecological cancers: Evaluating the impact on metabolic and inflammatory profiles and quality of life. *Gynecologic Oncology*, 124: March.
Not in PICO
- Mallmann, P. (2014) Early recognition of endometrial cancer. [German]. *Gynakologe*, 47: 340-345.
Narrative review
- Martin-Loeches, M., Orti, R. M., Asins, E. & Llixiona, J. (2003) The prognostic implications of anaemia in the outcome of patients with early stages of uterine cervix carcinoma. *Archives of Gynecology & Obstetrics*, 267: 121-125.
Not in PICO
- Miller, B. E. (11111) Diagnosis and staging of gynecological malignancies. *Oncology Spectrums*, 2: 2001.
Narrative review
- Morrison, J., Gillespie, S. & MacKenzie, I. Z. (2003) 'Two week wait' standards for suspected gynaecological malignancy. On target, but missing the point? *Journal of the British Menopause Society*, 9: 170-172.
Not in PICO
- Muruzabal Torquemada, J. C., Aguirre, S., Aranda, S. & Elizalde, F. J. (2009) Emergencies in oncological gynaecology. [Spanish]. *Anales del Sistema Sanitario de Navarra*, 32: 2009.
Narrative review
- Mwaka, A. D., Okello, E. S., Kiguli, J. & Rutebemberwa, E. (2014) - Understanding cervical cancer: an exploration of lay perceptions, beliefs and knowledge about cervical cancer among the Acholi in northern Uganda. - *BMC Women's Health*, 14: 84.
Not in PICO
- Naik, R. M., Pai, A., Guruprasad, Y. & Singh, R. (2013) Efficacy of colour Doppler ultrasound in diagnosis of cervical lymphadenopathy. *Journal of Maxillofacial & Oral Surgery*, 12: 123-129.
Not in PICO
- Newell, S. & Overton, C. (2002) Postmenopausal bleeding should be referred urgently. *Practitioner*, 256: 13-15.
Narrative review
- Oh, J. K. & Kim, K. H. (2013) Why are recurrent cervical cancers of the pelvic stump misdiagnosed as interstitial cystitis?: The urologist's point of view based on a case report. *Canadian Urological Association Journal*, 7: E359-E362.
Not in PICO
- Okadome, M., Saito, T., Tsukamoto, N., Nishi, K., Nishiyama, N. & Nagata, E. (2006) Endometrial scraping cytology in women with extragenital malignancies. *Acta Cytologica*, 50: 158-163.
Not in PICO
- Olagunju, A. T., Aina, O. F., Sarimiye, F. O. & Olagunju, T. O. (2014) Indications for integrated supportive care among individuals with cervical cancer: A view from a developing country. *Supportive Care in Cancer*, 22: S145.
Not in PICO
- Olesen, F. (1988) [Uterine cervical cancer and variations in taking cytological samples in general practice]. [Danish]. *Ugeskrift for Læger*, 150: 2247-2250.
Not in PICO
- Oliver, A. & Overton, C. (2002) Detecting ovarian disorders in primary care. *The Practitioner*, 258: 15-19, 2.
Narrative review
- Oliver, A. & Overton, C. (2002) - Detecting ovarian disorders in primary care. - *Practitioner*, 258: 15-19.
Duplicate

- Ordi, J., Stamatakos, M. D. & Tavassoli, F. A. (1997) Pure pleomorphic rhabdomyosarcomas of the uterus. *International Journal of Gynecological Pathology*, 16: October.
Narrative review
- Panda, J. K. (2002) One-stop clinic for postmenopausal bleeding. *Journal of Reproductive Medicine*, 47: 761-766.
Not in PICO
- Peipert, J. F., Wells, C. K., Schwartz, P. E. & Feinstein, A. R. (1993) The Impact of Symptoms and Comorbidity on Prognosis in Stage-Ib Cervical-Cancer. *American Journal of Obstetrics and Gynecology*, 169: 598-604.
Not in PICO
- Pinar, G., Algier, L., Dogan, N. & Kaya, N. (2008) Determination of the risk factors in individuals with gynecological cancer. [Turkish]. *UHOD - Uluslararası Hematoloji-Onkoloji Dergisi*, 18: 2008.
Not in PICO
- Protopapas, A. G., Diakomanolis, E. S., Milingos, S. D., Rodolakis, A. J., Markaki, S. N., Vlachos, G. D., Papadopoulos, D. E. & Michalas, S. P. (2004) Tubo-ovarian abscesses in postmenopausal women: Gynecological malignancy until proven otherwise? *European Journal of Obstetrics Gynecology and Reproductive Biology*, 114: 15.
Not in PICO
- Puig-Tintore, L. M. & Jou, C. P. (1983) [Early diagnosis of gynecological cancer]. [Spanish]. *Medicina Clinica*, 81: 131-135.
Narrative review
- Ramanathan, S. A., Baratiny, G., Stocks, N. P., Searles, A. M. & Redford, R. J. (2011) General practitioner referral patterns for women with gynaecological symptoms: a randomised incomplete block study design. *The Medical journal of Australia*, 195: 602-606.
Not in PICO
- Redman, C. W. (2000) An audit of the management of uterine malignancy within the West Midlands. West Midlands Gynaecological Oncology Group. *BJOG: An International Journal of Obstetrics & Gynaecology*, 107: 552-555.
Not in PICO
- Rim, S. H., Polonec, L., Stewart, S. L. & Gelb, C. A. (2011) A national initiative for women and healthcare providers: CDC's inside knowledge: Get the facts about gynecologic cancer campaign. *Journal of Women's Health*, 20: 01.
Not in PICO
- Rosenthal, A. N., Panoskaltsis, T., Smith, T. & Soutter, W. P. (2001) The frequency of significant pathology in women attending a general gynaecological service for postcoital bleeding. *British Journal of Obstetrics and Gynaecology*, 108: 103-106.
Not in PICO
- Salani, R., Hade, E., Husain, M. & Katz, M. (2012) The smoking gun: An assessment of patient awareness of endometrial cancer risk factors and symptoms. *Gynecologic Oncology.Conference: 43rd Annual Meeting of the Society of Gynecologic Oncology Austin, TX United States.Conference Start: 20120324 Conference End: 20120327.Conference Publication: (var.pagings)*, 125: March.
Not in PICO
- Sarkar, M., Konar, H. & Raut, D. (2010) Symptomatology of gynecological malignancies: experiences in the gynecology out-patient clinic of a tertiary care hospital in kolkata, India. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 11: 785-791.
Not in PICO
- Shalini, R., Amita, S. & Neera, M. A. (1998) How alarming is post-coital bleeding - A cytologic, colposcopic and histopathologic evaluation. *Gynecologic and Obstetric Investigation*, 45: 205-208.
Not in PICO

- Shapley, M., Jordan, K. & Croft, P. R. (11111) An epidemiological survey of symptoms of menstrual loss in the community. *British Journal of General Practice*, 54: May.
Not in PICO
- Shapley, M., Jordan, J. & Croft, P. R. (2006) A systematic review of postcoital bleeding and risk of cervical cancer. [Review] [77 refs]. *British Journal of General Practice*, 56: 453-460.
Not in PICO
- Shapley, M., Jordan, K. & Croft, P. R. (2007) Abnormal bleeding patterns associated with menorrhagia in women in the community and in women presenting to primary care. *Family Practice*, 24: December.
Not in PICO
- Shapley, M., Blagojevic-Bucknall, M., Jordan, K. P. & Croft, P. R. (2013) The epidemiology of self-reported intermenstrual and postcoital bleeding in the perimenopausal years. *BJOG: An International Journal of Obstetrics & Gynaecology*, 120: 1348-1355.
Not in PICO (not symptomatic patients presenting to the GP)
- Smith-Bindman, R., Weiss, E. & Feldstein, V. (2004) How thick is too thick? When endometrial thickness should prompt biopsy in postmenopausal women without vaginal bleeding. *Ultrasound in Obstetrics & Gynecology*, 24: 558-565.
Not in PICO
- Soleymani, M. H., Watermeyer, S., El, H. E. & Ismail, L. (2008) A postmenopausal women presenting with atypical symptoms and cervical cancer: a case report. *Cases journal*, 1: 401.
Not in PICO
- Staite, A. (1989) Cervical cytology in general practice. *New Zealand Nursing Journal*, 82: 18-19.
Narrative review
- Stapley, S. & Hamilton, W. (2011) Gynaecological symptoms reported by young women: examining the potential for earlier diagnosis of cervical cancer. *Family Practice*, 28: 592-598.
Not in PICO
- Sweet, M. G., Schmidt-Dalton, T. A., Weiss, P. M. & Madsen, K. P. (2012) Evaluation and Management of Abnormal Uterine Bleeding in Premenopausal Women. *American Family Physician*, 85: 35-43.
Narrative review
- Taylor, E., Campbell, J., Donnelly, M. & Hebden, J. (2014) A specialist iron deficiency anaemia clinic significantly reduces the need for secondary care follow up. *Gut*, 63: A222-A223.
Not in PICO
- Thomakos, N., Papadimitriou, C. A., Zagouri, F., Dimopoulos, M.-A. & Antsaklis, A. (2010) Venous thromboembolic events alert for gynecologic neoplasms. *Onkologie*, 33: November.
Narrative review
- Trajkovska, E., Dzikova, E., Dimitrov, G. & Andonova, I. (2011) Early detection of endometrial pathology in postmenopausal women using transvaginal ultrasonography. *International Journal of Gynecological Cancer. Conference: International Gynecologic Cancer Society Regional Meeting on Gynecologic Cancers, IGCS 2011 New Delhi India. Conference Start: 20110402 Conference End: 20110403. Conference Publication: (var.pagin, 21: May.*
Meeting abstract, does not appear to be in PICO
- Trichot, C., Barthier, S., Rivain, A. L., Prevot, S., Demoulin, G., Kai, G. S., Thubert, T. & Deffieux, X. (794) - [Diagnosis for uterine cervix and endometrial cancer]. [French]. - *Revue du Praticien*, 64: 789-791.
Guideline
- Tsai, M. C. & Goldstein, S. R. (2012) Office Diagnosis and Management of Abnormal Uterine Bleeding. *Clinical Obstetrics and Gynecology*, 55: 635-650.
Narrative review

Valentin, L. (2004) Transvaginal sonography in gynaecology. *Reviews in Gynaecological Practice*, 4: March.
Narrative review

Vandborg, M. P., Christensen, R. D., Kragstrup, J., Edwards, K., Vedsted, P., Hansen, D. G. & Mogensen, O. (2011) Reasons for diagnostic delay in gynecological malignancies. *International Journal of Gynecological Cancer*, 21: 967-974.
Not in PICO

Viikki, M., Pukkala, E. & Hakama, M. (1998) Bleeding symptoms and subsequent risk of gynecological and other cancers. *Acta Obstetricia et Gynecologica Scandinavica*, 77: 1998.
Not in PICO

Walker, S., Hyde, C. & Hamilton, W. (2013) Risk of uterine cancer in symptomatic women in primary care: case-control study using electronic records. *British Journal of General Practice*, 63: 643-648.
Not in PICO (included under endometrial cancer)

Washington, D. L., Danz, M. & Cordasco, K. M. (2014) Development of quality indicators for the care of women with abnormal uterine bleeding. *Journal of General Internal Medicine*, 29: S68-S69.
Not in PICO

Wethington, S. L., Herzog, T. J., Burke, W. M., Sun, X., Lerner, J. P., Lewin, S. N. & Wright, J. D. (2011) Risk and predictors of malignancy in women with endometrial polyps. *Annals of Surgical Oncology*, 18: 3819-3823.
Not in PICO

White, L. N. (1993) An Overview of Screening and Early Detection of Gynecologic Malignancies. *Cancer*, 71: 1400-1405.
Narrative review

Williams, S., Butler-Manuel, S., Taylor, A. & Madhuri, T. (2013) Ovarian metastases from squamous cell carcinoma of cervix: A rare finding. *BJOG: An International Journal of Obstetrics and Gynaecology*, 120: 247-248.
Not in PICO

Winfrey, L. E., Henretta, M. S., Hallowell, P. T. & Modesitt, S. C. (2010) Pre-operative gynecologic evaluation of bariatric surgery patients: Improving cancer detection in a high-risk population. *Journal of the American College of Surgeons*, 211: August.
Not in PICO

You, W., Dainty, L. A., Rose, G. S., Krivak, T., McHale, M. T., Olsen, C. H. & Elkas, J. C. (2005) Gynecologic malignancies in women aged less than 25 years. *Obstetrics and Gynecology*, 105: June.
Not in PICO

Zanotti, K. M. & Kennedy, A. W. (1999) Screening for gynecologic cancer. *Medical Clinics of North America*, 83.
Narrative review

Review question:

Which investigations of symptoms of suspected cervix cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	917	138	10/06/2013
<i>Premedline</i>	1980-2013	158	6	10/06/2013
<i>Embase</i>	1980-2013	2221	114	11/06/2013

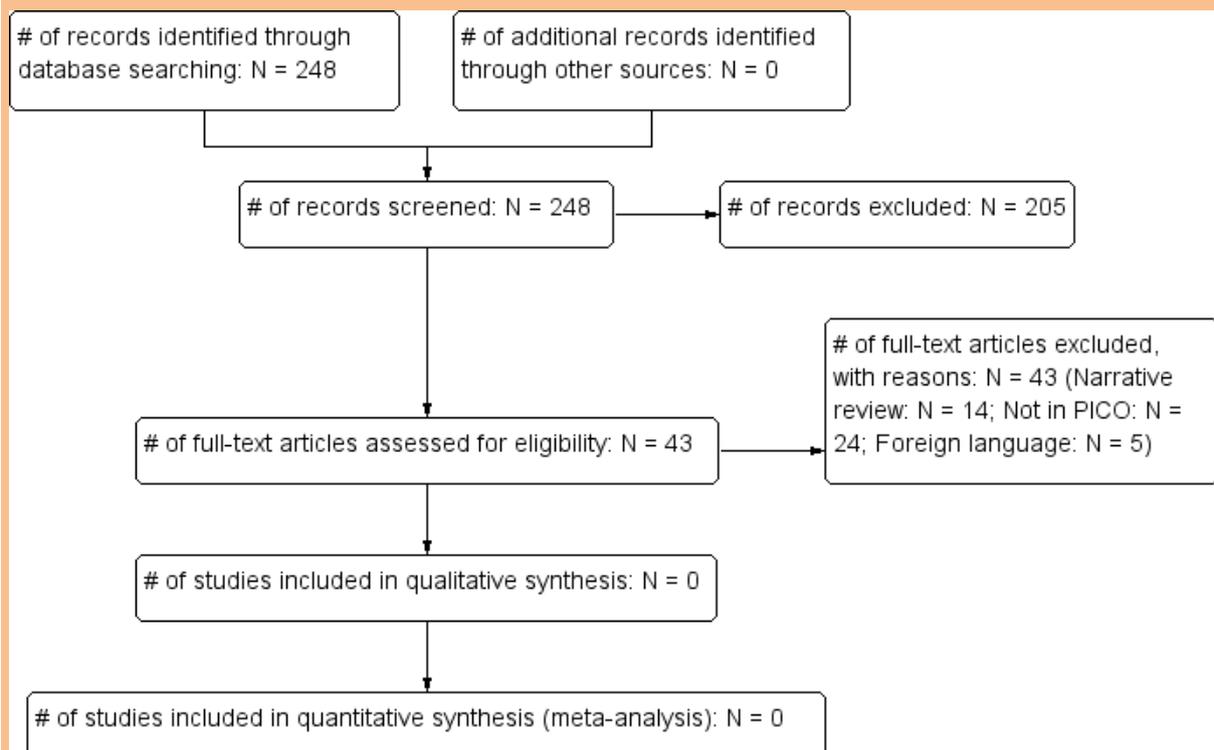
<i>Cochrane Library</i>	1980-2013	275	18	11/06/2013
<i>Psychinfo</i>	1980-2013	8	1	11/06/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	108	12	11/06/2013

Total References retrieved (after de-duplication): 245

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	6/2013-13/08/2014	170	2	13/08/2014
<i>Premedline</i>	6/2013-13/08/2014	44	1	13/08/2014
<i>Embase</i>	6/2013-13/08/2014	32	0	13/08/2014
<i>Cochrane Library</i>	6/2013-13/08/2014	34	0	13/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	6/2013-13/08/2014	15	0	13/08/2014

Total References retrieved (after de-duplication): 3



Study results

No evidence was identified pertaining to the diagnostic accuracy of cervical smear in patients with suspected cervix cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

- Abike, F., Bingol, B., Kilic, G. S., Dunder, I. & Tapisiz, O. L. (2011) Cervical cancer and tumor markers. *Turk Jinekolojik Onkoloji Dergisi*, 14: 1-9.
Narrative review
- Abu, J. & Davies, Q. (2005) Endocervical curettage at the time of colposcopic assessment of the uterine cervix. [Review] [315 refs]. *Obstetrical & Gynecological Survey*, 60: 315-320.
Narrative review
- Abu, J., Davies, Q. & Ireland, D. (2006) Should women with postcoital bleeding be referred for colposcopy? *Journal of Obstetrics & Gynaecology*, 26: 45-47.
Not in PICO
- Acharya, B. C. & Jihong, L. (2009) Sentinel lymph node detection in patients with early cervical cancer. *Jnma, Journal of the Nepal Medical Association*, 48: 287-291.
Not in PICO
- Adam, Y., van Gelderen, C. J., de, B. G., McIntyre, J. A., Turton, D. A. & Martinson, N. A. (2008) Predictors of persistent cytologic abnormalities after treatment of cervical intraepithelial neoplasia in Soweto, South Africa: A cohort study in a HIV high prevalence population. *BMC Cancer*, 8.
Not in PICO
- Adcock, L. L., Julian, T. M. & Okagaki, T. (1982) Carcinoma of the uterine cervix FIGO stage I-B. *Gynecologic Oncology*, 14: 199-208.
Not in PICO
- Afnas'eva, K. G., Ugrumova, R. P., Blagushina, L. G., Plisova, T. E. & Sorokina, L. M. (1980) Experience with using luminescence microscopy in the early diagnosis of cervical cancer. [Russian]. *Voprosy Onkologii*, 26: 90-91.
In Russian, not enough information can be extracted.
- Alleyne, G. (1996) Early detection of cervical cancer. *Bulletin of the Pan American Health Organization*, 30: 283-284.
Narrative review
- American Academy of Family Physicians (2012) Five things physicians and patients should question. *Journal - Oklahoma State Medical Association*, 105: 370-371.
Not in PICO
- Anthony, P. P. (1999) Who should be reporting gynaecological cytopathology? *Cytopathology*, 10: 366-368.
Comment
- Aparicio, L. A. & Morera, S. M. (2009) [Evaluation of the "Early detection and opportune attention of cervicouterine cancer" program]. [Spanish]. *Atencion Primaria*, 41: 300-305.
Not in PICO
- Apgar, B. S., Kaufman, A. J., Bettcher, C. & Parker-Featherstone, E. (2013) Gynecologic procedures: colposcopy, treatments for cervical intraepithelial neoplasia and endometrial assessment. [Review]. *American Family Physician*, 87: 836-843.
Narrative review
- Arroyave, A. M., Penaranda, E. K. & Lewis, C. L. (2011) Organizational change: a way to increase colon, breast and cervical cancer screening in primary care practices (DARE structured abstract). *Journal of Community Health*, 36: 281-288.
Not in PICO
- Ashfaq, R., Gibbons, D., Vela, C., Saboorian, M. H. & Iliya, F. (1999) ThinPrep Pap Test. Accuracy for glandular disease. *Acta Cytologica*, 43: 81-85.
Not in PICO

- Au Yong, T. K., Wong, C. P., Leung, Y. K., Chu, K. S. & Tong, W. C. M. (2005) Evaluation of positron-emission tomography in the diagnosis of primary tumours in patients presenting with metastases: Prospective study. *Journal of the Hong Kong College of Radiologists*, 8: 9-14.
Not in PICO
- Ayhan-Tuncay, Y., Sezginsoy, S., Omurcan, C., Kirecci, A. & Yucel, N. (2005) To evaluate cervical biopsy pathologies. [Turkish]. *Goztepe Tip Dergisi*, 20: 77-79.
Not in PICO
- Baldauf, J. J. & Ritter, J. (1999) [ANAES: review of the literature on the reproducibility of low grade lesions and of atypical cells of indeterminate significance (ASCUS). Decision trees on treating abnormal cervical smears. Clinical problems engendered by the diagnosis]. [Review] [20 refs] [French]. *Annales de Pathologie*, 19: Suppl-4.
Narrative review
- Beal, M. W. (1915) Understanding cervical cytology. *Nurse Practitioner*, 12: 8-10.
Narrative review
- Bean, S. M., Kurtycz, D. F. & Colgan, T. J. (2011) Recent developments in defining microinvasive and early invasive carcinoma of the uterine cervix. [Review]. *Journal of Lower Genital Tract Disease*, 15: 146-157.
Narrative review
- Benard, V. B., Lawson, H. W., Ehemann, C. R., Anderson, C. & Helsel, W. (2005) Adherence to guidelines for follow-up of low-grade cytologic abnormalities among medically underserved women. *Obstetrics & Gynecology*, 105: 1323-1328.
Not in PICO
- Benard, V. B., Howe, W., Saraiya, M., Helsel, W. & Lawson, H. W. (2008) Assessment of follow-up for low-grade cytological abnormalities in the National Breast and Cervical Cancer Early Detection Program, 2000-2005. *Journal of Lower Genital Tract Disease*, 12: 300-306.
Not in PICO
- Benard, V. B., Berkman, N. D., Kuo, T., Martin, C. K. & Richardson, L. C. (2010) Follow-up for cervical abnormalities in a managed care plan, 1999-2004. *Preventive Medicine*, 50: 81-85.
Not in PICO
- Bence, S. A. (2000) Stop cervical cancer in its tracks. *Nursing*, 30: suppl-7.
Narrative review
- Benedet, J. L. & Anderson, G. H. (1981) Cervical intraepithelial neoplasia in British Columbia: a comprehensive program for detection, diagnosis, and treatment. *Gynecologic Oncology*, 12: t-91.
Not in PICO
- Bergeron, C., Bishop, J., Lemarie, A., Cas, F., Ayivi, J., Huynh, B. & Barrasso, R. (2001) Accuracy of thin-layer cytology in patients undergoing cervical cone biopsy. *Acta Cytologica*, 45: 519-524.
Not in PICO
- Berner, A., Hoeg, K. & Oppedal, B. R. (1980) Smear biopsies. A cause of negative follow-up biopsies in patients with premalignant conditions of the uterine cervix. *Diagnostic Gynecology and Obstetrics*, 2: 99-102.
Not in PICO
- Bhargava, V. L., Verma, K., Sharma, R., Batra, S. & Anandalakshmy, P. N. (1993) A hospital-based study on the use of paramedical personnel for clinical downstaging of cancer cervix. *The Indian journal of medical research*, 98: 65-68.
Not in PICO
- Bishai, D. M., Ferris, D. G. & Litaker, M. S. (2003) What is the least costly strategy to evaluate cervical abnormalities in rural women? Comparing telemedicine, local practitioners, and expert physicians. *Medical Decision Making*, 23: 463-470.
Not in PICO

- Boon, M. E., Kwikkel, H. J. & Rietveld, W. (1986) The predictive value of immature dysplastic cells in CIN I and II smears. *Diagnostic Cytopathology*, 2: 36-39.
Not in PICO
- Boukes, F. S., Meijer, L. J., Flikweert, S., Assendelft, W. J. & Nederlands, H. G. (2002) [Summary of the standard "Vaginal bleeding" (first revision) of the Dutch College of General Practitioners]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 146: 2179-2183.
Narrative review
- Broderick, D., Matityahu, D., Dudhbbhai, M. & Alter, S. (2002) Histologic and colposcopic correlates of ASCUS pap smears in pregnancy. *Journal of Lower Genital Tract Disease*, 6: 116-119.
Not in PICO
- Brotzman, G. L. & Schellhase, K. G. (2004) Colposcopic proficiency-disease spectrum in a single family practice colposcopists' clinic. *Wisconsin Medical Journal*, 103: 61-65.
Not in PICO
- Buis, P., Van Den Heuvel, L., Balfourt, A., Chorus, R. & Van, D. P. (2006) Cervical smears taken by the practice assistants are of lower quality than smears taken by general practitioners. [Dutch]. *Huisarts en Wetenschap*, 49: 24-27.
Not in PICO
- Butureanu, S., Pricop, F., Stratan, E., Radulescu, D., Patras, C., Dragomir, D., Dumitrache, F., Gheorghita, V., Popovici, C. & Popovici, R. (1990) [The role of biopsy in the early diagnosis of cancer of the cervix uteri]. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 94: 129-131.
Not in PICO
- Byrnes, E. C. (1992) A new age in Pap testing. [Review] [12 refs]. *Advance for Nurse Practitioners*, 6: 65-66.
Narrative review
- Cantor, S. B., Mitchell, M. F., Tortolero, L. G., Bratka, C. S., Bodurka, D. C. & Richards, K. R. (1998) Cost-effectiveness analysis of diagnosis and management of cervical squamous intraepithelial lesions (Structured abstract). *Obstetrics and Gynecology*, 91: 270-277.
Not in PICO
- Cardin, V. A., Grimes, R. M., Jiang, Z. D., Pomeroy, N., Harrell, L. & Cano, P. (2001) Low-income minority women at risk for cervical cancer: a process to improve adherence to follow-up recommendations. *Public Health Reports*, 116: 608-616.
Not in PICO
- Carey, P. & Gjerdingen, D. K. (1993) Follow-up of abnormal Papanicolaou smears among women of different races. *Journal of Family Practice*, 37: 583-587.
Not in PICO
- Carpenter, A. B. & Davey, D. D. (1999) ThinPrep Pap Test: performance and biopsy follow-up in a university hospital. *Cancer*, 87: 105-112.
Not in PICO
- Cavanagh, D. & Roberts, W. S. (1985) Early detection of uterine cancer. *Journal of the Florida Medical Association*, 72: 36-40.
Narrative review
- Chacho, M. S., Mattie, M. E. & Schwartz, P. E. (2003) Cytohistologic correlation rates between conventional Papanicolaou smears and ThinPrep cervical cytology: A comparison. *Cancer Cytopathology*, 99: 135-140.
Not in PICO
- Chen, E. T., Eder, M., Elder, N. C. & Hickner, J. (2010) Crossing the finish line: follow-up of abnormal test results in a multisite community health center. *Journal of the National Medical Association*, 102: 720-725.
Not in PICO

- Chhabra, S., Bhavani, M. & Deshpande, A. (2014) Trends of vulvar cancer. *Journal of Obstetrics & Gynaecology*, 34: 165-168.
Not in PICO
- Chirenje, Z. M. (1994) Management of the patient with an abnormal Papanicolaou smear. [Review] [11 refs]. *Central African Journal of Medicine*, 40: 131-134.
Narrative review
- Chong, A., Ha, J. M., Jeong, S. Y., Song, H. C., Min, J. J., Bom, H. S. & Choi, H. S. (2013) Clinical Usefulness of (18)F-FDG PET/CT in the Detection of Early Recurrence in Treated Cervical Cancer Patients with Unexplained Elevation of Serum Tumor Markers. *Chonnam Medical Journal*, 49: 20-26.
Not in PICO
- Chung, H. H., Jo, H., Kang, W. J., Kim, J. W., Park, N. H., Song, Y. S., Chung, J. K., Kang, S. B. & Lee, H. P. (2007) Clinical impact of integrated PET/CT on the management of suspected cervical cancer recurrence. *Gynecologic Oncology*, 104: 529-534.
Not in PICO
- Clement, K. D. & Christenson, P. D. (1990) Papanicolaou smear cell recovery techniques used by primary care physicians. *Journal of the American Board of Family Practice*, 3: 253-258.
Not in PICO
- Cooper, P., Kirby, A. J., Spiegelhalter, D. J., Whitehead, A. L. & Patterson, A. (1992) Management of women with a cervical smear showing a mild degree of dyskaryosis: a review of policy. *Cytopathology*, 3: 331-339.
Not in PICO
- Costa, S., De, N. M., Rubino, A., Rambelli, V., Marinelli, M., Santini, D., Cristiani, P. & Bucchi, L. (2003) Independent determinants of inaccuracy of colposcopically directed punch biopsy of the cervix. *Gynecologic Oncology*, 90: 57-63.
Not in PICO
- Cronjé, H. S., Rensburg, E., Cooreman, B. F., Niemand, I. & Beyer, E. (2000) Speculoscopy vs. the acetic acid test for cervical neoplasia. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, 69: 249-253.
Not in PICO
- Czekanowski, R., Pietrzak, M. & Kukulski, P. (1999) [Correlation between oncologically suspicious cytologic smears and colposcopic images of the uterine cervix and results of histopathologic examination taken from material provided by the Gynecology Department of the Pruszkow Municipal Hospital from 1995 to 1997]. [Polish]. *Przegląd Lekarski*, 56: 48-50.
Not in PICO
- Dangore, S. B., Degwekar, S. S. & Bhowate, R. R. (2008) Evaluation of the efficacy of colour Doppler ultrasound in diagnosis of cervical lymphadenopathy. *Dentomaxillofacial Radiology*, 37: 205-212.
Not in PICO
- de Bie, R. P., Massuger, L. F., van Dongen, R. A., Snijders, M. P., Bulten, J., Melchers, W. J. & Bekkers, R. L. (2011) To treat or not to treat; the clinical dilemma of atypical squamous cells of undetermined significance (ASC-US). *Acta Obstetrica et Gynecologica Scandinavica*, 90: 313-318.
Not in PICO
- DeMay, R. M. (2000) Should we abandon pap smear testing?. [Review] [35 refs]. *American Journal of Clinical Pathology*, 114: Suppl-51.
Narrative review
- Denny, L. A., Soeters, R., Dehaeck, K. & Bloch, B. (1995) Does colposcopically directed punch biopsy reduce the incidence of negative LLETZ? *British Journal of Obstetrics & Gynaecology*, 102: 545-548.
Not in PICO
- DeSimone, C. P., Day, M. E., Tovar, M. M., Dietrich, C. S., III, Eastham, M. L. & Modesitt, S. C. (2006) Rate of pathology from atypical glandular cell Pap tests classified by the Bethesda 2001

- nomenclature. *Obstetrics & Gynecology*, 107: 1285-1291.
Not in PICO
- Ding, A. H. (124) N2 laser in diagnosis of early cervical cancer. [Chinese]. *Zhonghua fu chan ke za zhi*, 26: 95-96, 124.
Not in PICO
- Dolatowski, R. & Zoltowski, M. (1986) [Diagnostic accuracy of vaginal smears and histopathologic studies in the early detection of cervical cancer]. [Polish]. *Ginekologia Polska*, 57: 64-67.
Not in PICO
- Dolatowski, R. & Zoltowski, M. (1986) Diagnostic accuracy of vaginal smears and histopathologic studies in the early detection of cervical cancer. [Polish]. *Ginekologia Polska*, 57: 64-67.
Duplicate
- Dolatowski, R. & Zoltowski, M. (1986) Agreement between cytological examinations of vaginal smears and histopathological examinations in early detection of cervical carcinoma. [Polish]. *Ginekologia Polska*, 57: 64-67.
Duplicate
- Dolman, G., Tan, J. & Quinn, M. (2005) Should the Pap smear be repeated at the first colposcopy visit? *Australian & New Zealand Journal of Obstetrics & Gynaecology*, 45: 514-517.
Not in PICO
- Dubuisson, J., Boukrid, M. & Petignat, P. (1936) [Management of post-coital bleeding: should all women be referred?]. [French]. *Revue Medicale Suisse*, 9: 1933-1934.
Narrative review
- Ebeling, K. (1986) Practical points of reference for the prevention and early detection of cervical cancer. [German]. *Zeitschrift fur Arztliche Fortbildung*, 80: 306-310.
Narrative review
- Ebeling, K. (1987) [Early diagnosis of cervical cancer]. [German]. *Zeitschrift fur Arztliche Fortbildung (Jena)*, 81: 763-769.
Narrative review
- Edelin, K. C. & Hamid, M. A. (1930) When to refer. Abnormal Pap smears. *Hospital Practice (Office Edition)*, 20: 23-27.
Narrative review
- Eggleston, K. S., Coker, A. L., Das, I. P., Cordray, S. T. & Luchok, K. J. (2007) Understanding barriers for adherence to follow-up care for abnormal Pap tests (DARE structured abstract). *Journal of Women's Health*, 16: 311-330.
Not in PICO
- Elit, L., Levine, M. N., Julian, J. A., Sellors, J. W., Lytwyn, A., Chong, S., Mahony, J. B., Gu, C., Finch, T. & Zeferino, L. C. (2011) Expectant management versus immediate treatment for low-grade cervical intraepithelial neoplasia. *Cancer*, 117: 1438-1445.
Not in PICO
- Ellman, R. (1990) Problems of follow-up for abnormal cervical smears: discussion paper. *Journal of the Royal Society of Medicine*, 83: 94-95.
Narrative review
- Elwood, J. M., Cotton, R. E., Johnson, J., Jones, G. M., Curnow, J. & Beaver, M. W. (1984) Are patients with abnormal cervical smears adequately managed? *British Medical Journal Clinical Research Ed.*, 289: 891-894.
Not in PICO
- Engelstad, L. P., Stewart, S. L., Nguyen, B. H., Bedeian, K. L., Rubin, M. M., Pasick, R. J. & Hiatt, R. A. (2001) Abnormal Pap smear follow-up in a high-risk population. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*, 10: 1015-1020.
Not in PICO

- Etherington, I. J., Luesley, D. M., Shafi, M. I., Dunn, J., Hiller, L. & Jordan, J. A. (1997) Observer variability among colposcopists from the West Midlands region. *British Journal of Obstetrics & Gynaecology*, 104: 1380-1384.
Not in PICO
- Evans, D. M., Hibbard, B. M., Jones, J. M. & Sweetnam, P. (1981) The Cardiff Cervical Cytology Study: prevalence of cytological grades and initial histological findings. *British Medical Journal Clinical Research Ed.*, 282: 689-691.
Not in PICO
- Evans, D. M., Hudson, E. A., Brown, C. L., Boddington, M. M., Hughes, H. E. & Mackenzie, E. F. (1987) Management of women with abnormal cervical smears: supplement to terminology in gynaecological cytopathology. *Journal of Clinical Pathology*, 40: 530-531.
Not in PICO
- Everett, W. D., Solomon, P. & Wheeler, L. (1991) Experience with colposcopy in a family practice center. *Family Practice Research Journal*, 11: 283-290.
Not in PICO
- Eze, J. N., Emeka-Irem, E. N. & Edege, F. O. (2013) A six-year study of the clinical presentation of cervical cancer and the management challenges encountered at a state teaching hospital in southeast Nigeria. *Clinical Medicine Insights.Oncology*, 7: 151-158.
Not in PICO
- Fakokunde, B. & Selo-Ojeme, D. (2008) Impact of prolonged referral interval on colposcopic outcomes in women with moderate or severe dysplasia. *International Journal of Gynaecology & Obstetrics*, 101: 245-247.
Not in PICO
- Falcone, T. & Parker, W. H. (2013) Surgical management of leiomyomas for fertility or uterine preservation. [Review]. *Obstetrics & Gynecology*, 121: 856-868.
Narrative review
- Farley, J. H., Hickey, K. W., Carlson, J. W., Rose, G. S., Kost, E. R. & Harrison, T. A. (2003) Adenosquamous histology predicts a poor outcome for patients with advanced-stage, but not early-stage, cervical carcinoma. *Cancer*, 97: 2196-2202.
Not in PICO
- Ferris, D. G., Payne, P. & Frisch, L. E. (1993) Cervicography: an intermediate triage test for the evaluation of cervical atypia. *Journal of Family Practice*, 37: 463-468.
Not in PICO
- Ferris, D. G., Payne, P., Frisch, L. E., Milner, F. H., Dipaola, F. M. & Petry, L. J. (1993) Cervicography - Adjunctive Cervical-Cancer Screening by Primary-Care Clinician. *Journal of Family Practice*, 37: 158-164.
Not in PICO
- Ferris, D. G. (1997) Office procedures. Colposcopy. [Review] [8 refs]. *Primary Care; Clinics in Office Practice*, 24: 241-267.
Narrative review
- Flannely, G., Anderson, D., Kitchener, H. C., Mann, E. M., Campbell, M., Fisher, P., Walker, F. & Templeton, A. A. (1994) Management of women with mild and moderate cervical dyskaryosis. *BMJ*, 308: 1399-1403.
Not in PICO
- Flannely, G. & Kitchener, H. (1995) Every woman with an abnormal cervical smear should be referred for treatment: debate. [Review] [20 refs]. *Clinical Obstetrics & Gynecology*, 38: 585-591.
Narrative review
- Flannely, G. (2010) The management of women with abnormal cervical cytology in pregnancy. *Best Practice & Research in Clinical Obstetrics & Gynaecology*, 24: 51-60.
Narrative review

- Fleury, A. C., Birsner, M. L. & Fader, A. N. (2012) Management of the abnormal Papanicolaou smear and colposcopy in pregnancy: an evidenced-based review. [Review]. *Minerva Ginecologica*, 64: 137-148.
Narrative review
- Foster, J. (1982) A simple test for cancer. *Nursing Mirror*, 154: 26-29.
Narrative review
- Franco, E. S., Hyppolito, S. B., Franco, R. G., Oria, M. O., Almeida, P. C., Pagliuca, L. M. & Rocha, N. F. (2008) [Digital cervicography criteria: improving sensitivity in uterine cervical cancer diagnosis]. [Portuguese]. *Cadernos de Saude Publica*, 24: 2653-2660.
Not in PICO
- Frisch, L. E. (1986) Effectiveness of a case management protocol in improving follow-up and referral of Papanicolaou smears indicating cervical intraepithelial neoplasia. *Journal of American College Health*, 35: 112-115.
Not in PICO
- Fujii, T., Nakamura, M., Kameyama, K., Saito, M., Nishio, H., Ohno, A., Hirao, N., Iwata, T., Tsukazaki, K. & Aoki, D. (2010) Digital colposcopy for the diagnosis of cervical adenocarcinoma using a narrow band imaging system. *International Journal of Gynecological Cancer*, 20: 605-610.
Not in PICO
- Galic, V., Herzog, T. J., Lewin, S. N., Neugut, A. I., Burke, W. M., Lu, Y.-S., Hershman, D. L. & Wright, J. D. (2012) Prognostic significance of adenocarcinoma histology in women with cervical cancer. *Gynecologic Oncology*, 125: 287-291.
Not in PICO
- Gallwas, J., Chiapponi, C., Turk, L., Ochsenkuehn, R., Friese, K. & Dannecker, C. (2010) [Optical coherence tomography: preliminary results with a new noninvasive technique for evaluating uterine cervical tissue and vulvar epithelium]. [Italian]. *Minerva Ginecologica*, 62: 395-401.
Not in PICO
- Gallwas, J., Gaschler, R., Stepp, H., Friese, K. & Dannecker, C. (2012) 3D optical coherence tomography of cervical intraepithelial neoplasia--early experience and some pitfalls. *European Journal of Gynaecological Oncology*, 33: 37-41.
Not in PICO
- Ghidoni, D., Fabbris, E., Folicaldi, S., Amadori, A., Medri, M., Bucchi, L. & Bondi, A. (1998) [The PAPNET system in the rescreening of negative cervical/vaginal smears. A study from the Imola cytology laboratory]. [Italian]. *Pathologica*, 90: 357-363.
Not in PICO
- Girardi, F. (1995) Colposcopy of the uterine cervix. [German]. *Medizinische Welt*, 46: 26-31.
Narrative review
- Gocze, P. & Vahrson, H. (1992) [Significance of determination of squamous cell carcinoma antigen in the follow up of patients with cancer of the uterine cervix]. [Hungarian]. *Orvosi Hetilap*, 133: 3191-3194.
Not in PICO
- Gortzak-Uzan, L., Jimenez, W., Nofech-Mozes, S., Ismiil, N., Khalifa, M. A., Dube, V., Rosen, B., Murphy, J., Laframboise, S. & Covens, A. (2010) Sentinel lymph node biopsy vs. pelvic lymphadenectomy in early stage cervical cancer: Is it time to change the gold standard? *Gynecologic Oncology*, 116: 28-32.
Not in PICO
- Guido, R., Schiffman, M., Solomon, D. & Burke, L. (2003) Postcolposcopy management strategies for women referred with low-grade squamous intraepithelial lesions or human papillomavirus DNA-positive atypical squamous cells of undetermined significance: a two-year prospective study. *American Journal of Obstetrics and Gynecology*, 188: 1401-1405.
Not in PICO

- Hadwin, R., Eggington, S., Brennan, A., Walker, P., Patnick, J. & Pilgrim, H. (2008) Modelling the cost-effectiveness and capacity impact of changes to colposcopy referral guidelines for women with mild dyskaryosis in the UK Cervical Screening Programme (Structured abstract). *BJOG. An International Journal of Obstetrics and Gynaecology*, 115: 749-757.
Not in PICO
- Halder, K., Chachra, K. L., Sodhani, P. & Gupta, S. (2008) Utility of imprint cytology for early presumptive diagnosis in clinically suspicious cervical cancer. *Acta Cytologica*, 52: 286-293.
Not in PICO
- Hall, J. M., Han, J. J. & Fadare, O. (2011) The value of repeated cytology at the time of first colposcopy: a retrospective analysis of 1,087 cases. *American Journal of Clinical Pathology*, 135: 628-636.
Not in PICO
- Hanuszek, K. (1980) [Diagnostic accuracy of colposcopy in the detection of precancerous conditions and early forms of cervical cancer]. [Polish]. *Polski Tygodnik Lekarski*, 35: 1521-1524.
Not in PICO
- Harrison, W. N., Mohammed, M. A., Wall, M. K. & Marshall, T. P. (2004) Analysis of inadequate cervical smears using Shewhart control charts. *BMC Public Health*, 4: 1-6.
Not in PICO
- Havrilesky, L. J., Wong, T. Z., Secord, A. A., Berchuck, A., Clarke-Pearson, D. L. & Jones, E. L. (2003) The role of PET scanning in the detection of recurrent cervical cancer. *Gynecologic Oncology*, 90: 186-190.
Not in PICO
- Heatley, M. K. (1995) A critical evaluation of the use of the Schiller test in selecting blocks from the uterine cervix in suspected intraepithelial neoplasia. *The Ulster medical journal*, 64: 147-150.
Not in PICO
- Heinzl, S. (2004) [The clarification of a suspect cervical smear--are dysplasia units needed?]. [German]. *Gynakologisch-Geburtshilfliche Rundschau*, 44: 138-141.
Narrative review
- Hermens, R. P., Siebers, B. G., Hulscher, M. E., Braspenning, J. C., Doremalen, J. H., Hanselaar, A., Grol, R. P. & Weel, C. (2005) Follow-up of abnormal or inadequate cervical smears using two guidance systems: RCT on effectiveness. *Preventive Medicine*, 41: 809-814.
Not in PICO
- Hippisley-Cox, J. & Coupland, C. (2013) Symptoms and risk factors to identify women with suspected cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice*, 63: e11-e21.
Not in PICO
- Hollingworth, J., Kotecha, K., Dobbs, S. P., Shaw, P. A. V. & Ireland, D. (2000) Cervical disease in women referred to colposcopy following inadequate smears. *Cytopathology*, 11: 45-52.
Not in PICO
- Howard, M., Sellors, J. W., Lytwyn, A., Roth, P. & Mahony, J. B. (2004) Combining human papillomavirus testing or cervicography with cytology to detect cervical neoplasia. *Archives of Pathology & Laboratory Medicine*, 128: 1257-1262.
Not in PICO
- Howe, D. T. & Vincenti, A. C. (1991) Is large loop excision of the transformation zone (LLETZ) more accurate than colposcopically directed punch biopsy in the diagnosis of cervical intraepithelial neoplasia? *British Journal of Obstetrics and Gynaecology*, 98: 588-591.
Not in PICO
- Hughes, C. (2009) Cervical cancer: prevention, diagnosis, treatment and nursing care. *Nursing standard (Royal College of Nursing (Great Britain) : 1987)*, 23: 48-56.
Narrative review

- Hunt, J. M., Irwig, L. M. & Towler, B. P. (1994) The management of women with initial minor Pap smear abnormalities. *Medical Journal of Australia*, 160: 558-563.
Not in PICO
- Igdbashian, S., Maggioni, A., Casadio, C., Boveri, S., Cristoforoni, P. & Sideri, M. (2009) Sentinel Pap smears in 261 invasive cervical cancer patients in Italy. *Vaccine*, 27: A34-A38.
Not in PICO
- Izadi, B., Khazaei, S. & Mirbahari, S. G. (2011) A survey on association of P16 protein and uterine cervical dysplasia. [Arabic]. *Journal of Isfahan Medical School*, 28: 904-910.
Not in PICO
- Jahic, M. (2006) [The significance of the colposcopy and PAP test in the primary health care]. [Bosnian]. *Medicinski Arhiv*, 60: Suppl-7.
Not in PICO
- Jefferies, H., Sutton, A. & Chan, K. K. (2009) Does direct referral after an abnormal smear improve patient experience? *Nursing Times*, 105: 26-29.
Not in PICO
- Johnson, D. B. & Rowlands, C. J. (1989) Diagnosis and treatment of cervical intraepithelial neoplasia in general practice. *BMJ*, 299: 1083-1086.
Not in PICO
- Johnson, S. J. & Wadehra, V. (2001) How predictive is a cervical smear suggesting invasive squamous cell carcinoma? *Cytopathology*, 12: 144-150.
Not in PICO
- Johnston, W. W., Myers, B., Creasman, W. T. & Owens, S. M. (1982) Cytopathology and the management of early invasive cancer of the uterine cervix. *Obstetrics and Gynecology*, 60: 350-353.
Not in PICO
- jr, J. C. & Marine, C. S. (1989) Early detection of gynecologic malignancies. *Seminars in Surgical Oncology*, 5: 176-178.
Narrative review
- Kalir, T., Simsir, A., Demopoulos, H. B. & Demopoulos, R. I. (2005) Obstacles to the early detection of endocervical adenocarcinoma. *International Journal of Gynecological Pathology*, 24: 399-403.
Not in PICO
- Kane, B. R., Berger, M. S. & Lisney, M. (1997) Pap smear adequacy: the role of clinician experience. *Family Medicine*, 29: 315-317.
Not in PICO
- Karag'ozov, A. (1981) Diagnostic and treatment problems and prospects in precancerous and early stages of cervical cancer. [Bulgarian]. *Akusherstvo i Ginekologija*, 20: 331-337.
In Bulgarian, not enough information can be extracted, but I think it is "Not in PICO".
- Karimi, Z. M., Binesh, F., Kazemi, Z., Teimoori, S., Soltani, H. R. & Chiti, Z. (2011) Value of colposcopy in the early diagnosis of cervical cancer in patients with abnormal pap smears at Shahid Sadoughi hospital, Yazd. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 12: 3439-3441.
Not in PICO
- Keane, D. P., Turner, M. J., Lenehan, P. M., Kelehan, P. & Murphy, J. F. (1991) Do atypia in a cervical smear warrant colposcopy? *Journal of Obstetrics and Gynaecology*, 11: 373-375.
Not in PICO
- Kelly, B. A. & Black, A. S. (1990) The inflammatory cervical smear: a study in general practice. *The British journal of general practice : the journal of the Royal College of General Practitioners*, 40: 238-240.
Not in PICO
- Khalid, S., Carcopino, X., Michail, G., Metchette, S., Conroy, R. & Prendiville, W. (2011) Compliance with follow up cytology after discharge from the colposcopy clinic. *Irish Medical Journal*, 104:

167-170.

Not in PICO

Khan, Z., Appleton, F. & Turner, J. (2008) Is cervical intra-epithelial neoplasia symptomatic? *Journal of Obstetrics and Gynaecology*, 28: 336-337.

Not in PICO

Khattab, A. F., Ewies, A. A., Appleby, D. & Cruickshank, D. J. (2005) The outcome of referral with postcoital bleeding (PCB). *Journal of Obstetrics & Gynaecology*, 25: 279-282.

Not in PICO

Kim, S. J., Ha, S. Y., Choi, B. M., Lee, M. Y., Jin, J. Y., Yeom, S. J., Kim, T. W., Kim, Y. M. & Lee, K. (2013) The prevalence and clinical characteristics of cancer among anemia patients treated at an outpatient clinic. *Blood Research*, 48: 46-50.

Not in PICO (secondary care)

Kingery, J. E. & Noble, W. G. (2012) Endometrial biopsy. *Osteopathic Family Physician*, 4: 144-148.

Narrative review

Kohn, E. C., Mills, G. B. & Liotta, L. (2003) Promising directions for the diagnosis and management of gynecological cancers. [Review] [46 refs]. *International Journal of Gynaecology & Obstetrics*, 83: Suppl-9.

Narrative review

Korach, J., Menczer, J. & Lusky, A. (1995) A comparison between referral and hospital cervical cytology laboratory reports. *Israel Journal of Medical Sciences*, 31: 352-355.

Not in PICO

Kostova, P. & Zlatkov, V. (2013) [Pregnancy and malignant diseases. Part V. Some rare gynecological tumors during pregnancy]. [Bulgarian]. *Akusherstvo i ginekologii{combining double inverted breve}a*, 52: 48-50.

Narrative review

Krizanac, S., Jukic, S. & Bolanca, M. (1987) Accompanying histological changes in the cervix uteri in carcinoma in situ and early invasive carcinoma. [Serbian]. *Lijecnicki Vjesnik*, 109: 418-421.

Not in PICO

Kurihara, M. & Nozawa, S. (1989) [Diagnosis of carcinoma of the uterine cervix]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics.Spec No:349-57, 1989 Jan.*, 349-357.

In Japanese, not enough information can be extracted to ascertain relevance (I think it is a narrative review)

Kyrgiou, M., Koliopoulos, G., Martin-Hirsch, P., Kehoe, S., Flannelly, G., Mitrou, S., Arbyn, M., Prendiville, W. & Paraskevidis, E. (2007) Management of minor cervical cytological abnormalities: a systematic review and a meta-analysis of the literature (DARE structured abstract). *Cancer Treatment Reviews*, 33: 514-520.

Not in PICO

Lam, K. D. & Cheung, K. B. (2004) Common gynaecological problems in general practice. *Hong Kong Practitioner*, 26: 271-276.

Narrative review

Lansac, J. (1982) Detection of carcinoma of the uterine cervix. [French]. *Revue de Medecine*, 23: 1223-1226.

Narrative review

Lelievre, L., Camatte, S., Le Frere-Belda, M. A., Kerrou, K., Froissart, M., Taurelle, R., Vilde, F. & Lecuru, F. (2004) [Sentinel lymph node biopsy in cervical and endometrial cancers: a feasibility study]. [French]. *Bulletin du Cancer*, 91: 379-384.

Not in PICO

Liang, J., Mittal, K. R., Wei, J. J., Yee, H., Chiriboga, L. & Shukla, P. (2007) Utility of p16INK4a, CEA, Ki67, P53 and ER/PR in the differential diagnosis of benign, premalignant, and malignant glandular lesions of the uterine cervix and their relationship with Silverberg scoring system for

- endocervical glandular lesions. *International Journal of Gynecological Pathology*, 26: 71-75.
Not in PICO
- Liao, S. Y. & Stanbridge, E. J. (1996) Expression of the MN antigen in cervical papanicolaou smears is an early diagnostic biomarker of cervical dysplasia. *Cancer Epidemiology, Biomarkers & Prevention*, 5: 549-557.
Not in PICO
- Lickrish, G. M., Colgan, T. J. & Wright, V. C. (1993) Colposcopy of adenocarcinoma in situ and invasive adenocarcinoma of the cervix. [Review] [19 refs]. *Obstetrics & Gynecology Clinics of North America*, 20: 111-122.
Narrative review
- Link, M. (1996) Early detection of cervix carcinoma: Conditions, methods and consequences. [German]. *Gynakologe*, 29: 781-794.
Narrative review
- Liu, B. Q., Yan, Z. W., Yao, H. X. & Cai, J. F. (2007) [Evaluation of liquid based cytology test (LCT) in avoiding medical tangles]. [Chinese]. *Fa i Hsueh Tsa Chih Journal of Forensic Medicine*, 23: 274-276.
Not in PICO
- Lopez, G. N., Recio, S. S. & Garcia, G. A. (1985) Colposcopy and early diagnosis of cancer of the uterine cervix. [Spanish]. *Revista Espanola de Oncologia*, 32: 671-680.
Narrative review
- Madrigal de la Campa Mde, Lazcano Ponce, E. C. & Infante, C. C. (2005) [Overuse of colposcopy service in Mexico]. [Spanish]. *Ginecologia y Obstetricia de Mexico*, 73: 637-647.
Not in PICO
- Maggi, R., Gilardi, L. & Cristofori, E. (1982) What factors delimit the "levels of intervention" for early diagnosis and prevention of cervix carcinoma in the consultation environment?. [Italian]. *Annali di Ostetricia, Ginecologia, Medicina Perinatale*, 103: 366-371.
Not in PICO
- Majeed, F. A., Cook, D. G., Anderson, H. R., Hilton, S., Bunn, S. & Stones, C. (1994) Using patient and general practice characteristics to explain variations in cervical smear uptake rates. *British Medical Journal*, 308: 1272-1276.
Not in PICO
- Makwela, M. R. (2009) Should a smear result of H-SIL always be followed by a biopsy? *Obstetrics and Gynaecology Forum*, 19: 47-49.
Narrative review
- Mantouvalos, C. (1982) Early diagnosis of carcinoma of the cervix uteri. The significance of correlation between beta-glucuronidase estimation and cytology. *Clinical Trials Journal*, 19: 85-90.
Not in PICO
- Matsukuma, K., Tsukamoto, N., Kaku, T., Matsumura, M., Toki, N., Toh, N. & Nakano, H. (1989) Early adenocarcinoma of the uterine cervix - Its histologic and immunohistologic study. *Gynecologic Oncology*, 35: 38-43.
Not in PICO
- Matsuura, Y., Kawagoe, T., Toki, N., Sugihara, K. & Kashimura, M. (1996) Early cervical neoplasia confirmed by conization. Diagnostic accuracy of cytology, colposcopy and punch biopsy. *Acta Cytologica*, 40: 241-246.
Not in PICO
- McCartney, M. (2014) - Doctors and patients confuse cervical screening with diagnostic tests. - *BMJ*, 348: g3334.
Not in PICO
- McCrorry, D. C., Matchar, D. B., Bastian, L., Datta, S., Hasselblad, V., Hickey, J., Myers, E. & Nanda, K. (1999) Evaluation of cervical cytology. [Review] [0 refs]. *Evidence Report: Technology Assessment*

- (Summary). (5):1-6, 1999 Jan., 1-6.
Not in PICO (screening)
- McKee, M. D., Schechter, C., Burton, W. & Mulvihill, M. (2001) Predictors of follow-up of atypical and ASCUS papanicolaou tests in a high-risk population. *Journal of Family Practice*, 50: 609.
Not in PICO
- Meana, M., Stewart, D. E., Lickrish, G. M., Murphy, J. & Rosen, B. (1999) Patient preference for the management of mildly abnormal Papanicolaou smears. *Journal of Womens Health & Gender-Based Medicine*, 8: 941-947.
Not in PICO
- Melguizo, J. M., Lopez, V. F., Castro Gomez, J. A., Tomas, G. J., Bailon, M. E. & de la Revilla, A. L. (1989) The evaluation of a program for the early diagnosis of cervix cancer at a health center (1981-1987). [Spanish]. *Atencion primaria / Sociedad Espanola de Medicina de Familia y Comunitaria*, 6: 300-303.
Not in PICO
- Messer, L., Steckler, A. & Dignan, M. (1999) Early detection of cervical cancer among Native American women: a qualitative supplement to a quantitative study. *Health Education & Behavior*, 26: 547-562.
Not in PICO
- Miller, K. S., Yunger, J., Single, N. & Kunz, J. (1996) Prevalence of abnormal Pap smears in rural family practice. *Journal of Rural Health*, 12: 33-38.
Not in PICO
- Mossa, B., Ebano, V. & Marziani, R. (2010) Reliability of outpatient endometrial brush cytology vs biopsy in postmenopausal symptomatic women. *European Journal of Gynaecological Oncology*, 31: 621-626.
Not in PICO
- Murata, P. J. & Li, J. E. (1992) Relationship between Pap smear performance and physician ordering a mammogram. *Journal of Family Practice*, 35: 644-648.
Not in PICO
- Naik, R. M., Pai, A., Guruprasad, Y. & Singh, R. (2013) Efficacy of colour Doppler ultrasound in diagnosis of cervical lymphadenopathy. *Journal of Maxillofacial & Oral Surgery*, 12: 123-129.
Not in PICO
- Narine, N. & Young, W. (2007) Transformation zone sampling rate is a useful performance indicator for practitioners collecting cervical samples using SurePath liquid-based cytology system. *Cytopathology*, 18: 220-224.
Not in PICO
- Nelson, J., Averette, H. E. & Richart, R. M. (1984) Dysplasia, carcinoma in situ, and early invasive cervical carcinoma. *Ca-A Cancer Journal for Clinicians*, 34: 306-327.
Not in PICO
- Nene, B. M., Deshpande, S., Jayant, K., Budukh, A. M., Dale, P. S., Deshpande, D. A., Chiwate, A. S., Malvi, S. G., Deokar, S., Parkin, D. M. & Sankaranarayanan, R. (1996) Early detection of cervical cancer by visual inspection: a population-based study in rural India. *International Journal of Cancer*, 68: 770-773.
Not in PICO
- Newell, S. & Overton, C. (2002) Postmenopausal bleeding should be referred urgently. *Practitioner*, 256: 13-15.
Narrative review
- Njoroge, E., Alty, S. R., Gani, M. R. & Alkatib, M. (2006) Classification of cervical cancer cells using FTIR data. *Conference Proceedings: ...Annual International Conference of the IEEE Engineering in Medicine & Biology Society*, 1: 5338-5341.
Not in PICO

- Noda, K. (1984) Early diagnosis of uterine cancer. *Asian Medical Journal*, 27: 624-630.
Narrative review
- Nuovo, J., Melnikow, J. & Paliescheskey, M. (1995) Management of patients with atypical and low-grade Pap smear abnormalities. *American Family Physician*, 52: 2243-2250.
Narrative review
- Nuovo, J., Melnikow, J., Hutchison, B. & Paliescheskey, M. (1997) Is cervicography a useful diagnostic test? A systematic overview of the literature. [Review] [41 refs]. *Journal of the American Board of Family Practice*, 10: 390-397.
Not in PICO
- Oh, J. K. & Kim, K. H. (2013) Why are recurrent cervical cancers of the pelvic stump misdiagnosed as interstitial cystitis?: The urologist's point of view based on a case report. *Canadian Urological Association Journal*, 7: E359-E362.
Not in PICO
- Olaniyan, O. B. (2002) Validity of colposcopy in the diagnosis of early cervical neoplasia--a review. *African Journal of Reproductive Health*, 6: 59-69.
Not in PICO
- Olesen, F. (1988) [Uterine cervical cancer and variations in taking cytological samples in general practice]. [Danish]. *Ugeskrift for Laeger*, 150: 2247-2250.
Not in PICO
- Olesen, F. & Lauritzen, T. (1997) Do general practitioners want guidelines? Attitudes toward a county-based and a national college-based approach. *Scandinavian Journal of Primary Health Care*, 15: 141-145.
Not in PICO
- Otero, L., Sanz, B. & Blasco, T. (2011) Early detection of cervical cancer according to the discourses of primary care midwives in Segovia, Spain. *Revista de Saude Publica*, 45: 824-830.
Not in PICO
- Pairwuti, S. (1990) Pap smear examinations of women at the out-patient department of Siriraj Hospital. *Journal of the Medical Association of Thailand*, 73: 473-478.
Not in PICO
- Palm, B. T., Kant, A. C., Visser, E. A., Vooijs, G. P., Bosch, W. J. & Weel, C. (1997) The effect of the family physician on improving follow-up after an abnormal PAP smear. *International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua.*, 9: 277-282.
Not in PICO
- Papillo, J. L., Zarka, M. A. & John, T. L. (1998) Evaluation of the ThinPrep Pap test in clinical practice. A seven-month, 16,314-case experience in northern Vermont. *Acta Cytologica*, 42: 203-208.
Not in PICO
- Peedicayil, A., Regi, A., Mathai, M. & Jasper, P. (1994) Colposcopy in women with a normal Papanicolaou smear. *National Medical Journal of India*, 7: 208-209.
Not in PICO
- Perez, D. J., Santamaria, M., Jurado, M., Cabezon, C., Dominquez, J., de la Fuente, F. & Lopez, G. G. (1980) [Diagnosis of cervical dysplasias]. [Spanish]. *Revista de Medicina de la Universidad de Navarra*, 24: 26-29.
Narrative review
- Pfenninger, J. L. (1992) Colposcopy in A Family-Practice Residency - the 1St 200 Cases. *Journal of Family Practice*, 34: 67-72.
Not in PICO
- Pisal, N. V., Sindos, M., Desai, S., Mansell, E. & Singer, A. (2003) How significant is a cervical smear showing glandular dyskaryosis? *European Journal of Obstetrics, Gynecology, & Reproductive Biology*, 108: 209-212.
Not in PICO

- Polterauer, S., Grimm, C., Seebacher, V., Rahhal, J., Tempfer, C., Reinthaller, A. & Hefler, L. (2010) The inflammation-based Glasgow Prognostic Score predicts survival in patients with cervical cancer. *International Journal of Gynecological Cancer*, 20: 1052-1057.
Not in PICO
- Poomtavorn, Y., Suwannarurk, K., Thaweekul, Y. & Maireang, K. (2011) Risk factors for high-grade cervical intraepithelial neoplasia in patients with atypical squamous cells of undetermined significance (ASC-US) Papanicolaou smears. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 12: 235-238.
Not in PICO
- Prendiville, W. & Walker, P. (1995) Every woman with an abnormal cervical smear should not be referred for colposcopy: debate. [Review] [16 refs]. *Clinical Obstetrics & Gynecology*, 38: 592-599.
Narrative review
- Prislin, M. D., Dinh, T. & Giglio, M. (1997) On-site colposcopy services in a family practice residency clinic: impact on physician test-ordering behavior, patient compliance, and practice revenue generation. *Journal of the American Board of Family Practice*, 10: 259-264.
Not in PICO
- Puig-Tintore, L. M. & Jou, C. P. (1983) [Early diagnosis of gynecological cancer]. [Spanish]. *Medicina Clinica*, 81: 131-135.
Narrative review
- Rao, R. S., Kamath, V. G., Chandrashekar, S., Rao, L. & Pratap, K. (2007) Downstaging for cervical cancer: a community-based study in the rural areas of Udupi district, Karnataka, India. *Tropical Doctor*, 37: 73-75.
Not in PICO
- Ratinahirana, S., Razanamparany, P.-V., Razafintsalama, B., Randriamampandry, A., Ravaoarison, J., Rabarijaona, L., Ranjatoarivelo, J. & Andriamanalina, N. (1995) Study of 79 cases of invasive cervical carcinoma by the Department of Oncology of Antananarivo. Can the delays in diagnosis be improved?. [French]. *Cahiers Sante*, 5: 195-198.
Not in PICO
- Ravarino, A., Nemolato, S., Macciocu, E., Frascini, M., Senes, G., Faa, G. & Negri, G. (2012) CINtec PLUS immunocytochemistry as a tool for the cytologic diagnosis of glandular lesions of the cervix uteri. *American Journal of Clinical Pathology*, 138: 652-656.
Not in PICO
- Ray, P. & Kaul, V. (2008) Prevalence of high-grade squamous intraepithelial neoplasia (HiSIL) in symptomatic women referred to the colposcopy clinic with negative cytology. *Archives of Gynecology & Obstetrics*, 277: 501-504.
Not in PICO
- Ray, P., Thumuluru, K. M. & Kaul, V. (2009) Primary care sector versus treatment centre follow up for post-treatment cervical squamous intraepithelial neoplasia (SIL). *Archives of Gynecology and Obstetrics*, 279: 109-111.
Not in PICO
- Raymond, L., Obradovic, M. & Riotton, G. (1984) A case control study for the evaluation of the cytological detection of cancer of the cervix. [French]. *Revue d'epidemiologie et de sante publique*, 32: 10-15.
Not in PICO
- Raymond, L., Obradovic, M. & Riotton, G. (1984) A case control study to estimate the detection of cancer of the cervix uteri by cytology. [French]. *Revue d'epidemiologie et de sante publique*, 32: 10-15.
Not in PICO
- Ritter, J., Baldauf, J. J. & Gandar, R. (1985) Early cytological detection of cancer of the cervix. [French]. *Revue Francaise de Gynecologie et d'Obstetrique*, 80: 341-352.
Narrative review

- Rochanawutanon, M. & Srisupandit, S. (2007) The histopathologic patterns of cervical lesions and visual inspection with acetic acid on excised uterine cervixes. *International Journal of Gynecological Cancer*, 17: 827-832.
Not in PICO
- Roderick, E., Anderson, J., Birket, I., Cox, J., Donald, C., Fakes, W., Farndale, J., Gardner, D., Gray, P., Herd, B., Horne, A., Howarth, J., Jay, S., Jones, R., McKay, W. G., Mitchell, I., Stevenson, M., Swindells, R. & Taylor, M. (1991) Sampling endocervical cells on cervical smears: A comparison of two instruments used in general practice. *British Journal of General Practice*, 41: 192-193.
Not in PICO
- Rosenthal, A. N., Panoskaltsis, T., Smith, T. & Soutter, W. P. (2001) The frequency of significant pathology in women attending a general gynaecological service for postcoital bleeding. *British Journal of Obstetrics and Gynaecology*, 108: 103-106.
Not in PICO
- Rosvold, E. O., Hjartaker, A., Bjertness, E. & Lund, E. Breast self-examination and cervical cancer testing among Norwegian female physicians: A nation-wide comparative study. [References]. *Social Science & Medicine* 52[2], 249-258. 2001.
Ref Type: Generic
Ref ID: 145
Reprint: Not in File
Abstract: Examined breast self-examination (BSE) practices and cervical cancer Pap smear testing in female physicians. 284 female physicians (aged 24-67 yrs) residing in Norway completed questionnaires. Results show that 30.6% of Ss performed BSE at least once monthly; 54.6% of Ss had a Pap smear test once every 3rd yr at least. BSE was never practiced among 19.2% of the physicians: primary cited reasons for this included forgetting, membership in a low risk group, or having no symptoms of disease. 16.2% of Ss had never undergone routine Pap smears, claiming that they were in a low risk group, they had no symptoms of disease, they had a problem in finding a physician to attend, or they forgot. Compared with 738 Norwegian females, a subgroup of 135 physicians (aged 35-49 yrs) practiced BSE monthly or more often compared with other university educated women. However, a significantly lower percentage of the physicians had Pap smear tests every 3rd yr or more frequently. (PsycINFO Database Record (c) 2012 APA, all rights reserved)
Notes: DB - PsycINFO
AN - Peer Reviewed Journal: 2000-14380-006
SO - Social Science & Medicine. Vol.52(2), Jan 2001, pp. 249-258
- Ryu, S. Y., Kim, M. H., Choi, S. C., Choi, C. W. & Lee, K. H. (2003) Detection of early recurrence with 18F-FDG PET in patients with cervical cancer. *Journal of Nuclear Medicine*, 44: 347-352.
Not in PICO
- Sandvik, R. M., Jensen, P. T., Hendel, H. W. & Palle, C. (2011) Positron emission tomography-computed tomography has a clinical impact for patients with cervical cancer. *Danish Medical Bulletin*, 58: A4240.
Not in PICO
- Sauvaget, C., Fayette, J. M., Muwonge, R., Wesley, R. & Sankaranarayanan, R. (2011) Accuracy of visual inspection with acetic acid for cervical cancer screening (DARE structured abstract). *International Journal of Gynecology and Obstetrics*, 113: 14-24.
Not in PICO
- Savas, H. G. & Taskin, L. (2011) Determining nurse-midwives' knowledge of the Pap-smear test and their rate of being tested in Turkey. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 12: 1353-1360.
Not in PICO
- Schorn, M. (2004) What are the current Pap test guidelines? *Nursing*, 34: 26.
Not in PICO

- Seamon, L. G., Tarrant, R. L., Fleming, S. T., Vanderpool, R. C., Pachtman, S., Podzielinski, I., Branscum, A. J., Feddock, J. M., Randall, M. E. & DeSimone, C. P. (2011) Cervical cancer survival for patients referred to a tertiary care center in Kentucky. *Gynecologic Oncology*, 123: 565-570.
Not in PICO
- Segal, A., Frost, F. A., Miranda, A., Fletcher, C. & Sterrett, G. F. (2003) Predictive value of diagnoses of endocervical glandular abnormalities in cervical smears. *Pathology*, 35: 198-203.
Not in PICO
- Selim, M. A. & Razi, A. (1980) Cryosurgery for intraepithelial neoplasia of the cervix. *Cancer*, 46: 2315-2318.
Not in PICO
- Serur, E., Fruchter, R. G., Maiman, M., McGuire, J., Arrastia, C. D. & Gibbon, D. (1995) Age, substance abuse, and survival of patients with cervical carcinoma. *Cancer*, 75: 2530-2538.
Not in PICO
- Sethom, F., Besbes, K. & Cammoun, M. (1989) For an early diagnosis of cervical cancer by systematic vaginal smears--clinical and psychological approach. [French]. *La Tunisie medicale*, 67: 505-511.
In French, not enough information can be extracted/is reported to ascertain relevance (i.e., setting) for study 1; study 2 not in PICO
- Shahida, S. M., Mirza, T. T., Saleh, A. F. & Islam, M. A. (2012) Colposcopic evaluation of pre-invasive and early cervical carcinoma with histologic correlation. *Mymensingh Medical Journal: MMJ*, 21: 200-206.
Not in PICO
- Shapley, M., Blagojevic-Bucknall, M., Jordan, K. P. & Croft, P. R. (2013) The epidemiology of self-reported intermenstrual and postcoital bleeding in the perimenopausal years. *BJOG: An International Journal of Obstetrics & Gynaecology*, 120: 1348-1355.
Not in PICO (not symptomatic patients presenting to the GP)
- Shivkumar, P. V. (2012) To study the cases of cervical abnormalities and to correlate their clinical cyto-histopathological findings in a rural population of central india. *International Journal of Gynecology and Obstetrics*, 119: S484.
Not in PICO
- Shukla, S., Rajput, D., Acharya, S., Acharya, N., Grover, S., Samal, N. & Vagha, S. (2013) A study on the nucleolar organizer regions-as a tumour proliferative marker in cervical smears. *Journal of Clinical and Diagnostic Research*, 7: 278-283.
Not in PICO
- Siddiq, T. S., Twigg, J. P. & Hammond, R. H. (2006) Assessing the accuracy of colposcopy at predicting the outcome of abnormal cytology in pregnancy. *European Journal of Obstetrics Gynecology and Reproductive Biology*, 124: 93-97.
Not in PICO
- Siebers, A. G., Klinkhamer, P. J. J. M., Grefte, J. M. M., Massuger, L. F. A. G., Vedder, J. E. M., Beijers-Broos, A., Bulten, J. & Arbyn, M. (2009) Comparison of Liquid-Based Cytology With Conventional Cytology for Detection of Cervical Cancer Precursors A Randomized Controlled Trial. *Jama-Journal of the American Medical Association*, 302: 1757-1764.
Not in PICO
- Simsir, A., Ioffe, O. B., Bourquin, P., Brooks, S. E. & Henry, M. (2001) Repeat cervical cytology at the time of colposcopy: is there an added benefit? (Structured abstract). *Acta Cytologica*, 45: 23-27.
Not in PICO
- Singh, V., Verma, K. & Bhargava, V. L. (1983) Cytological & colposcopic evaluation in premalignant & early malignant lesions of the cervix. *Indian Journal of Medical Research*, 78: Suppl-9.
Not in PICO
- Skaarland, E. (1986) New concept in diagnostic endometrial cytology: diagnostic criteria based on composition and architecture of large tissue fragments in smears. *Journal of Clinical Pathology*,

- 39: 36-43.
Not in PICO (secondary/tertiary care)
- Skehan, M., Soutter, W. P., Lim, K., Krausz, T. & Pryse-Davies, J. (1990) Reliability of colposcopy and directed punch biopsy. *British Journal of Obstetrics & Gynaecology*, 97: 811-816.
Not in PICO
- Snyder, M. J., Robboy, S. J., Vollmer, R. T. & Dodd, L. G. (2004) An abnormal cervicovaginal cytology smear in uterine carcinosarcoma is an adverse prognostic sign: analysis of 25 cases. *American Journal of Clinical Pathology*, 122: 434-439.
Not in PICO
- Soutter, W. P., Wisdom, S., Brough, A. K. & Monaghan, J. M. (1986) Should patients with mild atypia in a cervical smear be referred for colposcopy? *British Journal of Obstetrics & Gynaecology*, 93: 70-74.
Not in PICO
- Soutter, W. P. (1994) Management of women with mild dyskaryosis. Immediate referral to colposcopy is safer. *BMJ*, 309: 591-592.
Not in PICO
- Spagnolo, A., Torrini, V., Cavallari, L. & Patella, A. (1985) Uterine cervix: Colposcopic, cytologic, histologic correlations in 5602 women observed. [Italian]. *Giornale Italiano di Oncologia*, 5: 295-300.
In Italian, limited information provided about patients, but I believe it is "Not in PICO"
- Spoelhof, G. D. (1994) Colposcopy in a private family practice: a one year experience. *Family Practice Research Journal*, 14: 97-103.
Not in PICO
- Srivannaboon, S. & Phijaisanit, P. (1982) Detection of early cervical cancer by the irrigation smear technic. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet*, 65: 361-365.
Not in PICO
- Staite, A. (1989) Cervical cytology in general practice. *New Zealand Nursing Journal*, 82: 18-19.
Narrative review
- Stapley, S. & Hamilton, W. (2011) Gynaecological symptoms reported by young women: examining the potential for earlier diagnosis of cervical cancer. *Family Practice*, 28: 592-598.
Not in PICO
- Stokes-Lampard, H., Wilson, S., Waddell, C. & Bentley, L. (2011) Vaginal vault cytology tests: analysis of a decade of data from a UK tertiary centre. *Cytopathology*, 22: 121-129.
Not in PICO
- Stoler, M. H., Vichnin, M. D., Ferenczy, A., Ferris, D. G., Perez, G., Paavonen, J., Joura, E. A., Djursing, H., Sigurdsson, K., Jefferson, L., Alvarez, F., Sings, H. L., Lu, S., James, M. K., Saah, A., Haupt, R. M. & Future, I. (2011) The accuracy of colposcopic biopsy: analyses from the placebo arm of the Gardasil clinical trials. *International journal of cancer. Journal international du cancer*, 128: 1354-1362.
Not in PICO
- Suwannarurk, K., Bhamarapavati, S., Thaweekul, Y., Mairaing, K., Poomtavorn, Y. & Pattaraarchachai, J. (2009) The accuracy of cervical cancer and cervical intraepithelial neoplasia diagnosis with loop electrosurgical excisional procedure under colposcopic vision. *Journal of Gynecologic Oncology*, 20: 35-38.
Not in PICO
- Sykes, P. H., Harker, D. Y., Miller, A., Whitehead, M., Neal, H., Wells, J. E. & Peddie, D. (2008) A randomised comparison of SurePath liquid-based cytology and conventional smear cytology in a colposcopy clinic setting. *BJOG: An International Journal of Obstetrics & Gynaecology*, 115: 1375-1381.
Not in PICO

- Takashima, E. (1985) Usefulness of hysteroscopy for detection of cancer in the endocervical canal. [Japanese]. *Acta Obstetrica et Gynaecologica Japonica*, 37: 2401-2409.
Not in PICO
- Tariq, T. A., Mason, W. P. & Steele, T. (1993) Role of colposcopy in the diagnosis and outpatient treatment of cervical intraepithelial neoplasia. *JPMA - Journal of the Pakistan Medical Association*, 43: 86-89.
Not in PICO
- Teter, J. (1982) Detection of cervix dysplasia and early forms of cervical cancer. [Polish]. *Nowotwory*, 32: 201-208.
Not in PICO
- Toplis, P. J., Casemore, V., Hallam, N. & Charnock, M. (1986) Evaluation of colposcopy in the postmenopausal woman. *British Journal of Obstetrics & Gynaecology*, 93: 843-851.
Not in PICO
- Towler, B. P., Irwig, L. M. & Shelley, J. M. (1993) The adequacy of management of women with CIN 2 and CIN 3 Pap smear abnormalities. *Medical Journal of Australia*, 159: 523-528.
Not in PICO
- Trivers, K. F., Benard, V. B., Ehemann, C. R., Royalty, J. E., Ekwueme, D. U. & Lawson, H. W. (2009) Repeat pap testing and colposcopic biopsies in the underserved. *Obstetrics & Gynecology*, 114: 1049-1056.
Not in PICO
- Underwood, S. M., Ramsay-Johnson, E., Dean, A., Russ, J. & Ivalis, R. (2009) Expanding the scope of nursing research in low resource and middle resource countries, regions, and states focused on cervical cancer prevention, early detection, and control. [Review] [79 refs]. *Journal of National Black Nurses Association*, 20: 42-54.
Narrative review
- Ursic-Vrscelj, M., Rakar, S., Mozina, A., Takac, I., Subic, Z., Kodric, T. & Smrkolj, S. (2005) Clinical audit of patients with cervical cancer in slovenia - Data analysis for the year 2003. *European Journal of Gynaecological Oncology*, 26: 537-542.
Not in PICO
- van der Veldt, A. A., Hooft, L., van Diest, P. J., Berkhof, J., Buist, M. R., Comans, E. F., Hoekstra, O. S. & Molthoff, C. F. (2006) Microvessel density and p53 in detecting cervical cancer by FDG PET in cases of suspected recurrence. *European Journal of Nuclear Medicine & Molecular Imaging*, 33: 1408-1416.
Not in PICO
- van Hemel, B. M., Buikema, H. J., Groen, H. & Suurmeijer, A. J. (2009) Accuracy of a low priced liquid-based method for cervical cytology in 632 women referred for colposcopy after a positive Pap smear. *Diagnostic Cytopathology*, 37: 579-583.
Not in PICO
- Wainer, J., Willis, E., Dwyer, J., King, D. & Owada, K. (2012) The treatment experiences of Australian women with gynaecological cancers and how they can be improved: a qualitative study. *Reproductive Health Matters*, 20: 38-48.
Not in PICO
- Ward, B. G. & Broe, S. J. (2003) Outpatient management of abnormal smears. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 43: 50-53.
Not in PICO
- Wetta, L. A., Matthews, K. S., Kemper, M. L., Whitworth, J. M., Fain, E. T., Huh, W. K., Kendrick, J. E. & Straughn, J. (2009) The management of cervical intraepithelial neoplasia during pregnancy: Is colposcopy necessary? *Journal of Lower Genital Tract Disease*, 13: 182-185.
Not in PICO
- Wheelock, J. B. & Kaminski, P. F. (1989) Value of repeat cytology at the time of colposcopy for the evaluation of cervical intraepithelial neoplasia on Papanicolaou smears. *Journal of Reproductive*

- Medicine*, 34: 815-817.
Not in PICO
- Wilkinson, C. E., Peters, T. J., Harvey, I. M. & Stott, N. C. (1994) Feasibility, reliability and women's views of a risk scoring system for cervical neoplasia in primary care. *British Journal of General Practice*, 44: 306-308.
Not in PICO
- Wilkinson, C. E., Peters, T. J., Stott, N. C. H. & Harvey, I. M. (1994) Prospective Evaluation of A Risk Scoring System for Cervical Neoplasia in Primary-Care. *British Journal of General Practice*, 44: 341-344.
Not in PICO (screening)
- Williams, M. P., Husband, J. E., Heron, C. W., Cherryman, G. R. & Koslin, D. B. (1989) Magnetic resonance imaging in recurrent carcinoma of the cervix. *British Journal of Radiology*, 62: 544-550.
Not in PICO
- Williams, S., Butler-Manuel, S., Taylor, A. & Madhuri, T. (2013) Ovarian metastases from squamous cell carcinoma of cervix: A rare finding. *BJOG: An International Journal of Obstetrics and Gynaecology*, 120: 247-248.
Not in PICO
- Wilson, J. D., Hill, A. S. & Hicks, D. A. (1988) Value of colposcopy in genitourinary departments. *Genitourinary Medicine*, 64: 100-102.
Not in PICO
- Wright, V. C. (1959) When to suspect squamous cancer at colposcopy. [Review] [22 refs]. *Nurse Practitioner*, 26: 50-56.
Narrative review
- Yamazaki, T., Inaba, F., Takeda, N., Furuno, M., Kamemori, T., Kosaka, N., Ohta, Y., Fukasawa, I. & Inaba, N. (2006) A study of abnormal cervical cytology in pregnant women. *Archives of Gynecology and Obstetrics*, 273: 355-359.
Not in PICO
- Yen, T. C., Lai, C. H., Ma, S. Y., Huang, K. G., Huang, H. J., Hong, J. H., Hsueh, S., Lin, W. J., Ng, K. K. & Chang, T. C. (2006) Comparative benefits and limitations of 18F-FDG PET and CT-MRI in documented or suspected recurrent cervical cancer. *European Journal of Nuclear Medicine & Molecular Imaging*, 33: 1399-1407.
Not in PICO
- Yu, B. K., Kuo, B., I, Yen, M. S., Twu, N. F., Lai, C. R., Chen, P. J., Chien, P. S., Chao, K. C. & Yuan, C. C. (2003) Improved early detection of cervical intraepithelial lesions by combination of conventional Pap smear and speculoscopy (Structured abstract). *European Journal of Gynaecological Oncology*, 24: 495-499.
Not in PICO (screening)
- Zeqiri, F., Pacarada, M., Zeqiri, V., Kongjeli, G., Kongjeli, N. & Zejnullahu-Raci, P. (2010) Colposcopy and cytodiagnosis in the prevention of cervical malignancies. *Nigerian Journal of Medicine: Journal of the National Association of Resident Doctors of Nigeria*, 19: 157-161.
Not in PICO

VULVAL CANCER

Review question:

What is the risk of vulval cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

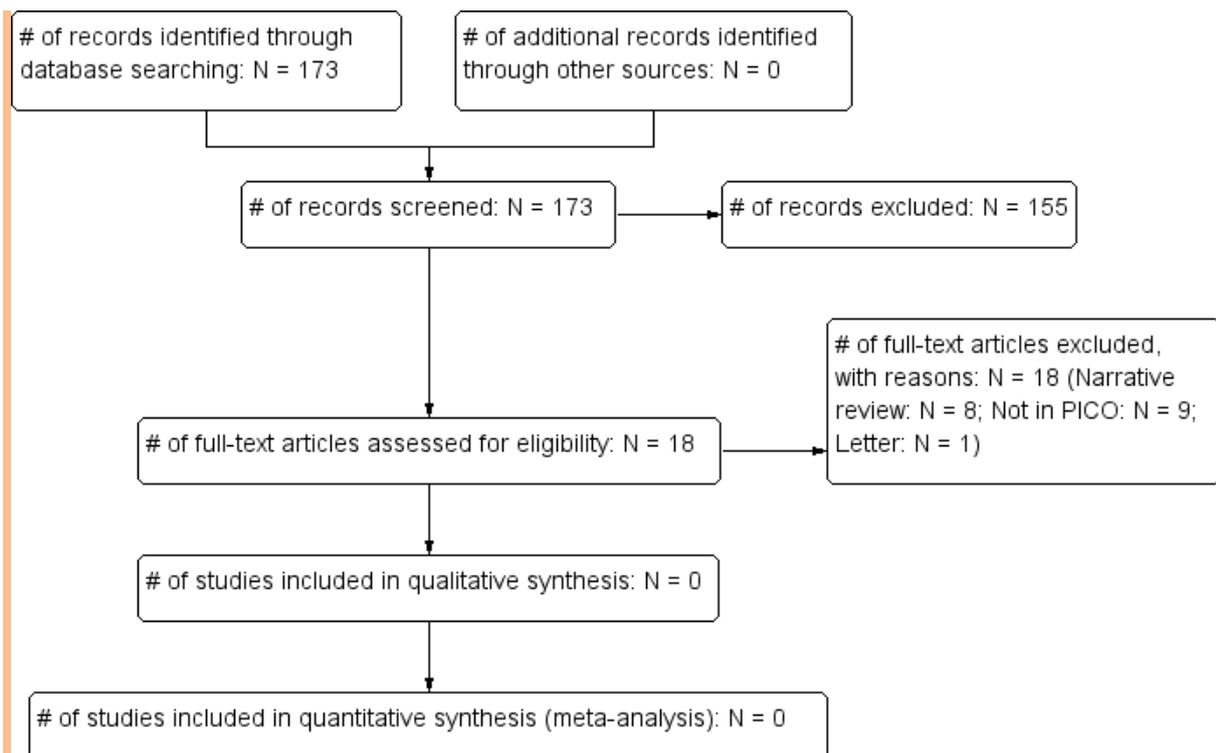
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	373	93	27/09/2012
<i>Premedline</i>	All-2012	9	2	27/09/2012
<i>Embase</i>	All-2012	474	125	01/10/2012
<i>Cochrane Library</i>	All-2012	23	0	27/09/2012
<i>Psychinfo</i>	All-2012	0	0	27/09/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	3	2	27/09/2012
<i>Biomed Central</i>	All-2012	73	2	27/09/2012

Total References retrieved (after de-duplication): 167

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	9/2012-27/08/2014	42	0	27/08/2014
<i>Premedline</i>	9/2012-27/08/2014	36	4	27/08/2014
<i>Embase</i>	9/2012-27/08/2014	56	3	27/08/2014
<i>Cochrane Library</i>	9/2012-27/08/2014	17	0	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	9/2012-27/08/2014	8	0	27/08/2014

Total References retrieved (after de-duplication): 6



Study results

No evidence was identified.

References

Included studies

None

Excluded studies (with excl reason)

Practice guidelines: vulvar cancer. Society of Gynecologic Oncologists Clinical Practice Guidelines. Oncology (Williston Park) 12[2], 275-282. 1998.

Excl reason: Guideline

Information from your family doctor. Vulvar cancer. American Family Physician 66[7], 1276. 1-10-2002.

Excl reason: Patient education material

Abdel-Mesih, A., Daya, D., Onuma, K., Akhtar-Danesh, N., Boutross-Tadross, O., Ceballos, K., Chapman, W., Colgan, T., Deb, P., Nucci, M. R., Oliva, E., Sur, M., Tang, S., and Lytwyn, A. Inter-observer agreement among pathologists for assessing invasion in early vulvar squamous cell carcinoma: Still a diagnostic challenge. Laboratory Investigation 90, 232A. 2010. Nature Publishing Group.

Excl reason: Not in PICO

Athavale, R., Naik, R., Godfrey, K. A., Cross, P., Hatem, M. H., and de Barros, Lopes A. Vulvar intraepithelial neoplasia-The need for auditable measures of management. European Journal of Obstetrics Gynecology and Reproductive Biology 137[1], 97-102. 2008.

Excl reason: Not in PICO

Baderca, F., Cojocaru, S., Lazar, E., Lazureanu, C., Lighezan, R., Alexa, A., Raica, M., and Nicola, T. Amelanotic vulvar melanoma: case report and review of the literature. [Review] [25 refs]. Romanian Journal of Morphology & Embryology 49[2], 219-228. 2008.

Excl reason: Not in PICO

- Balat, O. Contemporary management of groin lymph nodes in early vulvar cancer: diagnosis and treatment. *European Journal of Gynaecological Oncology* 23[5], 378-382. 2002.
Excl reason: Not in PICO
- Baltzer, J. [Precancerous conditions and early stages of vulvar cancer]. [Review] [8 refs] [German]. *Archives of Gynecology & Obstetrics* 245[1-4], 498-503. 1989.
Excl reason: Narrative review
- Baltzer, J. and Poleska, W. Metastatic vaginal neoplasia - A diagnostic and therapeutic problem. [Polish, English]. *Ginekologia Onkologiczna* 4[4], 250-255. 2006.
Excl reason: Not in PICO
- Bapir, M., Hoh, J., and Al-Inizi, S. Leiomyosarcoma of the vulva. *BJOG: An International Journal of Obstetrics and Gynaecology* 119, 186. 2012. Blackwell Publishing Ltd.
Excl reason: Not in PICO
- Basta, A., Adamek, K., and Pitynski, K. Intraepithelial neoplasia and early stage vulvar cancer. Epidemiological, clinical and virological observations. *European Journal of Gynaecological Oncology* 20[2], 111-114. 1999.
Excl reason: Not in PICO
- Basta, A. [Tactical diagnostic-therapeutic procedures in early stages of vulvar cancer]. [Polish]. *Przegląd Lekarski* 56[1], 89-93. 1999.
Excl reason: Not in PICO
- Bifulco, G., Mandato, V. D., Piccoli, R., Giampaolino, P., Mignogna, C., Mignogna, M. D., Costagliola, L., and Nappi, C. Early invasive vulvar squamous cell carcinoma arising in a woman with vulvar pemphigus vulgaris and systemic lupus erythematosus. *BMC Cancer* 10, 324. 2010.
Excl reason: Not in PICO
- Blair, A. R. and Casas, C. M. Gynecologic cancers. [Review] [45 refs]. *Primary Care; Clinics in Office Practice* 36[1], 115-130. 20-11-2009.
Excl reason: Narrative review
- Boice, C. R., Seraj, I. M., Thrasher, T., and King, A. Microinvasive squamous carcinoma of the vulva: present status and reassessment. [Review] [13 refs]. *Gynecologic Oncology* 18[1], 71-76. 1984.
Excl reason: Not in PICO
- Bornstein, J., Pascal, B., Sova, Y., Rosenfeld, Y., and Abramovici, H. The vulvar clinic. [Hebrew]. *Harefuah* 119[12], 413-416. 16-12-1990.
Excl reason: Not in PICO
- Brannigan, J. and McCullough, A. Setting up a vulval clinic. *Nursing Times* 83[14], 30-32. 8-4-1987.
Excl reason: Not in PICO
- Burbos, N. and Rufford, B. Predictive value of urgent referrals for women with suspected gynecologic malignancies. *Gynecologic Oncology* 116[3 SUPPL. 1], S53. 2010. Academic Press Inc.
Excl reason: Not in PICO
- Burbos, N., Musonda, P., and Rufford, B. Diagnostic performance of urgent referrals for suspected gynaecological malignancies. *Archives of Gynecology & Obstetrics* 284[6], 1495-1500. 2011.
Excl reason: Not in PICO
- Buscema, J., Stern, J. L., and Woodruff, J. D. Early invasive carcinoma of the vulva. *American Journal of Obstetrics & Gynecology* 140[5], 563-569. 1-7-1981.
Excl reason: Not in PICO
- Caglar, H., Tamer, S., and Hreshchyshyn, M. M. Vulvar intraepithelial neoplasia. *Obstetrics & Gynecology* 60[3], 346-349. 1982.
Excl reason: Not in PICO
- Canavan, T. P. and Cohen, D. Vulvar cancer. [Review] [19 refs]. *American Family Physician* 66[7], 1269-1274. 1-10-2002.
Excl reason: Narrative review
- Candiani, P., Caru, A., Klinger, M., Campiglio, G. L., and Colonna, M. Vulvar dystrophy: The past and the present in the reconstructive treatment. [Italian]. *Rivista Italiana di Chirurgia Plastica* 23,

270-274. 1991.

Excl reason: Not in PICO

Carlson, J. A., Ambros, R., Malfetano, J., Ross, J., Grabowski, R., Lamb, P., Figge, H., and Mihm, M. C., Jr. Vulvar lichen sclerosus and squamous cell carcinoma: a cohort, case control, and investigational study with historical perspective; implications for chronic inflammation and sclerosis in the development of neoplasia. [Review] [187 refs]. *Human Pathology* 29[9], 932-948. 1998.

Excl reason: Not in PICO

Carter, J. S. and Downs, L. S., Jr. Vulvar and vaginal cancer. *Obstetrics & Gynecology Clinics of North America* 39[2], 213-231. 2012.

Excl reason: Narrative review

Caschetto, S., Caragliano, L., Cassaro, N., Consalvo, P., Bianca, G., and Garozzo, G. [Screening strategies for vulvar preneoplastic and neoplastic lesions]. [Italian]. *Minerva Ginecologica* 52[12], 491-495. 2000.

Excl reason: Not in PICO

Castellano, A., Scassellati, Sforzolini G., and Bartolomucci, L. [Epidemiology and clinical presentation of vulvar cancer]. [Review] [23 refs] [Italian]. *Rivista Europea Per le Scienze Mediche e Farmacologiche* 14[5], 341-345. 1992.

Excl reason: Narrative review

Castellano, A., Scassellati, Sforzolini G., and Bartolomucci, L. Vulvar cancer: Epidemiology and clinical presentation. [Italian]. *European Review for Medical and Pharmacological Sciences* 14[5], 341-345. 1992.

Excl reason: Narrative review

Cattaneo, A., De, Magnis A., Botti, E., Piciocchi, L., and Carli, P. [Principles of the clinical evaluation of the vulvar region]. [Review] [6 refs] [Italian]. *Minerva Ginecologica* 48[10], 429-433. 1996.

Excl reason: Narrative review

Cavanagh, D., Praphat, H., and Ruffolo, E. H. Cancer of the vulva. *Obstetrics and Gynecology Annual Vol.*, 303-339. 1982.

Excl reason: Narrative review

Chhabra, S., Bhavani, M. & Deshpande, A. (2014) Trends of vulvar cancer. *Journal of Obstetrics & Gynaecology*, 34: 165-168.

Not in PICO

Chu, J., Tamimi, H. K., and Figge, D. C. Femoral node metastases with negative superficial inguinal nodes in early vulvar cancer. *American Journal of Obstetrics & Gynecology* 140[3], 337-339. 1-6-1981.

Excl reason: Not in PICO

Clayton, R. D. and Barton, D. P. J. Recent trends in the management of vulval cancer. *Reviews in Gynaecological Practice* 3[4], 206-216. 2003.

Excl reason: Narrative review

Cockayne, S. E., Rassl, D. M., and Thomas, S. E. Squamous cell carcinoma arising in Hailey-Hailey disease of the vulva. *British Journal of Dermatology* 142[3], 540-542. 2000.

Excl reason: Not in PICO

Cooper, C.P.; Gelb, C.A.; Rodriguez, J.; Hawkins, N.A. (2014). Promoting gynecologic cancer awareness at a critical juncture--where women and providers meet. *Journal of Cancer Education*, 29, 247-51.

Not in PICO

Creasman, W. T., Phillips, J. L., and Menck, H. R. The National Cancer Data Base report on early stage invasive vulvar carcinoma. The American College of Surgeons Commission on Cancer and the American Cancer Society. *Cancer* 80[3], 505-513. 1-8-1997.

Excl reason: Not in PICO

Crofton, H. S. & Carter, P. (2013) An evaluation of suspected cervical and vulval cancer referrals determining common causes of error. *BJOG: An International Journal of Obstetrics and Gynaecology*, 120: 280-281.
Not in PICO

Crosbie, E. J., Slade, R. J., and Ahmed, A. S. The management of vulval cancer. [Review] [83 refs]. *Cancer Treatment Reviews* 35[7], 533-539. 2009.
Excl reason: Narrative review

D'Arcy, T. J., Roy, A., Thomas, A., McIndoe, A., and Soutter, W. P. Standards for the management of cervical and vulval carcinoma. *British Journal of Obstetrics and Gynaecology* 107[7], 846-848. 2000.
Excl reason: Not in PICO

de Hullu, J. A., Oonk, M. H. M., and van der Zee, A. G. J. Modern management of vulvar cancer. *Current Opinion in Obstetrics and Gynecology* 16[1], 65-72. 2004.
Excl reason: Not in PICO/narrative review

de Hullu, J. A., van der Avoort, I. A., Oonk, M. H., and van der Zee, A. G. Management of vulvar cancers. [Review] [63 refs]. *European Journal of Surgical Oncology* 32[8], 825-831. 2006.
Excl reason: Not in PICO

Dellacasa, I., Beffa, V., Neyroud, I., Pelte, M. F., Vlastos, G., Dubuisson, J. B., and Vlastos, A. T. Vulvar cancer in Geneva: A population based study. *Gynecological Surgery* 6, S197. 2009. Springer Verlag.
Excl reason: Not in PICO

Derrick, E. K. and Neill, S. Vulval dermatoses. *Medicine* 38[6], 300-305. 2010.
Excl reason: Narrative review

Dewdney, S., Kennedy, C. M., and Galask, R. P. Leiomyosarcoma of the vulva: A case report. *Journal of Reproductive Medicine for the Obstetrician and Gynecologist* 50[8], 630-632. 2005.
Excl reason: Not in PICO

Dhar, K. K. and Woolas, R. P. Changes in the management of vulval cancer. *Best Practice and Research: Clinical Obstetrics and Gynaecology* 17[4], 529-542. 2003.
Excl reason: Narrative review

Dittmer, C., Fischer, D., Diedrich, K., and Thill, M. Diagnosis and treatment options of vulvar cancer: a review. [Review]. *Archives of Gynecology & Obstetrics* 285[1], 183-193. 2012.
Excl reason: Not in PICO

Divine, L., Erickson, B., Leath, C. & Straughn, J. (2013) Cost-effectiveness analysis of sentinel lymph node biopsy in the treatment of early-stage vulvar cancer. *Gynecologic Oncology*, 131: 280.
Not in PICO

Dongankar, D., Agale, S. V., Lanjewar, D. N., and Chitale, A. Vulvar carcinoma in HIV infected women: A report of two cases. *Journal of Obstetrics and Gynaecology* 31, 45. 2011. Informa Healthcare.
Excl reason: Not in PICO

Door, A. Less common gynecologic malignancies. [Review] [90 refs]. *Seminars in Oncology Nursing* 18[3], 207-222. 2002.
Excl reason: Narrative review

Doxanakis, A., Bradshaw, C., Fairley, C., and Pokorny, C. S. Vulval itch: All that itches is not thrush. *Medicine Today* 5[6], 54-63. 2004.
Excl reason: Narrative review

Duarte-Franco, Eliane and Franco, Eduardo. Other Gynecologic Cancers: endometrial, ovarian, vulvar and vaginal cancers. *BMC Women's Health* 4[Suppl 1], S14. 2004.
Excl reason: Narrative review

Dumitriu, S., Radulescu, D., Costea, C., Dumitriu, A., Ungureanu, C., Stolnicu, S., Morosanu, E., and Butcovan, D. Prognostic factors in carcinoma of the vulva. *Virchows Archiv* 457[2], 211. 2010. Springer Verlag.
Excl reason: Not in PICO

Duong, T. H. and Flowers, L. C. Vulvo-vaginal cancers: risks, evaluation, prevention and early detection. [Review] [100 refs]. *Obstetrics & Gynecology Clinics of North America* 34[4], 783-802. 20-11-2007.

Excl reason: Narrative review

Dursun, N., Leblebici, C., Zengin, M., Gunver, F., and Bozkurt, E. R. Four cases of simplex (differentiated) variant of vulvar intraepithelial neoplasia. *Virchows Archiv* 459, S232. 2011. Springer Verlag.

Excl reason: Not in PICO

Edwards, C. L., Tortolero-Luna, G., Linares, A. C., Malpica, A., Baker, V. V., Cook, E., Johnson, E., and Follen, Mitchell M. Vulvar intraepithelial neoplasia and vulvar cancer. [Review] [81 refs]. *Obstetrics & Gynecology Clinics of North America* 23[2], 295-324. 1996.

Excl reason: Narrative review

Eliezri, Y. D. The toluidine blue test: an aid in the diagnosis and treatment of early squamous cell carcinomas of mucous membranes. *Journal of the American Academy of Dermatology* 18[6], 1339-1349. 1988.

Excl reason: Not in PICO

Eva, L. J. Screening and follow up of vulval skin disorders. [Review]. *Best Practice & Research in Clinical Obstetrics & Gynaecology* 26[2], 175-188. 2012.

Excl reason: Narrative review

Finan, M. A. and Barre, G. Bartholin's gland carcinoma, malignant melanoma and other rare tumours of the vulva. *Best Practice and Research: Clinical Obstetrics and Gynaecology* 17[4], 609-633. 2003.

Excl reason: Narrative review

Fiorica, J. V., Lapolla, J. P., and Cavanagh, D. Diagnosis and management of vulvar carcinoma. [Review] [13 refs]. *Comprehensive Therapy* 14[5], 24-28. 1988.

Excl reason: Narrative review

Fischer, M. and Marsch, W. C. Vulvodynia: an indicator or even an early symptom of vulvar cancer. *Cutis* 67[3], 235-238. 2001.

Excl reason: Narrative review

Fuller, A. F., Jr. Role of the primary physician in the detection and treatment of gynecologic cancer. *Primary Care; Clinics in Office Practice* 8[1], 111-129. 1981.

Excl reason: Narrative review

Gerber, S., Tonna, Sienkiewicz D., and Delaloye, J. F. [A new classification of vulvar intraepithelial neoplasia (VIN)]. [French]. *Revue Medicale Suisse* 4[176], 2281-2282. 2284.

Excl reason: Narrative review

Ghosh, K., Belani, K., and Chen, M. D. Gynecologic malignancies and anesthesia. *Anesthesiology Clinics of North America* 16[3], 629-644. 1998.

Excl reason: Narrative review

Ghurani, G. B. and Penalver, M. A. An update on vulvar cancer. [Review] [27 refs]. *American Journal of Obstetrics & Gynecology* 185[2], 294-299. 2001.

Excl reason: Narrative review

Girardi, F., Pickel, H., Joura, E. A., Breiteneker, G., Gitsch, G., Graf, A. H., and Neunteufel, W. [Guidelines for diagnosis and therapy of intraepithelial neoplasia and early invasive carcinoma of the female lower genital system (cervix uteri, vagina, vulva) established by the AGK (Colposcopy Work Group in the OGGG [Austrian Society of Gynecology and Obstetrics])]. [German]. *Gynakologisch-Geburtshilfliche Rundschau* 41[3], 197-200. 2001.

Excl reason: Not in PICO

Gormley, R. H. and Kovarik, C. L. Human papillomavirus-related genital disease in the immunocompromised host: Part II. [Review]. *Journal of the American Academy of Dermatology* 66[6], 883-17. 899.

Excl reason: Narrative review

Gotlieb, W. H. The assessment and surgical management of early-stage vulvar cancer. [Review] [52 refs]. *Best Practice & Research in Clinical Obstetrics & Gynaecology* 17[4], 557-569. 2003.
Excl reason: Narrative review

Grant, J. M. Revised FIGO staging for early invasive carcinoma of the vulva and cervix. *British Journal of Obstetrics & Gynaecology* 103[5], xxi-xxii. 1996.
Excl reason: Not in PICO

Gusberg, S. B. The diagnosis of gynecologic cancer. *Cancer* 51[12:Suppl], Suppl-9. 15-6-1983.
Excl reason: Narrative review

Hacker, N. F. Current management of early vulvar cancer. [Review] [28 refs]. *Annals of the Academy of Medicine, Singapore* 27[5], 688-692. 1998.
Excl reason: Narrative review

Hall, K. L., Dewar, M. A., and Perchalski, J. Screening for gynecologic cancer. Vulvar, vaginal, endometrial, and ovarian neoplasms. [Review] [62 refs]. *Primary Care; Clinics in Office Practice* 19[3], 607-620. 1992.
Excl reason: Not in PICO

Hefler, L. A., Sliutz, G., Leodolter, S., Speiser, P., Joura, E., Reinthaller, A., and Kohlberger, P. Squamous cell carcinoma antigen serum levels as prognostic parameter in patients with early stage vulvar cancer. *Gynecologic Oncology* 97[3], 904-907. 2005.
Excl reason: Not in PICO

Hengge, U. R. and Meurer, M. [Pigmented lesions of the genital mucosa]. [Review] [83 refs] [German]. *Hautarzt* 56[6], 540-549. 2005.
Excl reason: Not in PICO

Iwasaka, T. Current trends in the management of vulvar carcinoma. [Japanese]. *Gan to Kagaku Ryoho Cancer*[8], 1121-1127. 2005.
Excl reason: Not in PICO

Jefferies, H. The lived experience of younger women with vulval cancer: the impact of delayed diagnosis. *Nursing Times* 106[6], 21-24. 16-2-2010.
Excl reason: Not in PICO

Jefferies, H. and Clifford, C. All change: the lived experience of younger women with cancer of the vulva. *Journal of Clinical Nursing* 21[15-16], 2327-2335. 2012.
Excl reason: Not in PICO

Jones, R. W., Scurry, J., Neill, S., and MacLean, A. B. Guidelines for the follow-up of women with vulvar lichen sclerosus in specialist clinics. *American Journal of Obstetrics & Gynecology* 198[5], 496-3. 2008.
Excl reason: Narrative review

Joura, E. A. Epidemiology and precursors of vulvar cancer. *Journal of Women's Imaging* 4[3], 126-129. 2002.
Excl reason: Narrative review

Kagie, M. J., Kenter, G. G., Hermans, J., Trimbos, J. B., and Fleuren, G. J. The relevance of various vulvar epithelial changes in the early detection of squamous cell carcinoma of the vulva. *International Journal of Gynecological Cancer* 7[1], 50-57. 1997.
Excl reason: Not in PICO

Kapczuk, K., Lewandowska, L., Friebe, Z., and Wochowiak, J. Vulvar rhabdomyosarcoma in a 15-year-old girl (case report). *Ceska Gynekologie* 68[6], 458-461. 2003.
Excl reason: Not in PICO

Kietpeerakool, C., Changkasisri, B., Khunamornpong, S., Siriaunkgul, S., and Srisomboon, J. Pathology slide review is mandatory before planning treatment for referral patients with gynecologic cancer. *Asia-Pacific Journal of Clinical Oncology* 2[2], 104-108. 2006.
Excl reason: Not in PICO

Kini, U. Squamous cell carcinoma of the vulva in association with mixed vulvar dystrophy. A brief report with review of literature. *Indian Journal of Cancer* 34[2], 92-95. 1997.
Excl reason: Not in PICO

Klyszejko, C., Ilnicki, W., Klyszejko, D., Kozma, J., Porada, J., and Szymczak, G. Detection of neoplasms of female reproductive organs in Paluk region in the years 1979-1997 before and after expanded prophylactic investigation. [Polish]. *Ginekologia Polska* 69[5], 353-357. 1998.
Excl reason: Not in PICO

Knight, K., Wade, S., and Balducci, L. Prevalence and outcomes of anemia in cancer: A systematic review of the literature. *American Journal of Medicine* 116[7 SUPPL. 1], 11-26. 5-4-2004.
Excl reason: Not in PICO

Krathen, M. S., Liu, C. L., and Loo, D. S. Vulvar melanoma: a missed opportunity for early intervention? *Journal of the American Academy of Dermatology* 66[4], 697-698. 2012.
Excl reason: Not in PICO

Kreienberg, R. Early recognition of carcinoma of cervix vulva and vagina. [German]. *Gynakologe* 34[11], 1079-1086. 2001.
Excl reason: Narrative review

Kuppers, V. and Schnurch, H.-G. Current state of early diagnosis of female genital cancer. [German]. *Gynakologe* 30[8], 624-630. 1997.
Excl reason: Narrative review

Lamb, M. Vulvar cancer: patient information booklet. *Oncology Nursing Forum* 13[6], 79-82. 1986.
Excl reason: Patient information booklet

Lanneau, G. S., Argenta, P. A., Lanneau, M. S., Riffenburgh, R. H., Gold, M. A., McMeekin, D. S., Webster, N., and Judson, P. L. Vulvar cancer in young women: demographic features and outcome evaluation. *American Journal of Obstetrics & Gynecology* 200[6], 645. 2009.
Excl reason: Not in PICO

Larrabee, R. and Kylander, D. J. Benign vulvar disorders: Identifying features, practical management of nonneoplastic conditions and tumors. *Postgraduate Medicine* 109[5], 151-164. 2001.
Excl reason: Narrative review

Lawhead, Jr and Majmudar, B. Early diagnosis of vulvar neoplasia as a result of vulvar self-examination. *Journal of Reproductive Medicine for the Obstetrician and Gynecologist* 35[12], 1134-1137. 1990.
Excl reason: Not in PICO

Lawhead, R. A. Vulvar self-examination. *American Journal of Obstetrics & Gynecology* 158[5], 1238. 1988.
Excl reason: Letter

Lawhead, R. A., Jr. and Majmudar, B. Early diagnosis of vulvar neoplasia as a result of vulvar self-examination. *Journal of Reproductive Medicine* 35[12], 1134-1137. 1990.
Excl reason: Duplicate

Lea, J. S. and Miller, D. S. Optimum screening interventions for gynecologic malignancies. [Review] [41 refs]. *Texas Medicine* 97[2], 49-55. 2001.
Excl reason: Not in PICO

Liaquat, N. F. and Noorani, K. Causes of post-menopausal bleeding - A study of 328 cases. *Journal of the College of Physicians and Surgeons Pakistan* 10[4], 134-137. 2000.
Excl reason: Not in PICO

Lindsey, W. F., Wood, D. K., and Briele, H. A. Pelvic exenteration. *Journal of Surgical Oncology* 30[4], 231-234. 1985.
Excl reason: Not in PICO

Lorente, A. I., Morillo, M., De, Z. T., Gonzalez, J. & Conejo-Mir, J. (2013) Verrucous squamous cell carcinoma of vulva simulating multiple epidermal inclusion cysts. *Indian Journal of Dermatology*, 58: 318-319.
Not in PICOLundvall, F. [Early diagnosis of vulvar neoplasms]. [Danish]. *Ugeskrift for Laeger*

142[17], 1106-1107. 21-4-1980.

Excl reason: Narrative review

MacLean, A. B., Roberts, D. T., and Reid, W. M. N. Review of 1000 women seen at two specially designated vulval clinics. *Current Obstetrics and Gynaecology* 8[3], 159-162. 1998.

Excl reason: Not in PICO

Madsen, B. S., Jensen, H. L., Van Den Brule, A. J. C., Wohlfahrt, J., and Frisch, M. Risk factors for invasive squamous cell carcinoma of the vulva and vagina - Population-based case-control study in Denmark. *International Journal of Cancer* 122[12], 2827-2834. 15-6-2008.

Excl reason: Not in PICO

Mais, V., Cirronis, M. G., Piras, B., Silveti, E., Cossu, E., and Melis, G. B. Intraoperative lymphatic mapping techniques for endometrial cancer. [Review]. *Expert Review of Anticancer Therapy* 11[1], 83-93. 2011.

Excl reason: Narrative review

Mazdziarz, A., Zielinska, A., Alkhalayla, H. & Spiewankiewicz, B. (2013) Comparison of efficiency of photodynamic diagnostics with topical use of the 3% and 15% aminolevulinic acid in the detection of vulvar lesions. *Photodiagnosis & Photodynamic Therapy*, 10: 422-428.

Not in PICO

Medeiros, F., Nascimento, A. F., and Crum, C. P. Early vulvar squamous neoplasia: advances in classification, diagnosis, and differential diagnosis. [Review] [32 refs]. *Advances in Anatomic Pathology* 12[1], 20-26. 2005.

Excl reason: Narrative review

Menczer, J. Diagnosis and treatment delay in gynecological malignancies. Does it affect outcome? *International Journal of Gynecological Cancer* 10[2], 89-94. 2000.

Excl reason: Not in PICO

Merisio, C., Berretta, R., Gualdi, M., Pultrone, D. C., Anfuso, S., Agnese, G., Aprile, C., Mereu, L., Salamano, S., Tateo, S., and Melpignano, M. Radioguided sentinel lymph node detection in vulvar cancer. *International Journal of Gynecological Cancer* 15[3], 493-497. 2005.

Excl reason: Not in PICO

Michalska, M., Sajdak, S., Obrebowska, A., and Spaczynski, M. Malignant melanoma of the vulva: 2 case reports]. [Polish]. *Ginekologia Polska* 69[5], 344-348. 1998.

Excl reason: Not in PICO

Milojkovic, M., Rubin, M., and Mrcela, M. Risk factor evaluation used as indicators in early detection of recurrent vulvar cancer. [Croatian]. *Gynaecologia et Perinatologia* 13[3], 113-116. 2004.

Excl reason: Not in PICO

Mirhashemi, R., Nieves-Neira, W., and Averette, H. E. Gynecologic malignancies in older women. [Review] [67 refs]. *Oncology (Williston Park)* 15[5], 580-586. 592.

Excl reason: Narrative review

Morris, P. G. Granular cell myoblastoma of the vulva: report of two cases and review of the literature. *Journal of Obstetrics and Gynaecology* 2[3], 178-180. 1982.

Excl reason: Not in PICO

Nauth, H. F. and Schilke, E. Cytology of the vulva, a morphological study in a large series. [German]. *Geburtshilfe und Frauenheilkunde* 42[10], 739-746. 1982.

Excl reason: Not in PICO

Nauth, H. F. Early diagnosis of carcinoma of the vulva. [German]. *Diagnostik* 15[16], 1220-1223. 1982.

Excl reason: Narrative review

Nauth, H. F. Current vulvar diagnostic methods, with special reference to vulvar cytology. *Journal of Reproductive Medicine* 31[9], 788-795. 1986.

Excl reason: Not in PICO/narrative review

Onnis, A., Marchetti, M., Maggino, T., and De, Toffoli J. Clinical experience in gynecological cancer management. b) Vulvar cancer: report from the Gynecologic Institutes of Padua University

(1963-1989). *European Journal of Gynaecological Oncology* 11[3], 161-169. 1990.
 Excl reason: Not in PICO

Onnis, A., Marchetti, M., and Maggino, T. Carcinoma of the vulva: critical analysis of survival and treatment of recurrences. *Clinical & Experimental Obstetrics & Gynecology* 19[2], 87-92. 1992.
 Excl reason: Narrative review

Oonk, M. H., Eijsink, J. J., Volders, H. H., Hollema, H., Wisman, G. B., Schuurings, E., and van der Zee, A. G. Identification of inguinofemoral lymph node metastases by methylation markers in vulvar cancer. *Gynecologic Oncology* 125[2], 352-357. 2012.
 Excl reason: Not in PICO

Oonk, M. H. M., de Hullu, J. A., Hollema, H., Mourits, M. J. E., Pras, E., Wymenga, A. N. M., and van der Zee, A. G. J. The Value of Routine Follow-Up in Patients Treated for Carcinoma of the Vulva. *Cancer* 98[12], 2624-2629. 15-12-2003.
 Excl reason: Not in PICO

Ozbebit, U., Eskitascioglu, T., and Gunay, G. K. Basal cell carcinoma of the labium majus. [Turkish]. *Erciyes Tip Dergisi* 30[1], 052-054. 2008.
 Excl reason: Not in PICO

Patel, A., Ratnavelu-Nithya, D. G., Martin-Hirsch-Pierre, P. L., Naik, R., Bryant, A. & Ralte, A. (2013) Sentinel node assessment for diagnosis of groin lymph node involvement in vulvar cancer. *Cochrane.Database.of Systematic.Reviews.*.
 Not in PICO

Penney, G. C., Kitchener, H. C., and Templeton, A. The management of carcinoma of the vulva: current opinion and current practice among consultant gynaecologists in Scotland. *Health Bulletin* 53[1], 47-54. 1995.
 Excl reason: Not in PICO

Petrillo, Marco, Corrado, Giacomo, Carbone, Arnaldo, Macchia, Gabriella, and Ferrandina, Gabriella. Vulvar squamous cell carcinoma with sarcoma-like stroma: A case report and review of the literature. *Diagnostic Pathology* 6[1], 95. 2011.
 Excl reason: Not in PICO

Petry, K. U., Kochel, H., Bode, U., Schedel, I., Niesert, S., Glaubitz, M., Maschek, H., and Kuhnle, H. Human papillomavirus is associated with the frequent detection of warty and basaloid high-grade neoplasia of the vulva and cervical neoplasia among immunocompromised women. *Gynecologic Oncology* 60[1], 30-34. 1996.
 Excl reason: Not in PICO

Pickel, H. [Precancerous and early stages of vulvar cancer]. [German]. *Gynakologisch-Geburtshilfliche Rundschau* 32, Suppl. 1992.
 Excl reason: Not in PICO/Narrative review

Pickel, T. H. The early stages of vulvar carcinoma. Diagnostic problems. *Journal of Reproductive Medicine* 27[8], 465-470. 1982.
 Excl reason: Not in PICO

Prat, J. Pathology of vulvar intraepithelial lesions and early invasive carcinoma. [Review] [39 refs]. *Human Pathology* 22[9], 877-883. 1991.
 Excl reason: Not in PICO

Puig-Soler, M. and Vilamala-Muns, M. Pruritus, itching and vulvar pain: Approach from primary care. [Spanish]. *FMC Formacion Medica Continuada en Atencion Primaria* 12[10], 654-668. 2010.
 Excl reason: Narrative review

Regauer, S., Liegl, B., and Reich, O. Early vulvar lichen sclerosus: a histopathological challenge. [Review] [29 refs]. *Histopathology* 47[4], 340-347. 2005.
 Excl reason: Narrative review

Robinson, Z., Edey, K., and Murdoch, J. Invasive vulval cancer. *Obstetrics, Gynaecology and Reproductive Medicine* 21[5], 129-136. 2011.
 Excl reason: Narrative review

Rodolakis, A., Diakomanolis, E., Voulgaris, Z., Akrivos, T., Vlachos, G., and Michalas, S. Squamous vulvar cancer: A clinically based individualization of treatment. *Gynecologic Oncology* 78[3 I], 346-351. 2000.
Excl reason: Not in PICO

Rodriguez, M. I. and Leclair, C. M. Benign vulvar dermatoses. *Obstetrical and Gynecological Survey* 67[1], 55-63. 2012.
Excl reason: Narrative review

Rome, R. M. Early diagnosis of gynaecological malignancy. *Australian Family Physician* 12[11], 778-782. 1983.
Excl reason: Narrative review

Rowley, K. C., Gallion, H. H., Donaldson, E. S., van Nagell, J. R., Higgins, R. V., Powell, D. E., Kryscio, R. J., and Pavlik, E. J. Prognostic factors in early vulvar cancer. *Gynecologic Oncology* 31[1], 43-49. 1988.
Excl reason: Not in PICO

Ruiz Moreno, J. A., Garcia, Gomez R., Tun, Sanchez R., and Ortega Alvarado, R. M. [The results of a selective program to detect intraepithelial neoplasms of the vulva]. [Spanish]. *Ginecologia y Obstetricia de Mexico* 60, 55-59. 1992.
Excl reason: Not in PICO

Sagili, H. and Prabhu, K. Unilateral acquired vulval lymphangiectasia mimicking a vulval tumour. *Journal of Obstetrics and Gynaecology* 30[5], 527-528. 2010.
Excl reason: Not in PICO

Salhan, S. Clinico-pathological profile of carcinoma of the vulva. *European Journal of Gynaecological Oncology* 21[2], 205-208. 2000.
Excl reason: Narrative review

Sandella, J. Vulvar self examination (VSE). *Oncology Nursing Forum* 14[6], 71-73. 1987.
Excl reason: Not in PICO

Sauthier, P. and Petignat, P. [Diagnosis and management of vulvar intraepithelial neoplasias and invasive vulvar cancers]. [German]. *Gynakologisch-Geburtshilfliche Rundschau* 47[2], 88-93. 2007.
Excl reason: Not in PICO/narrative review

Scheistroen, M., Nesland, J. M., and Trope, C. Have patients with early squamous carcinoma of the vulva been overtreated in the past? The Norwegian experience 1977-1991. *European Journal of Gynaecological Oncology* 23[2], 93-103. 2002.
Excl reason: Not in PICO

Schluter, W. and Hamann, D. [Early cancer detection--advanced vulvar cancer: a contradiction?]. [German]. *Zentralblatt fur Gynakologie* 115[10], 466-467. 1993.
Excl reason: Narrative review

Selim, M. A. and Hoang, M. P. A histologic review of vulvar inflammatory dermatoses and intraepithelial neoplasm. [Review]. *Dermatologic Clinics* 28[4], 649-667. 2010.
Excl reason: Narrative review

Senn, B., Eicher, M., Mueller, M. D., Engberg, S., and Spirig, R. [Needs based nursing care in gynecology. "My symptom diary"]. [German]. *Krankenpflege - Soins Infirmiers* 105[5], 32-33. 2012.
Excl reason: Not in PICO

Shamini, N., Tay, E. H., and Ho, T. H. Vulvar cancer--what do we know about our patients? *Singapore Medical Journal* 42[7], 292-296. 2001.
Excl reason: Not in PICO

Sharma, A. and Menon, U. Screening for gynaecological cancers. *European Journal of Surgical Oncology* 32[8], 818-824. 2006.
Excl reason: Not in PICO

Sherman, V., Mcpherson, T., Baldo, M., Salim, A., Xing-Hua, G., and Wojnarowska, F. T. An observational cohort study shows a high rate of familial Lichen sclerosus and associated vulval cancer suggesting a genetic contribution. *British Journal of Dermatology* 161, 2. 2009. Blackwell Publishing Ltd.
Excl reason: Not in PICO

Siegle, R. J., Headington, J. T., and Swanson, N. A. Early invasive carcinoma of the vulva treated with the Mohs technique of microscopically controlled surgery. *American Journal of Obstetrics and Gynecology* 147[4], 459-461. 1983.
Excl reason: Not in PICO

Skapa, P., Zamecnik, J., Hamsikova, E., Salakova, M., Smahelova, J., Jandova, K., Robova, H., Rob, L., and Tachezy, R. Human papillomavirus (HPV) profiles of vulvar lesions: Possible implications for the classification of vulvar squamous cell carcinoma precursors and for the efficacy of prophylactic HPV vaccination. *American Journal of Surgical Pathology* 31[12], 1834-1843. 2007.
Excl reason: Not in PICO

Spencer, R. J., Young, R. H., and Goodman, A. The risk of squamous cell carcinoma in persistent vulvar ulcers. *Menopause* 18[10], 1067-1071. 2011.
Excl reason: Not in PICO

Spitzer, M. Lower genital tract intraepithelial neoplasia in HIV-infected women: Guidelines for evaluation and management. *Obstetrical and Gynecological Survey* 54[2], 131-137. 1999.
Excl reason: Narrative review

Stroup, A. M., Harlan, L. C., and Trimble, E. L. Demographic, clinical, and treatment trends among women diagnosed with vulvar cancer in the United States. *Gynecologic Oncology* 108, 577-583. 2008.
Excl reason: Not in PICO

Sukur, Y. E., Gozukucuk, M., and Berker, B. Hypercalcemia associated with early recurrence of vulvar cancer. *Archives of Gynecology & Obstetrics* 281[1], 117-118. 2010.
Excl reason: Not in PICO

Sykes, P., Smith, N., McCormick, P., and Frizelle, F. A. High-grade vulval intraepithelial neoplasia (VIN 3): a retrospective analysis of patient characteristics, management, outcome and relationship to squamous cell carcinoma of the vulva 1989-1999. *Australian & New Zealand Journal of Obstetrics & Gynaecology* 42[1], 69-74. 2002.
Excl reason: Not in PICO

Talaat, A., Brinkmann, D., Nagar, Y., Hogston, P., Khoury, G., and Woolas, R. Experience in the management of patients older than 80 years with vulval cancer. *International Journal of Gynecological Cancer* 19[4], 752-755. 2009.
Excl reason: Not in PICO

Tan, A. L., Jones, R., Mcpherson, G., and Rowan, D. Audit of a multidisciplinary vulvar clinic in a gynecologic hospital. *Journal of Reproductive Medicine for the Obstetrician and Gynecologist* 45[8], 655-658. 2000.
Excl reason: Not in PICO

Tham, K. F., Shepherd, J. H., Lowe, D. G., Hudson, C. N., and Van Dam, P. A. Early vulval cancer: the place of conservative management. *European Journal of Surgical Oncology* 19[4], 361-367. 1993.
Excl reason: Not in PICO

Thill, M., Bohlmann, M. K., Dittmer, C., Diedrich, K., and Fischer, D. Diagnosis and treatment options in vulvar and vaginal cancer. [German]. *Onkologie* 15[1], 28-39. 2009.
Excl reason: Not in PICO/Narrative review

Thorstensen, K. A. and Birenbaum, D. L. Recognition and management of vulvar dermatologic conditions: lichen sclerosus, lichen planus, and lichen simplex chronicus. [Review]. *Journal of Midwifery & Women's Health* 57[3], 260-275. 2012.
Excl reason: Narrative review

Tidy, J. A., Soutter, W. P., Luesley, D. M., MacLean, A. B., Buckley, C. H., and Ridley, C. M. Management of lichen sclerosus and intraepithelial neoplasia of the vulva in the UK. *Journal of the Royal Society of Medicine* 89[12], 699-701. 1996.
Excl reason: Not in PICO

Tsuji, M., Nakai, N., Ueda, E., Takenaka, H., Katoh, N., and Kishimoto, S. Double cancer of plantar malignant melanoma and vulvar extramammary Paget's disease. *Journal of Dermatology* 37[5], 484-487. 2010.
Excl reason: Not in PICO

Tyagi, S.; Tripathi, R.; Batra, S. (2014). Clinical scoring system to detect malignant and premalignant vulval lesions. *Journal of Obstetrics and Gynecology of India*, 64, 41-6.
Not in PICO

Tyring, S. K. Vulvar squamous cell carcinoma: guidelines for early diagnosis and treatment. [Review] [70 refs]. *American Journal of Obstetrics & Gynecology* 189[3:Suppl], Suppl-23. 2003.
Excl reason: Narrative review

Usmani, A. T., Ayub, S., and Basharat, A. Oncological referral patterns of gynaecological cancer patients over 2010-2011. the need for gynaecologic oncology subspecialty services. *BJOG: An International Journal of Obstetrics and Gynaecology* 119, 182-183. 2012. Blackwell Publishing Ltd.
Excl reason: Not in PICO

van, der, V, van Lindert, A. C., Gimbrere, C. H., Oosting, H., and Heintz, A. P. Epidemiologic data on vulvar cancer: comparison of hospital with population-based data. *Gynecologic Oncology* 62[3], 379-383. 1996.
Excl reason: Not in PICO

van, der, V. Elderly patients with vulvar carcinoma: should we use standard treatment?. [Dutch]. *Tijdschrift Voor Gerontologie En Geriatrie* 28[6], 272-276. 1997.
Excl reason: Not in PICO

van, der, V. Advances in the management of vulval cancer. *International Journal of Gynecology and Obstetrics* 107, S89. 2009. Elsevier Ireland Ltd.
Excl reason: Not in PICO/Narrative review

van, der, V and Fons, G. Regarding "reasons for diagnostic delay in gynecological malignancies". *International Journal of Gynecological Cancer* 22[3], 342. 2012.
Excl reason: Not in PICO

van, Seters M., ten Kate, F. J., van, Beurden M., Verheijen, R. H., Meijer, C. J., Burger, M. P., and Helmerhorst, T. J. In the absence of (early) invasive carcinoma, vulvar intraepithelial neoplasia associated with lichen sclerosus is mainly of undifferentiated type: new insights in histology and aetiology. *Journal of Clinical Pathology* 60[5], 504-509. 2007.
Excl reason: Not in PICO

Vandborg, M. P., Christensen, R. D., Kragstrup, J., Edwards, K., Vedsted, P., Hansen, D. G., and Mogensen, O. Reasons for diagnostic delay in gynecological malignancies. *International Journal of Gynecological Cancer* 21[6], 967-974. 2011.
Excl reason: Not in PICO

Warner, E. A. and Parsons, A. K. Screening and early diagnosis of gynecologic cancers. *Medical Clinics of North America* 80[1], 45-61. 1996.
Excl reason: Narrative review

Weiderpass, E., Ye, W., Tamimi, R., Trichopolous, D., Nyren, O., Vainio, H., and Adami, H. O. Alcoholism and risk for cancer of the cervix uteri, vagina, and vulva. *Cancer Epidemiology, Biomarkers & Prevention* 10[8], 899-901. 2001.
Excl reason: Not in PICO

Weintraub, N. T. and Freedman, M. L. Gynecologic malignancies of the elderly. *Clinics in Geriatric Medicine* 3[4], 669-694. 1987.
Excl reason: Narrative review

Williams, T. S., Callen, J. P., and Owen, L. G. Vulvar disorders in the prepubertal female. [Review] [63 refs]. *Pediatric Annals* 15[8], 588-589. 1982.

Excl reason: Narrative review

Woodruff, J. D. Early invasive carcinoma of the vulva. *Clinics in Oncology* 1[2], 349-354. 1982.

Excl reason: Not in PICO

Wu, X., Xin, Y., Yao, J., Hasui, K., Tsuyama, S., Yonezawa, S., and Murata, F. Expression of epithelial growth factor receptor and its two ligands, transforming growth factor-alpha and epithelial growth factor, in normal and neoplastic squamous cells in the vulva: an immunohistochemical study. *Medical Electron Microscopy* 34[3], 179-184. 2001.

Excl reason: Not in PICO

Yamashiro, T., Hasumi, K., and Masubuchi, K. [Clinical study of 84 primary vulvar carcinomas]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]* 16[4:Pt 2-3], t-3. 1989.

Excl reason: Not in PICO

Yoder, B. J., Rufforny, I., Massoll, N. A., and Wilkinson, E. J. Stage IA vulvar squamous cell carcinoma: An analysis of tumor invasive characteristics and risk. *American Journal of Surgical Pathology* 32[5], 765-772. 2008.

Excl reason: Not in PICO

Yu, B. K., Lai, C. R., Yen, M. S., Tou, N. F., Chao, K. C., and Yuan, C. C. Extramammary Paget's disease found by abnormal vulvar brush sampling. *European Journal of Gynaecological Oncology* 23[1], 35-36. 2002.

Excl reason: Not in PICO

Zanoio, L., Zacche, G., and Cartolari, I. The Richart-Collins test in the screening of vulvar neoplasia. [Italian]. *Minerva Ginecologica* 36[12], 793-795. 1984.

Excl reason: Not in PICO

Review question:

Which investigations of symptoms of suspected vulval cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	196	37	06/06/2013
<i>Premedline</i>	1980-2013	17	1	06/06/2013
<i>Embase</i>	1980-2013	212	57	06/06/2013
<i>Cochrane Library</i>	1980-2013	24	1	06/06/2013
<i>Psychinfo</i>	1980-2013	1	0	06/06/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	25	5	06/06/2013

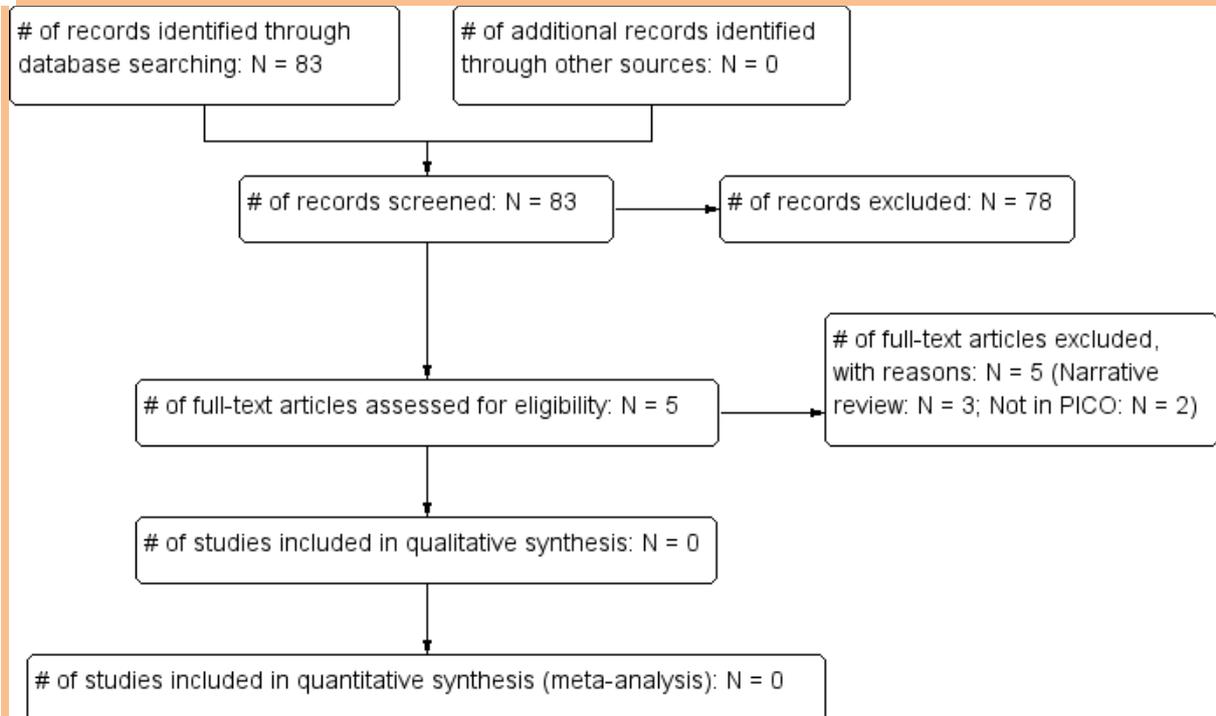
Total References retrieved (after de-duplication): 77

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	6/2013-27/08/2014	5	0	27/08/2014
<i>Premedline</i>	6/2013-27/08/2014	24	6	27/08/2014

Embase	6/2013-27/08/2014	30	1	27/08/2014
Cochrane Library	6/2013-27/08/2014	12	1	27/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	6/2013-27/08/2014	5	0	27/08/2014

Total References retrieved (after de-duplication): 6



Study results

No evidence was identified pertaining to the diagnostic accuracy of biopsy in patients with suspected vulvar cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Agarwal, S. & Bodurka, D. C. (2010) Symptom research in gynecologic oncology: A review of available measurement tools. *Gynecologic Oncology*, 119: 384-389.

Not in PICO

Baltzer, J. (1989) Precancerous conditions and early stages of vulvar cancer. [German]. *Archives of Gynecology and Obstetrics*, 245: 498-503.

Narrative review

Basta, A. (1989) Diagnostic and therapeutic procedures in the vulvar intraepithelial neoplasia (VIN) and early invasive cancer of the vulva. *European Journal of Gynaecological Oncology*, 10: 55-59.

Not in PICO

- Boecker, W. & Stegner, H.-E. (1981) Vulvar preneoplasias. [German]. *Archives of Gynecology*, 232: 1-12.
Narrative review
- Bornstein, J., Pascal, B., Sova, Y., Rosenfeld, Y. & Abramovici, H. (1990) The vulvar clinic. [Hebrew]. *Harefuah*, 119: 413-416.
Not in PICO
- Burbos, N., Musonda, P. & Rufford, B. (2011) Diagnostic performance of urgent referrals for suspected gynaecological malignancies. *Archives of Gynecology and Obstetrics*, 284: 1495-1500.
Not in PICO
- Byrne, M. A., Walker, M. M., Leonard, J., Pryce, D. & Taylor-Robinson, D. (1989) Recognising covert disease in women with chronic vulval symptoms attending an STD clinic: Value of detailed examination including colposcopy. *Genitourinary Medicine*, 65: 46-49.
Not in PICO
- Caglar, H., Tamer, S. & Hreshchyshyn, M. M. (1982) Vulvar intraepithelial neoplasia. *Obstetrics and Gynecology*, 60: 346-349.
Not in PICO
- Canavan, T. P. & Cohen, D. (2002) Vulvar cancer. *American Family Physician*, 66: 1269-1274+1276.
Narrative review
- Carter, J., Evans, C., Ghebre, R., Glubka, B. & Downs, L. (2012) Superficially invasive squamous cell carcinoma of the vulva: Is radical excision necessary? *Gynecologic Oncology*, 125: S83.
Not in PICO
- Castellano, A., Scassellati, S. G. & Bartolomucci, L. (1992) Vulvar cancer: Epidemiology and clinical presentation. [Italian]. *European Review for Medical and Pharmacological Sciences*, 14: 341-345.
Narrative review
- Castellano, A., Scassellati, S. G. & Bartolomucci, L. (1992) [Epidemiology and clinical presentation of vulvar cancer]. [Review] [23 refs] [Italian]. *Rivista Europea Per le Scienze Mediche e Farmacologiche*, 14: 341-345.
Narrative review
- Chhabra, S., Bhavani, M. & Deshpande, A. (2014) Trends of vulvar cancer. *Journal of Obstetrics & Gynaecology*, 34: 165-168.
Not in PICO
- Creasman, W. T., Phillips, J. L. & Menck, H. R. (1997) The National Cancer Data Base report on early stage invasive vulvar carcinoma. The American College of Surgeons Commission on Cancer and the American Cancer Society. *Cancer*, 80: 505-513.
Not in PICO
- Crofton, H. S. & Carter, P. (2013) An evaluation of suspected cervical and vulval cancer referrals determining common causes of error. *BJOG: An International Journal of Obstetrics and Gynaecology*, 120: 280-281.
Not in PICO
- Crosbie, E. J., Slade, R. J. & Ahmed, A. S. (2009) The management of vulval cancer. *Cancer Treatment Reviews*, 35: 533-539.
Narrative review
- de Hullu, J. A., Hollema, H., Piers, D. A., Verheijen, R. H., van Diest, P. J., Mourits, M. J., Aalders, J. G. & van Der Zee, A. G. (2000) Sentinel lymph node procedure is highly accurate in squamous cell carcinoma of the vulva. *Journal of Clinical Oncology*, 18: 2811-2816.
Not in PICO
- Di Paola, G. R. (1980) The problem of the so-called precancerous lesions of the vulva. Ten years of prospective experience. *European Journal of Gynaecological Oncology*, 1: 20-28.
Not in PICO

- Dittmer, C., Fischer, D., Diedrich, K. & Thill, M. (2012) Diagnosis and treatment options of vulvar cancer: A review. *Archives of Gynecology and Obstetrics*, 285: 183-193.
Narrative review
- Divine, L., Erickson, B., Leath, C. & Straughn, J. (2013) Cost-effectiveness analysis of sentinel lymph node biopsy in the treatment of early-stage vulvar cancer. *Gynecologic Oncology*, 131: 280.
Not in PICO
- Door, A. (2002) Less common gynecologic malignancies. *Seminars in Oncology Nursing*, 18: 207-222.
Narrative review
- Doxanakis, A., Bradshaw, C., Fairley, C. & Pokorny, C. S. (2004) Vulval itch: All that itches is not thrush. *Medicine Today*, 5: 54-63.
Narrative review
- Duong, T. H. & Flowers, L. C. (2007) Vulvo-Vaginal Cancers: Risks, Evaluation, Prevention and Early Detection. *Obstetrics and Gynecology Clinics of North America*, 34: 783-802.
Narrative review
- Dursun, N., Leblebici, C., Zengin, M., Gunver, F. & Bozkurt, E. R. (2011) Four cases of simplex (differentiated) variant of vulvar intraepithelial neoplasia. *Virchows Archiv*, 459: S232.
Not in PICO
- Eliezri, Y. D. (1988) The toluidine blue test: an aid in the diagnosis and treatment of early squamous cell carcinomas of mucous membranes. *Journal of the American Academy of Dermatology*, 18: 1339-1349.
Not in PICO
- Farnsworth, A. & Hacker, N. F. (1990) Pathology of the vulva. *Current Opinion in Obstetrics and Gynecology*, 2: 448-455.
Narrative review
- Gallwas, J., Chiapponi, C., Turk, L., Ochsenkuehn, R., Friese, K. & Dannecker, C. (2010) Optical coherence tomography: Preliminary results with a new noninvasive technique for evaluating uterine cervical tissue and vulvar epithelium. [Italian]. *Minerva Ginecologica*, 62: 395-401.
Not in PICO
- Ghurani, G. B. & Penalver, M. A. (2001) An update on vulvar cancer. *American Journal of Obstetrics and Gynecology*, 185: 294-299.
Narrative review
- Giammarile, F., Bozkurt, M. F., Cibula, D., Pahisa, J., Oyen, W. J., Paredes, P., Olmos, R. V. & Sicart, S. V. (2014) - The EANM clinical and technical guidelines for lymphoscintigraphy and sentinel node localization in gynaecological cancers. - *European Journal of Nuclear Medicine & Molecular Imaging*, 41: 1463-1477.
Not in PICO
- Girardi, F., Pickel, H., Joura, E. A., Breiteneker, G., Gitsch, G., Graf, A.-H. & Neunteufel, W. (2001) Guidelines for diagnosis and treatment of intraepithelial neoplasias and early invasive carcinomas of the female lower genital tract (cervix uteri, vagina, vulva). [German]. *Gynakologisch-Geburtshilfliche Rundschau*, 41: 197-200.
Guideline
- Goolamali, S., Lewis, F., Calonje, E. & Neill, S. (2009) Vulval hyperpigmentation. *British Journal of Dermatology*, 161: 49-50.
Narrative review
- Gotlieb, W. H. (2003) The assessment and surgical management of early-stage vulvar cancer. *Best Practice and Research: Clinical Obstetrics and Gynaecology*, 17: 557-569.
Narrative review
- Grant, N. & Nunns, D. (2012) Vulval pruritus and vaginal discharge. *Obstetrics, Gynaecology and Reproductive Medicine*, 22: 309-314.
Narrative review

- Hakam, A., Nasir, A., Raghuwanshi, R., Smith, P. V., Crawley, S., Kaiser, H. E., Grendys, E. & Fiorica, J. F. (2004) Value of multilevel sectioning for improved detection of micrometastases in sentinel lymph nodes in invasive squamous cell carcinoma of the vulva. *Anticancer Research*, 24: 1281-1286.
Not in PICO
- HAMPL, M., Hantschmann, P., Michels, W. & Hillemanns, P. (2008) Validation of the accuracy of the sentinel lymph node procedure in patients with vulvar cancer: Results of a multicenter study in Germany. *Gynecologic Oncology*, 111: 282-288.
Not in PICO
- HARRY, V. N., Deans, H., Ramage, E., Parkin, D. E. & Gilbert, F. J. (2009) Magnetic resonance imaging in gynecological oncology. *International Journal of Gynecological Cancer*, 19: 186-193.
Not in PICO
- HENGGE, U. R. & Meurer, M. (2005) [Pigmented lesions of the genital mucosa]. [Review] [83 refs] [German]. *Hautarzt*, 56: 540-549.
Narrative review
- JONES, R. W., Scurry, J., Neill, S. & MacLean, A. B. (2008) Guidelines for the follow-up of women with vulvar lichen sclerosus in specialist clinics. *American Journal of Obstetrics & Gynecology*, 198: 496-3.
Not in PICO
- JOURA, E. A. (2002) Epidemiology and precursors of vulvar cancer. *Journal of Women's Imaging*, 4: 126-129.
Narrative review
- KLÁT, J., Sevcík, L., Simetka, O., Gráf, P., Waloschek, T., Kraft, O., Jaluvková, Z. & Procházka, M. (2009) Characteristics of sentinel lymph nodes' metastatic involvement in early stage of vulvar cancer. *The Australian & New Zealand journal of obstetrics & gynaecology.*, 49: 672-676.
Not in PICO
- KOROM, I., Erika, V., Erika, K., Judit, O. & Lajos, K. (2011) Benign and malignant tumors of the vulva. *American Journal of Dermatopathology*, 33: 220.
Narrative review
- KUPPERS, V. & Schnurch, H.-G. (1997) Current state of early diagnosis of female genital cancer. [German]. *Gynakologe*, 30: 624-630.
Narrative review
- LARRABEE, R. & Kylander, D. J. (2001) Benign vulvar disorders: Identifying features, practical management of nonneoplastic conditions and tumors. *Postgraduate Medicine*, 109: 151-164.
Narrative review
- LAWHEAD, J. & Majmudar, B. (1990) Early diagnosis of vulvar neoplasia as a result of vulvar self-examination. *Journal of Reproductive Medicine for the Obstetrician and Gynecologist*, 35: 1134-1137.
Not in PICO
- LAWRIE, T. A., Patel, A., Martin-Hirsch, P. P., Bryant, A., Ratnavelu, N. D., Naik, R. & Ralte, A. (2014) - Sentinel node assessment for diagnosis of groin lymph node involvement in vulval cancer. - *Cochrane Database of Systematic Reviews*, 6: CD010409.
Not in PICO
- LIOTTA, M., Drake, R., Yang, B., Escobar, P., Chiesa-Vottero, A. & Rose, P. (2010) Vulvar intraepithelial neoplasia 3 simplex type is a distinct entity associated with invasive carcinoma of the vulva. *Gynecologic Oncology*, 116: S94.
Not in PICO
- LOIUDICE, L., Schonauer, S., Cramarossa, D. & Orsini, G. (1980) Comparison between histological pattern and other diagnostic tests in the detection of the vulvar cancer. [Italian]. *Folia Oncologica*, 3: 53-59.
NOT in PICO

- Lorente, A. I., Morillo, M., De, Z. T., Gonzalez, J. & Conejo-Mir, J. (2013) Verrucous squamous cell carcinoma of vulva simulating multiple epidermal inclusion cysts. *Indian Journal of Dermatology*, 58: 318-319.
Not in PICO
- Lundvall, F. (1980) Early diagnosis of vulvar neoplasms. [Danish]. *Ugeskrift for Laeger*, 142: 1106-1107.
Narrative review
- Mazdziarz, A., Zielinska, A., Alkhalayla, H. & Spiewankiewicz, B. (2013) Comparison of efficiency of photodynamic diagnostics with topical use of the 3% and 15% aminolevulinic acid in the detection of vulvar lesions. *Photodiagnosis & Photodynamic Therapy*, 10: 422-428.
Not in PICO
- McGee, J. & Covens, A. (2009) State of the art of sentinel lymph node biopsy in vulvar carcinoma. *Women's Health*, 5: 555-563.
Narrative review
- Medeiros, F., Nascimento, A. F. & Crum, C. P. (2005) Early vulvar squamous neoplasia: Advances in classification, diagnosis, and differential diagnosis. *Advances in Anatomic Pathology*, 12: 20-26.
Narrative review
- Menczer, J. (2000) Diagnosis and treatment delay in gynecological malignancies. Does it affect outcome? *International Journal of Gynecological Cancer*, 10: 89-94.
Not in PICO
- Merisio, C., Berretta, R., Gualdi, M., Pultrone, D. C., Anfusio, S., Agnese, G., Aprile, C., Mereu, L., Salamano, S., Tateo, S. & Melpignano, M. (2005) Radioguided sentinel lymph node detection in vulvar cancer. *International Journal of Gynecological Cancer*, 15: 493-497.
Not in PICO
- Naldini, A., Rossitto, C., Morciano, A., Panico, G., Campagna, G., Paparella, P. & Scambia, G. (2014) - The first leg video endoscopic groin lymphadenectomy in vulvar cancer: A case report. - *International Journal of Surgery Case Reports*, 5: 455-458.
Not in PICO
- Nauth, H. F. (1982) Early diagnosis of carcinoma of the vulva. [German]. *Diagnostik*, 15: 1220-1223.
Narrative review
- Nauth, H. F. & Schilke, E. (1982) Cytology of the vulva, a morphological study in a large series. [German]. *Geburtshilfe und Frauenheilkunde*, 42: 739-746.
Not in PICO
- Nauth, H. F. (1984) Exfoliative cytology of the vulva with consideration of histological and clinical aspects. [German]. *Fortschritte der Medizin*, 102: 872-875.
Narrative review
- Nauth, H. F. (1986) Current vulvar diagnostic methods, with special reference to vulvar cytology. *Journal of Reproductive Medicine*, 31: 788-795.
Narrative review
- Nordin, A., Mohammed, K. A., Naik, R., de Barros, L. A. & Monaghan, J. (2001) Does long-term follow-up have a role for node negative squamous carcinoma of the vulva? The Gateshead experience. *European Journal of Gynaecological Oncology*, 22: 36-39.
Not in PICO
- O'Keefe, R. J., Scurry, J. P., Dennerstein, G., Sfameni, S. & Brennan, J. (1995) Audit of 114 non-neoplastic vulvar biopsies. *British Journal of Obstetrics and Gynaecology*, 102: 780-786.
Not in PICO
- Ouldamer, L., Chraïbi, Z., Arbion, F., Barillot, I. & Body, G. (2013) Bartholin's gland carcinoma: Epidemiology and therapeutic management. *Surgical Oncology*, 22: 117-122.
Narrative review
- Patel, A., Ratnavelu-Nithya, D. G., Martin-Hirsch-Pierre, P. L., Naik, R., Bryant, A. & Ralte, A. (2013) Sentinel node assessment for diagnosis of groin lymph node involvement in vulvar cancer.

Cochrane.Database.of.Systematic.Reviews..

Not in PICO

Penney, G. C., Kitchener, H. C. & Templeton, A. (1995) The management of carcinoma of the vulva: current opinion and current practice among consultant gynaecologists in Scotland. *Health Bulletin*, 53: 47-54.

Not in PICO

Pickel, T. H. (1982) The early stages of vulvar carcinoma. Diagnostic problems. *Journal of Reproductive Medicine for the Obstetrician and Gynecologist*, 27: 465-470.

Not in PICO

Puig, C. O., Bajen, M., Rodriguez-Gasen, A., Notta, P., Ricart, Y., Sabate-Llobera, A., Ponce, J. & Martin-Comin, J. (2011) Reliability of sentinel node biopsy in early stage vulvar carcinoma. *European Journal of Nuclear Medicine and Molecular Imaging*, 38: S369.

Not in PICO

Rabbie, R., Nielsen, M. J. & Kirwan, J. (2011) Ultrasound-guided fine needle aspiration cytology of groin lymph nodes - A surveillance tool in early-stage vulval cancer. *International Journal of Gynecological Cancer*, 21: S934.

Not in PICO

Regauer, S., Liegl, B. & Reich, O. (2005) Early vulvar lichen sclerosus: A histopathological challenge. *Histopathology*, 47: 340-347.

Narrative review

Robinson, Z., Edey, K. & Murdoch, J. (2011) Invasive vulval cancer. *Obstetrics, Gynaecology and Reproductive Medicine*, 21: 129-136.

Narrative review

Robison, K., Holman, L. L. & Moore, R. G. (2011) Update on sentinel lymph node evaluation in gynecologic malignancies. *Current Opinion in Obstetrics and Gynecology*, 23: 8-12.

Not in PICO

Rome, R. M. (1983) Early diagnosis of gynaecological malignancy. *Australian Family Physician*, 12: 778-782.

Narrative review

Ruiz Moreno, J. A., Garcia, G. R., Tun, S. R. & Ortega Alvarado, R. M. (1992) [The results of a selective program to detect intraepithelial neoplasms of the vulva]. [Spanish]. *Ginecologia y Obstetricia de Mexico*, 60: 55-59.

Not in PICO

Salhan, S. (2000) Clinico-pathological profile of carcinoma of the vulva. *European Journal of Gynaecological Oncology*, 21: 205-208.

Narrative review

Salvesen, H. B. (2001) [Routine follow up after treatment for gynecological cancer]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 121: 1253-1255.

Not in PICO

Santoso, J. T. & Likes, W. (2014) - Colposcopic acetowhitening of vulvar lesion: a validity study. - *Obstetrics & Gynecology*, 123 Suppl 1: 181S.

Not in PICO

Sauthier, P. & Petignat, P. (2007) Diagnosis and management of vulvar intraepithelial neoplasias and invasive vulvar cancers. [French]. *Gynakologisch-Geburtshilfliche Rundschau*, 47: 88-93.

Narrative review

Selim, M. A. & Hoang, M. P. (2010) A histologic review of vulvar inflammatory dermatoses and intraepithelial neoplasm. [Review]. *Dermatologic Clinics*, 28: 649-667.

Narrative review

Shamini, N., Tay, E. H. & Ho, T. H. (2001) Vulvar cancer--what do we know about our patients? *Singapore Medical Journal*, 42: 292-296.

Not in PICO

- Sideri, M., De, C. C., Maggioni, A., Colombo, N., Bocciolone, L., Trifiro, G., De, N. M., Mangioni, C. & Paganelli, G. (2000) Detection of sentinel nodes by lymphoscintigraphy and gamma probe guided surgery in vulvar neoplasia. *Tumori*, 86: 359-363.
Not in PICO
- Simpson, R. C., Littlewood, S. M., Cooper, S. M., Cruickshank, M. E., Green, C. M., Derrick, E., Yell, J., Chiang, N., Bell, H., Owen, C., Javed, A., Wilson, C. L., McLelland, J. & Murphy, R. (2012) Real-life experience of managing vulvar erosive lichen planus: a case-based review and U.K. multicentre case note audit. *British Journal of Dermatology*, 167: 85-91.
Not in PICO
- Spencer, R. J., Young, R. H. & Goodman, A. (2011) The risk of squamous cell carcinoma in persistent vulvar ulcers. *Menopause*, 18: 1067-1071.
Not in PICO
- Tan, A. L., Jones, R., Mcpherson, G. & Rowan, D. (2000) Audit of a multidisciplinary vulvar clinic in a gynecologic hospital. *Journal of Reproductive Medicine for the Obstetrician and Gynecologist*, 45: 655-658.
Not in PICO
- Thill, M. & Adamietz, I. A. (2011) Diagnosis and treatment options of vulvar and vaginal cancer. [German]. *Onkologe*, 17: 1163-1180.
Narrative review
- Tyagi, S., Tripathi, R. & Batra, S. (2014) Clinical scoring system to detect malignant and premalignant vulval lesions. *Journal of Obstetrics and Gynecology of India*, 64: 41-46.
Not in PICO
- Vandborg, M. P., DePont, C. R., Kragstrup, J., Edwards, K., Vedsted, P., Hansen, D. G. & Mogensen, O. (2011) Reasons for diagnostic delay in gynecological malignancies. *International Journal of Gynecological Cancer*, 21: 967-974.
Not in PICO
- Wessels, R., Bruin De, D. M., Faber, D. J., Boven van, H. H., Vincent, A., Leeuwen van, T. G., Beurden, v. M. & Ruers, T. J. M. (2012) Optical coherence tomography in vulvar intraepithelial neoplasia. *European Journal of Surgical Oncology*, 38: 769.
Not in PICO
- Zekan, J., Mutvar, A., Huic, D., Petrovic, D., Karelavic, D. & Mitrovic, L. (2012) Reliability of sentinel node assay in vulvar cancer: The first Croatian validation trial. *Gynecologic Oncology*, 126: 99-102.
Not in PICO
- Zivanovic, O., Khoury-Collado, F., Abu-Rustum, N. R. & Gemignani, M. L. (2009) Sentinel Lymph Node Biopsy in the Management of Vulvar Carcinoma, Cervical Cancer, and Endometrial Cancer. *The Oncologist*, 14: 695-705.
Narrative review

VAGINA CANCER

Review question:

What is the risk of vagina cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

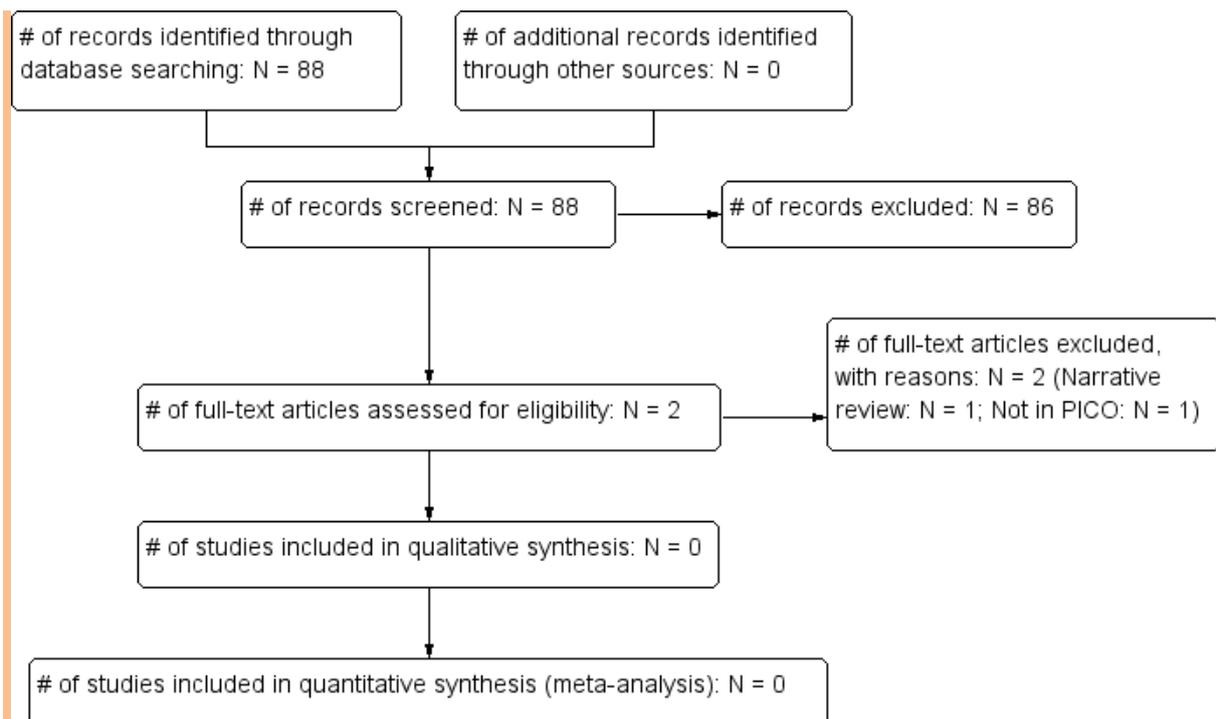
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	248	50	24/09/2012
<i>Premedline</i>	All-2012	6	2	24/09/2012
<i>Embase</i>	All-2012	293	54	27/09/2012
<i>Cochrane Library</i>	All-2012	83	0	24/09/2012
<i>Psychinfo</i>	All-2012	3	0	24/09/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	4	1	27/09/2012
<i>Biomed Central</i>	All-2012	108	2	27/09/2012

Total References retrieved (after de-duplication): 83

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	9/2012-27/08/2014	8	1	27/08/2014
<i>Premedline</i>	9/2012-27/08/2014	20	1	27/08/2014
<i>Embase</i>	9/2012-27/08/2014	36	2	27/08/2014
<i>Cochrane Library</i>	9/2012-27/08/2014	99	0	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	9/2012-27/08/2014	32	2	27/08/2014

Total References retrieved (after de-duplication): 5



Study results

No evidence was identified.

References

Included studies

None

Excluded studies (with excl reason)

Society of Gynecologic Oncologists Clinical Practice Guidelines. Practice guidelines: vaginal cancer. *Oncology (Williston Park)* 12[3], 449-452. 1998.

Excl reason: Guideline

Alipour, P., Arjmandi, K., and Hallaji, F. Vaginal clear cell adenocarcinoma with early pulmonary metastasis in a child. *Pediatric Hematology & Oncology* 25[7], 679-684. 2008.

Excl reason: Not in PICO

Amaral, E., Zeferino, A., Nadruz, W., Antonio, M. A., Sarian, L., Inhaia, C., Leite, R. C., and Mennin, S. P. Successful accomplishment of educational goals with clinical experience at public primary care facilities. *Medical Teacher* 29[6], 600-605. 2007.

Excl reason: Not in PICO

Arora, M., Shrivastav, R. K., and Jaiprakash, M. P. A rare germ-cell tumor site: vaginal endodermal sinus tumor. *Pediatric Surgery International* 18[5-6], 521-523. 2002.

Excl reason: Not in PICO

Artioli, G., Cassaro, M., Pedrini, L., Borgato, L., Corti, L., Cappetta, A., Lombardi, G., and Nicoletto, M. O. Rare presentation of endometrial carcinoma with singular bone metastasis. *European Journal of Cancer Care* 19[5], 694-698. 2010.

Excl reason: Not in PICO

Baltzer, J. and Poleska, W. Metastatic vaginal neoplasia - A diagnostic and therapeutic problem. [Polish, English]. *Ginekologia Onkologiczna* 4[4], 250-255. 2006.

Excl reason: Not in PICO

Basta, A., Adamek, K., and Pitynski, K. Intraepithelial neoplasia and early stage vulvar cancer. Epidemiological, clinical and virological observations. *European Journal of Gynaecological Oncology* 20[2], 111-114. 1999.
Excl reason: Not in PICO

Burbos, N. and Rufford, B. Predictive value of urgent referrals for women with suspected gynecologic malignancies. *Gynecologic Oncology* 116[3 SUPPL. 1], S53. 2010. Academic Press Inc.
Excl reason: Not in PICO

Carter, J. S. and Downs, L. S., Jr. Vulvar and vaginal cancer. *Obstetrics & Gynecology Clinics of North America* 39[2], 213-231. 2012.
Excl reason: Narrative review

Catipovic, M., Crnojevic-Ivanusic, R., Dujsin, M., Batinica, S., Cacic, M., and Markoja, I. Vaginal yolk sac tumor in a nine-month-old female child. *Croatian Medical Journal* 39[1], 66-68. 1998.
Excl reason: Not in PICO

Compton, W. C. Gynecological malignancy. *Alaska Medicine* 23[2], 13-17. 1981.
Excl reason: Narrative review

Cooper, C. P., Polonec, L., and Gelb, C. A. Women's knowledge and awareness of gynecologic cancer: a multisite qualitative study in the United States. *Journal of Women's Health* 20[4], 517-524. 2011.
Excl reason: Not in PICO

Dijkwel, G. A. and van Huisseling, J. C. [Two post-menopausal women with vaginal bleeding due to non-gynaecological malignancies]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde* 149[48], 2649-2652. 26-11-2005.
Excl reason: Not in PICO

Door, A. Less common gynecologic malignancies. [Review] [90 refs]. *Seminars in Oncology Nursing* 18[3], 207-222. 2002.
Excl reason: Narrative review

Duong, T. H. and Flowers, L. C. Vulvo-vaginal cancers: risks, evaluation, prevention and early detection. [Review] [100 refs]. *Obstetrics & Gynecology Clinics of North America* 34[4], 783-802. 20-11-2007.
Excl reason: Narrative review

Eddy, G. L., Singh, K. P., and Gansler, T. S. Superficially invasive carcinoma of the vagina following treatment for cervical cancer: a report of six cases. *Gynecologic Oncology* 36[3], 376-379. 1990.
Excl reason: Not in PICO

Elagoz, S., Arici, D. S., Aker, H., Tasyurt, A., and Arikan, G. Amelanotic malignant melanoma of the vagina. *Turkish Journal of Cancer* 30[3], 126-130. 2000.
Excl reason: Not in PICO

Fontaine, P.L.; Saslow, D.; King, V.J. (2012). ACS/ASCCP/ASCP guidelines for the early detection of cervical cancer. *American Family Physician*, 86, 6.
Excl reason: Guideline

Foroudi, F., Bull, C. A., and Gebiski, V. Primary invasive cancer of the vagina: outcome and complications of therapy. *Australasian Radiology* 43[4], 472-475. 1999.
Excl reason: Not in PICO

Funada, T. and Fujita, S. A case of vaginal metastasis from a rectal cancer. *Japanese Journal of Clinical Oncology* 40[5], 482. 2010.
Excl reason: Not in PICO

Ghosh, S. B., Tripathi, R., Mala, Y. M., and Khurana, N. Primary invasive carcinoma of vagina with third degree uterovaginal prolapse: a case report and review of literature. *Archives of Gynecology & Obstetrics* 279[1], 91-93. 2009.
Excl reason: Not in PICO

Girardi, F., Pickel, H., Joura, E. A., Breiteneker, G., Gitsch, G., Graf, A. H., and Neunteufel, W. [Guidelines for diagnosis and therapy of intraepithelial neoplasia and early invasive carcinoma of

the female lower genital system (cervix uteri, vagina, vulva) established by the AGK (Colposcopy Work Group in the OGGG [Austrian Society of Gynecology and Obstetrics])). [German]. *Gynakologisch-Geburtshilfliche Rundschau* 41[3], 197-200. 2001.

Excl reason: Not in PICO

Gostout, B. S., Strome, S. E., Clayton, A. C., McGovern, R. M., Olsen, K. D., and Webb, M. J. Two cases of coincident carcinomas of the head and neck and the uterine cervix. *Gynecologic Oncology* 85[2], 376-380. 2002.

Excl reason: Not in PICO

Gregoriou, O., Grigoriadis, C., Hatzidakis, V. E., Mantzavinos, S., and Kondi-Pafiti, A. Removal of a large bizarre uterine leiomyoma by operative hysteroscopy. Case report and review of the literature. *Clinical and Experimental Obstetrics & Gynecology* 39[1], 124-126. 2012.

Excl reason: Not in PICO

Grigsby, P. W. Vaginal cancer. [Review] [16 refs]. *Current Treatment Options in Oncology* 3[2], 125-130. 2002.

Excl reason: Narrative review

Hagen, B., Tingulstad, S., Onsrud, M., Moen, M., Kiserud, T., Eik-Nes, S., Halvorsen, T., and Nustad, K. [Preoperative identification of malignancy among women with a pelvic mass. Evaluation of a risk index based on ultrasound findings. CA 125 in serum and menopausal status]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening* 115[7], 820-822. 10-3-1995.

Excl reason: Not in PICO

Hall, K. L., Dewar, M. A., and Perchalski, J. Screening for gynecologic cancer. Vulvar, vaginal, endometrial, and ovarian neoplasms. [Review] [62 refs]. *Primary Care; Clinics in Office Practice* 19[3], 607-620. 1992.

Excl reason: Not in PICO

Hanley, K. Z., Tadros, T. S., Briones, A. J., Birdsong, G. G., and Mosunjac, M. B. Hematologic malignancies of the female genital tract diagnosed on liquid-based Pap test: Cytomorphologic features and review of differential diagnoses. *Diagnostic Cytopathology* 37[1], 61-67. 2009.

Excl reason: Narrative review

Heim, K., Hopfl, R., Muller-Holzner, E., Bergant, A., and Dapunt, O. Multiple blue nevi of the vagina: A case report. *Journal of Reproductive Medicine for the Obstetrician and Gynecologist* 45[1], 42-44. 2000.

Excl reason: Not in PICO

Heller, D. S. Lower genital tract disease in children and adolescents - A review. *Journal of Pediatric and Adolescent Gynecology* 18[2], 75-83. 2005.

Excl reason: Narrative review

Horejsi, J. and Rob, L. [Malignant tumors of the female genitalia in childhood--yesterday, today and tomorrow]. [Review] [8 refs] [Czech]. *Casopis Lekarů Ceských* 142[2], 84-87. 2003.

Excl reason: Narrative review

Horejsi, J. and Rob, L. Malignant genital tumors in childhood - Yesterday, today and tomorrow. [Czech]. *Casopis Lekarů Ceských* 142[2], 84-87. 2003.

Excl reason: Duplicate? Narrative review

Howard, J. R. Dyspareunia in women: Managing a common problem. *Medicine Today* 6[8], 24-34. 2005.

Excl reason: Narrative review

Huang, W., Li, L., Yu, D. Q., Huang, Y. L., Liu, Y., Chen, X. Q., Tang, B. J., Xu, H., Ma, G., Dong, L. H., Li, L., Qiu, Y., Bai, H., Nong, W. Z., Li, L., Zeng, D. Y., Jiang, F. Y., Lan, Y., Ye, Y., Tang, X. Z., Wang, D. X., Li, H. Z., Pan, Y. B., Mo, A. X., Wu, X. Y., Lei, Z. Y., Zhou, G. P., Liu, C., and Su, Q. H. [Constitutive characteristics and change trend of gynecological malignant tumors in 8009 hospitalized patients in Guangxi Zhuang Autonomous Region]. [Chinese]. *Chung-Hua Fu Chan Ko Tsa Chih [Chinese Journal of Obstetrics & Gynecology]* 42[1], 22-25. 2007.

Excl reason: Not in PICO

- Jahnke, A., Domke, R., Makovitzky, J., Nizze, H., and Briese, V. Vaginal metastasis of lung cancer: a case report. *Anticancer Research* 25[3A], 1645-1648. 2005.
Excl reason: Not in PICO
- Jerant, A. F. Adenocarcinoma of the uterine cervix. *Journal of the American Board of Family Practice* 10[1], 36-42. 1997.
Excl reason: Not in PICO
- Johann, S. and Mueller, M. D. Follow-up after malignant tumours of the uterus (cancer of the uterine corpus / cervical cancer). [German]. *Therapeutische Umschau* 65[6], 341-346. 2008.
Excl reason: Not in PICO
- Joseph, R. E., Enghardt, M. H., Doering, D. L., Brown, B. F., Shaffer, D. W., and Raval, H. B. Small cell neuroendocrine carcinoma of the vagina. *Cancer* 70[4], 784-789. 15-8-1992.
Excl reason: Not in PICO
- Joura, E. A., Garland, S. M., Paavonen, J., Ferris, D. G., Perez, G., Ault, K. A., Huh, W. K., Sings, H. L., James, M. K., Haupt, R. M., and FUTURE, I. and, II. Effect of the human papillomavirus (HPV) quadrivalent vaccine in a subgroup of women with cervical and vulvar disease: retrospective pooled analysis of trial data. *BMJ* 344, e1401. 2012.
Excl reason: Not in PICO
- Kawano, A., Suzuki, R., and Shigeta, H. A case of large cell neuroendocrine carcinoma. *International Journal of Gynecological Cancer* 21[12 SUPPL. 3], S283. 2011. Lippincott Williams and Wilkins.
Excl reason: Not in PICO
- Kneba, M., Bergholz, M., Schauer, A., Nagel, G. A., and Krieger, G. [Vaginal tumor--an initial manifestation of malignant histiocytosis]. [German]. *Deutsche Medizinische Wochenschrift* 113[15], 602-604. 15-4-1988.
Excl reason: Not in PICO
- Kondoh, N., Nakamura, M., Nakano, E., and Sakaguchi, T. [A case of serous papillary adenocarcinoma of the ovary initially suspected to be a uretero-vaginal fistula]. [Japanese]. *Hinyokika Kyo - Acta Urologica Japonica* 33[6], 953-956. 1987.
Excl reason: Not in PICO
- Kostova, P.; Zlatkov, V. (2013). Pregnancy and malignant diseases. Part V. Some rare gynecological tumors during pregnancy. *Akusherstvo i Ginekologija*, 52, 48-50.
Excl reason: Narrative review
- Kreienberg, R. Early recognition of carcinoma of cervix vulva and vagina. [German]. *Gynakologe* 34[11], 1079-1086. 2001.
Excl reason: Narrative review
- Laiyemo, R., Disu, S., Vijaya, G., and Wise, B. Post-menopausal vaginal angiomyofibroblastoma: a case report. *Archives of Gynecology & Obstetrics* 273[2], 129-130. 2005.
Excl reason: Not in PICO
- Lea, J. S. and Miller, D. S. Optimum screening interventions for gynecologic malignancies. [Review] [41 refs]. *Texas Medicine* 97[2], 49-55. 2001.
Excl reason: Not in PICO
- Liaquat, N. F. and Noorani, K. Causes of post-menopausal bleeding - A study of 328 cases. *Journal of the College of Physicians and Surgeons Pakistan* 10[4], 134-137. 2000.
Excl reason: Not in PICO
- Meeuwis, K. A., van Rossum, M. M., van de Kerkhof, P. C., Hoitsma, A. J., Massuger, L. F., and de Hullu, J. A. Skin cancer and (pre)malignancies of the female genital tract in renal transplant recipients. *Transplant International* 23[2], 191-199. 2010.
Excl reason: Not in PICO
- Moore, D. H., Wilson, D. K., Hurteau, J. A., Look, K. Y., Stehman, F. B., and Sutton, G. P. Gynecologic cancers metastatic to the breast. *Journal of the American College of Surgeons* 187[2], 178-181. 1998.
Excl reason: Not in PICO

- Murakami, T., Hoshino, K., Hasumi, H., Makiyama, K., Miyoshi, Y., Yoshida, M., Nakaigawa, N., Ogawa, T., Uemura, H., Yao, M., and Kubota, Y. [Only metastasis to uterine corpus from superficial bladder cancer that of no original recurrence]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 53[1], 75-77. 2007.
Excl reason: Not in PICO
- Murta, E. F. C., Neves, Jr, Sempionato, L. R. F., Costa, M. C., and Maluf, P. J. Vaginal intraepithelial neoplasia: Clinical-therapeutic analysis of 33 cases. *Archives of Gynecology and Obstetrics* 272[4], 261-264. 2005.
Excl reason: Not in PICO
- Mwaka,A.D.; Okello,E.S.; Kiguli,J.; Rutebemberwa,E. (2014). Understanding cervical cancer: an exploration of lay perceptions, beliefs and knowledge about cervical cancer among the Acholi in northern Uganda. *BMC Women's Health*, 14, 84.
Excl reason: Not in PICO
- Newell, S. and Overton, C. Postmenopausal bleeding should be referred urgently. *Practitioner* 256[1749], 13-15. 20-11-2002.
Excl reason: Narrative review
- Nour Eldine,N.M.; Abdelnabi,A.R.A.; Lawrence,A. (2012). Two week waits: What are we waiting for? *International Journal of Gynecology and Obstetrics*, 119, S438-9.
Excl reason: Not in PICO
- Otton, G. R., Nicklin, J. L., Dickie, G. J., Niedetzky, P., Tripcony, L., Perrin, L. C., and Crandon, A. J. Early-stage vaginal carcinoma--an analysis of 70 patients. *International Journal of Gynecological Cancer* 14[2], 304-310. 2004.
Excl reason: Not in PICO
- Pan, C. C. and Lee, W. L. Vaginal obliteration in a woman with a history of cutaneous T-cell lymphoma: the results of combined chemotherapy-induced gonadal toxicity and lymphoma relapse. *Taiwanese Journal of Obstetrics & Gynecology* 49[1], 69-71. 2010.
Excl reason: Not in PICO
- Parikh, J. H., Barton, D. P., Ind, T. E., and Sohaib, S. A. MR imaging features of vaginal malignancies. [Review] [55 refs]. *Radiographics* 28[1], 49-63. 20-11-0322.
Excl reason: Not in PICO
- Petrillo, Marco, Corrado, Giacomo, Carbone, Arnaldo, Macchia, Gabriella, and Ferrandina, Gabriella. Vulvar squamous cell carcinoma with sarcoma-like stroma: A case report and review of the literature. *Diagnostic Pathology* 6[1], 95. 2011.
Excl reason: Not in PICO
- Petru, E., Luck, H. J., Stuart, G., Gaffney, D., Millan, D., Vergote, I., and Gynecologic Cancer Intergroup, GCIG. Gynecologic Cancer Intergroup (GCIG) proposals for changes of the current FIGO staging system. *European Journal of Obstetrics, Gynecology, & Reproductive Biology* 143[2], 69-74. 2009.
Excl reason: Not in PICO
- Pinar, G., Topuz, S., An, S., Dogan, N., Kaya, N., and Algier, L. [Baskent University Ankara Hospital Gynecology and Obstetrics, HPV VACCINE AND CERVICAL CANCER INFORMATION ABOUT THE LEVELS OF WOMEN]. *Turk Jinekolojik Onkoloji Dergisi* 13[1], 11-18. 2010.
Excl reason: Not in PICO
- Priebe, A.-M., Sareen, P., and Strickland, J. L. Abnormal vaginal bleeding in children and adolescents. *Journal of Pediatric and Adolescent Gynecology* 25[2], e33-e34. 2012. Elsevier USA.
Excl reason: Not in PICO
- Rekhi, Bharat, Qureshi, Sajid, Basak, Ranjan, Desai, Sangeeta, Medhi, Seema, Kurkure, Purna, Menon, Santosh, Maheshwari, Amita, and Jambhekar, Nirmala. Primary vaginal Ewing's sarcoma or primitive neuroectodermal tumor in a 17-year-old woman: a case report. *Journal of Medical Case Reports* 4[1], 88. 2010.
Excl reason: Not in PICO

- Sadan, O., Kruger, S., and Van, Iddekinge B. Vaginal tumors in pregnancy. Case report and review of the literature. *Acta Obstetrica et Gynecologica Scandinavica* 66[6], 559-562. 1987.
Excl reason: Not in PICO
- Sarkar, M.; Konar, H.; Raut, D. (2013). Clinico-pathological Features of Gynecological Malignancies in a Tertiary Care Hospital in Eastern India: Importance of Strengthening Primary Health Care in Prevention and Early Detection. *Asian Pacific Journal of Cancer Prevention*, 14, 3541-7.
Excl reason: Not in PICO
- Scambia, G., Benedetti, Panici P., Baiocchi, G., Coli, A., Ferrone, S., Natali, P. G., and Mancuso, S. A primary amelanotic melanoma of the vagina diagnosed by immunocytochemistry. [Review] [21 refs]. *International Journal of Gynaecology & Obstetrics* 29[2], 159-164. 1989.
Excl reason: Not in PICO
- Schober, J. M. Cancer of the neovagina. *Journal of pediatric urology* 3[3], 167-170. 2007.
Excl reason: Not in PICO
- Sharma, A. and Menon, U. Screening for gynaecological cancers. [Review] [76 refs]. *European Journal of Surgical Oncology* 32[8], 818-824. 2006.
Excl reason: Not in PICO
- Sherman, J. F., Mount, S. L., Evans, M. F., Skelly, J., Simmons-Arnold, L., and Eltabbakh, G. H. Smoking increases the risk of high-grade vaginal intraepithelial neoplasia in women with oncogenic human papillomavirus. *Gynecologic Oncology* 110[3], 396-401. 2008.
Excl reason: Not in PICO
- Shibata, R., Umezawa, A., Takehara, K., Aoki, D., Nozawa, S., and Hata, J. Primary carcinosarcoma of the vagina. *Pathology International* 53[2], 106-110. 2003.
Excl reason: Not in PICO
- Sinha, B., Stehman, F., Schilder, J., Clark, L., and Cardenes, H. Indiana University experience in the management of vaginal cancer. *International Journal of Gynecological Cancer* 19[4], 686-693. 2009.
Excl reason: Not in PICO
- Solomon, L. A., Zurawin, R. K., and Edwards, C. L. Vaginoscopic resection for rhabdomyosarcoma of the vagina: a case report and review of the literature. [Review] [10 refs]. *Journal of Pediatric & Adolescent Gynecology* 16[3], 139-142. 2003.
Excl reason: Not in PICO
- Soultanakis, E. N., Irelan, W., Oppenheimer, K., and Brard, L. Human papillomavirus infection and subtyping in primary vaginal carcinomas. *Gynecologic Oncology* 112[2 SUPPL. 1], S94-S95. 2009. Academic Press Inc.
Excl reason: Not in PICO
- Storfa, A., Davidson, S., and Singh, M. Polypoid lesions of the lower female genital tract. *Oncology* 20[4], 417-420. 2006.
Excl reason: Not in PICO
- Strehl, J. D., Mehlhorn, G., Koch, M. C., Harrer, E. G., Harrer, T., Beckmann, M. W., and Agaimy, A. HIV-associated hypertrophic herpes simplex genitalis with concomitant early invasive squamous cell carcinoma mimicking advanced genital cancer: Case report and literature review. *International Journal of Gynecological Pathology* 31[3], 286-293. 2012.
Excl reason: Not in PICO
- Sundersingh, S., Majhi, U., Chandrasekar, S. K., Seshadri, R. A., Dakshinamurthy, S. K., and Narayanaswamy, K. Metastatic malignant melanoma of the small bowel--report of two cases. *Journal of Gastrointestinal Cancer* 43[2], 332-335. 2012.
Excl reason: Not in PICO
- Thill, M. and Adamietz, I. A. Diagnosis and treatment options of vulvar and vaginal cancer. [German]. *Onkologie* 17[12], 1163-1180. 2011.
Excl reason: Narrative review

Tjalma, W. A. and Somville, J. Fibula metastasis as the presenting feature of vaginal cancer. *European Journal of Gynaecological Oncology* 32[1], 114-116. 2011.

Excl reason: Not in PICO

Triolo, O., Antico, F., Mancuso, A., Salimbeni, V., and Nicotina, P. A. Postmenopausal bleeding and vaginal nodules as the first presenting sign of adenocarcinoma of the gallbladder. *European Journal of Gynaecological Oncology* 26[5], 543-544. 2005.

Excl reason: Not in PICO

Tsai, M. C. and Goldstein, S. R. Office diagnosis and management of abnormal uterine bleeding. *Clinical Obstetrics and Gynecology* 55[3], 635-650. 2012.

Excl reason: Narrative review

Uehara, T., Onda, T., Sasajima, Y., Sawada, M., and Kasamatsu, T. A case of vaginal clear cell adenocarcinoma complicated with congenital anomalies of the genitourinary tract and metanephric remnant without prenatal diethylstilbestrol exposure. *Journal of Obstetrics & Gynaecology Research* 36[3], 681-685. 2010.

Excl reason: Not in PICO

Usmani, A. T., Ayub, S., and Basharat, A. Oncological referral patterns of gynaecological cancer patients over 2010-2011. the need for gynaecologic oncology subspecialty services. *BJOG: An International Journal of Obstetrics and Gynaecology* 119, 182-183. 2012. Blackwell Publishing Ltd.

Excl reason: Not in PICO

Valdera Simbron, C. J., Nievas, Soriano M., Marti Romero, M. T., Pulido, Fernandez F., and Fiol, Ruiz G. Vaginal leiomyoma. [Spanish]. *Progresos de Obstetricia y Ginecologia* 55[3], 130-133. 2012.

Excl reason: Not in PICO

Villa, Alcazar M., Pacheco, Cumani M., Navalon, Burgos J., and Lopez-Ibor, Alino B. "Don't mistreat a tumor"... Vaginal bleeding in a 10-month-old girl. [Spanish]. *Acta Pediatrica Espanola* 66[4], 195-197. 2008.

Excl reason: Not in PICO

Vorobiev, A. and Makatsaria, A. Inherent and acquired thrombophilia in cancer patient with thrombosis in past history. *Thrombosis Research* 127, S149. 2011. Elsevier Ltd.

Excl reason: Not in PICO

Weiderpass, E., Ye, W., Tamimi, R., Trichopolous, D., Nyren, O., Vainio, H., and Adami, H. O. Alcoholism and risk for cancer of the cervix uteri, vagina, and vulva. *Cancer Epidemiology, Biomarkers & Prevention* 10[8], 899-901. 2001.

Excl reason: Not in PICO

Wharton, J. T., Tortolero-Luna, G., Linares, A. C., Malpica, A., Baker, V. V., Cook, E., Johnson, E., and Follen, Mitchell M. Vaginal intraepithelial neoplasia and vaginal cancer. [Review] [32 refs]. *Obstetrics & Gynecology Clinics of North America* 23[2], 325-345. 1996.

Excl reason: Narrative review

Williams, W. C. and Herman, J. M. Vaginal intraepithelial neoplasia: methodologic problems in a case-control study. *Family Practice Research Journal* 10[1], 27-35. 1990.

Excl reason: Not in PICO

Yi, K. W., Song, S. H., Kim, K. A., Jung, W. Y., Lee, J. K., and Hur, J. Y. Giant endocervical polyp mimicking cervical malignancy: primary excision and hysteroscopic resection. *Journal of Minimally Invasive Gynecology* 16[4], 498-500. 2009.

Excl reason: Not in PICO

Review question:

Which investigations of symptoms of suspected vaginal cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

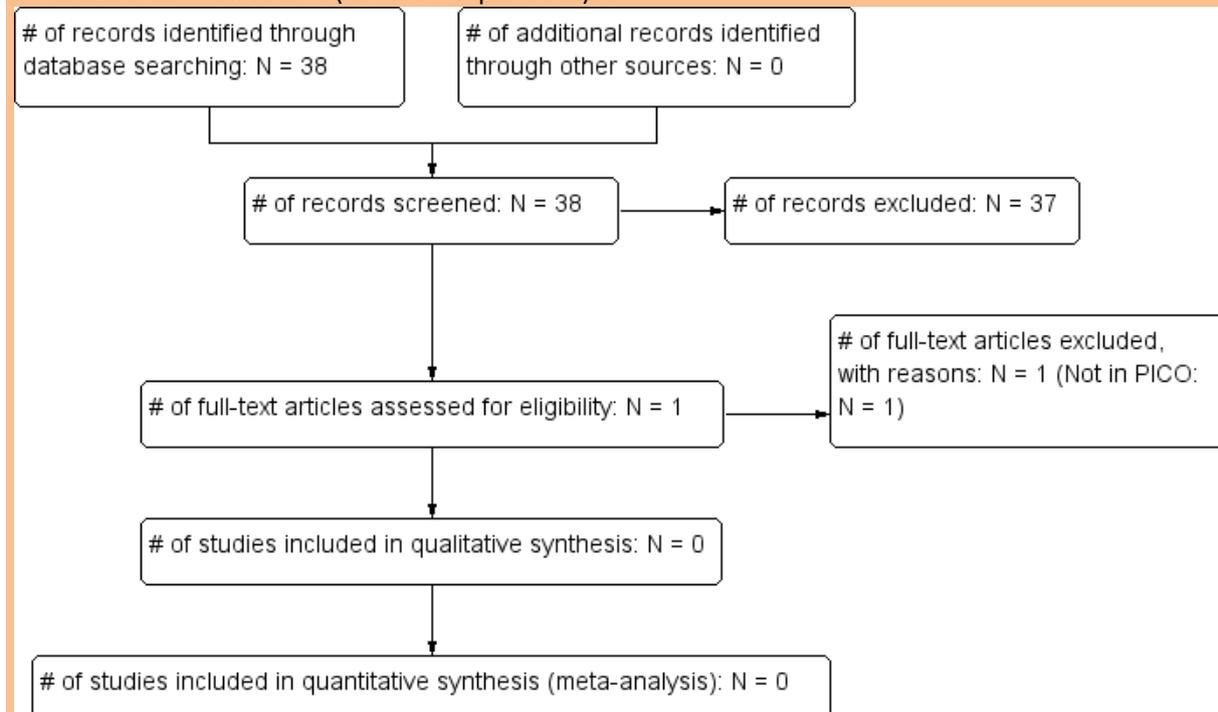
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	151	16	05/06/2013
<i>Premedline</i>	1980-2013	10	1	05/06/2013
<i>Embase</i>	1980-2013	142	10	05/06/2013
<i>Cochrane Library</i>	1980-2013	104	0	05/06/2013
<i>Psychinfo</i>	1980-2013	4	0	05/06/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	76	8	05/06/2013

Total References retrieved (after de-duplication): 34

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	6/2013-27/08/2014	6	0	27/08/2014
<i>Premedline</i>	6/2013-27/08/2014	10	0	27/08/2014
<i>Embase</i>	6/2013-27/08/2014	18	2	27/08/2014
<i>Cochrane Library</i>	6/2013-27/08/2014	75	0	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	6/2013-27/08/2014	19	2	27/08/2014

Total References retrieved (after de-duplication): 4



Study results

No evidence was identified pertaining to the diagnostic accuracy of tests in patients with suspected vaginal cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

- (2013) Clinical practice guidelines: Presumed benign ovarian tumors - Short text. *Journal de Gynecologie Obstetrique et Biologie de la Reproduction*, 42: 856-866.
Guideline
- Alipour, P., Arjmandi, K. & Hallaji, F. (2008) Vaginal clear cell adenocarcinoma with early pulmonary metastasis in a child. *Pediatric Hematology & Oncology*, 25: 679-684.
Not in PICO
- Baltzer, J. & Poleska, W. (2006) Metastatic vaginal neoplasia - A diagnostic and therapeutic problem. [Polish, English]. *Ginekologia Onkologiczna*, 4: 250-255.
Narrative review
- Chappell, C. A., West, A. M., Kabbani, W. & Werner, C. L. (2010) Off-label high-risk HPV DNA testing of vaginal ASC-US and LSIL cytologic abnormalities at Parkland hospital. *Journal of Lower Genital Tract Disease*, 14: 352-355.
Not in PICO
- Clark, T. J., Mann, C. H., Shah, N., Khan, K. S., Song, F. J. & Gupta, J. K. (2002) Accuracy of outpatient endometrial biopsy in the diagnosis of endometrial cancer: a systematic quantitative review. *Bjog-An International Journal of Obstetrics and Gynaecology*, 109: 313-321.
Not in PICO
- Creasman, W. T., Phillips, J. L. & Menck, H. R. (1998) The National Cancer Data Base report on cancer of the vagina. *Cancer*, 83: 1033-1040.
Not in PICO
- Dijkwel, G. A. & van Huisseling, J. C. (2005) [Two post-menopausal women with vaginal bleeding due to non-gynaecological malignancies]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 149: 2649-2652.
Not in PICO
- Flint, A., Terhart, K., Murad, T. M. & Taylor, P. T. (1982) Confirmation of metastases by fine needle aspiration biopsy in patients with gynecologic malignancies. *Gynecologic Oncology*, 14: 382-391.
Not in PICO
- Fontaine, P. L.; Saslow, D.; King, V. J. (2012). ACS/ASCCP/ASCP guidelines for the early detection of cervical cancer. *American Family Physician*, 86, 6.
Guideline
- Ghosh, T. K. & Cera, P. J. (1983) Transition of benign vaginal adenosis to clear cell carcinoma. *Obstetrics & Gynecology*, 61: 126-130.
Not in PICO
- Giannella, L., Mfuta, K., Setti, T., Cerami, L. B., Bergamini, E. & Boselli, F. (2014) A risk-scoring model for the prediction of endometrial cancer among symptomatic postmenopausal women with endometrial thickness > 4 mm. *BioMed Research International*, 2014.
Not in PICO
- Girardi, F., Pickel, H., Joura, E. A., Breitenacker, G., Gitsch, G., Graf, A. H. & Neunteufel, W. (2001) [Guidelines for diagnosis and therapy of intraepithelial neoplasia and early invasive carcinoma of the female lower genital system (cervix uteri, vagina, vulva) established by the AGK (Colposcopy Work Group in the OGGG [Austrian Society of Gynecology and Obstetrics])].

- [German]. *Gynakologisch-Geburtshilfliche Rundschau*, 41: 197-200.
Guideline
- Grant, N. & Nunns, D. (2012) Vulval pruritus and vaginal discharge. *Obstetrics, Gynaecology and Reproductive Medicine*, 22: 309-314.
Narrative review
- Gunderson, C. C., Nugent, E. K., Elfrink, S. H., Gold, M. A. & Moore, K. N. (2013) A contemporary analysis of epidemiology and management of vaginal intraepithelial neoplasia. *American Journal of Obstetrics and Gynecology*, 208: 410.
Not in PICO
- Heller, D. S., Moomjy, M., Koulos, J. & Smith, D. (1994) Vulvar and Vaginal Melanoma - A Clinicopathological Study. *Journal of Reproductive Medicine*, 39: 945-948.
Not in PICO
- Jahnke, A., Domke, R., Makovitzky, J., Nizze, H. & Briese, V. (2005) Vaginal metastasis of lung cancer: a case report. *Anticancer Research*, 25: 1645-1648.
Not in PICO
- Jerant, A. F. (1997) Adenocarcinoma of the uterine cervix. *Journal of the American Board of Family Practice*, 10: 36-42.
Not in PICO
- Kostova, P.; Zlatkov, V. (2013). Pregnancy and malignant diseases. Part V. Some rare gynecological tumors during pregnancy. *Akusherstvo i Ginekologija*, 52, 48-50.
Narrative review
- Langer, M., Langer, R., Schumacher, K. A. & Maier, W. (1981) [The localization and differential diagnosis of benign and malignant gynaecological tumours in the axial computer assisted tomogram (author's transl)]. [German]. *Geburtshilfe und Frauenheilkunde*, 41: 551-555.
Not in PICO
- Newell, S. & Overton, C. (2002) Postmenopausal bleeding should be referred urgently. *Practitioner*, 256: 13-15.
Narrative review
- Nour Eldine, N. M., Abdelnabi, A. R. A. & Lawrence, A. (2012) Two week waits: What are we waiting for? *International Journal of Gynecology and Obstetrics*, 119: S438-S439.
Not in PICO
- Orfanelli, T., Doulaveris, G., Jeong, J. M., Holcomb, K. M., Caputo, T. A., Gupta, D. & Witkin, S. S. (2014) Inhibition of autophagy by vaginal fluid from women with malignant adnexal masses. *Gynecologic Oncology*, 133: 108.
Not in PICO
- Parikh, J. H., Barton, D. P., Ind, T. E. & Sohaib, S. A. (1111) MR imaging features of vaginal malignancies. [Review] [55 refs]. *Radiographics*, 28: 49-63.
Narrative review
- Priebe, A.-M., Sareen, P. & Strickland, J. L. (2012) Abnormal vaginal bleeding in children and adolescents. *Journal of Pediatric and Adolescent Gynecology*, 25: e33-e34.
Not in PICO
- Ratnavelu, N., Patel, A., Fisher, A., Galaal, K., Cross, P. & Naik, R. (2013) High-grade vaginal intraepithelial neoplasia: can we be selective about who we treat? *BJOG: An International Journal of Obstetrics & Gynaecology*, 120: 887-893.
Not in PICO
- Rome, R. M. & England, P. G. (2000) Management of vaginal intraepithelial neoplasia: A series of 132 cases with long-term follow-up. *International Journal of Gynecological Cancer*, 10: 382-390.
Not in PICO
- Ruiz Moreno, J. A., Garcia, G. R., Tun, S. R. & Ortega Alvarado, R. M. (1992) [The results of a selective program to detect intraepithelial neoplasms of the vulva]. [Spanish]. *Ginecologia y Obstetricia*

- de Mexico*, 60: 55-59.
Not in PICO
- Sadan, O., Kruger, S. & van, I. B. (1987) Vaginal tumors in pregnancy. Case report and review of the literature. *Acta Obstetrica et Gynecologica Scandinavica*, 66: 559-562.
Not in PICO
- Sethom, F., Besbes, K. & Cammoun, M. (1989) For an early diagnosis of cervical cancer by systematic vaginal smears--clinical and psychological approach. [French]. *La Tunisie medicale*, 67: 505-511.
Not in PICO (cervical cancer)
- Shibata, R., Umezawa, A., Takehara, K., Aoki, D., Nozawa, S. & Hata, J. (2003) Primary carcinosarcoma of the vagina. *Pathology International*, 53: 106-110.
Not in PICO
- Slawson, D. C., Bennett, J. H. & Herman, J. M. (1992) Are Papanicolaou Smears Enough - Acetic-Acid Washes of the Cervix As Adjunctive Therapy - A Harnet Study. *Journal of Family Practice*, 35: 271-277.
Not in PICO
- Stapley, S. & Hamilton, W. (2011) Gynaecological symptoms reported by young women: examining the potential for earlier diagnosis of cervical cancer. *Family Practice*, 28: 592-598.
Not in PICO
- Stokes-Lampard, H., Wilson, S., Allan, T., Waddell, C. & Kehoe, S. (2005) Vaginal vault smears - 'know more - do less': a questionnaire survey of primary health care practitioners. *Cytopathology*, 16: 244-251.
Not in PICO
- Stokes-Lampard, H., Wilson, S., Waddell, C. & Bentley, L. (2011) Vaginal vault cytology tests: analysis of a decade of data from a UK tertiary centre. *Cytopathology*, 22: 121-129.
Not in PICO
- Terada, S., Suzuki, N., Tomimatsu, N. & Akasofu, K. (1992) Vaginal schwannoma. *Archives of Gynecology & Obstetrics*, 251: 203-206.
Not in PICO
- Tsai, M. C. & Goldstein, S. R. (2012) Office diagnosis and management of abnormal uterine bleeding. *Clinical Obstetrics and Gynecology*, 55: 635-650.
Narrative review
- Vandborg, M. P., Christensen, R. D., Kragstrup, J., Edwards, K., Vedsted, P., Hansen, D. G. & Mogensen, O. (2011) Reasons for Diagnostic Delay in Gynecological Malignancies. *International Journal of Gynecological Cancer*, 21: 967-974.
Not in PICO
- Vesoulis, Z. & Erhardt, C. A. (2001) Cytologic diagnosis of vaginal papillary squamotransitional cell carcinoma. A case report. *Acta Cytologica*, 45: 465-469.
Not in PICO
- Zarcone, R., Bellini, P., Carfora, E. & Cardone, A. (1997) A case of malignant melanoma of the vagina during pregnancy: immunological problems. *European Journal of Gynaecological Oncology*, 18: 136-138.
Not in PICO

UROLOGICAL CANCERS

PROSTATE CANCER

Review question:

What is the risk of prostate cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

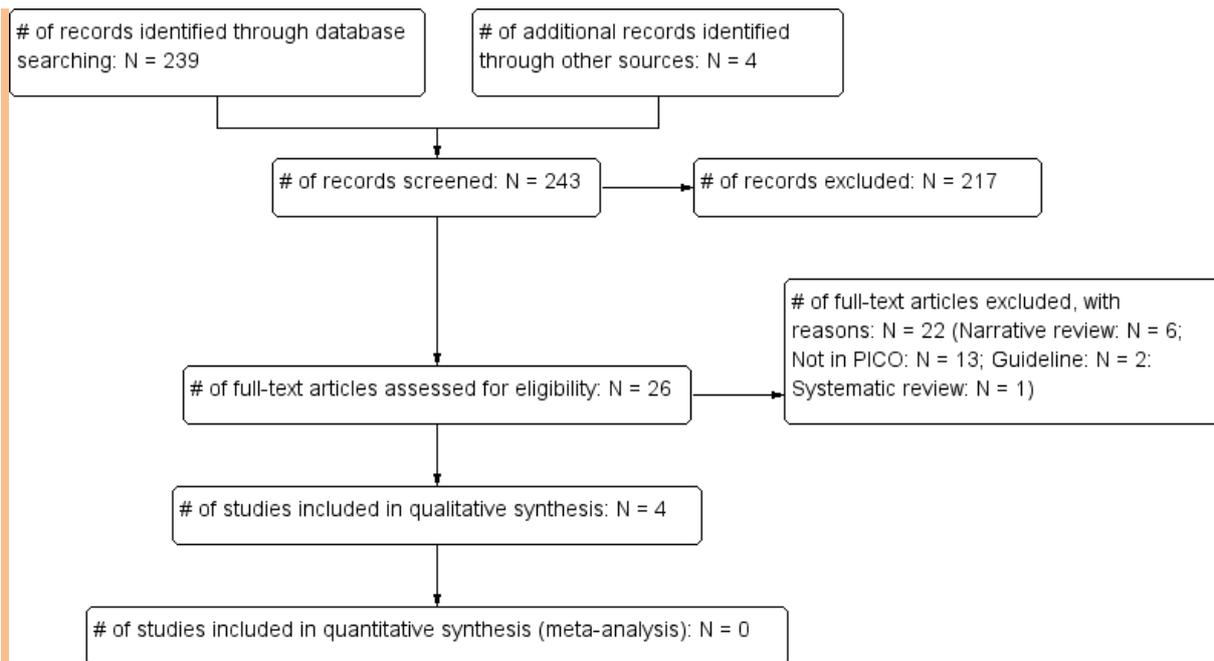
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	858	103	27/11/2012
<i>Premedline</i>	All-2012	33	3	27/11/2012
<i>Embase</i>	All-2012	2023	82	28/11/2012
<i>Cochrane Library</i>	All-2012	134	0	28/11/2012
<i>Psychinfo</i>	All-2012	33	4	27/11/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	540	66	28/11/2012
<i>Biomed Central</i>	All-2012	29	4	28/11/2012

Total References retrieved (after de-duplication): 215

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	11/2012-26/08/2014	115	11	26/08/2014
<i>Premedline</i>	11/2012-26/08/2014	57	1	26/08/2014
<i>Embase</i>	11/2012-26/08/2014	289	10	26/08/2014
<i>Cochrane Library</i>	11/2012-26/08/2014	77	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	11/2012-26/08/2014	160	5	26/08/2014

Total References retrieved (after de-duplication): 24



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issue to note is that 4/5 studies employed samples of patients that are not directly representative of an unselected symptomatic population of patients presenting to the UK-based GP and the 5th study employed a case-control design which has been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors may have gone some way in counteracting this influence. Three of the studies also employed reference standards that are subject to an unclear risk of bias; all of which must be born in mind when evaluating the evidence contributed by these studies.

	<u>Risk of Bias</u>				<u>Applicability Concerns</u>		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Bouwman (2007)	?	+	?	?	?	+	+
Deyo (1988)	?	+	?	+	-	+	+
Friedlander (2014)	+	+	?	+	?	+	+
Hallissey (1990)	+	+	+	+	?	+	+
Hamilton (2006)	-	+	+	+	+	+	+

- High	? Unclear	+ Low
---	---	--

Study results

Table 1: Prostate cancer: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)%
Bouwman (2007)	Urinary symptoms	Males aged ≥ 50 years	7.37 (5-10.7) 26/353
Deyo (1988)	Back pain	Male patients	0.13 (0.007-0.9) 1/750
Friedlander (2014)	Haematuria	All patients	0.61 (0.36-1.03) 15/2455
Hamilton (2006)	Haematuria	All patients	1 (0.57-1.8) Cases: 54/217 Controls: 33/1080
Hamilton (2006)	Haematuria (reported twice)	All patients	1.6 (0.8-3.2)
Hamilton (2006)	Loss of weight	All patients	0.75 (0.38-1.4) Cases: 48/217 Controls: 21/1080
Hamilton (2006)	Loss of weight (reported twice)	All patients	2.1 (NR)
Hamilton (2006)	Nocturia	All patients	2.2 (1.2-3.6) Cases: 49/217 Controls: 63/1080
		Patients 40-69 years	1.1 (NR)
		Patients ≥ 70 years	5.9 (NR)
Hamilton (2006)	Nocturia (reported twice)	All patients	3.3 (NR)
Hamilton (2006)	Hesitancy	All patients	3 (1.5-5.5) Cases: 21/217 Controls: 37/1080
Hamilton (2006)	Hesitancy (reported twice)	All patients	2 (NR)
Hamilton (2006)	Rectal exam: Benign enlargement	All included patients	2.8 (1.6-4.6) Cases: 37/217 Controls: 61/1080
		Patients 40-69 years	0.85 (NR)
		Patients ≥ 70 years	8.7 (NR)
Hamilton (2006)	Rectal exam: Malignant enlargements	All patients	12 (5-37) Cases: 5/217 Controls: 41/1080
Hamilton (2006)	Frequency/urgency	All patients	2.2 (1.1-3.5) Cases: 77/217 Controls: 102/1080
Hamilton (2006)	Frequency/urgency (reported twice)	All patients	3.1 (1.9-5.5)
Hamilton (2006)	Frequency	Patients 40-69 years	0.61 (NR)
		Patients ≥ 70 years	7.4 (NR)
Hamilton (2006)	Retention	All patients	3.1 (1.5-6)

			Cases: 18/217 Controls: 33/1080
		* excluding 39 patients with unsuspected cancer	1.6 (NR)
Hamilton (2006)	Impotence	All patients	3 (1.7-4.9) Cases: 38/217 Controls: 67/1080
		Patients 40-69 years	1.1 (NR)
		Patients ≥ 70 years	8.4 (NR)
Hamilton (2006)	When PSA was added to a small multivariate analysis (N = 208; N = 137 patients and N = 71 controls) with the following otherwise significant variables: urinary retention, second presentation with loss of weight, impotence, frequency, hesitancy, nocturia, haematuria, and rectal examination, these variables ceased to be significant predictors of prostate cancer while PSA > 4 ng/ml was significant (OR = 29, 95% CI 3.9-220; p = .001).		
Hallissey (1990)	Dyspepsia	All patients	0.08 (0.01-0.3) 2/2585

CI = Confidence interval. *The authors report that a sub-analysis excluding the 39 patients who had previously unsuspected cancer identified at prostatectomy, showed that the PPVs of symptoms were little changed, other than for retention.

Table 2: Prostate cancer: Symptom combinations

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)%
Hamilton (2006)	Haematuria + nocturia	All patients	1.9 (NR)
Hamilton (2006)	Haematuria + benign rectal exam	All patients	3.3 (NR)
Hamilton (2006)	Haematuria + malignant rectal exam	All patients	3.9 (NR)
Hamilton (2006)	Haematuria + frequency/urgency	All patients	1.8 (0.9-3.9)
Hamilton (2006)	Loss of weight + nocturia	All patients	12 (NR)
Hamilton (2006)	Loss of weight + benign rectal exam	All patients	9.4 (NR)
Hamilton (2006)	Loss of weight + frequency/urgency	All patients	1.8 (NR)
Hamilton (2006)	Nocturia + hesitancy	All patients	2.8 (NR)
Hamilton (2006)	Nocturia + benign rectal exam	All patients	3.9 (2.1-7.8)
Hamilton (2006)	Nocturia + malignant rectal exam	All patients	15 (NR)
Hamilton (2006)	Nocturia + frequency/urgency	All patients	3.2 (1.9-6)
Hamilton (2006)	Hesitancy + benign rectal exam	All patients	3.3 (NR)
Hamilton (2006)	Hesitancy + malignant rectal exam	All patients	10 (NR)
Hamilton (2006)	Hesitancy + frequency/urgency	All patients	4.7 (NR)

Hamilton (2006)	Benign rectal exam + frequency/urgency	All patients	4 (2.3-7.4)
Hamilton (2006)	Malignant rectal exam + frequency/urgency	All patients	13 (NR)

CI = Confidence interval.

Evidence statement(s):

The positive predictive values for prostate cancer of single symptoms presenting in a primary care setting ranged from 0.08% (for dyspepsia) to 12% (for malignant rectal exam; 5 studies, N = 7440). The studies were associated with 1-4 bias or applicability concerns (see also Table 1).

The positive predictive values for prostate cancer of symptom pairs presenting in a primary care setting ranged from 1.8% (for haematuria + frequency/urgency) to 15% (for nocturia + malignant rectal exam; 1 study, N = 1297). This study was a case-control study (i.e, high risk of bias for patient selection; see also Table 2).

Evidence tables

Bouwman (2007)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Database study using data from the Registration Network Groningen (RNG) from 2003 and 2004, which is a database registering continuous automatic recorded data from, on average, 17 GPs working in practices in Groningen, Hoozevee and Hoozevee-Sappemeer (population of approximately 30000 people) in the Netherlands.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	In the whole sample there were 4422 men aged ≥ 50 years in the period 2003 to 2004. Of these 353 men consulted the GP for urinary symptoms. <i>No further details reported.</i> <u>Inclusion criteria:</u> Male patients aged ≥ 50 years in the period 2003 to 2004 who visited participating practices because of urinary symptoms (see "Index test" for further details) for the first time. <u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> Primary care in the Netherlands.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	The following ICPC codes were used: U01 (painful urination), U02 (increased urinary frequency / urgency), U04 (urinary incontinence), other micturition U05) and Y06 (symptoms / complaints prostate) and some minor codes: U07

	(other symptoms / complaints urine) and U13 (other symptoms / complaints bladder). The code Y85 for BPH / LUTS was not included in this selection because the RNG agreements apply to the use of the different parts of the ICPC. This agreement is that a health problem is initially registered as a symptom or complaint until by advancing knowledge and further research a diagnosis code may be added to the records.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
<u>A. risk of bias</u>	
Reference standard(s)	The reference standard consisted checking the database to see if a BHP diagnosis (ICPC code Y85) or prostate carcinoma diagnosis (ICPC code Y77) had been registered by 2005.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
<u>A. risk of bias</u>	
Flow and timing	There is very little information about the included patients and the patient pool from which they were drawn. It is therefore not possible to ascertain whether all patients are accounted for.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk
NOTES	Original paper is published in Dutch
Deyo (1988)	
PATIENT SELECTION	
<u>A. risk of bias</u>	
Patient sampling	Prospective consecutive? patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)

Could the selection of patients have introduced bias?		Unclear risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 1975, mean (SD; range) age = 39.5 (15.4; 15-86) years, 62% females. 54% of the patients were seeking medical care for back pain for the first time and 76% of the patients had had back pain for < 3 months. 3% had a history of back pain surgery. Maximal back pain in the low back (84%) or in the upper back (16%).</p> <p><u>Inclusion criteria:</u> Patients who sought treatment between March 1982 and September 1984 in the walk-in clinic of a public hospital where virtually all patients are self-referred. In each case back pain was part of the chief complaint.</p> <p><u>Exclusion criteria:</u> Neck pain.</p> <p><u>Clinical setting:</u> Walk-in clinic of a public hospital; this clinic is a source of primary care for indigent persons in a county in the USA with a population of approximately 1 million.</p>	
Are there concerns that the included patients and setting do not match the review question?		High concern
INDEX TEST		
A. Risk of bias		
Index test	Back pain; not further specified.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	<p>The reference standard consisted of a search on each patient name in the institutional tumour registry \geq 6 months after the index visit. The registry included every patient with a histological diagnosis of cancer made in the authors' hospital system regardless of site of care. The authors point out that "while this method might fail to identify cancer patients who sought care elsewhere, it is likely that most patients sought follow-up for a particular illness at the same facility.</p>	
Is the reference standard likely to correctly classify the target condition?	Unclear	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		

Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	It is a concern that some patients with cancer might have been missed due to the choice of reference standard because this would result in an underestimation of the positive predictive value. 38/1975 patients were found in the tumour registry. Of those 38, 13 patients had tumours that were probable causes of back pain, and 4 of these 13 patients already had a diagnosis of cancer at presentation. The 9/1975 patients who had undiagnosed cancer that the back pain could be attributed to had: Lymphoma (NOS; 2), cancer of unknown primary (1), prostate cancer (1), retroperitoneal liposarcoma (1), lung cancer (1), renal cell (1), multiple myeloma (1), mucinous adenocarcinoma (of gallbladder?; 1)

Friedlander (2014)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective cohort study, using claims data and laboratory values from the Vanderbilt University Medical Centre's (VUMC) Research Derivative, which is a "data repository that contains administrative and clinical information, including a complete record of visits and admissions, laboratory data, and diagnosis and procedure codes, on every patient treated in the Vanderbilt health system" (p 634) located in Tennessee in the USA.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2455 patients, 724 males / 1731 females, median (inter-quartile range) age = 58 (49-68) years; smoking history: current smoker (N = 406), former smoker (N = 473), non-smoker (N = 1514). <u>Inclusion criteria:</u> "Patients aged ≥ 40 years with a first diagnosis of hematuria" "between 2004 and 2012 by urinalysis (>3 red blood counts per high power field) or International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes for hematuria (599.7, 599.70, 599.71 or 599.72) at one of the VUMC's 19 primary care clinics. To be included in the study, patients must have had records for 1 year before the date of hematuria diagnosis." <u>Exclusion criteria:</u> "Patients were excluded if they had a urinary tract infection (defined as a urinalysis positive for both leukocyte esterase and urine nitrites, or a positive urine culture) within 4 weeks before or 1 week after the index hematuria episode (n = 590, 9.0%) or had a prior explanatory diagnoses and procedures that would preclude the need for a hematuria evaluation (according to a convened panel of content experts;

	prostate/renal/bladder/other cancer, benign prostate/renal/bladder/other mass, prostate dysplasia, cystitis, urethritis, epididymitis/orchitis, prostatitis, pyelonephritis, urolithiasis, prostatic enlargement, trauma, medical renal disease, haematologic/thrombotic disease?, anatomic abnormality, prostatectomy, prostate biopsy, transurethral incision of prostate, resection of prostate, cystoscopy, cystectomy, ureteroscopy, nephrectomy, pyeloplasty, ureteral reimplantation).” We then used Physicians Current Procedural Terminology Coding System, 4th Edition and ICD-9 codes to exclude patients with an explanatory diagnosis or procedure within 180 days preceding their hematuria diagnosis (n = 3540, 53.8%).” Clinical setting: Primary care, USA.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	First diagnosis of hematuria” “by urinalysis (>3 red blood counts per high power field) or International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes for hematuria (599.7, 599.70, 599.71 or 599.72)”.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	The reference standard consisted checking the database for diagnoses of genitourinary neoplasms within 180 days after haematuria diagnosis, as determined by ICD-9 codes.
Is the reference standard likely to correctly classify the target condition?	Unclear (is 180 days enough time to get a diagnosis of all cancers?)
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

NOTES	There were 66 patients with cancer: Bladder (N = 33), renal cell (N = 16), prostate (N = 15). The types of cancer for the remaining two cases were not reported.	
Hallissey (1990)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Propective consecutive patient series from a group of 10 general practices in England.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia. <u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, England.	
Are there concerns that the included patients and setting do not match the review question?	Unclear concern	
INDEX TEST		
A. Risk of bias		
Index test	Dyspepsia of any degree	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	

FLOW AND TIMING	
A. risk of bias	
Flow and timing	2659 patients were seen and 2585 attended for investigation
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), cirrhomatosis of unknown primary (7).

Hamilton (2006)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based case-control study, involving all 21 general practices in Exeter, Devon, UK.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> 217 male patients; age at diagnosis: < 60 years: N = 15 (7%); 60-69 years: N = 51 (24%); 70-79 years: N = 100 (46%); ≥ 80 years: N = 51 (24%); median number of consultations in the 2 years preceding diagnosis = 14 (IQR = 10-21).</p> <p><u>Controls:</u> 1080 male patients; age at diagnosis: < 60 years: N = 79 (7%); 60-69 years: N = 253 (23%); 70-79 years: N = 494 (46%); ≥ 80 years: N = 254 (24%); median number of consultations in the 2 years preceding diagnosis = 14 (IQR = 10-21).</p> <p><u>Inclusion criteria:</u> Cases: All patients aged 40 years or over with prostate cancer, diagnosed from 1998 to 2002 inclusive, were identified from the cancer registry at the Royal Devon and Exeter Hospital (the only hospital offering urological services to Exeter patients). Computerised searches at every practice identified any cases missing from the register. Cases without positive histology were included if the records contained a consultant urologist</p>

	<p>diagnosis of cancer based on strong clinical evidence.</p> <p>Controls: Five male controls were matched to each case on general practice and on age (to 1-year bands if possible, increased in 1-year multiples to a maximum of 5 years). Controls were eligible if they were alive at the time of diagnosis of their case.</p> <p><u>Exclusion criteria:</u> Unobtainable records; no consultations in the 2 years before diagnosis; previous prostate cancer; or residence outside Exeter at the time of diagnosis.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	All entries into the primary care records for 2 years before diagnosis were coded, blinded to case/control status, using the International Classification of Primary Care-2. Only variables occurring in >2.5% of cases or controls were analysed.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Prostate cancer code, from 1998 to 2002 inclusive, in the cancer registry at the Royal Devon and Exeter Hospital or the general practice records
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes

Could the patient flow have introduced bias?	Low risk
NOTES	

References

Included studies

- Bouwman, I., Van Der Heide, W. K., Van Der Veen, W. J., and Van Der Meer, K. GPs and patients still think that lower urinary tract symptoms are an indication of prostate cancer. [Dutch]. *Huisarts en Wetenschap* 50[7], 321-325. 2007.
- Deyo, R. A. and Diehl, A. K. Cancer as a cause of back pain: Frequency, clinical presentation, and diagnostic strategies. *Journal of General Internal Medicine* 3, 230-238. 1-11-1988.
- Friedlander, D.F., Resnick, M.J., You, C., Bassett, J., Yarlagadda V., Penson, D.F., Barocas D.A. Variation in the intensity of hematuria evaluation: A target for primary care quality improvement. *American Journal of Medicine*, 127, 633-640. 2014.
- Hallisey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.
- Hamilton, W., Sharp, D. J., Peters, T. J., and Round, A. P. Clinical features of prostate cancer before diagnosis: a population-based, case-control study. *British Journal of General Practice* 56[531], 756-762. 2006.

Excluded studies (with excl reason)

- Acheson, H. W. & Henley, M. H. (1984) Clinical knowledge and education for general practice. *Journal of the Royal College of General Practitioners - Occasional Paper.(27):1-28, 1984 Oct., 1-28.*
Not in PICO
- Afifi, A. H. A. A., Etaby, A. N., Ahmad, M. A. Y. & Farghaly, Y. T. (2013) Value of diffusion weighted magnetic resonance imaging in the prediction of cancer prostate. *Alexandria Journal of Medicine*, 49: 57-66.
Not in PICO
- Ahaghotu, C., Baffoe-Bonnie, A., Kittles, R., Pettaway, C., Powell, I., Royal, C., Wang, H., Vijayakumar, S., Bennett, J., Hoke, G., Mason, T., Bailey-Wilson, J., Boykin, W., Berg, K., Carpten, J., Weinrich, S., Trent, J., Dunston, G. & Collins, F. (2004) Clinical characteristics of African-American men with hereditary prostate cancer: the AAHPC study. *Prostate Cancer and Prostatic Diseases*, 7: 165-169.
Not in PICO
- Ahmad, S., Cao, R., Varghese, T., Bidaut, L. & Nabi, G. (2013) Transrectal quantitative shear wave elastography in the detection and characterisation of prostate cancer. *Surgical Endoscopy and Other Interventional Techniques*, 27: 3280-3287.
Not in PICO
- Allen, D., Popert, R. & O'Brien, T. (2004) The two-week-wait cancer initiative in urology: useful modernization? *Journal of the Royal Society of Medicine*, 97: 279-281.
Not in PICO
- Allgar, V. L. & Neal, R. D. (2005) General practitioners' management of cancer in England: secondary analysis of data from the National Survey of NHS Patients - Cancer. *European Journal of Cancer Care*, 14: 409-416.
Not in PICO
- Allgar, V. L., Neal, R. D., Ali, N., Leese, B., Heywood, P., Proctor, G. & Evans, J. (2006) Urgent GP referrals for suspected lung, colorectal, prostate and ovarian cancer. *British Journal of General Practice*, 56: 355-362.
Not in PICO
- Anast, J. W., Andriole, G. L. & Grubb, R. L. (2007) Managing the local complications of locally advanced prostate cancer. [Review] [24 refs]. *Current Urology Reports*, 8: 211-216.
Narrative review

- Antunes, A. A., Srougi, M., Dall'oglio, M. F., Vicentini, F., Paranhos, M. & Freire, G. C. (2008) The role of BPH, lower urinary tract symptoms, and PSA levels on erectile function of Brazilian men who undergo prostate cancer screening. *Journal of Sexual Medicine*, 5: 1702-1707.
Not in PICO
- Arumainayagam, N., Ahmed, H. U., Moore, C. M., Freeman, A., Allen, C., Sohaib, S. A., Kirkham, A., van der Meulen, J. & Emberton, M. (2013) Multiparametric MR imaging for detection of clinically significant prostate cancer: a validation cohort study with transperineal template prostate mapping as the reference standard. *Radiology*, 268: 761-769.
Not in PICO
- Babaian, R. J., Miyashita, H., Evans, R. B., Voneschenbach, A. C. & Ramirez, E. I. (1991) Early Detection Program for Prostate-Cancer - Results and Identification of High-Risk Patient Population. *Urology*, 37: 193-197.
Not in PICO
- Bagi, C. M. (2003) Skeletal implications of prostate cancer. *Journal of Musculoskeletal Neuronal Interactions*, 3: 112-117.
Narrative review
- Bailey, C. & Broadbent, A. Cutaneous metastases of prostate cancer. [References]. *Journal of Palliative Medicine* 10[4], 980-982. 2007.
Not in PICO
- Bajramovic, S. & Junuzovic, D. (2013) Detection of prostate cancer at low volume prostate and low PSA range. *European Urology, Supplements*, 12: e1286.
Not in PICO
- Barkin, J. (2008) Management of benign prostatic hyperplasia by the primary care physician in the 21st century: the new paradigm. *The Canadian journal of urology*, 15: 21-30.
Narrative review
- Barkin, J., Rosenberg, M. T. & Miner, M. (2014) A guide to the management of urologic dilemmas for the primary care physician (PCP). *Canadian Journal of Urology*, 21: 55-63.
Narrative review
- Barrett, J. & Hamilton, W. (2005) Pathways to the diagnosis of prostate cancer in a British city. A population-based study. *Scandinavian Journal of Urology and Nephrology*, 39: 267-270.
Not in PICO
- Basha, R., Baker, C. H. & Abdelrahim, M. (2009) Biomarkers clinical relevance in cancer: Emphasis on breast cancer and prostate cancer. *Current Trends in Biotechnology and Pharmacy*, 3: 1-7.
Narrative review
- Bastide, C., Beuzeboc, P., Cormier, L., Fromont, G., Hennequin, C., Mongiat-Artus, P., Peyromaure, M., Ploussard, G., Renard-Penna, R., Rozet, F., Richaud, P., Soulie, M., Salomon, L., Azria, D., Coloby, P., Molinie, V., Ravery, V., Rebillard, X., Villers, A. & Les membres du, C. C. A. F. (2013) [CCAFU Recommendations 2013: Prostate cancer]. [French]. *Progres En Urologie*, 23: Suppl-S101.
Guideline
- Baughan, P., O'Neill, B. & Fletcher, E. (2009) Auditing the diagnosis of cancer in primary care: the experience in Scotland. *British Journal of Cancer*, 101: Suppl-91.
Not in PICO
- Baughan, P., Keatings, J. & O'Neill, B. (2011) Urgent suspected cancer referrals from general practice: Audit of compliance with guidelines and referral outcomes. *British Journal of General Practice*, 61: e700-e706.
Not in PICO
- Berney, D. M. (2012) Early prostate cancer. *Journal of Pathology*, 226: S3.
Narrative review
- Bhojani, N., Perrotte, P., Hutterer, G., Suardi, N., Jeldres, C., Shariat, S. F., Capitanio, U., Arjane, P., Widmer, H., Benard, F., Peloquin, F., Montorsi, F. & Karakiewicz, P. (2008) Body mass index and its association with genitourinary disorders in men undergoing prostate cancer screening. *Journal*

- of *Sexual Medicine*, 5: 2141-2151.
Not in PICO
- Bianco, F. J., Jr., McHone, B. R., Wagner, K., King, A., Burgess, J., Patierno, S. & Jarrett, T. W. (2009) Prevalence of erectile dysfunction in men screened for prostate cancer. *Urology*, 74: 89-93.
Not in PICO
- Billington, A. (1998) Prostate cancer and its effect on sexuality. *Community Nurse*, 4: 33-34.
Not in PICO
- Bjurlin, M. A., Carter, H. B., Schellhammer, P., Cookson, M. S., Gomella, L. G., Troyer, D., Wheeler, T. M., Schlossberg, S., Penson, D. F. & Taneja, S. S. (2013) Optimization of initial prostate biopsy in clinical practice: sampling, labeling and specimen processing. [Review]. *Journal of Urology*, 189: 2039-2046.
Not in PICO
- Bjurlin, M. A. & Taneja, S. S. (2014) Standards for prostate biopsy. *Current Opinion in Urology*, 24: 155-161.
Narrative review
- Blanker, M. H., Bernsen, R. M., Bosch, J. L., Thomas, S., Groeneveld, F. P., Prins, A. & Bohnen, A. M. (2002) Relation between nocturnal voiding frequency and nocturnal urine production in older men: a population-based study. [Erratum appears in *Urology*. 2003 Jan;61(1):259.]. *Urology*, 60: 612-616.
Not in PICO
- Blanker, M. H., Bernsen, R. M., Ruud Bosch, J. L., Thomas, S., Groeneveld, F. P., Prins, A. & Bohnen, A. M. (2002) Normal values and determinants of circadian urine production in older men: a population based study. *Journal of Urology*, 168: t-7.
Not in PICO
- Blanker, M. H., Driessen, L. F. C., Ruud Bosch, J. L. H., Bohnen, A. M., Thomas, S., Prins, A., Bernsen, R. M. D. & Groeneveld, F. P. M. J. (2002) Health status and its correlates among Dutch community-dwelling older men with and without lower urogenital tract dysfunction. *European Urology*, 41: 602-607.
Not in PICO
- Blanker, M. H., Bernsen, R. M. D., Bosch, J. L. H. R., Thomas, S., Groeneveld, F. P. M. J., Prins, A. & Bohnen, A. M. (2002) Relation between nocturnal voiding frequency and nocturnal urine production in older men: A population-based study. *Urology*, 60: 612-616.
Not in PICO
- Blanker, M. H., Klomp, M. A., van den Donk, M., van der Heide, W. K., Opstelten, W. & Burgers, J. S. (2013) [Summary of the NHG practice guideline 'Lower urinary tract symptoms in men']. [Review] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 157: A6178.
Narrative review/guideline
- Bodelle, B., Naguib, N. N., Schulz, B., Eichler, K., Muller, C., Hansmann, M. L., Hammerstingl, R., Hubner, F., Vogl, T. J. & Zangos, S. (2013) 1.5-T magnetic resonance-guided transgluteal biopsies of the prostate in patients with clinically suspected prostate cancer: technique and feasibility. *Investigative Radiology*, 48: 458-463.
Not in PICO
- Booth, C. M., Chaudry, A. A., Smith, K. & Griffiths, K. (1996) The benefits of a shared-care prostate clinic. *British Journal of Urology*, 77: 830-835.
Not in PICO
- Borneman, T., Koczywas, M., Sun, V., Piper, B. F., Smith-Idell, C., Laroya, B., Uman, G. & Ferrell, B. (2011) Effectiveness of a clinical intervention to eliminate barriers to pain and fatigue management in oncology. *Journal of Palliative Medicine*, 14: 197-205.
Not in PICO
- Borneman, T., Piper, B. F., Koczywas, M., Munevar, C. M., Sun, V., Uman, G. C. & Ferrell, B. R. (2012) A qualitative analysis of cancer-related fatigue in ambulatory oncology. *Clinical Journal of*

- Oncology Nursing*, 16: E26-E32.
Not in PICO
- Bos, E. (2008) "It is not going to happen to me". Andros male clinic: A diagnostic center for typical male problems. [Dutch]. *Pharmaceutisch Weekblad*, 143: 30-34.
Narrative review
- Braun, K. P., May, M., Grassmell, Y., Fuhrer, S., Hoschke, B. & Braun, V. (2008) The General Practitioner's part in the initiation of diagnostic procedures in prostate cancer. *Aktuelle Urologie*, 39: 141-146.
Not in PICO (referred population)
- Brawer, M. K. (1993) The diagnosis of prostatic carcinoma. *Problems in Urology*, 7: 129-136.
Narrative review
- Bundred, N. J., Walls, J. & Ratcliffe, W. A. (1996) Parathyroid hormone-related protein, bone metastases and hypercalcaemia of malignancy. *Annals of the Royal College of Surgeons of England*, 78: 354-358.
Not in PICO
- Bunting, P. S., Goel, V., Williams, J. I. & Iscoe, N. A. (1999) Prostate-specific antigen testing in Ontario: reasons for testing patients without diagnosed prostate cancer. *Canadian Medical Association Journal*, 160: 70-75.
Not in PICO
- Buntinx, F. & Wauters, H. (1997) The diagnostic value of macroscopic haematuria in diagnosing urological cancers: A meta-analysis. *Family Practice*, 14: 63-68.
SR, but no studies conducted in primary care included
- Burnett, A. L. & Wein, A. J. (2006) Benign prostatic hyperplasia in primary care: What you need to know. *Journal of Urology*, 175: S19-S24.
Narrative review
- Cahill, D. (2005) The GP's role in lower urinary tract obstruction. *Practitioner*, 249: 38-42.
Narrative review
- Calhoun, E. A., Clemens, J. Q., Litwin, M. S., Walker-Corkery, E., Markossian, T., Kusek, J. W. & McNaughton-Collins, M. (2009) Primary care physician practices in the diagnosis, treatment and management of men with chronic prostatitis/chronic pelvic pain syndrome. *Prostate Cancer and Prostatic Diseases*, 12: 288-295.
Not in PICO
- Carey, M., Bryant, J., Yoong, S. L., Russell, G., Barker, D. & Sanson-Fisher, R. (2013) Prostate specific antigen testing in family practice: a cross sectional survey of self-reported rates of and reasons for testing participation and risk disclosure. *BMC Family Practice*, 14: 186.
Not in PICO
- Carlsson, L., Hakansson, A. & Nordenskjold, B. (2001) Common cancer-related symptoms among GP patients - Opportunistic screening in primary health care. *Scandinavian Journal of Primary Health Care*, 19: 199-203.
Not in PICO
- Cescon, D. W., Canil, C., Le, L. W. & Tannock, I. F. (2009) Use of the Prostate Cancer-specific Quality of Life Instrument (PROSQOLI) in clinical practice. *Journal of Clinical Oncology*, 27: e20569.
Not in PICO
- Chang, V. T., Hwang, S. S., Kasimis, B. & Thaler, H. T. (2004) Shorter symptom assessment instruments: The condensed Memorial Symptom Assessment Scale (CMSAS). *Cancer Investigation*, 22: 526-536.
Not in PICO
- Chisholm, G. D., Carne, S. J., Fitzpatrick, J. M., George, N. J. R., Gingell, J. C., Keen, J. W., Kirby, R. S., Kirk, D., Odonoghue, E. P. N., Peeling, W. B., Shearer, R. J. & Williams, G. B. (1995) Prostate Disease - Management Options for the Primary Health-Care Team - Report of A Working Party of

- the British Prostate Group. *Postgraduate Medical Journal*, 71: 136-142.
Narrative review
- Clements, A., Watson, E., Rai, T., Bukach, C., Shine, B. & Austoker, J. (2007) The PSA testing dilemma: GPs' reports of consultations with asymptomatic men: a qualitative study. *BMC Family Practice*, 8: 35.
Not in PICO
- Coeurdacier, P., Staerman, F., Thoquenne, G., Cipolla, B., Guille, F. & Lobel, B. (1996) [General practitioners' approach to urination disorders in men over the age of 50. A survey of 250 physicians in Brittany]. [French]. *Progres En Urologie*, 6: 52-59.
Not in PICO
- Collins, M. (1997) Increasing prostate cancer awareness in African American men. *Oncology Nursing Forum*, 24: 91-95.
Not in PICO
- Collins, M. M., Barry, M., Roberts, R. G., Oesterling, J. E. & Fowler, F. J. (1997) Diagnosis and treatment of benign prostatic hyperplasia - Practice patterns of primary care physicians. *Journal of General Internal Medicine*, 12: 224-229.
Not in PICO
- Collins, M. M., O'Leary, M. P. & Barry, M. J. (1998) Prevalence of bothersome genitourinary symptoms and diagnoses in younger men on routine primary care visits. *Urology*, 52: 422-427.
Not in PICO
- Couzi, L., Cluzeau, J., Skopinski, S., Constans, J. & Conri, C. (2002) Henoch-Schonlein purpura and prostatic carcinoma. [French]. *Revue de Medecine Interne*, 23: 717-719.
Not in PICO
- Cunningham, R. S. (2006) Clinical practice guideline use by oncology advanced practice nurses. *Applied Nursing Research*, 19: 126-133.
Not in PICO
- D'Ambrosio, G. G., Campo, S., Cancian, M., Pecchioli, S. & Mazzaglia, G. (2010) Opportunistic prostate-specific antigen screening in Italy: 6 years of monitoring from the Italian general practice database. *European Journal of Cancer Prevention*, 19: 413-416.
Not in PICO
- Dalla, P. L., Ricci, C. & Magnaldi, S. (1995) Referral criteria for selection of patients and diagnostic procedures. *Radiation Protection Dosimetry*, 57: 3-8.
Narrative review
- Davalli, P., Rizzi, F., Caporali, A., Pellacani, D., Davoli, S., Bettuzzi, S., Brausi, M. & D'Arca, D. (2012) Anticancer activity of green tea polyphenols in prostate gland. [Review]. *Oxidative medicine & cellular longevity*, 2012: 984219.
Narrative review
- Delgado-Guay, M. O., Yennurajalingam, S. & Bruera, E. (2008) Delirium with severe symptom expression related to hypercalcemia in a patient with advanced cancer: an interdisciplinary approach to treatment. *Journal of Pain and Symptom Management*, 36: 442-449.
Not in PICO
- Delongchamps, N. B., Peyromaure, M., Schull, A., Beuvon, F., Bouazza, N., Flam, T., Zerbib, M., Muradyan, N., Legman, P. & Cornud, F. (2013) Prebiopsy magnetic resonance imaging and prostate cancer detection: comparison of random and targeted biopsies. *Journal of Urology*, 189: 493-499.
Not in PICO
- Drummond, F., Carsin, A. E., Sharp, L. & Comber, H. (2009) Factors prompting PSA-testing of asymptomatic men in a country with no guidelines: a national survey of general practitioners. *BMC Family Practice*, 10: 3.
Not in PICO

- Durmus, T., Goldmann, U., Baur, A. D., Huppertz, A., Schwenke, C., Hamm, B. & Franiel, T. (2013) MR-guided biopsy of the prostate: comparison of diagnostic specimen quality with 18 G and 16 G biopsy needles. *European Journal of Radiology*, 82: e749-e754.
Not in PICO
- Ebrahimi, M., Assadi, M. & Rezaei, M. M. (2012) New bone pain palliation radiopharmaceuticals in Iran. *Iranian Journal of Nuclear Medicine*, 20: 135.
Narrative review
- Edwards, J. L. (2008) Diagnosis and management of benign prostatic hyperplasia. *American Family Physician*, 77: 1403-1410+1413.
Narrative review
- Emery, J. D., Walter, F. M., Gray, V., Sinclair, C., Howting, D., Bulsara, M., Bulsara, C., Webster, A., Auret, K., Saunders, C., Nowak, A. & Holman, C. D. (2013) Diagnosing cancer in the bush: a mixed-methods study of symptom appraisal and help-seeking behaviour in people with cancer from rural Western Australia. *Family Practice*, 30: 294-301.
Not in PICO
- Fawzy, A., Fontenot, C., Guthrie, R. & Baudier, M. M. (1997) Practice patterns among primary care physicians in benign prostatic hyperplasia and prostate cancer. *Family Medicine*, 29: 321-325.
Not in PICO
- Fernandez, J. C., Olmo, J. M. C., Fernandez-Pro, A., Martin, J. A., Bermudez, F. J. B., Pulido, E. N., Molero, J. M. & Morales, D. P. (2010) Referral criteria for benign prostatic hyperplasia in primary care. *Actas Urologicas Espanolas*, 34: 24-34.
Narrative review
- Fiset, P. O., Aprikian, A. & Brimo, F. (2013) Length of prostate biopsy cores: does it impact cancer detection? *Canadian Journal of Urology*, 20: 6848-6853.
Not in PICO
- Fitzpatrick, P., Corcoran, N. & Fitzpatrick, J. M. (1998) Prostate cancer: how aware is the public? *British Journal of Urology*, 82: 43-48.
Not in PICO
- Fletcher, S. G., Clark, S. J., Overstreet, D. L. & Steers, W. D. (1126) An improved approach to followup care for the urological patient: drop-in group medical appointments. *Journal of Urology*, 176: 1122-1126.
Not in PICO
- Forbes, L. J. L., Warburton, F., Richards, M. A. & Ramirez, A. J. (2014) Risk factors for delay in symptomatic presentation: A survey of cancer patients. *British Journal of Cancer*, 111: 581-588.
Not in PICO
- Franc, B. L., Cho, S. Y., Rosenthal, S. A., Cui, Y., Tsui, B., Vandewalker, K. M., Holz, A. L., Poonamallee, U., Pomper, M. G. & James, R. B. (2013) Detection and localization of carcinoma within the prostate using high resolution transrectal gamma imaging (TRGI) of monoclonal antibody directed at prostate specific membrane antigen (PSMA)--proof of concept and initial imaging results. *European Journal of Radiology*, 82: 1877-1884.
Not in PICO
- Franiel, T., Vargas, H. A., Mazaheri, Y., Bohmer, S., Hricak, H., Akin, O. & Beyersdorff, D. (2013) Role of endorectal prostate MRI in patients with initial suspicion of prostate cancer.[Erratum appears in Rofo. 2013 Sep;184(10):E5 Note: Vargas, A H [corrected to Vargas, H A]]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 184: 967-974.
Not in PICO
- Fransson, P. (2008) Quality of life for members of Swedish Prostate Cancer Patient Associations. *Cancer Nursing*, 31: 23-31.
Not in PICO

- Frydenberg, M. & Wijesinha, S. (2007) Diagnosing prostate cancer - What GPs need to know. *Australian Family Physician*, 36: 345-347.
Narrative review
- Fukagai, T., Maruyama, K., Nagata, M., Morita, M., Naoe, M. & Yoshida, H. (2007) Practice patterns regarding prostate cancer and benign prostatic hyperplasia in Japanese primary care practitioners. *International Journal of Urology*, 14: 412-415.
Not in PICO
- Gades, N. M., Jacobson, D. J., Girman, C. J., Roberts, R. O., Lieber, M. M. & Jacobsen, S. J. (2005) Prevalence of conditions potentially associated with lower urinary tract symptoms in men. *BJU International*, 95: 549-553.
Not in PICO
- Ganie, F. A., Wani, M. S., Shaheen, F., Wani, M. L., Ganie, S. A., Mir, M. F., Wani, S. N. & Masaratul, G. (2013) Endorectal coil MRI and MR-spectroscopic imaging in patients with elevated serum prostate specific antigen with negative trus transrectal ultrasound guided biopsy. *Urology annals*, 5: 172-178.
Not in PICO
- Gao, X., Porter, A. T., Grignon, D. J., Pontes, J. E. & Honn, K. V. (1997) Diagnostic and prognostic markers for human prostate cancer. [Review] [185 refs]. *Prostate*, 31: 264-281.
Narrative review
- Gentile, M., Carini, M., Morgia, G., Selvaggi, F. P., Randone, D. & Rosati, A. (2001) Management of patients with LUTS suggestive of BPH. *European Urology*, 40: 5-8.
Narrative review
- Giordana, M. T., Cordera, S. & Boghi, A. (2000) Cerebral metastases as first symptom of cancer: a clinico-pathologic study. *Journal of Neuro-Oncology*, 50: 265-273.
Narrative review
- Gittens, P. R., Lallas, C. D., Pe, M. L., Perkel, R., Folia, C. & Gomella, L. G. (2008) Uro pharmacology for the primary care physician. [Review] [86 refs]. *Canadian Journal of Urology*, 15: Suppl-91.
Narrative review
- Gjengsto, P., Eide, J., Frugard, J., Bakke, A. & Hoisaeter, P. A. (2004) The potentially curable prostate cancer patient and the pathways leading to diagnosis and treatment. *Scandinavian Journal of Urology and Nephrology*, 38: 15-18.
Not in PICO
- Godley, P. A. & Carpenter, W. R. (2007) Case-control prostate cancer screening studies should not exclude subjects with lower urinary tract symptoms. *Journal of Clinical Epidemiology*, 60: 176-180.
Narrative review
- Goedendorp, M. M., Gielissen, M. F., Verhagen, C. A., Peters, M. E. & Bleijenberg, G. (2008) Severe fatigue and related factors in cancer patients before the initiation of treatment. *British Journal of Cancer*, 99: 1408-1414.
Not in PICO
- Gonsalves, L., Cartmel, B. & Mueller, L. (2012) The burden of cancer in Connecticut. *Connecticut Medicine*, 76: 335-351.
Not in PICO
- Gottesman, J. & Baum, N. (1997) Common urologic disorders: When to treat and when to refer. *Postgraduate Medicine*, 102: 235-246.
Narrative review
- Gourova, L. W., van de Beek, C., Spigt, M. G., Nieman, F. H. & van Kerrebroeck, P. E. (2006) Predictive factors for nocturia in elderly men: a cross-sectional study in 21 general practices. *BJU International*, 97: 528-532.
Not in PICO

- Gratzke, C., Schlenker, B., Weidlich, P., Seitz, M., Reich, O. & Stief, C. G. (2007) Benign prostatic hyperplasia: Background and diagnosis. [German]. *MMW-Fortschritte der Medizin*, 149: 25-28.
Narrative review
- Gray, M. A., Crampton, P., Weinstein, P. & Nacey, J. N. (2004) Differences in prostate disease symptoms and visits to the general practitioner among three ethnic groups in New Zealand. *BJU International*, 94: 96-100.
Not in PICO
- Greenwald, H. P., Bonica, J. J. & Bergner, M. (1987) The prevalence of pain in four cancers. *Cancer*, 60: 2563-2569.
Not in PICO
- Gui, Q., Xu, C., Zhao, X., Wang, X., Yang, L., Duan, X., Li, H., Yang, Z. & Hu, W. (2013) Diagnostic value of transrectal real-time elastography in prostatic benign and malignant lesions. *Chinese Journal of Andrology*, 27: 14-17+21.
Not in PICO
- Gutierrez, C., Hernansanz, S., Rubiales, A. S., Del Valle, M. L., Cuadrillero, R. F., Flores, L. A. & Garcia, C. (2006) Clinical manifestations and care in tumors with pelvic involvement: Is there a pelvic syndrome in Palliative Care?. [Spanish]. *Medicina Paliativa*, 13: 32-36.
Not in PICO
- Hamilton, W. & Sharp, D. (2004) Symptomatic diagnosis of prostate cancer in primary care: a structured review. *British Journal of General Practice*, 54: 617-621.
Narrative review
- Hamilton, W. (2009) The CAPER studies: five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients. *British Journal of Cancer*, 101: Suppl-6.
Narrative review
- Hamilton, W. (2009) Five misconceptions in cancer diagnosis. *British Journal of General Practice*, 59: 441-447.
Narrative review
- Hamilton, W. (2010) Cancer diagnosis in primary care. *British Journal of General Practice*, 60: 121-128.
Narrative review
- Hansen, R., Vedsted, P., Sokolowski, I., Sondergaard, J. & Olesen, F. (2011) Time intervals from first symptom to treatment of cancer: a cohort study of 2,212 newly diagnosed cancer patients. *BMC Health Services Research*, 11: 284.
Not in PICO
- Hawary, A. M., Warburton, H. E., Brough, R. J., Collins, G. N., Brown, S. C., O'Reilly, P. H. & Adeyoku, A. A. (2008) The '2-week wait' rule for referrals for suspected urological cancers--urgent need for refinement of criteria. *Annals of the Royal College of Surgeons of England*, 90: 517-522.
Not in PICO
- Heedman, P. A. & Strang, P. (2003) Pain and pain alleviation in hospital-based home care: demographic, biological and treatment factors. *Supportive Care in Cancer*, 11: 35-40.
Not in PICO
- Heins, M. J., Korevaar, J. C., Rijken, P. M. & Schellevis, F. G. (2013) For which health problems do cancer survivors visit their General Practitioner? *European Journal of Cancer*, 49: 211-218.
Not in PICO
- Heinzer, H. & Steuber, T. (2009) Prostate cancer in the elderly. *Urologic Oncology*, 27: 668-672.
Narrative review
- Helmy, H., Rasheed, M. & Al-Abd, S. (2009) Vardenafil improves erectile function and urinary symptoms in men with erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia: A randomized, double-blind, placebo controlled trial. *European*

- Urology, Supplements*, 8: 238.
Not in PICO
- Herman, C. J., Hoffman, R. M. & Altobelli, K. K. (1999) Variation in recommendations for cancer screening among primary care physicians in New Mexico. *Journal of Community Health*, 24: 253-267.
Not in PICO
- Hicks, R. J. & Cook, J. B. (1995) Managing patients with benign prostatic hyperplasia. *American Family Physician*, 52: 135-142.
Narrative review
- Higano, C. S. (2014) - To treat or not to treat, that is the question: the role of bone-targeted therapy in metastatic prostate cancer. - *Journal of Clinical Oncology*, 32: 1107-1111.
Not in PICO
- Hodgson, F., Obertova, Z., Brown, C. & Lawrenson, R. (2012) PSA testing in general practice. *Journal of Primary Health Care*, 4: 199-204.
Not in PICO
- Hofstetter, A. (2004) The 10-minute consultation. With weak discharge often past the target... [German]. *MMW Fortschritte der Medizin*, 146: 67-68.
Narrative review
- Holden, J. & Emery, C. B. (2004) Prostate cancer. Primary care providers play critical role. *Advance for Nurse Practitioners*, 12: 28-35.
Narrative review
- Horchani, A., Binous, M. Y., Ben, H. A., Sallami, S., El, A. H. & Naji, A. (2007) [Prevalence of benign prostatic hyperplasia in general practice and practical approach of the Tunisian general practitioner (Prevapt study)]. [French]. *Tunisie Medicale*, 85: 619-624.
Not in PICO
- Huang, S., Lin, J., Guo, N., Zhang, M., Yun, X., Liu, S., Zhou, J., He, E. & Skog, S. (2011) Elevated serum thymidine kinase 1 predicts risk of pre/early cancerous progression. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 12: 497-505.
Not in PICO
- Hughes, A. M., Sladden, M. J., Hirst, G. H. & Ward, J. E. (2000) Community study of uncomplicated lower urinary tract symptoms among male Italian immigrants in Sydney, Australia. *European Urology*, 37: 191-198.
Not in PICO
- Ikoma, F., Mori, Y., Arima, M., Shimada, K., Shima, H., Terakawa, T., Kanokogi, M., Yabumoto, H., Fujisue, K. & Tsujimoto, S. (1988) Clinical statistics on outpatients, inpatients and operations in 1986. [Japanese]. *Hinyokika kyo, Acta*: 2047-2052.
Not in PICO
- Jarvis, S. (2003) The CHARM study: Implications for general practice a commentary from primary care. *British Journal of Cardiology*, 10: 337-338.
Not in PICO
- Jichlinski, P. (2014) Urology. [French]. *Revue Medicale Suisse*, 10: 127-129.
Duplicate
- Jichlinski, P. (2014) - [Urology]. [Review] [French]. - *Revue Medicale Suisse*, 10: 127-129.
Narrative review
- Jolly, S., Howson, J., Catto, J., Haynes, M., Cutinha, P., Yates, D. & Rosario, D. (2013) Clinical microsystems in designing trus-biopsy services - A closed-loop audit of a specialist nurse-led triage clinic for men with suspected prostate cancer. *International Journal of Surgery*, 11: 727.
Not in PICO
- Jordan, K. P., Hayward, R. A., Blagojevic-Bucknall, M. & Croft, P. (2013) Incidence of prostate, breast, lung and colorectal cancer following new consultation for musculoskeletal pain: A cohort study

- among UK primary care patients. *International Journal of Cancer*, 133: 713-720.
Duplicate
- Jordan, K. P., Hayward, R. A., Blagojevic-Bucknall, M. & Croft, P. (2013) Incidence of prostate, breast, lung and colorectal cancer following new consultation for musculoskeletal pain: a cohort study among UK primary care patients. *International Journal of Cancer*, 133: 713-720.
Cannot extract outcome in PICO (PPVs) as cancer data only reported in total for 10-year follow up
- Kamalov, A. A., Maksimov, V. A., Takhirzade, T. B., Gevorkian, A. R., Okhobotov, D. A., Avakian, A. I. & Vasil'eva, E. G. (2012) [Detection of prostate cancer based on monitoring of prostate-specific antigen in outpatient clinic]. [Russian]. *Urologiia (Moscow, Russia)*.(6):58-60, 2012 Sep-Oct., 58-60.
Not in PICO
- Kaplan, S. & Naslund, M. (2006) Public, patient, and professional attitudes towards the diagnosis and treatment of enlarged prostate: A landmark national US survey. *International Journal of Clinical Practice*, 60: 1157-1165.
Not in PICO
- Kapoor, A. (2012) Benign prostatic hyperplasia (BPH) management in the primary care setting. *Canadian Journal of Urology*, 19: Suppl-7.
Narrative review
- Karakiewicz, P. I., Aprikian, A. G., Bazinet, M. & Elhilali, M. M. (1997) Patient attitudes regarding treatment-related erectile dysfunction at time of early detection of prostate cancer. *Urology*, 50: 704-709.
Not in PICO
- Katz, B., Srougi, M., Dall'Oglio, M., Nesrallah, A. J., Sant'anna, A. C., Pontes, J., Jr., Reis, S. T., Sanudo, A., Camara-Lopes, L. H. & Leite, K. R. (2012) Are we able to correctly identify prostate cancer patients who could be adequately treated by focal therapy? *Urologic Oncology*, 30: 794-797.
Not in PICO
- Khan, M. A., Shaw, G. & Paris, A. M. (2002) Is microscopic haematuria a urological emergency? *BJU International*, 90: 355-357.
Not in PICO
- Khoury, S., Cockett, A., Aso, Y., Chatelain, C., Andersson, L., Abrams, P., Griffiths, K. & Denis, L. (2000) International Consultation on Urological Diseases: a decade of progress. *Prostate*, 45: 194-199.
Narrative review
- Kim, Y. M., Kim, J., Park, S., Lee, J. H., Ryu, D. S., Choi, S. H. & Cheon, S. H. (2013) Role of prostate volume in the early detection of prostate cancer in a cohort with slowly increasing prostate specific antigen. *Yonsei Medical Journal*, 54: 1202-1206.
Not in PICO
- Kimura, T., Ikemoto, I. & Ohishi, Y. (2000) [Clinical profiles of prostate cancer in our hospital: association between primary symptoms and clinical stage]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica*, 46: 83-86.
Not in PICO
- Kirkham, A. P., Haslam, P., Keanie, J. Y., McCafferty, I., Padhani, A. R., Punwani, S., Richenberg, J., Rottenberg, G., Sohaib, A., Thompson, P., Turnbull, L. W., Kurban, L., Sahdev, A., Clements, R., Carey, B. M. & Allen, C. (2013) Prostate MRI: who, when, and how? Report from a UK consensus meeting. *Clinical Radiology*, 68: 1016-1023.
Narrative review
- Kiyota, H., Onodera, S., Ohishi, Y., Tsukamoto, T. & Matsumoto, T. (2003) Questionnaire survey of Japanese urologists concerning the diagnosis and treatment of chronic prostatitis and chronic pelvic pain syndrome. *International Journal of Urology*, 10: 636-642.
Not in PICO
- Koo, J. H., Kim, C. K., Choi, D., Park, B. K., Kwon, G. Y. & Kim, B. (2013) Diffusion-weighted magnetic resonance imaging for the evaluation of prostate cancer: optimal B value at 3T. *Korean Journal of*

- Radiology*, 14: 61-69.
Not in PICO
- Krause, B. J., Souvatzoglou, M. & Treiber, U. (2013) Imaging of prostate cancer with PET/CT and radioactively labeled choline derivatives. [Review]. *Urologic Oncology*, 31: 427-435.
Narrative review
- Kumar, P., Kapoor, S. & Nargund, V. (2006) Haemospermia - a systematic review. [Review] [15 refs]. *Annals of the Royal College of Surgeons of England*, 88: 339-342.
Narrative review
- Lamy, P. J., Montels, F., Tosi, D., Leizour, B., Bascoul-Mollevis, C., Castan, F., Roques, S., Nielloud, F. & Rebillard, X. (2013) [Evaluation of (-2)proPSA in combination with total PSA and free PSA for the early detection of prostate cancer]. [French]. *Annales de Biologie Clinique*, 71: 537-544.
Not in PICO
- Lane, J. A., Hamdy, F. C., Martin, R. M., Turner, E. L., Neal, D. E. & Donovan, J. L. (2010) Latest results from the UK trials evaluating prostate cancer screening and treatment: The CAP and ProtecT studies. *European Journal of Cancer*, 46: 3095-3101.
Not in PICO
- Leader, A., Daskalakis, C., Braddock, C. H., III, Kunkel, E. J., Cocroft, J. R., Berekenyei, S., Riggio, J. M., Capkin, M. & Myers, R. E. (2012) Measuring informed decision making about prostate cancer screening in primary care. *Medical Decision Making*, 32: 327-336.
Not in PICO
- Lee, S. J., Hwang, I., Hwang, E. C., Jung, S. I., Kang, T. W., Kwon, D. D. & Park, K. (2013) Are more low-risk prostate cancers detected by repeated biopsy? A retrospective pilot study. *Korean Journal of Urology*, 54: 364-368.
Not in PICO
- Lenk, V. S. (2005) [Diagnosis of the "aging male"--what is recommended?]. [Review] [27 refs] [German]. *Urologe (Auszg.A)*, 44: 1167-1172.
Narrative review
- Li, L., Wang, L., Feng, Z., Hu, Z., Wang, G., Yuan, X., Wang, H. & Hu, D. (2013) Prostate cancer magnetic resonance imaging (MRI): multidisciplinary standpoint. *Quantitative Imaging in Medicine & Surgery*, 3: 100-112.
Narrative review
- Lippi, G., Plebani, M., Franchini, M., Guidi, G. C. & Favaloro, E. J. (2009) Prostate-specific antigen, prostate cancer, and disorders of hemostasis. [Review] [111 refs]. *Seminars in Thrombosis & Hemostasis*, 35: 654-664.
Narrative review
- Litwin, M. S., Lubeck, D. P., Henning, J. M. & Carroll, P. R. (1998) Differences in urologist and patient assessments of health related quality of life in men with prostate cancer: results of the CaPSURE database. *Journal of Urology*, 159: 1988-1992.
Not in PICO
- Liu, J., Yue, Q.-X., Zhou, Y., Yu, G.-H. & Li, S. (2013) Application of transrectal real-time elastography in prostate biopsy. [Chinese]. *Chinese Journal of Interventional Imaging and Therapy*, 10: 101-103.
Not in PICO
- Mannini, D., Ferri, C., Maver, P., Corrado, G., Stasi, G., Querze, R., Bacchini, P. & Galanti, G. (1992) Nonspecific granulomatous prostatitis (PGA): Diagnosis and follow-up. [Italian]. *Acta Urologica Italica*, 6: 479-480.
Not in PICO
- Mansson, J. & Bengtsson, C. (1994) Prostate cancer. From the general practitioner's point of view. *Neoplasma*, 41: 237-240.
Not in PICO

- Mansson, J., Bjorkelund, C. & Hultborn, R. (1999) Symptom pattern and diagnostic work-up of malignancy at first symptom presentation as related to level of care. A retrospective study from the primary health care centre area of Kungsbacka, Sweden. *Neoplasma*, 46: 93-99.
Not in PICO
- Mansson, J., Marklund, B. & Hultborn, R. (2001) The diagnosis of cancer in the "roar" of potential cancer symptoms of patients in primary health care. Research by means of the computerised journal. *Scandinavian Journal of Primary Health Care*, 19: 83-89.
Symptoms not linked with cancers; analysis based on number of codes, not patients.
- Mansson, J., Marklund, B. & Carlsson, P. (2006) Costs in primary care of investigating symptoms suspicious of cancer in a defined population. *Scandinavian Journal of Primary Health Care*, 24: 243-250.
Symptoms not linked with cancers; analysis based on number of codes, not patients
- Martin, R. M., Vatten, L., Gunnell, D., Romundstad, P. & Nilsen, T. I. (2008) Lower urinary tract symptoms and risk of prostate cancer: the HUNT 2 Cohort, Norway. *International Journal of Cancer*, 123: 1924-1928.
Not in PICO
- Mason, M. D., Bosnyak, Z., Malmberg, A. & Neijber, A. (2014) Lower urinary tract symptoms (LUTS) in prostate cancer (PC) patients treated with GnRH antagonist compared to agonist: Results of a pooled analysis. *Journal of Clinical Oncology*, 32.
Not in PICO
- Matthew, A. G., Currie, K. L., Irvine, J., Ritvo, P., Santa, M. D., Jamnicky, L., Nam, R. & Trachtenberg, J. (2007) Serial personal digital assistant data capture of health-related quality of life: a randomized controlled trial in a prostate cancer clinic. *Health & Quality of Life Outcomes*, 5: 38.
Not in PICO
- Mazzola, C. R., Ghoneim, T. & Shariat, S. F. (2011) [Emerging biomarkers for the diagnosis, staging and prognosis of prostate cancer]. [Review] [French]. *Progres En Urologie*, 21: 1-10.
Narrative review
- McCombie, S., Logan, C., Hawks, C., Ling, O. W. & Hayne, D. (2014) The 'one stop' prostate clinic: A report on Fremantle Hospital's first 200 patients. *BJU International*, 113: 37.
Not in PICO
- McNaughton-Collins, M. & Barry, M. J. (2005) Managing patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. *American Journal of Medicine*, 118: 1331-1339.
Narrative review
- McVary, K. T., Monnig, W., Camps, J., Young, J. M., Tseng, L.-J. & van den Ende, G. (2007) Sildenafil Citrate Improves Erectile Function and Urinary Symptoms in Men With Erectile Dysfunction and Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia: A Randomized, Double-Blind Trial. *Journal of Urology*, 177: 1071-1077.
Not in PICO
- Melia, J., Moss, S. & Johns, L. (2004) Rates of prostate-specific antigen testing in general practice in England and Wales in asymptomatic and symptomatic patients: a cross-sectional study. *BJU International*, 94: 51-56.
Not in PICO
- Melia, J., Coulson, P., Coleman, D. & Moss, S. (2008) Urological referral of asymptomatic men in general practice in England. *British Journal of Cancer*, 98: 1176-1181.
Not in PICO
- Melia, J., Coulson, P., Moss, S. & Coleman, D. (2010) Effects of a prostate awareness pilot on GP consultations and PSA requests. *Family Practice*, 27: 69-76.
Not in PICO
- Mengus, C., Le, M. C., Trella, E., Yousef, K., Bubendorf, L., Provenzano, M., Bachmann, A., Heberer, M., Spagnoli, G. C. & Wyler, S. (2011) Elevated levels of circulating IL-7 and IL-15 in patients with

- early stage prostate cancer. *Journal of Translational Medicine*, 9: 162.
Not in PICO
- Merino, M., Gonzales, E. L. M., Rodriguez, L. & Roehrborn, C. G. (2009) The Health Improvement Network (THIN) database: Focused safety study of acute urinary retention (AUR) in men. *Journal of Urology*, 181: 593.
Not in PICO
- Mischi, M., Saidov, T., Kompatsiari, K., Engelbrecht, M. R., Breeuwer, M. & Wijkstra, H. (2013) Prostate cancer localization by novel magnetic resonance dispersion imaging. *Conference Proceedings: ...Annual International Conference of the IEEE Engineering in Medicine & Biology Society*, 2013: 2603-2606.
Narrative review
- Miser, W. F. (2007) Cancer screening in the primary care setting - The role of the primary care physician in screening for breast, cervical, colorectal, lung, ovarian, and prostate cancers. *Primary Care*, 34: 137-+.
Narrative review
- Mishina, T. (1992) [Clinical statistics on outpatients at Mishina urological office between July, 1984 and December, 1990]. [Japanese]. *Hinyokika Kyo - Acta Urologica Japonica*, 38: 367-372.
Not in PICO
- Mohamed, Z. K., Dominguez-Escrig, J., Vasdev, N., Bharathan, B. & Greene, D. (2013) The prognostic value of transrectal ultrasound guided biopsy in patients over 70 years old with a prostate specific Antigen (PSA) level <15 ng/ml and normal digital rectal examination: A 10-year prospective follow-up study of 427 consecutive patients. *Urologic Oncology: Seminars and Original Investigations*, 31: 1489-1496.
Not in PICO
- Mold, J. W., Holtgrave, D. R., Bissoni, R. S., Marley, D. S., Wright, R. A. & Spann, S. J. (1992) The Evaluation and Treatment of Men with Asymptomatic Prostate Nodules in Primary Care - A Decision-Analysis. *Journal of Family Practice*, 34: 561-568.
Not in PICO
- Molero, J. M., Morales, D. P., Bermudez, F. J. B., Pulido, E. N., Fernandez-Pro, A., Martin, J. A., Fernandez, J. C. & Olmo, J. M. C. (2010) Referral criteria for benign prostatic hyperplasia in primary care. *Atencion Primaria*, 42: 36-46.
Narrative review
- Molina, R., Bosch, X., Auge, J. M., Filella, X., Escudero, J. M., Molina, V., Sole, M. & Lopez-Soto, A. (2012) Utility of serum tumor markers as an aid in the differential diagnosis of patients with clinical suspicion of cancer and in patients with cancer of unknown primary site. *Tumor Biology*, 33: 463-474.
Not in PICO
- Monreal, M., Fernandez-Llamazares, J., Perandreu, J., Urrutia, A., Sahuquillo, J. C. & Contel, E. (1997) Occult cancer in patients with venous thromboembolism: which patients, which cancers. *Thrombosis & Haemostasis*, 78: 1316-1318.
Not in PICO
- Monreal, M. & Prandoni, P. (1999) Venous thromboembolism as first manifestation of cancer. [Review] [31 refs]. *Seminars in Thrombosis & Hemostasis*, 25: 131-136.
Narrative review
- Morris, L., Gorayski, P. & Turner, S. (2014) - Back pain in a cancer patient: a case study. - *Australian Family Physician*, 43: 529-530.
Not in PICO
- Mouraviev, V., Verma, S., Kalyanaraman, B., Zhai, Q. J., Gaitonde, K., Pugnale, M. & Donovan, J. F. (2013) The feasibility of multiparametric magnetic resonance imaging for targeted biopsy using novel navigation systems to detect early stage prostate cancer: the preliminary experience.

Journal of Endourology, 27: 820-825.

Not in PICO

Mouton, W. G., Kienle, Y., Muggli, B., Naef, M. & Wagner, H. E. (2009) Tumors associated with superficial thrombophlebitis. *Vasa - Journal of Vascular Diseases*, 38: 167-170.

Not in PICO

Mowatt, G., Scotland, G., Boachie, C., Cruickshank, M., Ford, J. A., Fraser, C., Kurban, L., Lam, T. B., Padhani, A. R., Royle, J., Scheenen, T. W. & Tassie, E. (2001) The diagnostic accuracy and cost-effectiveness of magnetic resonance spectroscopy and enhanced magnetic resonance imaging techniques in aiding the localisation of prostate abnormalities for biopsy: a systematic review and economic evaluation. *Health technology assessment (Winchester, England)*, 17: vii-281.

Not in PICO

Naslund, M. J., Gilseman, A. W., Midkiff, K. D., Bown, A., Wolford, E. T. & Wang, J. (2007) Prevalence of lower urinary tract symptoms and prostate enlargement in the primary care setting. *International Journal of Clinical Practice*, 61: 1437-1445.

Not in PICO

Neal, R. D., Allgar, V. L., Ali, N., Leese, B., Heywood, P., Proctor, G. & Evans, J. (2007) Stage, survival and delays in lung, colorectal, prostate and ovarian cancer: Comparison between diagnostic routes. *British Journal of General Practice*, 57: 212-219.

Not in PICO

Neal, R. D., Pasterfield, D., Wilkinson, C., Hood, K., Makin, M. & Lawrence, H. (2008) Determining patient and primary care delay in the diagnosis of cancer - lessons from a pilot study of patients referred for suspected cancer. *BMC Family Practice*, 9.

Not in PICO

Neheman, A., Shotland, Y., Metz, Y. & Stein, A. (1988) [Screening for early detection of prostate cancer (first experience in Israel)]. [Hebrew]. *Harefuah*, 140: 4-10.

Not in PICO

Neppi-Huber, C., Zappa, M., Coebergh, J. W., Rapiti, E., Rachtan, J., Holleczeck, B., Rosso, S., Aareleid, T., Brenner, H., Gondos, A. & EUNICE Survival Working Group (2012) Changes in incidence, survival and mortality of prostate cancer in Europe and the United States in the PSA era: additional diagnoses and avoided deaths. *Annals of Oncology*, 23: 1325-1334.

Not in PICO

Ng, Y. H., Seeley, J. P. & Smith, G. (2013) Haemospermia as a presenting symptom: Outcomes of investigation in 300 men. *Surgeon-Journal of the Royal Colleges of Surgeons of Edinburgh and Ireland*, 11: 35-38.

Not in PICO

Ng, Y. H., Seeley, J. P. & Smith, G. (2013) Haemospermia as a presenting symptom: outcomes of investigation in 300 men. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 11: 35-38.

Not in PICO

Ngo, T. C., Turnbull, B. B., Lavori, P. W. & Presti, J. C. (2011) The Prostate Cancer Risk Calculator From the Prostate Cancer Prevention Trial Underestimates the Risk of High Grade Cancer in Contemporary Referral Patients. *Journal of Urology*, 185: 483-487.

Not in PICO

Nielsen, T. N., Hansen, R. P. & Vedsted, P. (2010) [Symptom presentation in cancer patients in general practice]. [Danish]. *Ugeskrift for Laeger*, 172: 2827-2831.

Not in PICO

Numao, N., Yoshida, S., Komai, Y., Ishii, C., Kagawa, M., Kijima, T., Yokoyama, M., Ishioka, J., Matsuoka, Y., Koga, F., Saito, K., Masuda, H., Fujii, Y., Kawakami, S. & Kihara, K. (2013) Usefulness of pre-biopsy multiparametric magnetic resonance imaging and clinical variables to reduce initial prostate biopsy in men with suspected clinically localized prostate cancer. *Journal of Urology*,

190: 502-508.

Not in PICO

Nunes, J., Naymark, M., Sauer, L., Muhammad, A., Keun, H., Sturge, J., Stebbing, J., Waxman, J. & Pchejetski, D. (2012) Circulating sphingosine-1-phosphate and erythrocyte sphingosine kinase-1 activity as novel biomarkers for early prostate cancer detection. *British Journal of Cancer*, 106: 909-915.

Not in PICO

Nunez, C., Angulo, J., Sanchez-Chapado, M., Alonso, S., Portillo, J. A. & Villavicencio, H. (2012) [Variability of the urological clinical practice in prostate cancer in Spain]. [Spanish]. *Actas Urologicas Espanolas*, 36: 333-339.

Not in PICO

O'Leary, M. P., Gee, W. F., Holtgrewe, H. L., Blute, M. L., Cooper, T. P., Miles, B. J., Nellans, R. E., Thomas, R., Painter, M. R., Meyer, J. J., Naslund, M. J., Gormley, E. A., Blizzard, R. & Fenninger, R. B. (2000) 1999 American Urological Association Gallup Survey: changes in physician practice patterns, treatment of incontinence and bladder cancer, and impact of managed care. *Journal of Urology*, 164: 1311-1316.

Not in PICO

O'Rourke, M. E. (2000) Urinary incontinence as a factor in prostate cancer treatment selection. *Journal of wound, ostomy, and continence nursing : official publication of The Wound, Ostomy and Continence Nurses Society / WOCN*, 27: 146-154.

Narrative review

Obertova, Z., Brown, C., Hodgson, F. & Lawrenson, R. (2013) What do men say about diagnostic pathways? From prostate-specific antigen (PSA) test to prostate cancer. *BJU International*, 112: 14.

Not in PICO

Oh, J. H., Lotan, Y., Gurnani, P., Rosenblatt, K. P. & Gao, J. (2009) Prostate cancer biomarker discovery using high performance mass spectral serum profiling. *Computer Methods & Programs in Biomedicine*, 96: 33-41.

Not in PICO

Ok, J. H., Meyers, F. J. & Evans, C. P. (2005) Medical and surgical palliative care of patients with urological malignancies. [Review] [48 refs]. *Journal of Urology*, 174: t-82.

Narrative review

Onur, M. R., Turgut, A. T. & Dogra, V. (2014) Ultrasound-guided biopsy of the prostate: New updates. *Ultrasound Clinics*, 9: 81-94.

Narrative review

Opalinska, E., Stoma, F., Michalak, A., Latalski, M. & Goniewicz, M. (2002) Benign prostatic hyperplasia, prostate cancer and other prostate diseases diagnosed as a result of screening procedure among 1,004 men in the Lublin district. *Annales Universitatis Mariae Curie-Skłodowska - Sectio d - Medicina*, 57: 493-501.

Not in PICO

Oranusi, C. K., Mbieri, U. T., Oranusi, I. O. & Nwofor, A. M. E. (2012) Prostate cancer awareness and screening among male public servants in Anambra state, Nigeria. *African Journal of Urology*, 18: 72-74.

Not in PICO

Orom, H., Underwood, W., Homish, D. L., Homish, G. G., Brasel, A. & Nelson, C. J. (2012) Treatment decision-making self-efficacy predicts better quality of life in prostate cancer patients managed with active surveillance. *Psycho-Oncology*, 21: 19.

Not in PICO

Paneesha, S., McManus, A., Arya, R., Scriven, N., Farren, T., Nokes, T., Bacon, S., Nieland, A., Cooper, D., Smith, H., O'Shaughnessy, D. & Rose, P. (2010) Frequency, demographics and risk (according to tumour type or site) of cancer-associated thrombosis among patients seen at outpatient DVT

- clinics. *Thrombosis and Haemostasis*, 103: 338-343.
Not in PICO (referred patients)
- Paparella, S. & Rocco, F. (2010) Degarelix: A new GnRH antagonist in the treatment of prostate cancer. [Italian]. *Geriatric and Medical Intelligence*, 19: 119-124.
Not in PICO
- Paranhos, M., Antunes, A., Andrade, E., Freire, G. & Srougi, M. (2009) The prevalence of erectile dysfunction among Brazilian men screened for prostate cancer. *BJU International*, 104: 1130-1133.
Not in PICO
- Parsons, B. A., Evans, S. & Wright, M. P. (2009) Prostate cancer and urinary incontinence. [Review] [70 refs]. *Maturitas*, 63: 323-328.
Narrative review
- Payne, H. & Cornford, P. (2011) Prostate-specific antigen: an evolving role in diagnosis, monitoring, and treatment evaluation in prostate cancer. [Review]. *Urologic Oncology*, 29: 593-601.
Narrative review
- Perez, C. E., Simonet Aineto, P. J., Vargas, B. C., Castells, E. M. & Parellada, E. N. (2000) [The diagnostic situation with prostatic cancer in primary care]. [Spanish]. *Atencion Primaria*, 25: 137-141.
Not in PICO
- Pieczyrak, R., Kotulska, A. & Kucharz, E. (2010) Neoplasia in patients with symptoms of inflammatory connective tissue diseases. *Internal Medicine Journal*, 40: 150.
Not in PICO
- Pinedo, H. M. (2003) Thrombosis, prevalence and new evidence on current perceptions of risk. *Cancer Treatment Reviews*, 29: 3-5.
Not in PICO
- Plawker, M. W., Fleisher, J. M., Nitti, V. W. & Macchia, R. J. (1996) Primary care practitioners: An analysis of their perceptions of voiding dysfunction and prostate cancer. *Journal of Urology*, 155: 601-604.
Not in PICO
- Potvin, K. & Winquist, E. (2008) Hormone-refractory prostate cancer: a primer for the primary care physician. *Canadian Journal of Urology*, 15: 14-20.
Narrative review
- Prystajeky, M., Lang, E., Wang, D., Lonergan, K., Simon, J., Sinnarajah, A., Martin, T. L. W., Murray, A., Hagen, N., Waller, A., Bultz, B., Carlson, L., Groff, S., McRae, A. & Thomas, B. (2012) Emergency department utilization by adult cancer patients: A prospective cohort study. *Canadian Journal of Emergency Medicine*, 14: S7-S8.
Not in PICO
- Quinlan, M. R., O'Daly, B. J., O'Brien, M. F., Gardner, S., Lennon, G., Mulvin, D. W. & Quinlan, D. M. (2009) The value of appropriate assessment prior to specialist referral in men with prostatic symptoms. *Irish Journal of Medical Science*, 178: 281-285.
Not in PICO
- Ramachandran, S., Foster, M. C., Thomas, D. R., Roalfe, A. K. & Hall, R. A. (1998) An audit of prostate-specific antigen and clinical symptoms in general practice. *Postgraduate Medical Journal*, 74: 28-32.
Not in PICO (no symptoms per patient reported; population?)
- Rana, A., Chisholm, G. D., Rashwan, H. M., Salim, A., Merrick, M. V. & Elton, R. A. (1994) Symptomatology of metastatic prostate cancer: prognostic significance. *British Journal of Urology*, 73: 683-686.
Not in PICO

- Rao, G. & Card, A. (2014) An unusual case of acute back pain. *Journal of General Internal Medicine*, 29: S312-S313.
Not in PICO
- Rees, J., Waldron, D., O'Boyle, C., Ewings, P. & MacDonagh, R. (2003) Prospective vs retrospective assessment of lower urinary tract symptoms in patients with advanced prostate cancer: the effect of 'response shift'. *BJU International*, 92: 703-706.
Not in PICO
- Reggio, E., de, B. J., Jr., Junqueira, R. G., Timm, O., Jr., Sette, M. J., Sansana, V. & Gomes, C. M. (2007) Correlation between lower urinary tract symptoms and erectile dysfunction in men presenting for prostate cancer screening. *International Journal of Impotence Research*, 19: 492-495.
Not in PICO
- Rodriguez, L. A. G., Merino, M. E. M., Gonzales, E. L. M. & Roehrborn, C. G. (2009) The health improvement network (THIN) database: Focused safety study of acute urinary retention (AUR) in men. *European Urology, Supplements*, 8: 236.
Not in PICO
- Roehrborn, C. G. (2011) Male lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH). [Review]. *Medical Clinics of North America*, 95: 87-100.
Narrative review
- Rohayem, J. & Kliesch, S. (565) [Androgen deprivation therapy in prostate cancer. Indication and systemic consequences]. [German]. *Urologe (Ausg.A)*, 51: 557-564.
Narrative review
- Rosenberg, M. T., Miner, M. M., Riley, P. A. & Staskin, D. R. (2010) STEP: simplified treatment of the enlarged prostate. [Review]. *International Journal of Clinical Practice*, 64: 488-496.
Narrative review
- Roth, A. J., Nelson, C., Rosenfeld, B., Scher, H., Slovin, S., Morris, M., O'Shea, N., Arauz, G. & Breitbart, W. (2010) Methylphenidate for fatigue in ambulatory men with prostate cancer. *Cancer*, 116: 5102-5110.
Not in PICO
- Rothke, M., Blondin, D., Schlemmer, H. P. & Franiel, T. (2013) [PI-RADS classification: structured reporting for MRI of the prostate]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 185: 253-261.
Not in PICO
- Ruiz-Torrejon, A., Ramos-Monserrat, M. & Llobera-Canaves, J. (2006) [Family practice and diagnosis of cancer]. [Spanish]. *Atencion Primaria*, 37: 16-21.
Not in PICO
- Sanchez-Martinez, L. C., Paredes-Solis, C. A., Hernandez-Ordonez, O. F. & Sanchez-Ruvalcaba, I. R. (2013) [Prostate-specific antigen. The role in the prostate cancer diagnosis]. [Spanish]. *Revista Medica del Instituto Mexicano del Seguro Social*, 51: 124-126.
Narrative review
- Sausville, J. & Naslund, M. (2010) Benign prostatic hyperplasia and prostate cancer: an overview for primary care physicians. [Review]. *International Journal of Clinical Practice*, 64: 1740-1745.
Narrative review
- Saw, S. & Aw, T. C. (2000) Age-related reference intervals for free and total prostate-specific antigen in a Singaporean population. *Pathology*, 32: 245-249.
Narrative review
- Schiff, G. D. (2014) Diagnosis and diagnostic errors: Time for a new paradigm. *BMJ Quality and Safety*, 23: 1-3.
Not in PICO
- Schmid, M., Hansen, J., Rink, M., Fisch, M. & Chun, F. (2013) The development of nomograms for stratification of men at risk of prostate cancer prior to prostate biopsy. *Biomarkers in Medicine*, 7:

- 843-850.
Narrative review
- Seamonds, B., Whitaker, B. & Yang, N. (1986) Evaluation of prostate-specific antigen and prostatic acid phosphatase as prostate cancer markers. *Urology*, 28: 472-479.
Not in PICO
- Seftel, A. (2005) Correlation between LUTS (AUA-SS) and erectile dysfunction (SHIM) in an age-matched racially diverse male population: data from the prostate cancer awareness week (PCAW). *Journal of Urology*, 174: 1940.
Not in PICO
- Shahab, A. A., Soebadi, D. M., Djatisoesanto, W., Hardjowijoto, S., Soetojo, S. & Hakim, L. (2013) Prostate-specific antigen and prostate-specific antigen density cutoff points among Indonesian population suspected for prostate cancer. *Prostate International*, 1: 23-30.
Not in PICO
- Shapley, M., Mansell, G., Jordan, J. L. & Jordan, K. P. (2010) Positive predictive values of $\geq 5\%$ in primary care for cancer: systematic review. [Review]. *British Journal of General Practice*, 60: e366-e377.
Systematic review. Relevant included studies are already included in our review.
- Shariat, S. F., Scherr, D. S., Gupta, A., Bianco, F. J., Jr., Karakiewicz, P. I., Zeltser, I. S., Samadi, D. B. & Akhavan, A. (2011) Emerging biomarkers for prostate cancer diagnosis, staging, and prognosis. [Review]. *Archivos Espanoles de Urologia*, 64: 681-694.
Narrative review
- Sharp, V. J., Takacs, E. B. & Powell, C. R. (2010) Prostatitis: Diagnosis and treatment. *American Family Physician*, 82: 397-406.
Narrative review
- Shinotoh, K. & Takigawa, H. (1999) [Voiding condition in elderly males examined prostate cancer screening in total health check and the effect of subjective urinary symptoms on quality of life]. [Japanese]. *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology*, 90: 32-40.
Not in PICO
- Siguel, E. Balancing the harms and benefits of early detection of prostate cancer. [References]. *Cancer* 117[15], 3533-3534. 2011.
Comment
- Sing, R. I. & Singal, R. K. (2012) What is significant hematuria for the primary care physician? *Canadian Journal of Urology*, 19: Suppl-41.
Narrative review
- Skillinge, D., Langan, R., Krafczyk, M. & McGarey, M. (2011) Benign prostate hyperplasia: A clinical review. *Osteopathic Family Physician*, 3: 182-186.
Narrative review
- Sladden, M. J., Hughes, A. M., Hirst, G. H. & Ward, J. E. (2000) A community study of lower urinary tract symptoms in older men in Sydney, Australia. *Australian & New Zealand Journal of Surgery*, 70: 322-328.
Not in PICO
- Smith, S. D. & Birtwhistle, R. (2012) Exploring patient perceptions of PSA screening for prostate cancer: Risks, effectiveness, and importance. *Canadian Family Physician*, 58: e502-e507.
Not in PICO
- Sohn, M. W., Zhang, H., Taylor, B., Fischer, M., Yano, E., Saigal, C., Wilt, T. & the Urologic Diseases in America Project (2006) Prevalence and trends of selected urologic conditions for VA healthcare users. *BMC Urology*, 6: 30.
Not in PICO
- Song, J. M., Kim, C. B., Chung, H. C. & Kane, R. L. (2005) Prostate-specific antigen, digital rectal examination and transrectal ultrasonography: A meta-analysis for this diagnostic triad of prostate

- cancer in symptomatic Korean men. *Yonsei Medical Journal*, 46: 414-424.
Not in PICO
- Sorensen, F. B. & Marcussen, N. (1989) Non-specific granulomatous prostatitis. [Danish]. *Ugeskrift for Laeger*, 151: 287-290.
Narrative review
- Sorum, P. C., Shim, J., Chasseigne, G., Bonnin-Scaon, S., Cogneau, J. & Mullet, E. (2003) Why do primary care physicians in the United States and France order prostate-specific antigen tests for asymptomatic patients? *Medical Decision Making*, 23: 301-313.
Not in PICO
- Sothilingam, S., Sundram, M., Malek, R. & Sahabuddin, R. M. (2010) Prostate cancer screening perspective, Malaysia. *Urologic Oncology*, 28: 670-672.
Not in PICO
- Spain, P., Carpenter, W. R., Talcott, J. A., Clark, J. A., Do, Y. K., Hamilton, R. J., Galanko, J. A., Jackman, A. & Godley, P. A. (2008) Perceived family history risk and symptomatic diagnosis of prostate cancer: the North Carolina Prostate Cancer Outcomes study. *Cancer*, 113: 2180-2187.
Not in PICO
- Starreveld, J. S., Wolters, R. J., Romeijnders, A. C., Pijnenborg, L. & Goudswaard, A. N. (2005) [Summary of the practice guideline 'Lower urinary-tract symptoms in middle-aged and elderly men' (second revision) from the Dutch College of General Practitioners]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 149: 1568-1572.
Narrative review
- Stefanovic, K. B., Gregg, P. C. & Soung, M. (2009) Evaluation and treatment of hematospermia. *American Family Physician*, 80: 1421-1427.
Narrative review
- Sturgeon, C. M., Duffy, M. J., Stenman, U. H., Lilja, H., Brunner, N., Chan, D. W., Babaian, R., Bast, R. C., Jr., Dowell, B., Esteva, F. J., Haglund, C., Harbeck, N., Hayes, D. F., Holten-Andersen, M., Klee, G. G., Lamerz, R., Looijenga, L. H., Molina, R., Nielsen, H. J., Rittenhouse, H., Semjonow, A., Shih, I., Sibley, P., Soletormos, G., Stephan, C., Sokoll, L., Hoffman, B. R., Diamandis, E. P. & National Academy of Clinical Biochemistry (2008) National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers. *Clinical Chemistry*, 54: e11-e79.
Narrative review
- Tanguay, S., Awde, M., Brock, G., Casey, R., Kozak, J., Lee, J., Nickel, J. C. & Saad, F. (2009) Diagnosis and management of benign prostatic hyperplasia in primary care. *Cuaj-Canadian Urological Association Journal*, 3: S92-S100.
Narrative review
- Tasian, G. E., Cooperberg, M. R., Cowan, J. E., Keyashian, K., Greene, K. L., Daniels, N. A., Carroll, P. R. & Chan, J. M. (2012) Prostate specific antigen screening for prostate cancer: knowledge of, attitudes towards, and utilization among primary care physicians. *Urologic Oncology*, 30: 155-160.
Not in PICO
- Thiruchelvam, N. (2014) Benign prostatic hyperplasia. *Surgery (United Kingdom)*, 32: 314-322.
Narrative review
- Tohfe, M., Baki, S. A., Saliba, W., Ghandour, F., Ashou, R., Ghazal, G., Bahous, J. & Chamseddine, N. (2008) Metastatic prostate adenocarcinoma presenting with pulmonary symptoms: a case report and review of the literature. *Cases journal*, 1: 316.
Not in PICO
- Tsang, K. K. & Garraway, W. M. (1993) Impact of benign prostatic hyperplasia on general well-being of men. *Prostate*, 23: 1-7.
Not in PICO

- Tscholl, R. (1989) [Check-ups from the urologic viewpoint]. [German]. *Therapeutische Umschau*, 46: 378-383.
Narrative review
- Turner, J. A., Ciol, M. A., Von Korff, M. & Berger, R. (2005) Health concerns of patients with nonbacterial prostatitis/pelvic pain. *Archives of Internal Medicine*, 165: 1054-1059.
Not in PICO
- Umehara, T., Kumamoto, Y., Mikuma, N., Yamaguchi, Y., Tsukamoto, T., Miura, T., Watanabe, H. & Ooe, H. (1990) [Mass screening of prostate in Shiribeshi area in Hokkaido--incidence and clinical symptoms of benign prostatic hypertrophy and prostatic carcinoma]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica*, 36: 415-423.
Not in PICO
- Van der Meer, S., Kollen, B. J., Hirdes, W. H., Steffens, M. G., Hoekstra-Weebers, J. E., Nijman, R. M. & Blanker, M. H. (2013) Impact of the European Randomized Study of Screening for Prostate Cancer (ERSPC) on prostate-specific antigen (PSA) testing by Dutch general practitioners. *BJU International*, 112: 26-31.
Not in PICO
- Van Gils, M. P. M. Q. & Mulders, P. F. A. (2005) The standard of the Dutch College of General Practitioners on micturition disorder in elderly men. [Dutch]. *Nederlands Tijdschrift voor Urologie*, 13: 207-214.
Guideline
- Vasdev, N. & Thorpe, A. C. (2011) Has the introduction of the '2 week rule' in the UK led to an earlier diagnosis of urological malignancy? *ecancermedicalscience*, 5.
Not in PICO
- Vickers, A. J. (2013) Counterpoint: Prostate-specific antigen velocity is not of value for early detection of cancer. *Journal of the National Comprehensive Cancer Network*, 11: 286-290.
Narrative review
- Voskanyan, G. A., Glybochko, P. V., Vinarov, A. Z., Korobkin, A. S., Ternovoy, S. K. & Shariya, M. A. (2013) Anticipating metabolic changes: Magnetic resonance spectroscopy as a diagnostic tool for early detection of prostate cancer. *European Urology, Supplements*, 12: 149-150.
Not in PICO
- Wagg, A., Harari, D., Lowe, D. & Potter, J. (2011) Use of the dre in male continence/luts assessment; a dying art? Data from a national audit. *Neurourology and Urodynamics*, 30: 993-994.
Not in PICO
- Walker, N. A. & Challacombe, B. (2013) Managing epididymo-orchitis in general practice. *Practitioner*, 257: 21-25.
Narrative review
- Walz, J., Suardi, N., Hutterer, G. C., Perrotte, P., Gallina, A., Benard, F., Valiquette, L., McCormack, M., Graefen, M., Montorsi, F. & Karakiewicz, P. I. (2008) Lower urinary tract symptoms affect one-third of men in a prostate cancer screening population. *Journal of Endourology*, 22: 369-376.
Not in PICO
- Warshaw, G. (2009) Providing quality primary care to older adults. *Journal of the American Board of Family Medicine: JABFM*, 22: 239-241.
Comment
- Wayte, N., Da, S. L., Chenevix-Trench, G. & Lakhani, S. R. (2008) What's in a cancer syndrome? Genes, phenotype and pathology. *Pathology*, 40: 247-259.
Narrative review
- Webb, V. & Holmes, A. (2000) Urological cancers: do early detection strategies exist? *BJU International*, 86: 996-1000.
Not in PICO
- Wei, J. T., Dunn, R. L., Litwin, M. S., Sandler, H. M. & Sanda, M. G. (2000) Development and validation of the expanded prostate cancer index composite (EPIC) for comprehensive assessment of

- health-related quality of life in men with prostate cancer. *Urology*, 56: 899-905.
Not in PICO
- Wei, J. T., Calhoun, E. & Jacobsen, S. J. (2005) Urologic diseases in America project: Benign prostatic hyperplasia. *Journal of Urology*, 173: 1256-1261.
Not in PICO
- Weight, C. J., Kim, S. P., Jacobson, D. J., McGree, M. E., Boorjian, S. A., Thompson, R. H., Leibovich, B. C., Karnes, R. J. & St, S. J. (2013) The effect of benign lower urinary tract symptoms on subsequent prostate cancer testing and diagnosis. *European Urology*, 63: 1021-1027.
Not in PICO
- Whelan, T. J., Mohide, E. A., Willan, A. R., Arnold, A., Tew, M., Sellick, S., Gafni, A. & Levine, M. N. (1997) The supportive care needs of newly diagnosed cancer patients attending a regional cancer center. *Cancer*, 80: 1518-1524.
Not in PICO
- Williams, R. M. & Naz, R. K. (2010) Novel biomarkers and therapeutic targets for prostate cancer. [Review] [43 refs]. *Frontiers in Bioscience*, 2: 677-684.
Narrative review
- Wirth, M. P., Froschermaier, S. E. & Pilarsky, C. P. (1995) Early detection of prostate cancer. [German]. *Onkologie*, 18: 56-60.
Narrative review
- Wolters, R., Wensing, M., Klomp, M., Van Weel, C. & Grol, R. (2004) Shared care and the management of lower urinary tract symptoms. *BJU International*, 94: 1287-1290.
Not in PICO
- Wolters, R., Wensing, M., Klomp, M., Lagro-Jansen, T., Weel, C. & Grol, R. (2005) Effects of distance learning on clinical management of LUTS in primary care: a randomised trial. *Patient Education & Counseling*, 59: 212-218.
Not in PICO
- Wong, J. G. & Feussner, J. R. (1993) Screening for prostate cancer. Does it make a difference? *North Carolina Medical Journal*, 54: 568-571.
Not in PICO
- Wong, M. Y. C. (2011) Update of LUTS & BPH. Guidelines for the family physician in the management of benign prostatic hyperplasia (BPH). *Journal of Men's Health*, 8: S110-S111.
Narrative review
- Yafi, F. A., Aprikian, A. G., Tanguay, S. & Kassouf, W. (2010) Practice and referral patterns among primary care physicians with regards to the use of 5-alpha reductase inhibitors and BPH. *Journal of Urology*, 183: e690.
Not in PICO
- Yakimovapolyzou, V., Georgiou, S., Soukouli, P., Bandis, E. & Babaliaris, K. (2011) Clinical findings and grade of malignancy at the time of diagnosis of prostate cancer. *International Journal of Cancer*, 128: 47.
Not in PICO
- Yatani, R., Yabana, T. & Soga, T. (1985) Atypical hyperplasia and latent carcinoma of the prostate as an early stage of carcinoma. [Japanese]. *Gan to Kagaku Ryoho*, Cancer: 714-719.
Not in PICO
- Yazici, C. M. & Dogan, C. (2014) Can Non-Urological Doctors Play a Role in Early Prostate Cancer Detection? *Urology Journal*, 11: 1429-1434.
Not in PICO
- You, J., Cozzi, P., Walsh, B., Willcox, M., Kearsley, J., Russell, P. & Li, Y. (2010) Innovative biomarkers for prostate cancer early diagnosis and progression. [Review] [127 refs]. *Critical Reviews in Oncology-Hematology*, 73: 10-22.
Narrative review

Zaenker, P. & Ziman, M. R. (2013) Serologic autoantibodies as diagnostic cancer biomarkers--a review. *Cancer Epidemiology, Biomarkers & Prevention*, 22: 2161-2181.

Narrative review

Zeng, L. A., Zhang, L. Y., Culleton, S., Jon, F., Holden, L., Kwong, J., Khan, L., Tsao, M., Danjoux, C., Sahgal, A., Barnes, E. & Chow, E. (2011) Edmonton Symptom Assessment Scale as a Prognosticative Indicator in Patients with Advanced Cancer. *Journal of Palliative Medicine*, 14: 337-342.

Not in PICO

Zucca, A. C., Boyes, A. W., Linden, W. & Girgis, A. (2012) All's well that ends well? Quality of life and physical symptom clusters in long-term cancer survivors across cancer types. *Journal of Pain and Symptom Management*, 43: 720-731.

Not in PICO

Review question:

Which investigations of symptoms of suspected prostate cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

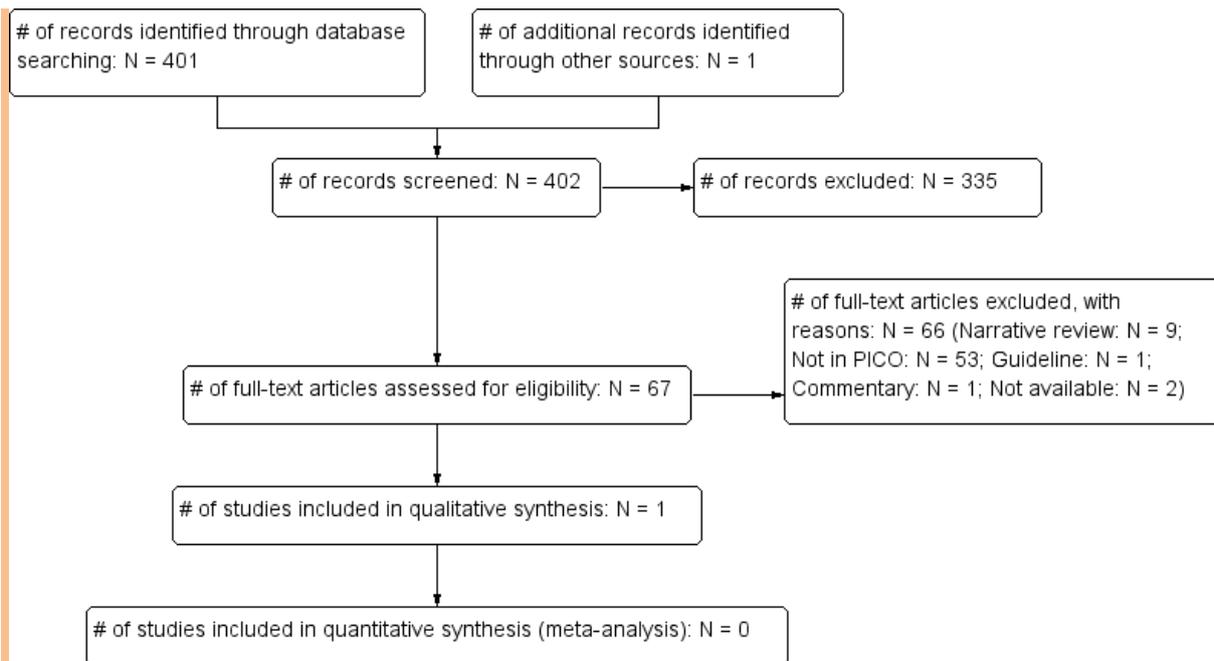
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	3732	59	04/02/2013
<i>Premedline</i>	1980-2013	179	22	04/02/2013
<i>Embase</i>	1980-2013	1695	122	04/02/2013
<i>Cochrane Library</i>	1980-2013	139	15	31/01/2013
<i>Psychinfo</i>	1980-2013	73	3	04/02/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	491	99	31/01/2013
<i>Biomed Central</i>	1980-2013	695	2	31/01/2013

Total References retrieved (after de-duplication): 317

Update Search

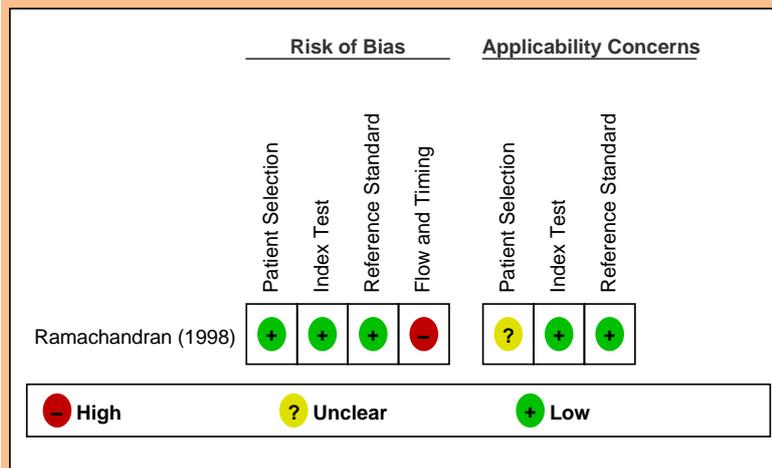
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-26/08/2014	189	21	26/08/2014
<i>Premedline</i>	2013-26/08/2014	196	43	26/08/2014
<i>Embase</i>	2013-26/08/2014	179	42	26/08/2014
<i>Cochrane Library</i>	2013-26/08/2014	38	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-26/08/2014	76	14	26/08/2014

Total References retrieved (after de-duplication): 84



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included study in the figure below. The main risk of bias in this study pertains to the ca 20% of missing data in this study. It is not possible to ascertain whether these data are missing in a systematic manner and whether they are likely to substantially influence the test accuracy estimates provided by this study. The only applicability concern identified for this study concerns the underspecification of the patients, that is, it is not clear from the study whether all the patients were symptomatic patients presenting to primary care, and to the extent they are not from this patient group, the applicability to the current guideline is limited.



Study results

Table 1: Prostate cancer: PSA

Study	Test	Prevalence	Sensitivity (95% CI)	Specificity (95% CI)	Other results
Ramacha	PSA 4 ng/ml	54/582	88.9%	70%	False negativity rate = 11.1%

ndran (1998)		(NR)	(NR)	
	PSA 5 ng/ml	88.9% (NR)	78% (NR)	False negativity rate = 11.1%
	PSA 6 ng/ml	87% (NR)	82.6% (NR)	False negativity rate = 13%
	PSA 7 ng/ml	83.3% (NR)	86% (NR)	False negativity rate = 16.7%
	PSA 8 ng/ml	83.3% (NR)	88.3% (NR)	False negativity rate = 16.7%
	PSA 9 ng/ml	83.3% (NR)	89% (NR)	False negativity rate = 16.7%
	PSA 10 ng/ml	77.8% (NR)	90.2% (NR)	False negativity rate = 22.2%

No evidence was found for MRI.

Evidence statement(s):

PSA testing (1 study, N = 582) conducted in patients presenting in a primary/hospital care setting is associated with sensitivities that ranged from 77.8-88.9%, specificities that ranged from 70-90.2% and false negativity rates that ranged from 11.1-22.2% for prostate cancer. The study was associated with one bias and one applicability concern (see also Table 1).

Evidence tables

Ramachandran (1998)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Audit of laboratory database, England.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 582. <i>No further detail reported.</i> <u>Inclusion criteria:</u> All patients who had a prediagnostic PSA estimation between August 1991 and December 1992 in the laboratory "Telepath" database. <i>Unclear if they are all symptomatic and if they are all from primary care.</i> <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary/hospital (?) care, England.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	PSA

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up for min 18 months using GP, Family Services Health Authority, hospice and hospital records
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 721 patients met the inclusion criteria. However, complete data were only available for 582 patients.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Unclear
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	2-by-2 tables cannot be extracted

References

Included studies

Ramachandran, S., Foster, M. C., Thomas, D. R., Roalfe, A. K., and Hall, R. A. An audit of prostate-specific antigen and clinical symptoms in general practice. *Postgraduate Medical Journal* 74[867], 28-32. 1998.

Excluded studies (with excl reason)

(2001) American cancer society guidelines for the early detection of cancer. *Ca-A Cancer Journal for Clinicians*, 51: 87-88.

Not in PICO

(2005) Prostate specific antigen (PSA) near patient testing for diagnosis and management of prostate cancer (Structured abstract). *Health Technology Assessment Database.*, 49.

Not in PICO

Aarnink, R. G., De La Rosette, J. J. M. C., Witjes, J. A., Debruyne, F. M. J. & Wijkstra, H. (1997) Diagnosis of prostate cancer in patients with prostate related problems in urological clinic:

- Current status and future developments. [Dutch]. *Tijdschrift Voor Gerontologie En Geriatrie*, 28: 264-271.
Not in PICO
- Aarnink, R. G., de la Rosette, J. J., Witjes, J. A., Debruyne, F. M. & Wijkstra, H. (1997) [Diagnosis of prostate cancer in urination disorders in urological practice: current status and future developments]. [Dutch]. *Tijdschrift Voor Gerontologie En Geriatrie*, 28: 264-271.
Not in PICO
- Abul, F. T., Arun, N., Abu-Assi, M. A. & Asbeutah, A. M. (2007) Transrectal ultrasound guided biopsy for detecting prostate cancer: can random biopsies be reduced using the 4-dimensional technique? *International Urology & Nephrology*, 39: 517-524.
Not in PICO
- Acino, S. & Resnick, M. I. (1988) Office urologic ultrasound. [Review] [34 refs]. *Urologic Clinics of North America*, 15: 577-588.
Narrative review
- Affifi, A. H. A. A., Etaby, A. N., Ahmad, M. A. Y. & Farghaly, Y. T. (2013) Value of diffusion weighted magnetic resonance imaging in the prediction of cancer prostate. *Alexandria Journal of Medicine*, 49: 57-66.
Not in PICO
- Ahmad, S., Cao, R., Varghese, T., Bidaut, L. & Nabi, G. (2013) Transrectal quantitative shear wave elastography in the detection and characterisation of prostate cancer. *Surgical Endoscopy and Other Interventional Techniques*, 27: 3280-3287.
Not in PICO
- Ahmed, M. (2011) Prostate cancer diagnosis in a resource-poor setting: the changing role of digital rectal examination. *Tropical Doctor*, 41: 141-143.
Not in PICO
- Akbayir, S., Muslu, N., Erden, S. & Bozlu, M. (2014) Detection of micrnas' diagnostic value in prostate cancer patients with 2-10 ng/ml prostate specific antigen (PSA) levels. *Clinical Chemistry and Laboratory Medicine*, 52: S359.
Not in PICO
- Ali, M. & Rashwan, H. (2010) Impact of lower urinary tract symptoms on sexual function in patients with symptomatic prostatic disorders. *Urology*, 76: S53.
Not in PICO
- Alioune, S., Yaya, S., Ibou, T., Boubacar, F., Babacar, D., Ahmed, F. P., Mamadou, B., Meissa, T. & Assane, D. B. (2011) Early detection of prostate cancer in Senegalese men 40-50years old. [French]. *Progres En Urologie*, 21: 260-263.
Not in PICO
- Allard, C. B., Dason, S., Lusic, J. & Kapoor, A. (2012) Prostate cancer screening: Attitudes and practices of family physicians in Ontario. *Canadian Urological Association Journal*, 6: 188-193.
Not in PICO
- Allepuz Losa, C. A., Gil Sanz, M. J., Gonzalvo, I. A., Blas, M. M., Sanz Velez, J. I. & Rioja Sanz, L. A. (1997) The early diagnosis of prostate cancer in a selected population. The usefulness of PSAD, PSAD ad. and age-adjusted PSA in patients with a PSA between 4-10 ngr./ml. [Spanish]. *Actas Urologicas Espanolas*, 21: 344-353.
Not in PICO
- Allhoff, E. P., Liedke, S. G., Gonnermann, O., Stief, C. G., Jonas, U. & Schneider, B. (1993) Efficient pathway for early detection of prostate cancer concluded from a 5-year prospective study. *World Journal of Urology*, 11: 201-205.
Not in PICO
- Andruss, C. M., Dinella, T. J., Macpherson, D. S., Pietropaoli, A. P., Tsao, L., Wachman, J., Whittle, J., Cameron, M. L., Hines, J. M., Mcneil, M., Conigliaro, J., Good, C. B., Labkoff, S. E., Cohen, M. G., Deswal, A., Gulinson, M. D., Hankin, L. M., Heinle, M. S., Higham, C. J., Hoffmann, E. L., Hunn, R.

- H., Hunter, T. M., Kam, L. W., Leon, R. J., Lilie, S., Lipinski, J. L., Marr, L. A., Mccullum, K. J., Michelson, G. C., Nace, D. A., Orourke, D. J., Osborn, J. L., Pendergast, W. J., Provencano, M. A., Ramsey, L. C., Reardon, L. C., Sandberg, M. L., Szawaluk, J. J., Vancleeff, S., Young, M. A., Yee, E. L., Zeldin, R. K., Bushman, K. E., Richards, S. A., Balderston, V., Caldwell, K. E., Collins, M. E., Diansi, E. G., Dale, C. G., Dippl, J. M., Finikiotis, M. W., Finkel, R. G., Friedland, D. M., Gorby, R. S., Guilinger, R. A., Hally, R. J., Hammerman, S. I., Harris, J. V., Keyes, J. V., Leuzzi, R. A., Lubick, C. J., Mcguinness, M. A., Needleman, D. C., Pritchard, R. J., Rodman, M. T., Rohn, S. G., Santora, D. M., Schloss, E. J., Selvaggi, T. A., Shuster, T. D., Stein, A. R., Sweet, L. J., Tee, S. T., Thomas, A., Hogan, R. C., Kosar, E. M. & Murtaugh, T. I. (1995) Effect of Digital Rectal Examination on Serum Prostate-Specific Antigen in A Primary-Care Setting. *Archives of Internal Medicine*, 155: 389-392.
Not in PICO
- Applewhite, J. C., Matlaga, B. R., McCullough, D. L. & Hall, M. C. (2001) Transrectal ultrasound and biopsy in the early diagnosis of prostate cancer. [Review] [56 refs]. *Cancer Control*, 8: 141-150.
Not in PICO
- Arumainayagam, N., Ahmed, H. U., Moore, C. M., Freeman, A., Allen, C., Sohaib, S. A., Kirkham, A., van der Meulen, J. & Emberton, M. (2013) Multiparametric MR imaging for detection of clinically significant prostate cancer: a validation cohort study with transperineal template prostate mapping as the reference standard. *Radiology*, 268: 761-769.
Not in PICO
- Audenet, F., Roupert, M., Perrin, P. & de La, T. A. (2011) [How to select the best candidates for prostate biopsies? The role of traditional tools and contribution of new biomarkers in prostate cancer]. [French]. *Progres En Urologie*, 21: Suppl-92.
Narrative review
- Avery, K. N., Metcalfe, C., Blazeby, J. M., Lane, J. A., Neal, D. E., Hamdy, F. C. & Donovan, J. L. (2008) Prostate-specific antigen testing and prostate biopsy: are self-reported lower urinary tract symptoms and health-related quality of life associated with the decision to undergo these investigations? *Bju International*, 102: 1629-1633.
Not in PICO
- Avery, K. N. L., Blazeby, J. M., Lane, J. A., Neal, D. E., Hamdy, F. C. & Donovan, J. L. (2008) Decision-making about PSA testing and prostate biopsies: A qualitative study embedded in a primary care randomised trial. *European Urology*, 53: 1186-1193.
Not in PICO
- Babaian, R. J., Miyashita, H., Evans, R. B., Voneschenbach, A. C. & Ramirez, E. I. (1991) Early Detection Program for Prostate-Cancer - Results and Identification of High-Risk Patient Population. *Urology*, 37: 193-197.
Not in PICO (screening)
- Babaian, R. J., Dinney, C. P., Ramirez, E. I. & Evans, R. B. (1993) Diagnostic testing for prostate cancer detection: less is best. *Urology*, 41: 421-425.
Not in PICO
- Bajramovic, S. & Junuzovic, D. (2013) Detection of prostate cancer at low volume prostate and low PSA range. *European Urology, Supplements*, 12: e1286.
Not in PICO
- Barak, M., Cohen, M., Mecz, Y., Stein, A., Rashkovitzki, R., Laver, B. & Lurie, A. (1997) The additional value of free prostate specific antigen to the battery of age-dependent prostate-specific antigen, prostate-specific antigen density and velocity. *European Journal of Clinical Chemistry and Clinical Biochemistry*, 35: 475-481.
Not in PICO (147/3470 received reference test)
- Barakzai, M. A., Mubarak, M. & Kazi, J. I. (2011) Histopathological lesions in transrectal ultrasound guided biopsies of prostate in patients with raised serum prostate specific antigen: A preliminary report. *Nephro-Urology Monthly*, 3: 186-190.
Not in PICO

- Bardon, Y., De la Taille, A., Chartier-Kastler, E., Moreau, J. L., Davin, J. L., Mignard, J. P. & Coulanges, C. (2007) The prostate : how to treat this symbol of male vulnerability ? An Association Francaise d'Urologie (AFU)-IPSOS qualitative survey. *Progres En Urologie*, 17: 199-202.
Not in PICO
- Barkin, J. (2008) Management of benign prostatic hyperplasia by the primary care physician in the 21(st) century: the new paradigm. *Canadian Journal of Urology*, 15: 21-30.
Not in PICO
- Barkin, J., Rosenberg, M. T. & Miner, M. (2014) A guide to the management of urologic dilemmas for the primary care physician (PCP). *Canadian Journal of Urology*, 21: 55-63.
Narrative review
- Barrett, J. & Hamilton, W. (2005) Pathways to the diagnosis of prostate cancer in a British city. A population-based study. *Scandinavian Journal of Urology and Nephrology*, 39: 267-270.
Not in PICO
- Basky, G., Belon, R., Boutin, B., McGowan, V., Nisbet, B. & Tonita, J. (1995) Prostate specific antigen (PSA) testing (Structured abstract). *Health Technology Assessment Database*.
Not available. Unlikely to be relevant (mass screening).
- Bastide, C., Beuzeboc, P., Cormier, L., Fromont, G., Hennequin, C., Mongiat-Artus, P., Peyromaure, M., Ploussard, G., Renard-Penna, R., Rozet, F., Richaud, P., Soulie, M., Salomon, L., Azria, D., Coloby, P., Molinie, V., Ravery, V., Rebillard, X., Villers, A. & Les membres du, C. C. A. F. (2013) [CCAFU Recommendations 2013: Prostate cancer]. [French]. *Progres En Urologie*, 23: Suppl-S101.
Guideline
- Beemsterboer, P. M., Koning, H. J., Kranse, R., Trienekens, P. H., Maas, P. J. & Schröder, F. H. (2000) Prostate specific antigen testing and digital rectal examination before and during a randomized trial of screening for prostate cancer: European randomized study of screening for prostate cancer, Rotterdam. *The Journal of urology*, 164: 1216-1220.
Not in PICO
- Belas, O., Klap, J., Cornud, F., Beuvon, F., Peyromaure, M., Zerbib, M. & Delongchamps, N. B. (2012) Prebiopsy multiparametric MRI of the prostate: The end of randomized biopsies?. [French]. *Progres En Urologie*, 22: 583-589.
Not in PICO (38/71 patients had cancer)
- Billia, M., Burtnyk, M., Kuru, T., Pahernik, S., Roethke, M., Schlemmer, H. P., Romagnoli, C. & Chin, J. (2014) MRI-guided transurethral ultrasound ablation of prostate cancer: Preliminary outcomes of a phase I clinical trial. *European Urology, Supplements*, 13: e1133.
Not in PICO
- Bjurlin, M. A., Carter, H. B., Schellhammer, P., Cookson, M. S., Gomella, L. G., Troyer, D., Wheeler, T. M., Schlossberg, S., Penson, D. F. & Taneja, S. S. (2013) Optimization of initial prostate biopsy in clinical practice: sampling, labeling and specimen processing. [Review]. *Journal of Urology*, 189: 2039-2046.
Not in PICO
- Bjurlin, M. A. & Taneja, S. S. (2014) - Standards for prostate biopsy. - *Current Opinion in Urology*, 24: 155-161.
Narrative review
- Bjurlin, M. A. & Taneja, S. S. (2014) Standards for prostate biopsy. *Current Opinion in Urology*, 24: 155-161.
Narrative review
- Blanker, M. H., Klomp, M. A., van den Donk, M., van der Heide, W. K., Opstelten, W. & Burgers, J. S. (2013) [Summary of the NHG practice guideline 'Lower urinary tract symptoms in men']. [Review] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 157: A6178.
Narrative review/guideline
- Bodelle, B., Naguib, N. N., Schulz, B., Eichler, K., Muller, C., Hansmann, M. L., Hammerstingl, R., Hubner, F., Vogl, T. J. & Zangos, S. (2013) 1.5-T magnetic resonance-guided transgluteal biopsies

- of the prostate in patients with clinically suspected prostate cancer: technique and feasibility. *Investigative Radiology*, 48: 458-463.
Not in PICO
- Boman, H. & Hedelin, H. (2005) Each fifth man above the age of 50 years who is referred to a urologist has cancer. PSA is important to get the priorities right. [Swedish]. *Lakartidningen*, 102: 1519-1521.
Not in PICO
- Boman, H. & Hedelin, H. (2005) [One man of five aged 50 years and over referred to a urologist is diagnosed with cancer. PSA analysis is important for correct prioritization of the referrals]. [Swedish]. *Lakartidningen*, 102: 1519-1521.
Duplicate
- Booth, C. M., Chaudry, A. A., Smith, K. & Griffiths, K. (1996) The benefits of a shared-care prostate clinic. *British Journal of Urology*, 77: 830-855.
Not in PICO
- Bories, P.-N., Younes, P., Zerbib, M., Denjean, L., Popovici, T., Cynober, L. & Delongchamps, N. B. (2013) TMPRSS2-ERG fusion transcripts in matched urine and needle rinse material after biopsy for the detection of prostate cancer. *Clinical Chemistry*, 59: 245-251.
Not in PICO
- Bosch, J. L. H. R., Bohnen, A. M. & Groeneveld, F. P. M. J. (2004) Validity of digital rectal examination and serum prostate specific antigen in the estimation of prostate volume in community-based men aged 50 to 78 years: The Krimpen study. *European Urology*, 46: 753-759.
Not in PICO
- Bouwman, I., van der Heide, W. K., Van Der Veen, W. J. & Van der Meer, K. (2007) GPs and patients still think that lower urinary tract symptoms are an indication of prostate cancer. [Dutch]. *Huisarts en Wetenschap*, 50: 321-325.
Not in PICO
- Brackett, C., Kearing, S., Cochran, N., Tosteson, A. N. A. & Brooks, W. B. (2010) Strategies for distributing cancer screening decision aids in primary care. *Patient Education and Counseling*, 78: 166-168.
Not in PICO
- Braun, K.-P., May, M., Grassmel, Y., Fuhrer, S., Hoschke, B. & Braun, V. (2008) The general practitioner's part in the initiation of diagnostic procedures in prostate cancer. [German]. *Aktuelle Urologie*, 39: 141-146.
Not in PICO
- Braun, K. P., Brookman-Amisshah, S., May, M., Grassmel, Y., Hoschke, B. & Braun, V. (2009) The Assessment of Pathological PSA Values by the General Practitioner - Observation or Intervention? *Aktuelle Urologie*, 40: 171-174.
Not in PICO
- Brett, J., Watson, E., Hewitson, P., Bukach, C., Edwards, A., Elwyn, G. & Austoker, J. (2005) PSA testing for prostate cancer: an online survey of the views and reported practice of General Practitioners in the UK. *Bmc Family Practice*, 6: 24.
Not in PICO
- Brett, T. (2005) Low prostate specific antigen levels and normal digital rectal examination--a report on a follow up cohort in general practice. *Australian Family Physician*, 34: 301-302.
Not in PICO
- Brett, T. (2011) Prostate specific antigen. [Review][Summary for patients in Aust Fam Physician. 2011 Jul;40(7):501; PMID: 21743855]. *Australian Family Physician*, 40: 497-500.
Narrative review
- Brett, T. D. (1998) An analysis of digital rectal examination and serum-prostate-specific antigen in the early detection of prostate cancer in general practice. *Family Practice*, 15: 529-533.
Not in PICO

- Brewster, S., Tuerkeri, L., Brausi, M., Ravery, V. & Djavan, B. (2010) A prospective survey of current prostate biopsy practices among oncological urologists. *Canadian Journal of Urology*, 17: 5071-5076.
Not in PICO
- Bunting, P. S., Goel, V., Williams, J. I. & Iscoe, N. A. (1999) Prostate-specific antigen testing in Ontario: reasons for testing patients without diagnosed prostate cancer. *Canadian Medical Association Journal*, 160: 70-75.
Not in PICO
- Burin, B., Bouchot, O. & Rigaud, J. (2006) Practices of general practitioners in the Loire-Atlantique region and their patients' knowledge about prostate cancer screening. *Progres En Urologie*, 16: 559-563.
Not in PICO
- Burnett, A. L. & Wein, A. J. (2006) Benign prostatic hyperplasia in primary care: What you need to know. *Journal of Urology*, 175: S19-S24.
Not in PICO
- Calvo, N., Henriquez, L., I, Pujol, F., Milia, L., Pont, A., Grino, J., Elias, J., Monllau, V., Pont, M. & Parada, J. (2010) Utility of magnetic resonance spectroscopy and guided biopsies in patients with previous negative biopsies and suspicious of prostate cancer. *Radiotherapy and Oncology*, 96: S419.
Not in PICO
- Cam, K., Ozveri, H., Turkeri, L. & Akdas, A. (2001) The significance of hypoechoic lesion directed and transition zone biopsies in improving the diagnostic ability in prostate cancer. *Brazilian Journal of Urology*, 27: 222-226.
Not in PICO
- Candas, B., Cusan, L., Gomez, J. L., Diamond, P., Suburu, R. E., Lévesque, J., Brousseau, G., Bélanger, A. & Labrie, F. (2000) Evaluation of prostatic specific antigen and digital rectal examination as screening tests for prostate cancer. *The Prostate*, 45: 19-35.
Not in PICO
- Carducci, M. A. & Carroll, P. R. (2005) Multidisciplinary management of advanced prostate cancer: changing perspectives on referring patients and enhancing collaboration between oncologists and urologists in clinical trials. *Urology*, 65: Suppl-22.
Not in PICO
- Carey, M., Bryant, J., Yoong, S. L., Russell, G., Barker, D. & Sanson-Fisher, R. (2013) Prostate specific antigen testing in family practice: a cross sectional survey of self-reported rates of and reasons for testing participation and risk disclosure. *Bmc Family Practice*, 14.
Duplicate
- Carey, M., Bryant, J., Yoong, S. L., Russell, G., Barker, D. & Sanson-Fisher, R. (2013) Prostate specific antigen testing in family practice: a cross sectional survey of self-reported rates of and reasons for testing participation and risk disclosure. *Bmc Family Practice*, 14: 186.
Not in PICO
- Carter, H. B. & Pearson, J. D. (1999) Prostate-specific antigen testing for early diagnosis of prostate cancer: Formulation of guidelines. *Urology*, 54: 780-786.
Narrative review
- Carter, H. B. (2011) Management of low (favourable)-risk prostate cancer. [Review]. *Bju International*, 108: 1684-1695.
Not in PICO
- Castelli, T., Cimino, S., Magno, C. & Morgia, G. (2010) Molecular markers for prostatic cancer. [Review] [139 refs]. *Frontiers in Bioscience*, 2: 641-656.
Narrative review
- Cevik, I., Turkeri, L. N., Ozveri, H., Ilker, Y. & Akdas, A. (1996) Short-term effect of digital rectal examination on serum prostate-specific antigen levels. A prospective study. *European Urology*,

- 29: 403-406.
Not in PICO
- Chadwick, D. J., Kemple, T., Astley, J. P., MacIver, A. G., Gillatt, D. A., Abrams, P. & Gingell, J. C. (1991) Pilot study of screening for prostate cancer in general practice. *Lancet*, 338: 613-616.
Not in PICO
- Chan, A. Y. T., Yiu, M. K. & Yiu, T. F. (1999) Diagnosis of benign prostatic hyperplasia and when to refer. *Hong Kong Practitioner*, 21: 116-124.
Not in PICO
- Chan, E. C. Y., Barry, M. J., Vernon, S. W. & Ahn, C. (2006) Brief report: Physicians and their personal prostate cancer-screening practices with prostate-specific antigen. *Journal of General Internal Medicine*, 21: 257-259.
Not in PICO
- Chappell, B. & McLoughlin, J. (2005) Technical considerations when obtaining and interpreting prostatic biopsies from men with suspicion of early prostate cancer: part 2. [Review] [58 refs]. *Bju International*, 95: 1141-1145.
Not in PICO
- Chappell, B. & McLoughlin, J. (2005) Technical considerations when obtaining and interpreting prostatic biopsies from men with suspicion of early prostate cancer: part I. [Review] [83 refs]. *Bju International*, 95: 1135-1140.
Not in PICO
- Chapple, A., Ziebland, S., Hewitson, P. & McPherson, A. (2008) Why men in the United Kingdom still want the prostate specific antigen test. *Qualitative Health Research*, 18: 56-64.
Not in PICO
- Chepurov, A. K., Vladimirov, V. G., Zarinskaia, S. A., Meshkov, V. V., Kobaladze, K. M. & Iremashvili, V. V. (2010) [On extended biopsy of the prostatic gland]. [Russian]. *Urologiia (Moscow, Russia)*.(1):52-5, 2010 Jan-Feb., 52-55.
Not in PICO
- Chesa, P. N. & Orengo Valverde, J. C. (2002) [Knowledge about PSA among primary care physicians]. [Spanish]. *Archivos Espanoles de Urologia*, 55: 113-116.
Not in PICO
- Chisholm, G. D., Carne, S. J., Fitzpatrick, J. M., George, N. J., Gingell, J. C., Keen, J. W., Kirby, R. S., Kirk, D., O'Donoghue, E. P. & Peeling, W. B. (1995) Prostate disease: management options for the primary healthcare team. Report of a working party of the British Prostate Group. *Postgraduate Medical Journal*, 71: 136-142.
Narrative review
- Cho, S., Matsuno, D., Isshiki, S., Kojima, S., Sato, N. & Furuya, Y. (2006) Trends in systematic prostatic biopsy in Teikyo University Chiba Medical Center, 1996 to 2005. [Japanese]. *Teikyo Medical Journal*, 29: 353-358.
Not in PICO
- Chung, M. S., Lee, S. H., Lee, D. H., Kim, S. J., Kim, C. S., Lee, K. S., Jung, I. J., Kim, S. W., Lee, Y. S. & Chung, B. H. (2012) Practice Patterns of Korean Urologists for Screening and Managing Prostate Cancer according to PSA Level. *Yonsei Medical Journal*, 53: 1136-1141.
Not in PICO
- Ciatto, S., Houssami, N., Martinelli, F., Giusti, F. & Zappa, M. (2008) PSA use and incidence of prostate biopsy in the Tuscany region: is opportunistic screening discounting biopsy in subjects with PSA elevation? *Tumori*, 94: 518-522.
Not in PICO
- Coley, C. M., Barry, M. J., Fleming, C. & Mulley, A. G. (1997) Early detection of prostate cancer. Part I: Prior probability and effectiveness of tests. *Annals of Internal Medicine*, 126: 394-406.
Unclear if systematic review; no data synthesis; any relevant individual studies will be included separately.

- Collin, S. M., Metcalfe, C., Donovan, J. L., Athene, L. J., Davis, M., Neal, D. E., Hamdy, F. C. & Martin, R. M. (2009) Associations of sexual dysfunction symptoms with PSA-detected localised and advanced prostate cancer: a case-control study nested within the UK population-based ProtecT (Prostate testing for cancer and Treatment) study. *European journal of cancer (Oxford, England : 1990)*, 45: 3254-3261.
Not in PICO
- Collins, M. M., Fowler, J., Roberts, R. G., Oesterling, J. E., Annas, G. J. & Barry, M. J. (2003) Medical malpractice implications of PSA testing for early detection of prostate cancer. *The Journal of law, medicine & ethics : a journal of the American Society of Law, Medicine & Ethics*, 25: 234-242, 230.
Not in PICO
- Collins, M. M., Barry, M., Roberts, R. G., Oesterling, J. E. & Fowler, F. J. (1997) Diagnosis and treatment of benign prostatic hyperplasia - Practice patterns of primary care physicians. *Journal of General Internal Medicine*, 12: 224-229.
Not in PICO
- Concato, J. & Wells, C. K. (2006) Prostate-specific antigen 'velocity' as a diagnostic test for prostate cancer. *Journal of Investigative Medicine*, 54: 361-364.
Not in PICO
- Cooper, C. P., Merritt, T. L., Ross, L. E., John, L. V. & Jorgensen, C. M. (2004) To screen or not to screen, when clinical guidelines disagree: primary care physicians' use of the PSA test. *Preventive Medicine*, 38: 182-191.
Not in PICO
- Corcoran, A. T., Smaldone, M. C., Egleston, B. L., Simhan, J., Ginzburg, S., Morgan, T. M., Walton, J., Chen, D. Y. T., Viterbo, R., Greenberg, R. E., Uzzo, R. G. & Kutikov, A. (2013) Comparison of prostate cancer diagnosis in patients receiving unrelated urological and non-urological cancer care. *Bju International*, 112: 161-168.
Not in PICO
- Costa, D. N., Pedrosa, I., Roehrborn, C. & Rofsky, N. M. (2014) - Multiparametric magnetic resonance imaging of the prostate: technical aspects and role in clinical management. - *Topics in Magnetic Resonance Imaging*, 23: 243-257.
Narrative review
- Cramer, R. & Dahm, F. J. (2005) [The follow-up of PSA tests for the early detection of prostate cancer. The responsibility of the physician to explain treatment methods which are not covered by public health insurance plans]. [German]. *Urologe (Ausg.A)*, 44: 798-800.
Narrative review
- Curran, V., Solberg, S., Mathews, M., Church, J., Buehler, S., Wells, J. & Lopez, T. (2005) Prostate cancer screening attitudes and continuing education needs of primary care physicians. *Journal of Cancer Education*, 20: 162-166.
Not in PICO
- D'Ambrosio, G. G., Campo, S., Cancian, M., Pecchioli, S. & Mazzaglia, G. (2010) Opportunistic prostate-specific antigen screening in Italy: 6 years of monitoring from the Italian general practice database. *European Journal of Cancer Prevention*, 19: 413-416.
Not in PICO
- Da, P. L., Scattoni, V., Mazzocoli, B., Rigatti, P., Manferrari, F., Martorana, G., Pietropaolo, F., Belgrano, E., Prezioso, D., Lotti, T., Villari, D. & Nicita, G. (2007) Tissue-resonance interaction method for the noninvasive diagnosis of prostate cancer: analysis of a multicentre clinical evaluation. *Bju International*, 100: 1055-1059.
Not in PICO
- Dalla, P. L., Ricci, C. & Magnaldi, S. (1995) Referral criteria for selection of patients and diagnostic procedures. *Radiation Protection Dosimetry*, 57: 3-8.
Narrative review

- Dason, S., Allard, C. B., Barrett, K., Wright, I. & Shayegan, B. (2014) Transurethral (TURP) biopsy of suspected anterior prostate cancers identified by MRI: Pilot study of a novel technique. *Journal of Clinical Oncology*, 32.
Not in PICO
- Davis, K., Haisfield, L., Dorfman, C., Krist, A. & Taylor, K. L. (2011) Physicians' Attitudes About Shared Decision Making for Prostate Cancer Screening. *Family Medicine*, 43: 260-266.
Not in PICO
- De, V. P., Oosterlinck, W., De, M. G. & Villeirs, G. (2010) Clinical and imaging tools in the early diagnosis of prostate cancer, a review. *JBR-BTR*, 93: 62-70.
Narrative review
- Delongchamps, N. B., Peyromaure, M., Schull, A., Beuvon, F., Bouazza, N., Flam, T., Zerbib, M., Muradyan, N., Legman, P. & Cornud, F. (2013) Prebiopsy magnetic resonance imaging and prostate cancer detection: comparison of random and targeted biopsies. *Journal of Urology*, 189: 493-499.
Not in PICO
- Diefenbach, M. A. (2012) - To screen or not to screen: A comment on Lepore et al. [References]. - *Annals of Behavioral Medicine*, Vol.44: 299-300.
Not in PICO
- Dijkstra, S., van der Heijden, A. G., Schaafsma, H. E. & Mulders, P. F. (2012) Synchronous penile metastasis from a high-grade adenocarcinoma of the prostate. *Case Reports Urology*, 2012: 193787.
Not in PICO
- Dijkstra, S., Mulders, P. F. & Schalken, J. A. (2014) - Clinical use of novel urine and blood based prostate cancer biomarkers: a review. - *Clinical Biochemistry*, 47: 889-896.
Narrative review
- Djavan, B., Zlotta, A. R., Byttebier, G., Shariat, S., Omar, M., Schulman, C. C. & Marberger, M. (1998) Prostate specific antigen density of the transition zone for early detection of prostate cancer. *Journal of Urology*, 160: 411-419.
Not in PICO
- Djavan, B., Zlotta, A. R., Remzi, M., Ghawidel, K., Bursa, B., Hruby, S., Wolfram, R., Schulman, C. C. & Marberger, M. (1999) Total and transition zone prostate volume and age: How do they affect the utility of PSA-based diagnostic parameters for early prostate cancer detection? *Urology*, 54: 846-852.
Not in PICO
- Djavan, B., Zlotta, A., Kratzik, C., Remzi, M., Seitz, C., Schulman, C. C. & Marberger, M. (1999) PSA, PSA density, PSA density of transition zone, free/total PSA ratio, and PSA velocity for early detection of prostate cancer in men with serum PSA 2.5 to 4.0 ng/mL. *Urology*, 54: 517-522.
Not in PICO
- Djavan, B., Zlotta, A. R., Remzi, M., Ghawidel, K., Bursa, B., Hruby, S., Wolfram, R., Schulman, C. C. & Marberger, M. (1999) Total and transition zone prostate volume and age: how do they affect the utility of PSA-based diagnostic parameters for early prostate cancer detection? *Urology*, 54: 846-852.
Duplicate
- Donovan, J., Hamdy, F., Neal, D., Peters, T., Oliver, S., Brindle, L., Jewell, D., Powell, P., Gillatt, D., Dedman, D., Mills, N., Smith, M., Noble, S. & Lane, A. (2003) Prostate Testing for Cancer and Treatment (ProtecT) feasibility study. *Health technology assessment (Winchester, England)*, 7: 1-88.
Not in PICO
- Dubey, D. (2009) The routine use of prostate-specific antigen for early detection of cancer prostate in India: Is it justified? *Indian Journal of Urology*, 25: 177-184.
Not in PICO

- Durmus, T., Goldmann, U., Baur, A. D., Huppertz, A., Schwenke, C., Hamm, B. & Franiel, T. (2013) MR-guided biopsy of the prostate: comparison of diagnostic specimen quality with 18 G and 16 G biopsy needles. *European Journal of Radiology*, 82: e749-e754.
Not in PICO
- Durmus, T., Baur, A. & Hamm, B. (2014) - Multiparametric magnetic resonance imaging in the detection of prostate cancer. - *Aktuelle Urologie*, 45: 119-126.
Narrative review
- Durmus, T., Baur, A. & Hamm, B. (2014) - Multiparametric magnetic resonance imaging in the detection of prostate cancer. [Review]. - *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 186: 238-246.
Narrative review
- Dwivedi, D. K., Kumar, V., Javali, T., Dinda, A. K., Thulkar, S., Jagannathan, N. R. & Kumar, R. (2012) A positive magnetic resonance spectroscopic imaging with negative initial biopsy may predict future detection of prostate cancer. *Indian Journal of Urology*, 28: 243-245.
Not in PICO
- Emokpae, M. A., Das, S. C., Orok, T., Mohammed, A. Z. & Hassan, S. A. (2004) Early detection of prostate cancer: evaluating the diagnostic performance of prostate specific antigen by comparing with histological technique among africans. *Indian Journal of Clinical Biochemistry*, 19: 62-66.
Not in PICO
- Engehausen, D. G., Engelhard, K., Schwab, S. A., Uder, M., Wach, S., Wullich, B. & Krause, F. S. (2012) Magnetic resonance image-guided biopsies with a high detection rate of prostate cancer. *TheScientificWorldJournal*, 2012: 975971.
Not in PICO
- Evans, R., Elwyn, G., Edwards, A., Newcombe, R., Kinnersley, P., Wright, P., Griffiths, J., Austoker, J. & Grol, R. (2007) A randomised controlled trial of the effects of a web-based PSA decision aid, Prosdex. Protocol. *Bmc Family Practice*, 8: 58.
Not in PICO
- Evans, R., Edwards, A. G. K., Elwyn, G., Watson, E., Grol, R., Brett, J. & Austoker, J. (2007) 'It's a maybe test': men's experiences of prostate specific antigen testing in primary care. *British Journal of General Practice*, 57: 303-310.
Not in PICO
- Falsaperla, M., Morgia, G., Giammusso, B., Condorelli, S. V., Saita, A., Marchese, F., Spampinato, A. & Motta, M. (2003) Role of Ca 15-3 in patients with biochemically suspected prostate cancer and multiple negative ultrasound-guided prostate biopsies. *Prostate Cancer and Prostatic Diseases*, 6: 45-49.
Not in PICO
- Fernandez, J. C., Olmo, J. M. C., Fernandez-Pro, A., Martin, J. A., Bermudez, F. J. B., Pulido, E. N., Molero, J. M. & Morales, D. P. (2010) Referral criteria for benign prostatic hyperplasia in primary care. *Actas Urologicas Espanolas*, 34: 24-34.
Not in PICO
- Fischer, K., Loertzer, H. & Fornara, P. (2005) The use of complexed PSA for the early detection of prostate cancer. *Anticancer Research*, 25: 1591-1596.
Not in PICO
- Fiset, P. O., Aprikian, A. & Brimo, F. (2013) Length of prostate biopsy cores: does it impact cancer detection? *Canadian Journal of Urology*, 20: 6848-6853.
Not in PICO
- Fowke, J. H., Motley, S. S., Cookson, M. S., Concepcion, R., Chang, S. S., Wills, M. L. & Smith, J. (2007) The association between body size, prostate volume and prostate-specific antigen. *Prostate Cancer and Prostatic Diseases*, 10: 137-142.
Not in PICO

- Franc, B. L., Cho, S. Y., Rosenthal, S. A., Cui, Y., Tsui, B., Vandewalker, K. M., Holz, A. L., Poonamallee, U., Pomper, M. G. & James, R. B. (2013) Detection and localization of carcinoma within the prostate using high resolution transrectal gamma imaging (TRGI) of monoclonal antibody directed at prostate specific membrane antigen (PSMA)--proof of concept and initial imaging results. *European Journal of Radiology*, 82: 1877-1884.
Not in PICO
- Franiel, T., Vargas, H. A., Mazaheri, Y., Bohmer, S., Hricak, H., Akin, O. & Beyersdorff, D. (2013) Role of endorectal prostate MRI in patients with initial suspicion of prostate cancer.[Erratum appears in *Rofo*. 2013 Sep;184(10):E5 Note: Vargas, A H [corrected to Vargas, H A]]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 184: 967-974.
Not in PICO
- Franiel, T., Eckardt, N., Waginger, M. & Horstmann, M. (2014) - [Prostate cancer]. [German]. - *Radiologe*, 54: 491-506.
Narrative review
- Frydenberg, M. & Wijesinha, S. (2007) Diagnosing prostate cancer - What GPs need to know. *Australian Family Physician*, 36: 345-347.
Narrative review
- Fukagai, T., Maruyama, K., Nagata, M., Morita, M., Naoe, M. & Yoshida, H. (2007) Practice patterns regarding prostate cancer and benign prostatic hyperplasia in Japanese primary care practitioners. *International Journal of Urology*, 14: 412-415.
Not in PICO
- Gambert, S. R. (2001) Prostate cancer - When to offer screening in the primary care setting. *Geriatrics*, 56: 22-+.
Not in PICO
- Ganie, F. A., Wani, M. S., Shaheen, F., Wani, M. L., Ganie, S. A., Mir, M. F., Wani, S. N. & Masaratul, G. (2013) Endorectal coil MRI and MR-spectroscopic imaging in patients with elevated serum prostate specific antigen with negative trus transrectal ultrasound guided biopsy. *Urology annals*, 5: 172-178.
Not in PICO
- Ganie, F. A., Wanie, M. S., Ganie, S. A., Lone, H., Gani, M., Mir, M. F. & Khan, N. A. (2014) - Correlation of transrectal ultrasonographic findings with histo pathology in prostatic cancer. - *Journal of Education & Health Promotion*, 3: 38.
Not in PICO
- Gann P.H., Hennekens, C. H. & Stampfer, M. J. (1995) A prospective evaluation of plasma prostate-specific antigen for detection of prostatic cancer. *Journal of the American Medical Association*, 273: 289-294.
Not in PICO (not symptomatic population)
- Gattellari, M., Young, J. M. & Ward, J. E. (2003) GP and patient predictors of PSA screening in Australian general practice. *Family Practice*, 20: 294-303.
Not in PICO
- Gattellari, M., Donnelly, N., Taylor, N., Meerkin, M., Hirst, G. & Ward, J. E. (2005) Does 'peer coaching' increase GP capacity to promote informed decision making about PSA screening? A cluster randomised trial. *Family Practice*, 22: 253-265.
Not in PICO
- Gentile, M., Carini, M., Morgia, G., Selvaggi, F. P., Randone, D. & Rosati, A. (2001) Management of patients with LUTS suggestive of BPH. *European Urology*, 40: 5-8.
Not in PICO
- Getzenberg, R. (2008) What is the future of prostate-specific antigen for the early detection of prostate cancer? *Bju International*, 102: 157-158.
Commentary

- Giguere, A., Legare, F., Grad, R., Pluye, P., Haynes, R. B., Cauchon, M., Rousseau, F., Argote, J. A. & Labrecque, M. (2012) Decision boxes for clinicians to support evidence-based practice and shared decision making: the user experience. *Implementation Science*, 7: 72.
Not in PICO
- Gjengsto, P., Eide, J., Frugard, J., Bakke, A. & Hoisaeter, P. A. (2004) The potentially curable prostate cancer patient and the pathways leading to diagnosis and treatment. *Scandinavian Journal of Urology and Nephrology*, 38: 15-18.
Not in PICO
- Gonzalez, H. M., West, B. & Underwood, W. (2005) PSA testing in office-based clinics: Are we testing as much as we think? *Journal of the American College of Surgeons*, 201: 906-912.
Not in PICO
- Gormley, G. J., Catney, D., Mccall, J. R., Reilly, P. M. & Gavin, A. T. (2006) Prostate-specific antigen testing: uncovering primary care influences. *Bju International*, 98: 996-1000.
Not in PICO
- Gottesman, J. & Baum, N. (1997) Common urologic disorders: When to treat and when to refer. *Postgraduate Medicine*, 102: 235-246.
Narrative review
- Grasso-Leanza, F., Pepe, P., Panella, P. & Pennisi, M. (1995) PSA and prostatic adenocarcinoma. Experience with 805 patients. [Italian]. *Minerva urologica e nefrologica = The Italian journal of urology and nephrology*, 47: 161-165.
Not in PICO
- Gravalos, G. J. D., Fernandez, G. P., Gorriz, I. C., Garcia, M. A., Araujo, S. A. & Dacosta, M. G. (2007) Survival of patients diagnosed with prostate cancer and monitored in primary care. *Atencion Primaria*, 39: 603-608.
Not in PICO
- Greene, K. L., Albertsen, P. C., Babaian, R. J., Carter, H. B., Gann, P. H., Han, M., Kuban, D. A., Sartor, A. O., Stanford, J. L., Zietman, A. & Carroll, P. (2009) Prostate Specific Antigen Best Practice Statement: 2009 Update. *Journal of Urology*, 182: 2232-2241.
Narrative review
- Greene, K. L., Albertsen, P. C., Babaian, R. J., Carter, H. B., Gann, P. H., Han, M., Kuban, D. A., Sartor, A. O., Stanford, J. L., Zietman, A. & Carroll, P. (2013) Prostate Specific Antigen Best Practice Statement: 2009 Update. *Journal of Urology*, 189: S2-S11.
Narrative review
- Guerra, C. E., Gimotty, P. A., Shea, J. A., Pagan, J. A., Schwartz, J. S. & Armstrong, K. (2008) Effect of guidelines on primary care physician use of PSA screening: Results from the community tracking study physician survey. *Medical Decision Making*, 28: 681-689.
Not in PICO
- Gueye, S. M., Zeigler-Johnson, C. M., Friebel, T., Spangler, E., Jalloh, M., MacBride, S., Malkowicz, S. B. & Rebbeck, T. R. (2003) Clinical characteristics of prostate cancer in African Americans, American whites, and Senegalese men. *Urology*, 61: 987-992.
Not in PICO
- Gui, Q., Xu, C., Zhao, X., Wang, X., Yang, L., Duan, X., Li, H., Yang, Z. & Hu, W. (2013) Diagnostic value of transrectal real-time elastography in prostatic benign and malignant lesions. *Chinese Journal of Andrology*, 27: 14-17+21.
Not in PICO
- Guichard, G., Larre, S., Gallina, A., Lazar, A., Faucon, H., Chemama, S., Allory, Y., Patard, J. J., Vordos, D., Hoznek, A., Yiou, R., Salomon, L., Abbou, C. C. & De la Taille, A. (2007) Extended 21-sample needle biopsy protocol for diagnosis of prostate cancer in 1000 consecutive patients. *European Urology*, 52: 430-435.
Not in PICO

- Gustafsson, O., Carlsson, P., Norming, U., Nyman, C. R. & Svensson, H. (1995) Cost-effectiveness analysis in early detection of prostate cancer: an evaluation of six screening strategies in a randomly selected population of 2,400 men (Structured abstract). *Prostate*, 26: 299-309.
Not in PICO
- Haider, M. A., Krieger, A., Elliott, C., Da Rosa, M. R. & Milot, L. (2014) - Prostate imaging: evaluation of a reusable two-channel endorectal receiver coil for MR imaging at 1.5 T. - *Radiology*, 270: 556-565.
Not in PICO
- Hall, I. J., Taylor, Y. J., Ross, L. E., Richardson, L. C., Richards, T. B. & Rim, S. H. (2011) Discussions About Prostate Cancer Screening Between US Primary Care Physicians and Their Patients. *Journal of General Internal Medicine*, 26: 1098-1104.
Not in PICO
- Hamoen, E. H. J., Reukers, D. F. M., Numans, M. E., Barentsz, J. O., Witjes, J. A. & Rovers, M. M. (2013) Discrepancies between guidelines and clinical practice regarding prostate-specific antigen testing. *Family Practice*, 30: 648-654.
Not in PICO
- Hansen, M. V. & Gronberg, A. (1995) Attitudes of European urologists to early prostatic carcinoma. I. Diagnostic work-up on suspected prostatic cancer cases. *European Urology*, 28: 189-195.
Not in PICO
- Harvey, P., Basuita, A., Endersby, D., Curtis, B., Iacovidou, A. & Walker, M. (2009) A systematic review of the diagnostic accuracy of prostate specific antigen (Structured abstract). *BMC Urology*, 9.
Not in PICO
- He, H., Fan, S., Li, Y., Ke, M., Li, Y., Chen, B. & Yu, H. (2014) - [Value of magnetic resonance imaging for early diagnosis of prostatic carcinoma in central zone]. [Chinese]. - *Chung-Hua i Hsueh Tsa Chih [Chinese Medical Journal]*, 94: 1051-1054.
Not in PICO
- He, H., Fan, S., Ke, M., Li, Y., Chen, B. & Yu, H. (2014) Value of magnetic resonance imaging for early diagnosis of prostatic carcinoma in central zone. [Chinese]. *National Medical Journal of China*, 94: 1051-1054.
Not in PICO
- Heins, M. J., Korevaar, J. C., Rijken, P. M. & Schellevis, F. G. (2013) For which health problems do cancer survivors visit their General Practitioner? *European Journal of Cancer*, 49: 211-218.
Not in PICO
- Helmy, H., Rasheed, M. & Al-Abd, S. (2009) Vardenafil improves erectile function and urinary symptoms in men with erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia: A randomized, double-blind, placebo controlled trial. *European Urology, Supplements*, 8: 238.
Not in PICO
- Helpap, B. & Oehler, U. (2012) [Importance of second opinions on histology of prostate biopsy specimens]. [German]. *Pathologe*, 33: 103-112.
Not in PICO
- Herranz, A. F., Verdu, T. F., Diez Cordero, J. M., Sanchez, C. F., Lledo, G. E., Bueno, C. G. & Leal, H. F. (1997) Yield of transrectal ultrasonography in the diagnosis of prostatic cancer in symptomatic patients with normal rectal digital test. [Spanish]. *Actas Urológicas Españolas*, 21: 565-571.
Not in PICO
- Herranz, A. F., Verdu, T. F., Diez Cordero, J. M., Saiz, C. A., Lledo, G. E., Rodriguez, F. E. & Bueno, C. G. (1997) [Yield of ultrasound-guided transrectal biopsy in the diagnosis of prostatic cancer in symptomatic patients]. [Spanish]. *Archivos Espanoles de Urologia*, 50: 283-288.
Not in PICO

- Herranz, A. F., Verdu, T. F., Diez Cordero, J. M., Bueno, C. G., Leal, H. F., Bielsa, C. A. & Garcia, B. J. (1999) Incidence of prostatic cancer in symptomatic patients with non-suspicious rectal palpation and PSA levels greater than 10 ng/ml. [Spanish]. *Actas Urologicas Espanolas*, 23: 316-322.
Not in PICO
- Herranz, A. F., Verdu, T. F., Diez Cordero, J. M., Leal, H. F., Bielsa, C. A., Garcia, B. J. & Subira, R. D. (2000) Usefulness of free PSA/total PSA ratio in the diagnosis of prostatic cancer in symptomatic patients with PSA levels ranging from 2.5 to 20 ng/ml. [Spanish]. *Actas Urologicas Espanolas*, 24: 24-30.
Not in PICO I believe (very little patient detail given but authors from "Servicio de Urologia" and cancer prevalence 25%).
- Heyns, C., Fisher, M., Lecuona, A. & Van Der Merwe, A. (2010) Evidence that initial PSA testing should be extended to men aged <45 years to detect those at risk of presenting with aggressive Prostate cancer at the age of <50 years. *Journal of Urology*, 183: e666-e667.
Not in PICO
- Heyns, C. F., Mathee, S., Isaacs, A., Kharwa, A., De Beer, P. M. & Pretorius, M. A. (2003) Problems with prostate specific antigen screening for prostate cancer in the primary healthcare setting in South Africa. *Bju International*, 91: 785-788.
Not in PICO
- Hillig, T., Sole-Tormos, G., Hansen, S. I. & Meyhoff, H. H. (2011) Diagnostic ability of tpsa and cpsa in a patient cohort referred to a Danish Urological Department. *European Journal of Cancer*, 47: S179.
Not in PICO
- Hocaoglu, Y., Seitz, M., Stief, C. G. & Bastian, P. J. (2012) [Early diagnosis of prostate cancer]. [German]. *MMW Fortschritte der Medizin*, 154: 43-46.
Not in PICO
- Hodgson, F., Obertova, Z., Brown, C. & Lawrenson, R. (2012) PSA testing in general practice. *Journal of Primary Health Care*, 4: 199-204.
Not in PICO
- Hodgson, F., Obertova, Z., Brown, C. & Lawrenson, R. (2012) PSA testing in general practice. *Journal of Primary Health Care*, 4: 199-204.
Not in PICO
- Hoffman, R. M., Clanon, D. L., Littenberg, B., Frank, J. J. & Peirce, J. C. (2000) Using the free-to-total prostate-specific antigen ratio to detect prostate cancer in men with nonspecific elevations of prostate-specific antigen levels (Structured abstract). *Journal of General Internal Medicine*, 15: 739-748.
Not in PICO
- Hoffman, R. M., Barry, M. J., Roberts, R. G. & Sox, H. C. (2012) Reconciling primary care and specialist perspectives on prostate cancer screening. *Annals of Family Medicine*, 10: 568-571.
Not in PICO
- Holmes, J. A., Wang, A. Z., Hoffman, K. E., Hendrix, L. H., Rosenman, J. G., Carpenter, W. R., Godley, P. A. & Chen, R. C. (2012) Is Primary Prostate Cancer Treatment Influenced by Likelihood of Extraprostatic Disease? A Surveillance, Epidemiology and End Results Patterns of Care Study. *International Journal of Radiation Oncology Biology Physics*, 84: 88-94.
Not in PICO
- Hong, C. W., Walton-Diaz, A., Rais-Bahrami, S., Hoang, A. N., Turkbey, B., Stamatakis, L., Xu, S., Amalou, H., Siddiqui, M. M., Nix, J. W., Vourganti, S., Merino, M. J., Choyke, P. L., Wood, B. J. & Pinto, P. A. (2014) - Imaging and pathology findings after an initial negative MRI-US fusion-guided and 12-core extended sextant prostate biopsy session. - *Diagnostic & Interventional Radiology*, 20: 234-238.
Not in PICO

- Hoogendam, A., Buntinx, F. & Vet, H. C. (1999) The diagnostic value of digital rectal examination in primary care screening for prostate cancer: a meta-analysis (Structured abstract). *Family Practice*, 16: 621-626.
Not in PICO
- Hori, S., Fuge, O., Trabucchi, K., Donaldson, P. & McLoughlin, J. (2013) Can a trained non-physician provider perform transrectal ultrasound-guided prostatic biopsies as effectively as an experienced urologist? *Bju International*, 111: 739-744.
Not in PICO
- Houlgatte, A., Vincendeau, S., Desfemmes, F., Ramirez, J., Benoist, N., Bensalah, K. & Durand, X. (2012) [Use of [-2] pro PSA and phi index for early detection of prostate cancer: a prospective of 452 patients]. [French]. *Progres En Urologie*, 22: 279-283.
Not in PICO
- Huber, J., Ihrig, A., Huber, C. G., Hadaschik, B., Pahernik, S. & Hohenfellner, M. (2011) [Patient centeredness and decision-making in localised prostate cancer: possible fields of health services research in urology]. [German]. *Urologe (Ausg.A)*, 50: 691-696.
Not in PICO
- Huber, S., Stenzl, A. & Schilling, D. (2009) Exploring new avenues to an early identification of a prostate carcinoma - Tumor-specific markers and imaging. [German]. *Klinikerarzt*, 38: 376-381.
Narrative review
- Hudson, S. V., Ohman-Strickland, P., Ferrante, J. M., Lu-Yao, G., Orzano, A. J. & Crabtree, B. F. (2009) Prostate-Specific Antigen Testing among the Elderly in Community-Based Family Medicine Practices. *Journal of the American Board of Family Medicine*, 22: 257-265.
Not in PICO
- Hultin, S., Hotston, M., Day, A., Taylor, A., Goodall, R., Thomas, P., Bahl, A., Persad, R. & Gjini, A. (2014) Audit of PSA requesting practices in primary care compared to guidelines established by the Prostate Cancer Risk Management programme in the Avon region of the South West of England. *Journal of Clinical Urology*, 7: 45-54.
Not in PICO
- Hwang, J. W., Bang, W. J., Oh, C. Y., Yoo, C. & Cho, J. S. (2014) - Factors influencing the acceptance of transrectal ultrasound-guided prostate biopsies. - *Korean Journal of Urology*, 55: 460-464.
Not in PICO
- Iqbal, N. & Chaughtai, N. (2005) Evaluation of the diagnostic use of free prostate specific antigen/total prostate specific antigen ratio in detecting prostate cancer. *Journal of the Pakistan Medical Association*, 55: 318-320.
Not in PICO
- Issa, M. M., Zasada, W., Ward, K., Hall, J. A., Petros, J. A., Ritenour, C. W., Goodman, M., Kleinbaum, D., Mandel, J. & Marshall, F. F. (2006) The value of digital rectal examination as a predictor of prostate cancer diagnosis among United States Veterans referred for prostate biopsy. *Cancer Detection & Prevention*, 30: 269-275.
Not in PICO
- Iwamoto, H., Yumioka, T., Yamaguchi, N., Inoue, S., Masago, T., Morizane, S., Yao, A., Honda, M., Sejima, T. & Takenaka, A. (2014) - The Efficacy of Target Biopsy of Suspected Cancer Lesions Detected by Magnetic Resonance Imaging and/or Transrectal Ultrasonography during Initial Prostate Biopsies: Comparison of Outcomes between Two Physicians. - *Yonago Acta Medica*, 57: 53-58.
Not in PICO
- Iwamoto, H., Yumioka, T., Yamaguchi, N., Inoue, S., Masago, T., Morizane, S., Yao, A., Honda, M., Sejima, T. & Takenaka, A. (2014) The efficacy of target biopsy of suspected cancer lesions detected by magnetic resonance imaging and/or transrectal ultrasonography during initial prostate biopsies: Comparison of outcomes between two physicians. *Yonago Acta Medica*, 57:

53-58.

Duplicate

Jamaspishvili, T., Kral, M., Khomeriki, I., Student, V., Kolar, Z. & Bouchal, J. (2010) Urine markers in monitoring for prostate cancer. [Review] [106 refs]. *Prostate Cancer & Prostatic Diseases*, 13: 12-19.

Narrative review

Jimbo, H., Totsuka, Y., Mashimo, T., Umeyama, T., Uehara, H. & Sinozaki, T. (1994) [Investigation of ultrasound guided systematic biopsy of the prostate]. [Japanese]. *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology*, 85: 964-967.

Not in PICO

Jolly, S., Howson, J., Catto, J., Haynes, M., Cutinha, P., Yates, D. & Rosario, D. (2013) Clinical microsystems in designing trus-biopsy services - A closed-loop audit of a specialist nurse-led triage clinic for men with suspected prostate cancer. *International Journal of Surgery*, 11: 727.

Not in PICO

Jonler, M., Eddy, B. & Poulsen, J. (2005) Prostate-specific antigen testing in general practice: A survey among 325 general practitioners in Denmark. *Scandinavian Journal of Urology and Nephrology*, 39: 214-218.

Not in PICO

Jordan, K. P., Hayward, R. A., Blagojevic-Bucknall, M. & Croft, P. (2013) Incidence of prostate, breast, lung and colorectal cancer following new consultation for musculoskeletal pain: a cohort study among UK primary care patients. *International Journal of Cancer*, 133: 713-720.

Cannot extract outcome in PICO (PPVs) as cancer data only reported in total for 10-year follow up

Jung, A. J., Westphalen, A. C., Kurhanewicz, J., Wang, Z. J., Carroll, P. R., Simko, J. P. & Coakley, F. V. (2014) - Clinical utility of endorectal MRI-guided prostate biopsy: Preliminary experience. - *Journal of Magnetic Resonance Imaging*, 40: 314-323.

Not in PICO

Jung, A. J., Westphalen, A. C., Kurhanewicz, J., Wang, Z. J., Carroll, P. R., Simko, J. P. & Coakley, F. V. (2014) Clinical utility of endorectal MRI-guided prostate biopsy: Preliminary experience. *Journal of Magnetic Resonance Imaging*, 40: 314-323.

Duplicate

Kamalov, A. A., Maksimov, V. A., Takhirzade, T. B., Gevorkian, A. R., Okhobotov, D. A., Avakian, A. I. & Vasil'eva, E. G. (2012) [Detection of prostate cancer based on monitoring of prostate-specific antigen in outpatient clinic]. [Russian]. *Urologiia (Moscow, Russia)*.(6):58-60, 2012 Sep-Oct., 58-60.

Not in PICO

Kaplan, S. & Naslund, M. (2006) Public, patient, and professional attitudes towards the diagnosis and treatment of enlarged prostate: A landmark national US survey. *International Journal of Clinical Practice*, 60: 1157-1165.

Not in PICO

Kapoor, A. (2012) Benign prostatic hyperplasia (BPH) management in the primary care setting. *Canadian Journal of Urology*, 19: 10-17.

Not in PICO

Kapoor, N., Surange, S., Gupta, K. N., Husainy, M. A. & Faizi, M. (2004) Diagnosis of malignancy of prostate. *Indian Journal of Pathology and Microbiology*, 47: 186-188.

Not in PICO

Katz, A., Katz, A. & Burchill, C. (2007) Androgen therapy: testing before prescribing and monitoring during therapy. *Canadian Family Physician*, 53: 1936-1942.

Not in PICO

Katz, B., Srougi, M., Dall'Oglio, M., Nesrallah, A. J., Sant'anna, A. C., Pontes, J., Jr., Reis, S. T., Sanudo, A., Camara-Lopes, L. H. & Leite, K. R. (2012) Are we able to correctly identify prostate cancer

- patients who could be adequately treated by focal therapy? *Urologic Oncology*, 30: 794-797.
Not in PICO
- Katz, B., Srougi, M., Dall'Oglio, M., Nesrallah, A. J., Sant'anna, A. C., Pontes, J., Jr., Reis, S. T., Sanudo, A., Camara-Lopes, L. H. & Leite, K. R. (2012) Are we able to correctly identify prostate cancer patients who could be adequately treated by focal therapy? *Urologic Oncology*, 30: 794-797.
Not in PICO
- Kell, J. S. (2010) Prostate-specific antigen tests and prostate cancer screening: an update for primary care physicians. *Canadian Journal of Urology*, 17: 18-25.
Narrative review
- Kiknavelidze, K., Tsintsadze, O., Goguadze, M., Pertia, A. & Managadze, L. (2006) Prostate cancer detection rate in patients with obstructive voiding symptoms by sextant biopsy: preliminary results. *Georgian Medical News*.(133):9-14, 2006 Apr., 9-14.
Not in PICO
- Kiknavelidze, K. G., Chanturaia, Z. M., Silagava, D. D., Nikoleishvili, D. O., Tsintsadze, O. V. & Managadze, L. G. (2006) Is sextant biopsy a valid method in diagnosis of prostatic cancer?. [Russian]. *Urologiia*, 32-35.
Not in PICO
- Kim, D. K., Kim, S. J., Moon, H. S., Park, S. Y., Kim, Y. T., Choi, H. Y., Lee, T. Y. & Park, H. Y. (2010) The Role of TURP in the Detection of Prostate Cancer in BPH Patients with Previously Negative Prostate Biopsy. *Korean Journal of Urology*, 51: 313-317.
Not in PICO
- Kim, J. Y., Kim, S. H., Kim, Y. H., Lee, H. J., Kim, M. J. & Choi, M. S. (2014) - Low-risk prostate cancer: the accuracy of multiparametric MR imaging for detection. - *Radiology*, 271: 435-444.
Not in PICO
- Kim, Y. M., Kim, J., Park, S., Lee, J. H., Ryu, D. S., Choi, S. H. & Cheon, S. H. (2013) Role of prostate volume in the early detection of prostate cancer in a cohort with slowly increasing prostate specific antigen. *Yonsei Medical Journal*, 54: 1202-1206.
Not in PICO
- Kimura, G., Nishimura, T., Kimata, R., Saito, Y. & Yoshida, K. (2005) Random systematic sextant biopsy versus power doppler ultrasound-guided target biopsy in the diagnosis of prostate cancer: positive rate and clinicopathological features. *Journal of Nippon Medical School = Nihon Ika Daigaku Zasshi*, 72: 262-269.
Not in PICO
- Kimura, T., Ikemoto, I. & Ohishi, Y. (2000) Clinical profiles of prostate cancer in our hospital: association between primary symptoms and clinical stage. [Japanese]. *Hinyokika kiyo, Acta*: 83-86.
Not in PICO
- Kirby, R. & Fitzpatrick, J. (2004) Prostate-specific antigen testing for the early detection of prostate cancer. *Bju International*, 94: 966-967.
Narrative review
- Kirkham, A. P., Haslam, P., Keanie, J. Y., McCafferty, I., Padhani, A. R., Punwani, S., Richenberg, J., Rottenberg, G., Sohaib, A., Thompson, P., Turnbull, L. W., Kurban, L., Sahdev, A., Clements, R., Carey, B. M. & Allen, C. (2013) Prostate MRI: who, when, and how? Report from a UK consensus meeting. *Clinical Radiology*, 68: 1016-1023.
Narrative review
- Klein, T., Palisaar, R. J., Holz, A., Brock, M., Noldus, J. & Hinkel, A. (2010) The impact of prostate biopsy and periprostatic nerve block on erectile and voiding function: A prospective study. *Journal of Urology*, 184: 1447-1452.
Not in PICO
- Kok, E. T., Groeneveld, F. P. M. J., Gouweloos, J., Jonkheijm, R., Bosch, J. L. H. R., Thomas, S. & Bohnen, A. M. (2006) Determinants of Seeking of Primary Care for Lower Urinary Tract

- Symptoms: The Krimpen Study in Community-Dwelling Men. *European Urology*, 50: 811-817.
Not in PICO
- Konety, B. R., Sharp, V. J., Verma, M. & Williams, R. D. (2006) Practice patterns in screening and management of prostate cancer in elderly men. *Urology*, 68: 1051-1056.
Not in PICO
- Kong, J. P. L., Bultitude, M. F., Longano, A., Grummet, J. & Corcoran, N. M. (2010) Metastatic prostate cancer presenting as a syndrome of inappropriate antidiuretic hormone secretion. *Bju International*, 105: 28.
Not in PICO
- Koo, J. H., Kim, C. K., Choi, D., Park, B. K., Kwon, G. Y. & Kim, B. (2013) Diffusion-weighted magnetic resonance imaging for the evaluation of prostate cancer: optimal B value at 3T. *Korean Journal of Radiology*, 14: 61-69.
Not in PICO
- Koo, V., McMahan, J., O'Brien, A., Young, M. & Marley, J. (2008) Outcome audit of nurse-led lower urinary tract symptoms clinic: lessons and challenges for practice. *International Journal of Urological Nursing*, 2: 72-77.
Not in PICO
- Korde, L. A. & Gadalla, S. M. (2009) Cancer Risk Assessment for the Primary Care Physician. *Primary Care - Clinics in Office Practice*, 36: 471-488.
Narrative review
- Kotsis, S. V., Spencer, S. L., Peyser, P. A., Montie, J. E. & Cooney, K. A. (2002) Early onset prostate cancer: Predictors of clinical grade. *Journal of Urology*, 167: 1659-1663.
Not in PICO
- Krause, B. J., Souvatzoglou, M. & Treiber, U. (2013) Imaging of prostate cancer with PET/CT and radioactively labeled choline derivatives. [Review]. *Urologic Oncology*, 31: 427-435.
Narrative review
- Kronz, J. D., Milord, R., Wilentz, R., Weir, E. G., Schreiner, S. R. & Epstein, J. I. (2003) Lesions missed on prostate biopsies in cases sent in for consultation. *Prostate*, 54: 310-314.
Not in PICO
- Kuo, N. W., Lin, H. C. & Lee, H. C. (2008) Physician Clinical Experience and Inappropriate Prostate Specific Antigen Screening: Evidence From an Asian Country. *Journal of Urology*, 180: 1954-1958.
Not in PICO
- Laguna Pes, M. P., Guinda, S. C., Zazo, R. A., Dominguez, J., Garcia, L. A., Borrego, H. J. & Gimeno, C. A. (2000) Clinical usefulness of free PSA/total PSA ratio in the early diagnosis of prostatic cancer. [Spanish]. *Archivos Espanoles de Urologia*, 53: 333-341.
Not in PICO (referred population)
- Lai, T. C. T., Tsu, J. H., Ng, C. M., Wong, E. M., Ho, K. L. & Yiu, M. K. (2014) Optimizing prostate cancer diagnosis: 10-core versus 12-core prostate biopsy protocol. *Bju International*, 113: 6.
Not in PICO
- Lamy, P. J., Montels, F., Tosi, D., Leizour, B., Bascoul-Mollevis, C., Castan, F., Roques, S., Nielloud, F. & Rebillard, X. (2013) [Evaluation of (-2)proPSA in combination with total PSA and free PSA for the early detection of prostate cancer]. [French]. *Annales de Biologie Clinique*, 71: 537-544.
Not in PICO
- Laufer, M., Keller, T., Gershman, V., Ferman, Z., Sarid, M. & Leibovitch, I. (2014) - [InoPro trial: collaboration between urologists and primary care physicians in the treatment of osteoporosis in prostate cancer patients]. [Hebrew]. - *Harefuah*, 153: 151-154.
Not in PICO
- Lawrence, E. M., Tang, S. Y., Barrett, T., Koo, B., Goldman, D. A., Warren, A. Y., Axell, R. G., Doble, A., Gallagher, F. A., Gnanapragasam, V. J., Kastner, C. & Sala, E. (2014) - Prostate cancer: performance characteristics of combined T2W and DW-MRI scoring in the setting of template

- transperineal re-biopsy using MR-TRUS fusion. - *European Radiology*, 24: 1497-1505.
Not in PICO
- Lawrentschuk, N., Daljeet, N., Ma, C. M., Hersey, K., Zlotta, A. & Fleshner, N. (2011) Prostate-specific antigen test result interpretation when combined with risk factors for recommendation of biopsy: a survey of urologist's practice patterns. *International Urology and Nephrology*, 43: 31-37.
Not in PICO
- Lebentrau, S., May, M., Maurer, O., Schostak, M., Lehsnau, M., Ecke, T., Al-Dumaini, S., Hallmann, S., Ahmed, A. M., Braun, V., Haferkamp, A., Bauer, R. M., Stief, C. G., Baumunk, D., Hoschke, B., Braun, H. P., Schafer, C., Hipp, M., Maurer, J., Braun, K. P., Wolff, I., Brookman-May, S. & Gilfrich, C. (2014) Rates of prostate-specific antigen testing for early detection of prostate cancer. A first comparison of German results with current international data. *Urologe*, 53: 715-724.
Not in PICO
- Lee, J., Yamaguchi, T., Abe, A., Shizukuishi, K., Uemura, H., Miyagi, E., Sakata, K. & Inoue, T. (2004) Clinical evaluation of choline measurement by proton MR spectroscopy in patients with malignant tumors. *Radiation Medicine*, 22: 148-154.
Not in PICO
- Lee, S. J., Hwang, I., Hwang, E. C., Jung, S. I., Kang, T. W., Kwon, D. D. & Park, K. (2013) Are more low-risk prostate cancers detected by repeated biopsy? A retrospective pilot study. *Korean Journal of Urology*, 54: 364-368.
Not in PICO
- Lee, T. H. (2001) By the way, doctor... I can't understand why there are reservations about the prostate-specific antigen (PSA) test. The "score" goes up when you have prostate cancer. So isn't getting a PSA test a good way of catching prostate cancer early? But my doctor seems reluctant to order it. What's the problem? *Harvard Health Letter*, 26: 8.
Not in PICO
- Lent, V., Baumbusch, F. & Weber, B. (2012) Criteria for errors in prostate-specific antigen diagnostics. [German]. *Urologe - Ausgabe A*, 51: 1558-1561.
Not in PICO
- Lentini, M., Marzano, D., Perrone, M., Annunziata, S. & Cianetti, A. (1997) Comparison of free/total PSA (F/T PSA) ratio and PSA density (PSAD) in the early diagnosis of cancer of the prostate. [Italian]. *Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica / Associazione ricerche in urologia*, 69: 101-104.
Narrative review
- Li, L., Wang, L., Feng, Z., Hu, Z., Wang, G., Yuan, X., Wang, H. & Hu, D. (2013) Prostate cancer magnetic resonance imaging (MRI): multidisciplinary standpoint. *Quantitative Imaging in Medicine & Surgery*, 3: 100-112.
Narrative review
- Li, Y.-H., Elshafei, A., Li, J., Gong, M., Susan, L., Fareed, K. & Jones, J. S. (2014) Transrectal saturation technique may improve cancer detection as an initial prostate biopsy strategy in men with prostate-specific antigen <10 ng/ml. *European Urology*, 65: 1178-1183.
Not in PICO
- Little, B., Ho, K. J., Gormley, G. & Young, M. (2003) PSA testing in general practice. *Prostate Cancer and Prostatic Diseases*, 6: 154-158.
Not in PICO
- Liu, J., Yue, Q.-X., Zhou, Y., Yu, G.-H. & Li, S. (2013) Application of transrectal real-time elastography in prostate biopsy. [Chinese]. *Chinese Journal of Interventional Imaging and Therapy*, 10: 101-103.
Not in PICO
- Loeb, S. & Cooperberg, M. R. (2014) - Early detection of prostate cancer. - *Urologic Clinics of North America*, 41: xiii.
Narrative review

- Lokuhetty, M. D., Wijesinghe, H. D., Abey Suriya, D. T., Samarasinghe, U. C. & Perera, N. D. (2009) Trans rectal ultra sound guided prostate biopsies: a single centre experience in Sri Lanka. *The Ceylon medical journal*, 54: 6-9.
Not in PICO
- Lopez-Saez, J.-B., Otero, M., Senra-Varela, A., Ojea, A., Saez Martin, J. L., Duran, M. B. & Vieito, F. J. (2004) Prospective observational study to assess value of prostate cancer diagnostic methods. *Journal of Diagnostic Medical Sonography*, 20: 383-393.
Not in PICO (same data as other Lopez-Saez)
- Lopez-Saez, J.-B., Otero, M., Villar, M. D., Penueles, A. L., Navarro, P. R., Moreira, P. G. & Senra-Varela, A. (2007) Diagnostic methods in the detection of prostate cancer: Prospective observational study. *Current Medical Imaging Reviews*, 3: 27-35.
Not in PICO (same data as other Lopez-Saez)
- Luboldt, H.-J., Swoboda, A., Borgermann, C., Fornara, P. & Rubben, H. (2001) Clinical usefulness of free PSA in early detection of prostate cancer. *Onkologie*, 24: 33-37.
Not in PICO
- Luboldt, H. J., Husing, J., Altwein, J. E., Bichler, K. H., Czaja, D., Fornara, P., Jockel, K. H., Schalkhauser, K., Weissbach, L., Wirth, M. & Rubben, H. (2000) [Early detection of prostatic carcinoma in urologic practice with digital rectal examination and prostate-specific antigen. Early Detection Project Group]. [German]. *Urologe (Auszg.)*, 39: 330-333.
Narrative review
- Lumbreras, B., Lopez-Garrigos, M. & Salinas, M. (2012) Variation in Prostate Specific Antigen (PSA) Test Ordering in Primary Care Centers: Tendencies 2002-2009. *Clinical Laboratory*, 58: 573-577.
Not in PICO
- Luo, Y., Gou, X., Huang, P. & Mou, C. (2014) The PCA3 test for guiding repeat biopsy of prostate cancer and its cut-off score: A systematic review and meta-analysis. *Asian Journal of Andrology*, 16: 487-492.
Not in PICO
- Malli, G. (2013) [Early Detection of Prostate Cancer by PSA Testing: The Results of a Qualitative Study on Barriers Caused by Physicians in Austria Implementing Informed Decision Making]. [German]. *Gesundheitswesen*, 75: 22-28.
Not in PICO
- Manolovic, D., Pejicic, T. & Milovic, N. (1994) Prostatic specific antigen: role and significance in urologic practice. [Croatian]. *Srpski Arhiv Za Celokupno Lekarstvo*, 122: 171-173.
Narrative review
- Mantelli, M., Iacono, R., Quattropanetti, S., Quattropanetti, R. & Begani, P. R. (1993) Validity of transrectal ultrasonography and echo-guided biopsy in the early diagnosis of prostatic neoplasms. Our experience on 100 cases. [Italian]. *Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica / Associazione ricerche in urologia*, 65: 413-415.
Not in PICO
- McNaughton, C. M., Stafford, R. S. & Barry, M. J. (2000) Age-specific patterns of prostate-specific antigen testing among primary care physician visits. *The Journal of family practice*, 49: 169-172.
Not in PICO
- Melia, J. & Moss, S. (2001) Survey of the rate of PSA testing in general practice. *British Journal of Cancer*, 85: 656-657.
Not in PICO
- Melia, J., Moss, S. & Johns, L. (2004) Rates of prostate-specific antigen testing in general practice in England and Wales in asymptomatic and symptomatic patients: a cross-sectional study. *Bju International*, 94: 51-56.
Not in PICO

- Melia, J., Coulson, P., Coleman, D. & Moss, S. (2008) Urological referral of asymptomatic men in general practice in England. *British Journal of Cancer*, 98: 1176-1181.
Not in PICO
- Melia, J., Coulson, P., Moss, S. & Coleman, D. (2010) Effects of a prostate awareness pilot on GP consultations and PSA requests. *Family Practice*, 27: 69-76.
Not in PICO
- Metcalfe, C., Evans, S., Ibrahim, F., Patel, B., Anson, K., Chinegwundoh, F., Corbishley, C., Gillatt, D., Kirby, R., Muir, G., Nargund, V., Popert, R., Persad, R. & Ben-Shlomo, Y. (2008) Pathways to diagnosis for Black men and White men found to have prostate cancer: The PROCESS cohort study. *British Journal of Cancer*, 99: 1040-1045.
Not in PICO
- Miao, H., Fukatsu, H. & Ishigaki, T. (2007) Prostate cancer detection with 3-T MRI: comparison of diffusion-weighted and T2-weighted imaging. *European Journal of Radiology*, 61: 297-302.
Not in PICO
- Minguez, M. R., Fernandez, B. A., Gomez, S. F., Ruiz, Z. C., Teba del, P. F., Romero Tejada, J. C., Arellano, G. R. & Pereira, S., I (1999) Early diagnosis of prostate cancer in patients with prostate symptoms by DRE, PSA, TRU and DPSA. [Spanish]. *Actas Urologicas Espanolas*, 23: 688-693.
Not in PICO
- Mischi, M., Saidov, T., Kompatsiari, K., Engelbrecht, M. R., Breeuwer, M. & Wijkstra, H. (2013) Prostate cancer localization by novel magnetic resonance dispersion imaging. *Conference Proceedings: ...Annual International Conference of the IEEE Engineering in Medicine & Biology Society*, 2013: 2603-2606.
Narrative review
- Mitchell, J. M. (2012) Urologists' self-referral for pathology of biopsy specimens linked to increased use and lower prostate cancer detection. *Health Affairs*, 31: 741-749.
Not in PICO
- Mohamed, Z. K., Dominguez-Escrig, J., Vasdev, N., Bharathan, B. & Greene, D. (2013) The prognostic value of transrectal ultrasound guided biopsy in patients over 70 years old with a prostate specific Antigen (PSA) level <15 ng/ml and normal digital rectal examination: A 10-year prospective follow-up study of 427 consecutive patients. *Urologic Oncology: Seminars and Original Investigations*, 31: 1489-1496.
Not in PICO
- Molero, J. M., Morales, D. P., Bermudez, F. J. B., Pulido, E. N., Fernandez-Pro, A., Martin, J. A., Fernandez, J. C. & Olmo, J. M. C. (2010) Referral criteria for benign prostatic hyperplasia in primary care. *Atencion Primaria*, 42: 36-46.
Narrative review
- Monda, J. M., Barry, M. J. & Oesterling, J. E. (1994) Prostate specific antigen cannot distinguish stage T1a (A1) prostate cancer from benign prostatic hyperplasia. *Journal of Urology*, 151: 1291-1295.
Not in PICO
- Morote, J., Raventos, C. X., Lorente, J. A., Lopez-Pacios, M. A., Encabo, G., de, T., I & Andreu, J. (1997) Comparison of percent free prostate specific antigen and prostate specific antigen density as methods to enhance prostate specific antigen specificity in early prostate cancer detection in men with normal rectal examination and prostate specific antigen between 4.1 and 10 ng./ml. *Journal of Urology*, 158: 502-504.
Not in PICO
- Morris, S. B., Hampson, S. J., Shearer, R. J. & Corbishley, C. M. (1994) Rapid processing in the management of prostatic cancer. *British Journal of Urology*, 73: 681-682.
Not in PICO
- Mosca, P. & Roy, J. B. (1980) Outpatient needle-biopsy of the prostate: a retrospective study. *Journal - Oklahoma State Medical Association*, 73: 3-6.
Not in PICO

- Mosli, H. A. (1997) Prostate cancer: Experience at King Abdulaziz University Hospital, Jeddah. *Annals of Saudi Medicine*, 17: 590-594.
Not in PICO
- Mosquera, M. J., Pinto, S., I, Enguix, A. A. & Sahagun Arguello, J. L. (2001) Usefulness of free/total PSA ratio and PSA density in distinguishing benign prostatic hypertrophy from prostatic cancer. [Spanish]. *Actas Urologicas Espanolas*, 25: 651-655.
Not in PICO
- Mouraviev, V., Verma, S., Kalyanaraman, B., Zhai, Q. J., Gaitonde, K., Pugnale, M. & Donovan, J. F. (2013) The feasibility of multiparametric magnetic resonance imaging for targeted biopsy using novel navigation systems to detect early stage prostate cancer: the preliminary experience. *Journal of Endourology*, 27: 820-825.
Not in PICO
- Mowatt, G., Scotland, G., Boachie, C., Cruickshank, M., Ford, J. A., Fraser, C., Kurban, L., Lam, T. B., Padhani, A. R., Royle, J., Scheenen, T. W. & Tassie, E. (2001) The diagnostic accuracy and cost-effectiveness of magnetic resonance spectroscopy and enhanced magnetic resonance imaging techniques in aiding the localisation of prostate abnormalities for biopsy: a systematic review and economic evaluation. *Health technology assessment (Winchester, England)*, 17: vii-281.
Not in PICO
- Murphy, D. G., Ahlering, T., Catalona, W. J., Crowe, H., Crowe, J., Clarke, N., Cooperberg, M., Gillatt, D., Gleave, M., Loeb, S., Roobol, M., Sartor, O., Pickles, T., Wootten, A., Walsh, P. C. & Costello, A. J. (2014) - The Melbourne Consensus Statement on the early detection of prostate cancer. [Review]. - *BJU International*, 113: 186-188.
Narrative review
- Myers, R. E., Daskalakis, C., Cocroft, J., Kunkel, E. J. S., Delmoor, E., Liberatore, M., Nydick, R. L., Brown, E. R., Gay, R. N., Powell, T. & Powell, R. L. (2005) Preparing African-American men in community primary care practices to decide whether or not to have prostate cancer screening. *Journal of the National Medical Association*, 97: 1143-1154.
Not in PICO
- Naslund, M. J., Gilseman, A. W., Midkiff, K. D., Bown, A., Wolford, E. T. & Wang, J. (2007) Prevalence of lower urinary tract symptoms and prostate enlargement in the primary care setting. *International Journal of Clinical Practice*, 61: 1437-1445.
Not in PICO
- Nepple, K. G., Joudi, F. N., Hillis, S. L. & Wahls, T. L. (2008) Prevalence of delayed clinician response to elevated prostate-specific antigen values. *Mayo Clinic Proceedings*, 83: 439-445.
Not in PICO
- Ng, Y. H., Seeley, J. P. & Smith, G. (2013) Haemospermia as a presenting symptom: Outcomes of investigation in 300 men. *Surgeon-Journal of the Royal Colleges of Surgeons of Edinburgh and Ireland*, 11: 35-38.
Not in PICO
- Ng, Y. H., Seeley, J. P. & Smith, G. (2013) Haemospermia as a presenting symptom: outcomes of investigation in 300 men. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 11: 35-38.
Not in PICO
- Ng, Y. H., Seeley, J. P. & Smith, G. (2013) Haemospermia as a presenting symptom: Outcomes of investigation in 300 men. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 11: 35-38.
Not in PICO
- Ngo, T. C., Turnbull, B. B., Lavori, P. W. & Presti, J. C. (2011) The Prostate Cancer Risk Calculator From the Prostate Cancer Prevention Trial Underestimates the Risk of High Grade Cancer in Contemporary Referral Patients. *Journal of Urology*, 185: 483-487.
Not in PICO

- Niang, L., Ndoye, M., Ouattara, A., Jalloh, M., Labou, M., Thiam, I., Kouka, S. C., Diaw, J. J. & Gueye, S. M. (2013) [Management of prostate cancer in Senegal: What is being done?]. [French]. *Progres En Urologie*, 23: 36-41.
Not in PICO
- Nortje, C. J. (2002) General practitioner's Radiology Case 3. *SADJ*, 57: 287-288.
Not in PICO
- Numao, N., Yoshida, S., Komai, Y., Ishii, C., Kagawa, M., Kijima, T., Yokoyama, M., Ishioka, J., Matsuoka, Y., Koga, F., Saito, K., Masuda, H., Fujii, Y., Kawakami, S. & Kihara, K. (2013) Usefulness of pre-biopsy multiparametric magnetic resonance imaging and clinical variables to reduce initial prostate biopsy in men with suspected clinically localized prostate cancer. *Journal of Urology*, 190: 502-508.
Not in PICO
- Numao, N., Matsuoka, Y., Ito, M., Yoshida, S., Ishikawa, Y., Uchida, Y., Toide, M., Higuchi, S., Nakayama, T., Inoue, M., Takeshita, H., Kijima, T., Nakanishi, Y., Ishioka, J., Saito, K., Yasuhisa, F. & Kazunori, K. (2014) Direct comparison of the ability to detect significant prostate cancer and assess cancer characteristics between magnetic resonance imaging targeted biopsy and systematic 14-core biopsy, including anterior samplings. *European Urology, Supplements*, 13: e949.
Not in PICO
- Nygaard, Y., Haukaas, S. A., Halvorsen, O. J., Gravdal, K., Frugard, J., Akslen, L. A. & Beisland, C. (2014) - A positive real-time elastography is an independent marker for detection of high-risk prostate cancers in the primary biopsy setting. - *BJU International*, 113: E90-E97.
Not in PICO
- Nygaard, Y., Haukaas, S. A., Halvorsen, O. J., Gravdal, K., Frugard, J., Akslen, L. A. & Beisland, C. (2014) A positive real-time elastography is an independent marker for detection of high-risk prostate cancers in the primary biopsy setting. *Bju International*, 113: E90-E97.
Duplicate
- Obertova, Z., Brown, C., Hodgson, F. & Lawrenson, R. (2013) What do men say about diagnostic pathways? From prostate-specific antigen (PSA) test to prostate cancer. *Bju International*, 112: 14.
Not in PICO
- Oesterling, J. E. (1994) PSA and early prostate cancer detection: the importance of age-specific reference ranges. *The Canadian journal of oncology*, 4: 52-56.
Not available. WWS not conducted as unlikely to be relevant.
- Oesterling, J. E. (1995) Prostate-Specific Antigen - Its Role in the Diagnosis and Staging of Prostate-Cancer. *Cancer*, 75: 1795-1804.
Narrative review
- Ojewola, R. W., Tijani, K. H., Jeje, E. A., Anunobi, C. C., Ogunjimi, M. A., Ezenwa, E. V. & Ogundiniyi, O. S. (2012) Is extended biopsy protocol justified in all patients with suspected prostate cancer? *Nigerian Journal of Clinical Practice*, 15: 315-319.
Not in PICO
- Okada, K. & Suzuki, Y. (2000) [Diagnosis of prostate cancer in general practice]. [Review] [13 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 58: Suppl-93.
Narrative review (asked Lily)
- Onishi, T., Akazawa, Y., Sakamaki, K., Shintani, T., Sugiyama, H., Senzaki, T., Numata, K., Sakaki, M., Fukawa, T., Yamamoto, Y., Izaki, H., Oka, N., Kanda, M., Takahashi, M., Naroda, T., Fukumori, T., Nishitani, M., Yamanaka, M., Kurokawa, Y., Miyamoto, T., Kanayama, H.-O. & Kagawa, S. (2002) Clinical statistics on outpatients in the Urology Clinic of Tokushima University Hospital between 1991 and 2000. [Japanese]. *Nishinohon Journal of Urology*, 64: 176-178.
Not in PICO

- Onur, M. R., Turgut, A. T. & Dogra, V. (2014) Ultrasound-guided biopsy of the prostate: New updates. *Ultrasound Clinics*, 9: 81-94.
Narrative review
- Onur, M. R., Turgut, A. T. & Dogra, V. (2014) Ultrasound-guided biopsy of the prostate: New updates. *Ultrasound Clinics*, 9: 81-94.
Narrative review
- Oranusi, C. K., Mbieri, U. T., Oranusi, I. O. & Nwofor, A. M. E. (2012) Prostate cancer awareness and screening among male public servants in Anambra state, Nigeria. *African Journal of Urology*, 18: 72-74.
Not in PICO
- Oremek, G. M., Sapoutzis, N., Eden, F. & Jonas, D. (2003) Complexed PSA in routine diagnosis. *Anticancer Research*, 23: 975-977.
Not in PICO
- Ornstein, D. K., Rao, G. S., Smith, D. S. & Andriole, G. L. (1997) The impact of systematic prostate biopsy on prostate cancer incidence in men with symptomatic benign prostatic hyperplasia undergoing transurethral resection of the prostate. *Journal of Urology*, 157: 880-884.
Not in PICO
- Ouzzane, A., Coloby, P., Mignard, J. P., Allegre, J. P., Soulie, M., Rebillard, X., Salomon, L., Villers, A., Committee of Infectious Diseases of the French Association of Urology (CIAFU) & Committee of Cancerology of the French Association of Urology (CCAFU) (2011) [Recommendations for best practice for prostate biopsy]. [Review] [French]. *Progres En Urologie*, 21: 18-28.
Not in PICO
- Overduin, C. G., Futterer, J. J. & Barentsz, J. O. (2013) MRI-Guided Biopsy for Prostate Cancer Detection: A Systematic Review of Current Clinical Results. *Current Urology Reports*, 14: 209-213.
Not in PICO
- Ozen, H., Aygun, C., Ergen, A., Sozen, S., Aki, F. T. & Uygur, M. C. (2001) Combined use of prostate-specific antigen derivatives decreases the number of unnecessary biopsies to detect prostate cancer. *American Journal of Clinical Oncology: Cancer Clinical Trials*, 24: 610-613.
Not in PICO
- Pan, D. & McCahy, P. (2012) Patient knowledge about prostate-specific antigen (PSA) and prostate cancer in Australia. *Bju International*, 109: Suppl-6.
Not in PICO
- Pascual, D. T., Gonzalez, R. J., Sanchez, S. E., Ruiz De La Roja, J. C., Berenguer, S. A. & Miravalles, G. E. (1996) Prostate specific antigen in the early detection of prostate cancer. [Spanish]. *Revista de la Sociedad Espanola de Quimica Clinica*, 15: 29-33.
Not in PICO
- Patel, N. S., Blick, C., Kumar, P. V. S. & Malone, P. R. (2009) The diagnostic value of abdominal ultrasound, urine cytology and prostate-specific antigen testing in the lower urinary tract symptoms clinic. *International Journal of Clinical Practice*, 63: 1734-1738.
Not in PICO
- Payne, H., Clarke, N., Huddart, R., Parker, C., Troup, J. & Graham, J. (2013) Nasty or Nice? Findings from a UK Survey to Evaluate the Impact of the National Institute for Health and Clinical Excellence (NICE) Clinical Guidelines on the Management of Prostate Cancer. *Clinical Oncology*, 25: 178-189.
Not in PICO
- Pelechano, G. P., Casanova Ramon-Borja, J. & Collado, S. A. (2014) - An update on imaging techniques to optimize active surveillance in prostate cancer. - *Archivos Espanoles de Urologia*, 67: 473-485.
Narrative review
- Perachino, M., Puppo, P., Scannapieco, G., Vitali, A. & Di, C. L. (1993) The diagnostic value of PSA compared to rectal monitoring and transrectal echography in the diagnosis of prostatic

- carcinoma in patients with obstructive diseases: Results of 202 cases. [Italian]. *Acta Urologica Italica*, 7: 7-8.
Not in PICO (referred patients; cancer rate 33.7%)
- Perachino, M., Di, C. L., Barbetti, V., Ardoino, S., Vitali, A., Introini, C., Vigliercio, G. & Puppo, P. (1997) Results of rebiopsy for suspected prostate cancer in symptomatic men with elevated PSA levels. *European Urology*, 32: 155-159.
Not in PICO
- Perez, C. E., Simonet Aineto, P. J., Vargas, B. C., Castells, E. M. & Parellada, E. N. (2000) [The diagnostic situation with prostatic cancer in primary care]. [Spanish]. *Atencion Primaria*, 25: 137-141.
Not in PICO
- Perez, C. E., Simonet Aineto, P. J., Vargas, B. C., Castells, E. M. & Parellada, E. N. (2000) The diagnostic situation with prostatic cancer in primary care. [Spanish]. *Atencion primaria / Sociedad Espanola de Medicina de Familia y Comunitaria*, 25: 137-141.
Not in PICO
- Perrin, P., Maquet, J. H., Bringeon, G. & Devonec, M. (1991) Screening for prostate cancer. Comparison of transrectal ultrasound, prostate specific antigen and rectal examination. *British Journal of Urology*, 68: 263-265.
Not in PICO
- Pinnock, C. B., Weller, D. P. & Marshall, V. R. (1998) Self-reported prevalence of prostate-specific antigen testing in South Australia: A community study. *Medical Journal of Australia*, 169: 25-28.
Not in PICO
- Pinnock, C. B. (2004) PSA testing in general practice: can we do more now? *Medical Journal of Australia*, 180: 379-381.
Narrative review
- Plawker, M. W., Fleisher, J. M., Nitti, V. W. & Macchia, R. J. (1996) Primary care practitioners: An analysis of their perceptions of voiding dysfunction and prostate cancer. *Journal of Urology*, 155: 601-604.
Not in PICO
- Plekhanov, A. I., Zhivov, A. V., Petrov, S. B., Veliev, E. I., Galanin, S. V., Urbanskii, A. I. & Lysenko, I. S. (2007) [Estimation of predictive prostate cancer probability with logistic regression equation]. [Russian]. *Urologiia (Moscow, Russia)*.(4):81-5, 2007 Jul-Aug., 81-85.
Not in PICO
- Pokorny, M. R., de, R. M., Duncan, E., Schroder, F. H., Parkinson, R., Barentsz, J. O. & Thompson, L. C. (2014) - Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound-guided biopsy versus magnetic resonance (MR) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. - *European Urology*, 66: 22-29.
Not in PICO
- Pollack, C. E., Platz, E. A., Bhavsar, N. A., Noronha, G., Green, G. E., Chen, S. & Carter, H. B. (2012) Primary Care Providers' Perspectives on Discontinuing Prostate Cancer Screening. *Cancer*, 118: 5518-5524.
Not in PICO
- Pourmand, G., Ramezani, R., Sabahgoulian, B., Nadali, F., Mehrsai, A., Nikoobakht, M., Allameh, F., Hossieni, S., Seraji, A., Rezai, M., Haidari, F., Dehghani, S., Razmandeh, R. & Pourmand, B. (2012) Preventing Unnecessary Invasive Cancer-Diagnostic Tests: Changing the Cut-off Points. *Iranian Journal of Public Health*, 41: 47-52.
Not in PICO
- Powles, L. A. R., Rolls, A. E., Lamb, B. W., Taylor, E. & Green, J. S. A. (2012) Can redesigning a laboratory request form reduce the number of inappropriate PSA requests without compromising clinical outcome. *British Journal of Medical and Surgical Urology*, 5: 67-73.
Not in PICO

- Presti, J. (2004) What is the most efficient biopsy regimen for detecting early prostate cancer? *Nature Clinical Practice Urology*, 1: 76-77.
Not in PICO
- Puppo, P., Perachino, M., Ricciotti, G., Vitali, A., Arduino, S. & Di, C. L. (1992) Comparison between digital rectal examination, prostate-specific antigen and transrectal ultrasound in symptomatic patients. Results on 141 cases. *European Urology*, 21: 87-91.
Not in PICO
- Puzone, R., Paleari, L., Montefiore, F., Ruggiero, L., Puntoni, M., Maffezzini, M., Bobbio, B., Marroni, P., Libener, R. & Betta, P. G. (2010) Osteopontin plasma level does not detect prostate cancer in patients referred for diagnostic prostate biopsy. *International Journal of Biological Markers*, 25: 200-206.
Not in PICO
- Qu, M., Ren, S. C. & Sun, Y. H. (2014) - Current early diagnostic biomarkers of prostate cancer. - *Asian Journal of Andrology*, 16: 549-554.
Narrative review
- Quentin, M., Pentang, G., Schimmoller, L., Kott, O., Muller-Lutz, A., Blondin, D., Arsov, C., Hiester, A., Rabenalt, R. & Wittsack, H. J. (2014) - Feasibility of diffusional kurtosis tensor imaging in prostate MRI for the assessment of prostate cancer: Preliminary results. - *Magnetic Resonance Imaging*, 32: 880-885.
Not in PICO
- Quinlan, M. R., Teahan, S., Mulvin, D. & Quinlan, D. M. (2007) Is digital rectal examination still necessary in the early detection of prostate cancer? *Irish Journal of Medical Science*, 176: 161-163.
Not in PICO
- Quinlan, M. R., O'Daly, B. J., O'Brien, M. F., Gardner, S., Lennon, G., Mulvin, D. W. & Quinlan, D. M. (2009) The value of appropriate assessment prior to specialist referral in men with prostatic symptoms. *Irish Journal of Medical Science*, 178: 281-285.
Not in PICO
- Radavoi, G. D., Petrescu, A., Berdan, M. G., Manea, N. F., Tanase, F. & Jinga, V. (2014) The use of multiplex biopsies as a cost-effective method in the diagnostic of prostate cancer. *European Urology, Supplements*, 13: e745.
Not in PICO
- Randrup, E. & Baum, N. (2011) Prostate-specific antigen testing for prostate cancer. Practical interpretation of values. [Review] [14 refs]. *Postgraduate Medicine*, 99: 227-228.
Narrative review
- Ravery, V., Schmid, H. P., Billebaud, T., Toublanc, M., Boccon-Gibod, L., Hermieu, J. F., Delmas, V. & Boccon-Gibod, L. (1996) Detection of prostate cancer in symptomatic patients with prostate specific antigen between 4 and 10 ng/ml. [French]. *Presse Medicale*, 25: 272-276.
Not in PICO
- Recker, F. (1996) Prostate specific antigen in the diagnosis of organ confined curable prostate cancer. [German]. *Schweizerische Medizinische Wochenschrift*, 126: 1881-1890.
Narrative review
- Rehsia, S. & Shayegan, B. (2012) PSA implications and medical management of prostate cancer for the primary care physician. *Canadian Journal of Urology*, 19: 28-35.
Not in PICO
- Reljic, A., Tomaskovic, I., Simundic, A.-M. & Kruslin, B. (2004) Diagnostic value of age specific prostate specific antigen in prostate cancer patients. *Acta Clinica Croatica*, 43: 379-383.
Not in PICO
- Richter, F., Dudley, A. W., Irwin, R. J. & Sadeghi-Nejad, H. (2001) Are we ordering too many PSA tests? Prostate cancer diagnosis and PSA screening patterns for a single Veterans Affairs Medical

- Center. *Journal of Cancer Education*, 16: 38-41.
Not in PICO
- Riedinger, C. B., Womble, P. R., Linsell, S. M., Ye, Z., Montie, J. E., Miller, D. C., Lane, B. R. & - Michigan Urological Surgery Improvement Collaborative (2014) - Variation in prostate cancer detection rates in a statewide quality improvement collaborative. - *Journal of Urology*, 192: 373-378.
Not in PICO
- Rinaldi, D., Fiocchi, F., Ligabue, G., Bianchi, G. & Torricelli, P. (2012) Role of diffusion-weighted magnetic resonance imaging in prostate cancer evaluation. *Radiologia Medica*, 117: 1429-1440.
Not in PICO
- Rinnab, L., Gottfried, H. W., Schnoller, T., Hautmann, R. E. & Kuefer, R. (2007) Clinical value of transrectal ultrasound in the diagnosis of suspected neoplasia in the small pelvis. *Ultraschall in der Medizin*, 28: 195-200.
Not in PICO
- Rochester, M. A., Donaldson, P. J. & McLoughlin, J. (2008) Perception of abnormal serum prostate-specific antigen (PSA) test results amongst family practitioners. *Annals of the Royal College of Surgeons of England*, 90: 398-402.
Not in PICO
- Roddam, A. W., Hamdy, F. C., Allen, N. E., Price, C. P. & UK Prostate Cancer Risk Management Program (2007) The impact of reducing the prostate-specific antigen threshold and including isoform reflex tests on the performance characteristics of a prostate-cancer detection programme. [Review] [19 refs]. *Bju International*, 100: 514-517.
Not in PICO
- Rodriguez-Cantalejo, F., Lopez-Garrigos, M., Benitez-Benitez, D., Sanchez-Fernandez, E., Moreno-Noguero, E., Rodriguez-Borja, E., Roldan-Fontana, E., Martin-Oncina, F. J., Gascon, F., Velasco-Pena, F., Miralles, F., Marcaida, G., Barrionuevo, M., Dominguez-Pascual, I., Herrera-Contreras, I., Ferrero, J. A. & Salinas, M. (2014) Differences in prostatic specific antigen requesting patterns in primary care setting: A pilot study in Spain. *Clinical Chemistry and Laboratory Medicine*, 52: S459.
Not in PICO
- Rodriguez, D. C., Aguillon, J. & Rodriguez, H. (1991) Occult cancer in patients with symptomatic benign prostatic hyperplasia. [Spanish]. *Archivos Espanoles de Urologia*, 44: 411-414.
Not in PICO
- Roehrborn, C. G., Pickens, G. J. & Carmody, T., III (1996) Variability of repeated serum prostate-specific antigen (PSA) measurements within less than 90 days in a well-defined patient population. *Urology*, 47: 59-66.
Not in PICO
- Roehrborn, C. G. (2011) Male lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH). [Review]. *Medical Clinics of North America*, 95: 87-100.
Narrative review
- Romagnoli, A., Giglio, M., Timossi, L., Bertolotto, F., Germinale, F. & Carmignani, G. (2002) [Ultrasonography-guided transperineal prostatic biopsy: optimization of sampling protocol after 1,352 biopsies]. [Italian]. *Archivio Italiano di Urologia, Andrologia*, 74: 285-289.
Not in PICO
- Roobol, M. J., Schröder, F. H., Kranse, R., ERSPC & Rotterdam (2006) A comparison of first and repeat (four years later) prostate cancer screening in a randomized cohort of a symptomatic men aged 55-75 years using a biopsy indication of 3.0 ng/ml (results of ERSPC, Rotterdam). *The Prostate*, 66: 604-612.
Not in PICO
- Roobol, M. J., van Vugt, H. A., Loeb, S., Zhu, X. Y., Bul, M., Bangma, C. H., van Leenders, A. G. L. J., Steyerberg, E. W. & Schroder, F. H. (2012) Prediction of Prostate Cancer Risk: The Role of Prostate Volume and Digital Rectal Examination in the ERSPC Risk Calculators. *European Urology*, 61: 577-

583.

Not in PICO

Rosario, D. J., Lane, J. A., Metcalfe, C., Donovan, J. L., Doble, A., Goodwin, L., Davis, M., Catto, J. W., Avery, K., Neal, D. E. & Hamdy, F. C. (2012) Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: prospective evaluation within ProtecT study. *BMJ*, 344: d7894.

Not in PICO

Rosenberg, M. T., Miner, M. M., Riley, P. A. & Staskin, D. R. (2010) STEP: Simplified Treatment of the Enlarged Prostate. *International Journal of Clinical Practice*, 64: 488-496.

Narrative review

Roshanai, A., Nordin, K. & Berglund, G. (2012) Factors influencing primary care physicians' decision to order prostate-specific antigen (PSA) test for healthy men. *Asia-Pacific Journal of Clinical Oncology*, 8: 249.

Not in PICO

Roshanai, A. H., Nordin, K. & Berglund, G. (2013) Factors influencing primary care physicians' decision to order prostate-specific antigen (PSA) test for men without prostate cancer. *Acta Oncologica*, 52: 1602-1608.

Not in PICO

Ross, L. E., Berkowitz, Z. & Ekwueme, D. U. (2008) Use of the prostate-specific antigen test among US men: Findings from the 2005 national health interview survey. *Cancer Epidemiology Biomarkers & Prevention*, 17: 636-644.

Not in PICO

Ross, L. E., Taylor, Y. J., Richardson, L. C. & Howard, D. L. (2009) Patterns in Prostate-Specific Antigen Test Use and Digital Rectal Examinations in the Behavioral Risk Factor Surveillance System, 2002-2006. *Journal of the National Medical Association*, 101: 316-324.

Not in PICO

Ross, L. E., Taylor, Y. J. & Howard, D. L. (2011) Trends in Prostate-Specific Antigen Test Use, 2000-2005. *Public Health Reports*, 126: 228-239.

Not in PICO

Rothke, M., Blondin, D., Schlemmer, H. P. & Franiel, T. (2013) [PI-RADS classification: structured reporting for MRI of the prostate]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 185: 253-261.

Not in PICO

Ruckle, H. C., Klee, G. G. & Oesterling, J. E. (1994) Prostate-specific antigen: critical issues for the practicing physician. [Review] [41 refs]. *Mayo Clinic Proceedings*, 69: 59-68.

Narrative review

Ruckle, H. C., Klee, G. G. & Oesterling, J. E. (1994) Prostate-specific antigen: Critical issues for the practicing physician. *Mayo Clinic Proceedings*, 69: 59-68.

Narrative review

Rud, E., Baco, E. & Eggesbo, H. B. (2012) MRI and ultrasound-guided prostate biopsy using soft image fusion. *Anticancer Research*, 32: 3383-3389.

Not in PICO

Sadchenko, A. V., Govorov, A. V., Pushkar', D. I., Sidorenkov, A. V., Vasil'ev, A. O., Kovylna, M. V. & Prilepskaia, E. A. (2014) [Perineal saturation biopsy of the prostate]. [Russian]. *Urologii{combining double inverted breve}a (Moscow, Russia : 1999)*, 33-36.

Not in PICO

Salinas, M., Lopez-Garrigos, M., Miralles, F., Chinchilla, V., Ortuno, M., Aguado, C., Marcaida, G., Guaita, M., Carratala, A., Diaz, J., Yago, M., Esteban, A., Laiz, B., Rodriguez-Borja, E., Lorente, M. A. & Uris, J. (2011) Evaluation of psa testing by general practitioners: Regional study in the autonomic community of valencia. *Archivos Espanoles de Urologia*, 64: 435-440.

Not in PICO

- Sanchez-Martinez, L. C., Paredes-Solis, C. A., Hernandez-Ordonez, O. F. & Sanchez-Ruvalcaba, I. R. (2013) [Prostate-specific antigen. The role in the prostate cancer diagnosis]. [Spanish]. *Revista Medica del Instituto Mexicano del Seguro Social*, 51: 124-126.
Narrative review
- Sanz Velez, J. I., Allepuz, L. C., Gil Sanz, M. J., Plaza, L., Castrillo, J., Cuesta Presedo, J. M. & Rioja Sanz, L. A. (1997) Early diagnosis of cancer of the prostate. 5-year analysis. [Spanish]. *Actas Urologicas Espanolas*, 21: 827-834.
Not in PICO
- Sarle, R., Zvara, P., Bunnell, M. L. & Plante, M. K. (2001) Statewide prostate cancer screening practices among primary care physicians. *American Journal of Managed Care*, 137-143.
Not in PICO
- Sato, C., Naganawa, S., Nakamura, T., Kumada, H., Miura, S., Takizawa, O. & Ishigaki, T. (2005) Differentiation of noncancerous tissue and cancer lesions by apparent diffusion coefficient values in transition and peripheral zones of the prostate. *Journal of Magnetic Resonance Imaging*, 21: 258-262.
Not in PICO
- Scales, C. D., Jr., Curtis, L. H., Norris, R. D., Schulman, K. A., Albala, D. M. & Moul, J. W. (2006) Prostate specific antigen testing in men older than 75 years in the United States. *Journal of Urology*, 176: 511-514.
Not in PICO
- Scheidler, J., Weores, I., Brinkschmidt, C., Zeitler, H., Panzer, S., Scharf, M., Heuck, A. & Siebels, M. (2012) Diagnosis of prostate cancer in patients with persistently elevated PSA and tumor-negative biopsy in ambulatory care: performance of MR imaging in a multi-reader environment. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 184: 130-135.
Not in PICO
- Schenk, J. M., Kristal, A. R., Arnold, K. B., Tangen, C. M., Neuhaus, M. L., Lin, D. W., White, E. & Thompson, I. M. (2011) Association of symptomatic benign prostatic hyperplasia and prostate cancer: results from the prostate cancer prevention trial. *American Journal of Epidemiology*, 173: 1419-1428.
Not in PICO
- Schiff, G. D. (2014) Diagnosis and diagnostic errors: Time for a new paradigm. *BMJ Quality and Safety*, 23: 1-3.
Not in PICO
- Schmid, M., Hansen, J., Rink, M., Fisch, M. & Chun, F. (2013) The development of nomograms for stratification of men at risk of prostate cancer prior to prostate biopsy. *Biomarkers in Medicine*, 7: 843-850.
Narrative review
- Shahab, A. A., Soebadi, D. M., Djatisoesanto, W., Hardjowijoto, S., Soetojo, S. & Hakim, L. (2013) Prostate-specific antigen and prostate-specific antigen density cutoff points among Indonesian population suspected for prostate cancer. *Prostate International*, 1: 23-30.
Not in PICO
- Shariat, S. F. & Roehrborn, C. G. (2008) Using biopsy to detect prostate cancer. *Reviews in Urology*, 10: 262-280.
Narrative review
- Shatov, A. V. & Ognerubov, N. A. (2004) [Magnetic resonance imaging in diagnosis of localized prostatic cancer]. [Russian]. *Urologiia (Moscow, Russia)*.(3):25-9, 2004 May-Jun., 25-29.
Not in PICO
- Sheikh, M., Al-Saeed, O., Kehinde, E. O., Sinan, T., Anim, J. T. & Ali, Y. (2005) Utility of volume adjusted prostate specific antigen density in the diagnosis of prostate cancer in Arab men. *International Urology & Nephrology*, 37: 721-726.
Not in PICO

- Shen, J., Lu, Y., Yang, Y., Zhao, W., Jiang, Z., Zhang, C., Ma, Q., Zhang, Y. & Shan, Y. (2014) Application evaluation of MR diffusion weighted imaging in the diagnosis and differential diagnosis of early prostate cancer. [Chinese]. *Chinese Journal of Radiology (China)*, 48: 114-118.
Not in PICO
- Shenker, B. S. & Stern, J. (2012) The effect of lowering the prostate-specific antigen normal cutoff on referral rates to urology. *Journal of the American Board of Family Medicine*, 25: 927-929.
Not in PICO
- Siddiqui, E., Mumtaz, F. H. & Gelister, J. (2004) Understanding prostate cancer. [Review] [8 refs]. *Journal of the Royal Society for the Promotion of Health*, 124: 219-221.
Narrative review
- Sing, R. I. & Singal, R. K. (2012) What is significant hematuria for the primary care physician? *Canadian Journal of Urology*, 19: Suppl-41.
Narrative review
- Smith, R. A., Cokkinides, V. & Eyre, H. J. (2006) American Cancer Society guidelines for the early detection of cancer, 2006. *Ca-A Cancer Journal for Clinicians*, 56: 11-25.
Guideline
- Smith, S. D. & Birtwhistle, R. (2012) Exploring patient perceptions of PSA screening for prostate cancer: Risks, effectiveness, and importance. *Canadian Family Physician*, 58: e502-e507.
Not in PICO
- Smith, S. D. & Birtwhistle, R. (2012) Exploring patient perceptions of PSA screening for prostate cancer: Risks, effectiveness, and importance. *Canadian Family Physician*, 58: e502-e507.
Not in PICO
- Snow, D. C. & Klein, E. A. (2010) Use of nomograms for early detection in prostate cancer. *JNCCN Journal of the National Comprehensive Cancer Network*, 8: 271-276.
Narrative review
- Song, J. M., Kim, C. B., Chung, H. C. & Kane, R. L. (2005) Prostate-specific antigen, digital rectal examination and transrectal ultrasonography: A meta-analysis for this diagnostic triad of prostate cancer in symptomatic Korean men. *Yonsei Medical Journal*, 46: 414-424.
Not in PICO (cancer prevalence rate = 25.4%)
- Sonn, G. A., Chang, E., Natarajan, S., Margolis, D. J., Macairan, M., Lieu, P., Huang, J., Dorey, F. J., Reiter, R. E. & Marks, L. S. (2014) - Value of targeted prostate biopsy using magnetic resonance-ultrasound fusion in men with prior negative biopsy and elevated prostate-specific antigen. - *European Urology*, 65: 809-815.
Not in PICO
- Sorum, P. C., Shim, J., Chasseigne, G., Bonnin-Scaon, S., Cogneau, J. & Mullet, E. (2003) Why do primary care physicians in the United States and France order prostate-specific antigen tests for asymptomatic patients? *Medical Decision Making*, 23: 301-313.
Not in PICO
- Sorum, P. C., Mullet, E., Shim, J., Bonnin-Scaon, S., Chasseigne, G. & Cogneau, J. (2004) Avoidance of anticipated regret: the ordering of prostate-specific antigen tests. *Medical Decision Making*, 24: 149-159.
Not in PICO
- Spencer, B. A., Babey, S. H., Etzioni, D. A., Ponce, N. A., Brown, E. R., Yu, H. J., Chawla, N. & Litwin, M. S. (2006) A population-based survey of prostate-specific antigen testing among California men at higher risk for prostate carcinoma. *Cancer*, 106: 765-774.
Not in PICO
- Sperandeo, G., Sperandeo, M., Morcaldi, M., Caturelli, E., Dimitri, L. & Camagna, A. (2003) Transrectal ultrasonography for the early diagnosis of adenocarcinoma of the prostate: a new maneuver designed to improve the differentiation of malignant and benign lesions. *Journal of Urology*, 169: 607-610.
Not in PICO

- Stamatiou, K., Alevizos, A., Karanasiou, V., Mariolis, A., Mihas, C., Papathanasiou, M., Bovis, K. & Sofras, F. (2007) Impact of additional sampling in the TRUS-guided biopsy for the diagnosis of prostate cancer. *Urologia Internationalis*, 78: 313-317.
Not in PICO
- Stapleton, A. M., Johns, R. L., Kopsaftis, T., Tamblyn, D. J. & Pinnock, C. B. (2008) Abnormal PSA tests -delays in referral. *Australian Family Physician*, 37: 84-88.
Not in PICO
- Stephan, C., Miller, K. & Jung, K. (2011) Is there an optimal prostate-specific antigen threshold for prostate biopsy? *Expert Review of Anticancer Therapy*, 11: 1215-1221.
Narrative review
- Stephenson, S. K., Chang, E. K. & Marks, L. S. (2014) - Screening and detection advances in magnetic resonance image-guided prostate biopsy. [Review]. - *Urologic Clinics of North America*, 41: 315-326.
Narrative review
- Stone, C. A., May, F. W., Pinnock, C. B., Elwood, M. & Rowett, D. S. (2005) Prostate cancer, the PSA test and academic detailing in Australian general practice: an economic evaluation. *Australian and New Zealand Journal of Public Health*, 29: 349-357.
Not in PICO
- Szabo, J., Vegh, A., Gasman, D., Hoznek, A., Chopin, D. K. & Abbou, C. C. (1998) Biopsy-based diagnosis of prostate cancer in 1290 patients referred for prostate examination: results according to the PSA level, digital rectal examination and ultrasonography. *Acta Chirurgica Hungarica*, 37: 95-100.
Not in PICO
- Takahashi, C. & Miyagawa, I. (1997) [Serum prostate-specific antigen in a urological outpatient clinic. Efficacy of age-specific and prostate volume-specific reference range in detection of prostate cancer]. [Japanese]. *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology*, 88: 612-617.
Not in PICO
- Taneja, S. S. (2003) Optimizing prostate biopsy strategies for the diagnosis of prostate cancer. *Reviews in Urology*, 5: 149-155.
Narrative review
- Taneja, S. S. (2014) - Early detection of prostate cancer. - *Urologic Clinics of North America*, 41: xi-xii.
Narrative review
- Tasian, G. E., Cooperberg, M. R., Potter, M. B., Cowan, J. E., Greene, K. L., Carroll, P. R. & Chan, J. M. (2012) PSA screening: determinants of primary-care physician practice patterns. *Prostate Cancer and Prostatic Diseases*, 15: 189-194.
Not in PICO
- Tasian, G. E., Cooperberg, M. R., Cowan, J. E., Keyashian, K., Greene, K. L., Daniels, N. A., Carroll, P. R. & Chan, J. M. (2012) Prostate specific antigen screening for prostate cancer: Knowledge of, attitudes towards, and utilization among primary care physicians. *Urologic Oncology-Seminars and Original Investigations*, 30: 155-160.
Not in PICO
- Thanigasalam, R., Mancuso, P., Tsao, K. & Rashid, P. (2009) Prostate-specific antigen velocity (PSAV): a practical role for PSA?. [Review] [31 refs]. *ANZ Journal of Surgery*, 79: 703-706.
Narrative review
- Tilburt, J. C., Kelley, S., DeCourtney, C. A., Humeniuk, K. M., Latini, J. & Kim, S. P. (2014) - Caring for Alaska Native prostate cancer survivors in primary care: a survey of Alaska Tribal Health System providers. - *International Journal of Circumpolar Health*, 73: 23637.
Not in PICO
- Tohfe, M., Baki, S. A., Saliba, W., Ghandour, F., Ashou, R., Ghazal, G., Bahous, J. & Chamseddine, N. (2008) Metastatic prostate adenocarcinoma presenting with pulmonary symptoms: a case report

- and review of the literature. *Cases journal*, 1: 316.
Not in PICO
- Tong, Y.-J., Wang, X.-Y., Li, F.-Y. & Jiang, X.-X. (2006) Value of MR in differential diagnosis of prostate carcinoma. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 22: 1061-1063.
Not in PICO
- Tsugawa, M., Sasaki, K., Senoo, T., Arata, R., Nasu, Y. & Kumon, H. (2000) Efficacy of ultrasound contrast agent in the diagnosis and treatment of prostate diseases. [Japanese]. *Nishinippon Journal of Urology*, 62: 176-181.
Not in PICO
- Tudiver, F., Guibert, R., Haggerty, J., Ciampi, A., Medved, W., Brown, J. B., Herbert, C., Katz, A., Ritvo, P., Grant, B., Goel, V., Smith, P., O'Beirne, M., Williams, J. I. & Moliner, P. (2002) What influences family physicians' cancer screening decisions when practice guidelines are unclear or conflicting? *Journal of Family Practice*, 51: 760-7U8.
Not in PICO
- Tuppin, P., Samson, S., Fagot-Campagna, A., Lukacs, B., Alla, F., Allemand, H., Paccaud, F., Thalabard, J. C., Vicaut, E., Vidaud, M. & Millat, B. (2014) - [PSA testing, biopsy and cancer and benign prostate hyperplasia in France]. [French]. - *Progres en Urologie*, 24: 572-580.
Not in PICO
- Umbehr, M., Bachmann, L. M., Held, U., Kessler, T. M., Sulser, T., Weishaupt, D., Kurhanewicz, J. & Steurer, J. (2009) Combined magnetic resonance imaging and magnetic resonance spectroscopy imaging in the diagnosis of prostate cancer: a systematic review and meta-analysis. [Review] [54 refs]. *European Urology*, 55: 575-590.
Not in PICO (referred population)
- van Bokhoven, M., Koch, H., van der Weijden, T., Weekers-Muyres, A., Bindels, P., Grol, R. & Dinant, G. J. (2012) The effect of watchful waiting compared to immediate test ordering instructions on general practitioners' blood test ordering behaviour for patients with unexplained complaints; a randomized clinical trial (ISRCTN55755886). *Implementation Science*, 7: 29.
Not in PICO
- Van der Meer, S., Lowik, S. A. M., Hirdes, W. H., Nijman, R. M., Van der Meer, K., Hoekstra-Weebers, J. E. H. M. & Blanker, M. H. (2012) Prostate specific antigen testing policy worldwide varies greatly and seems not to be in accordance with guidelines: a systematic review. *Bmc Family Practice*, 13.
Not in PICO
- Van der Meer, S., Kollen, B. J., Hirdes, W. H., Steffens, M. G., Hoekstra-Weebers, J. E., Nijman, R. M. & Blanker, M. H. (2013) Impact of the European Randomized Study of Screening for Prostate Cancer (ERSPC) on prostate-specific antigen (PSA) testing by Dutch general practitioners. *Bju International*, 112: 26-31.
Not in PICO
- van Renterghem, K., Van Koeveringe, G. & Van Kerrebroeck, P. (2007) Rising PSA in patients with minor LUTS without evidence of prostatic carcinoma: a missing link? *International Urology and Nephrology*, 39: 1107-1113.
Not in PICO
- Vedel, I., Puts, M. T. E., Monette, M., Monette, J. & Bergman, H. (2011) The decision-making process in prostate cancer screening in primary care with a prostate-specific antigen: A systematic review. *Journal of Geriatric Oncology*, 2: 161-176.
Not in PICO
- Venderbos, L. D. F. & Roobol, M. J. (2011) PSA-based prostate cancer screening: the role of active surveillance and informed and shared decision making. *Asian Journal of Andrology*, 13: 219-224.
Narrative review

- Verma, A., St, O. J., Dhillon, K. & Chorneyko, A. (2014) - PSA density improves prediction of prostate cancer. - *Canadian Journal of Urology*, 21: 7312-7321.
Not in PICO
- Vickers, A. J., Savage, C., O'Brien, M. F. & Lilja, H. (2009) Systematic review of pretreatment prostate-specific antigen velocity and doubling time as predictors for prostate cancer. [Review] [27 refs]. *Journal of Clinical Oncology*, 27: 398-403.
Not in PICO
- Vickers, A. J., Till, C., Tangen, C. M., Lilja, H. & Thompson, I. M. (2011) An Empirical Evaluation of Guidelines on Prostate-specific Antigen Velocity in Prostate Cancer Detection. *Journal of the National Cancer Institute*, 103: 462-469.
Not in PICO
- Vickers, A. J. (2013) Counterpoint: Prostate-specific antigen velocity is not of value for early detection of cancer. *Journal of the National Comprehensive Cancer Network*, 11: 286-290.
Narrative review
- Vincendeau, S., Moussa, M. A., Manunta, A., Patard, J. J., Guille, F. & Lobel, B. (2003) PSA: the difficult position of general practitioners between patients and urologists. *Progres En Urologie*, 13: 252-255.
Not in PICO
- von, E. A., Ho, R., Murphy, G. P., Cunningham, M. & Lins, N. (1997) American Cancer Society guidelines for the early detection of prostate cancer: update, June 10, 1997. *Cancer*, 80: 1805-1807.
Guideline
- Voskanyan, G. A., Glybochko, P. V., Vinarov, A. Z., Korobkin, A. S., Ternovoy, S. K. & Shariya, M. A. (2013) Anticipating metabolic changes: Magnetic resonance spectroscopy as a diagnostic tool for early detection of prostate cancer. *European Urology, Supplements*, 12: 149-150.
Not in PICO
- Wadhwa, K., Serrao, E., Frey, J., Gallagher, F., Koo, B. & Kastner, C. (2014) Diagnostic MRI prostate prebiopsy is associated with a significant false negative rate. *Bju International*, 113: 46-47.
Not in PICO
- Walker, N. A. & Challacombe, B. (2013) Managing epididymo-orchitis in general practice. *Practitioner*, 257: 21-25.
Narrative review
- Walker, P. L. C. & Crook, M. (2011) Tumour marker requesting in primary care and the role of the laboratory. *Journal of Clinical Pathology*, 64: 443-446.
Not in PICO
- Wallner, L. P., Frencher, S. K., Hsu, J. W. Y., Chao, C. R., Nichol, M. B., Loo, R. K. & Jacobsen, S. J. (2013) Changes in serum prostate-specific antigen levels and the identification of prostate cancer in a large managed care population. *Bju International*, 111: 1245-1252.
Not in PICO (screening)
- Walsh, P. C. (2012) Re: Urologists' self-referral for pathology of biopsy specimens linked to increased use and lower prostate cancer detection. *Journal of Urology*, 188: 1767.
Not in PICO
- Ward, J., Young, J. & Sladden, M. (1998) Australian general practitioners' views and use of tests to detect early prostate cancer. *Australian and New Zealand Journal of Public Health*, 22: 374-380.
Not in PICO
- Warshaw, G. (2009) Providing quality primary care to older adults. *Journal of the American Board of Family Medicine: JABFM*, 22: 239-241.
Not in PICO
- Watanabe, Y., Terai, A., Araki, T., Nagayama, M., Okumura, A., Amoh, Y., Ishimori, T., Ishibashi, M., Nakashita, S. & Dodo, Y. (2012) Detection and localization of prostate cancer with the targeted biopsy strategy based on ADC map: a prospective large-scale cohort study. *Journal of Magnetic*

- Resonance Imaging*, 35: 1414-1421.
Not in PICO
- Weight, C. J., Kim, S. P., Jacobson, D. J., McGree, M. E., Boorjian, S. A., Thompson, R. H., Leibovich, B. C., Karnes, R. J. & St, S. J. (2013) The effect of benign lower urinary tract symptoms on subsequent prostate cancer testing and diagnosis. *European Urology*, 63: 1021-1027.
Not in PICO
- Weller, D., May, F., Rowett, D., Esterman, A., Pinnock, C., Nicholson, S., Doust, J. & Silagy, C. (2003) Promoting better use of the PSA test in general practice: randomized controlled trial of educational strategies based on outreach visits and mailout. *Family Practice*, 20: 655-661.
Not in PICO
- Williams, N., Hughes, L. J., Turner, E. L., Donovan, J. L., Hamdy, F. C., Neal, D. E., Martin, R. M. & Metcalfe, C. (2011) Prostate-specific antigen testing rates remain low in UK general practice: a cross-sectional study in six English cities. *Bju International*, 108: 1402-1408.
Not in PICO
- Willis, S. R., Ahmed, H. U., Moore, C. M., Donaldson, I., Emberton, M., Miners, A. H. & van der Meulen, J. (2014) - Multiparametric MRI followed by targeted prostate biopsy for men with suspected prostate cancer: a clinical decision analysis. - *BMJ Open*, 4: e004895.
Not in PICO
- Willis, S. R., Ahmed, H. U., Moore, C. M., Donaldson, I., Emberton, M., Miners, A. H. & van der Meulen, J. (2014) Multiparametric MRI followed by targeted prostate biopsy for men with suspected prostate cancer: A clinical decision analysis. *BMJ Open*, 4.
Duplicate
- Wilson, C., Boyd, K., Mohammed, A. & Little, B. (2010) A single episode of haematospermia can be safely managed in the community. *International Journal of Clinical Practice*, 64: 1436-1439.
Not in PICO
- Wu, J. D., Lin, D. W., Page, S. T., Lundgren, A. D., True, L. D. & Plymate, S. R. (2009) Oxidative DNA damage in the prostate may predispose men to a higher risk of prostate cancer. *Clinical & translational oncology*, 2: 39-45.
Not in PICO
- Xoxakos, I., Sotiropoulou, G., Rompolis, D., Chatzinicolaou, V., Kalyvas, C., Louka, G. & Stokidis, D. (2009) Incidental prostate cancer. A malignancy while treating a benign disease. *Journal of Endourology*, 23: A15.
Not in PICO
- Xu, Y. M. (254) [Transperineal prostatic biopsy guided by ultrasound]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]*, 27: 231-232.
Not in PICO
- Yafi, F. A., Aprikian, A. G., Tanguay, S. & Kassouf, W. (2011) Are men on 5 alpha-reductase inhibitors appropriately referred to urology? A survey of primary care physicians. *Bju International*, 108: 1269-1273.
Not in PICO
- Yamaguchi, S., Baba, Y. & Naito, K. (1997) [Systematic ultrasound guided transrectal core prostate biopsy based on serum level of prostate-specific antigen]. [Japanese]. *Hinyokika Kyo - Acta Urologica Japonica*, 43: 641-645.
Not in PICO
- Yamamoto, M., Hibi, H. & Miyake, K. (1994) Role of prostate-specific antigen and digital rectal examination in the detection of prostate cancer. *International journal of urology : official journal of the Japanese Urological Association*, 1: 74-77.
Not in PICO (44/260 received reference standard)
- Yamazaki, H., Yoshigoe, F., Kobari, T., Takeuchi, H., Katoh, N. & Ohishi, Y. (1999) [Digital rectal examination, transrectal ultrasonography and prostate specific antigen for diagnosis of prostate cancer in clinical urological practice-detection of impalpable cancer]. [Japanese]. *Nippon*

- Hinyokika Gakkai Zasshi - Japanese Journal of Urology*, 90: 595-601.
Not in PICO
- Yazici, C. M. & Dogan, C. (2014) Can Non-Urological Doctors Play a Role in Early Prostate Cancer Detection? *Urology Journal*, 11: 1429-1434.
Not in PICO
- Yazici, C. M. & Dogan, C. (2014) - Can non-urological doctors play a role in early prostate cancer detection? - *Urology Journal*, 11: 1429-1434.
Duplicate
- Yerram, N., Volkin, D., Nix, J., Vourganti, S., Hoang, A., Ahmed, F., Gupta, G., Kruecker, J., Kadoury, S., Locklin, J., Gates, S., Xu, S., Merino, M., Linehan, W. M., Turkbey, I. B., Choyke, P. L., Wood, B. J. & Pinto, P. A. (2012) Multiparametric magnetic resonance imaging and ultrasound fusion biopsy detects prostate cancer in patients with prior negative trus biopsies. *Journal of Urology*, 187: e828.
Not in PICO
- Yoneyama, T., Tobisawa, Y., Hatakeyama, S., Narita, S., Habuchi, T., Mori, K., Koie, T. & Ohyama, C. (2014) Measurement of prostate cancer-associated aberrant glycosylation of prostate specific antigen can improve diagnostic accuracy. *European Urology, Supplements*, 13: e112-e112a.
Not in PICO
- Yoo, D. S., Woo, S. H., Cho, S., Kang, S. H., Kim, S. J., Park, S. Y., Lee, S. H., Jeon, S. H. & Park, J. (2014) Practice Patterns of Urologists in Managing Korean Men Aged 40 Years or Younger With High Serum Prostate-specific Antigen Levels. *Urology*, 83: 1339-1343.
Not in PICO
- Zaenker, P. & Ziman, M. R. (2013) Serologic autoantibodies as diagnostic cancer biomarkers--a review. *Cancer Epidemiology, Biomarkers & Prevention*, 22: 2161-2181.
Narrative review
- Zangos, S., Eichler, K., Engelmann, K., Ahmed, M., Dettmer, S., Herzog, C., Pegios, W., Wetter, A., Lehnert, T., Mack, M. G. & Vogl, T. J. (2005) MR-guided transgluteal biopsies with an open low-field system in patients with clinically suspected prostate cancer: technique and preliminary results. *European Radiology*, 15: 174-182.
Not in PICO
- Zhang, B., Ma, X., Zhan, W., Zhu, F., Li, M., Huang, J., Li, Y., Xue, L., Liu, L. & Wei, Y. (2014) - Real-time elastography in the diagnosis of patients suspected of having prostate cancer: a meta-analysis. - *Ultrasound in Medicine & Biology*, 40: 1400-1407.
Not in PICO
- Zhang, V. Y., Westphalen, A., Delos, S. L., Tabatabai, Z. L., Shinohara, K., Vigneron, D. B. & Kurhanewicz, J. (2014) - The role of metabolic imaging in radiation therapy of prostate cancer. - *NMR in Biomedicine*, 27: 100-111.
Not in PICO
- Zlotta, A. R. & Schulman, C. C. (1998) Use of transrectal ultrasonography in prostate pathology: determination and clinical usefulness of the prostate transition zone. [French]. *Revue Medicale de Bruxelles*, 19: 119-123.
Narrative review

BLADDER CANCER

Review question:

What is the risk of bladder cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

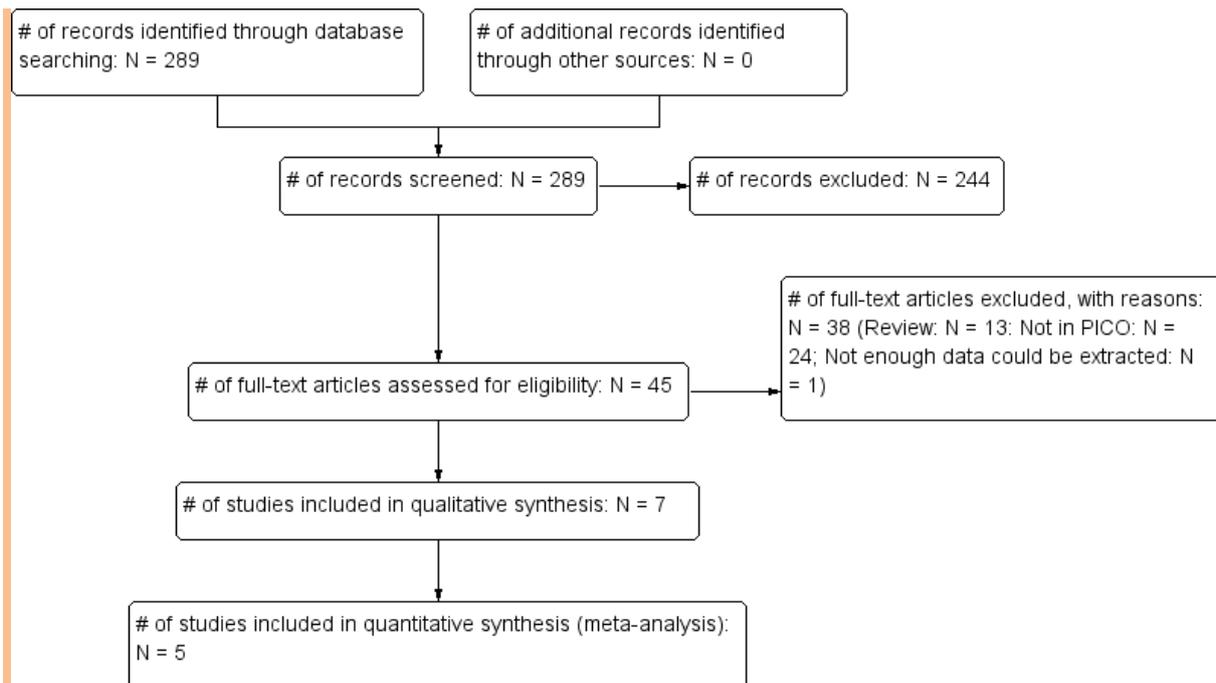
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All - 2012	1070	189	03/09/2012
<i>Premedline</i>	All - 2012	17	5	03/09/2012
<i>Embase</i>	All - 2012	2103	111	30/08/2012
<i>Cochrane Library</i>	All - 2012	126	1	03/09/2012
<i>Psychinfo</i>	All - 2012	2	0	03/09/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All - 2012	163	28	03/09/2012
<i>Biomed Central</i>	All - 2012	158	3	12/09/2012

Total References retrieved (after de-duplication): 263

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-11/08/2014	64	7	11/08/2014
<i>Premedline</i>	2013-11/08/2014	48	11	11/08/2014
<i>Embase</i>	2013-11/08/2014	283	18	11/08/2014
<i>Cochrane Library</i>	2013-11/08/2014	65	0	11/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-11/08/2014	68	3	11/08/2014

Total References retrieved (after de-duplication): 26



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main bias and validity issues to note are that one study was conducted in a Belgian primary care population (Bruyninckx, 2003) and another in US primary care setting (Friedlander, 2014) and these studies are therefore only applicable to the extent that the populations are comparable to a UK GP population, another study (Hippisley-Cox 2012) only presented data for 967681 out of 1240722 eligible patients and it is unclear why, a third study (Jones, 2007) report the results for both 6 months and 3 years after first symptom presentation and it is unclear whether 3 years is too long an interval to be confident that the symptom is a result of underlying cancer, similarly, Friedlander (2014) only followed up the included patients for 180 days, which may be too short a time period. The final study (Shephard, 2012) employed a case-control design which has been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Bruyninckx (2003)	+	+	+	+	?	+	+
Collins (2013)	+	+	+	+	+	+	+
Friedlander (2014)	+	+	?	+	?	+	+
Hippisley-Cox (2012)	+	+	+	-	+	+	+
Jones (2007)	+	+	+	+	+	+	+
Shephard/Price (2012/14)	-	+	+	+	+	+	+

 High	 Unclear	 Low
--	---	---

Study results

Table 1: Bladder cancer: Meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Bruyninckx (2003), Collins (2013), Friedlander (2014), Hippisley-Cox (2012), Jones (2007, at 6 months)	Haematuria	All patients (N = 70330)	4.43 (2.48-7.79)
Bruyninckx (2003), Collins (2013), Friedlander (2014), Hippisley-Cox (2012), Jones (2007, at 3 years)	Haematuria	All patients (N = 70330)	4.72 (2.63-8.32)

Please note that the data from Shephard (2012) are not included in these meta-analyses due to the case-control design of the study. These data are instead reported in the table below.

Table 2: Bladder cancer: Individual positive predictive values from the meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Bruyninckx (2003)	Haematuria	All patients	10.27 (7.6-13.7) 42/409
Collins (2013)	Haematuria	All patients	4.35 (4.1-4.6) 1645/37810
Friedlander (2014)	Haematuria	All included patients	1.34 (0.94-1.91) 33/2455
Hippisley-Cox (2012)	Haematuria	All patients	6.48 (6.1-6.8)

			1201/18548
Jones (2007, at 6 months),	Haematuria	All patients	4.2 (3.8-4.6) 466/11108
Jones (2007, at 3 years),	Haematuria	All patients	5.7 (5.3-6.2) 634/11108

Table 3: Bladder cancer: Additional results reported by the individual papers

Study	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Bruyningx (2003)	Macroscopic haematuria	Men (all ages)	14.2 (10.1-19.5)
Collins (2013)	Haematuria	Men (all ages)	5.5 (5.2-5.8) 1262/22810
Jones (2007)	Haematuria	Men (all ages) at 6 months	5.47 (4.9-6.1) 349/6385
Jones (2007)	Haematuria	Men (all ages) at 3 years	7.4 (6.8-8.1) 472/6385
Bruyningx (2003)	Macroscopic haematuria	Men < 40 years	0 (0-12)
Jones (2007)	Haematuria	Men < 45 years at 3 years	0.99 (0.53-1.69) 13/1311
Bruyningx (2003)	Macroscopic haematuria	Men 40-59 years	3.6 (.6-13.4)
Jones (2007)	Haematuria	Men 45-54 years at 3 years	4.35 (3.11-5.9) 39/897
Jones (2007)	Haematuria	Men 55-64 years at 3 years	8.51 (6.94-10.32) 94/1104
Bruyningx (2003)	Macroscopic haematuria	Men > 59 years	22.1 (15.8-30.1)
Jones (2007)	Haematuria	Men 65-74 years at 3 years	11.21 (9.66-12.9) 170/1517
Jones (2007)	Haematuria	Men 75-84 years at 3 years	10.27 (8.61-12.13) 123/1198
Jones (2007)	Haematuria	Men ≥ 85 years at 3 years	9.22 (6.43-12.7) 33/358
Bruyningx (2003)	Macroscopic haematuria	Women (all ages)	5.1 (2.5-9.8)
Collins (2013)	Haematuria	Women (all ages)	2.6 (2.3-2.8) 383/15000
Jones (2007)	Haematuria	Women (all ages) at 6 months	2.48 (2.1-3) 117/4723
Jones (2007)	Haematuria	Women (all ages) at 3 years	3.4 (2.9-4) 162/4723
Bruyningx (2003)	Macroscopic haematuria	Women < 40 years	0 (NR)
Jones (2007)	Haematuria	Women < 45 years at 3 years	0.22 (0.05-0.64) 3/1361
Bruyningx (2003)	Macroscopic haematuria	Women 40-59 years	6.4 (1.7-18.6)
Jones (2007)	Haematuria	Women 45-54 years at 3 years	1.34 (0.65-2.45) 10/745
Jones (2007)	Haematuria	Women 55-64 years at 3 years	3.42 (2.26-4.93) 27/790
Bruyningx (2003)	Macroscopic haematuria	Women > 59 years	8.3 (3.4-17.9)
Jones (2007)	Haematuria	Women 65-74 years at 3 years	5.91 (4.42-7.72) 50/846

Jones (2007)	Haematuria	Women 75-84 years at 3 years	6.83 (5.06-8.98) 47/688
Jones (2007)	Haematuria	Women ≥ 85 years at 3 years	8.53 (5.6-12.3) 25/293
Bruyninckx (2003)	Macroscopic haematuria	All patients < 60 years	2.6 (.9-6.2)
Shephard (2012)	Visible haematuria (coded data only)	All patients 40-59 years	3.1 (1-9.8)
Price (2014)	Visible haematuria (coded and uncoded data)	All patients 40-59 years	1.2 (0.64-2.3)
Shephard (2012)	Visible haematuria (coded data only)	All patients ≥ 60 years	3.9 (3.5-4.6)
Price (2014)	Visible haematuria (coded and uncoded data)	All patients ≥ 60 years	2.8 (2.5-3.1)
<i>Shephard (2012)</i>	<i>Visible haematuria</i>	<i>All patients</i>	<i>Cases: 2595/4915 Controls: 196/21718</i>
Shephard (2012)	Visible haematuria (second attendance)	All patients ≥ 60 years	6.1 (5.1-8.2)
Price (2014)	Non-visible haematuria (coded and uncoded data)	Patients 40-59 years	0.79 (0.11-5.6)
Price (2014)	Non-visible haematuria (coded and uncoded data)	All patients ≥ 60 years	1.6 (1.2-2.1)
Bruyninckx (2003)	Macroscopic haematuria + pain	All patients	5.3 (2.7-9.8)
Bruyninckx (2003)	Macroscopic haematuria + pain	Men > 60 years	17.8 (8.5-32.6)
Shephard (2012)	Visible haematuria + abdominal pain (coded data only)	All patients ≥ 60 years	3.2 (1.9-5.8)
Price (2014)	Visible haematuria + abdominal pain (coded and uncoded data)	All patients ≥ 60 years	2.3 (1.5-3.5)
Price (2014)	Non-visible haematuria + abdominal pain (coded and uncoded data)	All patients ≥ 60 years	1.7 (0.6-4.2)
Bruyninckx (2003)	Macroscopic haematuria without pain	All patients	10.9 (7.3-16)
Bruyninckx (2003)	Macroscopic haematuria without pain	Men > 60 years	18.9 (11.9-28.6)
Bruyninckx (2003)	Macroscopic haematuria + increased frequency of micturition	All patients	7.2 (3.8-12.8)
Bruyninckx (2003)	Macroscopic haematuria + increased frequency of micturition	Men > 60 years	22.6 (10.3-41.5)
Bruyninckx (2003)	Macroscopic haematuria without increased frequency of micturition	All patients	13.4 (9.4-18.7)

Bruyninckx (2003)	Macroscopic haematuria without increased frequency of micturition	Men > 60 years	22 (14.9-31.2)
Bruyninckx (2003)	Macroscopic haematuria + dysuria	All patients	5.6 (2.6-11)
Bruyninckx (2003)	Macroscopic haematuria + dysuria	Men > 60 years	24.1 (11-43.9)
Shephard (2012)	Visible haematuria + dysuria (coded data only)	All patients ≥ 60 years	6.4 (NR as N < 10)
Price (2014)	Visible haematuria + dysuria (coded and uncoded data)	All patients ≥ 60 years	4.1 (2.6-6.3)
Price (2014)	Non-visible haematuria + dysuria (coded and uncoded data)	All patients ≥ 60 years	4.5 (NR)
Bruyninckx (2003)	Macroscopic haematuria without dysuria	All patients	23.6 (17.1-31.5)
Bruyninckx (2003)	Macroscopic haematuria without dysuria	Men > 60 years	21.6 (14.6-30.6)
Bruyninckx (2003)	Macroscopic haematuria + nocturia	All patients	6.3 (2.4-14.8)
Bruyninckx (2003)	Macroscopic haematuria + nocturia	Men > 60 years	12.5 (3.3-33.5)
Bruyninckx (2003)	Macroscopic haematuria without nocturia	All patients	11.2 (8.1-15.2)
Bruyninckx (2003)	Macroscopic haematuria without nocturia	Men > 60 years	23.3 (16.3-32.1)
Bruyninckx (2003)	Macroscopic haematuria + weight loss	All patients	10 (.5-45.9)
Bruyninckx (2003)	Macroscopic haematuria + weight loss	Men > 60 years	33.3 (1.8-87.5)
Bruyninckx (2003)	Macroscopic haematuria without weight loss	All patients	8.3 (5.8-11.5)
Bruyninckx (2003)	Macroscopic haematuria without weight loss	Men > 60 years	18.2 (12.4-26)
Bruyninckx (2003)	Macroscopic haematuria + fatigue	All patients	20.8 (11-35.4)
Bruyninckx (2003)	Macroscopic haematuria + fatigue	Men > 60 years	30 (12.8-54.3)
Bruyninckx (2003)	Macroscopic haematuria without fatigue	All patients	8.9 (6.2-12.4)
Bruyninckx (2003)	Macroscopic haematuria without fatigue	Men > 60 years	20.8 (14.2-29.4)
Bruyninckx (2003)	Macroscopic haematuria with other symptoms	All patients	6.4 (4.3-9.3)
Bruyninckx (2003)	Macroscopic haematuria without other symptoms	All patients	3.9 (2.3-6.4)
Shephard (2012)	Visible haematuria + constipation (coded data only)	All patients ≥ 60 years	2.7 (1.6-4.5)

Price (2014)	Visible haematuria + constipation (coded and uncoded data)	All patients ≥ 60 years	2.2 (1.5-3.4)
Price (2014)	Non-visible haematuria + constipation (coded and uncoded data)	All patients ≥ 60 years	2 (NR)
Shephard (2012)	Visible haematuria + urinary tract infection (coded data only)	All patients ≥ 60 years	4.1 (3-6.2)
Price (2014)	Visible haematuria + urinary tract infection (coded and uncoded data)	All patients ≥ 60 years	2.2 (1.8-2.8)
Price (2014)	Non-visible haematuria + urinary tract infection (coded and uncoded data)	All patients ≥ 60 years	1.4 (0.8-2.4)
Shephard (2012)	Visible haematuria + raised inflammatory markers (coded data only)	All patients ≥ 60 years	5.6 (NR as N < 10)
Price (2014)	Visible haematuria + raised inflammatory markers (coded and uncoded data)	All patients ≥ 60 years	3.3 (2-5.4)
Price (2014)	Non-visible haematuria + raised inflammatory markers (coded and uncoded data)	All patients ≥ 60 years	1.25 (NR)
Shephard (2012)	Visible haematuria + raised creatinine (coded data only)	All patients ≥ 60 years	5.1 (3.4-8.4)
Price (2014)	Visible haematuria + raised creatinine (coded and uncoded data)	All patients ≥ 60 years	2.9 (2.1-3.9)
Price (2014)	Non-visible haematuria + raised creatinine (coded and uncoded data)	All patients ≥ 60 years	1.1 (0.6-2.2)
Shephard (2012)	Visible haematuria + raised white blood cell count (coded data only)	All patients ≥ 60 years	8.8 (NR as N < 10)
Price (2014)	Visible haematuria + raised white blood cell count (coded and uncoded data)	All patients ≥ 60 years	3.7 (2.1-6.3)
Price (2014)	Non-visible haematuria + raised white blood cell count (coded and uncoded data)	All patients ≥ 60 years	3.9 (NR)
Collins (2013)	Abdominal pain	All patients	0.11 (0.1-0.13)

			284/253344
		Men	0.2 (0.2-0.21) 187/105247
		Women	0.1 (0.1-0.1) 97/148097
Hippisley-Cox (2012)	Abdominal pain	All patients	0.2 (0.2-0.2) 182/93077
Shephard (2012)	Abdominal pain	All patients ≥ 60	0.2 (0.1-0.2)
<i>Shephard (2012)</i>	<i>Abdominal pain</i>	<i>All patients</i>	<i>Cases: 358/4915</i> <i>Controls: 787/21718</i>
Shephard (2012)	Abdominal pain (second attendance)	All patients ≥ 60	0.2 (0.1-0.2)
Shephard (2012)	Abdominal pain + dysuria	All patients ≥ 60	0.4 (0.3-0.7)
Shephard (2012)	Abdominal pain + constipation	All patients ≥ 60	0.2 (0.1-0.3)
Shephard (2012)	Abdominal pain + urinary tract infection	All patients ≥ 60	0.4 (0.3-0.6)
Shephard (2012)	Abdominal pain + raised inflammatory markers	All patients ≥ 60	0.2 (0.1-0.3)
Shephard (2012)	Abdominal pain + raised creatinine	All patients ≥ 60	0.3 (0.2-0.4)
Shephard (2012)	Abdominal pain + raised white blood cell count	All patients ≥ 60	0.2 (0.1-0.3)
Shephard (2012)	Dysuria	All patients ≥ 60	0.7 (0.6-0.8)
<i>Shephard (2012)</i>	<i>Dysuria</i>	<i>All patients</i>	<i>Cases: 444/4915</i> <i>Controls: 209/21718</i>
Shephard (2012)	Dysuria (second attendance)	All patients ≥ 60	1 (0.7-1.5)
Shephard (2012)	Dysuria + constipation	All patients ≥ 60	0.5 (0.3-0.9)
Shephard (2012)	Dysuria + urinary tract infection	All patients ≥ 60	0.7 (0.4-1.1)
Shephard (2012)	Dysuria + raised inflammatory markers	All patients ≥ 60	0.9 (0.5-1.7)
Shephard (2012)	Dysuria + raised creatinine	All patients ≥ 60	0.6 (0.4-1)
Shephard (2012)	Dysuria + raised white blood cell count	All patients ≥ 60	0.9 (0.5-1.9)
Shephard (2012)	Constipation	All patients ≥ 60	0.1 (0.1-0.2)
<i>Shephard (2012)</i>	<i>Constipation</i>	<i>All patients</i>	<i>Cases: 286/4915</i> <i>Controls: 708/21718</i>
Shephard (2012)	Constipation (second attendance)	All patients ≥ 60	0.1 (0.1-0.2)
Shephard (2012)	Constipation + urinary tract infection	All patients ≥ 60	0.5 (0.3-0.7)
Shephard (2012)	Constipation + raised inflammatory markers	All patients ≥ 60	0.2 (0.1-0.2)
Shephard (2012)	Constipation + raised creatinine	All patients ≥ 60	0.2 (0.2-0.3)
Shephard (2012)	Constipation + raised	All patients ≥ 60	0.3 (0.2-0.5)

	white blood cell count		
Shephard (2012)	Urinary tract infection	All patients ≥ 60	0.4 (0.3-0.4)
<i>Shephard (2012)</i>	<i>Urinary tract infection</i>	<i>All patients</i>	<i>Cases: 835/4915 Controls: 705/21718</i>
Shephard (2012)	Urinary tract infection (second attendance)	All patients ≥ 60	0.5 (0.4-1.6)
Shephard (2012)	Urinary tract infection + raised inflammatory markers	All patients ≥ 60	0.4 (0.3-0.7)
Shephard (2012)	Urinary tract infection + raised creatinine	All patients ≥ 60	0.5 (0.3-0.6)
Shephard (2012)	Urinary tract infection + raised white blood cell count	All patients ≥ 60	0.6 (0.4-0.9)
Shephard (2012)	Raised inflammatory markers	All patients ≥ 60	0.1 (0.1-0.2)
<i>Shephard (2012)</i>	<i>Raised inflammatory markers</i>	<i>All patients</i>	<i>Cases: 293/4915 Controls: 717/21718</i>
Shephard (2012)	Raised inflammatory markers + raised creatinine	All patients ≥ 60	0.3 (0.2-0.3)
Shephard (2012)	Raised inflammatory markers + raised white blood cell count	All patients ≥ 60	0.2 (0.1-0.3)
Shephard (2012)	Raised creatinine	All patients ≥ 60	0.1 (0.12-0.14) As reported, but PPV or CI not reported correctly
<i>Shephard (2012)</i>	<i>Raised creatinine</i>	<i>All patients</i>	<i>Cases: 660/4915 Controls: 1668/21718</i>
Shephard (2012)	Raised creatinine + raised white blood cell count	All patients ≥ 60	0.3 (0.2-0.4)
Shephard (2012)	Raised white blood cell count	All patients ≥ 60	0.2 (0.17-0.23)
<i>Shephard (2012)</i>	<i>Raised white blood cell count</i>	<i>All patients</i>	<i>Cases: 250/4915 Controls: 401/21718</i>
Collins (2013)	Appetite loss	Women	0.1 (0.04-0.3) 4/3481
Hippisley-Cox (2012)	Appetite loss	All patients	0.18 (0.07-0.4) 6/3330
Collins (2013)	Weight loss	Women	0.1 (0.1-0.2) 21/16037
Hippisley-Cox (2012)	Weight loss	All patients	0.41 (0.3-0.6) 38/9281
Collins (2013)	Anaemia	All patients	0.6 (0.5-0.7) 102/16961
		Men	1.4 (1.1-1.9) 57/3969
		Women	0.3 (0.3-0.5) 45/12992

Hippisley-Cox (2012)	Anaemia	All patients	0.69 (0.5-0.9) 68/9799
----------------------	---------	--------------	---------------------------

NR = Not reported. Please note the calculations of the positive predictive values differ between the studies with Bruyninckx (2003), Hippisley-Cox (2012) and Jones (2007) using (TP)/(TP+FP) and Shephard (2012) using Bayesian statistics due to the case-control design of this study.

Evidence statement(s):

Haematuria (6 studies, N = 89345) presenting in a primary care setting is associated with overall positive predictive values ranging from 1.34%-10.27% for bladder cancer, which tended to be higher in men (5.47%-14.2%) than in women (2.48%-5.1%; 3 studies, total N = 49327) and to increase with age in men (up 22.1%; 2 studies, total N = 11517) and much less so in women (up to 8.53%; 2 studies, total N = 11517). All the studies were associated with 0-2 bias or applicability concern (see also Tables 1-3).

Haematuria in combination with other symptoms presenting in a primary care setting was associated with positive predictive values ranging from 1.1% (non-visible with raised creatinine in patients \geq 60 years; 1 study, total N = 26633) to 33.3% (with weight loss in men $>$ 60 years old; 1 study, total N = 409) for bladder cancer. Both studies were associated with 1 bias or applicability concern (see also Table 3).

Other symptoms (than haematuria) presenting alone or in combination with each other (but not haematuria) in a primary care setting were all associated with positive predictive values \leq 1.5% for bladder cancer (3 studies, total N = 1284137). All the studies were associated with 0-1 bias or applicability concern (see also Table 3).

Evidence tables

Bruyninckx (2003)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive patient series using a register populated by GPs in Belgium. This register is based on the voluntary and constant registration of epidemiological data by GPs and is spread equally over the country. At the time of the study data (1993-1994) this GP network covered ca 1% of the Belgian population. GP participation rate was ca 90% (N = 83).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	A total of 83890 patient-years were registered. Patients with macroscopic haematuria: N = 409 (232 males/176 females/ 1 of unknown sex); mean (SD) age of patients with macroscopic haematuria but not cancer = 57 (20) years. <u>Inclusion criteria:</u> All patients complaining to their GP of macroscopic haematuria in 1993-1994 were included. Patients complaining repeatedly of

	haematuria were included only once. <u>Exclusion criteria:</u> None reported. <u>Clinical setting:</u> Primary care, Belgium.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Haematuria was registered if a patient complained to the GP of any blood of urological origin that had not necessarily been checked by the GP during the study period, irrespective of the duration of the complaint and irrespective of the existence or absence of other signs or symptoms. Registered associated signs and symptoms were fatigue, weight loss, pain, nocturia, dysuria or frequency of micturition.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Diagnosis of urological cancer during a clinical follow-up of ≥ 18 months was registered as the reference standard. Urological cancer was defined as any malignancy of the urological tract that was confirmed histologically or by cystoscopy, intravenous pyelogram, or ultrasound scan. Recall letters were sent to the practices every six months, to check the included cases again upon the emergence of a diagnosis of any urological cancer. To ensure that all cases of urological cancer diagnosed within the follow-up period were identified, at the end of the period each of the GPs was sent a list of all their patients with macroscopic haematuria who were included in the study, in order to check for any 'hidden' urological cancer diagnosis.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results but the number of true negatives and false negatives could not be ascertained from the reported results.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes

Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Type of urological cancer found in the 409 haematuria patients: Bladder: N = 34, other urological cancer: N = 8. All these cancers were included in the meta-analysis.
Collins (2013)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2145133 patients (1063355 men, 1081778 women) were identified from 364 practices.</p> <p><u>Symptoms:</u> Haemoglobin < 11 g/dl recorded in the last year (N = 16961; 3969 men, 12992 women), abdominal pain (N = 253344; 105247 men, 148097 women), appetite loss (N = 6097; 2616 men, 3481 women), weight loss (N = 29369; 13332 men, 16037 women), haematuria (N = 37810; 22810 men, 15000 women), previous diagnosis of cancer apart from renal tract cancer at study entry (N = 49303; 18130 men, 31173 women).</p> <p><u>Incident cases of renal tract cancer during the 2-year follow up period:</u> N = 2283 (1685 men, 598 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (e.g., haematuria, abdominal pain, weight loss, appetite loss, and anaemia), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of renal tract cancer, registered less than 12 months with the general practice, had invalid dates, < 30 years old or ≥ 85 years old.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Renal tract cancer, which was defined as incident diagnosis of cancer of the bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes. Patients without the outcome were censored at the earliest of the date of death, date of leaving the practice study of 2 years of follow up.	
Is the reference standard likely to correctly classify the target condition?		Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?		Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients seem to be accounted for	
Was there an appropriate interval between index test and reference standard?		Yes
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		Yes
Could the patient flow have introduced bias?		Low risk
NOTES	It is unclear why no data has been presented for men for the symptoms of appetite loss and weight loss.	
Friedlander (2014)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective cohort study, using claims data and laboratory values from the Vanderbilt University Medical Centre's (VUMC) Research Derivative, which is a "data repository that contains administrative and clinical information, including a complete record of visits and admissions, laboratory data, and diagnosis and procedure codes, on every patient treated in the Vanderbilt health system" (p 634) located in Tennessee in the USA.	
Was a consecutive or random sample of patients enrolled?		Yes
Was a case-control design avoided?		Yes
Did the study avoid inappropriate exclusions?		Yes (probably)
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and	N = 2455 patients, 724 males / 1731 females, median (inter-quartile range) age = 58 (49-68) years; smoking history: current smoker (N = 406), former	

setting	<p>smoker (N = 473), non-smoker (N = 1514).</p> <p><u>Inclusion criteria:</u> “Patients aged \geq 40 years with a first diagnosis of hematuria” “between 2004 and 2012 by urinalysis (>3 red blood counts per high power field) or International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes for hematuria (599.7, 599.70, 599.71 or 599.72) at one of the VUMC’s 19 primary care clinics. To be included in the study, patients must have had records for 1 year before the date of hematuria diagnosis.”</p> <p><u>Exclusion criteria:</u> “Patients were excluded if they had a urinary tract infection (defined as a urinalysis positive for both leukocyte esterase and urine nitrites, or a positive urine culture) within 4 weeks before or 1 week after the index hematuria episode (n = 590, 9.0%) or had a prior explanatory diagnoses and procedures that would preclude the need for a hematuria evaluation (according to a convened panel of content experts; prostate/renal/bladder/other cancer, benign prostate/renal/bladder/other mass, prostate dysplasia, cystitis, urethritis, epididymitis/orchitis, prostatitis, pyelonephritis, urolithiasis, prostatic enlargement, trauma, medical renal disease, haematologic/thrombotic disease?, anatomic abnormality, prostatectomy, prostate biopsy, transurethral incision of prostate, resection of prostate, cystoscopy, cystectomy, ureteroscopy, nephrectomy, pyeloplasty, ureteral reimplantation).” We then used Physicians Current Procedural Terminology Coding System, 4th Edition and ICD-9 codes to exclude patients with an explanatory diagnosis or procedure within 180 days preceding their hematuria diagnosis (n = 3540, 53.8%).”</p> <p><u>Clinical setting:</u> Primary care, USA.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	First diagnosis of hematuria” “by urinalysis (>3 red blood counts per high power field) or International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes for hematuria (599.7, 599.70, 599.71 or 599.72)”. ”
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	The reference standard consisted checking the database for diagnoses of genitourinary neoplasms within 180 days after haematuria diagnosis, as determined by ICD-9 codes.
Is the reference standard likely to correctly classify the target condition?	Unclear (is 180 days enough time to get a diagnosis of all cancers?)
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)

Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	There were 66 patients with cancer: Bladder (N = 33), renal cell (N = 16), prostate (N = 15). The types of cancer for the remaining two cases were not reported.

Hippisley-Cox (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1240722 patients were identified from 189 practices (622166 males, 618556 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Current symptoms and symptoms in the preceding year:</u> Current haematuria (N = 25553), current abdominal pain (N = 128721), current appetite loss (N = 5531), current weight loss (N = 14464), constipation in the last year (N = 8472), diarrhoea in the last year (N = 12171), tiredness in the last year (N = 12669), haemoglobin recoded in the last year (N = 216201), haemoglobin < 11 g/dl in the last year (N = 16169).</p> <p><u>Incident cases of renal tract cancer during the 2-year follow up period:</u> N = 1622; mean age at diagnosis = 70 years, 1187 males/ 435 females; Type of cancer: Bladder: N = 1292; Kidney: N = 307; Ureter: N = 21; Urethra: N = 2.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September</p>

	<p>2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months' registration prior to study entry. For patients with incident haematuria, appetite loss, weight loss, or abdominal pain, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of renal tract cancer at baseline, and patients with a recorded 'red-flag' (see "Definition of symptom" below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Renal tract cancer, which was defined as incident diagnosis of cancer of the bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 codes (188 or 189) or ICD-10 diagnostic codes (C64–67).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 101607 patients were excluded for the following reasons: No recorded Townsend score (N =

	70847), history of renal tract cancer (N = 1506), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 29254), leaving 1240722 patients. However, data is presented for 967681 / 1240722 patients. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	Please note, the included cancer cases were for renal tract cancer, not just bladder cancer.

Jones (2007)

PATIENT SELECTION

A. risk of bias

Patient sampling	Retrospective consecutive patient series using patients in the UK's General Practice Research Database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability

Patient characteristics and setting	<p>A total of 923605 patients were identified, of whom 762325 were aged \geq 15 years.</p> <p><u>Number of first occurrences in patients with no previous diagnosis of cancer:</u></p> <p><u>Haematuria:</u> N = 11138, mean (SD) age at first symptom = 58.5 (18.9) years. Patients excluded due to incomplete dates for their first symptom: N = 30. Sex (of final sample): 6385 males, 4723 females.</p> <p><u>Haemoptysis:</u> N = 4822, mean (SD) age at first symptom = 61.6 (18) years. Patients excluded due to incomplete dates for their first symptom: N = 10. Sex (of final sample): 2930 males, 1882 females.</p> <p><u>Dysphagia:</u> N = 6003, mean (SD) age at first symptom = 54.5 (19.4) years. Patients excluded due to incomplete dates for their first symptom: N = 4. Sex (of final sample): 2628 males, 3371 females.</p> <p><u>Rectal bleeding:</u> N = 15314, mean (SD) age at first symptom = 52.5 (18.8) years. Patients excluded due to incomplete dates for their first symptom: N = 25. Sex (of final sample): 7523 males, 7766 females.</p> <p><u>Inclusion criteria:</u> All patients from 128 general practices that provided data of a sufficient standard from 1 January 1994 to 31 December 2000 and which provided exclusively Read coded data, who were aged between 15 and 100 years, whose first ever recorded occurrence of each alarm symptom (haematuria, haemoptysis, dysphagia, or rectal bleeding) was after 31 December 1994 and who had not previously been diagnosed as having any cancer.</p> <p><u>Exclusion criteria:</u> Patients whose date of first symptom or first relevant diagnosis of cancer was before 1 January 1995 and patients with a diagnosis</p>
-------------------------------------	---

	of any other cancer than the ones of interest before the date of the first recorded symptom or before the index cancer diagnosis date if the related symptom was not recorded. <u>Clinical setting</u> : Primary care
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Identification of all patients who ever had symptoms recorded for haematuria, haemoptysis, dysphagia, or rectal bleeding.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Cancer code in the UK's General Practice Research Database: <u>Haematuria</u> : Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs. <u>Haemoptysis</u> : Respiratory tract neoplasms. <u>Dysphagia</u> : Oesophageal neoplasms. <u>Rectal bleeding</u> : Colorectal neoplasms.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Diagnoses of cancer were most often made in the first three months after the onset of alarm symptoms; very few diagnoses of cancer were made later than three years after symptom onset. In the 4th and 5th years of study, the small number of observed occurrences of cancer was similar to the number

	<p>expected from background incidence rates.</p> <p>Secondary analyses evaluating whether the incidence of neoplasms other than those prespecified was increased after the occurrence of alarm symptoms showed for:</p> <p><u>Haematuria</u>: Inclusion of cancers of the reproductive organs yielded 21 additional cancers in women and 158 cancers in men, mostly cancers of the prostate. Inclusion of these cancers in the analysis would give a positive predictive value of 3.9% in women and 9.9% in men.</p> <p><u>Dysphagia</u>: Inclusion of gastric cancers yielded 17 additional cancer diagnoses in women and 30 in men. Inclusion of these cancers gave positive predictive values of 5.2% in women and 6.9% in men.</p> <p><i>Estimates based on the pre-specified cancers may be thus conservative for these symptoms.</i></p> <p><u>Haemoptysis</u>: Extension of the diagnostic criteria yielded 6 additional cancers.</p> <p><u>Rectal bleeding</u>: Extension of the diagnostic criteria yielded 2 additional cancers.</p>
--	--

Shephard (2012)/Price (2014)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Matched case-control study using patients in the UK's General Practice Research Database.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases</u>:</p> <p>Males: 3563 patients, median age at diagnosis = 73 (IQR = 65-80) years, median number of consultations = 14 (IQR = 9-22), UK.</p> <p>Females: 1352 patients, median age at diagnosis = 75 (IQR = 67-82) years, median number of consultations = 15 (IQR = 10-23), UK.</p> <p><u>Controls</u>:</p> <p>Males: 15452 patients, median age at diagnosis = 73 (IQR = 66-79) years, median number of consultations = 8 (IQR = 4-15), UK.</p> <p>Females: 6266 patients, median age at diagnosis = 75 (IQR = 67-82) years, median number of consultations = 9 (IQR = 4-15), UK.</p> <p><u>Inclusion criteria</u>:</p> <p>Cases: Patients with a first record of bladder cancer between January 2000 and December 2009 inclusive, aged ≥ 40 years, with min. 1 year of data before diagnosis. The first instance of a bladder cancer code was assigned the data of diagnosis/index date.</p>

	<p>Controls: Up to 5 controls were matched on sex, general practice, and to 1 year of age of the case. The index date was the index date of the matched case.</p> <p><u>Exclusion criteria</u>: Metastatic cancer of the bladder from a non-bladder primary, diagnosis before 2000, or no consultations in the year before diagnosis.</p> <p><u>Clinical setting</u>: Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	<p>A list of symptoms, signs and investigations (features) potentially associated with bladder cancer was compiled from the authors' literature search, augmented by viewing material from bladder cancer support organisations and online chat rooms. Internet search terms included 'bladder cancer', 'bladder symptoms', and 'early signs/indications'. Visible and non-visible haematuria were studied separately. Only codes specifying the word 'microscopic' were assigned to the latter group, so generic codes such as the single word 'haematuria' were assumed to be visible haematuria. For each feature a list of relevant medical codes from the GPRD's master list of over 100,000 codes was assembled. Occurrences of these in the year before the index date were identified. Repeated consultations for the same complaint were also identified along with all codes for fractures as a test for any recording bias between cases and controls (making the assumption that the fracture rate would be approximately equal). Variables were retained only if they occurred in at least 5% of either cases or controls (this was always cases). Investigation results were deemed to be abnormal if they fell outside their local laboratory's normal range: for analysis, patients with a normal laboratory result were grouped with those who had not been tested.</p>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Bladder cancer code in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 29033 patients were identified, 24098 controls and 4935 cases. Of the controls the following exclusions were applied: bladder cancer post-2000 (N = 134), bladder control [?] pre-2000 (N = 125), metastatic cancer (N = 35), and no data in year pre-index date (N = 2086). Of the cases the following exclusions were applied: No controls (N = 13), metastatic cancer (N = 7).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	43 symptoms and 104 abnormal test results were considered initially. 6 symptoms and 7 abnormal test variables were present in $\geq 5\%$ of cases. The proportion of patients with a recorded fracture did not differ between cases (1.45%) and controls (1.46%). The authors have published extra analyses of the same data in an additional paper (Price, 2014) wherein the data analysis is extended to the uncoded data in the CPRD, namely 'free text' notes added by GPs to augment a coded entry in a patient's record. In particular, the authors "sought to identify whether there were sufficient additional non-visible haematuria entries to allow reliable estimates of its association with bladder cancer."

References

Included studies

- Bruyininckx, R., Buntinx, F., Aertgeerts, B., and Van, Casteren, V. The diagnostic value of macroscopic haematuria for the diagnosis of urological cancer in general practice. *British Journal of General Practice* 53[486], 31-35. 1-1-2003.
- Collins, G.S., and Altman, D.G. Identifying patients with undetected renal tract cancer in primary care: An independent and external validation of Qcancer (renal) prediction model. *Cancer Epidemiology*, 37, 115-120. 2013.
- Friedlander, D.F., Resnick, M.J., You, C., Bassett, J., Yarlagadda V., Penson, D.F., Barocas D.A. Variation in the intensity of hematuria evaluation: A target for primary care quality improvement. *American Journal of Medicine*, 127, 633-640. 2014.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected renal tract cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice* 62[597], e251-e260. 2012.
- Jones, R., Latinovic, R., Charlton, J., and Gulliford, M. C. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *BMJ* 334[7602], 1040. 19-5-2007.
- Price, S.J., Shephard, E. A., Stapley, S.A., Barraclough, K., and Hamilton, W. T. The risk of bladder cancer with non-visible haematuria: A primary care study using electronic records. *British Journal of General Practice* 64, e584-e589. 2014.
- Shephard, E. A., Stapley, S., Neal, R. D., Rose, P., Walter, F. M., and Hamilton, W. T. Clinical features of bladder cancer in primary care. *British Journal of General Practice* 62[602], 598-604. 2012.

Excluded studies (with excl reason)

Bladder cancer. Early detection is critical. Mayo Clinic health letter (English ed 16[3], 6. 1998.

Excl reason: Narrative review

Abbaszadeh, S., Taheri, S., and Nourbala, M. H. Bladder tumor in women with microscopic hematuria: an Iranian experience and a review of the literature. *Advances in Urology*.:231861, 2009. 231861. 2009.

Excl reason: Not in PICO (secondary care)

Adeniyi, A. American Urological Association--94th annual meeting. 1-6 May 1999, Dallas, USA. *Idrugs* 2[7], 656-658. 1999.

Excl reason: Narrative review/meeting summary

Akan, S., Yuksel, O., Ozbay, N., Uruc, F. & Verit, A. (2014) - A rare entity of benign bladder neoplasm: female lipoma. - *Georgian Medical News*, 17-20.

Not in PICO

Ali-El-Dein, B., El-Sobky, E., El-Baz, M., and Shaaban, A. A. Abdominal and pelvic extra-adrenal paraganglioma: A review of literature and a report on 7 cases. *In Vivo* 16[4], 249-254. 2002.

Excl reason: Not in PICO

Allen, D., Popert, R., and O'Brien, T. The two-week-wait cancer initiative in urology: useful modernization? *Journal of the Royal Society of Medicine* 97[6], 279-281. 2004.

Excl reason: Not in PICO

Altwein, J. E. [Dysuria. Typical symptoms for proper diagnosis]. [German]. *MMW Fortschritte der Medizin* 143, Suppl-30. 2001.

Excl reason: Narrative review

Amin, M. F. & Abd El Hamid, A. M. (2013) The diagnostic accuracy of multidetector computed tomography with multiplanar reformatted imaging and virtual cystoscopy in the early detection and evaluation of bladder carcinoma: comparison with conventional cystoscopy. *Abdominal Imaging*, 38: 184-192.

Not in PICO

Amling, C. L. Diagnosis and management of superficial bladder cancer. *Current Problems in Cancer* 25[4], 219-278. 2001.

Excl reason: Narrative review

Andreyev, H. J., Vlavianos, P., Blake, P., Dearnaley, D., Norman, A. R., and Tait, D. Gastrointestinal symptoms after pelvic radiotherapy: role for the gastroenterologist? *International Journal of Radiation Oncology, Biology, Physics* 62[5], 1464-1471. 1-8-2005.

Excl reason: Not in PICO

Arzimanoglou, I. I., Gilbert, F., and Barber, H. R. Microsatellite instability in human solid tumors. [Review] [132 refs]. *Cancer* 82[10], 1808-1820. 15-5-1998.

Excl reason: Not in PICO

Attallah, A. M., el-Didi, M., Seif, F., el-Mohamady, H., and Dalbagni, G. Comparative study between cytology and dot-ELISA for early detection of bladder cancer. *American Journal of Clinical Pathology* 105[1], 109-114. 1996.

Excl reason: Not in PICO

Banek, S., Schwentner, C., Tager, D., Pesch, B., Nasterlack, M., Leng, G., Gawrych, K., Bonberg, N., Johnen, G., Kluckert, M., Gakis, G., Todenhofer, T., Hennenlotter, J., Bruning, T. & Stenzl, A. (2013) Prospective evaluation of fluorescence-in situ-hybridization to detect bladder cancer: Results from the UroScreen-Study. *Urologic Oncology: Seminars and Original Investigations*, 31: 1656-1662.

Not in PICO

Baniel, J. and Vishna, T. Primary transitional cell carcinoma in vesical diverticula. *Urology* 50[5], 697-699. 1997.

Excl reason: Not in PICO

Basak, M., Ozkurt, H., Tanriverdi, O., Cay, E., Aydin, M., and Miroglu, C. Sixteen-slice multidetector computed tomographic virtual cystoscopy in the evaluation of a patient with suspected bladder tumor and history of bladder carcinoma operation. *Journal of Computer Assisted Tomography* 33[6], 867-871. 2009.

Excl reason: Not in PICO

Bassett, J. C., Gore, J. L., McCarthy, W. J., Morrison, C., Kwan, L., Bennett, C. J., Cookson, M. S., Penson, D. F. & Saigal, C. (2013) Introduction of a tobacco-screening initiative for those at risk for bladder cancer in a high volume urology clinic. *Journal of Clinical Oncology*, 31.

Not in PICO

Bassett, J., Alvarez, J. A., You, C., Koyama, T., Ni, S., Penson, D. & Barocas, D. (2014) Gender, race, and variation in the workup of hematuria. *Journal of Urology*, 191: e62-e63.

Published as abstract only. Not enough information can be extracted to ascertain the relevance of the study.

Batool, A., Ramachandran, R., Dubrovskaya, V. & Lee, D. (2013) Recurrent urothelial cancer masquerading as a large colonic mass and massive gastrointestinal hemorrhage. *American Journal of Gastroenterology*, 108: S458-S459.

Not in PICO

Baughan, P., O'Neill, B., and Fletcher, E. Auditing the diagnosis of cancer in primary care: the experience in Scotland. *British Journal of Cancer* 101, Suppl-91. 3-12-2009.

Excl reason: Not in PICO

Begara, Morillas F., Silmi, Moyano A., Espinosa, Fernandez B., Prieto, Chiparro L., Rapariz, Gonzalez M., Gonzalez Morales, M. L., Martin, Rodilla C., Bravo de Rueda, Accinelli C., and Resel, Estevez L. [Bladder amyloidosis in a female patient with suspected bladder carcinoma]. [Spanish]. *Archivos Espanoles de Urologia* 47[2], 176-179. 1994.

Excl reason: Not in PICO

Bevers, R. F., Battermann, J. J., Gietema, J. A., Hulsbergen-Van de Kaa CA, de Reijke, T. M., Feller, N., Witjes, J. A., De Nederlandse Vereniging voor Urologie, and Vereniging van Integrale Kankercentra (VIKC). [Guideline on urothelial carcinoma of the bladder]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde* 153, A956. 2009.

Excl reason: Guideline/narrative review

Bhatia, S. and Landier, W. Evaluating survivors of pediatric cancer. *Cancer Journal* 11[4], 340-354. 2005.

Excl reason: Not in PICO

Blanker, M. H., Bohnen, A. M., Groeneveld, F. P. M. J., Bernsen, R. M. D., Prins, A., Thomas, S., and Bosch, J. L. H. R. Erectile dysfunction amongst men aged 50 years and over: Prevalence, risk factors and inconvenience. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde* 145[29], 1404-1409. 21-7-2001.

Excl reason: Not in PICO

Blanker, M. H. [Diagnosis of urothelial carcinoma by the general practitioner--significance of haematuria]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde* 153, A1198. 2009.

Excl reason: Narrative review

Blick, C., Bailey, D., Haldar, N., Bdesha, A., Kelleher, J., and Muneer, A. The impact of the two-week wait rule on the diagnosis and management of bladder cancer in a single UK institution. *Annals of the Royal College of Surgeons of England* 92[1], 46-50. 2010.

Excl reason: Not in PICO

Blochlinger, A. M., Gasser, T. C., Stoffel, F., Laschke, S., and Buhring, C. Hematuria. [German]. *Therapeutische Umschau Revue*[9], 672-675. 1996.

Excl reason: Narrative review

- Bock-Oruma, A. A., Dienye, P. O. & Oghu, I. S. (2013) Prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia in primary care, Port Harcourt, Nigeria. *South African Family Practice*, 55: 467-472.
Not in PICO
- Boman, H., Hedelin, H., and Holmang, S. The results of routine evaluation of adult patients with haematuria analysed according to referral form information with 2-year follow-up. *Scandinavian Journal of Urology and Nephrology* 35[6], 497-501. 2001.
Excl reason: Not in PICO
- Borchini, R., Bonzini, M., Veronesi, G., Fava, C., Carezzi, M. C., Mombelli, S., Marconi, A., Bono, A. V., and Ferrario, M. M. [Validation of a screening method for occupational bladder cancer]. [Italian]. *Medicina del Lavoro* 100[6], 438-447. 2009.
Excl reason: Not in PICO
- Botteman, M. F., Pashos, C. L., Redaelli, A., Laskin, B., and Hauser, R. The Health Economics of Bladder Cancer: A Comprehensive Review of the Published Literature. *Pharmacoeconomics* 21[18], 1315-1330. 2003.
Excl reason: Not in PICO
- Bowden, E. A. and Foley, S. J. Haematuria; a late complication of TURP? *Prostate Cancer and Prostatic Diseases* 4[3], 178-179. 2001.
Excl reason: Not in PICO
- Bremnor, J. D. and Sadovsky, R. Evaluation of dysuria in adults. *American Family Physician* 65[8], 1589-1597. 15-4-2002.
Excl reason: Narrative review
- Britton, J. P., Dowell, A. C., and Whelan, P. Dipstick haematuria and bladder cancer in men over 60: results of a community study. *BMJ* 299[6706], 1010-1012. 21-10-1989.
Excl reason: Not in PICO
- Britton, J. P., Dowell, A. C., Whelan, P., and Harris, C. M. A community study of bladder cancer screening by the detection of occult urinary bleeding. *Journal of Urology* 148[3 I], 788-790. 1992.
Excl reason: Not in PICO
- Britton, J. P. Effectiveness of haematuria clinics. [Review] [37 refs]. *British Journal of Urology* 71[3], 247-252. 1993.
Excl reason: Narrative review
- Britton, J. P., Dowell, A. C. & Whelan, P. (1989) Dipstick haematuria and bladder cancer in men over 60: results of a community study. *BMJ*, 299: 1010-1012.
Not in PICO
- Brock, M., Martin, W., Sommerer, F., and Noldus, J. [Ductal Adenocarcinoma of the prostate with infiltration of the bladder. Can radical cystectomy and antiandrogen therapy cure the disease?]. [German]. *Urologe (Ausg.A)* 48[7], 770-773. 2009.
Excl reason: Not in PICO
- Buntinx, F. and Wauters, H. The diagnostic value of macroscopic haematuria in diagnosing urological cancers: A meta-analysis. *Family Practice* 14[1], 63-68. 1997.
Excl reason: SR, but no studies conducted in primary care included
- Burger, M., Grossman, H. B., Droller, M., Schmidbauer, J., Hermann, G., Dragoescu, O., Ray, E., Fradet, Y., Karl, A., Burgues, J. P., Witjes, J. A., Stenzl, A., Jichlinski, P. & Jocham, D. (2013) Photodynamic diagnosis of non-muscle-invasive bladder cancer with hexaminolevulinate cystoscopy: A meta-analysis of detection and recurrence based on raw data. *European Urology*, 64: 846-854.
Not in PICO
- Buteau, A., Seideman, C. A., Svatek, R. S., Youssef, R. F., Chakrabarti, G., Reed, G., Bhat, D. & Lotan, Y. (2014) What is evaluation of hematuria by primary care physicians? Use of electronic medical records to assess practice patterns with intermediate follow-up. *Urologic Oncology*, 32: 128-134.
Not in PICO

Caballero Alcantara, J. E., Castro Pita, M. A., Carrero, Lopez, V, Rodriguez, Antolin A., Pamplona, Casamayor M., and Leiva, Galvis O. [Leukemoid reaction as a paraneoplastic manifestation of bladder carcinoma]. [Spanish]. *Actas Urologicas Espanolas* 15[5], 496-499. 1991.
Excl reason: Not in PICO

Cai, T. and Bartoletti, R. Long-term outcome of hematuria home screening for bladder cancer in men. *Cancer* 109[9], 1923-1924. 2007.
Excl reason: Not in PICO

Chakarov, S. Hematuria. *General Medicine* 4[1], 14-19. 2002.
Excl reason: Narrative review

Chan, E. S., Ng, C. F., Hou, S. M., and Yip, S. K. Using urine microscopy and cytology for early detection of bladder cancer in male patients with lower urinary tract symptoms. *International Urology & Nephrology* 43[2], 289-294. 2011.
Excl reason: Not in PICO

Chen, K. S., Lai, M. K., Huang, C. C., Chu, S. H., and Leu, M. L. Urologic cancers in uremic patients. *American Journal of Kidney Diseases* 25[5], 694-700. 1995.
Excl reason: Not in PICO

Chiong, E., Gaston, K. E., and Grossman, H. B. Urinary markers in screening patients with hematuria. [Review] [44 refs]. *World Journal of Urology* 26[1], 25-30. 2008.
Excl reason: Narrative review

Chou, R. and Dana, T. Screening adults for bladder cancer: update of the 2004 evidence review for the U.S. Preventive Services Task Force (DARE structured abstract). *Agency for Healthcare Research and Quality*, 1. 2010.
Excl reason: Not in PICO

Crocetti, E., Arniani, S., and Buiatti, E. Synchronous and metachronous diagnosis of multiple primary cancers. *Tumori* 84[1], 9-13. 1998.
Excl reason: Not in PICO

Datta, S. N., Allen, G. M., Evans, R., Vaughton, K. C., and Lucas, M. G. Urinary tract ultrasonography in the evaluation of haematuria - A report of over 1000 cases. *Annals of the Royal College of Surgeons of England* 84[3], 203-205. 2002.
Excl reason: Not in PICO

De, Ridder D., Van, Poppel H., Demonty, L., D'Hooghe, B., Gonsette, R., Carton, H., and Baert, L. Bladder cancer in patients with multiple sclerosis treated with cyclophosphamide. *Journal of Urology* 159[6], 1881-1884. 1998.
Excl reason: Not in PICO

DeSouza, K., Chowdhury, S. & Hughes, S. (2003) - Prompt diagnosis key in bladder cancer. [Review]. - *Practitioner*, 258: 23-27.
Narrative review

Dondalski, M., White, E. M., Ghahremani, G. G., and Patel, S. K. Carcinoma arising in urinary bladder diverticula: Imaging findings in six patients. *American Journal of Roentgenology* 161[4], 817-820. 1993.
Excl reason: Not in PICO

Donohue, J. F. and Barber, N. J. How do we investigate haematuria and what role has finasteride? *BJU International* 93[1], 3-4. 2004.
Excl reason: Narrative review

Dregan, A., Moller, H., Charlton, J. & Gulliford, M. C. (2013) Are alarm symptoms predictive of cancer survival? Population-based cohort study. *British Journal of General Practice*, 63: E807-E812.
Not in PICO

Droller, M. J. Primary care update on kidney and bladder cancer - A urologic perspective. *Medical Clinics of North America* 88[2], 309+. 2004.
Excl reason: Narrative review

- Eissa, S., Badr, S., Elhamid, S. A., Helmy, A. S., Nour, M. & Esmat, M. (2013) The value of combined use of survivin mRNA and matrix metalloproteinase 2 and 9 for bladder cancer detection in voided urine. *Disease Markers*, 34: 57-62.
Not in PICO
- Eissa, S., Matboli, M., Mansour, A., Mohamed, S., Awad, N. & Kotb, Y. M. (2014) Evaluation of urinary HURP mRNA as a marker for detection of bladder cancer: relation to bilharziasis. *Medical Oncology*, 31: 804.
Not in PICO
- Elias, K., Svatek, R. S., Gupta, S., Ho, R., and Lotan, Y. High-risk patients with hematuria are not evaluated according to guideline recommendations. *Cancer* 116[12], 2954-2959. 15-6-2010.
Excl reason: Not in PICO
- Erbersdobler, A., Friedrich, M. G., Schwaibold, H., Henke, R. P., and Huland, H. Microsatellite alterations at chromosomes 9p, 13q, and 17p in nonmuscle-invasive transitional cell carcinomas of the urinary bladder. *Oncology Research* 10[8], 415-420. 1998.
Excl reason: Not in PICO
- Feifer, A. H., Steinberg, J., Tanguay, S., Aprikian, A. G., Brimo, F., and Kassouf, W. Utility of urine cytology in the workup of asymptomatic microscopic hematuria in low-risk patients. *Urology* 75[6], 1278-1282. 2010.
Excl reason: Not in PICO
- Feil, G. and Stenzl, A. [Tumor marker tests in bladder cancer]. [Review] [60 refs] [Spanish]. *Actas Urológicas Espanolas* 30[1], 38-45. 2006.
Excl reason: Not in PICO
- Ferre, A., Cordonnier, C., Demailly, M., Hakami, F., Sevestre, H. & Saint, F. (2013) [Bladder tumor targeting by Hexvix() fluorescence: 4 years results after prospective monocentric evaluation]. [French]. *Progres En Urologie*, 23: 195-202.
Not in PICO
- Fiore, D. C. & Fox, C. L. (2014) Urology and nephrology update: bladder and kidney cancer. *Fp Essentials*, 416: 26-29.
Narrative review
- Fiore, D. C. & Fox, C. L. (2014) - Section three: bladder and kidney cancer. - *Fp Essentials*, 416: 26-29.
Narrative review
- Flores-Carreras, O., Martinez-Espinoza, C. J., Gonzalez-Ruiz, M. I., and Montes-Casillas, Y. E. [Contribution of bladder biopsy to the study of urogynaecological patient]. [Spanish]. *Ginecologia y Obstetricia de Mexico* 78[3], 187-190. 2010.
Excl reason: Not in PICO
- Foo, K. T. (2013) The role of transabdominal ultrasound in office urology. *Proceedings of Singapore Healthcare*, 22: 125-130.
Narrative review
- Foresman, W. H. and Messing, E. M. Bladder cancer: Natural history, tumor markers, and early detection strategies. *Seminars in Surgical Oncology* 13[5], 299-306. 1997.
Excl reason: Not in PICO
- Forrest, J. B. Epidemiology and quality of life. [Review] [40 refs]. *Journal of Reproductive Medicine* 51[3:Suppl], Suppl-33. 2006.
Excl reason: Narrative review
- Fossa, S. D., Ous, S., Espetveit, S., and Langmark, F. Patterns of Primary Care and Survival in 336 Consecutive Unselected Norwegian Patients with Bladder-Cancer. *Scandinavian Journal of Urology and Nephrology* 26[2], 131-138. 1992.
Excl reason: Not in PICO
- Friedman, G. D., Hiatt, R. A., Quesenberry, C. P., Jr., Selby, J. V., and Weiss, N. S. Problems in assessing screening experience in observational studies of screening efficacy: example of

urinalysis screening for bladder cancer. *Journal of Medical Screening* 2[4], 219-223. 1995.

Excl reason: Not in PICO

Friedman, G. D., Carroll, P. R., Cattolica, E. V., and Hiatt, R. A. Can hematuria be a predictor as well as a symptom or sign of bladder cancer? *Cancer Epidemiology, Biomarkers & Prevention* 5[12], 993-996. 1996.

Excl reason: Not in PICO (screening population w/o symptoms, risk based analyses, setting?)

Gervino, G., Autino, E., Kolomoets, E., Leucci, G., and Balma, M. Diagnosis of bladder cancer at 465 MHz. *Electromagnetic Biology & Medicine* 26[2], 119-134. 2007.

Excl reason: Not in PICO

Gittens, P. R., Lallas, C. D., Pe, M. L., Perkel, R., Folia, C., and Gomella, L. G. Uro pharmacology for the primary care physician. *Canadian Journal of Urology* 15, 78-91. 2008.

Excl reason: Not in PICO

Gittes, R. F. and Nakamura, R. M. Female urethral syndrome. A female prostatitis? *Western Journal of Medicine* 164[5], 435-438. 1996.

Excl reason: Not in PICO

Goepel, M., Hoffmann, J. A., Piro, M., Rubben, H., and Michel, M. C. Prevalence and physician awareness of symptoms of urinary bladder dysfunction. *European Urology* 41[3], 234-239. 1-3-2002.

Excl reason: Not in PICO

Golijanin, D., Shapiro, A., and Pode, D. Immunostaining of cytokeratin 20 in cells from voided urine for detection of bladder cancer. *Journal of Urology* 164[6], 1922-1925. 2000.

Excl reason: Not in PICO

Gomella, L. G., Lallas, C. D., Perkel, R., Folia, C., Hirsch, I., Das, A., and Shenot, P. Uro pharmacology in primary care: 2010 update. *Canadian Journal of Urology* 17, 35-51. 2010.

Excl reason: Not in PICO

Gomella, L., Grossman, H. B., Droller, M., Schmidbauer, J., Hermann, G., Dragoescu, O., Ray, E., Witjes, A., Karl, A., Stenzl, A., Fradet, Y., Burgues, J. & Jocham, D. (2013) A meta-analysis of blue light cystoscopy with hexaminolevulinate in patients with non-muscle invasive bladder cancer. *Journal of Urology*, 189: e528.

Not in PICO

Gomes, C. A., de Figueiredo, A. A., Soares, Junior C., Bastos Netto, J. M., and Tassi, F. R. [Acute abdomen: spontaneous bladder rupture as an important differential diagnosis]. [Portuguese]. *Revista do Colegio Brasileiro de Cirurgioes* 36[4], 364-365. 2009.

Excl reason: Not in PICO

Gontero, P., Oderda, M., Altieri, V., Bartoletti, R., Cai, T., Colombo, R., Curotto, A., Di Stasi, S., Maffezzini, M., Tamagno, S., Serretta, V., Sogni, F., Terrone, C., Tizzani, A., Morgia, G., Mirone, V., and Carmignani, G. Are Referral Centers for Non-Muscle-Invasive Bladder Cancer Compliant to EAU Guidelines? A Report from the Vesical Antiplastic Therapy Italian Study. *Urologia Internationalis* 86[1], 19-24. 2011.

Excl reason: Not in PICO

Goodison, S., Rosser, C. J. & Urquidi, V. (2013) Bladder cancer detection and monitoring: assessment of urine- and blood-based marker tests. [Review]. *Molecular Diagnosis & Therapy*, 17: 71-84. Narrative review

Goonewardena, S. A. S., De Silva, W. A. S., and De Silva, M. V. C. Bladder cancer in Sri Lanka: Experience from a tertiary referral center. *International Journal of Urology* 11[11], 969-972. 2004.

Excl reason: Not in PICO

Gorich, J., Hasan, I., Kunze, V., Sittek, H., Brensing, K. A., Reiser, M., Layer, G., Rilinger, N., Sokiranski, R., and Steudel, A. [Intra-arterial treatment of therapy-resistant residual tumors of the pelvis]. [German]. *Strahlentherapie und Onkologie* 171[12], 671-678. 1995.

Excl reason: Not in PICO

- Gorich, J., Hasan, I., Kunze, V., Sittek, H., Brensing, K.-A., Reiser, M., Layer, G., Rilinger, N., Sokiranski, R., and Steudel, A. Evaluation of intraarterial cancer treatment in recurrent pelvic tumors. [German]. *Strahlentherapie und Onkologie* 171[12], 671-678. 1995.
Excl reason: Not in PICO
- Gourova, L. W., van de Beek, C., Spigt, M. G., Nieman, F. H., and van Kerrebroeck, P. E. Predictive factors for nocturia in elderly men: a cross-sectional study in 21 general practices. *BJU International* 97[3], 528-532. 2006.
Excl reason: Not in PICO
- Granberg, S., Wikland, M., and Norstrom, A. Endovaginal ultrasound scanning to identify bladder tumors as the source of vaginal bleeding in postmenopausal women. *Ultrasound in Obstetrics & Gynecology* 1[1], 63-65. 1-1-1991.
Excl reason: Not in PICO
- Griffiths, T. R. & Action on Bladder Cancer (2013) Current perspectives in bladder cancer management. [Review]. *International Journal of Clinical Practice*, 67: 435-448.
Narrative review
- Grossfeld, G. D., Wolf, J. S., Litwin, M. S., Hricak, H., Shuler, C. L., Agerter, D. C., and Carroll, P. R. Asymptomatic microscopic hematuria in adults: Summary of the AUA Best Practice Policy recommendations. *American Family Physician* 63[6], 1145-1154. 2001.
Excl reason: Guideline
- Hall, C. L. The patient with haematuria. *The Practitioner* 243[1600], 564-571. 5-7-0568.
Excl reason: Narrative review
- Hamid, A. A. (2013) The diagnostic accuracy of multidetector computed tomography with multiplanar reformatted imaging and virtual cystoscopy in the early detection and evaluation of bladder carcinoma: Comparison with conventional cystoscopy. *Journal of Endourology*, 27: A165.
Not in PICO
- Hansen, Rikke, Vedsted, Peter, Sokolowski, Ineta, Sondergaard, Jens, and Olesen, Frede. Time intervals from first symptom to treatment of cancer: a cohort study of 2,212 newly diagnosed cancer patients. *BMC Health Services Research* 11[1], 284. 2011.
Excl reason: Not in PICO
- Hargunani, R., Al-Dujaily, S., Abdulla, A. K. S., and Osborne, D. R. Haematuria as a presentation of metastatic oesophageal carcinoma. *International Seminars in Surgical Oncology* 2[1], 4. 2005.
Excl reason: Not in PICO
- Harima, M., Narita, K., Kobayakawa, H., Tsujino, T., Yamamoto, S., Fukushima, S., and Kishimoto, T. [A case of synchronous triple primary cancers of prostate, kidney and bladder]. [Review] [20 refs] [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 44[9], 675-678. 1998.
Excl reason: Not in PICO
- Harzmann, R. [Early diagnosis of urogenital tumors]. [German]. *Zeitschrift fur Hautkrankheiten* 62[9], 665-676. 681.
Excl reason: Narrative review
- Hasan, S. T., German, K., and Derry, C. D. Same day diagnostic service for new cases of haematuria - A District General Hospital experience. *British Journal of Urology* 73[2], 152-154. 1994.
Excl reason: Not in PICO
- Hattori, R., Matsuura, O., Takeuchi, N., Hashimoto, J., Ohshima, S., Ono, Y., Kinukawa, T., and Miyake, K. Clinical importance of microhematuria as an initial sign of bladder tumor. *Japanese Journal of Urology* 81[3], 414-419. 1990.
Excl reason: Not in PICO
- Hautmann, S., Lokeshwar, V. B., and Juenemann, K. P. [Urine-based diagnostics: an update on the Kiel Tumor Bank]. [Review] [21 refs] [German]. *Urologe (Ausg.A)* 48[6], 619-624. 2009.
Excl reason: Narrative review
- Hawary, A. M., Warburton, H. E., Brough, R. J., Collins, G. N., Brown, S. C., O'Reilly, P. H., and Adeyoju, A. A. The '2-week wait' rule for referrals for suspected urological cancers--urgent need

for refinement of criteria. *Annals of the Royal College of Surgeons of England* 90[6], 517-522. 2008.

Excl reason: Not in PICO

Hedelin, H., Boman, H., and Holmang, S. [When is it meaningful to investigate hematuria? Macroscopic hematuria--investigate always. Microscopic hematuria--symptoms and age decide]. [Swedish]. *Lakartidningen* 98[48], 5498-5500. 20-11-1103.

Excl reason: Not in PICO

Hedelin, H., Boman, H., and Holmang, S. When is it meaningful to investigate hematuria? Macroscopic hematuria--investigate always. Microscopic hematuria--symptoms and age decide. [Swedish]. *Lakartidningen* 98[48], 5498-5500, 5503. 28-3-1955.

Excl reason: Not in PICO

Hedelin, H., Jonsson, K., Salomonsson, K., and Boman, H. Screening for bladder tumours in men aged 60-70 years with a bladder tumour marker (UBC) and dipstick-detected haematuria using both white-light and fluorescence cystoscopy. *Scandinavian Journal of Urology & Nephrology* 40[1], 26-30. 2006.

Excl reason: Not in PICO

Hee, T. G., Shah, S. A., Ann, H. S., Hemdan, S. N., Shen, L. C., Al-Fahmi Abdul, G. N., Singam, P., Ho, C. C., Hong, G. E., Bahadzor, B. & Zainuddin, Z. M. (2013) Stratifying patients with haematuria into high or low risk groups for bladder cancer: a novel clinical scoring system. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 14: 6327-6330.

Not in PICO

Heins, M. J., Korevaar, J. C., Rijken, P. M. & Schellevis, F. G. (2013) For which health problems do cancer survivors visit their General Practitioner? *European Journal of Cancer*, 49: 211-218.

Not in PICO

Henning, A., Wehrberger, M., Madersbacher, S., Pycha, A., Martini, T., Comploj, E., Jeschke, K., Tripolt, C. & Rauchenwald, M. (2013) Do differences in clinical symptoms and referral patterns contribute to the gender gap in bladder cancer? *BJU International*, 112: 68-73.

Not in PICO

Henningsohn, L., Wijkstrom, H., Steven, K., Pedersen, J., Ahlstrand, C., Aus, G., Kallestrup, E. B., Bergmark, K., Onelov, E., and Steineck, G. Relative importance of sources of symptom-induced distress in urinary bladder cancer survivors. *European Urology* 43[6], 651-662. 2003.

Excl reason: Not in PICO

Herranz, Amo F., Diez Cordero, J. M., Verdu, Tartajo F., Bueno, Chomon G., Leal, Hernandez F., and Bielsa, Carrillo A. Abdominal pain in patients undergoing radical cystectomy for bladder cancer. [Spanish]. *Archivos Espanoles de Urologia* 51[4], 342-346. 1998.

Excl reason: Not in PICO

Herrera, Puerto J., Laguna, Alvarez E., Sevilla, Zabaleta M., Caballero, Gomez M., Soler, Fernandez J., Castano Casaseca, J. L., and Asuar, Aydillo S. [Bladder metastasis of a renal cell carcinoma]. [Spanish]. *Archivos Espanoles de Urologia* 43[6], 615-617. 1990.

Excl reason: Not in PICO

Hirshberg, A. J., Holliman, C. J., Wuerz, R. C., and Chapman, D. M. Case management by physician assistants and primary care physicians vs emergency physicians. *Academic Emergency Medicine* 4[11], 1046-1052. 1997.

Excl reason: Not in PICO

Ho, E. T., Johnston, S. R., and Keane, P. F. The haematuria clinic--referral patterns in Northern Ireland. *The Ulster medical journal* 67[1], 25-28. 1998.

Excl reason: Not in PICO

Hochreiter, W. Painful micturition (dysuria, alguria). [German]. *Therapeutische Umschau Revue*[9], 668-671. 1996.

Excl reason: Narrative review

Hollingsworth, J. M., Zhang, Y. S., Miller, D. C., Skolarus, T. A., Wood, D. P., Lee, C. T., Montie, J. E., and Hollenbeck, B. K. Identifying better practices for early-stage bladder cancer. *Medical Care* 49[12], 1112-1117. 2011.
Excl reason: Not in PICO

Holmang, S. and Johansson, S. L. Impact of diagnostic and treatment delay on survival in patients with renal pelvic and ureteral cancer. *Scandinavian Journal of Urology & Nephrology* 40[6], 479-484. 2006.
Excl reason: Not in PICO

Hooda, M. N., Siddique, F. H., Nabi, S., Islam, M. W., Ara, K. & Bhuiyan, Z. I. (2014) - Clinicopathologic features and treatment outcome of urinary bladder neoplasm. - *Mymensingh Medical Journal: MMJ*, 23: 341-344.
Not in PICO

House, A. A. and Cattran, D. C. Nephrology: 2. Evaluation of asymptomatic hematuria and proteinuria in adult primary care. *Canadian Medical Association Journal* 166[3], 348-353. 2002.
Excl reason: Narrative review

Huang, C. Y., Shun, C. T., Huang, K. H., Chen, J., and Pu, Y. S. Primary amyloidosis of the urinary bladder. *Journal of the Formosan Medical Association* 105[2], 164-167. 2006.
Excl reason: Not in PICO

Hussain, S. A., Stocken, D. D., Peake, D. R., Glaholm, J. G., Zarkar, A., Wallace, D. M., and James, N. D. Long-term results of a phase II study of synchronous chemoradiotherapy in advanced muscle invasive bladder cancer. *British Journal of Cancer* 90[11], 2106-2111. 1-6-2004.
Excl reason: Not in PICO

Iavarone, C., Forte, F., Bronzetti, E., Minocchi, L., Mezzetti, G., Greco, L., D'Orazi, V., Urciuoli, P., and Custureri, F. [Pseudosarcoma of the urinary bladder. Report of a case]. [Review] [8 refs] [Italian]. *Minerva Urologica e Nefrologica* 52[1], 45-48. 2000.
Excl reason: Not in PICO

Ibragimova, M. I., Chushnikov, V. N., Moiseev, V. N., Petukhov, V. I., Zheglov, E. P. & Cherepnev, G. V. (2013) [Electron paramagnetic resonance study of blood of anemic patients with urological cancer]. [Russian]. *Biofizika*, 58: 289-294.
Not in PICO

Jain, M., Kumari, N., Chhabra, P., and Gupta, R. K. Localized amyloidosis of urinary bladder: a diagnostic dilemma. *Indian Journal of Pathology & Microbiology* 51[2], 247-249. 2008.
Excl reason: Not in PICO

Jiang, X. Z., Xu, C., Zhang, N. Z., and Xu, Z. S. Influence of clinical characteristics and tumor size on symptoms of bladder leiomyoma: a pooled analysis of 61 cases. *Chinese Medical Journal* 125[14], 2436-2439. 2012.
Excl reason: Not in PICO

Jichlinski, P. (2014) - [Urology]. [Review] [French]. - *Revue Medicale Suisse*, 10: 127-129.
Narrative review

Jimbo, M. Evaluation and management of hematuria. [Review]. *Primary Care; Clinics in Office Practice* 37[3], 461-472. 20-11-2010.
Excl reason: Narrative review

Johnson, E. K., Daignault, S., Zhang, Y., and Lee, C. T. Patterns of hematuria referral to urologists: does a gender disparity exist? *Urology* 72[3], 498-502. 502.
Excl reason: Not in PICO

Jones, M. W., Cox, R., Davies, K. I., and Rose, M. B. The value of the pre-clinic intravenous urogram in the earlier diagnosis of the cause of haematuria. *British Journal of Urology* 62[1], 11-12. 1988.
Excl reason: Not in PICO

Kajita, Y., Megumi, Y., and Okabe, T. [Renal carcinoid tumor presenting as bladder tamponade: a case report and review of the Japanese cases]. [Review] [10 refs] [Japanese]. *Hinyokika Kiyo* -

Acta Urologica Japonica 51[7], 459-462. 2005.

Excl reason: Not in PICO

Kamat, A. M., Hegarty, P. K., Gee, J. R., Clark, P. E., Svatek, R. S., Hegarty, N., Shariat, S. F., Xylinas, E., Schmitz-Drager, B. J., Lotan, Y., Jenkins, L. C., Droller, M., van Rhijn, B. W., Karakiewicz, P. I. & International Consultation on Urologic Disease-European Association of Urology Consultation on Bladder Cancer (2013) ICUD-EAU International Consultation on Bladder Cancer 2012: Screening, diagnosis, and molecular markers. [Review]. *European Urology*, 63: 4-15.

Narrative review

Kaplan, J. and Loftus, L. Bladder cancer after pelvic irradiation for cervical cancer. *Southern Medical Journal* 78[9], 1068-1070. 1985.

Excl reason: Not in PICO

Karam, J. A., Kabbani, W., and Sagalowsky, A. I. Pseudosarcomatous fibromyxoid tumor of the bladder. *Urologic Oncology* 26[3], 291-294. 2008.

Excl reason: Not in PICO

Karl, A., Stief, C. & Zaak, D. (2013) [Photodynamic diagnostics of the bladder: current study results]. [Review] [German]. *Urologe (Auszg.A)*, 52: 504-508.

Narrative review

Kazi, J. I., Mubarak, M., Hashmi, A., Hussain, M., Naqvi, S. A., and Rizvi, S. A. H. Spectrum of pathological lesions in cystoscopic bladder biopsies - A clinicopathologic study. *Journal of the College of Physicians and Surgeons Pakistan* 12[12], 744-747. 1-12-2002.

Excl reason: Not in PICO

Keeble, S., Abel, G. A., Saunders, C. L., McPhail, S., Walter, F. M., Neal, R. D., Rubin, G. P. & Lyratzopoulos, G. (2014) - Variation in promptness of presentation among 10,297 patients subsequently diagnosed with one of 18 cancers: evidence from a National Audit of Cancer Diagnosis in Primary Care. - *International Journal of Cancer*, 135: 1220-1228.

Not in PICO

Kelly, J. D., Fawcett, D. P., and Goldberg, L. C. Assessment and management of non-visible haematuria in primary care. *British Medical Journal* 338. 2009.

Excl reason: Narrative review

Kelly, J. D., Dudderidge, T. J., Wollenschlaeger, A., Okoturo, O., Burling, K., Tulloch, F., Halsall, I., Prevost, T., Prevost, A. T., Vasconcelos, J. C., Robson, W., Leung, H. Y., Vasdev, N., Pickard, R. S., Williams, G. H., and Stoeber, K. Bladder Cancer Diagnosis and Identification of Clinically Significant Disease by Combined Urinary Detection of Mcm5 and Nuclear Matrix Protein 22. *Plos One* 7[7]. 2012.

Excl reason: Not in PICO

Khan, M. A., Shaw, G., and Paris, A. M. I. Is microscopic haematuria a urological emergency? *BJU International* 90[4], 355-357. 2002.

Excl reason: Not in PICO

Khandelwal, C. & Kistler, C. (2013) Diagnosis of urinary incontinence. *American Family Physician*, 87: 543-551.

Narrative review

Kikuchi, T., Yamada, Y., Satoh, T., Honda, N., Katoh, O., Fukatsu, H., and Segawa, A. [A case of paraganglioma of the urinary bladder]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 29[3], 333-337. 1983.

Excl reason: Not in PICO

King, K. & Steggall, M. (2014) - Haematuria: from identification to treatment. - *British Journal of Nursing*, 23: S28-S32.

Narrative review

Kjaer, S. K., Knudsen, J. B., Sorensen, B. L., and Moller, Jensen O. The Copenhagen case-control study of bladder cancer. V. Review of the role of urinary-tract infection. [Review] [33 refs]. *Acta*

Oncologica 28[5], 631-636. 1989.
 Excl reason: Not in PICO (risk, not symptoms)

Klein, F. A. and White, F. K. H. Flow cytometry deoxyribonucleic acid determinations and cytology of bladder washings: Practical experience. *Journal of Urology* 139[2], 275-278. 1988.
 Excl reason: Not in PICO

Kohler, C. and Varenhorst, E. Microscopic hematuria in adults--a diagnostic dilemma. Scientific guidelines for management are not available according to a review of the literature. [Swedish]. *Lakartidningen* 96[45], 4911-4916. 10-11-1999.
 Excl reason: Not in PICO (mixed population that cannot be disentangled)

Konety, B. R., Lavelle, J. P., Pirtskalaishvili, G., Dhir, R., Meyers, S. A., Nguyen, T. S., Hershberger, P., Shurin, M. R., Johnson, C. S., Trump, D. L., Zeidel, M. L., and Getzenberg, R. H. Effects of vitamin D (calcitriol) on transitional cell carcinoma of the bladder in vitro and in vivo. *Journal of Urology* 165[1], 253-258. 2001.
 Excl reason: Not in PICO

Konety, B. R., Joyce, G. F., and Wise, M. Bladder and upper tract urothelial cancer. *Journal of Urology* 177[5], 1636-1645. 2007.
 Excl reason: Not in PICO

Kruck, S., Scharpf, M., Stenzl, A. & Bedke, J. (2013) A rare case of synchronous renal cell carcinoma of the bladder presenting with gross hematuria. *Rare Tumors*, 5: 72-74.
 Not in PICO

Krupski, T. and Theodorescu, D. Orthotopic neobladder following cystectomy: indications, management, and outcomes. [Review] [27 refs]. *Journal of Wound, Ostomy, & Continence Nursing* 28[1], 37-46. 2001.
 Excl reason: Not in PICO

Kuyumcuoglu, U. and Kale, A. Unusual presentation of a dermoid cyst that derived from the bladder dome presenting as subserosal leiomyoma uteri. *Clinical & Experimental Obstetrics & Gynecology* 35[4], 309-310. 2008.
 Excl reason: Not in PICO

La, Vecchia C., Negri, E., D'Avanzo, B., Savoldelli, R., and Franceschi, S. Genital and urinary tract diseases and bladder cancer. *Cancer Research* 51[2], 629-631. 15-1-1991.
 Excl reason: Not in PICO

Lafuente, A., Rodriguez, A., Gibanel, R., Lafuente, M. J., Alonso, M., Molina, R., Ballesta, A., and Carretero, P. Limitations in the use of glutathione S-transferase P1 in urine as a marker for bladder cancer. *Anticancer Research* 18[5B], 3771-3772. 1998.
 Excl reason: Not in PICO

Larsson, G. Multiple leiomyomata of the urinary bladder in a hysterectomized woman. *Acta Obstetrica et Gynecologica Scandinavica* 73[1], 78-80. 1994.
 Excl reason: Not in PICO

Lazaro, Santander R., Castillo Gimeno, J. M., Garcia Prats, M. D., Andre, Gozalbo C., and Vera Roman, J. M. [Intravesical hemangiopericytoma]. [Review] [12 refs] [Spanish]. *Archivos Espanoles de Urologia* 52[7], 797-799. 1999.
 Excl reason: Not in PICO

Lee, M. Y., Tsou, M. H., Cheng, M. H., Chang, D. S., Yang, A. L., and Ko, J. S. Clinical application of NMP22 and urinary cytology in patients with hematuria or a history of urothelial carcinoma. *World Journal of Urology* 18[6], 401-405. 2000.
 Excl reason: Not in PICO

Lodde, M., Pycha, A., Palermo, S., Comploj, E., and Hohenfellner, R. Uretero-ureterocutaneostomy (wrapped by omentum). *BJU International* 95[3], 371-373. 2005.
 Excl reason: Not in PICO

- Lokeshwar, V. B. and Soloway, M. S. Current bladder tumor tests: does their projected utility fulfill clinical necessity?. [Review] [90 refs]. *Journal of Urology* 165[4], 1067-1077. 2001.
Excl reason: Not in PICO
- Lokeshwar, V. B., Habuchi, T., Grossman, H. B., Murphy, W. M., Hautmann, S. H., Hemstreet III, G. P., Bono, A. V., Getzenberg, R. H., Goebell, P., Schmitz-Drager, B. J., Schalken, J. A., Fradet, Y., Marberger, M., Messing, E., and Droller, M. J. Bladder tumor markers beyond cytology: International Consensus Panel on bladder tumor markers. *Urology* 66[6 SUPPL. 1], 35-63. 2005.
Excl reason: Not in PICO
- Lopes, R. I., Nogueira, L., Albertotti, C. J., Takahashi, D. Y., and Lopes, R. N. Comparison of virtual cystoscopy and transabdominal ultrasonography with conventional cystoscopy for bladder tumor detection. *Journal of Endourology* 22[8], 1725-1729. 2008.
Excl reason: Not in PICO
- Lotan, Y., Elias, K., Svatek, R. S., Bagrodia, A., Nuss, G., Moran, B., and Sagalowsky, A. I. Bladder cancer screening in a high risk asymptomatic population using a point of care urine based protein tumor marker. *Journal of Urology* 182[1], 52-57. 20-11-1958.
Excl reason: Not in PICO
- Ludecke, G., Pilatz, A., Hauptmann, A., Bschiepfer, T., and Weidner, W. Comparative analysis of sensitivity to blood in the urine for urine-based point-of-care assays (UBC rapid, NMP22 BladderChek and BTA-stat) in primary diagnosis of bladder carcinoma. Interference of blood on the results of urine-based POC tests. *Anticancer Research* 32[5], 2015-2018. 2012.
Excl reason: Not in PICO
- Lynch, T. H., Waymont, B., Dunn, J. A., Hughes, M. A., and Wallace, D. M. Rapid diagnostic service for patients with haematuria. *British Journal of Urology* 73[2], 147-151. 1994.
Excl reason: Same as Lynch 1994
- Lynch, T. H., Waymont, B., Dunn, J. A., Hughes, M. A., and Wallace, D. M. Repeat testing for haematuria and underlying urological pathology. *British Journal of Urology* 74[6], 730-732. 1994.
Excl reason: Not in PICO (selected referred population). Same as Lynch 1994
- Lyratzopoulos, G., Abel, G. A., McPhail, S., Neal, R. D. & Rubin, G. P. (2013) Gender inequalities in the promptness of diagnosis of bladder and renal cancer after symptomatic presentation: Evidence from secondary analysis of an English primary care audit survey. *BMJ Open*, 3.
Not in PICO
- Mack, D. and Jakse, G. [Bladder cancer as an incidental finding]. [German]. *Wiener Klinische Wochenschrift* 98[6], 175-178. 21-3-1986.
Excl reason: Not in PICO
- Maguire, A., Porta, M., Malats, N., Gallen, M., Pinol, J. L., Fernandez, E., Planas, J., Gomez, G., Digiacomio, S., Guallar, E., Calle, M. L., Grifol, E., and Saez, M. Cancer Survival and the Duration of Symptoms - An Analysis of Possible Forms of the Risk-Function. *European Journal of Cancer* 30A[6], 785-792. 1994.
Excl reason: Not in PICO
- Manassero, A., Chierchia, S. & Carone, R. (2013) Neurogenic lower urinary tract dysfunctions and bladder cancer: Our experience and proposal of evaluation algorithm. *Neurourology and Urodynamics*, 32: S15-S16.
Not in PICO
- Mansson, A., Anderson, H., and Colleen, S. Time lag to diagnosis of bladder cancer-influence of psychosocial parameters and level of health-care provision. *Scandinavian Journal of Urology and Nephrology* 27[3], 363-369. 1993.
Excl reason: Not in PICO
- Mantadakis, E., Panagiotidis, C., Delakas, D., and Samonis, G. Symptomatic relief of patients with advanced bladder carcinoma after regional intra-arterial chemotherapy. *Anticancer Research* 23[6D], 5143-5147. 2003.
Excl reason: Not in PICO

Mao, L. Genetic alterations as clonal markers for bladder cancer detection in urine. [Review] [39 refs]. *Journal of Cellular Biochemistry - Supplement* 25, 191-196. 1996.
Excl reason: Not in PICO

Mariani, A., Cha, S. S., Bergstralh, E. J., Boardman, L. A., Dowdy, S. C., Keeney, G. L., Podratz, K. C., and Melton, L. J., III. Referral and ascertainment bias in patients with synchronous and metachronous endometrial malignancy. *European Journal of Gynaecological Oncology* 31[1], 5-9. 2010.
Excl reason: Not in PICO

Marlin, E. S., Hyams, E. S., Dulabon, L., and Shah, O. Metastatic esophageal adenocarcinoma to the prostate presenting with bilateral ureteral obstruction. *Canadian Journal of Urology* 17[1], 5035-5037. 2010.
Excl reason: Not in PICO

Mason, T. J. and Vogler, W. J. Bladder cancer screening at the Dupont Chambers Works: a new initiative. *Journal of Occupational Medicine* 32[9], 874-877. 1990.
Excl reason: Not in PICO

Mason, T. J., Walsh, W. P., Lee, K., and Vogler, W. New opportunities for screening and early detection of bladder cancer. *Journal of Cellular Biochemistry Supplement.*, 13-22. 1992.
Excl reason: Not in PICO

Matsumoto, K., Irie, A., Satoh, T., Kuruma, H., Arakawa, T., and Baba, S. Occupational bladder cancer: From cohort study to biologic molecular marker. *Medical Science Monitor* 11[10], RA311-RA315. 2005.
Excl reason: Not in PICO

Matsuo, H., Kato, T., Hirai, T., Koderu, Y., Kito, T., and Nakamura, H. A case of cancerous familial adenomatous polyposis in urinary bladder due to migration of colonic mucosa through rectovesical fistula. *American Journal of Gastroenterology* 95[5], 1352-1354. 2000.
Excl reason: Not in PICO

Matzkin, H. and Merimsky, E. [Paraneoplastic syndromes in cancer of the bladder. Review of the literature]. [French]. *Journal d Urologie* 93[2], 77-79. 1987.
Excl reason: Not in PICO

Mayfield, M. P. and Whelan, P. Bladder tumours detected on screening: results at 7 years. *British Journal of Urology* 82[6], 825-828. 1998.
Excl reason: Not in PICO

Mayr, R. & Burger, M. (2013) Value of fluorescence cystoscopy in high risk non-muscle invasive bladder cancer. *Current Urology Reports*, 14: 90-93.
Narrative review

Mebel, M. and Vogler, H. Special problems of early detection of malignant tumors of the genitourinary system (author's transl). [German]. *Archiv fur Geschwulstforschung* 51[8], 679-684. 1981.
Excl reason: Not in PICO

Meeks, J. J., Herr, H. W., Bernstein, M., Al-Ahmadie, H. A. & Dalbagni, G. (2013) Preoperative accuracy of diagnostic evaluation of the urachal mass. *Journal of Urology*, 189: 1260-1262.
Not in PICO

Messing, E. M., Young, T. B., Hunt, V. B., Gilchrist, K. W., Newton, M. A., Bram, L. L., Hisgen, W. J., Greenberg, E. B., Kuglitsch, M. E., and Wegenke, J. D. Comparison of bladder cancer outcome in men undergoing hematuria home screening versus those with standard clinical presentations. *Urology* 45[3], 387-396. 396.
Excl reason: Not in PICO

Messing, E. M. and Vaillancourt, A. Hematuria screening for bladder cancer. *Journal of Occupational Medicine* 32[9], 838-845. 1990.
Excl reason: Not in PICO

- Messing, E. M., Young, T. B., Hunt, V. B., Roecker, E. B., Vaillancourt, A. M., Hisgen, W. J., Greenberg, E. B., Kuglitsch, M. E., and Wegenke, J. D. Home screening for hematuria: results of a multiclinic study. *Journal of Urology* 148[2:Pt 1], t-92. 1992.
Excl reason: Not in PICO
- Messing, E. M., Madeb, R., Young, T., Gilchrist, K. W., Bram, L., Greenberg, E. B., Wegenke, J. D., Stephenson, L., Gee, J., and Feng, C. Long-term outcome of hematuria home screening for bladder cancer in men. *Cancer* 107[9], 2173-2179. 1-11-2006.
Excl reason: Not in PICO
- Michaud, D. S., Spiegelman, D., Clinton, S. K., Rimm, E. B., Curhan, G. C., Willett, W. C., and Giovannucci, E. L. Fluid intake and the risk of bladder cancer in men. *New England Journal of Medicine* 340[18], 1390-1397. 6-5-1999.
Excl reason: Not in PICO
- Mishail, A., Shahsavari, M., Kim, J., Welliver, R. C., Vemulapalli, P., and Adler, H. L. Deficits in Urological Knowledge Among Medical Students and Primary Care Providers: Potential for Impact on Urological Care. *Journal of Urology* 180[5], 2140-2147. 2008.
Excl reason: Not in PICO
- Mishriki, S. F., Nabi, G. & Cohen, N. P. (2008) Diagnosis of urologic malignancies in patients with asymptomatic dipstick hematuria: prospective study with 13 years' follow-up. *Urology*, 71: 13-16.
Not in PICO (secondary care)
- Misra, V., Mukherjee, J., Gupta, S. C., Tandon, S., and Gupta, A. K. AgNORs in benign, borderline and transitional cell neoplasms of the urinary bladder. *APMIS* 106[10], 987-992. 1998.
Excl reason: Not in PICO
- Mitterberger, M., Pinggera, G. M., Neuwirt, H., Maier, E., Akkad, T., Strasser, H., Gradl, J., Pallwein, L., Bartsch, G., and Frauscher, F. Three-dimensional ultrasonography of the urinary bladder: preliminary experience of assessment in patients with haematuria. *BJU International* 99[1], 111-116. 2007.
Excl reason: Not in PICO
- Miyanaga, N., Akaza, H., Tsukamoto, T., Ishikawa, S., Noguchi, R., Ohtani, M., Kawabe, K., Kubota, Y., Fujita, K., Obata, K., Hirao, Y., Kotake, T., Ohmori, H., Kumazawa, J., and Koiso, K. Urinary nuclear matrix protein 22 as a new marker for the screening of urothelial cancer in patients with microscopic hematuria. *International Journal of Urology* 6[4], 173-177. 1999.
Excl reason: Not in PICO
- Miyoshi, Y., Asakura, T., Matsuzaki, J., Fukuda, M., Satomi, Y., and Akabane, H. [A case of CEA and CA19-9 producing recurrent transitional cell carcinoma in an Indiana pouch after total cystectomy]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 42[12], 961-964. 1996.
Excl reason: Not in PICO
- Mizusawa, H., Oguchi, T., Domen, T., Koizumi, K., Mimura, Y., Saito, T. & Kato, H. (2014) - [Two cases of lower abdominal tumors difficult to differentiate from urachal tumors]. [Japanese]. - *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology*, 105: 17-21.
Not in PICO
- Mkrtchian, L. N. and Ambartsumian, A. M. [The experience of the Armenian Republic Endoscopic Center in the active detection of tumors of the urinary system]. [Russian]. *Voprosy Onkologii* 35[6], 709-711. 1989.
Excl reason: Not in PICO
- Mobley, D. F. and Baum, N. Interstitial cystitis. When urgency and frequency mean more than routine inflammation. [Review] [16 refs]. *Postgraduate Medicine* 99[5], 201-204. 207.
Excl reason: Narrative review
- Mohammed, A., Khan, Z., Zamora, I., and Bhatti, A. Biological markers in the diagnosis of recurrent bladder cancer: an overview. [Review] [65 refs]. *Expert Review of Molecular Diagnostics* 8[1], 63-72. 2008.
Excl reason: Not in PICO

Mommsen, S., Aagaard, J., and Sell, A. Presenting symptoms, treatment delay and survival in bladder cancer. *Scandinavian Journal of Urology and Nephrology* 17[2], 163-167. 1983.
Excl reason: Not in PICO

Morant, S., Bloomfield, G., Vats, V., and Chapple, C. Increased sexual dysfunction in men with storage and voiding lower urinary tract symptoms. *Journal of Sexual Medicine* 6[4], 1103-1110. 2009.
Excl reason: Not in PICO

Morsi, M. I., Youssef, A. I., Hassouna, M. E., El-Sedafi, A. S., Ghazal, A. A., and Zaher, E. R. Telomerase activity, cytokeratin 20 and cytokeratin 19 in urine cells of bladder cancer patients. *Journal of Egyptian National Cancer Institute* 18[1], 82-92. 2006.
Excl reason: Not in PICO

Mostafid, H., Persad, R., Kockelbergh, R., and Fawcett, D. Is it time to re-design the haematuria clinic? *BJU International* 105[5], 585-588. 2010.
Excl reason: Narrative review

Mottola, A., Di, Cello, V., Saltutti, C., and Natali, A. [Paraneoplastic syndromes associated with bladder carcinoma. Apropos of 2 cases of hypercalcemia]. [Review] [22 refs] [Italian]. *Minerva Urologica e Nefrologica* 42[2], 99-101. 1990.
Excl reason: Not in PICO

Murakami, N., Tanabe, K., Murasugi, K., Kadoya, S., Matsumoto, Y., Yoshii, I., Fujikawa, Y., and Ohura, F. [A case report of a patient treatable by home palliative care, administered zoledronic acid used for bladder cancer with hypercalcemia]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]* 37[5], 939-942. 2010.
Excl reason: Not in PICO

Murakami, T., Hoshino, K., Hasumi, H., Makiyama, K., Miyoshi, Y., Yoshida, M., Nakaigawa, N., Ogawa, T., Uemura, H., Yao, M., and Kubota, Y. [Only metastasis to uterine corpus from superficial bladder cancer that of no original recurrence]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 53[1], 75-77. 2007.
Excl reason: Not in PICO

Murata, I., Makiyama, K., Funatsu, S., Kubo, K., Mizuta, Y., Nishihata, S., Imanishi, T., Hara, K., Nakamura, N., and Murase, K. A study involving early carcinomas of the gall bladder. [Japanese]. *Gan no rinsho Japan*[7], 867-874. 1988.
Excl reason: Not in PICO

Nakopoulou, L., Vourlakou, C., Zervas, A., Tzonou, A., Gakiopoulou, H., and Dimopoulos, M. A. The prevalence of bcl-2, p53, and Ki-67 immunoreactivity in transitional cell bladder carcinomas and their clinicopathologic correlates. *Human Pathology* 29[2], 146-154. 1998.
Excl reason: Not in PICO

Naslund, M. J., Gilseman, A. W., Midkiff, K. D., Bown, A., Wolford, E. T., and Wang, J. Prevalence of lower urinary tract symptoms and prostate enlargement in the primary care setting. *International Journal of Clinical Practice* 61[9], 1437-1445. 2007.
Excl reason: Not in PICO

Nasterlack, M., Feil, G., Leng, G., Pesch, B., Huber, S., Sievert, K. D., Johnen, G., Taeger, D., Mayer, T., Kluckert, M., Bruning, T., and Stenzl, A. [Bladder cancer screening with urine-based tumour markers - occupational medical experience]. [German]. *Aktuelle Urologie* 42[2], 128-134. 2011.
Excl reason: Not in PICO

Nasuti, J. F., Gomella, L. G., Ismial, M., and Bibbo, M. Utility of the BTA stat test kit for bladder cancer screening. *Diagnostic Cytopathology* 21[1], 27-29. 1999.
Excl reason: Not in PICO

Navon, J. D., Soliman, H., Khonsari, F., and Ahlering, T. Screening cystoscopy and survival of spinal cord injured patients with squamous cell cancer of the bladder. *Journal of Urology* 157[6], 2109-2111. 1997.
Excl reason: Not in PICO

Neal, R. D., Din, N. U., Hamilton, W., GBRoumunne, O. C., Carter, B., Stapley, S. & Rubin, G. (2014) Comparison of cancer diagnostic intervals before and after implementation of NICE guidelines: Analysis of data from the GBR General Practice Research Database. *British Journal of Cancer*, 110: 584-592.
Not in PICO

Nieder, A. M., Lotan, Y., Nuss, G. R., Langston, J. P., Vyas, S., Manoharan, M., and Soloway, M. S. Are patients with hematuria appropriately referred to Urology? A multi-institutional questionnaire based survey. *Urologic Oncology* 28[5], 500-503. 2010.
Excl reason: Not in PICO

Nisman, B., Barak, V., Shapiro, A., Golijanin, D., Peretz, T., and Pode, D. Evaluation of urine CYFRA 21-1 for the detection of primary and recurrent bladder carcinoma. *Cancer* 94[11], 2914-2922. 1-6-2002.
Excl reason: Not in PICO

Nitti, V. and Taneja, S. Overactive bladder: achieving a differential diagnosis from other lower urinary tract conditions. [Review] [43 refs]. *International Journal of Clinical Practice* 59[7], 825-830. 2005.
Excl reason: Narrative review

Nozais, J. P., Danis, M., and Gentilini, M. Symptoms and development of *Schistosoma haematobium* infestation seen in a metropolis. [French]. *La Revue du praticien* 43[4], 428-431. 15-2-1993.
Excl reason: Narrative review

O'Brien, T. S., Perkins, J. M. T., and Cranston, D. Efficiency in the outpatient department: The lessons from urology. *Annals of the Royal College of Surgeons of England* 77[4], 287-289. 1995.
Excl reason: Not in PICO

Obroniecka, I., Rojewska, J., and Wankowicz, Z. The value of urine sediment cytomorphology in the ambulatory differential diagnosis of hematuria. [Polish]. *Polski merkuriusz lekarski : organ Polskiego Towarzystwa Lekarskiego* 5[29], 285-287. 1998.
Excl reason: Not in PICO

Ojo, P., Abenthroth, A., Fiedler, P., and Yavorek, G. Migrating mesh mimicking colonic malignancy. *American Surgeon* 72[12], 1210-1211. 2006.
Excl reason: Not in PICO

Okuno, H., Kihara, Y., and Arai, Y. [Primary paraganglioma of the urinary bladder: a report of two cases]. [Japanese]. *Hinyokika Kiyō - Acta Urologica Japonica* 36[6], 691-696. 1990.
Excl reason: Not in PICO

Okuno, T., Masuda, M., Yamazaki, A., Hirokawa, M., Matsushita, K., and Asakura, S. [Malignant fibrous histiocytoma of the urinary bladder: a case report]. [Review] [13 refs] [Japanese]. *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology* 82[2], 312-315. 1991.
Excl reason: Not in PICO

Ollesch, J., Drees, S. L., Heise, H. M., Behrens, T., Bruning, T. & Gerwert, K. (2013) FTIR spectroscopy of biofluids revisited: an automated approach to spectral biomarker identification. *Analyst*, 138: 4092-4102.
Not in PICO

Ooi, W. L., Lee, F., Wallace, D. M., and Hayne, D. 'One stop' haematuria clinic in Fremantle Hospital, Western Australia: a report of the first 500 patients. *BJU International* 108, Suppl-6. 2011.
Excl reason: Not in PICO

Owens, J. L., DiPiero, J. M., Elson, P. & Hansel, D. E. (2013) Urine biobanking: Methods, validation, and research results. *Laboratory Investigation*, 93: 499A.
Not in PICO

Oya, M., Schmidt, B., Schmitz-Drager, B. J., and Schulz, W. A. Expression of G1-->S transition regulatory molecules in human urothelial cancer. *Japanese Journal of Cancer Research* 89[7], 719-726. 1998.
Excl reason: Not in PICO

Palmer, S., Sokolovski, S. G., Rafailov, E. & Nabi, G. (2013) Technologic developments in the field of photonics for the detection of urinary bladder cancer. *Clinical Genitourinary Cancer*, 11: 390-396. Narrative review

Park, J. W., Jeong, B. C., Seo, S. I., Jeon, S. S., Kwon, G. Y., and Lee, H. M. Leiomyoma of the urinary bladder: a series of nine cases and review of the literature. [Review]. *Urology* 76[6], 1425-1429. 2010.
Excl reason: Not in PICO

Parkin, D. E., Davis, J. A., and Symonds, R. P. Long-term bladder symptomatology following radiotherapy for cervical carcinoma. *Radiotherapy & Oncology* 9[3], 195-199. 1987.
Excl reason: Not in PICO

Parsons, B. A., Evans, S., and Wright, M. P. Prostate cancer and urinary incontinence. [Review] [70 refs]. *Maturitas* 63[4], 323-328. 20-8-2009.
Excl reason: Not in PICO

Pascual, Samaniego M., Torrecilla Garcia-Ripoll, J. R., Calleja, Escudero J., Egea, Camacho J., Rivera, Ferro J., and Fernandez del, Busto E. [Hypercalcemia, leukemoid reaction, and thrombocytosis as paraneoplastic presentation of transitional cell carcinoma of the kidney]. [Spanish]. *Actas Urologicas Espanolas* 25[5], 400-403. 2001.
Excl reason: Not in PICO

Paul, A. B., Collie, D. A., Wild, S. R., and Chisholm, G. D. An integrated haematuria clinic. *British Journal of Clinical Practice* 47[3], 128-130. 1993.
Excl reason: Not in PICO

Pedalino, M., Vercesi, E., Manini, C., Piras, D., Di Primio, O. G., Vella, R., and Marino, G. [A case of chronic schistosomiasis four years after infestation]. [Italian]. *Urologia (Treviso)* 77, Suppl-41. 2010.
Excl reason: Not in PICO

Plail, R. Detecting bladder cancer. *BMJ* 301[6752], 567-568. 22-9-1990.
Excl reason: Narrative review

Pode, D., Shapiro, A., Wald, M., Nativ, O., Laufer, M., and Kaver, I. Noninvasive detection of bladder cancer with the BTA stat test. *The Journal of urology* 161[2], 443-446. 1999.
Excl reason: Not in PICO

Pode, D., Golijanin, D., Sherman, Y., Lebensart, P., and Shapiro, A. Immunostaining of Lewis X in cells from voided urine, cytopathology and ultrasound for noninvasive detection of bladder tumors. *Journal of Urology* 159[2], 389-392. 19-12-7777.
Excl reason: Not in PICO

Pomara, G. & Francesca, F. (2013) [Endoscopic resection. Aspects of technique and optimization of outcomes. Current indications to PDD-guided resection]. [Italian]. *Urologia*, 80: 16-19. Narrative review

Ponsky, L. E., Sharma, S., Pandrangi, L., Kedia, S., Nelson, D., Agarwal, A., and Zippe, C. D. Screening and monitoring for bladder cancer: Refining the use of NMP22. *Journal of Urology* 166[1], 75-78. 2001.
Excl reason: Not in PICO

Porru, S., Assennato, G., Bergamaschi, E., Carta, P., Foa, V., Forni, A., Gabbani, G., Mastrangelo, G., and Sartorelli, P. [The toxicology and prevention of the risks of occupational exposure to aromatic polycyclic hydrocarbons. III. The effects: epidemiological evidence, early effects. Individual hypersusceptibility. Health surveillance]. [Review] [60 refs] [Italian]. *Giornale Italiano di Medicina del Lavoro ed Ergonomia* 19[4], 152-163. 1997.
Excl reason: Not in PICO

Poulakis, V., Witzsch, U., De, Vries R., Altmannsberger, H.-M., Manyak, M. J., and Becht, E. A comparison of urinary nuclear matrix protein-22 and bladder tumour antigen tests with voided urinary cytology in detecting and following bladder cancer: The prognostic value of false-positive

results. *BJU International* 88[7], 692-701. 2001.
 Excl reason: Not in PICO

Quek, P., Chin, C. M., and Lim, P. H. The role of BTA stat in clinical practice. *Annals of the Academy of Medicine, Singapore* 31[2], 212-216. 2002.
 Excl reason: Not in PICO

Rafique, M. Clinico-pathological features of bladder carcinoma in women in Pakistan and smokeless tobacco as a possible risk factor. *World Journal of Surgical Oncology* 3. 5-8-2005.
 Excl reason: Not in PICO

Rath, G. D. Bladder cancer, 1992. [Review] [23 refs]. *Postgraduate Medicine* 92[1], 105-112. 115.
 Excl reason: Narrative review

Restrepo, N. C. and Carey, P. O. Evaluating hematuria in adults. *American Family Physician* 40[2], 149-156. 1989.
 Excl reason: Narrative review

Rinsho, K., Ishikawa, S., Uchida, K., and Koiso, K. The value of ultrasonography in early detection of renal cell carcinoma. *Japanese Journal of Clinical Oncology* 14[3], 329-334. 1984.
 Excl reason: Not in PICO

Ripley, T. L., Havrda, D. E., Blevins, S., and Culkin, D. Early evaluation of hematuria in a patient receiving anticoagulant therapy and detection of malignancy. *Pharmacotherapy: The Journal of Human Pharmacology & Drug Therapy* 24[11], 1638-1640. 2004.
 Excl reason: Not in PICO

Ritchie, C. D., Bevan, E. A., and Collier, S. J. Importance of occult haematuria found at screening. *British Medical Journal Clinical Research Ed.* 292[6521], 681-683. 8-3-1986.
 Excl reason: Not in PICO

Rodgers, M. A., Hempel, S., Aho, T., Kelly, J. D., Kleijnen, J. & Westwood, M. (2006) Diagnostic tests used in the investigation of adult haematuria: a systematic review. *BMJ Int*, 98: 1154-1160.
 Systematic review, checked for relevant studies

Roobol, M. J., Bangma, C. H., el, Bouazzaoui S., Franken-Raab, C. G., and Zwarthoff, E. C. Feasibility study of screening for bladder cancer with urinary molecular markers (the BLU-P project). *Urologic Oncology* 28[6], 686-690. 2010.
 Excl reason: Not in PICO

Rosenberg, M. T., Hazzard, M. A., and Kuritzky, L. Chronic pelvic pain: When to suspect interstitial cystitis. *Consultant* 45[12], 1371-1381. 2005.
 Excl reason: Not in PICO

Rosenberg, M. T., Staskin, D. R., Kaplan, S. A., MacDiarmid, S. A., Newman, D. K., and Ohl, D. A. A practical guide to the evaluation and treatment of male lower urinary tract symptoms in the primary care setting. [Review] [53 refs]. *International Journal of Clinical Practice* 61[9], 1535-1546. 2007.
 Excl reason: Not in PICO

Rosser, C. J., Urquidi, V. & Goodison, S. (2013) Urinary biomarkers of bladder cancer: an update and future perspectives. *Biomarkers in Medicine*, 7: 779-790.
 Narrative review

Rous, S. N. Evaluation of gross and microscopic hematuria. *Primary Care; Clinics in Office Practice* 12[4], 647-659. 1985.
 Excl reason: Narrative review

Rozanski, T. A. and Grossman, H. B. Recent developments in the pathophysiology of bladder cancer. [Review] [30 refs]. *AJR. American Journal of Roentgenology* 163[4], 789-792. 1994.
 Excl reason: Narrative review

Sakamoto, W., Sugita, O., Nishijima, T., Kishimoto, T., and Maekawa, M. [Case report of primary carcinoma in situ in upper urinary tract and review of the Japanese literature]. [Review] [13 refs] [Japanese]. *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology* 80[4], 602-606. 1989.
 Excl reason: Not in PICO

- Sakamoto, Y., Tanaka, H., and Kawabata, G. [Inflammatory pseudotumor of the urinary bladder diagnosed using 3D-CT cystoscopy]. [Review] [9 refs] [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 49[10], 587-590. 2003.
Excl reason: Not in PICO
- Sallami, S., Ben, Rhouma S., Hafsia, G., Noura, Y., and Horchani, A. [Intradiverticular tumors of the bladder: diagnostic and therapeutic problems: report of 32 cases]. [French]. *Tunisie Medicale* 89[8-9], 663-667. 2011.
Excl reason: Not in PICO
- Sanchez-Carbayo, M., Urrutia, M., Silva, J. M., Romani, R., Gonzalez De Buitrago, J. M., and Navajo, J. A. Comparative predictive values of urinary cytology, urinary bladder cancer antigen, CYFRA 21-1 and NMP22 for evaluating symptomatic patients at risk for bladder cancer. *Journal of Urology* 165[5 1], 1462-1466. 2001.
Excl reason: Not in PICO
- Sanchini, M. A., Gunelli, R., Nanni, O., Bravaccini, S., Fabbri, C., Sermasi, A., Bercovich, E., Ravaioli, A., Amadori, D., and Calistri, D. Relevance of urine telomerase in the diagnosis of bladder cancer. *JAMA : the journal of the American Medical Association* 294[16], 2052-2056. 26-10-2005.
Excl reason: Not in PICO
- Sandhu, K. S., LaCombe, J. A., Fleischmann, N., Greston, W. M., Lazarou, G., and Mikhail, M. S. Gross and Microscopic Hematuria Guidelines for Obstetricians and Gynecologists. *Obstetrical & Gynecological Survey* 64[1], 39-49. 2009.
Excl reason: Not in PICO
- Sawczuk, I. S., Volfson, I. A., Bagiella, E., Sawczuk, A., and Ghafar, M. A. Detection of bladder cancer in patients with asymptomatic hematuria by urinary matrix protein 22, voided cytology and cystoscopy. *International Journal of Cancer Prevention* 2[1], 55-61. 2005.
Excl reason: Not in PICO
- See, W. A. and Williams, R. D. Tumors of the kidney, ureter, and bladder. [Review] [117 refs]. *Western Journal of Medicine* 156[5], 523-534. 1992.
Excl reason: Narrative review
- Sharfi, A. R. and Hassan, O. Evaluation of haematuria in Khartoum. *East African Medical Journal* 71[1], 29-31. 1994.
Excl reason: Not in PICO
- Sharp, V. J., Barnes, K. T. & Erickson, B. A. (2013) Assessment of asymptomatic microscopic hematuria in adults. *American Family Physician*, 88: 747-754.
Narrative review
- Sheldon, C. A., Clayman, R. V., Gonzalez, R., Williams, R. D., and Fraley, E. E. Malignant urachal lesions. [Review] [97 refs]. *Journal of Urology* 131[1], 1-8. 1984.
Excl reason: Not in PICO
- Shinagare, A. B., Silverman, S. G., Gershanik, E. F., Chang, S. L. & Khorasani, R. (2014) Evaluating hematuria: Impact of guideline adherence on urologic cancer diagnosis. *American Journal of Medicine*, 127: 625-632.
Not in PICO (setting)
- Shirodkar, S. P. and Lokeshwar, V. B. Potential new urinary markers in the early detection of bladder cancer. [Review] [47 refs]. *Current Opinion in Urology* 19[5], 488-493. 2009.
Excl reason: Not in PICO
- Siddiqui, I., Bhally, H. S., Niaz, Q., and Burney, I. A. Tumor-induced hypercalcemia: predictors of early mortality. *JPMA - Journal of the Pakistan Medical Association* 52[8], 361-364. 2002.
Excl reason: Not in PICO
- Siegel, M. J. Pelvic tumors in childhood. *Radiologic Clinics of North America* 35[6], 1455-1475. 1997.
Excl reason: Not in PICO
- Simon, J., Bartsch, G., Jr., Rinnab, L., Hautmann, R. E., and Volkmer, B. G. Transrectal ultrasound as diagnostic tool for the detection of local recurrence following cystectomy and urinary diversion.

Urologia Internationalis 82[1], 12-16. 2009.

Excl reason: Not in PICO

Smellie, W. S., Forth, J. O., McNulty, C. A. M., Hirschowitz, L., Lilić, D., Gosling, R., Bareford, D., Logan, E., Kerr, K. G., Spickett, G. P., Hoffman, J., Galloway, A., and Bloxham, C. A. Best practice in primary care pathology: review 2. *Journal of Clinical Pathology* 59[2], 113-120. 2006.

Excl reason: Not in PICO

Soga, N., Komeda, Y., Suzuki, R., and Kawamura, J. [Two cases of squamous cell carcinoma of the ureter]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 41[11], 879-882. 1995.

Excl reason: Not in PICO

Sommariva, M. L., Sandri, S. D., and Ceriani, V. Efficacy of sodium hyaluronate in the management of chemical and radiation cystitis. *Minerva Urologica e Nefrologica* 62[2], 145-150. 2010.

Excl reason: Not in PICO

Srivastava, A. K., Singh, P. K., Srivastava, K., Singh, D., Dalela, D., Rath, S. K., Goel, M. M. & Brahma Bhatt, M. L. (2013) Diagnostic role of survivin in urinary bladder cancer. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 14: 81-85.

Not in PICO

Stower, M. J. Delays in diagnosing and treating bladder cancer. *British Medical Journal Clinical Research Ed.* 296[6631], 1228-1229. 30-4-1988.

Excl reason: Not in PICO

Sturgeon, S. R., Hartge, P., Silverman, D. T., Kantor, A. F., Linehan, W. M., Lynch, C., and Hoover, R. N. Associations between bladder cancer risk factors and tumor stage and grade at diagnosis. *Epidemiology* 5[2], 218-225. 1994.

Excl reason: Not in PICO

Sugiono, M. and Hammonds, J. C. Do patients with frank haematuria referred under the two-week rule have a higher incidence of bladder cancer? *Annals of the Royal College of Surgeons of England* 88[1], 26. 2006.

Excl reason: Not in PICO

Sultana, S. R., Goodman, C. M., Byrne, D. J., and Baxby, K. Microscopic haematuria: Urological investigation using a standard protocol. *British Journal of Urology* 78[5], 691-698. 1996.

Excl reason: Not in PICO

Summerton, N., Mann, S., Rigby, A. S., Ashley, J., Palmer, S., and Hetherington, J. W. Patients with new onset haematuria: assessing the discriminant value of clinical information in relation to urological malignancies. [Review] [28 refs]. *British Journal of General Practice* 52[477], 284-289. 2002.

Excl reason: Not in PICO - secondary care

Svatek, R. S., Lotan, Y., Karakiewicz, P. I., and Shariat, S. F. Screening for bladder cancer using urine-based tumor markers. [Review] [26 refs]. *Minerva Urologica e Nefrologica* 60[4], 247-253. 2008.

Excl reason: Not in PICO

Svatek, R. S., Hollenbeck, B. K., Holmang, S., Lee, R., Kim, S. P., Stenzl, A. & Lotan, Y. (2014) The economics of bladder cancer: Costs and considerations of caring for this disease. *European Urology*, 66: 253-262.

Not in PICO

Tabata, T., Suzuki, H., Nakamura, Y., Morito, T., Yabuki, Y., Shibuya, A., and Ando, M. [Adult male with chronic renal failure due to reflux nephropathy that was possibly induced by neurogenic bladder since childhood]. [Japanese]. *Nippon Jinzo Gakkai Shi. Japanese Journal of Nephrology* 51[8], 1086-1090. 2009.

Excl reason: Not in PICO

Takai, K., Kakizoe, T., Tobisu, K., Tanaka, Y., Teshima, S., and Kishi, K. [A case of proliferative chronic cystitis, progressing to obstructive nephropathy, treated by total cystectomy and enterocystoplasty]. [Japanese]. *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology*

80[7], 1059-1062. 1989.

Excl reason: Not in PICO

Tan, P. K., Chang, H. C., and Sitoh, Y. Y. Haematuria clinic--a preliminary audit and considerations for a one-stop assessment centre. *Singapore Medical Journal* 39[11], 501-503. 1998.

Excl reason: Not in PICO

Taniguchi, H., Sakagami, J., Suzuki, N., Hasegawa, H., Shinoda, M., Tosa, M., Baba, T., Yasuda, H., Kataoka, K., and Yoshikawa, T. Adenoendocrine cell carcinoma of the gallbladder clinically mimicking squamous cell carcinoma. *International Journal of Clinical Oncology* 14[2], 167-170. 2009.

Excl reason: Not in PICO

Tawfik, H. N. Carcinoma of the urinary bladder associated with schistosomiasis in Egypt: the possible causal relationship. *Princess Takamatsu Symposia* 18, 197-209. 1987.

Excl reason: Not in PICO

Teichman, J. M. H., Weiss, B. D., and Solomon, D. Urological needs assessment for primary care practice: Implications for undergraduate medical education. *Journal of Urology* 161[4], 1282-1285. 1999.

Excl reason: Not in PICO

Thiruchelvam, N. and Mostafid, H. Do patients with frank haematuria referred under the two-week rule have a higher incidence of bladder cancer? *Annals of the Royal College of Surgeons of England* 87[5], 345-347. 2005.

Excl reason: Not in PICO

Tissot, W. D., Diokno, A. C., and Peters, K. M. A referral center's experience with transitional cell carcinoma misdiagnosed as interstitial cystitis. *Journal of Urology* 172[2], 478-480. 2004.

Excl reason: Not in PICO

Tsukagoshi, S. [ImmuCyst intravesical (freeze-dried preparation made from the connaught strain of Bacillus Calmette Guerin) for the treatment of superficial bladder cancer and carcinoma in situ of urinary bladder]. [Review] [30 refs] [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]* 30[7], 1027-1038. 2003.

Excl reason: Not in PICO

Turner, C. & Grady, M. (2013) 12-Year-old boy with back spasms. *Clinical Journal of Sport Medicine*, 23: e13.

Not in PICO

Ueda, T., Miura, N., Suzuki, K., Suzuki, F., Inomiya, H., Kotake, T., Nishikawa, Y., Yamaguchi, K., and Ito, H. [Metastatic bladder tumor from gastric carcinoma: a case report]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 38[10], 1175-1177. 1992.

Excl reason: Not in PICO

Vaidyanathan, S., Mansour, P., Ueno, M., Yamazaki, K., Wadhwa, M., Soni, B. M., Singh, G., Hughes, P. L., Watson, I. D., and Sett, P. Problems in early diagnosis of bladder cancer in a spinal cord injury patient: report of a case of simultaneous production of granulocyte colony stimulating factor and parathyroid hormone-related protein by squamous cell carcinoma of urinary bladder. *BMC Urology* 2[1], 8. 30-8-2002.

Excl reason: Not in PICO

Vaish, M., Mandhani, A., Mittal, R. D., and Mittal, B. Microsatellite instability as prognostic marker in bladder tumors: a clinical significance. *BMC Urology* 5, 2. 2005.

Excl reason: Not in PICO

Villalbi, J. R., Gelabert-Mas, A., Comin, E., and Coronado-Garcia, J. Cancer of the urothelium: background and characteristics of the care process related to the prognosis in a series of clinical cases. [Spanish]. *Actas Urologicas Espanolas* 14[2], 89-91. 1990.

Excl reason: Not in PICO

- Viswanath, S., Zehhof, B., Ho, E., Sethia, K., and Mills, R. Is routine urine cytology useful in the haematuria clinic? *Annals of the Royal College of Surgeons of England* 90[2], 153-155. 2008.
Excl reason: Not in PICO
- Volkmer, B. G., Kuefer, R., Bartsch, G. C., Jr., Gust, K., and Hautmann, R. E. Oncological followup after radical cystectomy for bladder cancer-is there any benefit? *Journal of Urology* 181[4], 1587-1593. 20-11-1593.
Excl reason: Not in PICO
- Volpe, A., Racioppi, M., D'Agostino, D., Cappa, E., Gardi, M., Totaro, A., Pinto, F., Sacco, E., Marangi, F., Palermo, G., and Bassi, P. F. Bladder tumor markers: a review of the literature. [Review] [145 refs]. *International Journal of Biological Markers* 23[4], 249-261. 2008.
Excl reason: Not in PICO
- Wadhwa, N., Jatawa, S. K. & Tiwari, A. (2013) Non-invasive urine based tests for the detection of bladder cancer. *Postgraduate Medical Journal*, 89: 352-357.
Narrative review
- Wadhwa, N., Jatawa, S. K. & Tiwari, A. (2013) Republished: non-invasive urine based tests for the detection of bladder cancer.[Reprint of *J Clin Pathol.* 2012 Nov;65(11):970-5; PMID: 22685259]. *Postgraduate Medical Journal*, 89: 352-357.
Narrative review
- Wakui, M. and Shiigai, T. Urinary tract cancer screening through analysis of urinary red blood cell volume distribution. *International Journal of Urology* 7[7], 248-253. 2000.
Excl reason: Not in PICO
- Wallace, D. M., Bryan, R. T., Dunn, J. A., Begum, G., Bathers, S., and West Midlands Urological Research Group. Delay and survival in bladder cancer. *BJU International* 89[9], 868-878. 2002.
Excl reason: Not in PICO
- Wang, J. and Wang, F. W. Clinical Characteristics and Outcomes of Patients with Primary Signet-Ring Cell Carcinoma of the Urinary Bladder. *Urologia Internationalis* 86[4], 453-460. 2011.
Excl reason: Not in PICO
- Ward, E., Halperin, W., Thun, M., Grossman, H. B., Fink, B., Koss, L., Osorio, A. M., and Schulte, P. Screening workers exposed to 4,4'-methylenebis(2-chloroaniline) for bladder cancer by cystoscopy. *Journal of Occupational Medicine* 32[9], 865-868. 1990.
Excl reason: Not in PICO
- Wawroschek, F. and Roth, S. Hematuria in cases of bladder cancer. [German]. *Urologe - Ausgabe A* 42[7], 902-907. 1-7-2003.
Excl reason: Not in PICO/narrative review
- Wax, J. R., Pinette, M. G., Blackstone, J., Cartin, A., and McCrann, D. J. Nonbilharzial bladder carcinoma complicating pregnancy: review of the literature. [Review] [25 refs]. *Obstetrical & Gynecological Survey* 57[4], 236-244. 2002.
Excl reason: Not in PICO
- Webb, V. and Holmes, A. Urological cancers: Do early detection strategies exist? *BJU International* 86[9], 996-1000. 2000.
Excl reason: Not in PICO
- Wise, G. J. and Shteynshlyuger, A. An update on lower urinary tract tuberculosis. [Review] [50 refs]. *Current Urology Reports* 9[4], 305-313. 2008.
Excl reason: Not in PICO
- Wu, C. F., Chang, P. L., Chen, C. S., Chuang, C. K., Weng, H. H., and Pang, S. T. The outcome of patients on dialysis with upper urinary tract transitional cell carcinoma. *Journal of Urology* 176[2], 477-481. 2006.
Excl reason: Not in PICO
- Wu, X., Amos, C. I., Zhu, Y., Zhao, H., Grossman, B. H., Shay, J. W., Luo, S., Hong, W. K., and Spitz, M. R. Telomere dysfunction: A potential cancer predisposition factor. *Journal of the National Cancer*

Institute 95[16], 1211-1218. 20-8-2003.

Excl reason: Not in PICO

Wu, Z., Zhang, Y., and Liu, D. [Relationship between the abnormal expression of CD44 gene and bladder cancer]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]* 34[11], 645-647. 1996.

Excl reason: Not in PICO

Yafi, F. A., Aprikian, A. G., Tanguay, S., and Kassouf, W. Patients with microscopic and gross hematuria: practice and referral patterns among primary care physicians in a universal health care system. *Canadian Urological Association Journal* 5[2], 97-101. 2011.

Excl reason: Not in PICO

Yakasai, A., Allam, M., and Thompson, A. J. Incidence of bladder cancer in a one-stop clinic. *Annals of African Medicine* 10[2], 112-114. 2011.

Excl reason: Not in PICO

Yang, C. C. and Clowers, D. E. Screening cystoscopy in chronically catheterized spinal cord injury patients. *Spinal Cord* 37[3], 204-207. 1999.

Excl reason: Not in PICO

Yeaton-Massey, A., Brookfield, K. F., Aziz, N., Mrazek-Pugh, B. & Chueh, J. (2013) Maternal bladder cancer diagnosed at routine first-trimester obstetric ultrasound examination. *Obstetrics & Gynecology*, 122: t-7.

Not in PICO

Yegin, Z., Gunes, S. & Buyukalpelli, R. (2013) Hypermethylation of TWIST1 and NID2 in tumor tissues and voided urine in urinary bladder cancer patients. *DNA & Cell Biology*, 32: 386-392.

Not in PICO

Yi, S. K., Yoder, M., Zaner, K., and Hirsch, A. E. Palliative radiation therapy of symptomatic recurrent bladder cancer. *Pain Physician* 10[2], 285-290. 2007.

Excl reason: Not in PICO

Yilmaz, Y., Aydin, S., Bayrakli, H., Ugras, S., Ozman, E., and Berktas, M. Using of NMP 22 only or together with the cytology in the diagnosis and follow-up of bladder tumors. [Turkish]. *Turk Uroloji Dergisi* 29[2], 138-145. 2003.

Excl reason: Not in PICO (secondary care)

Yip, S. K., Peh, W. C., Tam, P. C., Li, J. H., and Lam, C. H. Day case hematuria diagnostic service: use of ultrasonography and flexible cystoscopy. *Urology* 52[5], 762-766. 1998.

Excl reason: Not in PICO

Yip, S. K., Peh, W. C., Tam, P. C., Li, J. H., and Lam, C. H. Role of ultrasonography in screening for urological malignancies in patients presenting with painless haematuria. *Annals of the Academy of Medicine, Singapore* 28[2], 174-177. 1999.

Excl reason: Not in PICO

Yokoyama, S., Hirakawa, H., Ueno, S., Yabe, H., and Hiraoka, N. Neuroblastoma of the urinary bladder, preclinically detected by mass screening. *Pediatrics* 103[5], e67. 1999.

Excl reason: Not in PICO

Yun, E. J., Meng, M. V., and Carroll, P. R. Evaluation of the patient with hematuria. *Medical Clinics of North America* 88[2], 329-+. 2004.

Excl reason: Narrative review

Zhu, J., Zeng, Y. & Yang, B. (2013) Research progress of bladder cancer-related factors. [Chinese]. *Chinese Journal of Clinical Oncology*, 40: 741-744.

Narrative review

Zippe, C., Pandrangi, L., and Agarwal, A. NMP22 is a sensitive, cost-effective test in patients at risk for bladder cancer. *Journal of Urology* 161[1], 62-65. 1999.

Excl reason: Not in PICO

Review question:

Which investigations of symptoms of suspected bladder cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

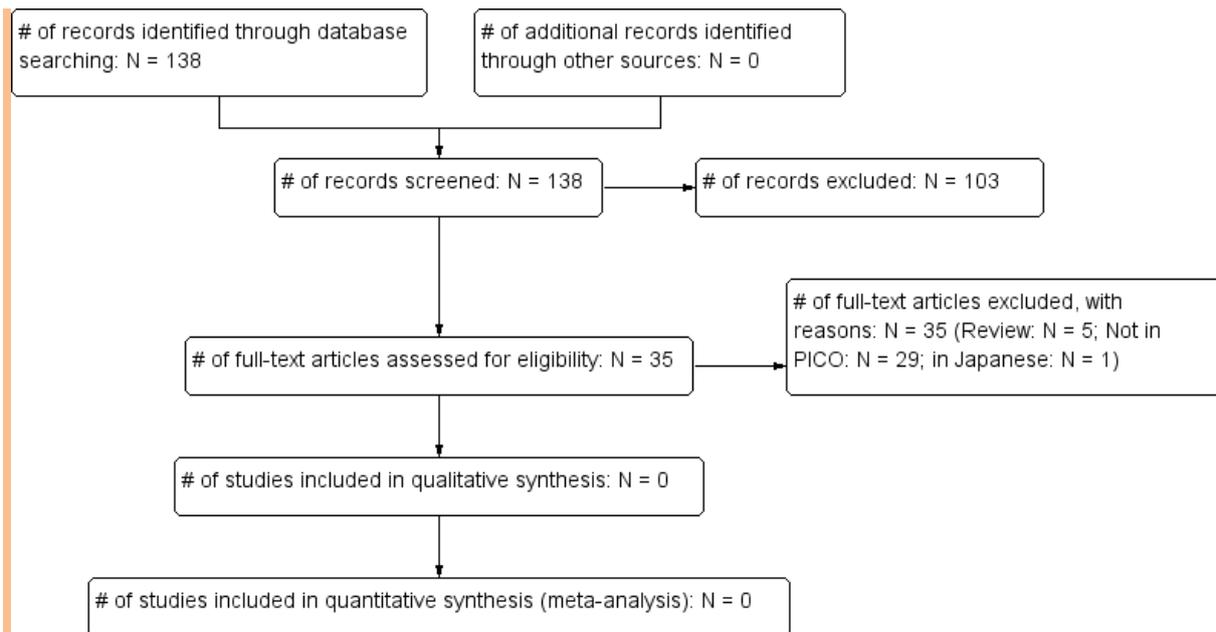
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	796	91	16/01/2013
<i>Premedline</i>	1980-2013	30	5	16/01/2013
<i>Embase</i>	1980-2013	358	40	17/01/2013
<i>Cochrane Library</i>	1980-2013	40	1	17/01/2013
<i>Psychinfo</i>	1980-2013	1	0	16/01/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	46	9	17/01/2013
<i>Biomed Central</i>	1980-2013	114	2	17/01/2013

Total number of references retrieved after de-duplication: 104

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-11/08/2014	37	14	11/08/2014
<i>Premedline</i>	2013-11/08/2014	52	10	11/08/2014
<i>Embase</i>	2013-11/08/2014	53	19	11/08/2014
<i>Cochrane Library</i>	2013-11/08/2014	25	0	11/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-11/08/2014	10	1	11/08/2014

Total References retrieved (after de-duplication): 34



Study results

No evidence was identified pertaining to the diagnostic accuracy of urine cytology, ultrasound, cystoscopy, blood HCG, urine marker NMP22, and urine marker MCM5 in patients with suspected bladder cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies

- (2002) Can blood tests detect cancer early? *Health News*, 8: 4.
Narrative review
- (2002) [Suspected bladder carcinoma. New rapid test with high sensitivity]. [German]. *MMW Fortschritte der Medizin*, 144: 65.
Not in PICO
- Abbaszadeh, S., Taheri, S. & Nourbala, M. H. (2009) Bladder tumor in women with microscopic hematuria: an Iranian experience and a review of the literature. *Advances in Urology*:231861, 2009., 231861.
Not in PICO
- Alameddine, M. & Nassir, A. (2012) The influence of urine cytology on our practice. *Urology annals*, 4: 80-83.
Not in PICO
- Allen, D., Popert, R. & O'Brien, T. (2004) The two-week-wait cancer initiative in urology: useful modernization? *Journal of the Royal Society of Medicine*, 97: 279-281.
Not in PICO
- Amin, M. F. & Abd El Hamid, A. M. (2013) The diagnostic accuracy of multidetector computed tomography with multiplanar reformatted imaging and virtual cystoscopy in the early detection and evaluation of bladder carcinoma: comparison with conventional cystoscopy. *Abdominal*

Imaging, 38: 184-192.

Not in PICO

Arora, V. K., Sarungbam, J., Bhatia, A., Singh, N., Agrawal, V. & Aggarwal, S. (2010) Usefulness of NMP22 as an adjunct to a typical urine cytology and low-grade urothelial carcinoma. *Diagnostic Cytopathology*, 38: 788-790.

Not in PICO

Banek, S., Schwentner, C., Tager, D., Pesch, B., Nasterlack, M., Leng, G., Gawrych, K., Bonberg, N., Johnen, G., Kluckert, M., Gakis, G., Todenhofer, T., Hennenlotter, J., Bruning, T. & Stenzl, A. (2013) Prospective evaluation of fluorescence-in situ-hybridization to detect bladder cancer: Results from the UroScreen-Study. *Urologic Oncology: Seminars and Original Investigations*, 31: 1656-1662.

Not in PICO

Barlandas-Rendon, E., Muller, M. M., Garcia-Latorre, E. & Heinschink, A. (2002) Comparison of urine cell characteristics by flow cytometry and cytology in patients suspected of having bladder cancer. *Clinical Chemistry & Laboratory Medicine*, 40: 817-823.

Not in PICO

Basak, M., Ozkurt, H., Tanriverdi, O., Cay, E., Aydin, M. & Miroglu, C. (2009) Sixteen-slice multidetector computed tomographic virtual cystoscopy in the evaluation of a patient with suspected bladder tumor and history of bladder carcinoma operation. *Journal of Computer Assisted Tomography*, 33: 867-871.

Not in PICO

Bassett, J. C., Gore, J. L., McCarthy, W. J., Morrison, C., Kwan, L., Bennett, C. J., Cookson, M. S., Penson, D. F. & Saigal, C. (2013) Introduction of a tobacco-screening initiative for those at risk for bladder cancer in a high volume urology clinic. *Journal of Clinical Oncology*, 31.

Not in PICO

Batool, A., Ramachandran, R., Dubrovskaya, V. & Lee, D. (2013) Recurrent urothelial cancer masquerading as a large colonic mass and massive gastrointestinal hemorrhage. *American Journal of Gastroenterology*, 108: S458-S459.

Not in PICO

Bhuiyan, J., Akhter, J. & O'Kane, D. J. (2003) Performance characteristics of multiple urinary tumor markers and sample collection techniques in the detection of transitional cell carcinoma of the bladder. *Clinica Chimica Acta*, 331: 69-77.

Not in PICO

Blanker, M. H. (2009) [Diagnosis of urothelial carcinoma by the general practitioner--significance of haematuria]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 153: A1198.

Narrative review

Blochlinger, A. M., Gasser, T. C., Stoffel, F., Laschke, S. & Buhning, C. (1996) [Hematuria]. [German]. *Therapeutische Umschau*, 53: 672-675.

Narrative review

Bock-Oruma, A. A., Dienye, P. O. & Oghu, I. S. (2013) Prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia in primary care, Port Harcourt, Nigeria. *South African Family Practice*, 55: 467-472.

Not in PICO

Bonner, R. B., Hemstreet, G. P., III, Fradet, Y., Rao, J. Y., Min, K. W. & Hurst, R. E. (1993) Bladder cancer risk assessment with quantitative fluorescence image analysis of tumor markers in exfoliated bladder cells. *Cancer*, 72: 2461-2469.

Not in PICO

Britton, J. P., Dowell, A. C. & Whelan, P. (1989) Dipstick haematuria and bladder cancer in men over 60: results of a community study. *BMJ*, 299: 1010-1012.

Not in PICO

- Browne, R. F., Murphy, S. M., Grainger, R. & Hamilton, S. (2005) CT cystography and virtual cystoscopy in the assessment of new and recurrent bladder neoplasms. *European Journal of Radiology*, 53: 147-153.
Not in PICO
- Budman, L. I., Kassouf, W. & Steinberg, J. R. (2008) Biomarkers for detection and surveillance of bladder cancer. *Canadian Urological Association Journal*, 2: 212-221.
Narrative review
- Burger, M., Grossman, H. B., Droller, M., Schmidbauer, J., Hermann, G., Dragoescu, O., Ray, E., Fradet, Y., Karl, A., Burgues, J. P., Witjes, J. A., Stenzl, A., Jichlinski, P. & Jocham, D. (2013) Photodynamic diagnosis of non-muscle-invasive bladder cancer with hexaminolevulinate cystoscopy: A meta-analysis of detection and recurrence based on raw data. *European Urology*, 64: 846-854.
Not in PICO
- Buteau, A., Seideman, C. A., Svatek, R. S., Youssef, R. F., Chakrabarti, G., Reed, G., Bhat, D. & Lotan, Y. (2014) What is evaluation of hematuria by primary care physicians? Use of electronic medical records to assess practice patterns with intermediate follow-up. *Urologic Oncology*, 32: 128-134.
Not in PICO
- Cauberg, E. C., Kloen, S., Visser, M., de la Rosette, J. J., Babjuk, M., Soukup, V., Pesl, M., Duskova, J. & de Reijke, T. M. (2010) Narrow band imaging cystoscopy improves the detection of non-muscle-invasive bladder cancer. *Urology*, 76: 658-663.
Not in PICO
- Chan, E. S., Ng, C. F., Hou, S. M. & Yip, S. K. (2011) Using urine microscopy and cytology for early detection of bladder cancer in male patients with lower urinary tract symptoms. *International Urology & Nephrology*, 43: 289-294.
Not in PICO
- Cohan, R. H., Caoili, E. M., Cowan, N. C., Weizer, A. Z. & Ellis, J. H. (2009) MDCT Urography: Exploring a new paradigm for imaging of bladder cancer. [Review] [47 refs]. *AJR.American Journal of Roentgenology*, 192: 1501-1508.
Narrative review
- Daniely, M., Rona, R., Kaplan, T., Olsfanger, S., Elboim, L., Zilberstien, Y., Friberger, A., Kidron, D., Kaplan, E., Lew, S. & Leibovitch, I. (2005) Combined analysis of morphology and fluorescence in situ hybridization significantly increases accuracy of bladder cancer detection in voided urine samples. *Urology*, 66: 1354-1359.
Not in PICO
- Datta, S. N., Allen, G. M., Evans, R., Vaughton, K. C. & Lucas, M. G. (2002) Urinary tract ultrasonography in the evaluation of haematuria—a report of over 1,000 cases. *Annals of the Royal College of Surgeons of England*, 84: 203-205.
Not in PICO
- Datta, S. N., Allen, G. M., Evans, R., Vaughton, K. C. & Lucas, M. G. (2002) Urinary tract ultrasonography in the evaluation of haematuria—a report of over 1,000 cases. *Ann R Coll Surg Engl*, 84: 200-205.
Duplicate
- De, G. N., D'Hallewin, M. A. & Baert, L. (1997) Contemporary non-imaging methods in diagnosis of bladder cancer: a review. [Review] [22 refs]. *Acta Urologica Belgica*, 65: 55-58.
Narrative review
- DeSouza, K., Chowdhury, S. & Hughes, S. (2003) - Prompt diagnosis key in bladder cancer. [Review]. - *Practitioner*, 258: 23-27.
Narrative review
- Dobrowolska-Glazar, B., Glazar, W., Dobrowolski, Z. & Lipczynski, W. (2010) [Bladder cancer biomarkers]. [Review] [Polish]. *Przegląd Lekarski*, 67: 479-483.
Narrative review

- Dobry, E. & Danuser, H. (2009) [Imaging of the kidney and the urinary tract]. [Review] [22 refs] [German]. *Therapeutische Umschau*, 66: 39-42.
Narrative review
- Doehn, C., Krockenberger, K., Zumbe, J., Rassler, J., Sommerauer, M., Feller, A. C., Gebhardt, M., Hemmelmann, C., Grozinger, K., Nolte, S., Breitling, C., Jocham, D. & Ziegler, A. (2014) Comparison of white-light, photodynamic diagnosis and narrow-band imaging for the detection of non-muscle invasive bladder cancer: Results from a randomized multicenter diagnostic phase-III study. *European Urology, Supplements*, 13: e23.
Not in PICO
- Dregan, A., Moller, H., Charlton, J. & Gulliford, M. C. (2013) Are alarm symptoms predictive of cancer survival? Population-based cohort study. *British Journal of General Practice*, 63: E807-E812.
Not in PICO
- Eissa, S., Shabayek, M. I., Ismail, M. F., El-Allawy, R. M. & Hamdy, M. A. (2010) Diagnostic evaluation of apoptosis inhibitory gene and tissue inhibitor matrix metalloproteinase-2 in patients with bladder cancer. *IUBMB Life*, 62: 394-399.
Not in PICO
- Eissa, S., Swellam, M., El-Khouly, I. M., Kassim, S. K., Shehata, H., Mansour, A., Esmat, M., Nossier, A. I., Hamdy, M. A., Awad, N. M. & El-Ahmady, O. (2011) Aberrant methylation of RARbeta2 and APC genes in voided urine as molecular markers for early detection of bilharzial and nonbilharzial bladder cancer. *Cancer Epidemiology, Biomarkers & Prevention*, 20: 1657-1664.
Not in PICO
- Eissa, S., Badr, S., Elhamid, S. A., Helmy, A. S., Nour, M. & Esmat, M. (2013) The value of combined use of survivin mRNA and matrix metalloproteinase 2 and 9 for bladder cancer detection in voided urine. *Disease Markers*, 34: 57-62.
Not in PICO
- Eissa, S., Matboli, M., Mansour, A., Mohamed, S., Awad, N. & Kotb, Y. M. (2014) Evaluation of urinary HURP mRNA as a marker for detection of bladder cancer: relation to bilharziasis. *Medical Oncology*, 31: 804.
Not in PICO
- Feil, G. & Stenzl, A. (2006) [Tumor marker tests in bladder cancer]. [Review] [60 refs] [Spanish]. *Actas Urologicas Espanolas*, 30: 38-45.
Narrative review
- Ferre, A., Cordonnier, C., Demailly, M., Hakami, F., Sevestre, H. & Saint, F. (2013) [Bladder tumor targeting by Hexvix() fluorescence: 4 years results after prospective monocentric evaluation]. [French]. *Progres En Urologie*, 23: 195-202.
Not in PICO
- Fiore, D. C. & Fox, C. L. (2014) Urology and nephrology update: bladder and kidney cancer. *Fp Essentials*, 416: 26-29.
Narrative review
- Flores-Carreras, O., Martinez-Espinoza, C. J., Gonzalez-Ruiz, M. I. & Montes-Casillas, Y. E. (2010) [Contribution of bladder biopsy to the study of urogynaecological patient]. [Spanish]. *Ginecologia y Obstetricia de Mexico*, 78: 187-190.
Not in PICO
- Foo, K. T. (2013) The role of transabdominal ultrasound in office urology. *Proceedings of Singapore Healthcare*, 22: 125-130.
Narrative review
- Friedlander, D. F., Resnick, M. J., You, C., Bassett, J., Yarlagadda, V., Penson, D. F. & Barocas, D. A. (2014) - Variation in the intensity of hematuria evaluation: a target for primary care quality improvement. - *American Journal of Medicine*, 127: 633-640.
Not in PICO

- Gervino, G., Autino, E., Kolomoets, E., Leucci, G. & Balma, M. (2007) Diagnosis of bladder cancer at 465 MHz. *Electromagnetic Biology & Medicine*, 26: 119-134.
Not in PICO
- Gomella, L., Grossman, H. B., Droller, M., Schmidbauer, J., Hermann, G., Dragoescu, O., Ray, E., Witjes, A., Karl, A., Stenzl, A., Fradet, Y., Burgues, J. & Jocham, D. (2013) A meta-analysis of blue light cystoscopy with hexaminolevulinate in patients with non-muscle invasive bladder cancer. *Journal of Urology*, 189: e528.
Not in PICO
- Goodison, S., Rosser, C. J. & Urquidi, V. (2013) Bladder cancer detection and monitoring: assessment of urine- and blood-based marker tests. [Review]. *Molecular Diagnosis & Therapy*, 17: 71-84.
Narrative review
- Griffiths, T. R. & Action on Bladder Cancer (2013) Current perspectives in bladder cancer management. [Review]. *International Journal of Clinical Practice*, 67: 435-448.
Narrative review
- Gutierrez Banos, J. L., Rebollo Rodrigo, M. H., Antolin, J. F., Martin, G. B., Hernandez, R. R., Portillo Martin, J. A., Correas Gomez, M. A., del Valle Schaan, J. I., Roca, E. A., de Diego, R. E. & Rado Velazquez, M. A. (2000) [Comparative study of BTA stat test, NMP-22, and cytology in the diagnosis of bladder cancer]. [Spanish]. *Archivos Espanoles de Urologia*, 53: 21-27.
Not in PICO
- Hamid, A. A. (2013) The diagnostic accuracy of multidetector computed tomography with multiplanar reformatted imaging and virtual cystoscopy in the early detection and evaluation of bladder carcinoma: Comparison with conventional cystoscopy. *Journal of Endourology*, 27: A165.
Not in PICO
- Harzmann, R. (681) [Early diagnosis of urogenital tumors]. [German]. *Zeitschrift fur Hautkrankheiten*, 62: 665-676.
Narrative review
- Hasan, S. T., German, K. & Derry, C. D. (1994) Same day diagnostic service for new cases of haematuria--a district general hospital experience. *British Journal of Urology*, 73: 152-154.
Not in PICO
- Hawary, A. M., Warburton, H. E., Brough, R. J., Collins, G. N., Brown, S. C., O'Reilly, P. H. & Adeyoju, A. A. (2008) The '2-week wait' rule for referrals for suspected urological cancers--urgent need for refinement of criteria. *Annals of the Royal College of Surgeons of England*, 90: 517-522.
Not in PICO
- Hee, T. G., Shah, S. A., Ann, H. S., Hemdan, S. N., Shen, L. C., Al-Fahmi Abdul, G. N., Singam, P., Ho, C. C., Hong, G. E., Bahadzor, B. & Zainuddin, Z. M. (2013) Stratifying patients with haematuria into high or low risk groups for bladder cancer: a novel clinical scoring system. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 14: 6327-6330.
Not in PICO
- Heins, M. J., Korevaar, J. C., Rijken, P. M. & Schellevis, F. G. (2013) For which health problems do cancer survivors visit their General Practitioner? *European Journal of Cancer*, 49: 211-218.
Not in PICO
- Henning, A., Wehrberger, M., Madersbacher, S., Pycha, A., Martini, T., Comploj, E., Jeschke, K., Tripolt, C. & Rauchenwald, M. (2013) Do differences in clinical symptoms and referral patterns contribute to the gender gap in bladder cancer? *BJU International*, 112: 68-73.
Not in PICO
- Hermann, G. G., Mogensen, K., Carlsson, S., Marcussen, N. & Duun, S. (2011) Fluorescence-guided transurethral resection of bladder tumours reduces bladder tumour recurrence due to less residual tumour tissue in Ta/T1 patients: a randomized two-centre study. *BJU International*, 108: t-303.
Not in PICO

- Herr, H. W. (2010) Narrow-band imaging cystoscopy to evaluate the response to bacille Calmette-Guerin therapy: preliminary results. *BJU International*, 105: 314-316.
Not in PICO
- Hollingsworth, J. M., Zhang, Y. S., Miller, D. C., Skolarus, T. A., Wood, D. P., Lee, C. T., Montie, J. E. & Hollenbeck, B. K. (2011) Identifying better practices for early-stage bladder cancer. *Medical Care*, 49: 1112-1117.
Not in PICO
- Ibragimova, M. I., Chushnikov, V. N., Moiseev, V. N., Petukhov, V. I., Zheglov, E. P. & Cherepnev, G. V. (2013) [Electron paramagnetic resonance study of blood of anemic patients with urological cancer]. [Russian]. *Biofizika*, 58: 289-294.
Not in PICO
- Jeon, S. S., Kang, I., Hong, J. H., Choi, H. Y. & Chai, S. E. (2001) Diagnostic efficacy of fluorescence cystoscopy for detection of urothelial neoplasms. *Journal of Endourology*, 15: 753-759.
Not in PICO
- Jichlinski, P. & Lovisa, B. (2011) High magnification cystoscopy in the primary diagnosis of bladder tumors. [Review]. *Current Opinion in Urology*, 21: 398-402.
Narrative review
- Jocham, D., Witjes, F., Wagner, S., Zeylemaker, B., van, M. J., Grimm, M. O., Muschter, R., Popken, G., Konig, F., Knuchel, R. & Kurth, K. H. (2005) Improved detection and treatment of bladder cancer using hexaminolevulinate imaging: a prospective, phase III multicenter study. *Journal of Urology*, 174: 862-866.
Not in PICO
- Jones, M. W., Cox, R., Davies, K. I. & Rose, M. B. (1988) The value of the pre-clinic intravenous urogram in the earlier diagnosis of the cause of haematuria. *British Journal of Urology*, 62: 11-12.
Not in PICO
- Kamat, A. M., Hegarty, P. K., Gee, J. R., Clark, P. E., Svatek, R. S., Hegarty, N., Shariat, S. F., Xylinas, E., Schmitz-Drager, B. J., Lotan, Y., Jenkins, L. C., Droller, M., van Rhijn, B. W., Karakiewicz, P. I. & International Consultation on Urologic Disease-European Association of Urology Consultation on Bladder Cancer (2013) ICUD-EAU International Consultation on Bladder Cancer 2012: Screening, diagnosis, and molecular markers. [Review]. *European Urology*, 63: 4-15.
Narrative review
- Karl, A., Stief, C. & Zaak, D. (2013) [Photodynamic diagnostics of the bladder: current study results]. [Review] [German]. *Urologe (Auszg.A)*, 52: 504-508.
Narrative review
- Khan, M. A., Shaw, G. & Paris, A. M. (2002) Is microscopic haematuria a urological emergency? *BJU International*, 90: 355-357.
Not in PICO
- Khandelwal, C. & Kistler, C. (2013) Diagnosis of urinary incontinence. *American Family Physician*, 87: 543-551.
Narrative review
- Kim, J. Y. & Kim, H. J. (2014) - A Comparison Between ThinPrep Monolayer and Cytospin Cytology for the Detection of Bladder Cancer. - *Korean Journal of Urology*, 55: 390-394.
Not in PICO
- King, K. & Steggall, M. (2014) - Haematuria: from identification to treatment. - *British Journal of Nursing*, 23: S28-S32.
Narrative review
- Kitahara, S., Iwatsubo, E., Yasuda, K., Ushiyama, T., Nakai, H., Suzuki, T., Yamashita, T., Sato, R., Kihara, T., Yamanishi, T. & Nohara, Y. (2006) Practice patterns of Japanese physicians in urologic surveillance and management of spinal cord injury patients. *Spinal Cord*, 44: 362-368.
Not in PICO

- Kivrak, A. S., Kiresi, D., Emlik, D., Odev, K. & Kilinc, M. (2009) Comparison of CT virtual cystoscopy of the contrast material-filled bladder with conventional cystoscopy in the diagnosis of bladder tumours. *Clinical Radiology*, 64: 30-37.
Not in PICO
- Kohler, C. & Varenhorst, E. (1999) [Microscopic hematuria in adults--a diagnostic dilemma. Scientific guidelines for management are not available according to a review of the literature]. [Review] [199 refs] [Swedish]. *Lakartidningen*, 96: 4911-4916.
Not in PICO
- Koiso, K., Kano, K., Nemoto, R., Ishikawa, H., Ohtani, M., Sato, T. & Iwasaki, A. (1989) [Detection and diagnosis of bladder cancer in the early stage]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 47: 1172-1177.
In Japanese. No translation available.
- Kruck, S., Scharpf, M., Stenzl, A. & Bedke, J. (2013) A rare case of synchronous renal cell carcinoma of the bladder presenting with gross hematuria. *Rare Tumors*, 5: 72-74.
Not in PICO
- Kundal, V. K., Pandith, A. A., Hamid, A., Shah, A., Kundal, R. & Wani, S. M. (2010) Role of NMP22 Bladder Check Test in early detection of bladder cancer with recurrence. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 11: 1279-1282.
Not in PICO
- Lahme, S., Bichler, K. H., Feil, G. & Krause, S. (2001) Comparison of cytology and nuclear matrix protein 22 for the detection and follow-up of bladder cancer. *Urologia Internationalis*, 66: 72-77.
Not in PICO
- Lokeshwar, V. B. & Soloway, M. S. (2001) Current bladder tumor tests: does their projected utility fulfill clinical necessity?. [Review] [90 refs]. *Journal of Urology*, 165: 1067-1077.
Narrative review
- Lopes, R. I., Nogueira, L., Albertotti, C. J., Takahashi, D. Y. & Lopes, R. N. (2008) Comparison of virtual cystoscopy and transabdominal ultrasonography with conventional cystoscopy for bladder tumor detection. *Journal of Endourology*, 22: 1725-1729.
Not in PICO
- Ludecke, G., Pilatz, A., Hauptmann, A., Bschleipfer, T. & Weidner, W. (2012) Comparative analysis of sensitivity to blood in the urine for urine-based point-of-care assays (UBC rapid, NMP22 BladderChek and BTA-stat) in primary diagnosis of bladder carcinoma. Interference of blood on the results of urine-based POC tests. *Anticancer Research*, 32: 2015-2018.
Not in PICO
- Lynch, T. H., Waymont, B., Dunn, J. A., Hughes, M. A. & Wallace, D. M. (1994) Rapid diagnostic service for patients with haematuria. *British Journal of Urology*, 73: 147-151.
Not in PICO
- Lyratzopoulos, G., Neal, R. D., Barbiere, J. M., Rubin, G. P. & Abel, G. A. (2012) Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. *Lancet Oncology*, 13: 353-365.
Not in PICO
- Lyratzopoulos, G., Abel, G. A., McPhail, S., Neal, R. D. & Rubin, G. P. (2013) Gender inequalities in the promptness of diagnosis of bladder and renal cancer after symptomatic presentation: Evidence from secondary analysis of an English primary care audit survey. *BMJ Open*, 3.
Not in PICO
- MacArthur, C., Pendleton, L. L. & Smith, A. (1985) Treatment delay in patients with bladder tumours. *Journal of Epidemiology & Community Health*, 39: 63-66.
Not in PICO
- Mack, D. & Jakse, G. (1986) [Bladder cancer as an incidental finding]. [German]. *Wiener Klinische Wochenschrift*, 98: 175-178.
Not in PICO

- Mady, H. H. E., Omar, A. M. A., Elgammal, M. A. A. & Ibrahim, G. H. M. (2014) Utility of urine cytology in evaluating hematuria with sonographically suspected bladder lesion in patients older than 50 years. *Urology annals*, 6: 212-217.
Not in PICO
- Mahnert, B. (2003) Measurements of complement factor H-related protein (BTA-TRAK (TM) assay) and nuclear matrix protein (NMP22 assay) - Useful diagnostic tools in the diagnosis of urinary bladder cancer? *Clinical Chemistry and Laboratory Medicine*, 41: 104-110.
Not in PICO
- Manassero, A., Chierchia, S. & Carone, R. (2013) Neurogenic lower urinary tract dysfunctions and bladder cancer: Our experience and proposal of evaluation algorithm. *Neurourology and Urodynamics*, 32: S15-S16.
Not in PICO
- Martingano, P., Stacul, F., Cavallaro, M., Casagrande, F., Cernic, S., Belgrano, M. & Cova, M. (2010) 64-Slice CT urography: 30 months of clinical experience. *Radiologia Medica*, 115: 920-935.
Not in PICO
- Mayr, R. & Burger, M. (2013) Value of fluorescence cystoscopy in high risk non-muscle invasive bladder cancer. *Current Urology Reports*, 14: 90-93.
Narrative review
- Meeks, J. J., Herr, H. W., Bernstein, M., Al-Ahmadie, H. A. & Dalbagni, G. (2013) Preoperative accuracy of diagnostic evaluation of the urachal mass. *Journal of Urology*, 189: 1260-1262.
Not in PICO
- Mian, C., Lodde, M., Comploj, E., Palermo, S., Mian, M., Maier, K. & Pycha, A. (2005) The value of the ImmunoCyt/uCyt+ test in the detection and follow-up of carcinoma in situ of the urinary bladder. *Anticancer Research*, 25: 3641-3644.
Not in PICO
- Mishriki, S. F., Nabi, G. & Cohen, N. P. (2008) Diagnosis of urologic malignancies in patients with asymptomatic dipstick hematuria: prospective study with 13 years' follow-up. *Urology*, 71: 13-16.
Not in PICO (secondary care)
- Mitra, A. P., Jorda, M. & Cote, R. J. (2012) Pathological possibilities and pitfalls in detecting aggressive bladder cancer. [Review]. *Current Opinion in Urology*, 22: 397-404.
Narrative review
- Mitterberger, M., Pinggera, G. M., Neuwirt, H., Maier, E., Akkad, T., Strasser, H., Gradl, J., Pallwein, L., Bartsch, G. & Frauscher, F. (2007) Three-dimensional ultrasonography of the urinary bladder: preliminary experience of assessment in patients with haematuria. *BJU International*, 99: 111-116.
Not in PICO
- Mohammed, A., Shergill, I. S., Vandal, M. T. & Gujral, S. S. (2010) Incidental urinary tract pathologies in the one-stop prostate cancer clinic.[Erratum appears in Arch Ital Urol Androl. 2010 Jun;82(2):III Note: Aza, Mohammed [corrected to Mohammed, Aza]; Iqbal, S Shergill [corrected to Shergill, Iqbal S]; Muhammad, M Vandal [corrected to Vandal, Muhammad T]; Sandeep, S Gujrai [corrected to Gujral, Sandeep S]]. *Archivio Italiano di Urologia, Andrologia*, 82: 15-17.
Not in PICO
- Monreal, M., Lafoz, E., Casals, A., Inaraja, L., Montserrat, E., Callejas, J. M. & Martorell, A. (1991) Occult cancer in patients with deep venous thrombosis. A systematic approach. *Cancer*, 67: 541-545.
Not in PICO
- Nakamura, K. (2009) Utility of serial urinary cytology in the initial evaluation of the patient with microscopic hematuria. *BMC Urology*, 9.
Not in PICO

- Naslund, I. (1988) Reliability and accuracy of Urotel test, a device for urinary cytology. *European Urology*, 15: 54-58.
Not in PICO
- Neal, R. D., Din, N. U., Hamilton, W., GBRoumunne, O. C., Carter, B., Stapley, S. & Rubin, G. (2014) Comparison of cancer diagnostic intervals before and after implementation of NICE guidelines: Analysis of data from the GBR General Practice Research Database. *British Journal of Cancer*, 110: 584-592.
Not in PICO
- Nemoto, S., Ishikawa, S., Takeshima, H., Iizumi, T., Uchida, K., Yazaki, T., Nemoto, R., Rinsho, K. & Kano, S. (1983) [Clinical study of urinary cytology: with special reference to bladder cancer]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica*, 29: 1611-1615.
Not in PICO
- Ng, K. L., Htun, T. H., Dublin, N., Ong, T. A. & Razack, A. H. (2012) Assessment and clinical significance of haematuria in Malaysian patients - relevance to early cancer diagnosis. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 13: 2515-2518.
Not in PICO
- Nicolau, C., Bunesch, L., Peri, L., Salvador, R., Corral, J. M., Mallofre, C. & Sebastia, C. (2011) Accuracy of contrast-enhanced ultrasound in the detection of bladder cancer. *British Journal of Radiology*, 84: 1091-1099.
Not in PICO
- Nitti, V. & Taneja, S. (2005) Overactive bladder: achieving a differential diagnosis from other lower urinary tract conditions. [Review] [43 refs]. *International Journal of Clinical Practice*, 59: 825-830.
Narrative review
- O'Donoghue, J. M., Horgan, P. G., Corcoran, M., Bredin, H., McGuire, M. & Given, H. F. (1991) Urinary cytology in the detection of bladder carcinoma. *Irish Journal of Medical Science*, 160: 352-353.
Not in PICO
- Ollesch, J., Drees, S. L., Heise, H. M., Behrens, T., Bruning, T. & Gerwert, K. (2013) FTIR spectroscopy of biofluids revisited: an automated approach to spectral biomarker identification. *Analyst*, 138: 4092-4102.
Not in PICO
- Owens, J. L., DiPiero, J. M., Elson, P. & Hansel, D. E. (2013) Urine biobanking: Methods, validation, and research results. *Laboratory Investigation*, 93: 499A.
Not in PICO
- Palmer, S., Sokolovski, S. G., Rafailov, E. & Nabi, G. (2013) Technologic developments in the field of photonics for the detection of urinary bladder cancer. *Clinical Genitourinary Cancer*, 11: 390-396.
Narrative review
- Park, J. W., Jeong, B. C., Seo, S. I., Jeon, S. S., Kwon, G. Y. & Lee, H. M. (2010) Leiomyoma of the urinary bladder: a series of nine cases and review of the literature. [Review]. *Urology*, 76: 1425-1429.
Not in PICO
- Patel, N. (2009) The diagnostic value of abdominal ultrasound, urine cytology and prostate-specific antigen testing in the lower urinary tract symptoms clinic. *International Journal of Clinical Practice*, 63: 1734-1738.
Not in PICO
- Paul, A. B., Collie, D. A., Wild, S. R. & Chisholm, G. D. (1993) An integrated haematuria clinic. *British Journal of Clinical Practice*, 47: 128-130.
Not in PICO
- Pode, D., Golijanin, D., Sherman, Y., Lebensart, P. & Shapiro, A. (1993) Immunostaining of Lewis X in cells from voided urine, cytopathology and ultrasound for noninvasive detection of bladder tumors. *Journal of Urology*, 159: 389-392.
Not in PICO

- Pomara, G. & Francesca, F. (2013) [Endoscopic resection. Aspects of technique and optimization of outcomes. Current indications to PDD-guided resection]. [Italian]. *Urologia*, 80: 16-19.
Narrative review
- Poulakis, V., Witzsch, U., De, V. R., Altmannsberger, H. M., Manyak, M. J. & Becht, E. (2001) A comparison of urinary nuclear matrix protein-22 and bladder tumour antigen tests with voided urinary cytology in detecting and following bladder cancer: the prognostic value of false-positive results. *BJU International*, 88: 692-701.
Not in PICO
- Purysko, A. S., Leao Filho, H. M. & Herts, B. R. (2012) Radiologic imaging of patients with bladder cancer. [Review]. *Seminars in Oncology*, 39: 543-558.
Narrative review
- Ren, H., Waltzer, W. C., Bhalla, R., Liu, J., Yuan, Z., Lee, C. S., Darras, F., Schulsinger, D., Adler, H. L., Kim, J., Mishail, A. & Pan, Y. (2009) Diagnosis of bladder cancer with microelectromechanical systems-based cystoscopic optical coherence tomography. *Urology*, 74: 1351-1357.
Not in PICO
- Restrepo, N. C. & Carey, P. O. (1989) Evaluating hematuria in adults. [Review] [27 refs]. *American Family Physician*, 40: 149-156.
Narrative review
- Rodgers, M. A., Hempel, S., Aho, T., Kelly, J. D., Kleijnen, J. & Westwood, M. (2006) Diagnostic tests used in the investigation of adult haematuria: a systematic review. *BMJ Int*, 98: 1154-1160.
Systematic review, checked for relevant studies
- Rosser, C. J., Urquidi, V. & Goodison, S. (2013) Urinary biomarkers of bladder cancer: an update and future perspectives. *Biomarkers in Medicine*, 7: 779-790.
Narrative review
- Sanchez-Carbayo, M., Urrutia, M., Silva, J. M., Romani, R., De Buitrago, J. M. & Navajo, J. A. (2001) Comparative predictive values of urinary cytology, urinary bladder cancer antigen, CYFRA 21-1 and NMP22 for evaluating symptomatic patients at risk for bladder cancer. *Journal of Urology*, 165: 1462-1467.
Not in PICO
- Schamhart, D. H., de Reijke, T. M., van der Poel, H. G., Witjes, J. A., de Boer, E. C., Kurth, K. & Schalken, J. A. (1998) The Bard BTA test: its mode of action, sensitivity and specificity, compared to cytology of voided urine, in the diagnosis of superficial bladder cancer. *European Urology*, 34: 99-106.
Not in PICO
- Schulze, S., Holm-Nielsen, A. & Mogensen, P. (1991) Transurethral ultrasound scanning in the evaluation of invasive bladder cancer. *Scandinavian Journal of Urology & Nephrology*, 25: 215-217.
Not in PICO
- Sharp, V. J., Barnes, K. T. & Erickson, B. A. (2013) Assessment of asymptomatic microscopic hematuria in adults. *American Family Physician*, 88: 747-754.
Narrative review
- Siemens, D. R., Morales, A., Johnston, B. & Emerson, L. (2003) A comparative analysis of rapid urine tests for the diagnosis of upper urinary tract malignancy. *Canadian Journal of Urology*, 10: 1754-1758.
Not in PICO
- Simon, J., Bartsch, G., Jr., Rinnab, L., Hautmann, R. E. & Volkmer, B. G. (2009) Transrectal ultrasound as diagnostic tool for the detection of local recurrence following cystectomy and urinary diversion. *Urologia Internationalis*, 82: 12-16.
Not in PICO
- Singh, R., Saleemi, A., Walsh, K., Popert, R. & O'Brien, T. (2003) Near misses in bladder cancer - an airline safety approach to urology. *Annals of the Royal College of Surgeons of England*, 85: 378-

381.

Not in PICO

Siracusano, S., Niccolini, B., Knez, R., Tiberio, A., Benedetti, E., Bonin, S., Ciciliato, S., Pappagallo, G. L., Belgrano, E. & Stanta, G. (2005) The simultaneous use of telomerase, cytokeratin 20 and CD4 for bladder cancer detection in urine. *European Urology*, 47: 327-333.

Not in PICO

Spencer, J., Lindsell, D. & Mastorakou, I. (1990) Ultrasonography compared with intravenous urography in the investigation of adults with haematuria. *BMJ*, 301: 1074-1076.

Not in PICO

Srivastava, A. K., Singh, P. K., Srivastava, K., Singh, D., Dalela, D., Rath, S. K., Goel, M. M. & Brahma Bhatt, M. L. (2013) Diagnostic role of survivin in urinary bladder cancer. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 14: 81-85.

Not in PICO

Subramonian, K. R., Puranik, S. & Mufti, G. R. (2003) How will the two-weeks-wait rule affect delays in management of urological cancers? *Journal of the Royal Society of Medicine*, 96: 398-399.

Not in PICO

Talbot, R. W., Bannister, J. J. & Hills, N. H. (1984) A haematuria diagnostic service in a district general hospital. *Annals of the Royal College of Surgeons of England*, 66: 348-350.

Not in PICO

Tan, P. K., Chang, H. C. & Sitoh, Y. Y. (1998) Haematuria clinic--a preliminary audit and considerations for a one-stop assessment centre. *Singapore Medical Journal*, 39: 501-503.

Not in PICO

Tanaka, M. (2011) Diagnosis and Management of Urothelial Carcinoma of the Bladder. *Postgraduate Medicine*, 123: 43-55.

Narrative review

Tauber, S., Liedl, B., Schneede, P., Liessmann, F., Waidelich, R. & Hofstetter, A. (2001) [Fluorescence cytology of the urinary bladder]. [German]. *Urologe (Ausg.A)*, 40: 217-221.

Not in PICO (at least 17/27 had cancer)

Thiruchelvam, N. & Mostafid, H. (2005) Do patients with frank haematuria referred under the two-week rule have a higher incidence of bladder cancer? *Annals of the Royal College of Surgeons of England*, 87: 345-347.

Not in PICO

Tissot, W. D., Diokno, A. C. & Peters, K. M. (2004) A referral center's experience with transitional cell carcinoma misdiagnosed as interstitial cystitis. *Journal of Urology*, 172: 478-480.

Not in PICO

Tomera, K. (2004) NMP22 (R) BladderChek (R) Test: point-of-care technology with life. and money-saving potential. *Expert Review of molecular diagnostics*, 4: 783-794.

Narrative review

Trivedi, D. (2009) Commentary: the role of cytologic analysis of voided urine in the work-up of asymptomatic microhematuria. *BMC Urology*, 9.

Narrative review

Turner, C. & Grady, M. (2013) 12-Year-old boy with back spasms. *Clinical Journal of Sport Medicine*, 23: e13.

Not in PICO

Vaish, M., Mandhani, A., Mittal, R. D. & Mittal, B. (2005) Microsatellite instability as prognostic marker in bladder tumors: a clinical significance. *BMC Urology*, 5: 2.

Not in PICO

Volpe, A., Racioppi, M., D'Agostino, D., Cappa, E., Gardi, M., Totaro, A., Pinto, F., Sacco, E., Marangi, F., Palermo, G. & Bassi, P. F. (2008) Bladder tumor markers: a review of the literature. [Review] [145 refs]. *International Journal of Biological Markers*, 23: 249-261.

Narrative review

- Wadhwa, N., Jatawa, S. K. & Tiwari, A. (2012) Non-invasive urine based tests for the detection of bladder cancer. *Journal of Clinical Pathology*, 65: 970-975.
Narrative review
- Wadhwa, N., Jatawa, S. K. & Tiwari, A. (2013) Non-invasive urine based tests for the detection of bladder cancer. *Postgraduate Medical Journal*, 89: 352-357.
Narrative review
- Wadhwa, N., Jatawa, S. K. & Tiwari, A. (2013) Republished: non-invasive urine based tests for the detection of bladder cancer.[Reprint of J Clin Pathol. 2012 Nov;65(11):970-5; PMID: 22685259]. *Postgraduate Medical Journal*, 89: 352-357.
Narrative review
- Wawroschek, F. & Roth, S. (2003) [Hematuria in cases of bladder cancer]. [Review] [28 refs] [German]. *Urologe (Auszg.A)*, 42: 902-907.
Narrative review
- Wilson, C., Boyd, K., Mohammed, A. & Little, B. (2010) A single episode of haematospermia can be safely managed in the community. *International Journal of Clinical Practice*, 64: 1436-1439.
Not in PICO
- Yafi, F. (2011) Patients with microscopic and gross hematuria: practice and referral patterns among primary care physicians in a universal health care system. *Canadian Urological Association Journal*, 5: 97-101.
Not in PICO
- Yakasai, A., Allam, M. & Thompson, A. J. (2011) Incidence of bladder cancer in a one-stop clinic. *Annals of African Medicine*, 10: 112-114.
Not in PICO
- Yeaton-Massey, A., Brookfield, K. F., Aziz, N., Mrazek-Pugh, B. & Chueh, J. (2013) Maternal bladder cancer diagnosed at routine first-trimester obstetric ultrasound examination. *Obstetrics & Gynecology*, 122: t-7.
Not in PICO
- Yegin, Z., Gunes, S. & Buyukalpelli, R. (2013) Hypermethylation of TWIST1 and NID2 in tumor tissues and voided urine in urinary bladder cancer patients. *DNA & Cell Biology*, 32: 386-392.
Not in PICO
- Yip, S. K., Peh, W. C., Tam, P. C., Li, J. H. & Lam, C. H. (1998) Day case hematuria diagnostic service: use of ultrasonography and flexible cystoscopy. *Urology*, 52: 762-766.
Not in PICO
- Yoo, J. H., Suh, B., Park, T. S., Shin, M. G., Choi, Y. D., Lee, C. H. & Choi, J. R. (2010) Analysis of fluorescence in situ hybridization, mtDNA quantification, and mtDNA sequence for the detection of early bladder cancer. *Cancer Genetics & Cytogenetics*, 198: 107-117.
Not in PICO
- Young, M. J. & Soloway, M. S. (1998) Office evaluation and management of bladder neoplasms. [Review] [43 refs]. *Urologic Clinics of North America*, 25: 603-611.
Narrative review
- Yun, E. (2004) Evaluation of the patient with hematuria. *Medical Clinics of North America*, 88: 329.
Narrative review
- Zhu, J., Zeng, Y. & Yang, B. (2013) Research progress of bladder cancer-related factors. [Chinese]. *Chinese Journal of Clinical Oncology*, 40: 741-744.
Narrative review
- Zippe, C., Pandrangi, L., Potts, J. M., Kursh, E., Novick, A. & Agarwal, A. (1999) NMP22: a sensitive, cost-effective test in patients at risk for bladder cancer. *Anticancer Research*, 19: 2621-2623.
Not in PICO
- Zippe, C., Pandrangi, L. & Agarwal, A. (1999) NMP22 is a sensitive, cost-effective test in patients at risk for bladder cancer. *Journal of Urology*, 161: 62-65.
Not in PICO



RENAL CANCER

Review question:

What is the risk of renal cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

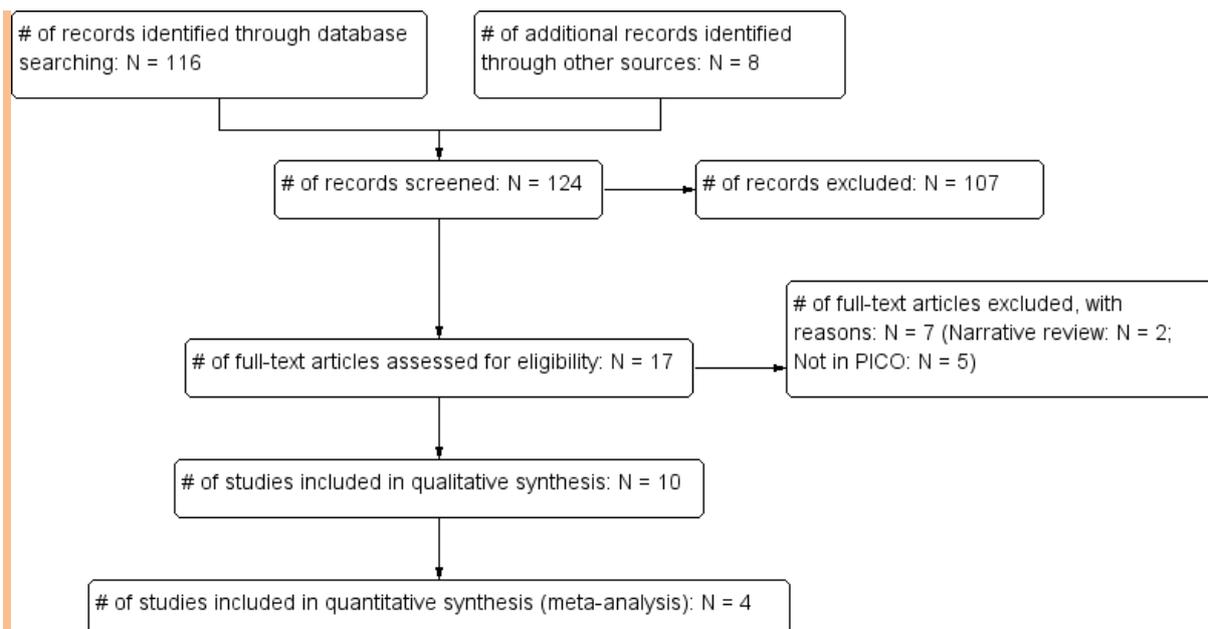
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	718	72	10/12/2012
<i>Premedline</i>	All-2012	29	2	10/12/2012
<i>Embase</i>	All-2012	662	57	10/12/2012
<i>Cochrane Library</i>	All-2012	289	0	11/12/2012
<i>Psychinfo</i>	All-2012	1	0	10/12/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	283	5	11/12/2012
<i>Biomed Central</i>	All-2012	18	0	11/12/2012

Total References retrieved (after de-duplication): 94

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-18/08/2014	49	8	18/08/2014
<i>Premedline</i>	2013-18/08/2014	67	7	18/08/2014
<i>Embase</i>	2013-18/08/2014	140	8	18/08/2014
<i>Cochrane Library</i>	2013-18/08/2014	207	0	18/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-18/08/2014	67	5	18/08/2014

Total References retrieved (after de-duplication): 22



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issue to note is that patient selection is associated with a number of bias or applicability concerns in most of the included studies, with some studies employing non-consecutive or non-random selection of patients and with some studies being employed in settings that are not clearly directly representative of UK-based primary care. Other areas of concern include missing data, compromised reference standards and underspecified presenting symptoms. These issues should all be born in mind when evaluating the evidence along with the fact that a large number of the included cancers were not renal cancers.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Collins (2013)	+	+	+	+	+	+	+
Deyo (1988)	?	+	?	+	-	+	+
Dommett (2012, 2013)	-	+	+	+	+	+	+
Friedlander (2014)	+	+	?	+	?	+	+
Hippisley-Cox (2012)	+	+	+	-	+	+	+
Jones (2007)	+	+	+	+	+	+	+
Muris (1995)	-	+	+	+	-	-	+
Oudega (2006)	+	+	+	+	?	+	+
Shephard (2013)	-	+	+	+	+	+	+

High	Unclear	Low
------	---------	-----

Study results

Table 1: Renal cancer: Meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Collins (2013), Friedlander (2014), Hippisley-Cox (2012), Jones (2007, at 6 months)	Haematuria	All patients (N = 69921)	3.05 (1.3-7.01)
Collins (2013), Friedlander (2014), Hippisley-Cox (2012), Jones (2007, at 3 years)	Haematuria	All patients (N = 69921)	3.3 (1.35-7.84)

Please note that the data from Shephard (2012) are not included in these meta-analyses due to the case-control design of the study. These data are instead reported in the table below.

Table 2: Renal cancer: Individual positive predictive values from the meta-analyses

Studies included	Symptom(s)	Patient group	Positive predictive value, % (95% CI)
Collins (2013)	Haematuria	All patients	4.35 (4.1-4.6) 1645/37810
Friedlander (2014)	Haematuria	All included patients	0.65 (0.39-1.83) 16/2455
Hippisley-Cox (2012)	Haematuria	All patients	6.48 (6.1-6.8)

			1201/18548
Jones (2007, at 6 months),	Haematuria	All patients	4.2 (3.8-4.6) 466/11108
Jones (2007, at 3 years),	Haematuria	All patients	5.7 (5.3-6.2) 634/11108

Table 3: Renal cancer: Patients aged > 14 years: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI)
Collins (2013)	Abdominal pain	All patients	0.11 (0.1-0.13) 284/253344
		Men	0.2 (0.2-0.21) 187/105247
		Women	0.1 (0.1-0.1) 97/148097
Hippisley-Cox (2012)	Abdominal pain	All patients	0.2 (0.2-0.2) 182/93077
Muris (1995)	Non-acute abdominal complaints	All patients	0.11 (0.01-0.7) 1/933
Shephard (2013)	Abdominal pain	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2013)	Abdominal pain: 2 presentations	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2013)	Constipation	Patients ≥ 60 years	0.1 (0.08-0.11)
Shephard (2013)	Constipation: 2 presentations	Patients ≥ 60 years	0.1 (0.06-0.12)
Shephard (2013)	Lower urinary tract infection	Patients ≥ 60 years	0.1 (0.09-0.12)
Shephard (2013)	Lower urinary tract infection: 2 presentations	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2013)	Fatigue	Patients ≥ 60 years	0.1 (0.09-0.13)
Shephard (2013)	Fatigue: 2 presentations	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2013)	Nausea	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2013)	Nausea: 2 presentations	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2013)	Raised inflammatory markers	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2013)	Thrombocytosis	Patients ≥ 60 years	0.3 (0.2-0.3)
Shephard (2013)	Microcytosis	Patients ≥ 60 years	0.3 (0.2-0.4)
Deyo (1988)	Back pain	All included patients	0.05 (0.002-0.3) TP = 1, FP = 1974 N = 8 had other types of cancer
Shephard (2013)	Back pain	Patients ≥ 60 years	0.1 (0.07-0.12)
Shephard (2013)	Back pain: 2 presentations	Patients ≥ 60 years	0.1 (0.07-0.12)
Collins (2013)	Anaemia	All patients	0.6 (0.5-0.7) 102/16961
		Men	1.4 (1.1-1.9)

			57/3969
		Women	0.3 (0.3-0.5) 45/12992
Hippisley-Cox (2012)	Anaemia	All patients	0.69 (0.5-0.9) 68/9799
Collins (2013)	Appetite loss	Women	0.1 (0.04-0.3) 4/3481
Hippisley-Cox (2012)	Appetite loss	All patients	0.18 (0.07-0.4) 6/3330
Oudega (2006)	Deep vein thrombosis	All patients	1.16 (0.4-2.9) 5/430
Collins (2013)	Weight loss	Women	0.1 (0.1-0.2) 21/16037
Hippisley-Cox (2012)	Weight loss	All patients	0.41 (0.3-0.6) 38/9281
Collins (2013)	Haematuria	Men	5.5 (5.2-5.8) 1262/22810
		Women	2.6 (2.3-2.8) 383/15000
Shephard (2013)	Visible haematuria	Patients 40-59 years	0.7 (0.4-1.3)
Shephard (2013)	Visible haematuria	Patients ≥ 60 years	1 (0.08-1.3)
Shephard (2013)	Visible haematuria: 2 presentations	Patients ≥ 60 years	1.2 (0.9-1.8)
Jones (2007)	Haematuria	Men (all ages) at 6 months	5.47 (4.9-6.1) 349/6385
Jones (2007)	Haematuria	Men (all ages) at 3 years	7.4 (6.8-8.1) 472/6385
Jones (2007)	Haematuria	Men < 45 years at 3 years	0.99 (0.53-1.69) 13/1311
Jones (2007)	Haematuria	Men 45-54 years at 3 years	4.35 (3.11-5.9) 39/897
Jones (2007)	Haematuria	Men 55-64 years at 3 years	8.51 (6.94-10.32) 94/1104
Jones (2007)	Haematuria	Men 65-74 years at 3 years	11.21 (9.66-12.9) 170/1517
Jones (2007)	Haematuria	Men 75-84 years at 3 years	10.27 (8.61-12.13) 123/1198
Jones (2007)	Haematuria	Men ≥ 85 years at 3 years	9.22 (6.43-12.7) 33/358
Jones (2007)	Haematuria	Women (all ages) at 6 months	2.48 (2.1-3) 117/4723
Jones (2007)	Haematuria	Women (all ages) at 3 years	3.4 (2.9-4) 162/4723
Jones (2007)	Haematuria	Women < 45 years at 3 years	0.22 (0.05-0.64) 3/1361
Jones (2007)	Haematuria	Women 45-54 years at 3 years	1.34 (0.65-2.45) 10/745
Jones (2007)	Haematuria	Women 55-64 years at 3 years	3.42 (2.26-4.93) 27/790
Jones (2007)	Haematuria	Women 65-74 years at	5.91 (4.42-7.72)

		3 years	50/846
Jones (2007)	Haematuria	Women 75-84 years at 3 years	6.83 (5.06-8.98) 47/688
Jones (2007)	Haematuria	Women ≥ 85 years at 3 years	8.53 (5.6-12.3) 25/293

TP = True positives, FP = False positives. Shephard (2013) calculated the positive predictive values using Bayesian statistics.

Table 4: Renal cancer: Patients aged ≥ 60 years: Symptom combinations

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI)
Shephard (2013)	Abdominal pain and back pain	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2013)	Abdominal pain and constipation	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2013)	Abdominal pain and lower urinary tract infections	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2013)	Abdominal pain and fatigue	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2013)	Abdominal pain and nausea	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2013)	Abdominal pain and raised inflammatory markers	Patients ≥ 60 years	0.2 (0.2-0.3)
Shephard (2013)	Abdominal pain and thrombocytosis	Patients ≥ 60 years	0.5 (0.3-1)
Shephard (2013)	Abdominal pain and microcytosis	Patients ≥ 60 years	> 5 (NR)
Shephard (2013)	Abdominal pain and visible haematuria	Patients ≥ 60 years	2.8 (NR)
Shephard (2013)	Visible haematuria and back pain	Patients ≥ 60 years	0.7 (0.4-1.3)
Shephard (2013)	Visible haematuria and constipation	Patients ≥ 60 years	1 (NR)
Shephard (2013)	Visible haematuria and lower urinary tract infections	Patients ≥ 60 years	0.6 (0.4-1)
Shephard (2013)	Visible haematuria and fatigue	Patients ≥ 60 years	0.9 (NR)
Shephard (2013)	Visible haematuria and nausea	Patients ≥ 60 years	1.1 (NR)
Shephard (2013)	Visible haematuria and raised inflammatory markers	Patients ≥ 60 years	1.3 (0.7-2.2)
Shephard (2013)	Visible haematuria and thrombocytosis	Patients ≥ 60 years	2.1 (NR)
Shephard (2013)	Visible haematuria and microcytosis	Patients ≥ 60 years	1.5 (NR)
Shephard (2013)	Constipation and back pain	Patients ≥ 60 years	0.2 (0.1-0.2)

Shephard (2013)	Constipation and lower urinary tract infections	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2013)	Constipation and fatigue	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2013)	Constipation and nausea	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2013)	Constipation and raised inflammatory markers	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2013)	Constipation and thrombocytosis	Patients ≥ 60 years	0.3 (0.2-0.5)
Shephard (2013)	Constipation and microcytosis	Patients ≥ 60 years	0.6 (NR)
Shephard (2013)	Back pain and lower urinary tract infections	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2013)	Back pain and fatigue	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2013)	Back pain and nausea	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2013)	Back pain and raised inflammatory markers	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2013)	Back pain and thrombocytosis	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2013)	Back pain and microcytosis	Patients ≥ 60 years	0.3 (0.1-0.6)
Shephard (2013)	Lower urinary tract infections and fatigue	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2013)	Lower urinary tract infections and nausea	Patients ≥ 60 years	0.2 (0.1-0.4)
Shephard (2013)	Lower urinary tract infections and raised inflammatory markers	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2013)	Lower urinary tract infections and thrombocytosis	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2013)	Lower urinary tract infections and microcytosis	Patients ≥ 60 years	0.4 (0.2-0.8)
Shephard (2013)	Fatigue and nausea	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2013)	Fatigue and raised inflammatory markers	Patients ≥ 60 years	0.2 (0.2-0.3)
Shephard (2013)	Fatigue and thrombocytosis	Patients ≥ 60 years	0.5 (0.3-0.9)
Shephard (2013)	Fatigue and microcytosis	Patients ≥ 60 years	0.4 (0.2-0.8)
Shephard (2013)	Nausea and raised inflammatory markers	Patients ≥ 60 years	0.2 (0.2-0.3)
Shephard (2013)	Nausea and thrombocytosis	Patients ≥ 60 years	0.4 (0.2-0.6)
Shephard (2013)	Nausea and microcytosis	Patients ≥ 60 years	0.5 (NR)
Shephard (2013)	Raised inflammatory markers and thrombocytosis	Patients ≥ 60 years	0.4 (0.3-0.5)
Shephard (2013)	Raised inflammatory markers and microcytosis	Patients ≥ 60 years	0.7 (0.5-1)

Shephard (2013)	Thrombocytosis and microcytosis	Patients \geq 60 years	0.6 (0.4-1)
-----------------	---------------------------------	--------------------------	-------------

NR = Not reported. TP = True positives, FP = False positives. Shephard (2013) calculated the positive predictive values using Bayesian statistics.

Table 5: Renal cancer: Positive predictive values for any childhood cancer: All patients

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2012)	Any NICE alert symptom 0-3 months before diagnosis	All included patients	0.055 (0.047-0.065) Cases: 342/1267 Control: 211/15318
Dommett (2012)	Any NICE alert symptom 0-12 months before diagnosis	All included patients	0.07 (0.064-0.078) Cases: 427/1267 Control: 829/15318
Dommett (2012)	Neurological symptoms 0-12 months before diagnosis	All included patients	0.083 (0.067-0.105) Cases: 108/1267 Control: 207/15318
Dommett (2012)	Headache 0-12 months before diagnosis	All included patients	0.064 (0.051-0.082) Cases: 90/1267 Control: 224/15318
Dommett (2013)	Headache 0-3 months before diagnosis	All included patients	0.06 (0.04-0.08) Cases: 73/1267 Control: 55/15318
Dommett (2013)	Headache 0-3 months before diagnosis and \geq 3 consultations	All included patients	0.13 (0.08-0.22)
Dommett (2012)	Lymphadenopathy 0-12 months before diagnosis	All included patients	0.096 (0.074-0.126) Cases: 82/1267 Control: 136/15318
Dommett (2013)	Lymphadenopathy 0-3 months before diagnosis	All included patients	0.09 (0.06-0.13) Cases: 69/1267 Control: 33/15318
Dommett (2013)	Lymphadenopathy 0-3 months before diagnosis and \leq 3 consultations	All included patients	0.2 (0.1-0.39)
Dommett (2012)	Lump/mass/swelling 0-12 months before diagnosis	All included patients	0.172 (0.119-0.25) Cases: 56/1267 Control: 52/15318
Dommett (2013)	Lump/mass/swelling below neck excluding abdomen 0-3 months before diagnosis	All included patients	0.11 (0.06-0.2) Cases: 42/1267 Control: 16/15318
Dommett (2013)	Lump/mass/swelling below neck excluding abdomen 0-3 months before diagnosis and \geq 3 consultations	All included patients	0.3 (0.09-0.99)
Dommett (2012)	Fatigue 0-12 months before diagnosis	All included patients	0.085 (0.06-0.121) Cases: 47/1267 Control: 88/15318

Dommett (2013)	Fatigue 0-12 months before diagnosis	All included patients	0.07 (0.04-0.12) Cases: 42/1267 Control: 24/15318
Dommett (2013)	Fatigue 0-12 months before diagnosis and ≥ 3 consultations	All included patients	0.12 (0.06-0.23)
Dommett (2012)	Back pain 0-12 months before diagnosis	All included patients	0.088 (0.06-0.128) Cases: 40/1267 Control: 73/15318
Dommett (2012)	Bruising 0-12 months before diagnosis	All included patients	0.08 (0.054-0.118) Cases: 38/1267 Control: 76/15318
Dommett (2013)	Bruising 0-3 months before diagnosis	All included patients	0.08 (0.05-0.13) Cases: 33/1267 Control: 18/15318
Dommett (2013)	Bruising 0-3 months before diagnosis and ≥ 3 consultations	All included patients	0.38 (0.09-1.64)
Dommett (2013)	Pallor 0-3 months before diagnosis	All included patients	0.41 (0.12-1.34) Cases: 33/1267 Control: 18/15318
Dommett (2013)	Pallor 0-3 months before diagnosis and ≥ 3 consultations	All included patients	0.76 (0.1-5.7)
Dommett (2013)	Lump mass swelling head and neck 0-3 months before diagnosis	All included patients	0.3 (0.1-0.84) Cases: 28/1267 Control: 4/15318
Dommett (2013)	Lump mass swelling head and neck 0-3 months before diagnosis and ≤ 3 consultations	All included patients	0.76 (0.1-5.7)
Dommett (2013)	Abnormal movement 0-3 months before diagnosis	All included patients	0.08 (0.04-0.14) Cases: 49/1267 Control: 26/15318
Dommett (2013)	Abnormal movement 0-3 months before diagnosis and ≥ 3 consultations	All included patients	0.15 (0.07-0.32)
Dommett (2013)	Bleeding 0-3 months before diagnosis	All included patients	0.06 (0.03-0.1) Cases: 28/1267 Control: 21/15318
Dommett (2013)	Bleeding 0-3 months before diagnosis and ≥ 3 consultations	All included patients	0.11 (0.04-0.31)
Dommett (2013)	Visual symptoms 0-3 months before diagnosis	All included patients	0.06 (0.03-0.10) Cases: 28/1267 Control: 21/15318
Dommett (2013)	Visual symptoms 0-3 months before diagnosis and ≤ 3 consultations	All included patients	0.23 (0.07-0.77)
Dommett (2013)	Pain 0-3 months before	All included patients	0.04 (0.03-0.06)

	diagnosis		Cases: 42/1267 Control: 41/15318
Dommett (2013)	Pain 0-3 months before diagnosis and ≥ 3 consultations	All included patients	0.14 (0.07-0.31)
Dommett (2013)	Musculoskeletal symptoms 0-3 months before diagnosis	All included patients	0.04 (0.03-0.07) Cases: 107/1267 Control: 102/15318
Dommett (2013)	Musculoskeletal symptoms 0-3 months before diagnosis and ≥ 3 consultations	All included patients	0.13 (0.08-0.19)
Dommett (2012)	Urinary symptoms 0-12 months before diagnosis	All included patients	0.266 (0.117-0.609) Cases: 15/1267 Control: 9/15318
Dommett (2013)	≥ 3 consultations	All included patients	0.02
Dommett (2013)	Childhood infection 0-3 months before diagnosis	All included patients	Cases: 54/1267 Control: 236/15318
Dommett (2013)	Upper respiratory tract infection 0-3 months before diagnosis	All included patients	Cases: 143/1267 Control: 942/15318
Dommett (2013)	Vomiting 0-3 months before diagnosis	All included patients	Cases: 86/1267 Control: 105/15318
Dommett (2013)	Cough 0-3 months before diagnosis	All included patients	Cases: 77/1267 Control: 654/15318
Dommett (2013)	Rash 0-3 months before diagnosis	All included patients	Cases: 63/1267 Control: 555/15318
Dommett (2013)	Abdominal pain 0-3 months before diagnosis	All included patients	Cases: 60/1267 Control: 137/15318
Dommett (2013)	Abdominal mass 0-3 months before diagnosis	All included patients	Cases: 48/1267 Control: 0/15318
Dommett (2013)	Fever 0-3 months before diagnosis	All included patients	Cases: 49/1267 Control: 166/15318
Dommett (2013)	Eye swelling 0-3 months before diagnosis	All included patients	Cases: 39/1267 Control: 238/15318
Dommett (2013)	Shortness of breath 0-3 months before diagnosis	All included patients	Cases: 35/1267 Control: 221/15318
Dommett (2013)	Constipation 0-3 months before diagnosis	All included patients	Cases: 26/1267 Control: 61/15318
Dommett (2012)	Hepatosplenomegaly 0-12 months before diagnosis	All included patients	2.19 (0.295-17.034) Cases: 14/1267 Control: 1/15318

The positive predictive values are calculated using Bayesian statistics.

Table 6: Renal cancer: Positive predictive values for any childhood cancer: Patients aged 0-4 years

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2012)	Any NICE alert symptom 0-3 months before diagnosis	Patients aged 0-4 years	0.081 (0.059-0.112) Cases: 96/436 Control: 55/4802

Dommett (2012)	Any NICE alert symptom 0-12 months before diagnosis	Patients aged 0-4 years	0.093 (0.077-0.113) Cases: 124/436 Control: 248/4802
Dommett (2012)	Neurological symptoms 0-12 months before diagnosis	Patients aged 0-4 years	0.076 (0.054-0.107) Cases: 43/436 Control: 105/4802
Dommett (2012)	Headache 0-12 months before diagnosis	Patients aged 0-4 years	0.135 (0.055-0.335) Cases: 8/436 Control: 11/4802
Dommett (2012)	Lymphadenopathy 0-12 months before diagnosis	Patients aged 0-4 years	0.061 (0.037-0.1) Cases: 20/436 Control: 61/4802
Dommett (2012)	Lump/mass/swelling 0-12 months before diagnosis	Patients aged 0-4 years	0.198 (0.099-0.399) Cases: 16/436 Control: 15/4802
Dommett (2012)	Fatigue 0-12 months before diagnosis	Patients aged 0-4 years	0.087 (0.048-0.16) Cases: 15/436 Control: 32/4802
Dommett (2012)	Back pain 0-12 months before diagnosis	Patients aged 0-4 years	0.186 (0.047-0.742) Cases: 4/436 Control: 4/4802
Dommett (2012)	Bruising 0-12 months before diagnosis	Patients aged 0-4 years	0.155 (0.086-0.279) Cases: 20/436 Control: 24/4802
Dommett (2012)	Urinary symptoms 0-12 months before diagnosis	Patients aged 0-4 years	0.739 (0.159-3.496) Cases: 8/436 Control: 2/4802
Dommett (2012)	Hepatosplenomegaly 0-12 months before diagnosis	Patients aged 0-4 years	1.286 (0.161-10.569) Cases: 7/436 Control: 1/4802

The positive predictive values are calculated using Bayesian statistics.

Table 7: Renal cancer: Positive predictive values for any childhood cancer: Patients aged 5-14 years

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2012)	Any NICE alert symptom 0-3 months before diagnosis	Patients aged 5-14 years	0.056 (0.047-0.068) Cases: 246/831 Control: 156/10516
Dommett (2012)	Any NICE alert symptom 0-12 months before diagnosis	Patients aged 5-14 years	0.075 (0.066-0.084) Cases: 303/831 Control: 581/10561
Dommett (2012)	Neurological symptoms 0-12 months before diagnosis	Patients aged 5-14 years	0.091 (0.067-0.123) Cases: 65/831 Control: 102/10516
Dommett (2012)	Headache 0-12 months before diagnosis	Patients aged 5-14 years	0.055 (0.043-0.07) Cases: 82/831 Control: 213/10516
Dommett (2012)	Lymphadenopathy 0-12 months before diagnosis	Patients aged 5-14 years	0.118 (0.085-0.164) Cases: 62/831 Control: 75/10516

Dommett (2012)	Lump/mass/swelling 0-12 months before diagnosis	Patients aged 5-14 years	0.154 (0.099-0.24) Cases: 40/831 Control: 37/10516
Dommett (2012)	Fatigue 0-12 months before diagnosis	Patients aged 5-14 years	0.082 (0.053-0.125) Cases: 32/831 Control: 56/10516
Dommett (2012)	Back pain 0-12 months before diagnosis	Patients aged 5-14 years	0.075 (0.05-0.111) Cases: 36/831 Control: 69/10516
Dommett (2012)	Bruising 0-12 months before diagnosis	Patients aged 5-14 years	0.049 (0.029-0.084) Cases: 18/831 Control: 52/10516
Dommett (2012)	Urinary symptoms 0-12 months before diagnosis	Patients aged 5-14 years	0.143 (0.05-0.407) Cases: 7/831 Control: 7/10516
Dommett (2012)	Hepatosplenomegaly 0-12 months before diagnosis	Patients aged 5-14 years	Cases: 7/831 Control: 0/10516

The positive predictive values are calculated using Bayesian statistics.

Evidence statement(s):

Patients aged > 14 years

Haematuria (5 studies, N = 87161) presenting in a primary care setting is associated with overall positive predictive values of 0.65-6.48% for renal cancer, which tended to be higher in men (5.47-5.5%) than in women (2.48-2.6%; 2 studies, N = 48918) and to increase with age in men (up to 11.21%; 1 study, N = 11108) and less so in women (up to 8.53%; 1 study, N = 11108). The evidence was, however, compromised by a large number of the included cancers being non-renal cancers. Each of the studies was associated with 0-2 bias concern (see also Tables 1-3).

For renal cancer the positive predictive values of single symptoms (excluding haematuria; 6 studies, N = 344897) presenting in primary care ranged from 0.05% (for back pain) to 1.4% (for anaemia in men). The evidence was, however, compromised by a large number of the included cancers being non-renal cancers and ≤ 3 bias or applicability concerns associated with 4 of the 6 included studies (see also Table 3).

For renal cancer the positive predictive values of symptom combinations (1 study, N = 17240) presenting in primary care ranged from 0.1% (for constipation in combination with either abdominal pain, nausea or lower urinary tract infection) to > 5% (for abdominal pain combined with microcytosis). The included study was associated with 1 bias concern (see also Table 4).

Patients aged < 15 years

The positive predictive values of having any childhood cancer ranged from 0.04% (for pain and musculoskeletal symptoms) to 2.19% (for hepatosplenomegaly) in all included patients, and from 0.061% (for lymphadenopathy) to 1.286% (for hepatosplenomegaly) for patients aged 0-4 years old, and from 0.049% (for bruising) to 0.154% (for 'lump/mass/swelling' [the PPV for hepatosplenomegaly could not be calculated as none of the controls experienced this symptom]) for patients aged 5-14 years old (all from 1 study, N = 16585). The evidence quality is somewhat compromised by the case-control design of the study (see also Tables 5-7).

Evidence tables

Collins (2013)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2145133 patients (1063355 men, 1081778 women) were identified from 364 practices.</p> <p><u>Symptoms:</u> Haemoglobin < 11 g/dl recorded in the last year (N = 16961; 3969 men, 12992 women), abdominal pain (N = 253344; 105247 men, 148097 women), appetite loss (N = 6097; 2616 men, 3481 women), weight loss (N = 29369; 13332 men, 16037 women), haematuria (N = 37810; 22810 men, 15000 women), previous diagnosis of cancer apart from renal tract cancer at study entry (N = 49303; 18130 men, 31173 women).</p> <p><u>Incident cases of renal tract cancer during the 2-year follow up period:</u> N = 2283 (1685 men, 598 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (e.g., haematuria, abdominal pain, weight loss, appetite loss, and anaemia), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of renal tract cancer, registered less than 12 months with the general practice, had invalid dates, < 30 years old or ≥ 85 years old.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference	Renal tract cancer, which was defined as incident diagnosis of cancer of the

standard(s)	bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes. Patients without the outcome were censored at the earliest of the date of death, date of leaving the practice study of 2 years of follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	It is unclear why no data has been presented for men for the symptoms of appetite loss and weight loss.
Deyo (1988)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive? patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 1975, mean (SD; range) age = 39.5 (15.4; 15-86) years, 62% females. 54% of the patients were seeking medical care for back pain for the first time and 76% of the patients had had back pain for < 3 months. 3% had a history of back pain surgery. Maximal back pain in the low back (84%) or in the upper back (16%).</p> <p><u>Inclusion criteria:</u> Patients who sought treatment between March 1982 and September 1984 in the walk-in clinic of a public hospital where virtually all patients are self-referred. In each case back pain was part of the chief complaint.</p> <p><u>Exclusion criteria:</u> Neck pain.</p> <p><u>Clinical setting:</u> Walk-in clinic of a public hospital; this clinic is a source of primary care for indigent persons in a county in the USA with a population of approximately 1 million.</p>

Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	Back pain; not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	The reference standard consisted of a search on each patient name in the institutional tumour registry ≥ 6 months after the index visit. The registry included every patient with a histological diagnosis of cancer made in the authors' hospital system regardless of site of care. The authors point out that "while this method might fail to identify cancer patients who sought care elsewhere, it is likely that most patients sought follow-up for a particular illness at the same facility.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	It is a concern that some patients with cancer might have been missed due to the choice of reference standard because this would result in an underestimation of the positive predictive value. 38/1975 patients were found in the tumour registry. Of those 38, 13 patients had tumours that were probable causes of back pain, and 4 of these 13 patients already had a diagnosis of cancer at presentation. The 9/1975 patients who had undiagnosed cancer that the back pain could be attributed to had: Lymphoma (NOS; 2), cancer of unknown primary (1), prostate cancer (1), retroperitoneal liposarcoma (1), lung cancer (1), renal cell (1), multiple

	myeloma (1), mucinous adenocarcinoma (of gallbladder?; 1)	
Dommett (2012, 2013)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Population-based nested case-control study using data from the General Practice Research Database (GPRD)	
Was a consecutive or random sample of patients enrolled?	No	
Was a case-control design avoided?	No	
Did the study avoid inappropriate exclusions?	Yes	
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes	
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes	
Could the selection of patients have introduced bias?	High risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p><u>Cases:</u> 1267 children; aged 0-4 years: N = 436; aged 5-14years: N = 831; 703 males/564 females. Cancer type: Leukemia: N = 368; brain: N = 270; lymphoma: N = 142; bone: N = 107; soft tissue sarcoma: N = 91; renal: N = 82; neuroblastoma: N = 75; other ICD codes: N = 132.</p> <p><u>Controls:</u> 15318 children; aged 0-4 years: N = 4802; aged 5-14years: N = 10516; 8461 males/6857 females.</p> <p><u>Inclusion criteria:</u> The sample comprised all children aged 0–14 years, inclusive, drawn from all general practices contributing research-standard data to the GPRD between 1 January 1988 and 31 December 2010. To be included, the practices had to have been contributing research-standard data for a minimum of 1 year before each child’s date of cancer diagnosis or the index date (see below) for matched controls. Cases: Patients diagnosed with the following cancers: leukaemia, lymphoma, neuroblastoma, soft tissue sarcoma, hepatic, renal, bone and central nervous system tumours, using pre-defined medical codes used in the GPRD. The date of diagnosis for cases was defined as the date of pathological diagnosis, but if this was unavailable, the date of the first cancer code entered in the GPRD was used. Controls: Up to 13 controls (children with no diagnosis of cancer at any time) were selected per case, using a computer-generated random sequence, matched on age (within 1 year), sex and practice, and had to be currently registered on the date of diagnosis of their matched case (the index date).</p> <p><u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> Primary care, UK.</p>	
Are there concerns that the included patients and setting do not match the review question?	Low concern	

INDEX TEST	
A. Risk of bias	
Index test	The GPRD uses just over 100 000 medical codes to encompass all primary care events, including both symptoms and diagnoses. From this list, libraries of codes were assembled representing individual alert symptoms derived from the NICE referral guidelines for suspected cancer in children. <i>No more information reported.</i>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Cancer diagnosis in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	This study is published in two papers.
Friedlander (2014)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective cohort study, using claims data and laboratory values from the Vanderbilt University Medical Centre's (VUMC) Research Derivative, which is a "data repository that contains administrative and clinical information, including a complete record of visits and

	admissions, laboratory data, and diagnosis and procedure codes, on every patient treated in the Vanderbilt health system” (p 634) located in Tennessee in the USA.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 2455 patients, 724 males / 1731 females, median (inter-quartile range) age = 58 (49-68) years; smoking history: current smoker (N = 406), former smoker (N = 473), non-smoker (N = 1514).</p> <p><u>Inclusion criteria:</u> “Patients aged \geq 40 years with a first diagnosis of hematuria” “between 2004 and 2012 by urinalysis ($>$3 red blood counts per high power field) or International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes for hematuria (599.7, 599.70, 599.71 or 599.72) at one of the VUMC’s 19 primary care clinics. To be included in the study, patients must have had records for 1 year before the date of hematuria diagnosis.”</p> <p><u>Exclusion criteria:</u> “Patients were excluded if they had a urinary tract infection (defined as a urinalysis positive for both leukocyte esterase and urine nitrites, or a positive urine culture) within 4 weeks before or 1 week after the index hematuria episode (n = 590, 9.0%) or had a prior explanatory diagnoses and procedures that would preclude the need for a hematuria evaluation (according to a convened panel of content experts; prostate/renal/bladder/other cancer, benign prostate/renal/bladder/other mass, prostate dysplasia, cystitis, urethritis, epididymitis/orchitis, prostatitis, pyelonephritis, urolithiasis, prostatic enlargement, trauma, medical renal disease, haematologic/thrombotic disease?, anatomic abnormality, prostatectomy, prostate biopsy, transurethral incision of prostate, resection of prostate, cystoscopy, cystectomy, ureteroscopy, nephrectomy, pyeloplasty, ureteral reimplantation).” We then used Physicians Current Procedural Terminology Coding System, 4th Edition and ICD-9 codes to exclude patients with an explanatory diagnosis or procedure within 180 days preceding their hematuria diagnosis (n = 3540, 53.8%).”</p> <p>Clinical setting: Primary care, USA.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	First diagnosis of hematuria” “by urinalysis ($>$ 3 red blood counts per high power field) or International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes for hematuria (599.7, 599.70, 599.71 or 599.72)”. ”.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low

REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	The reference standard consisted checking the database for diagnoses of genitourinary neoplasms within 180 days after haematuria diagnosis, as determined by ICD-9 codes.
Is the reference standard likely to correctly classify the target condition?	Unclear (is 180 days enough time to get a diagnosis of all cancers?)
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	There were 66 patients with cancer: Bladder (N = 33), renal cell (N = 16), prostate (N = 15). The types of cancer for the remaining two cases were not reported.

Hippisley-Cox (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	A total of 1240722 patients were identified from 189 practices (622166 males, 618556 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6). <u>Current symptoms and symptoms in the preceding year:</u> Current haematuria (N = 25553), current abdominal pain (N = 128721), current appetite loss (N = 5531), current weight loss (N = 14464), constipation in the last year (N = 8472), diarrhoea in the last year (N = 12171), tiredness in the last year (N = 12669), haemoglobin recoded in the last year (N = 216201), haemoglobin < 11 g/dl in the last year (N = 16169). <u>Incident cases of renal tract cancer during the 2-year follow up period:</u>

<p>N = 1622; mean age at diagnosis = 70 years, 1187 males/ 435 females; Type of cancer: Bladder: N = 1292; Kidney: N = 307; Ureter: N = 21; Urethra: N = 2.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months' registration prior to study entry. For patients with incident haematuria, appetite loss, weight loss, or abdominal pain, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of renal tract cancer at baseline, and patients with a recorded 'red-flag' (see "Definition of symptom" below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>	
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Renal tract cancer, which was defined as incident diagnosis of cancer of the bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 codes (188 or 189) or ICD-10 diagnostic codes (C64–67).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its	Low risk

interpretation have introduced bias?		
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	A total of 1342329 patients were initially identified of whom 101607 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of renal tract cancer (N = 1506), and ≥ one 'red flag' symptom recorded in the 12 months prior to study entry (N = 29254), leaving 1240722 patients. However, data is presented for 967681 / 1240722 patients. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Could the patient flow have introduced bias?	High risk	
NOTES		
Jones (2007)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective consecutive patient series using patients in the UK's General Practice Research Database.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>A total of 923605 patients were identified, of whom 762325 were aged ≥ 15 years.</p> <p><u>Number of first occurrences in patients with no previous diagnosis of cancer:</u></p> <p><u>Haematuria:</u> N = 11108, mean (SD) age at first symptom = 58.5 (18.9) years. Patients excluded due to incomplete dates for their first symptom: N = 30. Sex (of final sample): 6385 males, 4723 females.</p> <p><u>Haemoptysis:</u> N = 4822, mean (SD) age at first symptom = 61.6 (18) years. Patients excluded due to incomplete dates for their first symptom: N = 10. Sex (of final sample): 2930 males, 1882 females.</p> <p><u>Dysphagia:</u> N = 6003, mean (SD) age at first symptom = 54.5 (19.4) years. Patients excluded due to incomplete dates for their first symptom: N = 4. Sex (of final sample): 2628 males, 3371 females.</p> <p><u>Rectal bleeding:</u> N = 15314, mean (SD) age at first symptom = 52.5 (18.8) years. Patients excluded due to incomplete dates for their first symptom: N = 25. Sex (of final sample): 7523 males, 7766 females.</p>	

	<p><u>Inclusion criteria:</u> All patients from 128 general practices that provided data of a sufficient standard from 1 January 1994 to 31 December 2000 and which provided exclusively Read coded data, who were aged between 15 and 100 years, whose first ever recorded occurrence of each alarm symptom (haematuria, haemoptysis, dysphagia, or rectal bleeding) was after 31 December 1994 and who had not previously been diagnosed as having any cancer.</p> <p><u>Exclusion criteria:</u> Patients whose date of first symptom or first relevant diagnosis of cancer was before 1 January 1995 and patients with a diagnosis of any other cancer than the ones of interest before the date of the first recorded symptom or before the index cancer diagnosis date if the related symptom was not recorded.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Identification of all patients who ever had symptoms recorded for haematuria, haemoptysis, dysphagia, or rectal bleeding.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	<p>Cancer code in the UK's General Practice Research Database (the authors report cancer diagnosis at two time points, namely in the first 6 months and 3 years after the first alarm symptom):</p> <p><u>Haematuria:</u> Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs.</p> <p><u>Haemoptysis:</u> Respiratory tract neoplasms.</p> <p><u>Dysphagia:</u> Oesophageal neoplasms.</p> <p><u>Rectal bleeding:</u> Colorectal neoplasms.</p>
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	

Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	<p>Diagnoses of cancer were most often made in the first three months after the onset of alarm symptoms; very few diagnoses of cancer were made later than three years after symptom onset. In the 4th and 5th years of study, the small number of observed occurrences of cancer was similar to the number expected from background incidence rates.</p> <p>Secondary analyses evaluating whether the incidence of neoplasms other than those prespecified was increased after the occurrence of alarm symptoms showed for:</p> <p><u>Haematuria</u>: Inclusion of cancers of the reproductive organs yielded 21 additional cancers in women and 158 cancers in men, mostly cancers of the prostate. Inclusion of these cancers in the analysis would give a positive predictive value of 3.9% in women and 9.9% in men.</p> <p><u>Dysphagia</u>: Inclusion of gastric cancers yielded 17 additional cancer diagnoses in women and 30 in men. Inclusion of these cancers gave positive predictive values of 5.2% in women and 6.9% in men.</p> <p><i>Estimates based on the pre-specified cancers may be thus conservative for these symptoms.</i></p> <p><u>Haemoptysis</u>: Extension of the diagnostic criteria yielded 6 additional cancers.</p> <p><u>Rectal bleeding</u>: Extension of the diagnostic criteria yielded 2 additional cancers.</p>

Muris (1995)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 80/460 general practitioners in Limburg (Holland)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 933; 335 males, 598 females; age range = 18-75, aged > 30 years: N = 712, aged > 40 years: N = 517, aged > 60 years: N = 171.</p> <p><u>Inclusion criteria</u>: Patients who in 1989 consulted one of the participating GPs for new abdominal complaints lasting ≥ 2 weeks and with whom the GPs had a diagnostic problem.</p> <p><u>Exclusion criteria</u>: None listed.</p> <p><u>Clinical setting</u>: GPs in Holland</p>
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	

A. Risk of bias	
Index test	New abdominal complaints lasting ≥ 2 weeks. Not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Follow up for ≥ 12 months (mean = 18 months).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Other cancers diagnosed in these patients were: Stomach (2/933), pancreas (2/933), trachea/bronchus/lung (2/933), colorectal (4/933), cervix (1/933), other cancer of the female genital system (2/933), and other and unspecified sites (2/933).

Oudega (2006)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective study of all primary care physicians (N = 50) within a catchment area (ca 130000 inhabitants) of a non-teaching hospital in Holland.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	

Patient characteristics and setting	N = 430; 162 males, 268 females; mean age (SD) = 60.7 (18.2) years. <u>Inclusion criteria</u> : Consecutive patients who consulted their GP between January 1996 and July 2002 and who, after investigation (not referral) was confirmed to have deep vein thrombosis. <u>Exclusion criteria</u> : Patients with a known malignancy or a malignancy detected within 2 weeks of deep vein thrombosis diagnosis. <u>Clinical setting</u> : Primary care, Holland.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Deep vein thrombosis (suspicion based on painful swollen leg ≤ 30 days). Patients were classified as having secondary deep vein thrombosis if ≥ 1 of the following risk factors for deep vein thrombosis were present: Recent surgery, prolonged immobilisation, use of oral contraceptives or hormonal replacement therapy. If no risk factors were present patients were classified as having idiopathic deep vein thrombosis.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2 years follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 19 had cancer: 3 colorectal, 5 urogenital (not further subgrouped), 4 breast, 3 lung and 4 other. The urogenital data is added to the renal cancer evidence review.

Shephard (2013)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Matched case-control study using patients in the UK's General Practice Research Database (GPRD).
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> N = 3149, median age at diagnosis = 69 (IQR = 61-77) years, 1930 males / 1219 females; median number of consultations = 16 (IQR = 10-25), UK.</p> <p><u>Controls:</u> N = 14091, median age at diagnosis = 70 (IQR = 61-77) years, 8429 males / 5662 females; median number of consultations = 8 (IQR = 4-15), UK.</p> <p><u>Inclusion criteria:</u> Cases: Patients with a record of one of 22 GPRD kidney cancer codes between January 2000 and December 2009 inclusive, aged ≥ 40 years, with min. 1 year of data before diagnosis. The first instance of a kidney cancer code was assigned the data of diagnosis/index date. Controls: Up to 5 controls were matched to cases on sex, general practice, and to 1 year of age of the case. The index date was the index date of the matched case.</p> <p><u>Exclusion criteria:</u> Metastatic cancer to the kidney from a non-kidney primary, diagnosis before 2000, or no consultations in the year before diagnosis.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	A list of symptoms, signs and investigations (features) potentially associated with kidney cancer was compiled from the authors' literature search, augmented by viewing material from kidney cancer support organisations and online chat rooms. Internet search terms included 'kidney cancer', 'kidney cancer symptoms', and 'early signs/indications kidney cancer'. Visible and non-visible haematuria were studied separately. Only codes specifying the word 'microscopic' were assigned to the latter group, so generic codes such as the single word 'haematuria' were assumed to be visible haematuria. Over 1800 GPRD codes were compiled for the putative

	<p>features of kidney cancer from the GPRD's master list of over 100,000 codes. Occurrences of these features in the year before the index date were identified. Repeated consultations for the same complaint were also identified along with all codes for fractures as a test for any recording bias between cases and controls (making the assumption that the fracture rate would be approximately equal). Variables were retained only if they occurred in at least 5% of either cases or controls. Investigation results were deemed to be abnormal if they fell outside their local laboratory's normal range: for analysis, patients with a normal laboratory result were grouped with those who had not been tested.</p> <p>The raised inflammatory markers variable was a composite of any of abnormal erythrocyte sedimentation rate, plasma viscosity, or C-reactive protein; similarly abnormal liver function tests reflected a raised value of any of the hepatic enzymes reported by each laboratory.</p>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
<u>A. risk of bias</u>	
Reference standard(s)	Kidney cancer code in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
<u>A. risk of bias</u>	
Flow and timing	A total of 18890 patients were identified, 15707 controls and 3183 cases. Of the controls the following exclusions were applied: bladder cancer (N = 29), metastatic cancer (N = 104), and no data in year pre-index date (N = 1483). Of the cases the following exclusions were applied: No controls (N = 2), metastatic cancer (N = 24), and bladder cancer (N = 8).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes

Could the patient flow have introduced bias?	Low risk
NOTES	24 symptoms and 22 abnormal test results were considered initially. 10 symptoms and 11 abnormal test variables were present in $\geq 5\%$ of cases.

References

Included studies

- Collins, G.S., and Altman, D.G. Identifying patients with undetected renal tract cancer in primary care: An independent and external validation of QCancer (renal) prediction model. *Cancer Epidemiology*, 37, 115-120. 2013.
- Deyo, R. A. and Diehl, A. K. Cancer as a cause of back pain: Frequency, clinical presentation, and diagnostic strategies. *Journal of General Internal Medicine* 3, 230-238. 1988.
- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of childhood cancer in primary care: A population-based nested case-control study. *British Journal of Cancer* 106[5], 982-987. 28-2-2012.
- Dommett, R. M., Redaniel, T., Stevens, M. C. G., Martin, R. M., and Hamilton, W. Risk of childhood cancer with symptoms in primary care: A population-based case-control study. *British Journal of General Practice*; DOI:10.3399/bjgp13X660742. 2013.
- Friedlander, D.F., Resnick, M.J., You, C., Bassett, J., Yarlagadda V., Penson, D.F., Barocas D.A. Variation in the intensity of hematuria evaluation: A target for primary care quality improvement. *American Journal of Medicine*, 127, 633-640. 2014.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected renal tract cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice* 62[597], e251-e260. 2012.
- Jones, R., Latinovic, R., Charlton, J., and Gulliford, M. C. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *BMJ* 334[7602], 1040. 19-5-2007.
- Muris, J. W., Starmans, R., Fijten, G. H., Crebolder, H. F., Schouten, H. J., and Knottnerus, J. A. Non-acute abdominal complaints in general practice: diagnostic value of signs and symptoms. *British Journal of General Practice* 45[395], 313-316. 1995.
- Oudega, R., Moons, K. G. M., Nieuwenhuis, H. K., van Nierop, F. L., and Hoes, A. W. Deep vein thrombosis in primary care: Possible malignancy? *British Journal of General Practice* 56[530], 693-696. 2006.
- Shephard, E., Neal, R., Rose, P., Walter, F., and Hamilton, W. Clinical features of kidney cancer in primary care: A case-control study using primary care records. *British Journal of General Practice* DOI: 10.3399/bjgp13X665215. 2013

Excluded studies (with excl reason)

- Abouassaly, R., Finelli, A., Tomlinson, G. A., Urbach, D. R. & Alibhai, S. M. H. (2011) How often are patients with diabetes or hypertension being treated with partial nephrectomy for renal cell carcinoma? A population-based analysis. *BJU International*, 108: 1806-1812.
Not in PICO
- Ares, V. Y. (2009) [Correlation between symptoms and survival in patients with renal cell carcinoma]. [Spanish]. *Archivos Espanoles de Urologia*, 62: 201-206.
Not in PICO
- Ayllon, J., Verkarre, V., Scotte, F., Fournier, L., Correas, J. M., Mejean, A., Teghom, C. & Oudard, S. (2012) Renal malacoplakia: Case report of a differential diagnosis for renal cell carcinoma. *The American Journal of Case Reports*, 13: 38-40.
Not in PICO

- Barkin, J., Rosenberg, M. T. & Miner, M. (2014) A guide to the management of urologic dilemmas for the primary care physician (PCP). *Canadian Journal of Urology*, 21: 55-63.
Narrative review
- Barroca, H. & Bom-Successo, M. (2014) Fine needle biopsy with cytology in paediatrics: The importance of a multidisciplinary approach and the role of ancillary techniques. *Cytopathology*, 25: 6-20.
Narrative review
- Belani, J. S., Farooki, A., Prasad, S., Yan, Y., Heiken, J. P. & Kibel, A. S. (2005) Parenchymal imaging adds diagnostic utility in evaluating haematuria. *BJU International, Supplement*, 95: 64-67.
Not in PICO
- Bliznakova, D. (2003) Differential diagnosis of some kidney diseases in childhood. [Bulgarian]. *Bulgarian Medicine*, 11: 7-10.
Narrative review
- Buteau, A., Seideman, C. A., Svatek, R. S., Youssef, R. F., Chakrabarti, G., Reed, G., Bhat, D. & Lotan, Y. (2014) What is evaluation of hematuria by primary care physicians? Use of electronic medical records to assess practice patterns with intermediate follow-up. *Urologic Oncology*, 32: 128-134.
Not in PICO
- Carrafiello, G., Fontana, F., Mangini, M., Ierardi, A. M., Cotta, E., Piacentino, F., De, C. M., Floridi, C., Di, M. A., Marconi, A. M. & Fugazzola, C. (2012) Upper urinary tract biopsy: an old device for a new approach. *Radiologia Medica*, 117: 1152-1160.
Not in PICO
- Cave, D. G. (1994) Analyzing the content of physicians' medical practices. *Journal of Ambulatory Care Management*, 17: 15-36.
Not in PICO
- Chan, K. & Kamangar, N. (2012) Tuberous sclerosis complex manifesting with massive angiomyolipomas in multiple organs. *Chest*, 142.
Not in PICO
- Chen, D. Y. T. & Uzzo, R. G. (2011) Evaluation and Management of the Renal Mass. *Medical Clinics of North America*, 95: 179-+.
Narrative review
- Chow, W.-H., Dong, L. M. & Devesa, S. S. (2010) Epidemiology and risk factors for kidney cancer. *Nature Reviews Urology*, 7: 245-257.
Narrative review
- Coxon, J. P., Harris, H. J. & Watkin, N. A. (2003) A prospective audit of the implementation of the 2-week rule for assessment of suspected urological cancers. *Annals of the Royal College of Surgeons of England*, 85: 347-350.
Not in PICO
- Crispen, P. L., Soljic, A., Stewart, G., Kutikov, A., Davenport, D. & Uzzo, R. G. (2012) Enhancing renal tumors in patients with prior normal abdominal imaging: further insight into the natural history of renal cell carcinoma. *Journal of Urology*, 188: 1089-1093.
Not in PICO
- Cukier, J., Pascal, B. & Mangin, P. (1981) [Symptomatology manifesting cancer of the kidney in adults. Review of 184 observations]. [French]. *Acta Urologica Belgica*, 49: 259-262.
Not in PICO
- Dall'Oglio, M. F., Srougi, M., Goncalves, P. D., Leite, K., Nesrallah, L. & Hering, F. (2002) Incidental and symptomatic renal tumors: impact on patient survival. *Sao Paulo Medical Journal = Revista Paulista de Medicina*, 120: 165-169.
Not in PICO
- Debre, B., Peyromaure, M., Saighi, D. & Zerbib, M. (2004) [Advances in diagnosis and treatment of renal cell carcinoma]. [Review] [29 refs] [French]. *Bulletin de l'Academie Nationale de Medecine*,

188: 15-24.

Narrative review

DeSouza, K., Chowdhury, S. & Hughes, S. (2003) - Prompt diagnosis key in bladder cancer. [Review]. - *Practitioner*, 258: 23-27.

Narrative review

Dragoescu, E. A. & Liu, L. (2013) Indications for renal fine needle aspiration biopsy in the era of modern imaging modalities. *CytoJournal*, 10.

Not in PICO

Duque, J. L., Loughlin, K. R., O'Leary, M. P., Kumar, S. & Richie, J. P. (1998) Partial nephrectomy: alternative treatment for selected patients with renal cell carcinoma. [Review] [26 refs]. *Urology*, 52: 584-590.

Not in PICO

Edwards, T. J., Dickinson, A. J., Gosling, J., McInerney, P. D., Natale, S. & McGrath, J. S. (2011) Patient-specific risk of undetected malignant disease after investigation for haematuria, based on a 4-year follow-up. *BJU International*, 107: 247-252.

Not in PICO

Eisenberger, C. F., Schoenberg, M., Enger, C., Hortopan, S., Shah, S., Chow, N. H., Marshall, F. F. & Sidransky, D. (1999) Diagnosis of renal cancer by molecular urinalysis. *Journal of the National Cancer Institute*, 91: 2028-2032.

Not in PICO

Fall, B., Diao, B., Sow, Y., Sarr, A., Thiam, A., Fall, P. A., Ndoye, A. K., Sylla, C., Ba, M., Mendes, V. & Diagne, B. A. (2011) [Adult renal cancer in Senegal: Current epidemiological, clinical features, profile's evolution over the two past decades]. [French]. *Progres En Urologie*, 21: 521-526.

Not in PICO

Feldstein, M. S., Rhodes, D. J., Parker, A. S., Orford, R. R. & Castle, E. P. (2009) The haphazard approach to the early detection of asymptomatic renal cancer: results from a contemporary executive health programme. *BJU International*, 104: 53-56.

Not in PICO

Ferda, J., Ferdova, E., Hora, M., Hes, O., Finek, J., Topolcan, O. & Kreuzberg, B. (2013) 18F-FDG-PET/CT in potentially advanced renal cell carcinoma: a role in treatment decisions and prognosis estimation. *Anticancer Research*, 33: 2665-2672.

Not in PICO

Fernandez, R. E., Suarez, P. G., Blanco, D. A., Barbagelata, L. A., Ponce Diaz-Reixa, J. L., Novas, C. S., Ruibal, M. M., Gomez, V. F., Chantada, A., V & Gonzalez, M. M. (2005) [Clinical-pathological study of incidental renal cell carcinoma]. [Spanish]. *Archivos Espanoles de Urologia*, 58: 635-640.

Not in PICO

Ferzli, P. G., Millett, C. R., Newman, M. D. & Heymann, W. R. (2008) The dermatologist's guide to hereditary syndromes with renal tumors. *Cutis*, 81: 41-48.

Narrative review

Flamm, J. & Wober, L. (1981) [The malignant kidney tumour - a report on 117 cases (1969-1977) (author's transl)]. [German]. *Wiener Medizinische Wochenschrift*, 131: 579-585.

Not in PICO

Ghalayini, I. F. & Bani-Hani, I. H. (2003) Detection, staging and clinical implications of renal cell carcinoma. *Saudi Medical Journal*, 24: 79-83.

Not in PICO

Glick, R. D., Hicks, M. J., Nuchtern, J. G., Wesson, D. E., Olutoye, O. O. & Cass, D. L. (2004) Renal tumors in infants less than 6 months of age. [Review] [21 refs]. *Journal of Pediatric Surgery*, 39: 522-525.

Not in PICO

Gourova, L. W., van de Beek, C., Spigt, M. G., Nieman, F. H. & van Kerrebroeck, P. E. (2006) Predictive factors for nocturia in elderly men: a cross-sectional study in 21 general practices. *BJU*

- International*, 97: 528-532.
Not in PICO
- Gu, F. L. (1990) Imaging techniques for the diagnosis of renal tumors. *Proceedings of the Chinese Academy of Medical Sciences & the Peking Union Medical College*, 5: 75-78.
Not in PICO
- Gupta, N. P., Ishwar, R., Kumar, A., Dogra, P. N. & Seth, A. (2010) Renal tumors presentation: changing trends over two decades. *Indian Journal of Cancer*, 47: 287-291.
Not in PICO
- Guy, L., Alfidja, A. T., Chabrot, P., Ravel, A., Boiteux, J. P. & Boyer, L. (2007) Palliative transarterial embolization of renal tumors in 20 patients. *International Urology & Nephrology*, 39: 47-50.
Not in PICO
- Haliloglu, A. H., Gulpinar, O., Ozden, E. & Beduk, Y. (2011) Urinary ultrasonography in screening incidental renal cell carcinoma: is it obligatory? *International Urology & Nephrology*, 43: 687-690.
Not in PICO
- Hellsten, S., Berge, T. & Wehlin, L. (1981) Unrecognized renal cell carcinoma. Clinical and diagnostic aspects. *Scandinavian Journal of Urology & Nephrology*, 15: 269-272.
Not in PICO
- Henning, A., Wehrberger, M., Madersbacher, S., Pycha, A., Martini, T., Comploj, E., Jeschke, K., Tripolt, C. & Rauchenwald, M. (2013) Do differences in clinical symptoms and referral patterns contribute to the gender gap in bladder cancer? *BJU International*, 112: 68-73.
Not in PICO
- Henrique, R., Costa, V. L. & Jeronimo, C. (2007) Methylation-based biomarkers for early detection of urological cancer. [Review] [73 refs]. *Critical Reviews in Oncogenesis*, 13: 265-282.
Narrative review
- Higgins, J. C. & Arnold, M. J. (2013) When to worry about incidental renal and adrenal masses. *Journal of Family Practice*, 62: 476-483.
Narrative review
- Hofstetter, A., Rothenberger, K. H. & Kori-Lindner, C. (1981) [Urologic emergencies in general practice. 6. Diagnosis in hematuria]. [German]. *Fortschritte der Medizin*, 99: 1556-1561.
Narrative review
- Holley, J. L. (1998) Nephrologists as primary care providers: A review of the issues. *American Journal of Kidney Diseases*, 31: 574-583.
Narrative review
- Holmang, S., Lele, S. M. & Johansson, S. L. (2007) Squamous cell carcinoma of the renal pelvis and ureter: incidence, symptoms, treatment and outcome. *Journal of Urology*, 178: 51-56.
Not in PICO
- Hornak, M., Skablova, D., Bardos, A. & Ondrus, D. (1998) [Incidental renal carcinoma]. [Slovak]. *Bratislavské Lekárske Listy*, 99: 322-326.
Not in PICO
- Hruby, W., Stellamor, K., Zinner, G. & Marberger, M. (1983) [The renal pelvic tumor in the sonogram]. [German]. *Rofo: Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin*, 138: 469-472.
Not in PICO
- Ibragimova, M. I., Chushnikov, A. I., Moiseev, V. N., Petukhov, V. I. & Zheglov, E. P. (2011) [The abilities of the electron paramagnetic resonance technique to diagnose urological cancers]. [Russian]. *Klinicheskaja Laboratornaia Diagnostika*.(3):29-33, 2011 Mar., 29-33.
Not in PICO
- Iczkowski, K. A., Sweat, S. D. & Bostwick, D. G. (1999) Subepithelial pelvic hematoma of the kidney clinically mimicking cancer: Report of six cases and review of the literature. *Urology*, 53: 276-279.
Not in PICO

- Ikemoto, I., Oishi, Y., Onodera, S., Kishimoto, K., Kiyota, H., Furuta, N., Suzuki, Y., Asano, K. & Hasegawa, N. (2003) [Retrospective analysis of chief complaints of patients with urogenital malignancies over the past decade at the Jikei University Hospital]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica*, 49: 65-68.
Not in PICO
- Ishikawa, M., Takeda, M., Okabe, H., Kuwabara, S., Tsuyuguchi, M., Hirano, M., Kawamura, K., Mishima, M., Fujimoto, N., Saito, H., Sakurada, K., Shimamura, S., Sakai, S., Minase, T., Miyake, M. & Andou, M. (2000) Studies on incidental renal cell carcinoma detected by abdominal ultrasonography during health check-up. [Japanese]. *Nishinihon Journal of Urology*, 62: 563-567.
Not in PICO
- Izikson, L., English, J. C., III & Zirwas, M. J. (2006) The flushing patient: differential diagnosis, workup, and treatment. [Review] [101 refs]. *Journal of the American Academy of Dermatology*, 55: 193-208.
Narrative review
- Jayson, M. & Sanders, H. (1998) Increased incidence of serendipitously discovered renal cell carcinoma. [Review] [9 refs]. *Urology*, 51: 203-205.
Not in PICO
- Junuzovic, D., Kerleta, A. & Masic, I. (2013) The frequency of renal cell carcinoma in population of patients with kidney tumors. *Medicinski Arhiv*, 67: 27-30.
Not in PICO
- Kam, M. H., Barben, C. P., Eu, K. W. & Seow-Choen, F. (2004) Small bowel malignancies: A review of 29 patients at a single centre. *Colorectal Disease*, 6: 195-197.
Not in PICO
- Kawaciuk, I., Hyrsi, L., Dusek, P., Jarolim, L., Schmidt, M., Kaliska, V., Chocholaty, M. & Vesely, S. (2008) Influence of tumour-associated symptoms on the prognosis of patients with renal cell carcinoma. *Scandinavian Journal of Urology and Nephrology*, 42: 406-411.
Not in PICO
- Kawamura, T., Ohta, T., Ohno, Y., Wakai, K., Aoki, R., Tamakoshi, A., Maeda, K. & Mizuno, Y. (1995) Significance of urinalysis for subsequent kidney and urinary tract disorders in mass screening of adults. *Internal Medicine*, 34: 475-480.
Not in PICO
- Kim, S. W., Yoon, B. I., Ha, U. S., Sohn, D. W. & Cho, Y. H. (2013) Xanthogranulomatous pyelonephritis: clinical experience with 21 cases. *Journal of Infection & Chemotherapy*, 19: 1221-1224.
Not in PICO
- Krol, E., Rutkowski, B., Czekalski, S., Sulowicz, W., Wiecek, A., Lizakowski, S., Czarniak, P., Szubert, R., Karczewska-Maksymienko, L., Orlikowska, M., Kraszewska, E. & Magdon, R. (2005) [Early diagnosis of renal diseases--preliminary results from the pilot study PolNef]. [Polish]. *Przegląd Lekarski*, 62: 690-693.
Not in PICO
- Kurien, A., Mathew, A., Mishra, S., Ganpule, A., Sabnis, R. & Desai, M. (2009) Widening the plane of dissection in laparoscopic simple nephrectomy for symptomatic non-functioning kidneys keeping in mind the hidden upper track urothelial malignancy. *Journal of Endourology*, 23: A278.
Not in PICO
- Leslie, J. A. & Cain, M. P. (2006) Pediatric urologic emergencies and urgencies. [Review] [6 refs]. *Pediatric Clinics of North America*, 53: 513-527.
Narrative review
- Lin, M. S., Hung, Y. S., Wu, H. H., Kuo, M. C., Shiu, T. F., Chuang, C. K., Shih, L. Y. & Chu, P. H. (2009) Polycythemia vera as a presentation of renal angiomyolipoma: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 3: 90.
Not in PICO

- Lyratzopoulos, G., Abel, G. A., McPhail, S., Neal, R. D. & Rubin, G. P. (2013) Gender inequalities in the promptness of diagnosis of bladder and renal cancer after symptomatic presentation: evidence from secondary analysis of an English primary care audit survey. *BMJ Open*, 3: 2013.
Not in PICO
- Lyratzopoulos, G., Abel, G. A., McPhail, S., Neal, R. D. & Rubin, G. P. (2013) Gender inequalities in the promptness of diagnosis of bladder and renal cancer after symptomatic presentation: evidence from secondary analysis of an English primary care audit survey. *BMJ Open*, 3.
Not in PICO
- Macis, G., Di, G. S., Di, F. D. & Bonomo, L. (2013) [Future perspectives for diagnostic imaging in urology: from anatomic and functional to molecular imaging]. [Italian]. *Urologia (Treviso)*, 80: 29-41.
Not in PICO/Narrative review
- Masood, J., Lane, T., Koye, B., Vandal, M. T., Barua, J. M. & Hill, J. T. (2001) Renal cell carcinoma: incidental detection during routine ultrasonography in men presenting with lower urinary tract symptoms. *BJU International*, 88: 671-674.
Not in PICO
- Masuda, F., Suzuki, H., Kondo, I. & Furuta, N. (1991) [Clinical and pathological studies on incidental renal cell carcinoma]. [Japanese]. *Hinyokika Kyo - Acta Urologica Japonica*, 37: 1223-1227.
Not in PICO
- Matz, M., Fabricius, P. G. & Adler, F. (1981) [Considerations on possibilities of early diagnosis of tumors of the kidney parenchyma]. [German]. *Zeitschrift fur Arztliche Fortbildung (Jena)*, 75: 810-812.
Not in PICO
- Mayordomo, J. I., Guerra, J. M., Guijarro, C., Garcipratts, M. D., Gomez, A., Lopezbrea, M., Gonzalez, R., Hergueta, P., Lopezpino, M. A., Martineztello, F. & Cortesfunes, H. (1993) Neoplasms of Unknown Primary Site - A Clinicopathological Study of Autopsied Patients. *Tumori*, 79: 321-324.
Not in PICO
- McBride, D. (2010) Identification of proteins may lead to urinary test for kidney cancer. *ONS Connect*, 25: 17.
Not in PICO
- McCauley, L. R., Beckham, C. J., Hunter, T. B. & Nguyen, M. M. (2010) Gender and Renal Cancer: Do Variations in Clinical Presentation and Imaging Patterns Explain Observed Differences Between Males and Females? *Urology*, 76: 536-540.
Not in PICO
- McDonald, M. M., Swagerty, D. & Wetzel, L. (2006) Assessment of microscopic hematuria in adults. *American Family Physician*, 73: 1748-1754.
Narrative review
- McLernon, D. J., Dillon, J. F., Sullivan, F. M., Roderick, P., Rosenberg, W. M., Ryder, S. D. & Donnan, P. T. (2012) The utility of liver function tests for mortality prediction within one year in primary care using the algorithm for liver function investigations (ALFI). *PLoS ONE [Electronic Resource]*, 7: e50965.
Not in PICO
- Mevorach, R. A., Segal, A. J., Tersegno, M. E. & Frank, I. N. (1992) Renal cell carcinoma: Incidental diagnosis and natural history: Review of 235 cases. *Urology*, 39: 519-522.
Not in PICO
- Morbidelli, A., Zaniboni, N. & Bortolani, E. (1989) [Tumors of the upper excretory tract. Cases contribution and review of the literature]. [Review] [20 refs] [Italian]. *Minerva Chirurgica*, 44: 883-894.
Not in PICO

- Murphy, E., Bassett, J. H. & Williams, G. R. (2008) Disorders of calcium metabolism. [Review] [3 refs]. *Practitioner*, 250: 4-6.
Narrative review
- Narshimhaswamy, P., Jayaprakasha, G., Goyal, S., Soni, M. K., Ravishankar, T. H. S., Shivshankarappa, M. & Imdad, A. N. (2014) Renal cell carcinoma in an ENT clinic. *Indian Journal of Urology*, 30: S138.
Not in PICO
- Nelson, C. P. & Sanda, M. G. (2002) Contemporary diagnosis and management of renal angiomyolipoma. *Journal of Urology*, 168: 1315-1325.
Not in PICO
- Ng, Y. H., Seeley, J. P. & Smith, G. (2013) Haemospermia as a presenting symptom: Outcomes of investigation in 300 men. *Surgeon-Journal of the Royal Colleges of Surgeons of Edinburgh and Ireland*, 11: 35-38.
Not in PICO
- Oldbring, J., Glifberg, I., Mikulowski, P. & Hellsten, S. (1989) Carcinoma of the renal pelvis and ureter following bladder carcinoma: frequency, risk factors and clinicopathological findings. *Journal of Urology*, 141: 1311-1313.
Not in PICO
- Parekh, D. J., Cookson, M. S., Chapman, W., Harrell, F., Jr., Wells, N., Chang, S. S. & Smith, J. A., Jr. (2005) Renal cell carcinoma with renal vein and inferior vena caval involvement: clinicopathological features, surgical techniques and outcomes. *Journal of Urology*, 173: 1897-1902.
Not in PICO
- Patard, J. J. (1996) [Hematuria: current strategies]. [French]. *Annales d Urologie*, 30: 274-275.
Narrative review
- Patard, J. J., Bensalah, K., Vincendeau, S., Rioux-Leclercq, N., Guille, F. & Lobel, B. (2003) [Correlation between the mode of presentation of renal tumors and patient survival]. [French]. *Progres En Urologie*, 13: 23-28.
Not in PICO
- Patel, J. V., Chambers, C. V. & Gomella, L. G. (2008) Hematuria: etiology and evaluation for the primary care physician. [Review] [19 refs]. *Canadian Journal of Urology*, 15: Suppl-61.
Narrative review
- Pfister, D., Thuer, D. & Heidenreich, A. (2010) Pitfalls and outcome of nephrectomy for patients with polycystic kidney disease: Peri- and postoperative results. [German]. *Urologe - Ausgabe A*, 49: 1156-1162.
Not in PICO
- Pozzi-Mucelli, F., Medeot, A., Cernic, S., Calgaro, A., Braini, M. & Cova, M. (2011) Multimodal approach to the endovascular treatment of embolisation or exclusion of the renal arteries and their distal and/or polar branches: personal experience. *Radiologia Medica*, 116: 945-959.
Not in PICO
- Protzel, C., Woenckhaus, C., Zimmermann, U. & Klebingat, K.-J. (2001) Renal leiomyoma. An aspect of differential diagnosis of renal cell carcinoma with increasing clinical significance. [German]. *Urologe - Ausgabe A*, 40: 384-387.
Narrative review
- Puthenparambil, J., Lechner, K. & Kornek, G. (2010) Autoimmune hemolytic anemia as a paraneoplastic phenomenon in solid tumors: A critical analysis of 52 cases reported in the literature. [Review] [68 refs]. *Wiener Klinische Wochenschrift*, 122: 229-236.
Not in PICO
- Rais-Bahrami, S., Guzzo, T. J., Jarrett, T. W., Kavoussi, L. R. & Allaf, M. E. (2009) Incidentally discovered renal masses: Oncological and perioperative outcomes in patients with delayed

- surgical intervention. *BJU International*, 103: 1355-1358.
Not in PICO
- Schachter, L. R., Cookson, M. S., Chang, S. S., Smith, J. A., Jr., Dietrich, M. S., Jayaram, G. & Herrell, S. D. (2007) Second prize: frequency of benign renal cortical tumors and histologic subtypes based on size in a contemporary series: what to tell our patients. *Journal of Endourology*, 21: 819-823.
Not in PICO
- Schlomer, B., Figenshau, R. S., Yan, Y., Venkatesh, R. & Bhayani, S. B. (2006) Pathological features of renal neoplasms classified by size and symptomatology. *Journal of Urology*, 176: t-20.
Not in PICO
- Schwentner, C., Hennenlotter, J., Kuehs, U., Sleiman, H., Colleselli, D., Huber, S., Schilling, D., Sievert, K.-D. & Stenzl, A. (2010) Early detection of transitional cell carcinoma - Predictive power of urine-based tumor markers with regard to tumor grade and stage. *Journal of Urology*, 183: e454-e455.
Not in PICO
- Schwentner, C., Hennenlotter, J., Kuehs, U., Tews, V., Colleselli, D., Huber, S., Schilling, D., Sievert, K.-D. & Stenzl, A. (2010) Hematuria: Helpful or misleading for the early detection of transitional cell carcinoma-results from a cohort of 2008 patients. *Journal of Urology*, 183: e454.
Not in PICO
- Sells, H. & Cox, R. (2001) Undiagnosed macroscopic haematuria revisited: a follow-up of 146 patients. *BJU International*, 88: 6-8.
Not in PICO
- Shi, G. H., Chen, Y., Yao, X. D., Zhang, S. L., Dai, B., Feng, L. Q., Zhang, H. L., Shen, Y. J., Zhu, Y., Zhu, Y. P., Xiao, W. J., Ma, C. G., Wen, L. G., Qin, X. J., Yang, L. F. & Ye, D. W. (2013) Individualized renal mass biopsy strategy for Chinese patients with different subtypes and necrosis area. *Urologic Oncology*, 31: 920-923.
Not in PICO
- Shvarts, O., Han, K. R., Lam, J. S. & Belldegrun, A. S. (2004) Primary leiomyosarcoma of the inferior vena cava presenting as a renal mass. *Reviews in Urology*, 6: 39-42.
Not in PICO
- Siemer, S., Hack, M., Lehmann, J., Becker, F. & Stockle, M. (1243) Outcome of renal tumors in young adults. *Journal of Urology*, 175: 1240-1243.
Not in PICO
- Sigalow, D. A., Waldbaum, R. S. & Lowe, F. C. (1991) Identification of asymptomatic renal cell carcinomas utilizing modern radiographic techniques. *New York State Journal of Medicine*, 91: 200-202.
Not in PICO
- Slywotzky, C. M. & Bosniak, M. A. (2001) Localized cystic disease of the kidney. *AJR.American Journal of Roentgenology*, 176: 843-849.
Not in PICO
- Song, J., Tanagho, Y., Bhayani, S. & Figenshau, R. (2013) Factors predictive of symptomatic presentation in renal cell carcinoma. *Journal of Endourology*, 27: A383.
Not in PICO
- Stefanovic, K. B., Gregg, P. C. & Soung, M. (2009) Evaluation and treatment of hematospermia. *American Family Physician*, 80: 1421-1427.
Narrative review
- Steiner, M. S., Goldman, S. M., Fishman, E. K. & Marshall, F. F. (1993) The natural history of renal angiomyolipoma. *Journal of Urology*, 150: 1782-1786.
Not in PICO
- Szecs, A. & Szokoly, V. (1999) Retrospective clinical examination of incidentally detected kidney tumors. [Hungarian]. *Magyar Urologia*, 11: 349-356.
Not in PICO

- Taguchi, Y., Hori, S., Tomita, M., Matsuoka, Y., Suzuki, H., Odera, H. & Ishitani, H. (1994) Study of urine occult blood test with reagent strips - With special reference to results of workers' health check and ultrasonographic examination. [Japanese]. *Journal of Transportation Medicine*, 48: 276-280.
Not in PICO
- Takashi, M., Takagi, Y., Sakata, T., Shimoji, T. & Miyake, K. (1994) Clinicopathological characteristics of small renal cell carcinomas. *International Urology and Nephrology*, 26: 621-629.
Not in PICO
- Thaller, T. R. & Wang, L. P. (1154) Evaluation of asymptomatic microscopic hematuria in adults. [Review] [28 refs]. *American Family Physician*, 60: 1143-1152.
Narrative review
- Thariat, J., Vendrely, B., Roca, S., Ravaud, A., Bay, J. O., Lacout, A., Marcy, P. Y., Thyss, A. & Besancenot, J. F. (2012) [Renal involvement in cancer and renal paraneoplastic syndromes]. [Review] [French]. *Bulletin du Cancer*, 99: 263-275.
Narrative review
- Tijani, K. H., Anunobi, C. C., Ezenwa, E. V., Lawal, A., Habeebu, M. Y. M., Jeje, E. A., Ogunjimi, M. A. & Afolayan, M. O. (2012) Adult renal cell carcinoma in Lagos: Experience and challenges at the Lagos University Teaching Hospital. *African Journal of Urology*, 18: 20-23.
Not in PICO
- Tong, Y. C., Chieng, P. U., Tsai, T. C. & Lin, S. N. (1990) Renal angiomyolipoma: report of 24 cases. *British Journal of Urology*, 66: 585-589.
Not in PICO
- Tosaka, A., Ohya, K., Yamada, K., Ohashi, H., Kitahara, S., Sekine, H., Takehara, Y. & Oka, K. (1990) Incidence and properties of renal masses and asymptomatic renal cell carcinoma detected by abdominal ultrasonography. *Journal of Urology*, 144: 1097-1099.
Not in PICO
- Tsivian, M., Mouraviev, V., Kimura, M., Mayes, J., Albala, D., Robertson, C., Walther, P. & Polascik, T. (2009) Rationale for a less aggressive therapy for small renal tumors. *Urology*, 74: S19.
Not in PICO
- Valero-Aguilera, B., Bermudez-Tamayo, C., Garcia-Gutierrez, J. F., Jimenez-Pernett, J., Cozar-Olmo, J. M., Guerrero-Tejada, R. & Alba-Ruiz, R. (2014) - Information needs and Internet use in urological and breast cancer patients. - *Supportive Care in Cancer*, 22: 545-552.
Not in PICO
- Venables, Z., Ramaiya, A., Holden, S. & Millington, G. W. M. (2013) Three generations of hereditary leiomyomatosis associated with renal cell cancer. *British Journal of Dermatology*, 169: 21.
Not in PICO
- Vogelzang, N. J. & Stadler, W. M. (1998) Kidney cancer. *Lancet*, 352: 1691-1696.
Narrative review
- Wang, G. Y. (700) [Asymptomatic renal cell carcinoma and small renal cell carcinoma]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]*, 27: 656-657.
Not in PICO
- Wayte, N., Da, S. L., Chenevix-Trench, G. & Lakhani, S. R. (2008) What's in a cancer syndrome? Genes, phenotype and pathology. *Pathology*, 40: 247-259.
Narrative review
- Yamaguchi, K., Tominaga, T. & Nishimura, Y. (1995) Clinical study on incidental renal cell carcinoma. [Japanese]. *Hinyokika kyo*, Acta: 93-99.
Not in PICO
- Yap, N. Y., Ng, K. L., Ong, T. A., Pailoor, J., Gobe, G. C., Ooi, C. C., Razack, A. H., Dublin, N., Morais, C. & Rajandram, R. (2013) Clinical prognostic factors and survival outcome in renal cell carcinoma patients - a malaysian single centre perspective. *Asian Pacific Journal of Cancer Prevention: Apjcp*,

14: 7497-7500.

Not in PICO

Yazaki, T., Iiyama, T., Sato, S., Hata, R., Amemiya, H., Tomomasa, H., Muramatsu, H., Iizumi, T., Toyoshima, A. & Umeda, T. (1991) [Clinical study of renal cell carcinoma as incidental finding]. [Japanese]. *Nippon Jinzo Gakkai Shi. Japanese Journal of Nephrology*, 33: 409-415.

Not in PICO

Yeoh, M., Lai, N. K., Anderson, D. & Appadurai, V. (2013) Macroscopic haematuria--a urological approach. *Australian Family Physician*, 42: 123-126.

Narrative review

Yokom, D. W., Ihaddadene, R., Le, G. G., Moretto, P. & Carrier, M. (2013) Incidental venous thromboembolism in kidney cancer patients: A case-control study. *Journal of Thrombosis and Haemostasis*, 11: 330.

Not in PICO

Zielinski, H. (2005) Early detection of renal cancer. [Polish]. *Wspolczesna Onkologia*, 9: 98-100.

Narrative review

Zollner, S., Dirksen, U., Jurgens, H. & Ranft, A. (2013) Renal Ewing tumors. *Annals of Oncology*, 24: 2455-2461.

Not in PICO

Review question:

Which investigations of symptoms of suspected renal cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

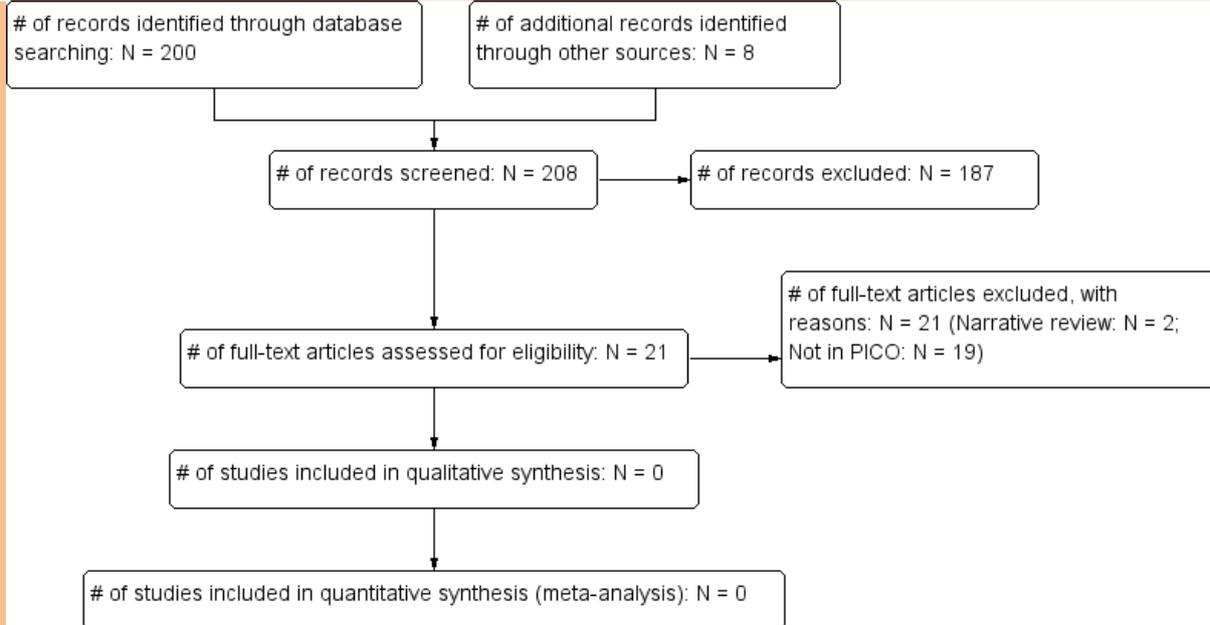
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	377	127	20/02/2013
Premedline	1980-2013	11	3	20/02/2013
Embase	1980-2013	457	94	21/03/2013
Cochrane Library	1980-2013	128	1	20/02/2013
Psychinfo	1980-2013	1	0	21/03/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	45	8	21/03/2013
Biomed Central	1980-2013	814	0	21/03/2013

Total References retrieved (after de-duplication): 189

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	2/2013-18/08/2014	10	1	18/08/2014
Premedline	2/2013-18/08/2014	15	3	18/08/2014
Embase	2/2013-18/08/2014	74	7	18/08/2014
Cochrane Library	2/2013-18/08/2014	70	0	18/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	2/2013-18/08/2014	11	2	18/08/2014

Total References retrieved (after de-duplication): 11



Study results

No evidence was identified pertaining to the diagnostic accuracy of abdominal ultrasound, urine cytology, x-ray, intravenous pyelogram, or CT scan of the abdomen and pelvis in patients with suspected renal cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Acino, S. & Resnick, M. I. (1988) Office urologic ultrasound. [Review] [34 refs]. *Urologic Clinics of North America*, 15: 577-588.

Narrative review

Aharony, S., Baniel, J., Tikva, P., Yossepowitch, O. & Hasharon, R. (2010) Clinically Unconfirmed positive Urine cytology - Oncological implications over long term follow-up. *Journal of Urology*, 183: e522.

Not in PICO

Ajit, D., Dighe, S. & Desai, S. (2010) Has urine cytology a role to play in the era of fluorescence in situ hybridization? *Acta Cytologica*, 54: 1118-1122.

Not in PICO

Ak, I. & Can, C. (2005) F-18 FDG PET in detecting renal cell carcinoma. *Acta Radiologica*, 46: 895-899.

Not in PICO

Akbari, A., Mayhew, A., Al-Alawi, M. A., Grimshaw, J., Winkens, R., Glidewell, E., Pritchard, C., Thomas, R. & Fraser, C. (2008) Interventions to improve outpatient referrals from primary care to secondary care. *Cochrane Database of Systematic Reviews*.

Not in PICO

Amendola, M. A. (1989) Comparison of MR imaging and CT in the evaluation of renal masses. [Review] [45 refs]. *Critical Reviews in Diagnostic Imaging*, 29: 117-150.

Narrative review

- Andresen, R. & Wegner, H. E. (1997) Intravenous urography revisited in the age of ultrasound and computerized tomography: diagnostic yield in cases of renal colic, suspected pelvic and abdominal malignancies, suspected renal mass, and acute pyelonephritis. *Urologia Internationalis*, 58: 221-226.
Not in PICO
- Arora, V. K., Sarungbam, J., Bhatia, A., Singh, N., Agrawal, V. & Aggarwal, S. (2010) Usefulness of NMP22 as an adjunct to a typical urine cytology and low-grade urothelial carcinoma. *Diagnostic Cytopathology*, 38: 788-790.
Not in PICO
- Aslaksen, A. & Gothlin, J. H. (1991) Imaging of solid renal masses. [Review] [37 refs]. *Current Opinion in Radiology*, 3: 654-662.
Narrative review
- Ayllon, J., Verkarre, V., Scotte, F., Fournier, L., Correas, J. M., Mejean, A., Teghom, C. & Oudard, S. (2012) Renal malacoplakia: Case report of a differential diagnosis for renal cell carcinoma. *The American Journal of Case Reports*, 13: 38-40.
Not in PICO
- Barroca, H. & Bom-Sucesso, M. (2014) Fine needle biopsy with cytology in paediatrics: The importance of a multidisciplinary approach and the role of ancillary techniques. *Cytopathology*, 25: 6-20.
Narrative review
- Battista, G., Sassi, C., Schiavina, R., Franceschelli, A., Baglivo, E., Martorana, G. & Canini, R. (2009) Computerized tomography virtual endoscopy in evaluation of upper urinary tract tumors: Initial experience. *Abdominal Imaging*, 34: 107-112.
Not in PICO
- Bayanati, H., Vakili, M. & Fasih, C. (2011) Syndromes in abdominal imaging-a case-based review of imaging findings. *American Journal of Roentgenology*, 196: A149.
Narrative review
- Beillard, C., Ardilouze, P. & Guillet, G. (2004) Dermatomyositis and kidney cancer: Interest of a thoraco-abdomino-pelvic scanner. [French]. *Nouvelles Dermatologiques*, 23: 543-545.
Not in PICO
- Beland, M. D., Mayo-Smith, W. W., Dupuy, D. E., Cronan, J. J. & DeLellis, R. A. (2007) Diagnostic yield of 58 consecutive imaging-guided biopsies of solid renal masses: should we biopsy all that are indeterminate? *AJR. American Journal of Roentgenology*, 188: 792-797.
Not in PICO
- Belville, J. S., Morgentaler, A., Loughlin, K. R. & Tumei, S. S. (1989) Spontaneous perinephric and subcapsular renal hemorrhage: evaluation with CT, US, and angiography. *Radiology*, 172: 733-738.
Not in PICO
- Bilal, M. M. & Brown, J. J. (1997) MR imaging of renal and adrenal masses in children. *Magnetic Resonance Imaging Clinics of North America*, 5: 179-197.
Narrative review
- Bloncourt, J., Dana, A., Galakhoff, C., Hospitel, S. & Michel, J. R. (1989) [Echography in pyelocaliceal tumors]. [French]. *Journal de Radiologie*, 70: 79-84.
Not in PICO
- Bonekamp, S., Corona-Villalobos, C. P. & Kamel, I. R. (2012) Oncologic applications of diffusion-weighted MRI in the body. *Journal of Magnetic Resonance Imaging*, 35: 257-279.
Narrative review
- Bos, S. D., Mellema, C. T. & Mensink, H. J. (2000) Increase in incidental renal cell carcinoma in the northern part of the Netherlands. *European Urology*, 37: 267-270.
Not in PICO

- Brown, F. M. (2000) Urine cytology. It is still the gold standard for screening?. [Review] [25 refs]. *Urologic Clinics of North America*, 27: 25-37.
Narrative review
- Budoff, M. J. & Gopal, A. (2007) Incidental findings on cardiac computed tomography. Should we look? *Journal of cardiovascular computed tomography*, 1: 97-105.
Narrative review
- Buteau, A., Seideman, C. A., Svatek, R. S., Youssef, R. F., Chakrabarti, G., Reed, G., Bhat, D. & Lotan, Y. (2014) What is evaluation of hematuria by primary care physicians? Use of electronic medical records to assess practice patterns with intermediate follow-up. *Urologic Oncology*, 32: 128-134.
Not in PICO
- Carrafiello, G., Fontana, F., Mangini, M., Ierardi, A. M., Cotta, E., Piacentino, F., De, C. M., Floridi, C., Di, M. A., Marconi, A. M. & Fugazzola, C. (2012) Upper urinary tract biopsy: an old device for a new approach. *Radiologia Medica*, 117: 1152-1160.
Not in PICO
- Cepulic, M., Cizmic, A., Petkovic, I., Fattorini, I., Nakic, M. & Stepan, G. J. (2003) Nephroblastomas - Wilms' tumor (WT). [Croatian]. *Paediatrica Croatica, Supplement*, 47: 75-80.
Narrative review
- Chahal, R., Taylor, K., Eardley, I., Lloyd, S. N. & Spencer, J. A. (2011) Patients at high risk for upper tract urothelial cancer: evaluation of hydronephrosis using high resolution magnetic resonance urography. *Journal of Urology*, 174: 478-482.
Not in PICO
- Chan, K. & Kamangar, N. (2012) Tuberous sclerosis complex manifesting with massive angiomyolipomas in multiple organs. *Chest*, 142.
Not in PICO
- Chen, D. Y. T. & Uzzo, R. G. (2011) Evaluation and management of the renal mass. *Medical Clinics of North America*, 95: 179-189.
Narrative review
- Chen, Y. F., Li, Y. W., Sheih, C. P. & Hsu, C. Y. (1999) Renal cell carcinoma: unusual pediatric renal tumors. *Journal of the Formosan Medical Association*, 98: 118-121.
Not in PICO
- Chisholm, R. A., Millet, B., Sherwood, T., Wraight, E. P. & Doyle, P. T. (1988) The investigation of painless haematuria - a comparison of intravenous urography and DMSA scintigraphy. *Clinical Radiology*, 39: 494-495.
Not in PICO
- Choyke, P. L. (2008) Radiologic evaluation of hematuria: Guidelines from the American College of Radiology's appropriateness criteria. *American Family Physician*, 78: 347-352.
Narrative review
- Collins, G. S. & Altman, D. G. (2013) Identifying patients with undetected renal tract cancer in primary care: An independent and external validation of Q Cancer (Renal) prediction model. *Cancer Epidemiology*, 37: 115-120.
Already included
- Craft, A. W., Parker, L., Stiller, C. & Cole, M. (1995) Screening for Wilms' tumour in patients with Aniridia, Beckwith syndrome, or hemihypertrophy. *Medical and Pediatric Oncology*, 24: 231-234.
Not in PICO
- Crispen, P. L., Soljic, A., Stewart, G., Kutikov, A., Davenport, D. & Uzzo, R. G. (2012) Enhancing renal tumors in patients with prior normal abdominal imaging: further insight into the natural history of renal cell carcinoma. *Journal of Urology*, 188: 1089-1093.
Not in PICO
- Croft, D. & Dickerson, M. (1994) Ultrasound differentiation of two pediatric abdominal masses. *Journal of Diagnostic Medical Sonography*, 10: 12-17.
Narrative review

- Czembirek, H. (1986) [Nephrology for general practice--roentgenologic diagnosis]. [German]. *Wiener Medizinische Wochenschrift*, 136: 17-19.
Narrative review
- Dalla, P. L., Pozzi-Mucelli, R., Magnaldi, S. & Pozzi-Mucelli, F. (1988) [Diagnostic imaging of renal tumors of small dimensions]. [Italian]. *Radiologia Medica*, 76: 590-596.
Not in PICO
- Dalla, P. L., Ricci, C. & Magnaldi, S. (1995) Referral criteria for selection of patients and diagnostic procedures. *Radiation Protection Dosimetry*, 57: 3-8.
Narrative review
- Damgaard-Pedersen, K. (1980) CT and IVU in the diagnosis of Wilms' tumour. A comparative study. *Pediatric Radiology*, 9: 207-211.
Not in PICO
- Datta, S. N., Allen, G. M., Evans, R., Vaughton, K. C. & Lucas, M. G. (2002) Urinary tract ultrasonography in the evaluation of haematuria--a report of over 1,000 cases. *Annals of the Royal College of Surgeons of England*, 84: 203-205.
Not in PICO
- Debre, B., Peyromaure, M., Saighi, D. & Zerbib, M. (2004) [Advances in diagnosis and treatment of renal cell carcinoma]. [Review] [29 refs] [French]. *Bulletin de l'Academie Nationale de Medecine*, 188: 15-24.
Narrative review
- Deidda, G., Paoni, A., Pischedda, A., Foddìs, G., Bottaru, M. & Bercovich, E. (1996) [Developments in the last 10 years in diagnostic imaging discovery of renal carcinoma]. [Italian]. *Archivio Italiano di Urologia, Andrologia*, 68: Suppl-51.
Not in PICO
- Delorme, S. & van, K. G. (1996) [Cui bono? Comments on cost-benefit analysis in ultrasound diagnosis]. [German]. *Radiologe*, 36: 285-291.
Narrative review
- Delorme, S. (2012) [Ultrasound in oncology: screening and staging]. [Review] [German]. *Internist*, 53: 271-281.
Narrative review
- Demirer, Z., Zor, M., Kurt, B., Bozkurt, Y. & Yildirim, I. (2012) Bilateral renal metastasis of an inguinal malignant solitary fibrous tumor, 9 years after primary surgical treatment. *Medical Principles & Practice*, 21: 585-587.
Not in PICO
- Descotes, J.-L. & Doublet, J.-D. (2006) Renal imaging and biopsy for diagnosis of renal masses. [French]. *Annales d'Urologie*, 40: S86-S90.
Narrative review
- Di, N. A. & Signoretti, S. (2009) Tissue biomarkers in renal cell carcinoma: issues and solutions. [Review] [44 refs]. *Cancer*, 115: Suppl-7.
Narrative review
- Dikranian, A. H., Petitti, D. B., Shapiro, C. E. & Kosco, A. F. (2005) Intravenous urography in evaluation of asymptomatic microscopic hematuria. *Journal of Endourology*, 19: 595-597.
Not in PICO
- Dirim, A., Tutar, N., Peskircioglu, L., Celik, H., Tekin, M. I. & Ozkardes, H. (2010) Can dynamic multidetector computerized tomography detect renal cell carcinoma subtypes? *Turkish Journal of Medical Sciences*, 40: 31-38.
Not in PICO
- Dobry, E. & Danuser, H. (2009) [Imaging of the kidney and the urinary tract]. [Review] [22 refs] [German]. *Therapeutische Umschau*, 66: 39-42.
Narrative review

- Dragoescu, E. A. & Liu, L. (2013) Indications for renal fine needle aspiration biopsy in the era of modern imaging modalities. *CytoJournal*, 10.
Not in PICO
- Ell, C. & Schott, G. (1994) [Suspected kidney tumor--diagnostic-therapeutic procedure]. [German]. *Fortschritte der Medizin*, 112: 123-124.
Narrative review
- Etemad, A., Brems-Dalgaard, E. & Thomsen, H. S. (2003) Outcome of intravenous urography in the year 2000. *Abdominal Imaging*, 28: 226-229.
Not in PICO
- Fekak, H., Bennani, S., Taha, A., Rabii, R., Joual, A., Sarf, S., Hafiani, M., el, M. M. & Benjelloun, S. (2001) [Kidney cancer. Report of 170 cases]. [French]. *Annales d'Urologie*, 35: 249-256.
Not in PICO
- Fekak, H., Bennani, S., Taha, A., Rabii, R., Joual, A., Sarf, S., Hafiani, M., el, M. M. & Benjelloun, S. (2001) The cancer of kidney. A report of 170 cases. [French]. *Annales d'Urologie*, 35: 249-256.
Not in PICO
- Ferda, J., Hora, M., Hes, O., Ferdova, E. & Kreuzberg, B. (2007) Assessment of the kidney tumor vascular supply by two-phase MDCT-angiography. *European Journal of Radiology*, 62: 295-301.
Not in PICO
- Ferda, J., Ferdova, E., Hora, M., Hes, O., Finek, J., Topolcan, O. & Kreuzberg, B. (2013) 18F-FDG-PET/CT in potentially advanced renal cell carcinoma: a role in treatment decisions and prognosis estimation. *Anticancer Research*, 33: 2665-2672.
Not in PICO
- Ferrer, M. D., Marti-Bonmati, L., Belloch, V., Moreno, F., Galant, J., Martinez-Rodrigo, J. & Casillas, C. (1993) Study of renal carcinoma in early stage by computerized tomography and magnetic resonance. [Spanish]. *Neoplasia*, 10: 201-205.
Not in PICO
- Fiegler, W., Felix, R., Schorner, W. & Kohler, D. (1985) [Diagnosis of kidney diseases with magnetic resonance tomography including the use of nuclear magnetic resonance contrast media]. [German]. *Urologe (Auszg.)*, 24: 264-269.
Narrative review
- Flanigan, R. C. (2007) Renal tumors: The good, the bad, and the ugly. *International Journal of Urology*, 14: 575-580.
Narrative review
- Foley, W. D. (2003) Renal MDCT. [Review] [8 refs]. *European Journal of Radiology*, 45: Suppl-8.
Narrative review
- Fornara, P. & Hoda, M. R. (2011) [Renal cell carcinoma]. [Review] [German]. *Urologe (Auszg.)*, 50: Suppl-22.
Narrative review
- Furtwangler, R., Schenk, J.-P., Reinhard, H., Leuschner, I., Rube, C., Von, S. D. & Graf, N. (2005) Nephroblastoma - Wilms' tumor. Genetics, radiological diagnostics and therapy concept - An overview. [German]. *Onkologie*, 11: 1077-1089.
Narrative review
- Ghani, K. R., Keeler, B. & Nargund, V. (2007) Haematuria 2: Imaging investigations, management and follow up. *British Journal of Hospital Medicine*, 68: 489-493.
Narrative review
- Gingu, C., Patrascoiu, S., Surcel, C., Chibelea, C., Harza, M., Zogas, V., Balsanu, C., Dick, A., Mirvald, C., Lupu, F., Domnisor, L. & Sinescu, I. (2012) Primary carcinoma of the male urethra-diagnosis and treatment. *European Urology, Supplements*, 11: e405-e405a.
Not in PICO
- Golan, S., Lifshitz, D., Livne, P. M., Baniel, J. & Nadu, A. (2012) The yield of ureteroscopy for upper tract urothelial carcinoma in the era of computerized tomography urography. *Journal of*

- Endourology*, 26: A94-A95.
Not in PICO
- Grossfeld, G. D., Wolf, J. S., Litwin, M. S., Hricak, H., Shuler, C. L., Agerter, D. C. & Carroll, P. R. (2001) Asymptomatic microscopic hematuria in adults: Summary of the AUA Best Practice Policy recommendations. *American Family Physician*, 63: 1145-1154.
Narrative review
- Gu, F. L. (1990) Imaging techniques for the diagnosis of renal tumors. *Proceedings of the Chinese Academy of Medical Sciences & the Peking Union Medical College*, 5: 75-78.
Not in PICO
- Guinan, P. & Rubenstein, M. (1987) Methods of early diagnosis in genitourinary cancer. [Review] [163 refs]. *Cancer*, 60: Suppl-76.
Narrative review
- Haendl, T., Strobel, D., Legal, W., Frieser, M., Hahn, E. G. & Bernatik, T. (2009) [Renal cell cancer does not show a typical perfusion pattern in contrast-enhanced ultrasound]. [German]. *Ultraschall in der Medizin*, 30: 58-63.
Not in PICO
- Hafron, J. & Kaouk, J. H. (2007) Ablative techniques for the management of kidney cancer. *Nature Clinical Practice Urology*, 4: 261-269.
Not in PICO
- Heikkinen, M., Rasanen, H. & Farkkila, M. (2005) Clinical value of ultrasound in the evaluation of dyspepsia in primary health care. *Scandinavian Journal of Gastroenterology*, 40: 980-984.
Not in PICO (Not diagnostic test accuracy study)
- Heilbrun, M. E., Yu, J., Smith, K. J., Dechet, C. B., Zagoria, R. J. & Roberts, M. S. (2012) The cost-effectiveness of immediate treatment, percutaneous biopsy and active surveillance for the diagnosis of the small solid renal mass: evidence from a Markov model (Structured abstract). *Journal of Urology*, 187: 39-43.
Not in PICO
- Helenon, O., Eiss, D., Debrito, P., Merran, S. & Correias, J. M. (2012) How to characterise a solid renal mass: a new classification proposal for a simplified approach. *Diagnostic and Interventional Imaging*, 93: 232-245.
Narrative review
- Henning, A., Wehrberger, M., Madersbacher, S., Pycha, A., Martini, T., Comploj, E., Jeschke, K., Tripolt, C. & Rauchenwald, M. (2013) Do differences in clinical symptoms and referral patterns contribute to the gender gap in bladder cancer? *BJU International*, 112: 68-73.
Not in PICO
- Hernandez, J. D., de la Torre, H. P., Alberola, B. J. & Amores, C. S. (2001) [Small renal mass. Diagnostic management]. [Review] [20 refs] [Spanish]. *Archivos Espanoles de Urologia*, 54: 593-601.
Narrative review
- Heynemann, H. (2008) [Current aspects in the diagnosis of renal cell cancer]. [German]. *Praxis*, 97: 421-425.
Narrative review
- Higgins, J. C. & Fitzgerald, J. M. (299) Evaluation of incidental renal and adrenal masses. *American Family Physician*, 63: 288-294.
Narrative review
- Higgins, J. C. & Arnold, M. J. (2013) When to worry about incidental renal and adrenal masses. *Journal of Family Practice*, 62: 476-483.
Narrative review
- Ho, K. K. L. (2002) Nephrotic syndrome in adults - A common clinical syndrome of kidney diseases. *Hong Kong Practitioner*, 24: 66-71.
Narrative review

- Hoefel, C., Pousset, M., Timsit, M. O., Elie, C., Mejean, A., Merran, S., Tranquart, F., Khairoune, A., Joly, D., Richard, S., Helenon, O. & Correas, J. M. (2010) Radiofrequency ablation of renal tumours: diagnostic accuracy of contrast-enhanced ultrasound for early detection of residual tumour. *European Radiology*, 20: 1812-1821.
Not in PICO
- Hricak, H. (1987) Urologic cancer. Methods of early detection and future developments. *Cancer*, 60: Suppl-85.
Narrative review
- Iczkowski, K. A., Sweat, S. D. & Bostwick, D. G. (1999) Subepithelial pelvic hematoma of the kidney clinically mimicking cancer: report of six cases and review of the literature. [Review] [12 refs]. *Urology*, 53: 276-279.
Not in PICO
- Jimbo, M. (2010) Evaluation and Management of Hematuria. *Primary Care*, 37: 461-+.
Narrative review
- Jinzaki, M., Matsumoto, K., Kikuchi, E., Sato, K., Horiguchi, Y., Nishiwaki, Y. & Silverman, S. G. (2011) Comparison of CT urography and excretory urography in the detection and localization of urothelial carcinoma of the upper urinary tract. *American Journal of Roentgenology*, 196: 1102-1109.
Not in PICO
- Junuzovic, D., Kerleta, A. & Masic, I. (2013) The frequency of renal cell carcinoma in population of patients with kidney tumors. *Medicinski Arhiv*, 67: 27-30.
Not in PICO
- Kang, N., Niu, Y., Zhang, J., Wang, J., Tian, X., Yan, Y., Yu, Z. & Xing, N. (2012) Intraoperative ultrasonography: a useful tool in retrolaparoscopic nephron-sparing surgery. *Urologia Internationalis*, 88: 338-342.
Not in PICO
- Kawaciuk, I., Hyrsi, L., Dusek, P., Jarolim, L., Schmidt, M., Kaliska, V., Chocholaty, M. & Vesely, S. (2008) Influence of tumour-associated symptoms on the prognosis of patients with renal cell carcinoma. *Scandinavian Journal of Urology & Nephrology*, 42: 406-411.
Not in PICO
- Kaya, K., Ayan, S., Gokce, G., Kilicarslan, H., Yildiz, E. & Gultekin, E. Y. (2005) Urinary nuclear matrix protein 22 for diagnosis of renal cell carcinoma. *Scandinavian Journal of Urology and Nephrology*, 39: 25-29.
Not in PICO
- Kim, J. (2006) Imaging findings of renal cell carcinoma. [Review] [43 refs]. *Expert Review of Anticancer Therapy*, 6: 895-904.
Narrative review
- Kim, S. W., Yoon, B. I., Ha, U. S., Sohn, D. W. & Cho, Y. H. (2013) Xanthogranulomatous pyelonephritis: clinical experience with 21 cases. *Journal of Infection & Chemotherapy*, 19: 1221-1224.
Not in PICO
- Knoflach, P., Judmaier, G., Reiner, A. & Mikuz, G. (1983) [Ultrasonically guided fine-needle biopsy]. [German]. *Wiener Medizinische Wochenschrift*, 133: 514-519.
Not in PICO
- Kreft, B. & Schild, H. H. (2003) [Cystic renal lesions]. [Review] [67 refs] [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 175: 892-903.
Narrative review
- Kumar, R., Chauhan, A., Lakhani, P., Xiu, Y., Zhuang, H. & Alavi, A. (2005) 2-Deoxy-2-[F-18]fluoro-D-glucose-positron emission tomography in characterization of solid renal masses. *Molecular Imaging & Biology*, 7: 431-439.
Not in PICO

- Lee, K. S., Zeikus, E., DeWolf, W. C., Rofsky, N. M. & Pedrosa, I. (2010) MR urography versus retrograde pyelography/ureteroscopy for the exclusion of upper urinary tract malignancy. *Clinical Radiology*, 65: 185-192.
Not in PICO
- Lee, S. Y., Landis, M. S., Ross, I. G., Goela, A. & Leung, A. E. (2012) Extraspinal findings at lumbar spine CT examinations: prevalence and clinical importance. *Radiology*, 263: 502-509.
Not in PICO
- Lee, Y., Kim, N., Cho, K. S., Kang, S. H., Kim, D. Y., Jung, Y. Y. & Kim, J. K. (2009) Bayesian classifier for predicting malignant renal cysts on MDCT: early clinical experience. *AJR.American Journal of Roentgenology*, 193: W106-W111.
Not in PICO
- Leinonen, A., Paivansalo, M. & Kontturi, M. (1984) Ultrasonography, arteriography and CT in the diagnosis of renal carcinoma. *Annals of Clinical Research*, 16: Suppl-30.
Not in PICO
- Leveridge, M. J., Finelli, A., Kachura, J. R., Evans, A., Chung, H., Shiff, D. A., Fernandes, K. & Jewett, M. A. (2011) Outcomes of small renal mass needle core biopsy, nondiagnostic percutaneous biopsy, and the role of repeat biopsy. *European Urology*, 60: 578-584.
Not in PICO
- Liedl, B., Liedl, T. & Hofstetter, A. G. (1992) Renal cell carcinoma. Diagnosis, differential diagnosis and prognosis. [German]. *Fortschritte der Medizin*, 110: 27-32.
Narrative review
- Long, J. A., Descotes, J. L. & Rambeaud, J. J. (2007) [Kidney cancer diagnosis]. [Review] [10 refs] [French]. *Revue du Praticien*, 57: 603-612.
Narrative review
- Luk'ianenok, P. I. (1989) [Magnetic resonance tomography in kidney tumors concomitant with symptomatic hypertension]. [Russian]. *Meditinskaja Radiologija*, 34: 41-44.
Not in PICO
- Luscher, T. F., Wanner, C., Otto, R., Hauri, D. & Vetter, W. (1987) [An incidental finding of renal cysts: routine occurrence or a finding deserving clarification?]. [Review] [60 refs] [German]. *Schweizerische Medizinische Wochenschrift.Journal Suisse de Medecine*, 117: 785-794.
Narrative review
- Lyratzopoulos, G., Abel, G. A., McPhail, S., Neal, R. D. & Rubin, G. P. (2013) Gender inequalities in the promptness of diagnosis of bladder and renal cancer after symptomatic presentation: evidence from secondary analysis of an English primary care audit survey. *BMJ Open*, 3: 2013.
Not in PICO
- Machida, T. & Ohnishi, T. (1983) [Diagnosis and treatment of renal cell carcinoma]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 10: 2103-2110.
Narrative review
- Machida, T. & Ohnishi, T. (1994) [Diagnosis for renal cell carcinoma]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 21: 12-16.
Narrative review
- Macis, G., Di, G. S., Di, F. D. & Bonomo, L. (2013) [Future perspectives for diagnostic imaging in urology: from anatomic and functional to molecular imaging]. [Italian]. *Urologia (Treviso)*, 80: 29-41.
Not in PICO/Narrative review
- Manenti, G., Di, R. M., Mancino, S., Bartolucci, D. A., Palmieri, G., Mastrangeli, R., Miano, R., Squillaci, E. & Simonetti, G. (2008) Malignant renal neoplasms: correlation between ADC values and cellularity in diffusion weighted magnetic resonance imaging at 3 T. *Radiologia Medica*, 113: 199-213.
Not in PICO

- Marhuenda, C., Ezzedine, M., Maldonado, J., Piro, C., Fuentes, E., Perez, A., Jimenez, A. I., Sanchez de, T. J. & Boix-Ochoa, J. (1989) [Bolande's tumor: significance of its early diagnosis and treatment]. [Spanish]. *Cirurgia Pediatrica*, 2: 196-199.
Not in PICO
- Masood, J., Lane, T., Koye, B., Vandal, M. T., Barua, J. M. & Hill, J. T. (2001) Renal cell carcinoma: Incidental detection during routine ultrasonography in men presenting with lower urinary tract symptoms. *BJU International*, 88: 671-674.
Not in PICO
- Masuda, F., Suzuki, H., Kondo, I. & Furuta, N. (1991) [Clinical and pathological studies on incidental renal cell carcinoma]. [Japanese]. *Hinyokika Kiyō - Acta Urologica Japonica*, 37: 1223-1227.
Not in PICO
- McCauley, L. R., Beckham, C. J., Hunter, T. B. & Nguyen, M. M. (2010) Gender and renal cancer: do variations in clinical presentation and imaging patterns explain observed differences between males and females? *Urology*, 76: 536-540.
Not in PICO
- McClennan, B. L. & Deyoe, L. A. (1994) The imaging evaluation of renal cell carcinoma: diagnosis and staging. *Radiologic Clinics of North America*, 32: 55-69.
Narrative review
- McDonald, M. M., Swagerty, D. & Wetzel, L. (2006) Assessment of microscopic hematuria in adults. *American Family Physician*, 73: 1748-1754.
Narrative review
- McHugh, K. (2007) Renal and adrenal tumours in children. [Review] [19 refs]. *Cancer Imaging*, 7: 41-51.
Narrative review
- McLernon, D. J., Dillon, J. F., Sullivan, F. M., Roderick, P., Rosenberg, W. M., Ryder, S. D. & Donnan, P. T. (2012) The utility of liver function tests for mortality prediction within one year in primary care using the algorithm for liver function investigations (ALFI). *PLoS ONE [Electronic Resource]*, 7: e50965.
Not in PICO
- Meyer, J. S., Harty, M. P. & Khademian, Z. (2002) Imaging of neuroblastoma and Wilms' tumor. [Review] [58 refs]. *Magnetic Resonance Imaging Clinics of North America*, 10: 275-302.
Narrative review
- Mian, C., Mazzoleni, G., Vikoler, S., Martini, T., Knuchel-Clark, R., Zaak, D., Lazica, A., Roth, S., Mian, M. & Pycha, A. (2010) Fluorescence in situ hybridisation in the diagnosis of upper urinary tract tumours. *European Urology*, 58: 288-292.
Not in PICO
- Milovanceva-Popovska, M. & Dzikova, S. (2008) Doppler ultrasonography: a tool for nephrologists--single centre experience. *Makedonska Akademija na Naukite i Umetnostite Oddelenie Za Biološki i Meditsinski Nauki Prilozi*, 29: 107-128.
Not in PICO
- Minamimoto, R., Senda, M., Terauchi, T., Jinnouchi, S., Inoue, T., Iinuma, T., Inoue, T., Ito, K., Iwata, H., Uno, K., Oku, S., Oguchi, K., Tsukamoto, E., Nakashima, R., Nishizawa, S., Fukuda, H., Murano, T. & Yoshida, T. (2011) Analysis of various malignant neoplasms detected by FDG-PET cancer screening program: based on a Japanese Nationwide Survey. *Annals of Nuclear Medicine*, 25: 45-54.
Not in PICO
- Miyakita, H., Tokunaga, M., Onda, H., Usui, Y., Kinoshita, H., Kawamura, N. & Yasuda, S. (2002) Significance of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) for detection of renal cell carcinoma and immunohistochemical glucose transporter 1 (GLUT-1) expression in the cancer. *International Journal of Urology*, 9: 15-18.
Not in PICO

- Morrissey, J. J., London, A. N., Luo, J. & Kharasch, E. D. (2010) Urinary biomarkers for the early diagnosis of kidney cancer. *Mayo Clinic Proceedings*, 85: 413-421.
Not in PICO
- Moslemi, M. K. & Mahfoozi, B. (2011) Urologist-operated ultrasound and its use in urological outpatient clinics. *Patient preference & adherence*, 5: 85-88.
Not in PICO (outcomes not relevant, referred population[?])
- Nakamura, L. & Ritchey, M. (2010) Current management of wilms' tumor. [Review] [58 refs]. *Current Urology Reports*, 11: 58-65.
Narrative review
- Ng, Y. H., Seeley, J. P. & Smith, G. (2013) Haemospermia as a presenting symptom: Outcomes of investigation in 300 men. *Surgeon-Journal of the Royal Colleges of Surgeons of Edinburgh and Ireland*, 11: 35-38.
Not in PICO
- Nicolai, N., Spreafico, C., Catanzaro, M., Torelli, T., Stagni, S., Biasoni, D., Piva, L., Necchi, A., Milani, A., Girotti, P., Marchiano, A. & Salvioni, R. (2010) Percutaneous cryoablation (PCA) for renal masses: Is something going to change? *Anticancer Research*, 30: 1398-1399.
Not in PICO
- O'Malley, M. E., Hahn, P. F., Yoder, I. C., Gazelle, G. S., McGovern, F. J. & Mueller, P. R. (2003) Comparison of excretory phase, helical computed tomography with intravenous urography in patients with painless haematuria. *Clinical Radiology*, 58: 294-300.
Not in PICO
- Olaniran, K., Cheng, W. & Pulinthanathu, R. (2014) - A 20-year-old female with hemoptysis and high blood pressure: An unusual case of papillary renal cell carcinoma. - *The American Journal of Case Reports*, 15: 254-257.
Not in PICO
- Oyama, N., Okazawa, H., Kusukawa, N., Kaneda, T., Miwa, Y., Akino, H., Fujibayashi, Y., Yonekura, Y., Welch, M. J. & Yokoyama, O. (2009) 11C-Acetate PET imaging for renal cell carcinoma. *European Journal of Nuclear Medicine & Molecular Imaging*, 36: 422-427.
Not in PICO
- Ozulker, T., Ozulker, F., Ozbek, E. & Ozpacaci, T. (2011) A prospective diagnostic accuracy study of F-18 fluorodeoxyglucose-positron emission tomography/computed tomography in the evaluation of indeterminate renal masses. *Nuclear Medicine Communications*, 32: 265-272.
Not in PICO
- Pace, G., Bozzini, G., Marengi, C., Picozzi, S. & Carmignani, L. (2012) The pocket ultrasound: The phonendoscope of the urologist. *European Urology, Supplements*, 11: e801-e801a.
Not in PICO
- Palazzo, S., Martino, P., Ditunno, P., Battaglia, M., De, C. G., Garofalo, L., Annunziata, G. & Selvaggi, F. P. (2000) [Incidental kidney neoplasm: anatomopathologic characteristics and clinical behavior]. [Review] [16 refs] [Italian]. *Archivio Italiano di Urologia, Andrologia*, 72: 216-220.
Not in PICO
- Palko, A., Kun, E., Greksa, E. & Khertelendi, A. (1991) [Computed tomography in the diagnosis of malignant renal neoplasms and their dissemination]. [Russian]. *Vestnik Rentgenologii i Radiologii*.(2):37-40, 1991 Mar-Apr., 37-40.
Not in PICO
- Palko, A., Kun, E., Greksa, E. & Khertelendi, A. (1991) [The role of computerized tomography in the diagnosis and evaluation of the dissemination of malignant kidney tumors]. [Russian]. *Vestnik Rentgenologii i Radiologii*.(2):37-40, 1991 Mar-Apr., 37-40.
Not in PICO
- Palmowski, M., Schifferdecker, I., Zwick, S., Macher-Goepfing, S., Laue, H., Haferkamp, A., Kauczor, H. U., Kiessling, F. & Hallscheidt, P. (2010) Tumor perfusion assessed by dynamic contrast-enhanced MRI correlates to the grading of renal cell carcinoma: initial results. *European*

Journal of Radiology, 74: e176-e180.

Not in PICO

Palsdottir, H. B., Hardarson, S., Petursdottir, V., Jonsson, A., Jonsson, E., Sigurdsson, M. I., Einarsson, G. V. & Gudbjartsson, T. (2012) Incidental detection of renal cell carcinoma is an independent prognostic marker: results of a long-term, whole population study. *Journal of Urology*, 187: 48-53.

Not in PICO

Park, S. H., Yoon, S. K., Cho, J. H., Oh, J. Y., Nam, K. J., Kwon, H. J., Kim, S. Y., Kang, M. J., Choi, S. & Sung, G. T. (2008) Radiofrequency ablation treatment for renal cell carcinoma: early clinical experience. *Korean Journal of Radiology*, 9: 340-347.

Not in PICO

Patard, J. J. (1996) [Hematuria: current strategies]. [French]. *Annales d Urologie*, 30: 274-275.

Narrative review

Patel, J. V., Chambers, C. V. & Gomella, L. G. (2008) Hematuria: etiology and evaluation for the primary care physician. *The Canadian journal of urology*, 15: 54-61.

Narrative review

Patel, N. S., Blick, C., Kumar, P. V. S. & Malone, P. R. (2009) The diagnostic value of abdominal ultrasound, urine cytology and prostate-specific antigen testing in the lower urinary tract symptoms clinic. *International Journal of Clinical Practice*, 63: 1734-1738.

Not in PICO

Patten, R. M., Byun, J. Y. & Freeny, P. C. (1993) CT of hypervascular hepatic tumors: are unenhanced scans necessary for diagnosis? *AJR.American Journal of Roentgenology*, 161: 979-984.

Not in PICO

Paul, A. B., Collie, D. A., Wild, S. R. & Chisholm, G. D. (1993) An integrated haematuria clinic. *British Journal of Clinical Practice*, 47: 128-130.

Not in PICO

Pieri, L., Tozzini, A., Orsitto, E., Bulleri, A. & Morelli, G. (1997) [Urotheliomas of the upper urinary tract. The role of computed tomography in integrated diagnostic imaging]. [Italian]. *Radiologia Medica*, 94: 202-207.

Not in PICO

Pirasteh, A., Snyder, L., Boncher, N., Passalacqua, M., Rosenblum, D. & Prologo, J. D. (2011) Cryoablation vs. radiofrequency ablation for small renal masses. *Academic Radiology*, 18: 97-100.

Not in PICO

Piscioli, F., Pusioli, T., Scappini, P. & Luciani, L. (1985) Urine cytology in the detection of renal adenocarcinoma. *Cancer*, 56: 2251-2255.

Not in PICO

Pluzarev, O. & Budimlija, Z. (1999) [Ultrasonography and computerized tomography in the evaluation of tumor invasion in renal adenocarcinoma]. [Croatian]. *Medicinski Pregled*, 52: 455-458.

Not in PICO

Porena, M., Vespasiani, G., Rosi, P., Costantini, E., Virgili, G., Mearini, E. & Micali, F. (1992) Incidentally detected renal cell carcinoma: role of ultrasonography. *Journal of Clinical Ultrasound*, 20: 395-400.

Not in PICO

Prando, A., Prando, D. & Prando, P. (2006) Renal cell carcinoma: unusual imaging manifestations. *Radiographics*, 26: 233-244.

Narrative review

Protzel, C., Woenckhaus, C., Zimmermann, U. & Klebingat, K.-J. (2001) Renal leiomyoma. An aspect of differential diagnosis of renal cell carcinoma with increasing clinical significance. [German]. *Urologe - Ausgabe A*, 40: 384-387.

Narrative review

- Ramdave, S., Thomas, G. W., Berlangieri, S. U., Bolton, D. M., Davis, I., Danguy, H. T., Macgregor, D. & Scott, A. M. (2001) Clinical role of F-18 fluorodeoxyglucose positron emission tomography for detection and management of renal cell carcinoma. *Journal of Urology*, 166: 825-830.
Not in PICO
- Razavi, S. A., Sadigh, G., Kelly, A. M. & Cronin, P. (2012) Comparative effectiveness of imaging modalities for the diagnosis of upper and lower urinary tract malignancy: a critically appraised topic. *Academic Radiology*, 19: 1134-1140.
Systematic review, have checked relevance of included papers
- Razdan, S., Johannes, J., Cox, M. & Bagley, D. H. (2005) Current practice patterns in urologic management of upper-tract transitional-cell carcinoma. *Journal of Endourology*, 19: 366-371.
Not in PICO
- Reichelt, O., Wunderlich, H., Weirich, T., Schlichter, A. & Schubert, J. (2001) Computerized contrast angiosonography: a new diagnostic tool for the urologist? *BJU International*, 88: 9-14.
Not in PICO
- Reiman, T. A., Siegel, M. J. & Shackelford, G. D. (1986) Wilms tumor in children: abdominal CT and US evaluation. *Radiology*, 160: 501-505.
Not in PICO
- Rendon, R. A., Stanietzky, N., Panzarella, T., Robinette, M., Klotz, L. H., Thurston, W. & Jewett, M. A. S. (2000) The natural history of small renal masses. *Journal of Urology*, 164: 1143-1147.
Not in PICO
- Richenberg, J. (2008) Haematuria. *Imaging*, 20: 57-72.
Narrative review
- Rinnab, L., Gottfried, H. W., Schnoller, T., Hautmann, R. E. & Kuefer, R. (2007) Clinical value of transrectal ultrasound in the diagnosis of suspected neoplasia in the small pelvis. *Ultraschall in der Medizin*, 28: 195-200.
Not in PICO
- Rinsho, K., Ishikawa, S., Uchida, K. & Koiso, K. (1984) The value of ultrasonography in early detection of renal cell carcinoma. *Japanese Journal of Clinical Oncology*, 14: 329-334.
Not in PICO
- Ritchey, M., Daley, S., Shamberger, R. C., Ehrlich, P., Hamilton, T., Haase, G. & Sawin, R. (2008) Ureteral extension in Wilms' tumor: a report from the National Wilms' Tumor Study Group (NWTSG). *Journal of Pediatric Surgery*, 43: 1625-1629.
Not in PICO
- Rousseau, T., Chretien, Y. & Dufour, B. (1991) Accidental diagnosis of cancer of the renal parenchyma in adults. [French]. *Journal d'urologie*, 97: 141-144.
Not in PICO
- Rousseau, T., Peyret, C., Zerbib, M., Thiounn, N., Flam, T. & Debre, B. (1994) [Circumstances of the detection of kidney cancer. Current part of accidental discoveries]. [Review] [37 refs] [French]. *Journal d Urologie*, 100: 189-195.
Not in PICO
- Saksena, M. & Gervais, D. (2009) Percutaneous renal tumor ablation. [Review] [40 refs]. *Abdominal Imaging*, 34: 582-587.
Not in PICO
- Schenk, J.-P., Engelmann, D., Rohrschneider, W., Zieger, B., Semler, O., Graf, N. & Troger, J. (2004) Rhabdoid tumors of the kidney in childhood - A retrospective radiomorphologic analysis of 22 patients as part of the nephroblastoma study SIOP 93/01-GPOH registered cases. [German]. *RoFo Fortschritte auf dem Gebiet der Rontgenstrahlen und der Bildgebenden Verfahren*, 176: 965-971.
Not in PICO
- Schlenker, B., Seitz, M., Bader, M. J., Ganzer, R., Tilki, D., Bayrle, F., Reich, O., Staehler, M., Bachmann, A., Stief, C. G. & Gratzke, C. (2010) Comparison of Guideline Recommendations with Daily Practice in Patients with Renal Cell Carcinoma. *European Journal of Medical Research*, 15:

253-257.

Not in PICO

Schoder, H. & Larson, S. M. (2004) Positron emission tomography for prostate, bladder, and renal cancer. [Review] [180 refs]. *Seminars in Nuclear Medicine*, 34: 274-292.

Narrative review

Schwentner, C., Hennenlotter, J., Kuehs, U., Tews, V., Colleselli, D., Huber, S., Schilling, D., Sievert, K. D. & Stenzl, A. (2010) Impact of urinary sampling and urinary tract infection on the diagnostic value of urine tests (urovysionr, uCyt+R) and cytology for transitional cell carcinoma - Results from a cohort of 2077 patients. *European Urology, Supplements*, 9: 50.

Abstract only so limited information, but I think it's not in PICO (referred patients because from Germany and authors from urology department)

Schwentner, C., Hennenlotter, J., Kuehs, U., Tews, V., Colleselli, D., Huber, S., Schilling, D., Sievert, K.-D. & Stenzl, A. (2010) Hematuria: Helpful or misleading for the early detection of transitional cell carcinoma-results from a cohort of 2008 patients. *Journal of Urology*, 183: e454.

Abstract only so limited information, but I think it's not in PICO (referred patients because from Germany and authors from urology department)

Schwentner, C., Hennenlotter, J., Kuehs, U., Tews, V., Colleselli, D., Huber, S., Schilling, D., Sievert, K.-D. & Stenzl, A. (2010) Impact of instrumented urinary sampling on the diagnostic value of urine tests (urovysionr, uCyt+r) and cytology for transitional cell carcinoma - Results from a cohort of 2077 patients. *Journal of Urology*, 183: e453-e454.

Abstract only so limited information, but I think it's not in PICO (referred patients because from Germany and authors from urology department)

Sears, C. L. G., Ward, J. F., Sears, S. T., Puckett, M. F., Kane, C. J. & Amling, C. L. (2002) Prospective comparison of computerized tomography and excretory urography in the initial evaluation of asymptomatic haematuria. *Journal of Urology*, 168: 2457-2460.

Not in PICO

Shah, O. & Taneja, S. S. (2004) Renal imaging: what the urologist wants to know. [Review] [101 refs]. *Magnetic Resonance Imaging Clinics of North America*, 12: 387-402.

Narrative review

Shi, G. H., Chen, Y., Yao, X. D., Zhang, S. L., Dai, B., Feng, L. Q., Zhang, H. L., Shen, Y. J., Zhu, Y., Zhu, Y. P., Xiao, W. J., Ma, C. G., Wen, L. G., Qin, X. J., Yang, L. F. & Ye, D. W. (2013) Individualized renal mass biopsy strategy for Chinese patients with different subtypes and necrosis area. *Urologic Oncology*, 31: 920-923.

Not in PICO

Shin, H. O., Kim, Y. S., Kim, K. D., Jang, I. H., Lee, S. Y., Kwon, Y. W. & Kim, T. H. (2008) Characteristics of incidentally detected renal cell carcinoma. [Korean]. *Korean Journal of Urology*, 49: 675-681.

Not in PICO

Shinagare, A. B., Silverman, S. G., Gershanik, E. F., Chang, S. L. & Khorasani, R. (2014) Evaluating hematuria: Impact of guideline adherence on urologic cancer diagnosis. *American Journal of Medicine*, 127: 625-632.

Not in PICO (setting; Willie agrees; also came up in bladder search)

Shvarts, O., Han, K. R., Seltzer, M., Pantuck, A. J. & Belldegrun, A. S. (2002) Positron emission tomography in urologic oncology. [Review] [52 refs]. *Cancer Control*, 9: 335-342.

Not in PICO

Sigalow, D. A., Waldbaum, R. S. & Lowe, F. C. (1991) Identification of asymptomatic renal cell carcinomas utilizing modern radiographic techniques. *New York State Journal of Medicine*, 91: 200-202.

Not in PICO

Silver, D. A., Morash, C., Brenner, P., Campbell, S. & Russo, P. (1997) Pathologic findings at the time of nephrectomy for renal mass. *Annals of Surgical Oncology*, 4: 570-574.

Not in PICO

- Siow, W. Y., Yip, S. K. H., Ng, L. G., Tan, P. H., Cheng, W. S. & Foo, K. T. (2000) Renal cell carcinoma: Incidental detection and pathological staging. *Journal of the Royal College of Surgeons of Edinburgh*, 45: 291-295.
Not in PICO
- Song, J., Tanagho, Y., Bhayani, S. & Figenshau, R. (2013) Factors predictive of symptomatic presentation in renal cell carcinoma. *Journal of Endourology*, 27: A383.
Not in PICO
- Speets, A. M., Kalmijn, S., Hoes, A. W., Van Der Graaf, Y. & Mali, W. P. T. (2006) Yield of abdominal ultrasound in patients with abdominal pain referred by general practitioners. *European Journal of General Practice*, 12: 135-137.
Not in PICO
- Stepan, J., Cepulic, M., Petkovic, I., Cizmic, A. & Nakic, M. (2007) Nephroblastomas - Wilm's tumor (WT). [Croatian]. *Paediatrica Croatica, Supplement*, 51: 92-97.
Narrative review
- Stutte, H., Bauer, B. & Grossmann, E. (1987) [Early sonographic recognition of renal cell carcinoma]. [German]. *Deutsche Medizinische Wochenschrift*, 112: 879-883.
Not in PICO
- Stutte, H., Bauer, B. & Grossmann, E. (1987) Early diagnosis of renal cell carcinoma by ultrasound. [German]. *Deutsche Medizinische Wochenschrift*, 112: 879-883.
Not in PICO
- Tada, S., Fukud, K., Aoyagi, Y. & Harada, J. (1980) CT of abdominal malignancies: dynamic approach. *AJR. American Journal of Roentgenology*, 135: 455-461.
Not in PICO
- Tada, S., Miura, S., Mizuma, K., Kurisu, Y. & Yasuda, M. (1988) Differential diagnosis of the early cancer: imaging diagnosis "CT". [Japanese]. *Gan no rinsho*, Japan: 1223-1226.
Narrative review
- Takahashi, N., Glockner, J. F., Hartman, R. P., King, B. F., Leibovich, B. C., Stanley, D. W., Fitz-Gibbon, P. D. & Kawashima, A. (2010) Gadolinium enhanced magnetic resonance urography for upper urinary tract malignancy. *Journal of Urology*, 183: 1330-1365.
Not in PICO
- Takebayashi, S., Hosaka, M., Takase, K., Kubota, N., Kishida, T. & Matsubara, S. (1999) Computerized tomography nephroscopic images of renal pelvic carcinoma. *Journal of Urology*, 162: 315-318.
Not in PICO
- Tamai, H., Takiguchi, Y., Oka, M., Shingaki, N., Enomoto, S., Shiraki, T., Furuta, M., Inoue, I., Iguchi, M., Yanaoka, K., Arij, K., Shimizu, Y., Nakata, H., Shinka, T., Sanke, T. & Ichinose, M. (2005) Contrast-enhanced ultrasonography in the diagnosis of solid renal tumors. *Journal of Ultrasound in Medicine*, 24: 1635-1640.
Not in PICO
- Tauber, S., Liedl, B., Schneede, P., Liessmann, F., Waidelich, R. & Hofstetter, A. (2001) [Fluorescence cytology of the urinary bladder]. [German]. *Urologe (Ausg.A)*, 40: 217-221.
Not in PICO (at least 17/27 had cancer)
- Taylor, P. M. (2002) Image-guided peritoneal access and management of complications in peritoneal dialysis. [Review] [25 refs]. *Seminars in Dialysis*, 15: 250-258.
Narrative review
- Teichman, J. M. H., Weiss, B. D. & Solomon, D. (1999) Urological needs assessment for primary care practice: Implications for undergraduate medical education. *Journal of Urology*, 161: 1282-1285.
Not in PICO (at least 17/27 had cancer)
- Telichko, F. F. & Iazykov, A. S. (1989) [Experimental and clinical rationale for the choice of optimal methods of x-ray diagnosis of kidney diseases]. [Russian]. *Vestnik Rentgenologii i Radiologii*.(5):62-7, 1989 Sep-Oct., 62-67.
Narrative review

- Teodorovich, O. V., Ternovoi, S. K., Vlasova, I. S., Zabrodina, N. B., Fominykh, E. V. & Kesov, I. (2006) [Comparative analysis of modern combined methods in diagnosis of renal cell carcinoma]. [Russian]. *Urologiia (Moscow, Russia)*.(5):3-6, 11, 2006 Sep-Oct., 3-6.
Not in PICO
- Terada, Y., Ueki, T. & Horiuchi, D. (1989) [A study on six cases of renal cell carcinoma detected by renal ultrasound during health screening]. [Japanese]. *Nippon Jinzo Gakkai Shi.Japanese Journal of Nephrology*, 31: 783-790.
Not in PICO
- Thompson, R. H., Hartman, R. P., Lowe, V. J., Kawashima, A. & Leibovich, B. C. (2004) Applications of positron emission tomography imaging, intraoperative ultrasonography, magnetic resonance imaging, and angiography in the evaluation of renal masses. [Review] [25 refs]. *Current Urology Reports*, 5: 30-34.
Narrative review
- Tiang, K. W., Ng, K. L., Vega-Vega, A. & Wood, S. (2014) A management dilemma of a rapidly enlarging chromophobe renal cell carcinoma during pregnancy. *BJU International*, 113: 70-71.
Not in PICO
- Tong, Y. C., Chieng, P. U., Tsai, T. C. & Lin, S. N. (1990) Renal angiomyolipoma: report of 24 cases. *British Journal of Urology*, 66: 585-589.
Not in PICO
- Tsvivan, M., Rampersaud, E. N., Pes, M. D. L., Joniau, S., Leveillee, R. J., Shingleton, W. B., Aron, M., Kim, C. Y., DeMarzo, A. M., Desai, M. M., Meler, J. D., Donovan, J. F., Klingler, H. C., Sopko, D. R., Madden, J. F., Marberger, M., Ferrandino, M. N. & Polascik, T. J. (2014) Small renal mass biopsy - how, what and when: report from an international consensus panel. *BJU International*, 113: 854-863.
Not in PICO
- Tsuboi, N., Horiuchi, K., Kimura, G., Kondoh, Y., Yoshida, K., Nishimura, T., Akimoto, M., Miyashita, T. & Subosawa, T. (2000) Renal masses detected by general health checkup. *International Journal of Urology*, 7: 404-408.
Not in PICO
- Ueda, T., Yasumasu, T., Uozumi, J. & Naito, S. (1991) Comparison of clinical and pathological characteristics in incidentally detected and suspected renal carcinoma. *British Journal of Urology*, 68: 470-472.
Not in PICO
- Ulu, E. M., Tutar, N. U., Coskun, M., Tore, H. G., Guvenc, Z. & Haberal, M. (2007) Abdominal computed tomography findings of malignant tumors in patients with solid organ transplants. *Transplantation Proceedings*, 39: 1066-1070.
Not in PICO
- van Weert, H. C. & Pinggen, F. (2009) Recurrent thrombophlebitis as a warning sign for cancer: a case report. *Cases journal*, 2: 153.
Not in PICO
- Van, C. R., Castillo, O., Aguirre, C., Azocar, G., Chamorro, A. & Medina, F. J. (1992) [Current diagnosis of renal cancer: clinical experience with 71 cases]. [Spanish]. *Revista Medica de Chile*, 120: 1118-1120.
Not in PICO
- Vasdev, N. & Thorpe, A. C. (2011) Has the introduction of the '2 week rule' in the UK led to an earlier diagnosis of urological malignancy? *ecancermedicalscience*, 5.
Not in PICO
- Vegso, G., Toronyi, E., Hajdu, M., Piros, L., Gorog, D., Deak, P. A., Doros, A., Peter, A. & Langer, R. M. (2011) Renal cell carcinoma of the native kidney: a frequent tumor after kidney transplantation with favorable prognosis in case of early diagnosis. *Transplantation Proceedings*, 43: 1261-1263.
Not in PICO

- Velkova, K. & Dimitrakov, D. (1992) Digital subtraction angiography in renal tumours. *Folia Medica (Plovdiv)*, 34: 39-45.
Not in PICO
- Venables, Z., Ramaiya, A., Holden, S. & Millington, G. W. M. (2013) Three generations of hereditary leiomyomatosis associated with renal cell cancer. *British Journal of Dermatology*, 169: 21.
Not in PICO
- Wang, G. Y. (700) [Asymptomatic renal cell carcinoma and small renal cell carcinoma]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]*, 27: 656-657.
Not in PICO
- Wang, L.-J., Wong, Y.-C., Huang, C.-C., Wu, C.-H., Hung, S.-C. & Chen, H.-W. (2010) Multidetector computerized tomography Urography is more accurate than excretory urography for diagnosing transitional cell carcinoma of the upper urinary tract in adults with hematuria. *Journal of Urology*, 183: 48-55.
Not in PICO
- Wessely, K., Biassoni, L. & McHugh, K. (2011) Pitfalls in paediatric oncology imaging. *Cancer Imaging*, 11: 144-154.
Narrative review
- Wiesbauer, P. (2008) [Nephrogenic tumors]. [German]. *Radiologe*, 48: 932-939.
Narrative review
- Wood, L. S. (2009) Renal cell carcinoma: screening, diagnosis, and prognosis. [Review] [29 refs]. *Clinical Journal of Oncology Nursing*, 13: Suppl-7.
Narrative review
- Wu, K. R. & Chen, Y. H. (191) [Early diagnosis of renal cell carcinoma]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]*, 26: 160-161.
Not in PICO
- Yap, N. Y., Ng, K. L., Ong, T. A., Pailoor, J., Gobe, G. C., Ooi, C. C., Razack, A. H., Dublin, N., Morais, C. & Rajandram, R. (2013) Clinical prognostic factors and survival outcome in renal cell carcinoma patients - a malaysian single centre perspective. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 14: 7497-7500.
Not in PICO
- Yashiro, N., Itai, Y., Ohtomo, K., Furui, S., Yoshikawa, K., Iio, M., Yoshida, H. & Asai, S. (1985) [Early renal carcinoma: clinical features, CT, and angiography]. [Japanese]. *Rinsho Hoshasen - Japanese Journal of Clinical Radiology*, 30: 875-881.
Not in PICO
- Yeoh, M., Lai, N. K., Anderson, D. & Appadurai, V. (2013) Macroscopic haematuria—a urological approach. *Australian Family Physician*, 42: 123-126.
Narrative review
- Yip, S. K., Peh, W. C., Tam, P. C., Li, J. H. & Lam, C. H. (1999) Role of ultrasonography in screening for urological malignancies in patients presenting with painless haematuria. *Annals of the Academy of Medicine, Singapore*, 28: 174-177.
Not in PICO (referred population)
- Yokom, D. W., Ihaddadene, R., Le, G. G. & Carrier, M. (2012) Incidental venous thromboembolism in kidney cancer patients: A retrospective case-control study. *Blood*, 120.
Not in PICO
- Yokom, D. W., Ihaddadene, R., Le, G. G., Moretto, P. & Carrier, M. (2013) Incidental venous thromboembolism in kidney cancer patients: A case-control study. *Journal of Thrombosis and Haemostasis*, 11: 330.
Not in PICO
- Yuan, X.-C., Wang, Y., Zhou, A.-Y., Chen, L., Den, L.-Y. & Liu, J. (2011) Comparison on contrast-enhanced ultrasonography and CT in diagnosing renal cell carcinoma. [Chinese]. *Chinese Journal*

of Medical Imaging Technology, 27: 2502-2505.

Not in PICO

Zeman, R. K., Zeiberg, A., Hayes, W. S., Silverman, P. M., Cooper, C. & Garra, B. S. (1996) Helical CT of renal masses: the value of delayed scans. *AJR.American Journal of Roentgenology*, 167: 771-776.

Not in PICO

Zieger, M., Buck, J. & Heuck, F. (1983) [Normal renal variations as a cause of sonographically suspect tumors]. [German]. *Radiologe*, 23: 256-259.

Not in PICO

Zieger, M., Buck, J. & Heuck, F. (1983) Physiological renal variations causing the sonographic tentative diagnosis of renal tumors. [German]. *Radiologe*, 23: 256-259.

Not in PICO

Zielinski, H. (2005) Early detection of renal cancer. [Polish]. *Wspolczesna Onkologia*, 9: 98-100.

Narrative review

Zollner, S., Dirksen, U., Jurgens, H. & Ranft, A. (2013) Renal Ewing tumors. *Annals of Oncology*, 24: 2455-2461.

Not in PICO

Zubarev, A. V., Nasnikova, I. I., Kozlov, V. P., Grishin, M. A. & Sal'nikov, D. V. (2001) [Ultrasound angiography: new perspectives in diagnosis of renal mass lesions]. [Russian]. *Terapevticheskii Arkhiv*, 73: 46-50.

Not in PICO

TESTICULAR CANCER

Review question:

What is the risk of testicular cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

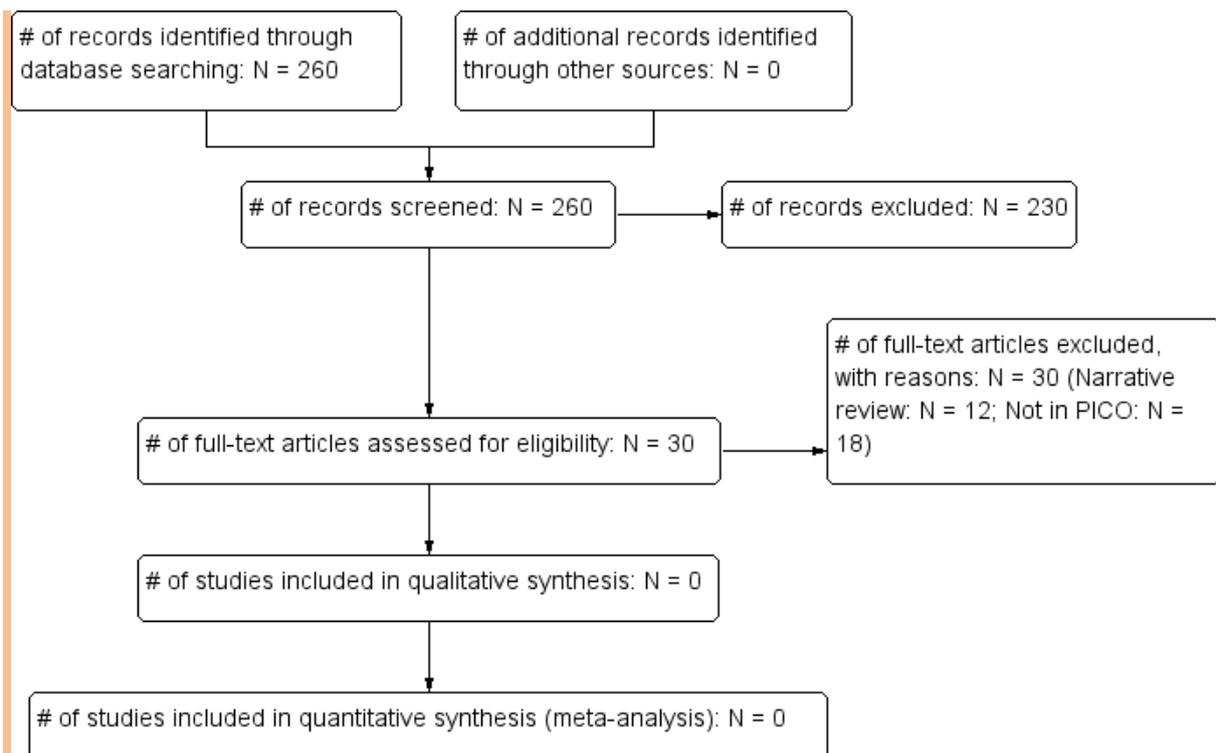
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	901	159	13/09/2012
<i>Premedline</i>	All-2012	24	6	13/09/2012
<i>Embase</i>	All-2012	871	167	20/09/2012
<i>Cochrane Library</i>	All-2012	23	1	20/09/2012
<i>Psychinfo</i>	All-2012	9	6	13/09/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	106	23	20/09/2012
<i>Biomed Central</i>	All-2012	2	0	20/09/2012

Total References retrieved (after de-duplication): 258

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	9/2012-27/08/2014	30	1	27/08/2014
<i>Premedline</i>	9/2012-27/08/2014	52	0	27/08/2014
<i>Embase</i>	9/2012-27/08/2014	77	2	27/08/2014
<i>Cochrane Library</i>	9/2012-27/08/2014	13	0	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	9/2012-27/08/2014	18	0	27/08/2014

Total References retrieved (after de-duplication): 2



Study results

No evidence was identified.

References

Included studies

None

Excluded studies (with excl reason)

Information from your family doctor. Testicular cancer. American Family Physician 69[3], 613-614. 1-2-2004.

Excl reason: Patient information booklet

Information from your family doctor: Testicular cancer: what to look for. American Family Physician 74[9], 1571-1572. 1-11-2006.

Excl reason: Patient information booklet

Aigner, F., De, Zordo T., Pallwein-Prettner, L., Junker, D., Schafer, G., Pichler, R., Leonhartsberger, N., Pinggera, G., Dogra, V. S., and Frauscher, F. Real-time sonoelastography for the evaluation of testicular lesions. Radiology 263[2], 584-589. 2012.

Excl reason: Not in PICO

Albers, P., Albrecht, W., Algaba, F., Bokemeyer, C., Cohn-Cedermark, G., Fizazi, K., Horwich, A., Laguna, M. P., and European Association of Urology. [EAU guidelines on testicular cancer: 2011 update. European Association of Urology]. [Spanish]. Actas Urologicas Espanolas 36[3], 127-145. 2012.

Excl reason: Guideline

Allen, D., Popert, R., and O'Brien, T. The two-week-wait cancer initiative in urology: useful modernization? Journal of the Royal Society of Medicine 97[6], 279-281. 2004.

Excl reason: Not in PICO

- Almstrup, K., Rajpert-De, Meyts E., Nielsen, J. E., Mogensen, H. O., Lippert, M. F., Foged, N. T., Hansen, J. D., and Skakkebaek, N. E. Non-invasive screening for early stage testicular cancer by cytological slide scanning and image analysis of semen samples. *APMIS* 119, 52-53. 2011. Blackwell Munksgaard.
Excl reason: Not in PICO
- Anderson, E. E. Early diagnosis of testicular carcinoma: self-examination of the testicle. *North Carolina Medical Journal* 46[7], 407-409. 1985.
Excl reason: Narrative review
- Arce, Terroba Y., Algaba-Arrea, F., and Villavicencio, Maverich H. [Segmental infarct of testicle: an infrequent pseudotumor]. [Spanish]. *Actas Urologicas Espanolas* 34[2], 194-200. 2010.
Excl reason: Not in PICO
- Austoker, J. Screening for ovarian, prostatic, and testicular cancers. *British Medical Journal* 309[6950], 315-320. 30-7-1994.
Excl reason: Not in PICO
- Austoker, J., Bankhead, C., Forbes, L. J. L., Atkins, L., Martin, F., Robb, K., Wardle, J., and Ramirez, A. J. Interventions to promote cancer awareness and early presentation: Systematic review. *British Journal of Cancer* 101, S31-S39. 2009.
Excl reason: Not in PICO
- Aviles-Salas, A., Turbiner-Miasnikova, J., Labardini-Mendez, J. R., and Sobrevilla-Calvo, P. D. J. Primary Testicular Lymphomas. Clinicopathologic Analysis of 10 Cases. Experience at the National Institute of Cancerology in Mexico City. [Spanish]. *Gaceta Medica de Mexico* 140[2], 123-128. 2004.
Excl reason: Not in PICO
- Barnhouse, K., Powers, A., and Smith, P. C. Clinical inquiries. How should you further evaluate an adult with a testicular mass? *Journal of Family Practice* 56[10], 851-853. 2007.
Excl reason: Narrative review
- Barrass, B. J. R., Scurrill, S., Banerjee, G., and Parry, J. R. W. Anxious patients with benign scrotal symptoms achieve excellent reassurance from imaging in a one-stop clinic. *British Journal of Medical and Surgical Urology* 3[3], 111-115. 2010.
Excl reason: Not in PICO
- Bell, D., Morash, C., Dranitsaris, G., Izawa, J., Short, T., Klotz, L. H., Fleshner, N., and Canadian surgical wait times (SWAT) initiative. Does prolonging the time to testicular cancer surgery impact long-term cancer control: a systematic review of the literature. [Review] [24 refs]. *Canadian Journal of Urology* 13, Suppl-6. 2006.
Excl reason: Not in PICO
- Bergholz, R. and Wenke, K. Polyorchidism: a meta-analysis. *Journal of Urology* 182[5], 2422-2427. 2009.
Excl reason: Not in PICO
- Bleyer, A. CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology* 36[3], 207-212. 2009.
Excl reason: Narrative review
- Bosl, G. J., Vogelzang, N. J., Goldman, A., Fraley, E. E., Lange, P. H., Levitt, S. H., and Kennedy, B. J. Impact of delay in diagnosis on clinical stage of testicular cancer. *Lancet* 2[8253], 970-973. 31-10-1981.
Excl reason: Not in PICO
- Bower, M., Ma, R., Savage, P., Abel, P., and Waxman, J. British urological surgery practice: 2. Renal, bladder and testis cancer. *British Journal of Urology* 81[4], 513-517. 1998.
Excl reason: Not in PICO
- Brahams, D. Missed diagnosis of testicular cancer. *Lancet* 339[8795], 734-735. 21-3-1992.
Excl reason: Not in PICO

Bridges, B. and Hussain, A. Testicular germ cell tumors. [Review] [45 refs]. *Current Opinion in Oncology* 18[3], 271-276. 2006.
Excl reason: Not in PICO

Brock, D., Fox, S., Gosling, G., Haney, L., Kneebone, P., Nagy, C., and Qualitza, B. Testicular cancer. [Review] [57 refs]. *Seminars in Oncology Nursing* 9[4], 224-236. 1993.
Excl reason: Narrative review

Buchler, T., Kubankova, P., Boublikova, L., Donatova, Z., Foldyna, M., Kanakova, J., Kordikova, D., Kupec, M., Nepomucka, J., Vorsilkova, E., and Abrahamova, J. Detection of second malignancies during long-term follow-up of testicular cancer survivors. *Cancer* 117[18], 4212-4218. 15-9-2011.
Excl reason: Not in PICO

Buckland, T. Hitting testicular cancer where it hurts: Through public awareness and post-treatment support. *Cancer Research* 71[8 SUPPL. 1], 15-4-2011. American Association for Cancer Research Inc.
Excl reason: Not in PICO

Carlsen, E., Giwercman, A., Keiding, N., and Skakkebaek, N. E. Declining Semen Quality and Increasing Incidence of Testicular Cancer - Is There A Common-Cause. *Environmental Health Perspectives* 103, 137-139. 1995.
Excl reason: Narrative review

Carmignani, L., Colombo, R., Gadda, F., Galasso, G., Lania, A., Palou, J., Algaba, F., Villavicencio, H., Colpi, G. M., Decobelli, O., Salvioni, R., Pizzocaro, G., Rigatti, P., and Rocco, F. Conservative Surgical Therapy for Leydig Cell Tumor. *Journal of Urology* 178[2], 507-511. 2007.
Excl reason: Not in PICO

Casey, R. G., Grainger, R., Butler, M., McDermott, T. E., and Thornhill, J. A. Scrotal signs and symptoms in the general population, the value of testis self-examination and the pitfalls of a scrotal screening programme: is the two-week rule relevant? *World Journal of Urology* 29[3], 387-391. 2011.
Excl reason: Not in PICO

Cavanaugh, Jr. Genital self-examination in adolescent males. *American Family Physician* 28[3], 199-201. 1983.
Excl reason: Not in PICO

Chapple, A., Ziebland, S., and McPherson, A. Qualitative study of men's perceptions of why treatment delays occur in the UK for those with testicular cancer. *British Journal of General Practice* 54[498], 25-32. 2004.
Excl reason: Not in PICO

Chevalier, N., Vega, A., Bouskine, A., Siddeek, B., Michiels, J. F., Chevallier, D., and Fenichel, P. GPR30, the non-classical membrane G protein related estrogen receptor, is overexpressed in human seminoma and promotes seminoma cell proliferation. *PLoS ONE [Electronic Resource]* 7[4], e34672. 2012.
Excl reason: Not in PICO

Chierigo, P., Puccetti, O., Visona, A., Bassan, F., Rahmati, M., Lazzarotto, M., and Franzolin, N. [High alpha-fetoprotein persistence after orchiectomy. On a case of uncommon etiology]. [Italian]. *Urologia (Treviso)* 77, Suppl-31. 2010.
Excl reason: Not in PICO

Chilvers, C. E. D., Forman, D., Oliver, R. T. D., Pike, M. C., Davey, G., Coupland, C. A. C., Baker, K., Dawson, S., Cartwright, R. A., Elwood, P. C., Birch, J., Tyrrell, C., Brett, R., Bush, T., Isbell, V., Cornwell, A., Steer, R., Thistlethwaite, S., Gellman, H., Hughes, J., Llewellyn, M., Ardernjones, A., Allen, A., Hilton, E., Lloyd, B., Mcveigh, S., Thorne, M., Trowbridge, P., and Reid, S. Social, Behavioral and Medical Factors in the Etiology of Testicular Cancer - Results from the Uk Study. *British Journal of Cancer* 70[3], 513-520. 1994.
Excl reason: Not in PICO

- Clarke, K., Howard, G. C., Elia, M. H., Hutcheon, A. W., Kaye, S. B., Windsor, P. M., and Yosef, H. M. Referral patterns within Scotland to specialist oncology centres for patients with testicular germ cell tumours. The Scottish Radiological Society and the Scottish Standing Committee of the Royal College of Radiologists. *British Journal of Cancer* 72[5], 1300-1302. 1995.
Excl reason: Not in PICO
- Congeni, J., Miller, S. F., and Bennett, C. L. Awareness of genital health in young male athletes. *Clinical Journal of Sport Medicine* 15[1], 22-26. 2005.
Excl reason: Not in PICO
- Connolly, J. G. Genitourinary malignancies. *Canadian Family Physician* 21[12], 38-43. 1975.
Excl reason: Narrative review
- Connolly, S. S., D'Arcy, F. T., Bredin, H. C., Callaghan, J., and Corcoran, M. O. Value of frozen section analysis with suspected testicular malignancy. *Urology* 67[1], 162-165. 2006.
Excl reason: Not in PICO
- Cook, N. Testicular cancer: testicular self-examination and screening. [Review] [52 refs]. *British Journal of Nursing* 9[6], 338-343. 23-3-2000.
Excl reason: Not in PICO
- Cummings, K. M., Lampon, D., Mettlin, C., and Pontes, J. E. What young men know about testicular cancer. *Preventive Medicine* 12[2], 326-330. 1983.
Excl reason: Not in PICO
- Daneliia, E. V., Gotsadze, D. T., and Pirtskhalaishvili, G. G. The lack of knowledgeability of men about testicular tumors as a cause for the late diagnosis of this disease. [Russian]. *Voprosy Onkologii* 38[10], 1254-1258. 1992.
Excl reason: Not in PICO
- Daneliya, E. V., Gotsadze, D. T., and Pirtskhalaishvili, G. G. Lack of knowledge about testicular cancer as a factor of untimely diagnosis. [Russian]. *Voprosy Onkologii* 38[10-12], 1254-1258. 1992.
Excl reason: Not in PICO
- Dawson, C. Testicular cancer: seek advice early. *Journal of Family Health Care* 12[1], 3. 2002.
Excl reason: Not in PICO
- De Backer A., Madern, G. C., Hakvoort-Cammel, F. G., Oosterhuis, J. W., and Hazebroek, F. W. Mediastinal germ cell tumors: clinical aspects and outcomes in 7 children. *European Journal of Pediatric Surgery* 16[5], 318-322. 2006.
Excl reason: Not in PICO
- De Padova S., Rosti, G., Scarpi, E., Salvioni, R., Amadori, D., De, Giorgi U., and Italian Germ Cell Cancer Group (. Expectations of survivors, caregivers and healthcare providers for testicular cancer survivorship and quality of life. *Tumori* 97[3], 367-373. 2011.
Excl reason: Not in PICO
- De, Nooijer J., Lechner, L., and De, Vries H. A qualitative study on detecting cancer symptoms and seeking medical help; an application of Andersen's model of total patient delay. *Patient Education and Counseling* 42[2], 145-157. 2001.
Excl reason: Not in PICO
- Descazeaud, A. and Mottet, N. [Cancers of the penis and testicle: news in 2008]. [French]. *Progres En Urologie* 18, Suppl-4. 2008.
Excl reason: Not in PICO
- Desgrandchamps, F. Undescended testes. Current state of knowledge. [French]. *Journal d'urologie* 96[8], 407-414. 1990.
Excl reason: Not in PICO
- Dieckmann, K.-P., Kulejewski, M., Heinemann, V., and Loy, V. Testicular biopsy for early cancer detection - objectives, technique and controversies. *International Journal of Andrology* 34[4 PART 2], e7-e13. 2011.
Excl reason: Not in PICO

- Dieckmann, K. P., Kulejewski, M., Pichlmeier, U., and Loy, V. Diagnosis of contralateral testicular intraepithelial neoplasia (TIN) in patients with testicular germ cell cancer: systematic two-site biopsies are more sensitive than a single random biopsy. *European Urology* 51[1], 175-183. 183.
Excl reason: Not in PICO
- Dieckmann, K. P., Becker, T., Dextl, A. M., and Bauer, H. W. [Early diagnosis in testicular tumors. Results of a survey]. [Review] [41 refs] [German]. *Medizinische Klinik* 82[18], 602-605. 4-9-1987.
Excl reason: Not in PICO
- Dieckmann, K. P., Kulejewski, M., Heinemann, V., and Loy, V. Testicular biopsy for early cancer detection--objectives, technique and controversies. [Review]. *International Journal of Andrology* 34[4:Pt 2], t-13. 2011.
Excl reason: Not in PICO
- Diotallevi, M. Testicular self-examination: are primary care physicians teaching this preventive measure? *Canadian Family Physician* 35, 1037-1039. 1989.
Excl reason: Not in PICO
- Docimo, S. G., Silver, R. I., and Cromie, W. The undescended testicle: diagnosis and management. [Review] [34 refs]. *American Family Physician* 62[9], 2037-2044. 2007.
Excl reason: Not in PICO
- Doherty, A. P., Bower, M., and Christmas, T. J. The role of tumour markers in the diagnosis and treatment of testicular germ cell cancers. [Review] [41 refs]. *British Journal of Urology* 79[2], 247-252. 1997.
Excl reason: Not in PICO
- Dube, C. E. and Fuller, B. K. A qualitative study of communication skills for male cancer screening discussions. *Journal of Cancer Education* 18[4], 182-187. 2003.
Excl reason: Not in PICO
- DuFour, J. L. Testicular cancer. Early action required. *Advance for Nurse Practitioners* 8[11], 77-78. 2000.
Excl reason: Narrative review
- Edelman, M. J., Meyers, F. J., and Siegel, D. The utility of follow-up testing after curative cancer therapy. A critical review and economic analysis. [Review] [133 refs]. *Journal of General Internal Medicine* 12[5], 318-331. 1997.
Excl reason: Not in PICO
- Evans, R. E., Simon, A. E., and Wardle, J. Public perceptions of the harms and benefits of testicular cancer education: a qualitative study. *Cancer Epidemiology* 34[2], 212-219. 2010.
Excl reason: Not in PICO
- Farrer, F. Cancer screening in primary care. *SA Pharmaceutical Journal* 77[9], 41-45. 2010.
Excl reason: Not in PICO
- Favilla, V., Cimino, S., Madonia, M., and Morgia, G. New advances in clinical biomarkers in testis cancer. [Review] [246 refs]. *Frontiers in Bioscience* 2, 456-477. 2010.
Excl reason: Not in PICO
- Foo, K. T. (2013) The role of transabdominal ultrasound in office urology. *Proceedings of Singapore Healthcare*, 22: 125-130.
Narrative review
- Forman, D., Pike, M. C., Davey, G., Dawson, S., Baker, K., Chilvers, C. E. D., Oliver, R. T. D., and Coupland, C. A. C. Aetiology of testicular cancer: Association with congenital abnormalities, age at puberty, infertility, and exercise. *British Medical Journal* 308[6941], 1393-1399. 1994.
Excl reason: Not in PICO
- Fossa, S. D., Klepp, O., and Elgjo, R. F. The effects of patient's delay and doctor's delay in patients with malignant germ cell tumours. *International Journal of Andrology* 4[Suppl. 4], 134-145. 1981.
Excl reason: Not in PICO
- Foster, P. W., Ritchie, A. W., and Jones, D. J. Prospective analysis of scrotal pathology referrals - are referrals appropriate and accurate? *Annals of the Royal College of Surgeons of England* 88[4],

363-366. 2006.

Excl reason: Not in PICO

Fredslund, Breinholt M. and Moller, Hansen T. Testicular yolk sac tumour in an 82 years old man. *APMIS* 119, 55. 2011. Blackwell Munksgaard.

Excl reason: Not in PICO

Friman, P. C., Finney, J. W., Glasscock, S. G., Weigel, J. W., and Christophersen, E. R. Testicular self-examination: validation of a training strategy for early cancer detection. *Journal of Applied Behavior Analysis* 19[1], 87-92. 1986.

Excl reason: Not in PICO

Garner, M. J., Turner, M. C., Ghadirian, P., and Krewski, D. Epidemiology of testicular cancer: an overview. [Review] [173 refs]. *International Journal of Cancer* 116[3], 331-339. 1-9-2005.

Excl reason: Narrative review

Gascoigne, P., Mason, M. D., and Roberts, E. Factors affecting presentation and delay in patients with testicular cancer: results of a qualitative study. *Psycho-Oncology* 8[2], 144-154. 1999.

Excl reason: Not in PICO

Geczi, L., Gomez, F., Horvath, Z., Bak, M., Kisbenedek, L., and Bodrogi, I. Three-year results of the first educational and early detection program for testicular cancer in Hungary. *Oncology* 60[3], 228-234. 2001.

Excl reason: Not in PICO (respondents to an awareness campaign)

Geczi, L., Gomez, F., Bak, M., and Bodrogi, I. The incidence, prognosis, clinical and histological characteristics, treatment, and outcome of patients with bilateral germ cell testicular cancer in Hungary. *Journal of Cancer Research & Clinical Oncology* 129[5], 309-315. 2003.

Excl reason: Not in PICO

Geiss, K., Meyer, M., Eberle, A., Luttmann, S., Stabenow, R., Hentschel, S., Nennecke, A., Kieschke, J., Sirri, E., Holleczeck, B., Emrich, K., Kajuter, H., Mattauch, V., Katalinic, A., Kraywinkel, K., Brenner, H., Gondos, A., and Hiripi, E. Survival from common and rare cancers in Germany in the early 21st century. *Annals of Oncology* 23[2], 472-479. 2012.

Excl reason: Not in PICO

Germa-Lluch, J. R., Garcia, del Muro, X, Maroto, P., Paz-Ares, L., Arranz, J. A., Guma, J., Alba, E., Sastre, J., Aparicio, J., Fernandez, A., Barnadas, A., Terrassa, J., Saenz, A., Almenar, D., Lopez-Brea, M., Climent, M. A., Sanchez, M. A., Lasso, de la, V, Berenguer, G., Perez, X., and Spanish Germ-Cell Cancer Group (. Clinical pattern and therapeutic results achieved in 1490 patients with germ-cell tumours of the testis: the experience of the Spanish Germ-Cell Cancer Group (GG). *European Urology* 42[6], 553-562. 562.

Excl reason: Not in PICO

Giesinger, J. M., Oberguggenberger, A., Kemmler, G., Gamper, E., Steiner, H., Sztankay, M., and Holzner, B. Electronic patient-reported outcome monitoring in testicular cancer patients. *Value in Health* 14[7], A460. 2011. Elsevier Ltd.

Excl reason: Not in PICO

Giwerzman, A. and Petersen, P. M. Cancer and male infertility. [Review] [79 refs]. *Best Practice & Research Clinical Endocrinology & Metabolism* 14[3], 453-471. 2000.

Excl reason: Not in PICO

Goldenring, J. M. and Purtell, E. Knowledge of testicular cancer risk and need for self-examination in college students: a call for equal time for men in teaching of early cancer detection techniques. *Pediatrics* 74[6], 1093-1096. 1984.

Excl reason: Not in PICO

Golovsky, D. Scrotal swellings: An approach for GPs. *Medicine Today* 6[5], 45-48. 2005.

Excl reason: Narrative review

Gottesman, J. and Baum, N. Common urologic disorders: When to treat and when to refer. *Postgraduate Medicine* 102[2], 235-246. 1997.

Excl reason: Narrative review

Grant, R. and Graus, F. Paraneoplastic movement disorders. [Review] [79 refs]. *Movement Disorders* 24[12], 1715-1724. 15-9-2009.
Excl reason: Not in PICO

Green, D. M. Testicular tumors in infants and children. [Review] [51 refs]. *Seminars in Surgical Oncology* 2[3], 156-162. 1986.
Excl reason: Narrative review

Gruschwitz, T. and Grimm, M.-O. Studieearly recognition in urology. [German]. *Onkologie* 18[3], 243-247. 2012.
Excl reason: Narrative review

Guinan, P. and Rubenstein, M. Methods of early diagnosis in genitourinary cancer. [Review] [163 refs]. *Cancer* 60[3:Suppl], Suppl-76. 1-8-1987.
Excl reason: Narrative review

Guthrie, J. A. and Fowler, R. C. Ultrasound diagnosis of testicular tumours presenting as epididymal disease. *Clinical Radiology* 46[6], 397-400. 1992.
Excl reason: Not in PICO

Hagerty, J. A. and Yerkes, E. B. Pediatric Scrotal Masses. *Clinical Pediatric Emergency Medicine* 10[1], 50-55. 2009.
Excl reason: Narrative review

Haggerty, B. J. Prevention and differential of scrotal cancer. *Nurse Practitioner* 8[10], 45-Dec. 1983.
Excl reason: Narrative review

Hanna, L. M., Taggart, L., and Cousins, W. Cancer prevention and health promotion for people with intellectual disabilities: an exploratory study of staff knowledge. *Journal of Intellectual Disability Research* 55[3], 281-291. 2011.
Excl reason: Not in PICO

Harris, M. F. and McKenzie, S. Men's health: What's a GP to do? *Medical Journal of Australia* 185[8], 440-444. 16-10-2006.
Excl reason: Not in PICO

Harzmann, R. [Early diagnosis of urogenital tumors]. [German]. *Zeitschrift fur Hautkrankheiten* 62[9], 665-676. 681.
Excl reason: Narrative review

Hawary, A. M., Warburton, H. E., Brough, R. J., Collins, G. N., Brown, S. C., O'Reilly, P. H., and Adeyoju, A. A. The '2-week wait' rule for referrals for suspected urological cancers--urgent need for refinement of criteria. *Annals of the Royal College of Surgeons of England* 90[6], 517-522. 2008.
Excl reason: Not in PICO

Haynes, J. H. Inguinal and scrotal disorders. *Surgical Clinics of North America* 86[2], 371-+. 2006.
Excl reason: Narrative review

Heidenreich, A., Krege, S., and Flasshove, M. [Interdisciplinary cooperation in the treatment of complex patients with advanced testicular germ cell tumor]. [Review] [35 refs] [German]. *Urologe (Auszg.)* 43[12], 1521-1530. 2004.
Excl reason: Not in PICO

Heidenreich, A., Bokemeyer, C., and Souchon, R. [Stage-specific treatment for testicular germ cell tumours]. [Review] [55 refs] [German]. *Urologe (Auszg.)* 48[4], 377-385. 2009.
Excl reason: Not in PICO

Hemminki, K., Sundquist, J., and Lorenzo, Bermejo J. Familial risks for cancer as the basis for evidence-based clinical referral and counseling. *The Oncologist* 13[3], 239-247. 2008.
Excl reason: Not in PICO

Hernandez-Rodriguez, J., Tan, C. D., Koenig, C. L., Khasnis, A. A., Rodriguez, E. R., and Hoffman, G. S. Testicular vasculitis: Findings differentiating isolated from systemic disease in 75 patients. *Arthritis and Rheumatism* 60, 1832. 2009. John Wiley and Sons Inc.
Excl reason: Not in PICO

Hernandez-Rodriguez, J., Tan, C. D., Koenig, C. L., Khasnis, A., Rodriguez, E. R., and Hoffman, G. S. Testicular vasculitis: findings differentiating isolated disease from systemic disease in 72 patients. *Medicine* 91[2], 75-85. 2012.
Excl reason: Not in PICO

Hernes, E. H., Harstad, K., and Fossa. Changing incidence and delay of testicular cancer in southern Norway (1981-1992). *European Urology* 30[3], 349-357. 1996.
Excl reason: Not in PICO

Hisamatsu, E., Takagi, S., Nakagawa, Y., Sugita, Y., Yoshino, K., Ueoka, K., and Tanikaze, S. Prepubertal testicular tumors: a 20-year experience with 40 cases. *International Journal of Urology* 17[11], 956-959. 2010.
Excl reason: Not in PICO

Horowitz, A. L., Reinert, S., and Caldamone, A. A. Teaching testicular self-examination in the pediatric outpatient setting: a survey of pediatricians and family doctors. *Medicine & Health, Rhode Island* 89[11], 370-371. 375.
Excl reason: Not in PICO

Houlgatte, A., Houdelette, P., Berlizot, P., Fournier, R., Bernard, O., and Schill, H. [Bilateral tumors of the testis: the role of the diagnosis of carcinoma in situ in early detection]. [French]. *Progres En Urologie* 5[4], 540-543. 1995.
Excl reason: Not in PICO

Howard, G. C., Nairn, M., and Guideline Development Group. Management of adult testicular germ cell tumours: summary of updated SIGN guideline. *BMJ* 342, d2005. 2011.
Excl reason: Not in PICO

Huddart, R. Learning lessons from the past: The path forward and new opportunities. *Radiotherapy and Oncology* 99, S224. 2011. Elsevier Ireland Ltd.
Excl reason: Narrative review

Iammarino, N. K. and Scardino, P. T. Testicular cancer: the role of the primary care physician in prevention and early detection. [Review] [33 refs]. *Texas Medicine* 87[5], 66-71. 1991.
Excl reason: Narrative review

Inatomi, H., Hamasaki, T., Ikuyama, T., Yamaguchi, R., Sato, H., Mineta, K., Takahashi, K., and Matsumoto, T. Testicular germ cell tumors in undescended testes: A report of five cases. [Japanese]. *Nishinippon Journal of Urology* 63[6], 395-398. 2001.
Excl reason: Not in PICO

Isidori, A. M. Ultrasonography: Testis and accessory glands. *International Journal of Andrology* 33, 25. 2010. Blackwell Publishing Ltd.
Excl reason: Not in PICO

Ivaz, Stella. Testicular cancer awareness. [References]. *Family Practice* 19[6], 707. 2002.
Excl reason: Not in PICO

Jeong, S. and Park, E. Neonatal scrotal disorder: Sonographic finding and anatomical consideration. *Pediatric Radiology* 41, S351. 2011. Springer Verlag.
Excl reason: Not in PICO

Jones, R. H. and Vasey, P. A. Part I: testicular cancer--management of early disease. [Review] [53 refs]. *Lancet Oncology* 4[12], 730-737. 2003.
Excl reason: Not in PICO

Jones, T. D., MacLennan, G. T., Bonnin, J. M., Varsegi, M. F., Blair, J. E., and Cheng, L. Screening for intratubular germ cell neoplasia of the testis using OCT4 immunohistochemistry. *American Journal of Surgical Pathology* 30[11], 1427-1431. 2006.
Excl reason: Not in PICO

Jones, W. and Appleyard, I. Early diagnosis of testicular cancer. *Practitioner* 233[1466], 509. 8-4-1989.
Excl reason: Narrative review

Josephides, E., Gala, A., and Chowdhury, S. GPs have key role in managing men with testicular cancer. *Practitioner* 258, 19-23. 2014.
Excl reason: Not in PICO

Junnila, J. and Lassen, P. Testicular masses. [Review] [21 refs]. *American Family Physician* 57[4], 685-692. 15-2-1998.
Excl reason: Narrative review

Junuzovic, D., Mehmedbasic, S., Mehmedbasic, E., and Spahovic, A. Incidence of testicular carcinoma, therapy and quality assesment. *Medicinski Arhiv* 65[3], 164-167. 2011.
Excl reason: Not in PICO

Karl, A., Seitz, M., Tritschler, S., Clevert, D., Gratzke, C., and Stief, C. [Scrotal masses]. [German]. *MMW Fortschritte der Medizin* 149[17], 44-48. 20-11-1949.
Excl reason: Narrative review

Kath, R., Schneider, C. P., and Hoffken, K. Measures for early detection in oncology: Secondary prevention. [German]. *Onkologe* 4[8], 731-739. 1998.
Excl reason: Not in PICO/narrative review

Kawai, T., Yamauchi, T., Tachibana, Y., Yoshino, S., and Kokuho, M. [Early detection of urogenital cancers: kidney, bladder, prostatic and testicular cancers]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics* 34[10], 1403-1407. 1988.
Excl reason: Narrative review

Kaufman, M. & Levine, D. L. (2013) A case of advanced testicular cancer in a society of racial and socioeconomic health disparity. *Journal of General Internal Medicine*, 28: S264-S265.
Not in PICO

Kay, R. Prepubertal testicular tumor registry. *Journal of Urology* 150[2 SUPPL.], 671-674. 1993.
Excl reason: Not in PICO

Kedzeriewicz, R., Chargari, C., Le, Moulec S., Jacques, Ferrandes N., Houlgatte, A., and Vedrine, L. Knowledge of testicular cancer and screening acceptance: Results from a prospective study. *Journal of Clinical Oncology* 29[7 SUPPL. 1]. 1-3-2011. American Society of Clinical Oncology.
Excl reason: Not in PICO

Kelsberg, G., Bishop, R., and Morton, J. When should a child with an undescended testis be referred to a urologist? *Journal of Family Practice* 55[4], 336-337. 2006.
Excl reason: Not in PICO

Kelsberg, G., Bishop, R., Morton, J., and Thomason, D. Clinical inquiries. When should a child with an undescended testis be referred to a urologist?. [Review] [9 refs]. *Journal of Family Practice* 55[4], 336-337. 2006.
Excl reason: Not in PICO

Khadra, A. and Oakeshott, P. Pilot study of testicular cancer awareness and testicular self-examination in men attending two South London general practices. *Family Practice* 19[3], 294-296. 2002.
Excl reason: Not in PICO

Kiss, A., Csontai, A., Merksz, M., Szonyi, P., and Goracz, G. Intrascrotal and testicular solid masses in childhood. *International Urology & Nephrology* 28[6], 787-792. 1996.
Excl reason: Not in PICO

Klein, J. F., Berry, C. C., and Felice, M. E. The development of a testicular self-examination instructional booklet for adolescents. *Journal of Adolescent Health Care* 11[3], 235-239. 1990.
Excl reason: Not in PICO

Kliesch, S. [Diagnosis and primary treatment of testicular tumor]. [Review] [21 refs] [German]. *Urologe (Auszg.A)* 43[12], 1494-1499. 2004.
Excl reason: Narrative review

Knapp, R. H., Hurt, R. D., Payne, W. S., Farrow, G. M., Lewis, B. D., Hahn, R. G., Muhm, J. R., and Earle, J. D. Malignant germ cell tumors of the mediastinum. *Journal of Thoracic & Cardiovascular*

Surgery 89[1], 82-89. 1985.

Excl reason: Not in PICO

Kobayashi, M. and Padival, S. Supraclavicular lymphadenopathy as initial presentation for testicular cancer: An important differential diagnosis for young men. *Journal of General Internal Medicine* 26, S470-S471. 2011. Springer New York.

Excl reason: Not in PICO

Kopp, H. G., Kuczyk, M., Classen, J., Stenzl, A., Kanz, L., Mayer, F., Bamberg, M., and Hartmann, J. T. Advances in the treatment of testicular cancer. [Review] [172 refs]. *Drugs* 66[5], 641-659. 2006.

Excl reason: Not in PICO

Kosan, M., Gonulalan, U., Ugurlu, O., Oztekin, V., Akdemir, O., and Adsan, O. Testicular microlithiasis in patients with scrotal symptoms and its relationship to testicular tumors. *Urology* 70[6], 1184-1186. 2007.

Excl reason: Not in PICO

Kumaraswamy, P., Cox, R., O'Rourke, J. S., and Willis, R. G. Audit of two-week rule referrals for suspected testicular cancer in Cornwall, 2003-2005. *Annals of the Royal College of Surgeons of England* 91[3], 239-244. 2009.

Excl reason: Not in PICO

Laguna, M. P., Pizzocaro, G., Klepp, O., Algaba, F., Kisbenedek, L., Leiva, O., and EAU Working Group on Oncological Urology. EAU guidelines on testicular cancer. *European Urology* 40[2], 102-110. 2001.

Excl reason: Guideline

Lantz, J. M., Fullerton, J. T., Harshburger, R. J., and Sadler, G. R. Promoting screening and early detection of cancer in men. *Nursing and Health Sciences* 3[4], 189-196. 2001.

Excl reason: Not in PICO

Leman, E. S. and Gonzalgo, M. L. Prognostic features and markers for testicular cancer management. *Indian Journal of Urology* 26[1], 76-81. 1-1-2010.

Excl reason: Not in PICO

Leskinen, M., Ala-Lipasti, M., Marttila, T., Paaso, I., and Raitanen, M. [Scrotal masses in adulthood]. [Finnish]. *Duodecim* 125[17], 1869-1876. 2009.

Excl reason: Narrative review

Lesnik, G., Nickl, S., Kuschnig, P., Sinzig, M., Hausegger, K., and Jeschke, K. [Sonography of the scrotum]. [Review] [50 refs] [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin* 178[2], 165-179. 2006.

Excl reason: Not in PICO

Leyh, H. Case history and palpation are the basis of early diagnosis of testicular tumors. [German]. *Medizinische Klinik* 79[22], 612-615. 1984.

Excl reason: Not in PICO

Li, M. & Jiang, T. (2013) MRI diagnosis of testicular neoplasm. [Chinese]. *Chinese Journal of Radiology (China)*, 47: 820-823.

Not in PICO

Loy, V. and Linke, J. Endocrine tumours of the testis. [German]. *Pathologe* 24[4], 308-313. 2003.

Excl reason: Narrative review

Lozano, J. M., Mestre, M. P., Lozano, M. A. M., Andres, P. M., and Lozano, C. M. Neoplasm of the testis in primary care: from the common to the very uncommon. *Swiss Medical Weekly* 139[33-34], 168S. 2009.

Excl reason: Not in PICO

Lyratzopoulos, G., Neal, R. D., Barbiere, J. M., Rubin, G. P., and Abel, G. A. Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. *Lancet Oncology* 13[4], 353-365. 2012.

Excl reason: Not in PICO

Lytras, A. and Tolis, G. Reproductive disturbances in multiple neuroendocrine tumor syndromes. *Endocrine-Related Cancer* 16[4], 1125-1138. 2009.
Excl reason: Not in PICO

MacVicar, G. R. and Pienta, K. J. Testicular cancer. [Review] [16 refs]. *Current Opinion in Oncology* 16[3], 253-256. 2004.
Excl reason: Not in PICO

Maddineni, S. B. and Clarke, N. W. Testis cancer: The UK as a model. [German]. *Urologe - Ausgabe A* 48[4], 386-392. 2009.
Excl reason: Narrative review

Mannuel, H. D. and Hussain, A. Update on testicular germ cell tumors. *Current Opinion in Oncology* 22[3], 236-241. 2010.
Excl reason: Not in PICO

Martin, B. and Tubiana, J. M. [Scrotal echography in the diagnosis of cancer of the testis: misleading images and echographic patterns]. [French]. *Annales de Radiologie* 32[2], 91-96. 1989.
Excl reason: Not in PICO

Mathers, M. J., Sperling, H., Rubben, H., and Roth, S. The undescended testis: diagnosis, treatment and long-term consequences. [Review] [56 refs]. *Deutsches Arzteblatt International* 106[33], 527-532. 2009.
Excl reason: Not in PICO

Mathew, A. and Desai, K. M. An audit of urology two-week wait referrals in a large teaching hospital in England. *Annals of the Royal College of Surgeons of England* 91[4], 310-312. 2009.
Excl reason: Not in PICO

McCullagh, J., Lewis, G., and Warlow, C. Promoting awareness and practice of testicular self-examination. *Nursing Standard* 19[51], 41-49. 31-8-2005.
Excl reason: Not in PICO

Mebel, M. and Vogler, H. [Special problems of early detection of malignant tumors of the genitourinary system (author's transl)]. [German]. *Archiv fur Geschwulstforschung* 51[8], 679-684. 1981.
Excl reason: Not in PICO

Meena, N. K. and Joshi, M. Small cell carcinoma presenting as limbic encephalopathy. *American Journal of Respiratory and Critical Care Medicine* 181[1 Meeting Abstracts]. 1-5-2010. American Thoracic Society.
Excl reason: Not in PICO

Mevcha, A. and Gillatt, D. Suspicious testicular lumps warrant urgent referral. *Practitioner* 253[1715], 23-24. 20-11-1926.
Excl reason: Narrative review

Miller, F. N., Rosairo, S., Clarke, J. L., Sriprasad, S., Muir, G. H., and Sidhu, P. S. Testicular calcification and microlithiasis: association with primary intra-testicular malignancy in 3,477 patients. *European Radiology* 17[2], 363-369. 2007.
Excl reason: Not in PICO

Minevich, E. Genitourinary emergencies in children. *Minerva Pediatrica* 61[1], 53-65. 2009.
Excl reason: Narrative review

Misener, T. R. and Fuller, S. G. Testicular versus breast and colorectal cancer screening: early detection practices of primary care physicians. *Cancer Practice* 3[5], 310-316. 1995.
Excl reason: Not in PICO

Moller, M. B. Association of testicular non-Hodgkin's lymphomas with elevated serum levels of human chorionic gonadotropin-like material. *Oncology* 53[2], 94-98. 1996.
Excl reason: Not in PICO

Morita, A. and Kamei, S. [Limbic encephalitis with antibodies against intracellular antigens]. [Review] [50 refs] [Japanese]. *Brain & Nerve / Shinkei Kenkyu no Shinpo* 62[4], 347-355. 2010.
Excl reason: Not in PICO

- Motzer, R. J., Bolger, G. B., Boston, B., Carducci, M. A., Fishman, M., Hancock, S. L., Hauke, R. J., Hudes, G. R., Jonasch, E., Kantoff, P., Kuzel, T. M., Lange, P. H., Levine, E. G., Logothetis, C., Margolin, K. A., Pohar, K. S., Redman, B. G., Robertson, C. N., Samlowski, W. E., Sheinfeld, J., and National Comprehensive Cancer Network. Testicular cancer. Clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network* 4[10], 1038-1058. 2006.
Excl reason: Guideline
- Moul, J. W., Paulson, D. F., Dodge, R. K., and Walther, P. J. Delay in diagnosis and survival in testicular cancer: impact of effective therapy and changes during 18 years. *Journal of Urology* 143[3], 520-523. 1990.
Excl reason: Not in PICO
- Moul, J. W. Timely diagnosis of testicular cancer. [Review] [77 refs]. *Urologic Clinics of North America* 34[2], 109-117. 2007.
Excl reason: Not in PICO
- Muller, T., Gozzi, C., Akkad, T., Pallwein, L., Bartsch, G., and Steiner, H. Management of incidental impalpable intratesticular masses of < or = 5 mm in diameter. *BJU International* 98[5], 1001-1004. 2006.
Excl reason: Not in PICO
- Mumperow, E., Lauke, H., Holstein, A. F., and Hartmann, M. Further practical experiences in the recognition and management of carcinoma in situ of the testis. *Urologia Internationalis* 48[2], 162-166. 1992.
Excl reason: Not in PICO
- Muramori, K., Nagata, K., and Handa, N. Infantile epididymitis with calcification. *Journal of Indian Association of Pediatric Surgeons* 13[1], 25-27. 2008.
Excl reason: Not in PICO
- Murchie, P., Campbell, N. C., Delaney, E. K., Dinant, G., Hannaford, P. C., Johansson, L., Lee, A. J., Rollano, P., and Spigt, M. Comparing diagnostic delay in cancer: A cross-sectional study in three european countries with primary care-led health care systems. *Family Practice* 29[1], 69-78. 2012.
Excl reason: Not in PICO
- Napal, Lecumberri S., Pascual, Piedrola, I, Arrondo Arrondo, J. L., and Ipiens, Aznar A. [Unusual presentation form of testicular neoplasms. Report of 5 cases]. [Spanish]. *Archivos Espanoles de Urologia* 45[1], 11-13. 1992.
Excl reason: Not in PICO
- Nay, C., Luthi, F., Ketterer, N., Bauer, J., and Leyvraz, S. Overview on cancer in young adults. [French]. *Revue Medicale Suisse* 3[112], 1305-1310. 23-5-2007.
Excl reason: Narrative review
- Nayyar, V., Bosman, D., and Laji, K. Bilateral testicular adrenal rests in congenital adrenal hyperplasia. *Endocrine Abstracts* 19, 30. 2009. BioScientifica.
Excl reason: Not in PICO
- Nichols, C. R. Testicular cancer. [Review] [294 refs]. *Current Problems in Cancer* 22[4], 187-274. 1998.
Excl reason: Not in PICO
- Noonan, A. M., Carney, D. N., and McCaffrey, J. Study to assess satisfaction of general practitioners (GP) with oncology services, GP awareness of follow-up guidelines for patients with cancer, and GP access to oncology services. *Journal of Clinical Oncology* 29[15 SUPPL. 1], 20-5-2011. American Society of Clinical Oncology.
Excl reason: Not in PICO
- Nordhaus, C., Stief, C. G., and Tullmann, E. M. [Inspection, palpation and ultrasound--the basics for clinical examination of the scrotum and testes]. [German]. *MMW Fortschritte der Medizin* 151[23], 39-40. 4-6-2009.
Excl reason: Narrative review

Nosov, A. K., Gafton, G. I., Meraboshvili, V. M., Mamizhev, E. M., Vorob'ev, A. V., and Petrov, S. B. [Testicular germ cell tumors, the state of diagnostics and staging in Saint-Petersburg]. [Russian]. *Voprosy Onkologii* 58[2], 238-242. 2012.
Excl reason: Narrative review

Nuver, J., Oosting, S. F., and Gietema, J. A. [Issues around testicular carcinoma]. [Review] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde* 155[45], A4092. 2011.
Excl reason: Narrative review

O'Brien, T. S., Perkins, J. M. T., and Cranston, D. Efficiency in the outpatient department: The lessons from urology. *Annals of the Royal College of Surgeons of England* 77[4], 287-289. 1995.
Excl reason: Not in PICO

O'Callaghan, A. and Mead, G. M. Testicular carcinoma. [Review] [23 refs]. *Postgraduate Medical Journal* 73[862], 481-486. 1997.
Excl reason: Not in PICO

Oliver, R. T. D., Ong, J., Blandy, J. P., and Altman, D. G. Testis conservation studies in germ cell cancer justified by improved primary chemotherapy response and reduced delay, 1978-1994. *British Journal of Urology* 78[1], 119-124. 1996.
Excl reason: Not in PICO

Oosterlinck, W., Dekuyper, P., Christiaens, T., and De, Maeseneer J. Audit of non-profit referrals of general practitioners to an (academic) urological consultation. [Dutch]. *Tijdschrift voor Geneeskunde* 62[10], 782-787. 15-5-2006.
Excl reason: Not in PICO

Opot, E. N. and Magoha, G. A. Testicular cancer at Kenyatta National Hospital, Nairobi. *East African Medical Journal* 77[2], 80-85. 2000.
Excl reason: Not in PICO

Osswald, M., Harlan, L. C., Penson, D., Stevens, J. L., and Clegg, L. X. Treatment of a population based sample of men diagnosed with testicular cancer in the United States. *Urologic Oncology* 27[6], 604-610. 2009.
Excl reason: Not in PICO

Ostwald, S. K. and Rothenberger, J. Development of a testicular self-examination program for college men. *Journal of the American College Health Association* 33[6], 234-239. 1985.
Excl reason: Not in PICO

Ott, J. J., Ullrich, A., and Miller, A. B. The importance of early symptom recognition in the context of early detection and cancer survival. *European Journal of Cancer* 45[16], 2743-2748. 2009.
Excl reason: Narrative review

Pamenter, B., De Bono, J. S., Brown, I. L., Nandini, M., Kaye, S. B., Russell, J. M., Yates, A. J., and Kirk, D. Bilateral testicular cancer: a preventable problem? Experience from a large cancer centre. *BJU International* 92[1], 43-46. 2003.
Excl reason: Not in PICO

Passman, C., Urban, D., Klemm, K., Lockhart, M., Kenney, P., and Kolettis, P. Testicular lesions other than germ cell tumours: feasibility of testis-sparing surgery. *BJU International* 103[4], 488-491. 2009.
Excl reason: Not in PICO

Pearse, I., Glick, R. D., Abramson, S. J., Gerald, W. R., Shamberger, R. C., and La Quaglia, M. P. Testicular-sparing surgery for benign testicular tumors. *Journal of Pediatric Surgery* 34[6], 1000-1003. 1999.
Excl reason: Not in PICO

Perimenis, P., Speakman, M. J., and Higgins, S. Chronic scrotal pain. A study of its causes and management. *International Urology and Nephrology* 26[3], 345-347. 1994.
Excl reason: Not in PICO/narrative review

Periyasamy, P., Subramaniam, S. R., and Rajalingham, S. An increasingly notorious mimicker of testicular tumours; crossing borders. *BMJ Case Reports* 2011, 2011. 2011.
Excl reason: Not in PICO

Polak, V. and Hornak, M. The value of scrotal ultrasound in patients with suspected testicular tumour. *International Urology & Nephrology* 22[5], 467-473. 1990.
Excl reason: Not in PICO

Raghavan, D. Towards the earlier diagnosis of testicular cancer. [Review] [20 refs]. *Australian Family Physician* 19[6], 865-875. 1990.
Excl reason: Narrative review

Raghavan, D. and Skinner, E. Genitourinary Cancer in the Elderly. *Seminars in Oncology* 31[2], 249-263. 2004.
Excl reason: Narrative review

Ravichandran, S., Smith, R., Cornford, P. A., and Fordham, M. V. Surveillance of testicular microlithiasis? Results of an UK based national questionnaire survey. *BMC Urology* 6, 8. 2006.
Excl reason: Not in PICO

Ray-Coquard, I., Guastalla, J.-P., Treilleux, I., Weber, B., Guardiola, E., Lotz, J.-P., Meeus, P., Mignot, L., Raudrant, D., Tournigand, C., Duvillard, P., and Pujade-Lorraine, E. Sex cord-stromal tumours, rare events in oncology necessitating multidisciplinary approach and referral pathways. *European Journal of Cancer, Supplement* 5[5], 247-253. 2007.
Excl reason: Not in PICO

Richie, J. P. and Sheinfeld, J. Introduction: International consultation on urologic diseases: testicular cancer: Societe Internationale d'Urologie/International Consultation on Urologic Diseases Consensus Meeting on Germ Cell Tumors (GCT), Shanghai 2009. *Urology* 78[4:Suppl], Suppl-6. 2011.
Excl reason: Narrative review

Riddick, A. Testicular lumps in general practice. [Review] [2 refs]. *Practitioner* 242[1590], 627-630. 1998.
Excl reason: Narrative review

Ringdahl, E., Claybrook, K., Teague, J. L., and Northrup, M. Testicular microlithiasis and its relation to testicular cancer on ultrasound findings of symptomatic men. *Journal of Urology* 172[5:Pt 1], t-6. 2004.
Excl reason: Not in PICO

Rochester, M., Scurrell, S., and Parry, J. R. Prospective evaluation of a novel one-stop testicular clinic. *Annals of the Royal College of Surgeons of England* 90[7], 565-570. 2008.
Excl reason: Not in PICO

Rodriguez, J. G., Velez, M., Serrano, E., and Casado, M. P. Adolescent student's compliance with testicular self examination. *Boletin de la Asociacion Medica de Puerto Rico* 87[3-4], 49-53. 1995.
Excl reason: Not in PICO

Rogers, M. and Todd, C. Information exchange in oncology outpatient clinics: Source, valence and uncertainty. *Psycho-Oncology* 11[4], 336-345. 2002.
Excl reason: Not in PICO

Rosella, J. D. Testicular cancer health education: an integrative review. [Review] [38 refs]. *Journal of Advanced Nursing* 20[4], 666-671. 1994.
Excl reason: Not in PICO

Rosenstein, D. and McAninch, J. W. Urologic emergencies. *Medical Clinics of North America* 88[2], 495-518. 2004.
Excl reason: Narrative review

Safah, H. and Weiner, R. S. The role of the primary physician in detecting cancer. [Review] [61 refs]. *Comprehensive Therapy* 19[5], 203-208. 1993.
Excl reason: Not in PICO

- Sah, R. P., Anaparthi, R., and Sugumar, A. A Case of Malignant Abdominal Pain. *Onkologie* 32[11], 666-668. 2009.
Excl reason: Not in PICO
- Saito, R., Ishizuka, E., Iwasaki, A., Chiba, K., Ambo, T., and Kobayashi, K. Malignant lymphoma of the testis: A case report. [Japanese]. *Nishinihon Journal of Urology* 57[9], 1016-1018. 1995.
Excl reason: Not in PICO
- Sanden, I., Larsson, U. S., and Eriksson, C. An interview study of men discovering testicular cancer. *Cancer Nursing* 23[4], 304-309. 2000.
Excl reason: Not in PICO
- Satie, A. P., Auger, J., Chevrier, C., Le, Bon C., Jouannet, P., Samson, M., and Jegou, B. Seminal expression of NY-ESO-1 and MAGE-A4 as markers for the testicular cancer. *International Journal of Andrology* 32[6], 713-719. 2009.
Excl reason: Not in PICO
- Saxon, P., Badler, R. L., Desser, T. S., Tublin, M. E., and Katz, D. S. Segmental testicular infarction: report of seven new cases and literature review. *Emergency Radiology* 19[3], 217-223. 2012.
Excl reason: Not in PICO
- Sayger, S. A., Fortenberry, J. D., and Beckman, R. J. Practice patterns of teaching testicular self-examination to adolescent patients. *Journal of Adolescent Health Care* 9[5], 441-442. 1988.
Excl reason: Not in PICO
- Schaffner, R. J. Knowledge of testicular self-exam. *Nurse Practitioner* 20[8], 10-12. 1995.
Excl reason: Not in PICO
- Schalamon, J., Ainoedhofer, H., Schleef, J., Singer, G., Haxhija, E. Q., and Hollwarth, M. E. Management of acute scrotum in children--the impact of Doppler ultrasound. *Journal of Pediatric Surgery* 41[8], 1377-1380. 2006.
Excl reason: Not in PICO (referred population)
- Scheiber, K. [Early diagnosis of testicular tumor]. [German]. *ZFA - Zeitschrift fur Allgemeinmedizin* 59[28], 1541-1543. 10-10-1983.
Excl reason: Narrative review
- Scher, H., Bosl, G., Geller, N., Cirrincione, C., Whitmore, W., and Golbey, R. Impact of symptomatic interval on prognosis of patients with stage III testicular cancer. *Urology* 21[6], 559-561. 1983.
Excl reason: Not in PICO
- Schickedanz, H. and Kleinteich, B. [Epidemiology and symptomatology of malignant testicular tumors in children]. [German]. *Kinderarztliche Praxis* 52[8], 370-376. 1984.
Excl reason: Not in PICO/narrative review
- Schickedanz, H. and Kleinteich, B. Epidemiology and symptomatology of scrotal tumours. [German]. *Zeitschrift fur Klinische Medizin* 40[7], 495-498. 1985.
Excl reason: Not in PICO
- Schumacher, H. Testicular involvement in internist-pediatric diseases. [German]. *Therapiewoche* 30[3], 310-319. 1980.
Excl reason: Narrative review
- Segal, R., Lukka, H., Klotz, L. H., Eady, A., Bestic, N., Johnston, M., and Cancer Care Ontario Practice Guidelines Initiative Genitourinary Cancer Disease Site Group. Surveillance programs for early stage non-seminomatous testicular cancer: a practice guideline. [Review] [27 refs]. *Canadian Journal of Urology* 8[1], 1184-1192. 2001.
Excl reason: Not in PICO
- Shaw, J. Diagnosis and treatment of testicular cancer. [Review] [37 refs]. *American Family Physician* 77[4], 469-474. 15-2-2008.
Excl reason: Not in PICO
- Sheth, K. R., Sharma, V., Zargaroff, S., Le, B., Dupree, J. M., and Brannigan, R. National incidence of testicular examination in men ages 15-45: Predictive factors and barriers. *Journal of Urology*

187[4 SUPPL. 1], e169-e170. 2012. Elsevier Inc.
 Excl reason: Not in PICO

Shindel, A. W., Akhavan, A., and Sharlip, I. D. Urologic aspects of HIV infection. *Medical Clinics of North America* 95[1], 129-151. 2011.
 Excl reason: Not in PICO

Shlebak, A. A. and Smith, D. B. Incidence of objectively diagnosed thromboembolic disease in cancer patients undergoing cytotoxic chemotherapy and/or hormonal therapy. *Cancer Chemotherapy & Pharmacology* 39[5], 462-466. 1997.
 Excl reason: Not in PICO

Shnorhavorian, M., Jacobs, M. A., Stearns, G., Mingin, G., and Koyle, M. A. Practice variation and clinical confusion regarding undescended testes and retractile testes among primary care respondents: A multi-regional survey study in the United States. *Pediatric Surgery International* 28[6], 635-639. 2012.
 Excl reason: Not in PICO

Shokar, Gurjeet S., Carlson, Carol A., Davis, Brian, and Shokar, Navkiran K. Testicular Cancer Screening in a Primary Care Setting. [References]. *International Journal of Men's Health* 2[3], 221-228. 2003.
 Excl reason: Not in PICO

Singer, A. J., Tichler, T., Orvieto, R., Finestone, A., and Moskovitz, M. Testicular carcinoma: a study of knowledge, awareness, and practice of testicular self-examination in male soldiers and military physicians. *Military Medicine* 158[10], 640-643. 1993.
 Excl reason: Not in PICO

Sladden, M. J. and Dickinson, J. A. General practitioners' attitudes to screening for prostate and testicular cancers. *Medical Journal of Australia* 162[8], 410-413. 17-4-1995.
 Excl reason: Not in PICO

Slaney, C., Livesey, E., and Carroll, D. Discontinuous spleno-gonadal fusion interpreted as a possible testicular malignancy-an important consideration in testicular imaging. *Pediatric Radiology* 41, S352. 2011. Springer Verlag.
 Excl reason: Not in PICO

Smart, C. R. The impact of the U.S. Preventive Services Task Force guidelines on cancer screening: perspective from the National Cancer Institute. *Journal of General Internal Medicine* 5[5:Suppl], Suppl-33. 1990.
 Excl reason: Not in PICO

Smith, F. C. T. and Gwynn, B. R. Direct access surgery. *Annals of the Royal College of Surgeons of England* 77[2], 94-96. 1995.
 Excl reason: Not in PICO

Snodgrass, W., Bush, N., Holzer, M., and Zhang, S. Current referral patterns and means to improve accuracy in diagnosis of undescended testis. *Pediatrics* 127[2], e382-e388. 2011.
 Excl reason: Not in PICO

Sokoloff, M. H., Joyce, G. F., and Wise, M. Testis cancer. *Journal of Urology* 177[6], 2030-2041. 2007.
 Excl reason: Narrative review

Sonpavde, G. and Einhorn, L. H. What to do when you discover testicular cancer: Helping patients overcome fear and choose treatment. *Postgraduate Medicine* 105[4], 229-236. 1999.
 Excl reason: Not in PICO

Spaan, J. A. and Van der Wouden, J. C. Delay in diagnosis of mammary, colorectal and testis tumors. Relationship with progression of the tumor and the part played by the general practitioner. [Dutch]. *Huisarts en Wetenschap* 32[4], 134-137. 1989.
 Excl reason: Not in PICO

Stotts, R. C. Cancers of the prostate, penis, and testicles: epidemiology, prevention, and treatment. [Review] [83 refs]. *Nursing Clinics of North America* 39[2], 327-340. 2004.
 Excl reason: Narrative review

Sturgeon, C. M., Duffy, M. J., Stenman, U. H., Lilja, H., Brunner, N., Chan, D. W., Babaian, R., Bast, R. C., Jr., Dowell, B., Esteva, F. J., Haglund, C., Harbeck, N., Hayes, D. F., Holten-Andersen, M., Klee, G. G., Lamerz, R., Looijenga, L. H., Molina, R., Nielsen, H. J., Rittenhouse, H., Semjonow, A., Shih, IeM, Sibley, P., Soletormos, G., Stephan, C., Sokoll, L., Hoffman, B. R., Diamandis, E. P., and National Academy of Clinical Biochemistry. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers. *Clinical Chemistry* 54[12], e11-e79. 2008.

Excl reason: Not in PICO

Suardi, N., Strada, E., Colombo, R., Freschi, M., Salonia, A., Lania, C., Cestari, A., Carmignani, L., Guazzoni, G., Rigatti, P., and Montorsi, F. Leydig cell tumour of the testis: presentation, therapy, long-term follow-up and the role of organ-sparing surgery in a single-institution experience. *BJU International* 103[2], 197-200. 2009.

Excl reason: Not in PICO

Subramonian, K. R., Puranik, S., and Mufti, G. R. How will the two-weeks-wait rule affect delays in management of urological cancers? *Journal of the Royal Society of Medicine* 96[8], 398-399. 1-8-2003.

Excl reason: Not in PICO

Swierz, J., Gomula, A., and Stawarz, B. [The role of clinical examination in early diagnosis of testicular malignancies]. [Polish]. *Wiadomosci Lekarskie* 45[23-24], 899-902. 1992.

Excl reason: Not in PICO

Tal, R., Holland, R., Belenky, A., Konichezky, M., and Baniel, J. Incidental testicular tumors in infertile men. *Fertility & Sterility* 82[2], 469-471. 2004.

Excl reason: Not in PICO

Tavolini, I. M., Zuliani, G., Norcen, M., Dal, Moro F., Abatangelo, G., and Oliva, G. [Prevention and early diagnosis of testicular neoplasms]. [Italian]. *Archivio Italiano di Urologia, Andrologia* 71[1], 27-30. 1999.

Excl reason: Not in PICO

Teichman, J. M., Weiss, B. D., and Solomon, D. Urological needs assessment for primary care practice: implications for undergraduate medical education. *Journal of Urology* 161[4], 1282-1285. 1999.

Excl reason: Not in PICO

Thorup, J. and Cortes, D. Surgical treatment and follow up on undescended testis. [Review] [50 refs]. *Pediatric Endocrinology Reviews* 7[1], 38-43. 2009.

Excl reason: Narrative review

Tiemstra, J. D. and Kapoor, S. Evaluation of scrotal masses. *American Family Physician* 78[10], 1165-1170. 15-11-2008.

Excl reason: Narrative review

Tilley, C. and Theaker, J. M. Pathology of tumours of the male genital tract. *Surgery* 28[12], 577-583. 2010.

Excl reason: Narrative review

Toklu, C., Ozen, H., Sahin, A., Rastadoskouee, M., and Erdem, E. Factors involved in diagnostic delay of testicular cancer. *International Urology & Nephrology* 31[3], 383-388. 1999.

Excl reason: Narrative review

Toner, G. C., Neerhut, G. J., Schwarz, M. A., Thursfield, V. J., Sandeman, T. F., Giles, G. G., and Snow, R. M. The management of testicular cancer in Victoria, 1988-1993. Urology Study Committee of the Victorian Co-operative Oncology Group. *Medical Journal of Australia* 174[7], 328-331. 2-4-2001.

Excl reason: Narrative review

Turner, D. Testicular cancer and the value of self-examination. *Nursing Times* 91[1], 30-31. 4-1-1995.

Excl reason: Not in PICO

- Ugboma, H. A. and Aburoma, H. L. Public awareness of testicular cancer and testicular self-examination in academic environments: a lost opportunity. *Clinics (Sao Paulo, Brazil)* 66[7], 1125-1128. 2011.
Excl reason: Not in PICO
- Underhill, C., Packer, C., Myers, R., Mamouney, K., Clouston, D., Byrne, J., Simons, K., Szer, J., McKendrick, J., Rosenthal, M., Mitchell, P., Gibbs, P., and Lewin, J. Urological cancer pathology project: Piloting a process for formalised second opinion pathology review for cancers of low incidence. *Asia-Pacific Journal of Clinical Oncology* 7, 194. 2011. Blackwell Publishing Ltd.
Excl reason: Not in PICO
- Vadaparampil, S. T., Moser, R. P., Loud, J., Peters, J. A., Greene, M. H., and Korde, L. Factors associated with testicular self-examination among unaffected men from multiple-case testicular cancer families. *Hereditary Cancer in Clinical Practice* 7. 2009.
Excl reason: Not in PICO
- Valentova, M. and Mladosevicova, B. Cardiovascular morbidity in patients after treatment for testicular cancer. [Slovak]. *Vnitřní Lekarství* 56[9], 915-919. 2010.
Excl reason: Not in PICO
- Varenhorst, E., Bjornlert, U., Herder, A., Nordenstam, G., and Alund, G. [Ultrasonic examination of the scrotum for the diagnosis of suspected testicular tumor]. [Swedish]. *Lakartidningen* 81[37], 3242-3243. 12-9-1984.
Excl reason: Not in PICO (patients with suspected testicular cancer)
- Vasdev, N. and Thorpe, A. C. Has the introduction of the '2 week rule' in the UK led to an earlier diagnosis of urological malignancy? *ecancermedicalscience* 5[1]. 31-8-2011.
Excl reason: Not in PICO
- Vasudev, N. S., Joffe, J. K., Cooke, C., Richards, F., and Jones, W. G. Delay in the diagnosis of testicular tumours - changes over the past 18 years. *British Journal of General Practice* 54[505], 595-597. 2004.
Excl reason: Not in PICO
- Vogt, H. B. and McHale, M. S. Testicular cancer: Role of primary care physicians in screening and education. *Postgraduate Medicine* 92[1], 93-100. 1992.
Excl reason: Narrative review
- Walsh, T. J., Dall'Era, M. A., Croughan, M. S., Carroll, P. R., and Turek, P. J. Prepubertal orchiopexy for cryptorchidism may be associated with lower risk of testicular cancer. [Review] [21 refs]. *Journal of Urology* 178[4:Pt 1], t-6. 2007.
Excl reason: Not in PICO
- Wampler, S. M. and Llanes, M. Common scrotal and testicular problems. [Review]. *Primary Care; Clinics in Office Practice* 37[3], 613-626. 20-11-2010.
Excl reason: Narrative review
- Wani, A. M., Al Zayyani, N. R., and Jacob, S. Unusual presentation of mixed germ cell tumour from testis in a 45-year-old man. *BMJ Case Reports* 2011, 2011. 2011.
Excl reason: Not in PICO
- Ward, K. D., Vander Weg, M. W., Read, M. C., Sell, M. A., and Beech, B. M. Testicular cancer awareness and self-examination among adolescent males in a community-based youth organization. *Preventive Medicine* 41[2], 386-398. 2005.
Excl reason: Not in PICO
- Wardle, J., Steptoe, A., Burckhardt, R., Vogele, C., Vila, J., and Zarczynski, Z. Testicular self-examination: Attitudes and practices among young men in Europe. *Preventive Medicine* 23[2], 206-210. 1994.
Excl reason: Not in PICO
- Webb, V. and Holmes, A. Urological cancers: do early detection strategies exist? *BJU International* 86[9], 996-1000. 2000.
Excl reason: Not in PICO

Weist, M. D. and Finney, J. W. Training in early cancer detection and anxiety in adolescent males: a preliminary report. *Journal of developmental and behavioral pediatrics* : JDBP 17[2], 98-99. 1996.
Excl reason: Not in PICO

Westlake, S. J. and Frank, J. W. Testicular self-examination: an argument against routine teaching. *Family Practice* 4[2], 143-148. 1987.
Excl reason: Not in PICO

Wheater, M. J., Manners, J., Nolan, L., Simmonds, P. D., Hayes, M. C., and Mead, G. M. The clinical features and management of testicular germ cell tumours in patients aged 60 years and older. *BJU International* 108[11], 1794-1799. 2011.
Excl reason: Not in PICO

Wiesenthal, J. D., Ettler, H., and Razvi, H. Testicular epidermoid cyst: a case report and review of the clinicopathologic features. [Review] [11 refs]. *Canadian Journal of Urology* 11[1], 2133-2135. 2004.
Excl reason: Not in PICO

Wijesinha, S. Male reproductive health--what is the GP's role?. [Review] [11 refs]. *Australian Family Physician* 32[6], 408-411. 2003.
Excl reason: Not in PICO

Wijesinha, S. S. What do family physicians need to know about men's sexual health? *Hong Kong Practitioner* 25[10], 486-490. 2003.
Excl reason: Not in PICO

Willson, P. C. and Judkins, A. F. Testicular and breast self-examinations: nurses' impact on early cancer detection. *Dimensions in Oncology Nursing* 4[3], 27-32. 1990.
Excl reason: Not in PICO

Wilson, C., Boyd, K., Mohammed, A., and Little, B. A single episode of haemospermia can be safely managed in the community. *International Journal of Clinical Practice* 64[10], 1436-1439. 2010.
Excl reason: Not in PICO

Winter, C. and Albers, P. Testicular germ cell tumors: pathogenesis, diagnosis and treatment. [Review]. *Nature Reviews Endocrinology* 7[1], 43-53. 2011.
Excl reason: Narrative review

Wohl, R. E. and Kane, W. M. Teachers' beliefs concerning teaching about testicular cancer and testicular self-examination. *Journal of School Health* 67[3], 106-111. 1997.
Excl reason: Not in PICO

Yeazel, M. W., Oeffinger, K. C., Gurney, J. G., Mertens, A. C., Hudson, M. M., Emmons, K. M., Chen, H. G., and Robison, L. L. The cancer screening practices of adult survivors of childhood cancer - A report from the childhood cancer survivor study. *Cancer* 100[3], 631-640. 2004.
Excl reason: Not in PICO

Review question:

Which investigations of symptoms of suspected testicular cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	266	54	22/03/2013
Premedline	1980-2013	14	6	22/03/2013
Embase	1980-2013	296	51	22/03/2013
Cochrane Library	1980-2013	0	0	22/03/2013

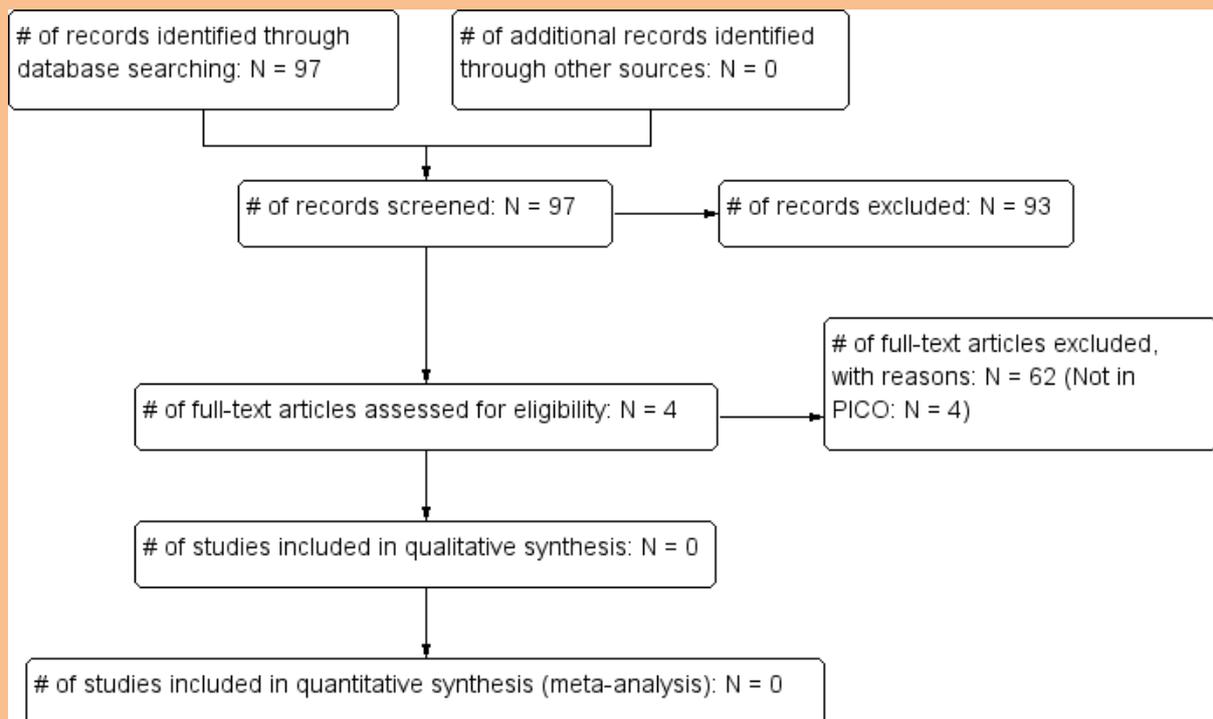
Psychinfo	1980-2013	0	0	22/03/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	51	2	22/03/2013

Total References retrieved (after de-duplication): 95

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	3/2013-27/08/2014	6	0	27/08/2014
<i>Premedline</i>	3/2013-27/08/2014	17	0	27/08/2014
<i>Embase</i>	3/2013-27/08/2014	36	2	27/08/2014
<i>Cochrane Library</i>	3/2013-27/08/2014	6	0	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	3/2013-27/08/2014	6	0	27/08/2014

Total References retrieved (after de-duplication): 2



Study results

No evidence was identified pertaining to the diagnostic accuracy of ultrasound in patients with suspected testicular cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

- Ahmad, I., Krishna, N. S., Clark, R., Nairn, R. & Al-Saffar, N. (2007) Testicular microlithiasis: prevalence and risk of concurrent and interval development of testicular tumor in a referred population. *International Urology & Nephrology*, 39: 1177-1181.
Not in PICO
- Aigner, A., Brachmann, P., Beyer, J., Jager, R., Raulais, D., Vigny, M., Neubauer, A., Heidenreich, A., Weinknecht, S., Czubayko, F. & Zugmaier, G. (2003) Marked increase of the growth factors pleiotrophin and fibroblast growth factor-2 in serum of testicular cancer patients. *Annals of Oncology*, 14: 1525-1529.
Not in PICO
- Aigner, F., De, Z. T., Pallwein-Prettner, L., Junker, D., Schafer, G., Pichler, R., Leonhartsberger, N., Pinggera, G., Dogra, V. S. & Frauscher, F. (2012) Real-time sonoelastography for the evaluation of testicular lesions. *Radiology*, 263: 584-589.
Not in PICO
- Albers, P., Goll, A., Bierhoff, E., Schoeneich, G. & Muller, S. C. (1999) Clinical course and histopathologic risk factor assessment in patients with bilateral testicular germ cell tumors. [Review] [20 refs]. *Urology*, 54: 714-718.
Not in PICO
- Albers, P., Albrecht, W., Algaba, F., Bokemeyer, C., Cohn-Cedermark, G., Fizazi, K., Horwich, A., Laguna, M. P. & European Association of Urology (2012) [EAU guidelines on testicular cancer: 2011 update. European Association of Urology]. [Spanish]. *Actas Urologicas Espanolas*, 36: 127-145.
Guideline
- Arce, T. Y., Algaba-Arrea, F. & Villavicencio, M. H. (2010) [Segmental infarct of testicle: an infrequent pseudotumor]. [Spanish]. *Actas Urologicas Espanolas*, 34: 194-200.
Not in PICO
- Badmos, K. B. (2012) Tuberculous epididymo-orchitis mimicking a testicular tumour: a case report. *African Health Sciences*, 12: 395-397.
Not in PICO
- Barnhouse, K., Powers, A. & Smith, P. C. (2007) Clinical inquiries. How should you further evaluate an adult with a testicular mass? *Journal of Family Practice*, 56: 851-853.
Narrative review
- Barrass, B. J. R., Scurrill, S., Banerjee, G. & Parry, J. R. W. (2010) Anxious patients with benign scrotal symptoms achieve excellent reassurance from imaging in a one-stop clinic. *British Journal of Medical and Surgical Urology*, 3: 111-115.
Not in PICO
- Bergholz, R. & Wenke, K. (2009) Polyorchidism: a meta-analysis. *Journal of Urology*, 182: 2422-2427.
Not in PICO
- Buchler, T., Simonova, K., Fencel, P. & Abrahamova, J. (2011) [Positron emission tomography in the diagnosis and monitoring of patients with nonseminomatous germ cell tumours]. [Czech]. *Klinicka Onkologie*, 24: 413-417.
Not in PICO
- Carmignani, L., Colombo, R., Gadda, F., Galasso, G., Lania, A., Palou, J., Algaba, F., Villavicencio, H., Colpi, G. M., Decobelli, O., Salvioni, R., Pizzocaro, G., Rigatti, P. & Rocco, F. (2007) Conservative Surgical Therapy for Leydig Cell Tumor. *Journal of Urology*, 178: 507-511.
Not in PICO
- Chapple, A., Ziebland, S. & McPherson, A. (2004) Qualitative study of men's perceptions of why treatment delays occur in the UK for those with testicular cancer. *British Journal of General Practice*, 54: 25-32.
Not in PICO
- Chierigo, P., Puccetti, O., Visona, A., Bassan, F., Rahmati, M., Lazzarotto, M. & Franzolin, N. (2010) [High alpha-fetoprotein persistence after orchiectomy. On a case of uncommon etiology].

- [Italian]. *Urologia (Treviso)*, 77: Suppl-31.
Not in PICO
- Church, D. N., Protheroe, A., Ian, S. D. R., Crane, G. L., Turner, G. D. & Verrill, C. (2012) Clinical relevance of specialist pathologic testicular tumor review. *Journal of Clinical Oncology*, 30.
Not in PICO
- Clarke, K., Howard, G. C. W., Elia, M. H., Hutcheon, A. W., Kaye, S. B., Windsor, P. M. & Yosef, H. M. A. (1995) Referral patterns within Scotland to specialist oncology centres for patients with testicular germ cell tumours. *British Journal of Cancer*, 72: 1300-1302.
Not in PICO
- Cook, J. L. & Dewbury, K. (2000) The changes seen on high-resolution ultrasound in orchitis. [Review] [22 refs]. *Clinical Radiology*, 55: 13-18.
Narrative review
- Dieckmann, K.-P. & Loy, V. (1998) The value of the biopsy of the contralateral testis in patients with testicular germ cell cancer: The recent German experience. *APMIS*, 106: 13-23.
Not in PICO
- Dieckmann, K.-P., Kulejewski, M., Pichlmeier, U. & Loy, V. (2007) Diagnosis of Contralateral Testicular Intraepithelial Neoplasia (TIN) in Patients with Testicular Germ Cell Cancer: Systematic Two-Site Biopsies Are More Sensitive Than a Single Random Biopsy. *European Urology*, 51: 175-185.
Not in PICO
- Dieckmann, K. P., Heinemann, V., Frey, U., Pichlmeier, U. & German Testicular Cancer Study Group (2005) How harmful is contralateral testicular biopsy?--an analysis of serial imaging studies and a prospective evaluation of surgical complications. *European Urology*, 48: 662-672.
Not in PICO
- Dieckmann, K. P., Kulejewski, M., Heinemann, V. & Loy, V. (2011) Testicular biopsy for early cancer detection--objectives, technique and controversies. [Review]. *International Journal of Andrology*, 34: t-13.
Narrative review
- Duffy, M. J. (2001) Clinical uses of tumor markers: a critical review. [Review] [129 refs]. *Critical Reviews in Clinical Laboratory Sciences*, 38: 225-262.
Not in PICO
- Fanti, S., Nanni, C., Ambrosini, V., Gross, M. D., Rubello, D. & Farsad, M. (2007) PET in genitourinary tract cancers. [Review] [82 refs]. *The Quarterly Journal of Nuclear Medicine & Molecular Imaging*, 51: 260-271.
Not in PICO
- Favilla, V., Cimino, S., Madonia, M. & Morgia, G. (2010) New advances in clinical biomarkers in testis cancer. [Review] [246 refs]. *Frontiers in Bioscience*, 2: 456-477.
Not in PICO
- Foo, K. T. (2013) The role of transabdominal ultrasound in office urology. *Proceedings of Singapore Healthcare*, 22: 125-130.
Narrative review
- Gallardo, A. E., Pena, G. E., Lopez, R. G., Ortega, G. E., Calabria de, D. A., Portillo Martin, J. A. & Martin, G. B. (1996) Testicular tumors. Echographic findings. [Spanish]. *Archivos Espanoles de Urologia*, 49: 622-626.
Not in PICO
- Geczi, L., Gomez, F., Horvath, Z., Bak, M., Kisbenedek, L. & Bodrogi, I. (2001) Three-year results of the first educational and early detection program for testicular cancer in Hungary. *Oncology*, 60: 228-234.
Not in PICO
- Gopalan, A., Dhall, D., Olgac, S., Fine, S. W., Korkola, J. E., Houldsworth, J., Chaganti, R. S., Bosl, G. J., Reuter, V. E. & Tickoo, S. K. (2009) Testicular mixed germ cell tumors: a morphological and immunohistochemical study using stem cell markers, OCT3/4, SOX2 and GDF3, with emphasis

- on morphologically difficult-to-classify areas. *Modern Pathology*, 22: 1066-1074.
Not in PICO
- Guinan, P. & Rubenstein, M. (1987) Methods of early diagnosis in genitourinary cancer. *Cancer*, 60: 668-676.
Not in PICO
- Guthrie, J. A. & Fowler, R. C. (1992) Ultrasound diagnosis of testicular tumours presenting as epididymal disease. *Clinical Radiology*, 46: 397-400.
Not in PICO
- Haas, R. J., Gobel, U., Harms, D., Schmidt, P. & Weissbach, L. (1988) Results of the cooperative Malignant Testicular Tumors 82 Study of the German Society of Pediatric Oncology on the therapy of malignant germ cell tumors in childhood. [German]. *Klinische Padiatrie*, 200: 230-235.
Not in PICO
- Haller, J., Gritzmann, N., Czembirek, H., Schmidbauer, C., Leitner, H., Sommer, G. & Tscholakoff, D. (1987) Occult and clinically suspected testicular tumor. Assessment using real-time sonography. [German]. *Der Radiologe*, 27: 113-117.
Not in PICO
- Hemminki, K., Mousavi, S. M., Brandt, A., Ji, J. & Sundquist, J. (2010) Histology-specific risks in testicular cancer in immigrants to Sweden. *Endocrine-Related Cancer*, 17: 329-334.
Not in PICO
- Hisamatsu, E., Takagi, S., Nakagawa, Y., Sugita, Y., Yoshino, K., Ueoka, K. & Tanikaze, S. (2010) Prepubertal testicular tumors: a 20-year experience with 40 cases. *International Journal of Urology*, 17: 956-959.
Not in PICO
- Holstein, A. F. & Lauke, H. (1996) Histologic diagnostics of early testicular germ-cell tumor. *International Journal of Urology*, 3: 165-172.
Not in PICO
- Isidori, A. M. (2010) Ultrasonography: Testis and accessory glands. *International Journal of Andrology*, 33: 25.
Narrative review
- Jones, W. & Appleyard, I. (1989) Early diagnosis of testicular cancer. *The Practitioner*, 233: 509.
Narrative review
- Kaufman, M. & Levine, D. L. (2013) A case of advanced testicular cancer in a society of racial and socioeconomic health disparity. *Journal of General Internal Medicine*, 28: S264-S265.
Not in PICO
- Kennedy, P. T., Elliott, J. M., Rice, P. F. & Kelly, B. E. (1999) Ultrasonography of intratesticular lesions: its role in clinical management. *Ulster Medical Journal*, 68: 54-58.
Not in PICO
- Kinkade, S. (2549) Testicular cancer. [Review] [26 refs]. *American Family Physician*, 59: 2539-2544.
Narrative review
- Kleinschmidt, K., Weissbach, L. & Holstein, A. F. (1989) Early diagnosis of the contralateral second cancer in patients with germ cell tumors by screening for carcinoma in situ testis. [German]. *Urologe - Ausgabe A*, 28: 281-284.
Not in PICO
- Kliesch, S. (2004) [Diagnosis and primary treatment of testicular tumor]. [Review] [21 refs] [German]. *Urologe (Ausg.A)*, 43: 1494-1499.
Narrative review
- Kontos, S., Doumanis, G., Karagianni, M., Politis, V., Simaioforidis, V., Kachrilas, S. & Koritsiadis, S. (2009) Burned-out testicular tumor with retroperitoneal lymph node metastasis: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 3: 8705.
Not in PICO

- Krege, S. & Rubben, H. (2005) [Lymphadenectomy for testicular cancer. Diagnostic and prognostic significance as well as therapeutic benefit]. [Review] [28 refs] [German]. *Urologe (Ausg.A)*, 44: 652-656.
Narrative review
- Krege, S., Beyer, J., Souchon, R., Albers, P., Albrecht, W., Algaba, F., Bamberg, M., Bodrogi, I., Bokemeyer, C., Cavallin-Stahl, E., Classen, J., Clemm, C., Cohn-Cedermark, G., Culine, S., Daugaard, G., De Mulder, P. H., De, S. M., de, W. M., de, W. R., Derigs, H. G., Dieckmann, K. P., Dieing, A., Droz, J. P., Fenner, M., Fizazi, K., Flechon, A., Fossa, S. D., del Muro, X. G., Gauler, T., Geczi, L., Gerl, A., Germa-Lluch, J. R., Gillessen, S., Hartmann, J. T., Hartmann, M., Heidenreich, A., Hoeltl, W., Horwich, A., Huddart, R., Jewett, M., Joffe, J., Jones, W. G., Kisbenedek, L., Klepp, O., Kliesch, S., Koehrmann, K. U., Kollmannsberger, C., Kuczyk, M., Laguna, P., Galvis, O. L., Loy, V., Mason, M. D., Mead, G. M., Mueller, R., Nichols, C., Nicolai, N., Oliver, T., Ondrus, D., Oosterhof, G. O., Ares, L. P., Pizzocaro, G., Pont, J., Pottek, T., Powles, T., Rick, O., Rosti, G., Salvioni, R., Scheiderbauer, J., Schmelz, H. U., Schmidberger, H., Schmoll, H. J., Schrader, M., Sedlmayer, F., Skakkebaek, N. E., Sohaib, A., Tjulandin, S., Warde, P., Weinknecht, S., Weissbach, L., Wittekind, C., Winter, E., Wood, L. & von der, M. H. (2008) European consensus conference on diagnosis and treatment of germ cell cancer: a report of the second meeting of the European Germ Cell Cancer Consensus group (EGCCCG): part I. [Review] [164 refs]. *European Urology*, 53: 478-496.
Not in PICO
- Kumaraswamy, P., Cox, R., O'Rourke, J. S. & Willis, R. G. (2009) Audit of two-week rule referrals for suspected testicular cancer in Cornwall, 2003-2005. *Annals of the Royal College of Surgeons of England*, 91: 239-244.
Not in PICO
- Lenz, S., Giwercman, A. & Skakkebaek, N. E. (1987) Ultrasound in detection of early neoplasia of the testis. *International Journal of Andrology*, 10: 187-190.
Not in PICO
- Lenz, S. (1991) Cancer of the testicle diagnosed by ultrasound and the ultrasonic appearance of the contralateral testicle. *Scandinavian Journal of Urology and Nephrology*, Supplementum.: 135-138.
Not in PICO
- Lenz, S. & Giwercman, A. (2008) Carcinoma-in-situ of the testis - Is ultrasound of the testes useful as a screening method? *Journal of Medical Ultrasound*, 16: 256-267.
Narrative review
- Leskinen, M., Ala-Lipasti, M., Marttila, T., Paaso, I. & Raitanen, M. (2009) [Scrotal masses in adulthood]. [Finnish]. *Duodecim*, 125: 1869-1876.
Narrative review
- Lesnik, G., Nickl, S., Kuschnig, P., Sinzig, M., Hausegger, K. & Jeschke, K. (2006) [Sonography of the scrotum]. [Review] [50 refs] [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 178: 165-179.
Narrative review
- Li, M. & Jiang, T. (2013) MRI diagnosis of testicular neoplasm. [Chinese]. *Chinese Journal of Radiology (China)*, 47: 820-823.
Not in PICO
- Lifschitz-Mercer, B., Elliott, D. J., Schreiber-Bramante, L., Leider-Trejo, L., Eisenthal, A. & Bar-Shira, M. B. (2001) Intratubular germ cell neoplasia: associated infertility and review of the diagnostic modalities. [Review] [41 refs]. *International Journal of Surgical Pathology*, 9: 93-98.
Not in PICO
- Lomena, F., Simo, M., Setoain, X. & Perez, G. (2001) [Positron emission tomography (PET): application in urogenital system oncologic diseases]. [Review] [39 refs] [Spanish]. *Archivos*

- Espanoles de Urologia*, 54: 649-660.
Not in PICO
- Mahmood, T., Farooq, K., Asghar, J. & Rashid, A. (2011) Evaluation of scrotal pathology on ultrasonography. *Pakistan Journal of Medical and Health Sciences*, 5: 341-343.
Narrative review
- Martin, B. & Conte, J. (1987) Ultrasonography of the acute scrotum. *Journal of Clinical Ultrasound*, 15: 37-44.
Not in PICO
- Martin, B. & Tubiana, J. M. (1989) Scrotal echography in the diagnosis of cancer of the testis: misleading images and echographic patterns. [French]. *Annales de Radiologie*, 32: 91-96.
Not in PICO
- Mathew, A. & Desai, K. M. (2009) An audit of urology two-week wait referrals in a large teaching hospital in England. *Annals of the Royal College of Surgeons of England*, 91: 310-312.
Not in PICO
- Miller, F. N., Rosairo, S., Clarke, J. L., Sriprasad, S., Muir, G. H. & Sidhu, P. S. (2007) Testicular calcification and microlithiasis: association with primary intra-testicular malignancy in 3,477 patients. *European Radiology*, 17: 363-369.
Not in PICO
- Milovanceva-Popovska, M. & Dzikova, S. (2008) Doppler ultrasonography: a tool for nephrologists--single centre experience. *Makedonska Akademija na Naukite i Umetnostite Oddelenie Za Bioloshki i Meditsinski Nauki Prilozi*, 29: 107-128.
Not in PICO
- Muller, T., Gozzi, C., Akkad, T., Pallwein, L., Bartsch, G. & Steiner, H. (2006) Management of incidental impalpable intratesticular masses of < or = 5 mm in diameter. *BJU International*, 98: 1001-1004.
Not in PICO
- Muramori, K., Nagata, K. & Handa, N. (2008) Infantile epididymitis with calcification. *Journal of Indian Association of Pediatric Surgeons*, 13: 25-27.
Not in PICO
- Napal, L. S., Pascual, P., I, Arrondo Arrondo, J. L. & Ipiens, A. A. (1992) Unusual presentation form of testicular neoplasms. Report of 5 cases. [Spanish]. *Archivos Espanoles de Urologia*, 45: 11-13.
Not in PICO
- Nguyen, M. M. & Ellison, L. M. (2005) Testicular cancer patterns in Asian-American males: an opportunity for public health education to impact outcomes. *Urology*, 66: 606-609.
Not in PICO
- Nordhaus, C., Stief, C. G. & Tullmann, E. M. (2009) [Inspection, palpation and ultrasound--the basics for clinical examination of the scrotum and testes]. [German]. *MMW Fortschritte der Medizin*, 151: 39-40.
Narrative review
- O'Brien, T. S., Perkins, J. M. T. & Cranston, D. (1995) Efficiency in the outpatient department: The lessons from urology. *Annals of the Royal College of Surgeons of England*, 77: 287-289.
Not in PICO
- Opot, E. N. & Magoha, G. A. (2000) Testicular cancer at Kenyatta National Hospital, Nairobi. *East African Medical Journal*, 77: 80-85.
Not in PICO
- Oszukowska, E., Slowikowska-Hilczer, J., Wolski, J. K., Kula, P., Sosnowski, M. & Kula, K. (2006) Surgery in andrology. [Polish, English]. *Chirurgia Polska*, 8: 207-222.
Not in PICO
- Parkinson, R. J., Walton, T. J. & Lemberger, R. J. (2009) Use and misuse of testicular ultrasound in routine clinical practice in a UK teaching hospital. *British Journal of Medical and Surgical*

- Urology*, 2: 105-110.
Not in PICO
- Perimenis, P., Speakman, M. J. & Higgins, S. (1994) Chronic scrotal pain. A study of its causes and management. *International Urology and Nephrology*, 26: 345-347.
Not in PICO
- Phillips, N. & Jequier, A. M. (2007) Early testicular cancer: A problem in an infertility clinic. *Reproductive BioMedicine Online*, 15: 520-525.
Not in PICO
- Polak, V. & Hornak, M. (1990) The value of scrotal ultrasound in patients with suspected testicular tumour. *International Urology and Nephrology*, 22: 467-473.
Not in PICO
- Pompino, H. J. (1980) Testicular biopsy in children - indications and risks. [German]. *Therapiewoche*, 30: 282-285.
Not in PICO
- Richenberg, J. & Brejt, N. (2012) Testicular microlithiasis: is there a need for surveillance in the absence of other risk factors? *European Radiology*, 22: 2540-2546.
Not in PICO
- Ringdahl, E., Claybrook, K., Teague, J. L. & Northrup, M. (2004) Testicular microlithiasis and its relation to testicular cancer on ultrasound findings of symptomatic men. *Journal of Urology*, 172: t-6.
Not in PICO
- Rochester, M., Scurrill, S. & Parry, J. R. (2008) Prospective evaluation of a novel one-stop testicular clinic. *Annals of the Royal College of Surgeons of England*, 90: 565-570.
Not in PICO
- Roy, C. & Tuchmann, C. (2003) Scrotal ultrasound. Part II: Cysts, tumors and rare non tumoral processes. [French]. *Journal de Radiologie*, 84: 667-680.
Narrative review
- Saxon, P., Badler, R. L., Desser, T. S., Tublin, M. E. & Katz, D. S. (2012) Segmental testicular infarction: Report of seven new cases and literature review. *Emergency Radiology*, 19: 217-223.
Not in PICO
- Schalamon, J., Ainoedhofer, H., Schleef, J., Singer, G., Haxhija, E. Q. & Hollwarth, M. E. (2006) Management of acute scrotum in children--the impact of Doppler ultrasound. *Journal of Pediatric Surgery*, 41: 1377-1380.
Not in PICO
- Shvarts, O., Han, K. R., Seltzer, M., Pantuck, A. J. & Beldegrun, A. S. (2002) Positron emission tomography in urologic oncology. [Review] [52 refs]. *Cancer Control*, 9: 335-342.
Not in PICO
- Soh, E., Berman, L. H., Grant, J. W., Bullock, N. & Williams, M. V. (2008) Ultrasound-guided core-needle biopsy of the testis for focal indeterminate intratesticular lesions. *European Radiology*, 18: 2990-2996.
Not in PICO
- Souchon, R. & Classen, J. (2007) Malignant testicular germ cell tumors: Early stages. [German]. *Onkologe*, 13: 1029-1044.
Narrative review
- Stoop, H., Honecker, F., van de Geijn, G. J., Gillis, A. J., Cools, M. C., de, B. M., Bokemeyer, C., Wolffenbittel, K. P., Drop, S. L., de Krijger, R. R., Dennis, N., Summersgill, B., McIntyre, A., Shipley, J., Oosterhuis, J. W. & Looijenga, L. H. (2008) Stem cell factor as a novel diagnostic marker for early malignant germ cells. *Journal of Pathology*, 216: 43-54.
Not in PICO
- Sturgeon, C. M., Duffy, M. J., Stenman, U. H., Lilja, H., Brunner, N., Chan, D. W., Babaian, R., Bast, R. C., Jr., Dowell, B., Esteva, F. J., Haglund, C., Harbeck, N., Hayes, D. F., Holten-Andersen, M., Klee,

- G. G., Lamerz, R., Looijenga, L. H., Molina, R., Nielsen, H. J., Rittenhouse, H., Semjonow, A., Shih, I., Sibley, P., Soletormos, G., Stephan, C., Sokoll, L., Hoffman, B. R., Diamandis, E. P. & National Academy of Clinical Biochemistry (2008) National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers. *Clinical Chemistry*, 54: e11-e79.
Not in PICO
- Teichman, J. M., Weiss, B. D. & Solomon, D. (1999) Urological needs assessment for primary care practice: implications for undergraduate medical education. *Journal of Urology*, 161: 1282-1285.
Not in PICO
- Torabi-Pour, N., Nouri, A. M., Perrett, D. & Oliver, R. T. (2000) The combined use of high performance liquid chromatography and immuno-biochemical techniques for protein isolation: a new approach for identification of an individual protein from a pool of proteins. *Biomedical Chromatography*, 14: 483-488.
Not in PICO
- Tsili, A. C., Argyropoulou, M. I., Astrakas, L. G., Ntoulia, E. A., Giannakis, D., Sofikitis, N. & Tsampoulas, K. (2013) Dynamic contrast-enhanced subtraction MRI for characterizing intratesticular mass lesions. *AJR.American Journal of Roentgenology*, 200: 578-585.
Not in PICO
- van Casteren, N. J., Stoop, H., Dohle, G. R., de, W. R., Oosterhuis, J. W. & Looijenga, L. H. (2008) Noninvasive detection of testicular carcinoma in situ in semen using OCT3/4. *European Urology*, 54: 153-158.
Not in PICO
- Vasdev, N. & Thorpe, A. C. (2011) Has the introduction of the '2 week rule' in the UK led to an earlier diagnosis of urological malignancy? *ecancermedicalscience*, 5.
Not in PICO
- Wakat, J. P., Zwicker, C. & Claussen, C. (1988) Scrotal changes in the 3.5 MHz ultrasound image. [German]. *Rontgen-Blatter; Zeitschrift fur Rontgen-Technik und medizinisch-wissenschaftliche Photographie*, 41: 304-309.
Not available, and doesn't appear to be relevant.
- Wheater, M. J., Manners, J., Nolan, L., Simmonds, P. D., Hayes, M. C. & Mead, G. M. (2011) The clinical features and management of testicular germ cell tumours in patients aged 60 years and older. *BJU International*, 108: 1794-1799.
Not in PICO
- Wiesenthal, J. D., Ettler, H. & Razvi, H. (2004) Testicular epidermoid cyst: a case report and review of the clinicopathologic features. [Review] [11 refs]. *Canadian Journal of Urology*, 11: 2133-2135.
Not in PICO
- Wilson, C., Boyd, K., Mohammed, A. & Little, B. (2010) A single episode of haematospermia can be safely managed in the community. *International Journal of Clinical Practice*, 64: 1436-1439.
Not in PICO
- Winstanley, A. M., Mikuz, G., Debryne, F., Schulman, C. C. & Parkinson, M. C. (2004) Handling and reporting of biopsy and surgical specimens of testicular cancer. *European Urology*, 45: 564-573.
Not in PICO
- Yee, W. S., Kim, Y. S., Kim, S. J., Choi, J. B., Kim, S. I. & Ahn, H. S. (2011) Testicular microlithiasis: prevalence and clinical significance in a population referred for scrotal ultrasonography. *Korean Journal of Urology*, 52: 172-177.
Not in PICO
- Zengerling, F., Hartmann, M., Heidenreich, A., Kregge, S., Albers, P., Karl, A., Wagner, W., Bedke, J., Schmelz, H. U., Retz, M., Kliesch, S., Winter, E., Kuczyk, M. & Schrader, M. (2012) Five years into the national second-opinion project of the German Testicular Cancer Group (GCTSG): Impact on guideline implementation and the quality of care for testicular cancer patients. *Journal of*

Clinical Oncology, 30.

Not in PICO

Zynger, D. L., Dimov, N. D., Luan, C., Teh, B. T. & Yang, X. J. (2006) Glypican 3: a novel marker in testicular germ cell tumors. *American Journal of Surgical Pathology*, 30: 1570-1575.

Not in PICO

Zynger, D. L., Everton, M. J., Dimov, N. D., Chou, P. M. & Yang, X. J. (2008) Expression of glypican 3 in ovarian and extragonadal germ cell tumors. *American Journal of Clinical Pathology*, 130: 224-230.

Not in PICO

PENILE CANCER

Review question:

What is the risk of penile cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

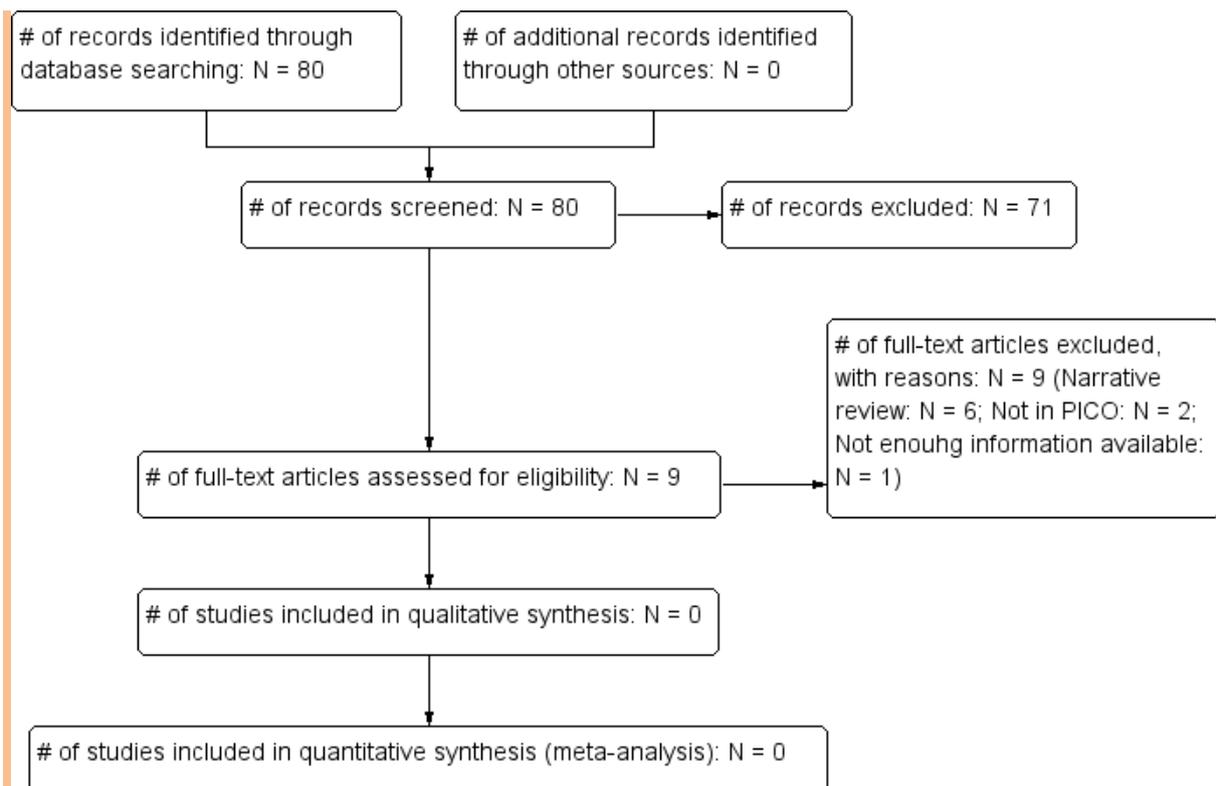
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	298	45	20/09/2012
<i>Premedline</i>	All-2012	3	1	20/09/2012
<i>Embase</i>	All-2012	400	44	20/09/2012
<i>Cochrane Library</i>	All-2012	32	0	21/09/2012
<i>Psychinfo</i>	All-2012	2	0	20/09/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	2	0	24/09/2012
<i>Biomed Central</i>	All-2012	52	2	24/09/2012

Total References retrieved (after de-duplication): 76

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	9/2012-26/08/2014	25	2	26/08/2014
<i>Premedline</i>	9/2012-26/08/2014	18	1	26/08/2014
<i>Embase</i>	9/2012-26/08/2014	57	2	26/08/2014
<i>Cochrane Library</i>	9/2012-26/08/2014	6	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	9/2012-26/08/2014	11	0	26/08/2014

Total References retrieved (after de-duplication): 4



Study results

No evidence was identified.

References

Included studies

None

Excluded studies (with excl reason)

Information from your family doctor. Penile cancer. *American Family Physician* 69[3], 617-618. 1-2-2004.

Excl reason: Information leaflet

Arya, M., Kalsi, J., Kelly, J. & Muneer, A. (2013) Malignant and premalignant lesions of the penis. [Review]. *BMJ*, 346: f1149.

Narrative review

Barbagli, G., Palminteri, E., Mirri, F., Guazzoni, G., Turini, D., and Lazzeri, M. Penile carcinoma in patients with genital lichen sclerosus: a multicenter survey. *Journal of Urology* 175[4], 1359-1363. 2006.

Excl reason: Not in PICO

Barocas, D. A. and Chang, S. S. Penile cancer: clinical presentation, diagnosis, and staging. *Urologic Clinics of North America* 37[3], 343-352. 2010.

Excl reason: Narrative review

Bastide, C. [Prevention and screening of penile cancer]. [Review] [44 refs] [French]. *Progres En Urologie* 13[5:Suppl 2], Suppl-42. 2003.

Excl reason: Not in PICO

Bigot, P. and Longvert, C. [Penile dermatological lesions: how to identify premalignant lesions?]. [French]. *Progres En Urologie* 21, Suppl-2. 2011.

Excl reason: Narrative review

Bleeker, M. C., Heideman, D. A., Snijders, P. J., Horenblas, S., Dillner, J., and Meijer, C. J. Penile cancer: epidemiology, pathogenesis and prevention. [Review] [99 refs]. *World Journal of Urology* 27[2], 141-150. 2009.
Excl reason: Narrative review

Bouchot, O. and Rigaud, J. [Penis tumours: techniques and indications]. [Review] [30 refs] [French]. *Annales d Urologie* 38[6], 285-297. 2004.
Excl reason: Narrative review

Bradway, C. and Rodgers, J. Evaluation and management of genitourinary emergencies. [Review] [24 refs]. *Nurse Practitioner* 34[5], 36-43. 1943.
Excl reason: Narrative review

Brady, K. L., Mercurio, M. G. & Brown, M. D. (2013) Malignant tumors of the penis. [Review]. *Dermatologic Surgery*, 39: 527-547.
Narrative review

Bray, F., Klint, A., Gislum, M., Hakulinen, T., Engholm, G., Tryggvadottir, L., and Storm, H. H. Trends in survival of patients diagnosed with male genital cancers in the Nordic countries 1964-2003 followed up until the end of 2006. *Acta Oncologica* 49[5], 644-654. 2010.
Excl reason: Not in PICO

Buechner, S. A. Common skin disorders of the penis. *BJU International* 90[5], 498-506. 2002.
Excl reason: Narrative review

Cathomas, R., Geldart, T. R., Iveson, T., Singh, N., and Rowen, D. An unusual differential diagnosis of penile warts: metastases from rectal carcinoma. *International Journal of STD & AIDS* 17[7], 491-492. 2006.
Excl reason: Not in PICO

Cherian, Jacob, Rajan, Sreekumar, Thwaini, Ali, Elmasry, Yaser, Shah, Tariq, and Puri, Rajiv. Secondary penile tumours revisited. *International Seminars in Surgical Oncology* 3[1], 33. 2006.
Excl reason: Not in PICO

Chiu, T.-Y., Huang, H.-S., Lai, M.-K., Chen, J., Hsieh, T.-S., and Chueh, S.-C. Penile cancer in Taiwan - 20 years' experience at National Taiwan University Hospital. *Journal of the Formosan Medical Association* 97[10], 673-678. 1998.
Excl reason: Not in PICO

Cottrell, A. M., Dickerson, D., and Oxley, J. D. Suspected penile cancer: a method to improve handling of pathology specimens. [Review] [3 refs]. *BJU International* 101[10], 1325-1328. 2008.
Excl reason: Not in PICO

David, N. and Tang, A. Efficacy and safety of penile biopsy in a GUM clinic setting. *International Journal of STD & AIDS* 13[8], 573-576. 2002.
Excl reason: Not in PICO

Dawson, C. and Whitfield, H. ABC of Urology. Urological emergencies in general practice. [Review] [0 refs]. *BMJ* 312[7034], 838-840. 30-3-1996.
Excl reason: Narrative review

De Freitas, Calmon M., Babeto, E., Mota, M. T. O., Candido, N. M., Girol, A. P., Oliani, S. M., Bonilha, J. L., Vassallo, J., and Rahal, P. Differential gene expression and HPV in penile carcinoma. *Cancer Research* 71[8 SUPPL. 1]. 15-4-2011. American Association for Cancer Research Inc.
Excl reason: Not in PICO

Dechev, I. and Banchev, A. More about the clinical characteristics of penile cancer. [Bulgarian]. *General Medicine* 8[4], 42-46. 2006.
Excl reason: Narrative review

Demeter, L. M., Stoler, M. H., Bonnez, W., Corey, L., Pappas, P., Strussenberg, J., and Reichman, R. C. Penile intraepithelial neoplasia: Clinical presentation and an analysis of the physical state of human papillomavirus DNA. *Journal of Infectious Diseases* 168[1], 38-46. 1993.
Excl reason: Not in PICO

Descazeaud, A. and Mottet, N. [Cancers of the penis and testicle: news in 2008]. [French]. *Progres En Urologie* 18, Suppl-4. 2008.
Excl reason: Not in PICO

Ficarra, V., Martignoni, G., Maffei, N., Cerruto, M. A., Novara, G., Cavalleri, S., and Artibani, W. Predictive pathological factors of lymph nodes involvement in the squamous cell carcinoma of the penis. *International Urology and Nephrology* 34[2], 245-250. 2002.
Excl reason: Not in PICO

Ficarra, V., Zattoni, F., Artibani, W., Fandella, A., Martignoni, G., Novara, G., Galetti, T. P., Zambolin, T., and Kattan, M. W. Nomogram Predictive of Pathological Inguinal Lymph Node Involvement in Patients With Squamous Cell Carcinoma of the Penis. *Journal of Urology* 175[5], 1700-1705. 2006.
Excl reason: Not in PICO

Fossa, S. D., Jones, W. G., Hamers, H. P., and van den Bogaert, W. Penile cancer. [Norwegian]. *Tidsskrift for Den Norske Laegeforening* 110[11], 1354-1356. 30-4-1990.
Excl reason: Narrative review

Fraley, E. E., Zhang, G., Sazama, R., and Lange, P. H. Cancer of the penis. Prognosis and treatment plans. *Cancer* 55[7], 1618-1624. 1985.
Excl reason: Not in PICO

Giannakopoulos, X., Basioukas, K., Dimou, S., and Agnantis, N. Squamous cell carcinoma of the penis arising from balanitis xerotica obliterans. *International Urology & Nephrology* 28[2], 223-227. 1996.
Excl reason: Not in PICO

Gingu, C., Patrascioiu, S., Surcel, C., Chibeleian, C., Harza, M. C., Zogas, V., Balsanu, C., Dick, A., Mirvald, C., Lupu, F., Domnisor, L., and Sinescu, I. Primary carcinoma of the male urethra - Diagnosis and treatment. *European Urology, Supplements* 10[9], 626. 2011. Elsevier.
Excl reason: Not in PICO

Grossman, H. B. Premalignant and early carcinomas of the penis and scrotum. *Urologic Clinics of North America* 19[2], 221-226. 1992.
Excl reason: Narrative review

Gulia, A. K., Mandhani, A., Muruganandham, K., Kapoor, R., Ansari, M. S., and Srivastava, A. Impact of delay in inguinal lymph node dissection in patients with carcinoma of penis. *Indian Journal of Cancer* 46[3], 214-218. 2009.
Excl reason: Not in PICO

Gutierrez, C., Hernansanz, S., Rubiales, A. S., Del Valle, M. L., Cuadrillero, Rodriguez F., Flores, L. A., and Garcia, C. Clinical manifestations and care in tumors with pelvic involvement: Is there a pelvic syndrome in Palliative Care?. [Spanish]. *Medicina Paliativa* 13[1], 32-36. 2006.
Excl reason: Not in PICO

Harzmann, R. Early diagnosis of urogenital tumors. [German]. *Zeitschrift fur Hautkrankheiten* 62[9], 665-682. 1-5-0681.
Excl reason: Narrative review

Hawary, A. M., Warburton, H. E., Brough, R. J., Collins, G. N., Brown, S. C., O'Reilly, P. H., and Adeyoju, A. A. B. The '2-week wait' rule for referrals for suspected urological cancers - Urgent need for refinement of criteria. *Annals of the Royal College of Surgeons of England* 90[6], 517-522. 2008.
Excl reason: Not in PICO

Horenblas, S., Jansen, L., Meinhardt, W., Hoefnagel, C. A., De Jong D., and Nieweg, O. E. Detection of occult metastasis in squamous cell carcinoma of the penis using a dynamic sentinel node procedure. *Journal of Urology* 163[1], 100-104. 2000.
Excl reason: Not in PICO

Inoue, T., Satou, M., Morii, H., and Matsuda, T. [Schwannoma of the penis: a case report]. [Review] [17 refs] [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 54[8], 569-572. 2008.
Excl reason: Not in PICO

Jones, W. G., Fossa, S. D., Hamers, H., and van den Bogaert, W. Penis cancer: A review by the joint radiotherapy committee of the European Organisation for Research and Treatment of Cancer (EORTC) Genitourinary and Radiotherapy Groups. *Journal of Surgical Oncology* 40[4], 227-231. 1989.
Excl reason: Narrative review

Kamat, A. M., Carpenter, S. M., Czerniak, B. A., and Pisters, L. L. Metastatic penile cancer in a young Caucasian male: impact of delayed diagnosis. *Urologic Oncology* 23[2], 130-131. 2005.
Excl reason: Not in PICO

Karanikas, Christos, Ptohis, Nikolaos, Mainta, Evgenia, Baltas, Christos, Athanasiadis, Dimitris, Lechareas, Simos, Katirtzoglou, Nikolaos, and Xynogalos, Spyros. Pulmonary adenocarcinoma presenting with penile metastasis: a case report. *Journal of Medical Case Reports* 6[1], 252. 2012.
Excl reason: Not in PICO

Kattan, M. W., Ficarra, V., Artibani, W., Cunico, S. C., Fandella, A., Martignoni, G., Novara, G., Galetti, T. P., and Zattoni, F. Nomogram Predictive of Cancer Specific Survival in Patients Undergoing Partial or Total Amputation for Squamous Cell Carcinoma of the Penis. *Journal of Urology* 175[6], 2103-2108. 2006.
Excl reason: Not in PICO

Katz, A. The top 13: What family physicians should know about prostate cancer. *Canadian Family Physician* 54[2], 198-203. 2008.
Excl reason: Not in PICO

Kohn, F. M. [Skin changes of the penis. Differentiation between local findings and systemic diseases!]. [German]. *MMW Fortschritte der Medizin* 144[12], 30-32. 1934.
Excl reason: Narrative review

Kreuter, A., Brockmeyer, N. H., Weissenborn, S. J., Gambichler, T., Stucker, M., Altmeyer, P., Pfister, H., Wieland, U., and German Competence Network HIV/AIDS. Penile intraepithelial neoplasia is frequent in HIV-positive men with anal dysplasia. *Journal of Investigative Dermatology* 128[9], 2316-2324. 2008.
Excl reason: Not in PICO

Kumar, P., Singh, S., Goddard, J. C., Terry, T. R., and Summerton, D. J. The development of a supraregional network for the management of penile cancer. *Annals of the Royal College of Surgeons of England* 94[3], 204-209. 2012.
Excl reason: Not in PICO

Leslie, J. A. and Cain, M. P. Pediatric Urologic Emergencies and Urgencies. *Pediatric Clinics of North America* 53[3], 513-527. 2006.
Excl reason: Narrative review

Lont, A. P., Kroon, B. K., Horenblas, S., Gallee, M. P., Berkhof, J., Meijer, C. J., and Snijders, P. J. Presence of high-risk human papillomavirus DNA in penile carcinoma predicts favorable outcome in survival. *International Journal of Cancer* 119[5], 1078-1081. 1-9-2006.
Excl reason: Not in PICO

Lucky, M. A., Rogers, B., and Parr, N. J. Referrals into a dedicated British penile cancer centre and sources of possible delay. *Sexually Transmitted Infections* 85[7], 527-530. 2009.
Excl reason: Not in PICO

Lutterbach, J., Pagenstecher, A., Weyerbrock, A., Schultze-Seemann, W., and Waller, C. F. Early-stage penile carcinoma metastasizing to brain: case report and literature review. [Review] [15 refs]. *Urology* 66[2], 432. 2005.
Excl reason: Not in PICO

- Markos, A. R. The presentation of anogenital cancers as sexually transmissible infection: a case for vigilance. *Sexual Health* 4[1], 79-80. 2007.
Excl reason: Narrative review
- Mebel, M. and Vogler, H. Special problems of early detection of malignant tumors of the genitourinary system. [German]. *Archiv fur Geschwulstforschung* 51[8], 679-684. 1981.
Excl reason: Not in PICO
- Minevich, E. Genitourinary emergencies in children. *Minerva Pediatrica* 61[1], 53-65. 2009.
Excl reason: Narrative review
- Misra, S., Chaturvedi, A., and Misra, N. C. Penile carcinoma: A challenge for the developing world. *Lancet Oncology* 5[4], 240-247. 1-4-2004.
Excl reason: Narrative review
- Miyamoto, T., Ikehara, A., Araki, M., Akaeda, T., and Mihara, M. Cutaneous metastatic carcinoma of the penis: suspected metastasis implantation from a bladder tumor. *Journal of Urology* 163[5], 1519. 2000.
Excl reason: Not in PICO
- Moiyadi, A. V., Tongaonkar, H. B., and Bakshi, G. K. Symptomatic intracranial metastasis in penile carcinoma. *Indian Journal of Urology* 26[4], 585-586. 2010.
Excl reason: Not in PICO
- Mosconi, A. M., Roila, F., Gatta, G., and Theodore, C. Cancer of the penis. [Review] [98 refs]. *Critical Reviews in Oncology-Hematology* 53[2], 165-177. 2005.
Excl reason: Narrative review
- Naumann, C. M., Filippow, N., Seif, C., van der Horst, C., Roelver, L., Braun, P. M., Juenemann, K. P., and Portillo, F. J. Penile carcinoma (pT1 G2): surveillance or inguinal lymph node dissection? *Onkologie* 28[3], 135-138. 2005.
Excl reason: Not in PICO
- Palamaras, I., Hamill, M., Sethi, G., Wilkinson, D., and Lamba, H. The usefulness of a diagnostic biopsy clinic in a genitourinary medicine setting: recent experience and a review of the literature. [Review] [21 refs]. *Journal of the European Academy of Dermatology & Venereology* 20[8], 905-910. 2006.
Excl reason: Not in PICO
- Persaud, S., Sebro, K., Saroop, S. & Goetz, L. (2012) Urethral cancer: A difficult diagnosis? *West Indian Medical Journal*, 61: 52.
Not in PICO
- Piccinelli, A., Romano, C., Ranieri, A., Chinaglia, D., and Lembo, A. [Precancerous lesions of the penis]. [Italian]. *Archivio Italiano di Urologia, Andrologia* 68[3], 133-135. 1996.
Excl reason: Narrative review
- Ritchie, A. W., Foster, P. W., Fowler, S., and BAUS Section of Oncology. Penile cancer in the UK: clinical presentation and outcome in 1998/99. *BJU International* 94[9], 1248-1252. 2004.
Excl reason: Not in PICO
- Rotolo, J. E. and Lynch, J. H. Penile cancer: Curable with early detection. *Hospital Practice* 26[6], 131-138. 1991.
Excl reason: Narrative review
- Rubben, H., Hering, F. J., Durben, G., and Lutzeyer, W. Value of screening for early detection of urological tumors (author's transl). [German]. *Urologia Internationalis* 37[1], 1-18. 1982.
Excl reason: Not in PICO
- Schoeneich, G. and Bruhl, P. Penile carcinoma. [German]. *Tumor Diagnostik und Therapie* 15[5], 163-167. 1994.
Excl reason: Narrative review
- Shigehara, K.; Sasagawa, T.; Kawaguchi, S.; Nakashima, K.; Nakashima, T.; Shimamura, M.; Furubayashi, K.; Namiki, M. (2014). Cytological evaluation using liquid-based cytology in the male urogenital tract infected with human papillomavirus. *Diagnostic Cytopathology*, 42, 491-7.

Not in PICO

Shim, T. N., Muneer, A., and Bunker, C. B. Chronic erosive and verrucous herpes simplex of the penis in chronic lymphocytic leukaemia. *British Journal of Dermatology* 167, 115-116. 2012. Blackwell Publishing Ltd.

Excl reason: Not in PICO

Siow, W. Y. and Cheng, C. Penile cancer: current challenges. [Review] [83 refs]. *Canadian Journal of Urology* 12, Suppl-23. 2005.

Excl reason: Narrative review

Sonpavde, G., Pagliaro, L. C., Buonerba, C., Dorff, T. B., Lee, R. J. & Di, L. G. (2013) Penile cancer: current therapy and future directions. [Review]. *Annals of Oncology*, 24: 1179-1189.

Narrative review

Spiess, P. E. & National Comprehensive, C. N. (2013) New treatment guidelines for penile cancer. *Journal of the National Comprehensive Cancer Network*, 11: Suppl-62.

Not in PICO

Stehr, M., Rohrbach, H., Schuster, T., and Dietz, H. G. [Leiomyoma of the glans penis]. [German]. *Urologe (Ausg.A)* 39[2], 171-173. 2000.

Excl reason: Not in PICO

Stotts, R. C. Cancers of the prostate, penis, and testicles: epidemiology, prevention, and treatment. [Review] [83 refs]. *Nursing Clinics of North America* 39[2], 327-340. 2004.

Excl reason: Narrative review

Teichman, J. M., Sea, J., Thompson, I. M., and Elston, D. M. Noninfectious penile lesions. [Review] [49 refs]. *American Family Physician* 81[2], 167-174. 15-1-2010.

Excl reason: Narrative review

Theiss, M., Tack, W., and Frohmuller, H. Screening examination for urological malignancies. [German]. *Medizinische Welt* 47[12], 493-497. 1996.

Excl reason: Not in PICO

Tsaur, I., Ochsendorf, F. R., Bug, R., and Jonas, D. [Primary syphilitic lesion mimicking penile cancer. Atypical manifestation with an unconventional diagnostic approach]. [German]. *Urologe (Ausg.A)* 48[10], 1210-1213. 2009.

Excl reason: Not in PICO

Tsen, H. F., Morgenstern, H., Mack, T., and Peters, R. K. Risk factors for penile cancer: results of a population-based case-control study in Los Angeles County (United States). *Cancer Causes & Control* 12[3], 267-277. 2001.

Excl reason: Not in PICO

Urrutia, Alonso J., Machuca, Santacruz J., Tallada, Bunuel M., Moreno, Jimenez J., Vicente, Prados J., Cozar Olmo, J. M., and Camara, Ortega M. [Epidermoid carcinoma of the male urethra. Our experience in 5 cases]. [Review] [25 refs] [Spanish]. *Archivos Espanoles de Urologia* 48[4], 355-363. 1995.

Excl reason: Not in PICO

Vasdev, N. and Thorpe, A. C. Has the introduction of the '2 week rule' in the UK led to an earlier diagnosis of urological malignancy? *ecancermedicalsience* 5[1]. 31-8-2011.

Excl reason: Not in PICO

Vincent, M. V. and Mackinnon, E. The response of clinical balanitis xerotica obliterans to the application of topical steroid-based creams. *Journal of Pediatric Surgery* 40[4], 709-712. 2005.

Excl reason: Not in PICO

Vogt, H., Schmidt, M., Bares, R., Brenner, W., Grunwald, F., Kopp, J., Reiners, C., Schober, O., Schumichen, C., Schicha, H., Sciuk, J., Sudbrock, F., and Wengenmair, H. [Procedure guideline for sentinel lymph node diagnosis]. [German]. *Nuclear-Medizin* 49[4], 167-172. 2010.

Excl reason: Not in PICO

Wessels, R., De Bruin, D. M., Faber, D. J., Horenblas, S., Van Rhijn, B. W. G., Vincent, A. D., Van Leeuwen, T. G. & Ruers, T. J. M. (2013) Optical coherence tomography (OCT) in neoplasia of the

penis. *European Journal of Cancer*, 49: S249.

Published as poster abstract only. Not enough information can be extracted to ascertain relevance, but I think it is not in PICO

Willson, P. Testicular, prostate and penile cancers in primary care settings: the importance of early detection. *The Nurse practitioner* 16[11], 18-26. 1991.

Excl reason: Narrative review

Wood, S. A guide to common conditions of the penis. [Review] [0 refs]. *Practitioner* 244[1614], 764-770. 2000.

Excl reason: Not in PICO

Wren, T. Penile and testicular disorders. [Review] [30 refs]. *Nursing Clinics of North America* 39[2], 319-326. 2004.

Excl reason: Narrative review

Yao, H. J., Ying, J., Wang, Z., Yao, D. H., Ren, X. M., and Bao, Y. Y. [One case report of primary penile malignant lymphoma (with a review of 24 case reports)]. [Chinese]. *Zhong Hua Nan Ke Xue* 12[6], 520-524. 20-11-0157.

Excl reason: Not in PICO

Zimet, G., Weiss, T., Rosenthal, S., Brennenman, S., and Klein, J. Physicians' sexual health discussions with adolescent males and attitudes about HPV vaccination. *Journal of Adolescent Health* 48[2 SUPPL. 1], S27-S28. 2011. Elsevier USA.

Excl reason: Not in PICO

Review question:

Which investigations of symptoms of suspected penile cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

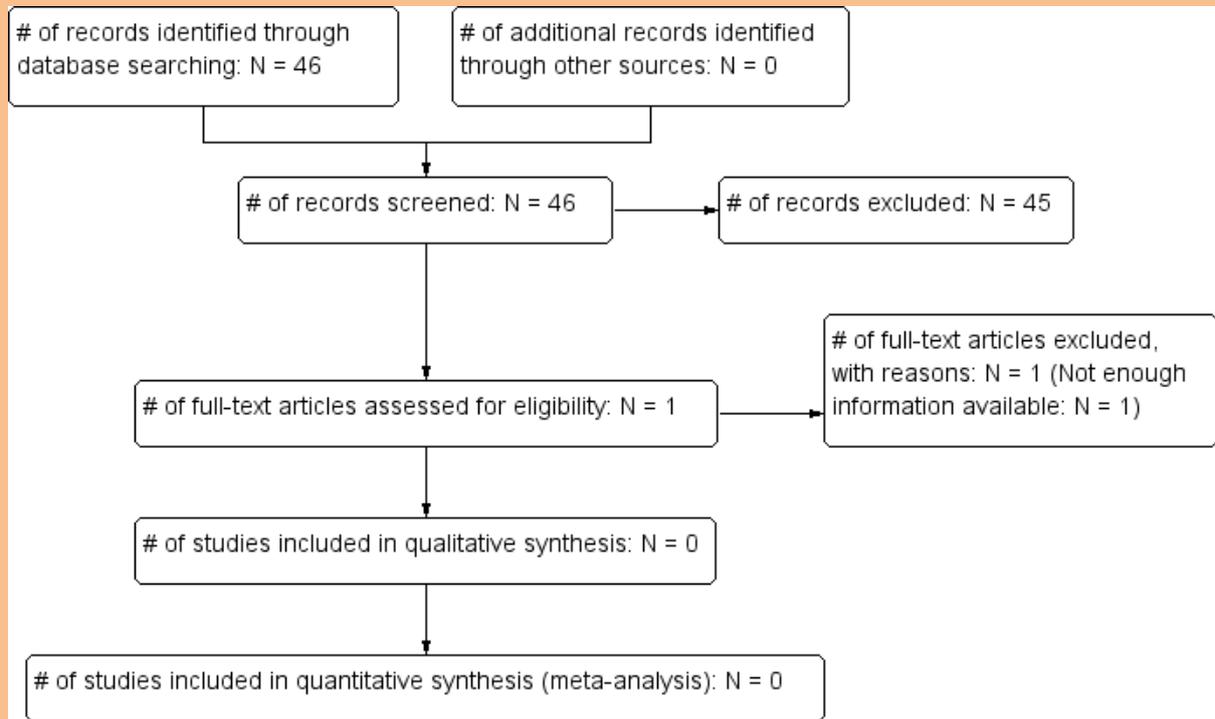
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	85	31	14/05/2013
Premedline	1980-2013	14	2	14/05/2013
Embase	1980-2013	122	25	14/05/2013
Cochrane Library	1980-2013	32	0	14/05/2013
Psychinfo	1980-2013	0	0	14/05/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	23	0	14/05/2013

Total References retrieved (after de-duplication): 43

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	5/2013-26/08/2014	4	2	26/08/2014
Premedline	5/2013-26/08/2014	5	0	26/08/2014
Embase	5/2013-26/08/2014	25	2	26/08/2014
Cochrane Library	5/2013-26/08/2014	2	0	26/08/2014
Web of Science (SCI &	5/2013-	1	0	26/08/2014

Total References retrieved (after de-duplication): 3



Study results

No evidence was identified pertaining to the diagnostic accuracy of tests used in patients with suspected penile cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

- Arya, M., Kalsi, J., Kelly, J. & Muneer, A. (2013) Malignant and premalignant lesions of the penis. [Review]. *BMJ*, 346: f1149.
Narrative review
- Azevedo Cavalcanti, R. F., Quirino, R., Monnerat, L. F., Ornellas, A. A. & Arcuri, R. (2004) Merkel cell carcinoma of penis. [French]. *Progres En Urologie*, 14: 558-560.
Not in PICO
- Barbagli, G., Palminteri, E., Mirri, F., Guazzoni, G., Turini, D. & Lazzeri, M. (2006) Penile carcinoma in patients with genital lichen sclerosus: A multicenter survey. *Journal of Urology*, 175: 1359-1363.
Not in PICO
- Barocas, D. A. & Chang, S. S. (2010) Penile Cancer: Clinical Presentation, Diagnosis, and Staging. *Urologic Clinics of North America*, 37: 343-352.
Narrative review
- Bhagat, S. K., Gopalakrishnan, G., Kekre, N. S., Chacko, N. K., Kumar, S., Manipadam, M. T. & Samuel, P. (2010) Factors predicting inguinal node metastasis in squamous cell cancer of penis. *World Journal of Urology*, 28: 93-98.
Not in PICO

- Bigot, P. & Longvert, C. (2011) [Penile dermatological lesions: how to identify premalignant lesions?]. [French]. *Progres en urologie : journal de l'Association francaise d'urologie et de la Societe francaise d'urologie*, 21: S50-S52.
Not in PICO
- Bleeker, M. C., Heideman, D. A., Snijders, P. J., Horenblas, S., Dillner, J. & Meijer, C. J. (2009) Penile cancer: epidemiology, pathogenesis and prevention. [Review] [99 refs]. *World Journal of Urology*, 27: 141-150.
Not in PICO
- Bouchot, O. & Rigaud, J. (2004) [Penis tumours: techniques and indications]. [Review] [30 refs] [French]. *Annales d Urologie*, 38: 285-297.
Narrative review
- Brady, K. L., Mercurio, M. G. & Brown, M. D. (2013) Malignant tumors of the penis. [Review]. *Dermatologic Surgery*, 39: 527-547.
Narrative review
- Buechner, S. A. (2002) Common skin disorders of the penis. [Review] [39 refs]. *BJU International*, 90: 498-506.
Not in PICO
- Chiu, T.-Y., Huang, H.-S., Lai, M.-K., Chen, J., Hsieh, T.-S. & Chueh, S.-C. (1998) Penile cancer in Taiwan - 20 years' experience at National Taiwan University Hospital. *Journal of the Formosan Medical Association*, 97: 673-678.
Not in PICO
- Cho, Y. S., Lee, J. A., Kim, S. B., Gong, S. J., Kim, J. H., Youn, S. M. & Kim, E. T. (2010) A case of synchronous double primary cancer of the penis and urinary bladder. *Cancer Research & Treatment*, 42: 53-56.
Not in PICO
- Cottrell, A. M., Dickerson, D. & Oxley, J. D. (2008) Suspected penile cancer: A method to improve handling of pathology specimens. *BJU International*, 101: 1325-1328.
Not in PICO
- David, N. & Tang, A. (2002) Efficacy and safety of penile biopsy in a GUM clinic setting. *International Journal of STD and AIDS*, 13: 573-576.
Not in PICO
- Dechev, I. & Banchev, A. (2006) More about the clinical characteristics of penile cancer. [Bulgarian]. *General Medicine*, 8: 42-46.
Not in PICO
- Descazeaud, A. & Mottet, N. (2008) Cancers of the penis and testicle: news in 2008. [French]. *Progres En Urologie*, 18: S130-S134.
Narrative review
- Eliezri, Y. D. (1988) The toluidine blue test: an aid in the diagnosis and treatment of early squamous cell carcinomas of mucous membranes. *Journal of the American Academy of Dermatology*, 18: 1339-1349.
Narrative review
- Ficarra, V., Zattoni, F., Artibani, W., Fandella, A., Martignoni, G., Novara, G., Galetti, T. P., Zambolin, T., Kattan, M. W. & Penile Cancer Project Members, U. O. N. E. (1704) Nomogram predictive of pathological inguinal lymph node involvement in patients with squamous cell carcinoma of the penis. *Journal of Urology*, 175: 1700-1704.
Not in PICO
- Ficarra, V., Martignoni, G., Maffei, N., Cerruto, M. A., Novara, G., Cavalleri, S. & Artibani, W. (2002) Predictive pathological factors of lymph nodes involvement in the squamous cell carcinoma of the penis. *International Urology and Nephrology*, 34: 245-250.
Not in PICO

- Gipponi, M. (2005) Clinical applications of sentinel lymph-node biopsy for the staging and treatment of solid neoplasms. [Review] [99 refs]. *Minerva Chirurgica*, 60: 217-233.
Not in PICO
- Hawary, A. M., Warburton, H. E., Brough, R. J., Collins, G. N., Brown, S. C., O'Reilly, P. H. & Adeyoku, A. A. B. (2008) The '2-week wait' rule for referrals for suspected urological cancers - Urgent need for refinement of criteria. *Annals of the Royal College of Surgeons of England*, 90: 517-522.
Not in PICO
- Horenblas, S., Jansen, L., Meinhardt, W., Hoefnagel, C. A., de, J. D. & Nieweg, O. E. (2000) Detection of occult metastasis in squamous cell carcinoma of the penis using a dynamic sentinel node procedure. *Journal of Urology*, 163: 100-104.
Not in PICO
- Jakobsen, J., Ording, O. K., Egbert Arnold, Z. K. & Bjerggaard, J. J. (2012) Sources of delay to a penile cancer referral centre in West Denmark. *Urology*, 80: S265-S266.
Not in PICO
- Kirrandar, P., Andren, O. & Windahl, T. (2013) Dynamic sentinel node biopsy in penile cancer: initial experiences at a Swedish referral centre. *BJU International*, 111: t-53.
Not in PICO
- Kumar, P., Singh, S., Goddard, J. C., Terry, T. R. & Summerton, D. J. (2012) The development of a supraregional network for the management of penile cancer. *Annals of the Royal College of Surgeons of England*, 94: 204-209.
Not in PICO
- Luciani, L., Pisciolli, F., Scappini, P. & Pusioli, T. (1984) Value and role of percutaneous regional node aspiration cytology in the management of penile carcinoma. *European Urology*, 10: 294-302.
Narrative review
- Minevich, E. (2009) Genitourinary emergencies in children. *Minerva Pediatrica*, 61: 53-65.
Narrative review
- Mosconi, A. M., Roila, F., Gatta, G. & Theodore, C. (2005) Cancer of the penis. *Critical Reviews in Oncology/Hematology*, 53: 165-177.
Narrative review
- Nicolai, N. (2013) Has dynamic sentinel node biopsy achieved its top performance in penile cancer? What clinicians still need to manage lymph nodes in early stage penile cancer. *European Urology*, 63: 664-666.
Not in PICO
- Palamaras, I., Hamill, M., Sethi, G., Wilkinson, D. & Lamba, H. (2006) The usefulness of a diagnostic biopsy clinic in a genitourinary medicine setting: recent experience and a review of the literature. [Review] [21 refs]. *Journal of the European Academy of Dermatology & Venereology*, 20: 905-910.
Not in PICO
- Persaud, S., Sebro, K., Saroop, S. & Goetz, L. (2012) Urethral cancer: A difficult diagnosis? *West Indian Medical Journal*, 61: 52.
Not in PICO
- Ritchie, A. W., Foster, P. W., Fowler, S. & BAUS Section of Oncology (2004) Penile cancer in the UK: clinical presentation and outcome in 1998/99. *BJU International*, 94: 1248-1252.
Not in PICO
- Rotolo, J. E. & Lynch, J. H. (1991) Penile cancer: curable with early detection. [Review] [10 refs]. *Hospital Practice (Office Edition)*, 26: 131-138.
Narrative review
- Saisorn, I., Lawrentschuk, N., Leewansangtong, S. & Bolton, D. M. (2006) Fine-needle aspiration cytology predicts inguinal lymph node metastasis without antibiotic pretreatment in penile carcinoma. *BJU International*, 97: 1225-1228.
Not in PICO

- Scher, B., Seitz, M., Reiser, M., Hungerhuber, E., Hahn, K., Tiling, R., Herzog, P., Reiser, M., Schneede, P. & Dresel, S. (2005) 18F-FDG PET/CT for staging of penile cancer. *Journal of Nuclear Medicine*, 46: 1460-1465.
Not in PICO
- Schoeneich, G. & Bruhl, P. (1994) Penile carcinoma. [German]. *Tumor Diagnostik und Therapie*, 15: 163-167.
Narrative review
- Shim, T. N., Muneer, A. & Bunker, C. B. (2012) Chronic erosive and verrucous herpes simplex of the penis in chronic lymphocytic leukaemia. *British Journal of Dermatology*, 167: 115-116.
Not in PICO
- Siow, W. Y. & Cheng, C. (2005) Penile cancer: current challenges. *The Canadian journal of urology*, 12: 18-23.
Narrative review
- Skeppner, E., Andersson, S.-O., Johansson, J.-E. & Windahl, T. (2012) Initial symptoms and delay in patients with penile carcinoma. *Scandinavian Journal of Urology and Nephrology*, 46: 319-325.
Not in PICO
- Sonpavde, G., Pagliaro, L. C., Buonerba, C., Dorff, T. B., Lee, R. J. & Di, L. G. (2013) Penile cancer: current therapy and future directions. [Review]. *Annals of Oncology*, 24: 1179-1189.
Narrative review
- Spiess, P. E. & National Comprehensive, C. N. (2013) New treatment guidelines for penile cancer. *Journal of the National Comprehensive Cancer Network*, 11: Suppl-62.
Not in PICO
- Teichman, J. M., Sea, J., Thompson, I. M. & Elston, D. M. (2010) Noninfectious penile lesions. [Review] [49 refs]. *American Family Physician*, 81: 167-174.
Narrative review
- Vasdev, N. & Thorpe, A. C. (2011) Has the introduction of the '2 week rule' in the UK led to an earlier diagnosis of urological malignancy? *ecancermedicalscience*, 5.
Not in PICO
- Vogt, H., Schmidt, M., Bares, R., Brenner, W., Grunwald, F., Kopp, J., Reiners, C., Schober, O., Schumichen, C., Schicha, H., Sciuk, J., Sudbrock, F. & Wengenmair, H. (2010) [Procedure guideline for sentinel lymph node diagnosis]. [German]. *Nuclear-Medizin*, 49: 167-172.
Narrative review
- Wajzman, Z. & Klimberg, I. (1987) Needle aspiration and needle biopsy procedures. *Urologic Clinics of North America*, 14: 103-113.
Narrative review
- Wawroschek, F., Harzmann, R. & Weckermann, D. (2005) [Value of sentinel node biopsy for urological tumors]. [Review] [15 refs] [German]. *Urologe (Ausg.A)*, 44: 630-634.
Narrative review
- Wessels, R., De Bruin, D. M., Faber, D. J., Horenblas, S., Van Rhijn, B. W. G., Vincent, A. D., Van Leeuwen, T. G. & Ruers, T. J. M. (2013) Optical coherence tomography (OCT) in neoplasia of the penis. *European Journal of Cancer*, 49: S249.
Published as poster abstract only. Not enough information can be extracted to ascertain relevance, but I think it is not in PICO
- Willson, P. (1923) Testicular, prostate and penile cancers in primary care settings: the importance of early detection. *The Nurse practitioner*, 16: 18-26.
Narrative review

SKIN CANCERS

MELANOMA

Review question:

What is the risk of melanoma in patients presenting in primary care with symptom(s)?

Results

Literature search

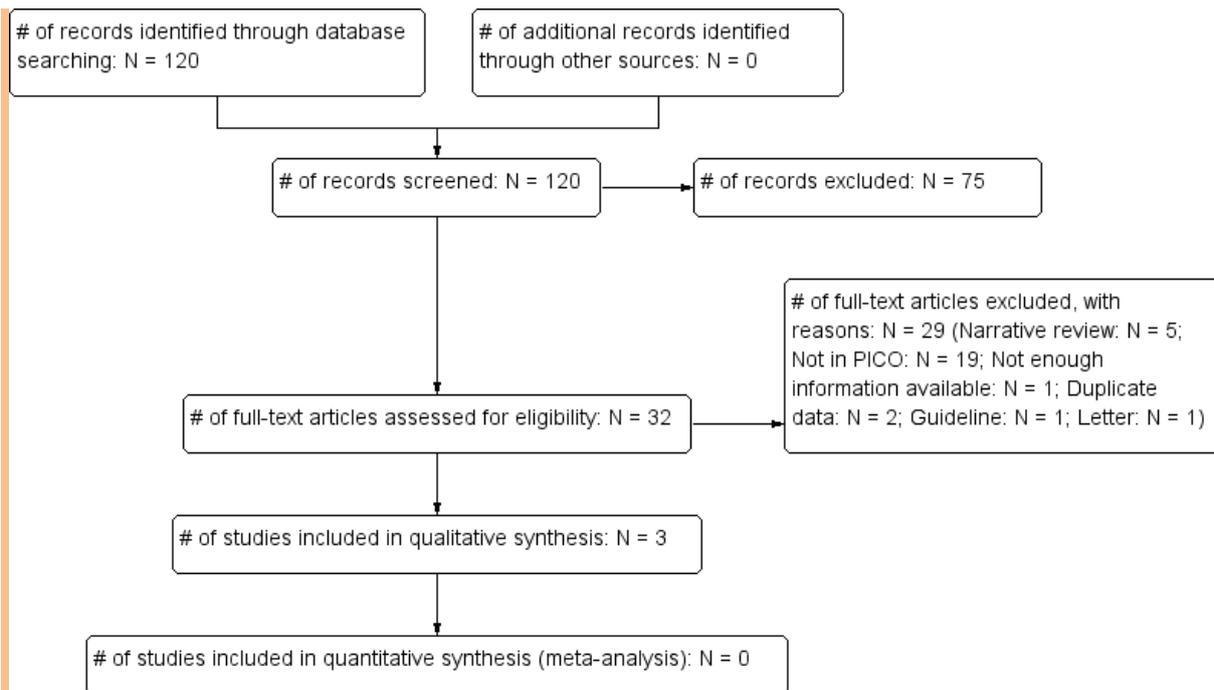
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	1403	49	08/04/2013
<i>Premedline</i>	1980-2013	50	1	08/04/2013
<i>Embase</i>	1980-2013	2470	47	09/04/2013
<i>Cochrane Library</i>	1980-2013	199	7	09/04/2013
<i>Psychinfo</i>	1980-2013	10	0	08/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	275	23	09/04/2013

Total References retrieved (after de-duplication): 101

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-19/08/2014	39	7	19/08/2014
<i>Premedline</i>	4/2013-19/08/2014	70	6	19/08/2014
<i>Embase</i>	4/2013-19/08/2014	184	11	19/08/2014
<i>Cochrane Library</i>	4/2013-19/08/2014	224	0	19/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	4/2013	162	3	19/08/2014

Total References retrieved (after de-duplication): 19



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main bias risks and applicability concerns that the studies are subject to relate to (1) the patient sampling method not clearly being consecutive or random, (2) the extent to which the study setting matches UK primary care, (3) the quality of the reference standard, which may not always reliably diagnose the symptoms, (4) the fact that the reference standard did not in all cases match that of the current question, namely histology, and 5) data missing .

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Emery (2010)	?	+	?	+	?	+	?
Walter (2012; 2013)	?	+	?	?	+	+	?

High	Unclear	Low
------	---------	-----

Study results

Table 1: Melanoma: Study results.

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI) Prevalence
Emery (2010)	Pigmented lesion	All included	1.4 (0.8-2.3)

Lesion-based analysis		patients	17/1211
		England sample	0.8 (0.3-2) 5/630
		Australia sample	1.9 (1-3.5) 11/581
Walter (2012) Lesion-based analysis	Suspicious pigmented lesions	All included patients	2.3 (1.6-3.2) 36/1573
Walter (2013) Lesion-based analysis	7PCL: Suspicious pigmented lesions: Change in size of lesion	All included patients	3.8 (2.5-5.5) 26/693
Walter (2013) Lesion-based analysis	7PCL: Suspicious pigmented lesions: Irregular pigmentation	All included patients	4.4 (3.1-6.3) 31/702
Walter (2013) Lesion-based analysis	7PCL: Suspicious pigmented lesions: Irregular border	All included patients	5.1 (3.4-7.5) 25/492
Walter (2013) Lesion-based analysis	7PCL: Suspicious pigmented lesions: Inflammation	All included patients	4.5 (1.9-10.1) 6/132
Walter (2013) Lesion-based analysis	7PCL: Suspicious pigmented lesions: Itch or altered sensation	All included patients	2.3 (1.1-4.4) 9/397
Walter (2013) Lesion-based analysis	7PCL: Suspicious pigmented lesions: Lesion larger than other (diameter > 7 mm)	All included patients	3.9 (2.6-5.7) 27/695
Walter (2013) Lesion-based analysis	7PCL: Suspicious pigmented lesions: Oozing/crusting of lesion	All included patients	4.9 (2.1-10.1) 7/144
Walter (2013) Lesion-based analysis	Original 7PCL: Score \geq 1*	All included patients	2.7 (1.9-3.8) 36/1334
Walter (2013) Lesion-based analysis	Original 7PCL: Score \geq 2*	All included patients	3.3 (2.4-4.7) 34/1016
Walter (2013) Lesion-based analysis	Original 7PCL: Score \geq 3*	All included patients	5.1 (3.5-7.4) 29/565
Walter (2013) Lesion-based analysis	Original 7PCL: Score \geq 4*	All included patients	8.2 (5.2-12.5) 20/245

Lesion-based analysis			
Walter (2013) Lesion-based analysis	Original 7PCL: Score \geq 5*	All included patients	12.3 (6.1-22.6) 9/73
Walter (2013) Lesion-based analysis	Original 7PCL: Score \geq 6*	All included patients	10.5 (1.8-34.5) 2/19
Walter (2013) Lesion-based analysis	Weighted 7PCL: Score \geq 1**	All included patients	2.7 (1.9-3.8) 36/1334
Walter (2013) Lesion-based analysis	Weighted 7PCL: Score \geq 2**	All included patients	2.9 (2.1-4.1) 36/1221
Walter (2013) Lesion-based analysis	Weighted 7PCL: Score \geq 3**	All included patients	3.4 (2.4-4.8) 33/969
Walter (2013) Lesion-based analysis	Weighted 7PCL: Score \geq 4**	All included patients	4.8 (3.4-6.8) 33/685
Walter (2013) Lesion-based analysis	Weighted 7PCL: Score \geq 5**	All included patients	5.9 (4-8.5) 27/459
Walter (2013) Lesion-based analysis	Weighted 7PCL: Score \geq 6**	All included patients	8.3 (5.4-12.6) 21/252
Walter (2013) Lesion-based analysis	Weighted 7PCL: Score \geq 7**	All included patients	10.9 (6.7-17.1) 17/156
Walter (2013) Lesion-based analysis	Weighted 7PCL: Score \geq 8**	All included patients	15.7 (7.5-29.1) 8/51
Walter (2013) Lesion-based analysis	Weighted 7PCL: Score \geq 9**	All included patients	8.3 (0.4-40.2) 1/12

*** Original 7PCL consists of 7 items (change in shape, size and/or colour, inflammation, crusting/bleeding, sensory change, diameter \geq 7 mm) and each present feature score 1 point. ** The Weighted 7PCL consists of the same 7 items, but these are divided into major (change in**

shape, size and/or colour) scoring 2 points each and minor (inflammation, crusting/bleeding, sensory change, diameter \geq 7 mm) scoring 1 point.

Evidence statement(s):

Pigmented skin lesions presenting in a primary care setting are associated with positive predictive values of 0.8-5.1% for melanoma (2 studies, N = 2784 *lesions*), and the positive predictive values increased proportionally to the number of different risk features the lesions displayed up to 15.7% (1 study, 1436 *lesions*). The studies were associated with 4 bias/applicability concerns (see also Table 1).

Evidence tables

Emery (2010)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective series of pigmented lesions recruited from England (6 general practices covering urban, suburban and rural areas with a registered population of 52913) and Australia (3 primary care skin cancer clinics operated by GPs from a metropolitan area)
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>England: N = 389 patients, mean age = 44.9 years, 68.6% females with interpretable images from N = 630 lesions. 0/630 lesions were squamous cell carcinoma, 0/630 lesions were basal cell carcinoma, 5/630 lesions were melanoma, and 0/630 lesions were lentigo maligna (melanoma).</p> <p>Australia: N = 469 patients, mean age = 50 years, 48% females, with interpretable images from N = 581 lesions. 0/581 lesions were squamous cell carcinoma, 22/581 lesions were basal cell carcinoma, 7/581 lesions were melanoma, and 4/581 lesions were lentigo maligna (melanoma).</p> <p><u>Inclusion criteria:</u> England: Patients aged > 18 years were recruited into the study by their GP if they presented with concerns about a pigmented skin lesion between January 2005 and January 2006. Australia: Patients aged > 18 years were recruited into the study by their GP if they presented with concerns about a pigmented skin lesion between April 2008 and January 2009. Additional lesions were also included when a pigmented skin lesion was identified as potentially suspicious during their clinical examination</p> <p><u>Exclusion criteria:</u> None reported.</p> <p><u>Clinical setting:</u> Primary care, UK, and primary care skin cancer practice, Queensland Australia.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern

INDEX TEST	
A. Risk of bias	
Index test	Pigmented skin lesions that concerned patients, which were evaluated using macroscopic clinical photographs, dermoscopic images and SIAscan.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histopathology or in-person clinical review of the lesion by one expert, including the 7-point melanoma checklist and digital dermoscopy or clinical diagnosis made on the basis of the 7-point melanoma checklist, photographic and dermoscopy images
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Analysis was on a per-lesion basis rather than a per-patient basis

Walter (2012; 2013)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective series of suspicious pigmented lesions
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1293 patients, mean age (SD) = 44.6 (16.8) years; 465 males / 828 females with N = 1573 lesions, of which 1 was squamous cell carcinoma, 10 basal cell carcinomas, and 36 melanomas. <u>Inclusion criteria:</u> Patients aged ≥ 18 years presenting to one of the 15

	participating general practices with a suspicious (any lesion presented buy a patient, or opportunistically seen by a family doctor or practice nurse, that could not immediately be diagnosed as benign and about which the patient could not be reassured) pigmented lesion from March 2008 to May 2010. <u>Exclusion criteria:</u> Patients who were unable to give informed consent or were considere3d inappropriate to include by their family doctor. <u>Clinical setting:</u> UK primary care.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Suspicious (any lesion presented buy a patient, or opportunistically seen by a family doctor or practice nurse, that could not immediately be diagnosed as benign and about which the patient could not be reassured) pigmented lesion
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Expert opinion by a histologist or dermatologist or review by two other dermatology experts of the recorded clinical history and examination, a digital photograph, and MoleMate images where available with or without follow up 3-6 months later.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes Tests: No signs & symptoms (S&S)
Could the patient flow have introduced bias?	Tests: Low risk; S&S: Unclear risk
NOTES	Data from this study published in 2 papers: Details above refer to the data from Walter (2012). Further publication-specific details for Walter (2013): Of the 1573 included lesions, 42 did not have a reference standard assessment and the 7PCL was not fully completed for a further 95 lesions. The analyses were therefore based on 1436 lesions from 1182 patients (mean age (SD) = 44.7 (16.6) years; 424 males / 758 females with 36 melanomas). Analysis was

on a per-lesion basis rather than a per-patient basis for both papers.

References

Included Studies

Emery, J.D., Hunter, J., Hall, P.N., Watson, A.J., Moncrieff, M., Walter, F.M. (2010). Accuracy of SIAscopy for pigmented skin lesions encountered in primary care: development and validation of a new diagnostic algorithm. *BMJ Dermatology*, 10:9.

Walter, F.M., Morris, H.C., Humphrys, E., Hall, P.N., Prevost, A.T., Burrows, N., Bradshaw, L., Wilson, E.C., Norris, P., Walls, J., Johnson, M., Kinmonth, A.L., Emery, J.D. (2012). Effect of adding a diagnostic aid to best practice to manage suspicious pigmented lesions in primary care: randomised controlled trial. *BMJ*, 345: e4110.

Walter, F.M., Prevost, A.T., Vasconcelos, J., Hall, P.N., Burrows, N., Morris, H.C., Kinmonth, A.L., Emery, J.D. (2013). Using the 7-point checklist as a diagnostic aid for pigmented skin lesions in general practice: A diagnostic validation study. *British Journal of General Practice*, DOI: 10.3399/bjgp13X667213.

Excluded Studies

Ackerman, A. B. & Ackerman, A. B. (1988) A "changing mole" is not the best clue to clinical detection of an "early" malignant melanoma. *Archives of Dermatological Research*, 280 Suppl: S13-S14.
Narrative review

Agarwal, S. (2001) Out patient waiting time for common skin conditions - Do general practitioners and dermatologists have the same priorities? A questionnaire-based survey. *Clinical and Experimental Dermatology*, 26: 13-15.

Not in PICO

Aitken, J. F., Janda, M., Elwood, M., Youl, P. H., Ring, I. T., Lowe, J. B., Aitken, J. F., Janda, M., Elwood, M., Youl, P. H., Ring, I. T. & Lowe, J. B. (2006) Clinical outcomes from skin screening clinics within a community-based melanoma screening program. *Journal of the American Academy of Dermatology*, 54: 105-114.

Not in PICO

Aldridge, R. B. Z. (2011) The 'ABCD' mnemonic does not function as a useful guide in assisting novices with the diagnosis of melanoma. *British Journal of Dermatology*, Conference: July.

Not in PICO

Allon, I., Allon, D. M., Gal, G., Anavi, Y., Chaushu, G. & Kaplan, I. (2013) Re-evaluation of common paradigms regarding the clinical appearance of oral mucosal malignancies. *Journal of Oral Pathology and Medicine*, 42: 670-675.

Not in PICO

Antonio, J. R., Soubhia, R. M., D'Avila, S. C., Caldas, A. C., Tridico, L. A. & Alves, F. T. (2013) Correlation between dermoscopic and histopathological diagnoses of atypical nevi in a dermatology outpatient clinic of the Medical School of Sao Jose do Rio Preto, SP, Brazil. *Anais Brasileiros de Dermatologia*, 88: 199-203.

Not in PICO

Askari, S. K., Schram, S. E., Wenner, R. A., Bowers, S., Liu, A., Bangerter, A. K. & Warshaw, E. M. (2007) Evaluation of prospectively collected presenting signs/symptoms of biopsy-proven melanoma, basal cell carcinoma, squamous cell carcinoma, and seborrheic keratosis in an elderly male population. *Journal of the American Academy of Dermatology*, 56: 739-747.

Not in PICO

Baade, P. D. B. (2005) Community perceptions of suspicious pigmented skin lesions: Are they accurate when compared to general practitioners? *Cancer Detection and Prevention*, 29: 267-275.

Not in PICO

Baade, P. D. D. (2005) Clinical diagnosis and management of suspicious pigmented skin lesions--a survey of GPs. *Australian Family Physician*, 34: 79-83.

Not in PICO

- Badertscher, N., Rosemann, T., Tandjung, R. & Braun, R. P. (2011) minSKIN does a multifaceted intervention improve the competence in the diagnosis of skin cancer by general practitioners? Study protocol for a randomised controlled trial. *Trials*, 12: 165.
Not in PICO
- Balois, T. & Amar, M. B. (2014) Morphology of melanocytic lesions in situ. *Science Reporter*, 4: 3622.
Not in PICO
- Barchuk, A. S., Anisimov, V. V., Vagner, R. I., Barchuk, A. S., Anisimov, V. V. & Vagner, R. I. (1996) [Clinical diagnosis of primary melanoma of the skin]. [Review] [18 refs] [Russian]. *Voprosy Onkologii*, 42: 96-100.
In Russian. Not enough information can be extracted to definitely ascertain whether it is in PICO, but I don't think so.
- Basra, M. (2012) An online survey of the awareness of malignant melanoma among general practitioners with special interest in dermatology. *British Journal of Dermatology*, Conference: July.
Not in PICO
- Bataille, V. & Bataille, V. (2003) Early detection of melanoma improves survival. *Practitioner*, 253: 29-32.
Narrative review
- Baughan, P., O'Neill, B., Fletcher, E., Baughan, P., O'Neill, B. & Fletcher, E. (2009) Auditing the diagnosis of cancer in primary care: the experience in Scotland. *British Journal of Cancer*, 101 Suppl 2: S87-S91.
Not in PICO
- Baughan, P., Keatings, J., O'Neill, B., Baughan, P., Keatings, J. & O'Neill, B. (2011) Urgent suspected cancer referrals from general practice: audit of compliance with guidelines and referral outcomes. *British Journal of General Practice*, 61: e700-e706.
Not in PICO
- Betti, R., Vergani, R., Tolomio, E., Santambrogio, R. & Crosti, C. (2003) Factors of delay in the diagnosis of melanoma. *European Journal of Dermatology*, 13: 183-188.
Not in PICO
- Biernikiewicz, M. (1998) Pigmented nevus in children as a diagnostic and treatment problem. *Polski merkuriusz lekarski : organ Polskiego Towarzystwa Lekarskiego*, 5: 72-73.
Not in PICO
- Bishop, J. N., Bataille, V., Gavin, A., Lens, M., Marsden, J., Mathews, T. & Wheelhouse, C. (2007) The prevention, diagnosis, referral and management of melanoma of the skin: concise guidelines. *Clinical Medicine*, 7: 283-290.
Narrative review
- Bogucki, P. (2013) Malignant melanoma, index and nonindex lesions. *Journal of the American Academy of Dermatology*, Conference: AB153.
Not in PICO
- Bonfa, R., Bonamigo, R. R., Bonfa, R., Duro, K. M., Furian, R. D. & Zelmanowicz, A. D. (2011) Early diagnosis of cutaneous melanoma: an observation in southern Brazil. *Anais Brasileiros de Dermatologia*, 86: 215-221.
Not in PICO
- Bourdeaud'hui, F., del, M., V, Bourdeaud'hui, F. & del Marmol, V. (2011) [Managing moles in general practice]. [French]. *Revue Medicale de Bruxelles*, 32: 205-209.
Narrative review
- Branstrom, R., Hedblad, M. A., Krakau, I., Ullen, H., Branstrom, R., Hedblad, M. A., Krakau, I. & Ullen, H. (2002) Laypersons' perceptual discrimination of pigmented skin lesions. *Journal of the American Academy of Dermatology*, 46: 667-673.
Not in PICO

- Brochez, L., Verhaeghe, E., Bleyen, L. & Naeyaert, J. M. (2001) Diagnostic ability of general practitioners and dermatologists in discriminating pigmented skin lesions. *Journal of the American Academy of Dermatology*, 44: 979-986.
Not in PICO
- Brodell, R. T., Helms, S. E., Brodell, R. T. & Helms, S. E. (1998) The changing mole. Additional warning signs of malignant melanoma. *Postgraduate Medicine*, 104: 145-148.
Not in PICO
- Bruce, A. J. & Brodland, D. G. (2000) Overview of skin cancer detection and prevention for the primary care physician. *Mayo Clinic Proceedings*, 75: 491-500.
Narrative review
- Brundel, K.-H. (1990) Skin cancer in general practice. *Dermatosen in Beruf und Umwelt*, 38: 54-57.
Not in PICO
- Buis, P. A. J. (2005) Value of histopathologic analysis of skin excisions by GPs. *British Journal of General Practice*, 55: 458-460.
Not in PICO (no symptoms)
- Burton, R. C. H. (1998) General practitioner screening for melanoma: Sensitivity, specificity, and effect of training. *Journal of Medical Screening*, 5: 156-161.
Not in PICO
- Carli, P., De, G., V, Nardini, P., Mannone, F., Palli, D., Giannotti, B., Carli, P., De Giorgi, V., Nardini, P., Mannone, F., Palli, D. & Giannotti, B. (2002) Melanoma detection rate and concordance between self-skin examination and clinical evaluation in patients attending a pigmented lesion clinic in Italy. *British Journal of Dermatology*, 146: 261-266.
Not in PICO
- Carli, P., De, G., V, Betti, R., Vergani, R., Catricala, C., Mariani, G., Simonacci, M., Bettacchi, A., Bottoni, U., Lo, S. G., Mulas, P., Giannotti, B., Carli, P., De Giorgi, V., Betti, R., Vergani, R., Catricala, C., Mariani, G., Simonacci, M., Bettacchi, A., Bottoni, U., Lo Scocco, G., Mulas, P. & Giannotti, B. (2003) Relationship between cause of referral and diagnostic outcome in pigmented lesion clinics: a multicentre survey of the Italian Multidisciplinary Group on Melanoma (GIPMe). *Melanoma Research*, 13: 207-211.
Not in PICO
- Casey, S., Dvorkin, L., Alsanjari, N., Dezso, B., Casey, S., Dvorkin, L., Alsanjari, N. & Dezso, B. (2011) Symptomatic malignant melanoma presenting as multiple gastrointestinal polyps. *BMJ Case Reports*, 2011, 2011..
Not in PICO
- Chattopadhyay, M. & Ha, T. (2013) How to examine a patient with suspected skin cancer. *Medicine (United Kingdom)*, 41: 400-401.
Narrative review
- Chen, S. C., Bravata, D. M., Weil, E. & Olkin, I. (2001) A comparison of dermatologists' and primary care physicians' accuracy in diagnosing melanoma. *Archives of Dermatology*, 137: 1627-1634.
Not in PICO
- Cheng, H., Oakley, A. & Rademaker, M. (2013) Please see this child with ? melanoma. *Australasian Journal of Dermatology*, 54: 35.
Not in PICO
- Cheng, H., Oakley, A. & Rademaker, M. (2014) - Change in a child's naevus prompts referral to a dermatology service. - *Journal of Primary Health Care*, 6: 123-128.
Not in PICO
- Ciocan, D., Barbe, C., Aubin, F., Granel-Brocard, F., Lipsker, D., Velten, M., Dalac, S., Truchetet, F., Michel, C., Mitschler, A., Arnoult, G., Buemi, A., Dalle, S., Bernard, P., Woronoff, A. S. & Grange, F. (2013) Distinctive features of melanoma and its management in elderly patients: a population-based study in France. *JAMA Dermatology*, 149: 1150-1157.
Not in PICO

- Corey, K. (2012) An analysis of terminology used by primary care physicians to describe concerning lesions referred to an urgent dermatology clinic. *Journal of Investigative Dermatology*, Conference: May.
Not in PICO
- Cox, N. H. (2004) Evaluation of the UK 2-week referral rule for skin cancer. *British Journal of Dermatology*, 150: 291-298.
Not in PICO
- Cox, N. H., Madan, V., Sanders, T., Cox, N. H., Madan, V. & Sanders, T. (2008) The U.K. skin cancer 'two-week rule' proforma: assessment of potential modifications to improve referral accuracy. *British Journal of Dermatology*, 158: 1293-1298.
Not in PICO
- Dewan, P. (2010) Are NICE skin cancer guidelines being followed in primary care? A re-audit to review changes in practice in an inner city setting. *British Journal of Dermatology*, Conference: July.
Not in PICO
- Du Vivier, A. W., Williams, H. C., Brett, J. V., Higgins, E. M., Du Vivier, A. W., Williams, H. C., Brett, J. V. & Higgins, E. M. (1991) How do malignant melanomas present and does this correlate with the seven-point check-list? *Clinical & Experimental Dermatology*, 16: 344-347.
Not in PICO
- Durbec, F., Vitry, F., Granel-Brocard, F., Lipsker, D., Aubin, F., Hedelin, G., Dalac, S., Truchetet, F., Michel, C., Batard, M. L., Domissy-Baury, B., Halna, J. M., Schmutz, J. L., Delvincourt, C., Reuter, G., Dalle, S., Bernard, P., Danzon, A. & Grange, F. (2010) The Role of Circumstances of Diagnosis and Access to Dermatological Care in Early Diagnosis of Cutaneous Melanoma A Population-Based Study in France. *Archives of Dermatology*, 146: 240-246.
Not in PICO
- El-Khalawany, M. (2014) - Acquired melanocytic nevi in Egyptian patients: a clinicopathological study. - *Acta Dermatovenerologica Alpina, Panonica et Adriatica*, 23: 5-11.
S&S: Population not in PICO; tests: Not a DTA study
- English, D. R., Burton, R. C., Mar, C. B., Donovan, R. J., Ireland, P. D. & Emery, G. (2003) Evaluation of aid to diagnosis of pigmented skin lesions in general practice: controlled trial randomised by practice. *BMJ (Clinical research ed.)*, 327: 375.
Not in PICO (excised lesions only)
- Foley, C. C., Corby, P. & Barnes, L. (1111) A dermatology outpatient waiting list initiative. *Irish Medical Journal*, 106: -August.
Not in PICO
- Friedman, R. J., Rigel, D. S., Kopf, A. W., Friedman, R. J., Rigel, D. S. & Kopf, A. W. (1985) Early detection of malignant melanoma: the role of physician examination and self-examination of the skin. *CA: A Cancer Journal for Clinicians*, 35: 130-151.
Narrative review
- Gallagher, R. P., Elwood, J. M., Rootman, J., Threlfall, W. J., Davis, J., Gallagher, R. P., Elwood, J. M., Rootman, J., Threlfall, W. J. & Davis, J. (1988) Symptoms and time to presentation and treatment in ocular melanoma: the Western Canada Melanoma Study. *Canadian Journal of Ophthalmology*, 23: 11-13.
Not in PICO
- Garmyn, M. (2007) How to recognize a malignant melanoma between the other pigmented spots. *Tijdschrift voor Geneeskunde*, 63: 1240-1243.
Narrative review
- Garmyn, M. (2009) How to recognize a malignant melanoma between the other pigmented spots. *Tijdschrift voor Geneeskunde*, 65: 9.
Narrative review

- Gazzani, P., Rothwell, J., Kasparis, C. & Gee, B. (2013) Progress towards integrating a melanoma diagnostic index into a U.K. dermatology department quality dashboard. *British Journal of Dermatology*, 169: 46-47.
Not in PICO
- Giacomet, J. & Zalaudek, I. (2013) Pink Lesions. *Dermatologic Clinics*, 31: 649-678.
Narrative review
- Giard, R. W. M. (2004) Diagnosis of pigmented skin lesions: How to recognize a malignant melanoma. *Nederlands Tijdschrift Voor Geneeskunde*, 148: 2261-2267.
Narrative review
- Gibbon, K. L. & Gibbon, K. L. (1998) Pigmented lesion clinics--are they a waste of resources? *Clinical & Experimental Dermatology*, 23: 3-8.
Narrative review
- Girardi, S., Gaudy, C., Gouvernet, J., Teston, J., Richard, M. A., Grob, J. J., Girardi, S., Gaudy, C., Gouvernet, J., Teston, J., Richard, M. A. & Grob, J. J. (2006) Superiority of a cognitive education with photographs over ABCD criteria in the education of the general population to the early detection of melanoma: a randomized study. *International Journal of Cancer*, 118: 2276-2280.
Not in PICO
- Grange, F., Hedelin, G., Halna, J. M., Grall, J. C., Kirstetter, H., Guillaume, J. C. & Michel, C. (2005) Assessment of a general practitioner training campaign for early detection of cutaneous melanoma in the Haut-Rhin department of France. *Annales de Dermatologie et de Venereologie*, 132: 956-961.
Not in PICO
- Grange, F., Barbe, C., Mas, L., Granel-Brocard, F., Lipsker, D., Aubin, F., Velten, M., Dalac, S., Truchetet, F., Michel, C., Mitschler, A., Arnoult, G., Buemi, A., Dalle, S., Reuter, G., Bernard, P., Woronoff, A. S. & Arnold, F. (2012) The role of general practitioners in diagnosis of cutaneous melanoma: a population-based study in France. *British Journal of Dermatology*, 167: 1351-1359.
Not in PICO
- Green, J., Murchie, P. & Lee, A. J. (2013) Does patients' place of residence affect the type of physician performing primary excision of cutaneous melanoma in northern Scotland? *Journal of Rural Health*, 29: Suppl-42.
Not in PICO
- Griffiths, W. A. & Griffiths, W. A. (2010) Improving melanoma diagnosis in primary care--a tele-dermatology project. *Journal of Telemedicine & Telecare*, 16: 185-186.
Not in PICO
- Gupta, A., Stacey, S. & Amissah-Arthur, K. N. (2014) Eyelid lumps and lesions. *BMJ (Online)*, 348.
Narrative review
- Gupta, M., Aggarwal, A., Ahuja, R., Pachauri, A. & Kumar, P. (2013) Significance of early detection of oral malignant melanoma: Some reasonable facts. *Clinical Cancer Investigation Journal*, 2: 178-180.
Narrative review
- Halkud, R., Shenoy, A. M., Naik, S. M., Chavan, P., Sidappa, K. T. & Biswas, S. (2014) Xeroderma Pigmentosum: Clinicopathological Review of the Multiple Oculocutaneous Malignancies and Complications. *Indian Journal of Surgical Oncology*, 5: 120-124.
Not in PICO
- Halpern, A. C. & Lieb, J. A. (2007) Early melanoma diagnosis: a success story that leaves room for improvement. *Current Opinion in Oncology*, 19: 109-115.
Narrative review
- Hamidi, R., Peng, D., Cockburn, M., Hamidi, R., Peng, D. & Cockburn, M. (2010) Efficacy of skin self-examination for the early detection of melanoma. [Review] [45 refs]. *International Journal of Dermatology*, 49: 126-134.
Narrative review

- Hansen, C., Wilkinson, D., Hansen, M., Argenziano, G., Hansen, C., Wilkinson, D., Hansen, M. & Argenziano, G. (2009) How good are skin cancer clinics at melanoma detection? Number needed to treat variability across a national clinic group in Australia. *Journal of the American Academy of Dermatology*, 61: 599-604.
Not in PICO (only excised lesions, not examined lesions; no information about symptoms/lesion features)
- Harris, J. (1999) Using the Internet to teach melanoma management guidelines to primary care physicians. *Journal of Evaluation in Clinical Practice*, 5: 199-211.
Not in PICO
- HealSmith, M. F. B. (1994) An evaluation of the revised seven-point checklist for the early diagnosis of cutaneous malignant melanoma. *British Journal of Dermatology*, 130: 48-50.
Not in PICO
- Higgins, E. M., Hall, P., Todd, P., Murthi, R., Du Vivier, A. W., Higgins, E. M., Hall, P., Todd, P., Murthi, R. & Du Vivier, A. W. (1992) The application of the seven-point check-list in the assessment of benign pigmented lesions. *Clinical & Experimental Dermatology*, 17: 313-315.
Not in PICO
- Hillner, B. E., Kirkwood, J. M. & Agarwala, S. S. (2001) Burden of illness associated with metastatic melanoma - An audit of 100 consecutive referral center cases. *Cancer*, 91: 1814-1821.
Not in PICO
- Holme, S. A. (2003) GPs have role in early detection of melanoma. [Review]. *Practitioner*, 257: 27-30.
Narrative review
- Humzah, M. D. E. (2003) Diagnosing pigmented skin lesions in general practice [2] (multiple letters). *British Medical Journal*, 327: 1167-1168.
Letter
- Jackson, A. (1995) Prevention, Early Detection and Team Management of Skin-Cancer in Primary-Care - Contribution to the Health-Of-The-Nation Objectives. *British Journal of General Practice*, 45: 97-101.
Narrative review
- Jackson, A. M., Morgan, D. R., Ellison, R., Jackson, A. M., Morgan, D. R. & Ellison, R. (2000) Diagnosis of malignant melanoma by general practitioners and hospital specialists. *Postgraduate Medical Journal*, 76: 295-298.
Not in PICO
- Jassim, O. W., Lind, A. C., Jassim, O. W. & Lind, A. C. (2010) Melanoma: from patient presentation to pathology report. [Review] [13 refs]. *Missouri Medicine*, 107: 101-106.
Narrative review
- Jemec, G. B. E. (1999) The diagnostic accuracy of Danish GPs in the diagnosis of pigmented skin lesions. *Family Practice*, 16: 619-620.
Not in PICO
- Kaminska-Winciorek, G. & Spiewak, R. (2013) [Dermoscopy on subungual melanoma]. [Polish]. *Postepy Higieny i Medycyny do Swiadczalnej (Online)*, 67: 380-387.
Narrative review
- Kelly, J. W., Shen, S., Pan, Y., Dowling, J. & McLean, C. A. (2014) Postexcisional melanocytic regrowth extending beyond the initial scar: A novel clinical sign of melanoma. *British Journal of Dermatology*, 170: 961-964.
Not in PICO
- Koelink, C. J. L., Kollen, B. J., Groenhof, F., van der Meer, K. & van der Heide, W. K. (2014) Skin lesions suspected of malignancy: an increasing burden on general practice. *Bmc Family Practice*, 15. Results only reported in 'number of contacts' for true positives, so PPV cannot be calculated.
- Kossard, S. (2001) An irregular, dappled, pigmented patch. *Medicine Today*, 2: 121.
Not in PICO

- Krige, J. E. J., Isaacs, S., Hudson, D. A., King, H. S., Strover, R. M. & Johnson, C. A. (1991) Delay in the Diagnosis of Cutaneous Malignant-Melanoma - A Prospective-Study in 250 Patients. *Cancer*, 68: 2064-2068.
Not in PICO
- Kundu, R. V. & Patterson, S. (2013) Dermatologic conditions in skin of color: part I. Special considerations for common skin disorders.[Summary for patients in Am Fam Physician. 2013 Jun 15;87(12):Online; PMID: 23939576]. *American Family Physician*, 87: 850-856.
Narrative review
- Kutcher, M. J. R. (1946) Fifteen inches from cancer: early recognition of facial lesions by the dentist. *Compendium of continuing education in dentistry (Jamesburg, N, J.: 939-942.*
Narrative review
- Lathlean, S. & Lathlean, S. (1999) Skin cancer in general practice in South Australia. A five year study. *Australian Family Physician*, 28 Suppl 1: S28-S31.
Not in PICO (only excised lesions, not examined lesions; no information about symptoms/lesion features)
- Lee, K. C., Jayarajan, R. & Daruwalla, M. (2013) Skin cancer diagnosis hit or miss? the leicester experience. *International Journal of Surgery*, 11: 683.
Not in PICO
- Lin, M. J. & Kelly, J. W. (2013) When is it melanoima? An update on diagnosis and management. *Medicine Today*, 14: 44-53.
Narrative review
- Lin, M. J., Mar, V., McLean, C., Wolfe, R. & Kelly, J. W. (2014) Diagnostic accuracy of malignant melanoma according to subtype. *Australasian Journal of Dermatology*, 55: 35-42.
Not in PICO
- Long, M. D. (2012) Cutaneous malignancies in patients with inflammatory bowel disease. *Gastroenterology and Hepatology*, 8: 467-471.
Narrative review
- Lyratzopoulos, G., Neal, R. D., Barbieri, J. M., Rubin, G. P. & Abel, G. A. (2012) Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. *Lancet Oncology*, 13: 353-365.
Not in PICO
- Maguire-Eisen, M., Frost, C., Maguire-Eisen, M. & Frost, C. (1994) Knowledge of malignant melanoma and how it relates to clinical practice among nurse practitioners and dermatology and oncology nurses. [Review] [26 refs]. *Cancer Nursing*, 17: 457-463.
Not in PICO
- Marghoob, A. A., Usatine, R. P. & Jaimes, N. (2013) Dermoscopy for the family physician. [Review]. *American Family Physician*, 88: 441-450.
Narrative review
- Marks, R. (1997) Who removes pigmented skin lesions? *Journal of the American Academy of Dermatology*, 36: 721-726.
Not in PICO
- Martinez, J. C. & Otley, C. C. (2001) The management of melanoma and nonmelanoma skin cancer: A review for the primary care physician. *Mayo Clinic Proceedings*, 76: 1253-1265.
Narrative review
- McCourt, C., Dolan, O. & Gormley, G. (2014) Malignant melanoma: A pictorial review. *Ulster Medical Journal*, 83: 103-110.
Not in PICO
- McGovern, T. W., Litaker, M. S., McGovern, T. W. & Litaker, M. S. (1992) Clinical predictors of malignant pigmented lesions. A comparison of the Glasgow seven-point checklist and the American Cancer Society's ABCDs of pigmented lesions. *Journal of Dermatologic Surgery &*

- Oncology*, 18: 22-26.
Not in PICO
- McWhirter, J. E. & Hoffman-Goetz, L. (2013) Visual images for patient skin self-examination and melanoma detection: a systematic review of published studies. [Review]. *Journal of the American Academy of Dermatology*, 69: 47-55.
Not in PICO
- Menzies, S. W., Moloney, F. J., Byth, K., Avramidis, M., Argenziano, G., Zalaudek, I., Braun, R. P., Malvehy, J., Puig, S., Rabinovitz, H. S., Oliviero, M., Cabo, H., Bono, R., Pizzichetta, M. A., Claesson, M., Gaffney, D. C., Soyer, H. P., Stanganelli, I., Scolyer, R. A., Guitera, P., Kelly, J., McCurdy, O., Llambrich, A., Marghoob, A. A., Zaballos, P., Kirchesch, H. M., Piccolo, D., Bowling, J., Thomas, L., Terstappen, K., Tanaka, M., Pellacani, G., Pagnanelli, G., Ghigliotti, G., Ortega, B. C., Crafter, G., Ortiz, A. M., Tromme, I., Karaarslan, I. K., Ozdemir, F., Tam, A., Landi, C., Norton, P., Kacar, N., Rudnicka, L., Slowinska, M., Simionescu, O., Di, S. A., Coates, E. & Kreuzsch, J. (2013) Dermoscopic evaluation of nodular melanoma. *JAMA Dermatology*, 149: 699-709.
Not in PICO
- Menzies, S. W. (2013) Evidence-Based Dermoscopy. *Dermatologic Clinics*, 31: 521-524.
Narrative review
- Menzies, S. W., Moloney, F. J., Byth, K., Avramidis, M., Argenziano, G., Zalaudek, I., Braun, R. P., Malvehy, J., Puig, S., Rabinovitz, H. S., Oliviero, M., Cabo, H., Bono, R., Pizzichetta, M. A., Claesson, M., Gaffney, D. C., Soyer, H. P., Stanganelli, I., Scolyer, R. A., Guitera, P., Kelly, J., McCurdy, O., Llambrich, A., Marghoob, A. A., Zaballos, P., Kirchesch, H. M., Piccolo, D., Bowling, J., Thomas, L., Terstappen, K., Tanaka, M., Pellacani, G., Pagnanelli, G., Ghigliotti, G., Ortega, B. C., Crafter, G., Perusquia Ortiz, A. M., Tromme, I., Karaarslan, I. K., Ozdemir, F., Tam, A., Landi, C., Norton, P., Kacar, N., Rudnicka, L., Slowinska, M., Simionescu, O., Di, S. A., Coates, E. & Kreuzsch, J. (2013) Dermoscopic evaluation of nodular melanoma. *JAMA Dermatology*, 149: 699-709.
Not in PICO
- Morrison, A., O'Loughlin, S. & Powell, F. C. (2001) Suspected skin malignancy: a comparison of diagnoses of family practitioners and dermatologists in 493 patients. *International Journal of Dermatology*, 40: 104-107.
Not in PICO
- Murchie, P., Raja, E. A., Lee, A. J. & Campbell, N. C. (2013) Mortality and morbidity after initial diagnostic excision biopsy of cutaneous melanoma in primary versus secondary care. *British Journal of General Practice*, 63: e563-e572.
Not in PICO
- Newell, E. L., Shaw, L. & Bragonier, R. (2014) Rising referrals for suspected paediatric melanoma via the 2-week rule referral system. *British Journal of Dermatology*, 170: e15.
Not in PICO
- Newell, E. L., Shaw, L. & Bragonier, R. (2014) Rising referrals for suspected paediatric melanoma via the 2-week rule referral system. *British Journal of Dermatology*, 170: e15.
Not in PICO
- Nielsen, T. N., Hansen, R. P., Vedsted, P., Nielsen, T. N., Hansen, R. P. & Vedsted, P. (2010) [Symptom presentation in cancer patients in general practice]. [Danish]. *Ugeskrift for Læger*, 172: 2827-2831.
Not in PICO
- Offidani, A., Simonetti, O., Bernardini, M. L., Alpagut, A., Cellini, A., Bossi, G., Offidani, A., Simonetti, O., Bernardini, M. L., Alpagut, A., Cellini, A. & Bossi, G. (2002) General practitioners' accuracy in diagnosing skin cancers. *Dermatology*, 205: 127-130.
Not in PICO
- Osborne, J. E., Bourke, J. F., Holder, J., Colloby, P., Graham-Brown, R. A., Osborne, J. E., Bourke, J. F., Holder, J., Colloby, P. & Graham-Brown, R. A. (1998) The effect of the introduction of a pigmented lesion clinic on the interval between referral by family practitioner and attendance at

- hospital. *British Journal of Dermatology*, 138: 418-421.
Not in PICO
- Patel, L. M., Lambert, P. J., Gagna, C. E., Maghari, A. & Lambert, W. C. (2011) Cutaneous signs of systemic disease. *Clinics in Dermatology*, 29: 511-522.
Narrative review
- Paul, E. (1990) The slow growth of malignant melanomas - The great chance of their early detection. *Regional Cancer Treatment*, 3: 107-110.
Narrative review
- Pereda, C., Traves, V., Requena, C., Serra-Guillen, C., Llombart, B., Sanmartin, O., Guillen, C. & Nagore, E. (2013) Clinical presentation of acral lentiginous melanoma: a descriptive study. *Actas Dermo-Sifiliograficas*, 104: 220-226.
Not in PICO
- Pfister, R. & Pfister, R. (1983) [Early symptoms of malignant skin changes]. [German]. *Fortschritte der Medizin*, 101: 445-450.
Not in PICO
- Pflugfelder, A., Kochs, C., Blum, A., Capellaro, M., Czeschik, C., Dettenborn, T., Dill, D., Dippel, E., Eigentler, T., Feyer, P., Follmann, M., Frerich, B., Ganten, M.-K., Gartner, J., Gutzmer, R., Hassel, J., Hauschild, A., Hohenberger, P., Hubner, J., Kaatz, M., Kleeberg, U. R., Kolbl, O., Kortmann, R.-D., Krause-Bergmann, A., Kurschat, P., Leiter, U., Link, H., Loquai, C., Loser, C., MacKensen, A., Meier, F., Mohr, P., Mohrle, M., Nashan, D., Reske, S., Rose, C., Sander, C., Satzger, I., Schiller, M., Schlemmer, H.-P., Strittmatter, G., Sunderkotter, C., Swoboda, L., Trefzer, U., Voltz, R., Vordermark, D., Weichenthal, M., Werner, A., Wesselmann, S., Weyergraf, A. J., Wick, W., Garbe, C. & Schadendorf, D. (2013) S3-Guideline "diagnosis, therapy and follow-up of melanoma" - Short version. [German, English]. *JDDG - Journal of the German Society of Dermatology*, 11: 593-602.
Guideline
- Porte, A. & Viguier, J. (2013) General practitioners and early detection of skin cancer Summary, Step 2 of the barometric survey. *Oncologie*, 15: 535-542.
Not in PICO
- Ramineni, M., Sonabend, M., Katta, R., Ramineni, M., Sonabend, M. & Katta, R. (2008) Tender growth on toe. *Journal of Family Practice*, 57: 473-475.
Not in PICO
- Reusch, M., Schaefer, I., Siebert, J., Kornek, T. & Augustin, M. (2013) Histological and epidemiological characteristics of cutaneous malignant melanoma in routine ambulatory care in germany. *JDDG - Journal of the German Society of Dermatology*, 11: 38-39.
Not in PICO
- Richard, M. A., Grob, J. J., Avril, M. F., Delaunay, M., Gouvernet, J., Wolkenstein, P., Souteyrand, P., Dreno, B., Bonerandi, J. J., Dalac, S., Machet, L., Guillaume, J. C., Chevrant-Breton, J., Vilmer, C., Aubin, F., Guillot, B., Beylot-Barry, M., Lok, C., Raison-Peyron, N. & Chemaly, P. (2000) Delays in diagnosis and melanoma prognosis (II): The role of doctors. *International Journal of Cancer*, 89: 280-285.
Not in PICO
- Robinson, J. K., Turrisi, R., Robinson, J. K. & Turrisi, R. (2006) Skills training to learn discrimination of ABCDE criteria by those at risk of developing melanoma. *Archives of Dermatology*, 142: 447-452.
Not in PICO
- Rosendahl, C., Hishon, M., Cameron, A., Barksdale, S., Weedon, D. & Kittler, H. (2014) - Nodular melanoma: five consecutive cases in a general practice with polarized and non-polarized dermatoscopy and dermatopathology. - *Dermatology Practical & Conceptual*, 4: 69-75.
Not in PICO
- Sahin, M. T., Ozturkcan, S., Ermertcan, A. T. & Gunes, A. T. (2004) A comparison of dermoscopic features among lentigo senilis/initial seborrheic keratosis, seborrheic keratosis, lentigo maligna

and lentigo maligna melanoma on the face. *Journal of Dermatology*, 31: 884-889.
Not in PICO

Schofield, J. (2011) The costs of diagnosing and treating skin cancer using the 2-week-wait referral process. *British Journal of Dermatology*, Conference: July.
Not in PICO

Shelton, R. M. (2001) Skin cancer: a review and atlas for the medical provider. *The Mount Sinai journal of medicine, New York*, 68: 243-252.
Narrative review

Steel, B. J. (2014) - Skin cancer - an overview for dentists. - *British Dental Journal*, 216: 575-581.
Narrative review

Stefano, Z., Cesare, B., Claudio, C., Fausto, C., Aldo, B., Natale, C., Stefano, Z., Cesare, B., Claudio, C., Fausto, C., Aldo, B. & Natale, C. (1992) Melanocytic neoplasia of the sole: diagnosis and therapeutic approach. *Journal of Dermatology*, 19: 280-284.
Not in PICO

Stollery, N. & Stollery, N. (2007) Pigmented lesions. [Review] [12 refs]. *Practitioner*, 251: 36-38.
Narrative review

Tloughan, B. E., Orlow, S. J. & Schaffer, J. V. (2013) Spitz nevi: beliefs, behaviors, and experiences of pediatric dermatologists. *JAMA Dermatology*, 149: 283-291.
Not in PICO

Tolpinrud, W. L., Viola, K. V., Kirsner, R. S., Gross, C. P., Imaeda, S. & Federman, D. G. (2011) Nondermatologists' Use of Predictive Terms for a Potentially Malignant Lesion. *Southern Medical Journal*, 104: 477-481.
Not in PICO

Turner, T. & Turner, T. (1993) Pigmented lesions--a plan for management in general practice. *Medical Journal of Australia*, 159: 809-814.
Narrative review

Urbancek, S., Simekova, P. & Tomkova, J. (2013) Misdiagnosis of melanoma: A 5 years analysis. *JDDG - Journal of the German Society of Dermatology*, 11: 31.
Not in PICO

van der Rhee, J. I., Bergman, W., Kukutsch, N. A., van der Rhee, J. I., Bergman, W. & Kukutsch, N. A. (2010) The impact of dermoscopy on the management of pigmented lesions in everyday clinical practice of general dermatologists: a prospective study. *British Journal of Dermatology*, 162: 563-567.
Not in PICO

Van Rijsingen, M. C. J., Van, B. B., Van Der Wilt, G. J., Lagro-Janssen, A. L. M. & Gerritsen, M. J. P. (2014) The current and future role of general practitioners in skin cancer care: An assessment of 268 general practitioners. *British Journal of Dermatology*, 170: 1366-1368.
Not in PICO

Van Rijsingen, M. C. J., Hanssen, S. C. A., Groenewoud, J. M. M., Van Der Wilt, G. J. & Gerritsen, M.-J. (2014) Referrals by general practitioners for suspicious skin lesions: The urgency of training. *Acta Dermato-Venereologica*, 94: 138-141.
Not in PICO

Walter, F. M., Humphrys, E., Tso, S., Johnson, M. & Cohn, S. (2010) Patient understanding of moles and skin cancer, and factors influencing presentation in primary care: a qualitative study. *Bmc Family Practice*, 11.
Narrative review

Walter, F. M., Morris, H. C., Humphrys, E., Hall, P. N., Kinmonth, A. L., Prevost, A. T., Wilson, E. C., Burrows, N., Norris, P., Johnson, M. & Emery, J. (2010) Protocol for the MoleMate UK Trial: a randomised controlled trial of the MoleMate system in the management of pigmented skin lesions in primary care [ISRCTN 79932379]. *Bmc Family Practice*, 11: 36.
Protocol

- Walter, F. M. P. (2012) The diagnostic accuracy of the 7-point checklist to assess pigmented skin lesions in primary care. *Asia-Pacific Journal of Clinical Oncology*, Conference: November. Same data as Walter 2012
- Walton, R. G. (1994) Recognition and importance of precursor lesions in the diagnosis of early cutaneous malignant melanoma. *International Journal of Dermatology*, 33: 302-307. Narrative review
- Ward, J. (1994) General practitioners' estimates of the ideal benign-to-malignant ratio for excised pigmented lesions. *Australian Journal of Public Health*, 18: 454-455. Not in PICO
- Watkins, J. & Watkins, J. (2010) Dermatology and the community nurse: actinic (solar) keratosis. [Review] [13 refs]. *British Journal of Community Nursing*, 15: 6-1. Narrative review
- Westbrook, R. H. G. (2006) Diagnostic accuracy for skin cancer: Comparison of general practitioner with dermatologist and dermatopathologist [1]. *Journal of Dermatological Treatment*, 17: 57-58. Not in PICO
- Whited, J. D., Hall, R. P., Simel, D. L. & Horner, R. D. (1997) Primary care clinicians' performance for detecting actinic keratoses and skin cancer. *Archives of Internal Medicine*, 157: 985-990. Not in PICO
- Wietfeldt, E. D., Thiele, J., Wietfeldt, E. D. & Thiele, J. (2009) Malignancies of the anal margin and perianal skin. *Clinics in Colon & Rectal Surgery*, 22: 127-135. Narrative review
- Wilson, E. C., Emery, J. D., Kinmonth, A. L., Prevost, A. T., Morris, H. C., Humphrys, E., Hall, P. N., Burrows, N., Bradshaw, L., Walls, J., Norris, P., Johnson, M. & Walter, F. M. (2013) The cost-effectiveness of a novel SIAscopic diagnostic aid for the management of pigmented skin lesions in primary care: a decision-analytic model. *Value in Health*, 16: 356-366. Same data as Walter (2012) already included.
- Wood, A., Morris, H., Emery, J., Hall, P. N., Cotton, S., Prevost, A. T., Walter, F. M., Wood, A., Morris, H., Emery, J., Hall, P. N., Cotton, S., Prevost, A. T. & Walter, F. M. (2008) Evaluation of the MoleMate training program for assessment of suspicious pigmented lesions in primary care. *Informatics in Primary Care*, 16: 41-50. Not in PICO (for signs and symptoms or for tests)
- Wray, E. V., Brant, B., Hussain, F. & Muller, F. M. (2013) A new model of teledermoscopy combining service and education. *British Journal of Dermatology*, 169: 139. Not in PICO
- Youl, P. H., Raasch, B. A., Janda, M., Aitken, J. F., Youl, P. H., Raasch, B. A., Janda, M. & Aitken, J. F. (2007) The effect of an educational programme to improve the skills of general practitioners in diagnosing melanocytic/pigmented lesions. *Clinical & Experimental Dermatology*, 32: 365-370. Not in PICO
- Youl, P. H., Baade, P. D., Janda, M., del Mar, C. B., Whiteman, D. C. & Aitken, J. F. (2007) Diagnosing skin cancer in primary care: how do mainstream general practitioners compare with primary care skin cancer clinic doctors? *Medical Journal of Australia*, 187: 215-220. Not in PICO: Data only reported for 3231[excised]/8790[examined] patients.
- Zortea, M., Schopf, T. R., Thon, K., Geilhufe, M., Hindberg, K., Kirchesch, H., Mollersen, K., Schulz, J., Skrovseth, S. O. & Godtlielsen, F. (2014) Performance of a dermoscopy-based computer vision system for the diagnosis of pigmented skin lesions compared with visual evaluation by experienced dermatologists. *Artificial Intelligence in Medicine*, 60: 13-26. Not in PICO

Review question:

Which investigations of symptoms of suspected melanoma should be done with clinical responsibility retained by primary care?

Results

Literature search

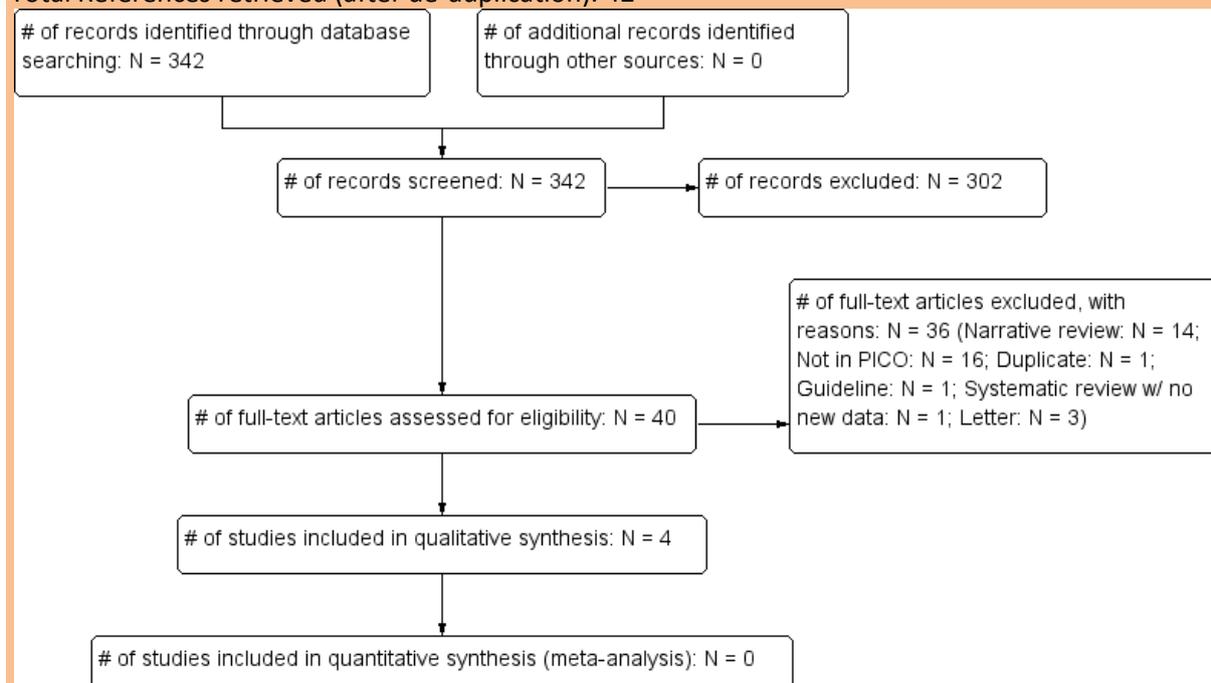
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	875	206	03/05/2013
<i>Premedline</i>	1980-2013	69	29	03/05/2013
<i>Embase</i>	1980-2013	1413	130	03/05/2013
<i>Cochrane Library</i>	1980-2013	129	9	08/05/2013
<i>Psychinfo</i>	1980-2013	9	1	08/05/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	431	98	08/05/2013

Total number of studies identified after de-duplication: 300

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-19/08/2014	34	2	19/08/2014
<i>Premedline</i>	2013-19/08/2014	105	17	19/08/2014
<i>Embase</i>	2013-19/08/2014	73	28	19/08/2014
<i>Cochrane Library</i>	2013-19/08/2014	52	0	19/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-19/08/2014	70	20	19/08/2014

Total References retrieved (after de-duplication): 42



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issues to note are that the study populations may not be directly representative of an unselected symptomatic population of patients presenting to the UK-based GP, that the criteria for malignancy of the index test are not specified in one case which may limit its external validity, and that the results presented are based on a best case scenario, and are therefore likely to be inflated, and only available for skin malignancy as a whole in some cases and not for melanoma separately. The reference standards employed were also subject to high or unclear risk of bias in the majority of the studies.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Emery (2010)	?	+	?	+	?	+	?
Menzies (2009)	+	+	-	-	?	+	+
Rosendahl (2011)	+	?	+	+	?	?	+
Walter (2012)	?	+	?	+	+	+	?

- High
 ? Unclear
 + Low

Study results

Table 1: Melanoma: SIAscan/MoleMate

Study	Intervention	Prevalence	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value % (95% CI)	False negativity rate %
Emery (2010)	SIAscan/MoleMate: Moncrieff scoring system	England development set: 24 "suspicious" and 3 melanomas /422 lesions	54 (35-72)	77 (73-81)	12 (7.5-20)	46
Emery (2010)	SIAscan/MoleMate: Primary scare scoring algorithm	England validation set: 6 "suspicious" and 2 melanomas /208 lesions	50 (18-81)	84 (78-88)	9 (3-22)	50
Emery (2010)	SIAscan/MoleMate: Primary scare scoring algorithm	Australia dataset: 45 "suspicious" and 11 melanomas /581 lesions	44 (32-58)	95 (93-97)	52 (38-66)	56

Walter (2012)	SIAscan/MoleMate	18 melanomas/ 766 lesions	100 (78.1-100)	71.79 (68.4-75)	7.86 (4.9-12.3)	0
---------------	------------------	---------------------------	----------------	-----------------	-----------------	---

Table 2: Melanoma: Dermoscopy/dermatoscopy

Study	Intervention	Prevalence	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value % (95% CI)	False negativity rate %
Menzies (2009)	Dermoscopy	Unclear/331 lesions	53.1 (34.7-70.9)	89 (84.9-92.3)	34 (21.2-48.8)	46.9
Menzies (2009)	Dermoscopy ± sequential digital dermoscopy imaging	Unclear/331 lesions	71.9 (53.3-86.3)	86.6 (82.2-90.3)	36.4 (24.7-49.6)	28.1
Menzies (2009)	Sequential digital dermoscopy imaging	Unclear/149 lesions	72.7 (39-94)	92.8 (87.1-96.5)	44.4 (21.5-69.2)	27.3
Rosendahl (2011)	Clinical images and dermatoscopy	138 malignancies/463 lesions	82.6	80	Not reported	17.4

There was no evidence relating to the diagnostic accuracy of biopsy or ophthalmoscopy for diagnosing melanoma in a primary care setting.

Evidence statement(s):

SIAscan/MoleMate (2 studies, N = 1977 lesions) performed in symptomatic patients presenting in a primary care setting is associated with sensitivities ranging between 44-100%, specificities ranging between 71.79-95%, positive predictive values ranging between 7.86-52%, and false negativity rates ranging between 0-56% for skin cancer/ melanoma. The studies were each associated with 3-4 bias/applicability concerns (see also Table 1).

Dermoscopy/dermoscopy with and without clinical images or sequential digital dermoscopy imaging (2 studies, N = 794 lesions) performed in symptomatic patients presenting in a primary care setting is associated with sensitivities ranging between 53.1- 82.6%, specificities ranging between 80-92.8%, positive predictive values ranging between 34-44.4%, and false negativity rates ranging between 17.4-46.9% for skin cancer/ melanoma. The studies were each associated with 3 bias/applicability concerns (see also Table 2).

Evidence tables

Emery (2010)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective series of pigmented lesions recruited from England (6 general practices covering urban, suburban and rural areas with a registered population of 52913) and Australia (3 primary care skin

	cancer clinics operated by GPs from a metropolitan area)
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>England: N = 389 patients, mean age = 44.9 years, 68.6% females with interpretable images from N = 630 lesions. 0/630 lesions were squamous cell carcinoma, 0/630 lesions were basal cell carcinoma, 5/630 lesions were melanoma, and 0/630 lesions were lentigo maligna (melanoma). For the evaluation of SIAscopy this sample was further split into 2 samples: Development: N = 422 lesions of which 0 were squamous cell carcinoma, 0 were basal cell carcinoma, 3 were melanoma and 0 were lentigo maligna. Validation: N = 208 lesions of which 0 were squamous cell carcinoma, 0 were basal cell carcinoma, 2 were melanoma and 0 were lentigo maligna.</p> <p>Australia: N = 469 patients, mean age = 50 years, 48% females, with interpretable images from N = 581 lesions. 0/581 lesions were squamous cell carcinoma, 22/581 lesions were basal cell carcinoma, 7/581 lesions were melanoma, and 4/581 lesions were lentigo maligna (melanoma).</p> <p><u>Inclusion criteria:</u> England: Patients aged > 18 years were recruited into the study by their GP if they presented with concerns about a pigmented skin lesion between January 2005 and January 2006. Australia: Patients aged > 18 years were recruited into the study by their GP if they presented with concerns about a pigmented skin lesion between April 2008 and January 2009. Additional lesions were also included when a pigmented skin lesion was identified as potentially suspicious during their clinical examination</p> <p><u>Exclusion criteria:</u> None reported.</p> <p><u>Clinical setting:</u> Primary care, UK, and primary care skin cancer practice, Queensland Australia.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	<p>Pigmented skin lesions that concerned patients, which were evaluated using macroscopic clinical photographs, dermoscopic images and SIAscan.</p> <p>SIAscan images and data (including the location of the lesion and the age group and sex of the patients) were assessed by a SIAscopy expert, who was blinded to the 7-item melanoma checklist results and clinical photographs. The SIAscopy expert scored the presence or absence of each specific SIAscopic feature including those previously associated with melanoma (Moncrieff et al. (2002) Br J Dermatol, 146: 448-57): Size of lesion, age of patient, dermal melanin, collagen holes and blood displacement with erythematous blush. Additional features that were also scored were blood vessels, white dots on the collagen view, blood lacunes and a cerebriform melanin pattern.</p> <p>From this information a primary care scoring algorithm was developed:</p>

	<p>All lesions -> Any collagen white dots OR cerebriform pattern? Yes -> Seborrheic keratosis STOP No -> Any blood lacunes? Yes -> Haemangioma STOP No -> Dermal melanin within the lesion: 3 points Presence of any blood vessels: 2 points Blood displacement with erythematous blush: 1 point Maximum diameter > 6 mm: 1 point For every COMPLETED 15 years of age: 1 point Score of 6 or more? Yes -> Suspicious No-> Not suspicious</p>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histopathology or in-person clinical review of the lesion by one expert, including the 7-point melanoma checklist and digital dermoscopy or clinical diagnosis made on the basis of the 7-point melanoma checklist, photographic and dermoscopy images
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Analysis was on a per-lesion basis rather than a per-patient basis. Please note the diagnostic accuracy results given above relates to the diagnosis of a "suspicious" lesion, and not just melanomas. The 2-by-2 tables could not be extracted.
Menzies (2009)	
PATIENT SELECTION	
A. risk of bias	

Patient sampling	Prospective consecutive patient series
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>102 GPs were initially recruited, 74 of whom completed the educational intervention and online assessment of learning. 63 GPs from 19 practices assessed 374 lesions as requiring referral or excision (median number of lesions per GP = 6, mean = 5.9, SD = 3). No other information reported.</p> <p><u>Inclusion criteria:</u> Consecutive patients with pigmented lesions (some brown, grey, blue or black colour within some part of the lesion) which, after routine naked eye examination by the GP would have been biopsied or referred (that is, a suspicious pigmented lesion) presenting to GPs who worked in practices in metropolitan Perth with a minimum of 3 doctors. The GPs and practices had to meet the following criteria: A history of excision or referral of at least 10 pigmented skin lesions over the previous 12-month period for each doctor, and available space for a sequential digital dermoscopy imaging device. During the pretrial period all GPs underwent a training program in the use of dermoscopy and sequential digital dermoscopy imaging. This included reading a textbook in dermoscopic diagnosis and the use of sequential digital dermoscopy imaging, and a tutorial on a CD-rom showing examples of changed and unchanged monitored lesions. In addition, GPs attended a 2 hour workshop on the use of diagnostic devices and recruitment procedures. The training was assessed through an online pre- and post-education intervention test of 245 lesions not seen in the textbook or on the CD-rom. Answers were provided during the post-test as a component of the educational intervention. Before formal patient recruitment began, GPs assessed at least one pretrial lesion to determine the quality of imaging with the sequential digital dermoscopy imaging device and undertake completion of the trial paperwork. GPs were allowed to practise using the dermoscopy device during this pretrial phase. The pretrial phase of education and run-in period occurred from May 2005 to January 2006.</p> <p><u>Exclusion criteria:</u> GPs who already used dermoscopy or sequential digital dermoscopy imaging in their routine practice.</p> <p><u>Clinical setting:</u> Primary care, Australia.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	<p>Dermoscopy examination performed using a hand-held oil immersion glass plate device (Delta 10 Dermatoscope: Heine Ltd, Herrsching, Germany). All lesions were then photographed with the dermoscopy imaging device (Sentry pilot; Polartechnics Ltd, Sydney, Australia). This incorporated a higher resolution megapixel camera which could be used for telemedicine diagnosis and for colour-calibrated sequential digital dermoscopy imaging. For melanocytic lesions that did not have dermoscopic evidence of melanoma, but were still considered to be suspicious, short term sequential digital dermoscopy imaging was performed over a period of 3 months.</p>

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Hierarchical diagnosis order of (1) histopathology, (2) unchanged lesions after sequential digital dermoscopy imaging indicating a benign diagnosis, (3) specialist opinion following referral, and (4) dermoscopy telemedicine. All sequential digital dermoscopy imaging and dermoscopy telemedicine images of nonexcised lesions were reviewed by an expert in dermoscopy and sequential digital dermoscopy imaging and a diagnosis recorded.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	The results only appear to be reported for 348/374 lesions for dermoscopy and dermoscopy ± sequential digital dermoscopy imaging (for melanoma: of which 9 had an unknown diagnosis and 8 had a diagnosis of basal cell carcinoma or Bowen disease – these were all excluded from the analyses) and for 160/192 lesions that received sequential digital dermoscopy imaging (for melanoma: of which 9 had an unknown diagnosis and 2 had a diagnosis of basal cell carcinoma or Bowen disease – these were all excluded from the analyses).
Was there an appropriate interval between index test and reference standard?	Unclear, but probably
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	Analysis appears to be on a per-lesion basis rather than a per-patient basis. The 2-by-2 tables could not be extracted.
Rosendahl (2011)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Consecutive series of lesions submitted for histology from the primary care skin cancer clinic of one of the authors.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Probably

Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 463 pigmented lesions from 389 patients, mean (SD) age = 57 (17) years, 32.6% females. Lesion location: Trunk: N = 241; extremities: N = 128; head and face: N = 82; palms and soles: N = 10. Histopathologically, 246 pigmented lesions turned out to be melanocytic and 217 were of non-melanocytic origin.</p> <p>Final diagnoses: Malignant lesions: Basal cell carcinoma: N = 72; squamous cell carcinoma: N = 37; melanoma: N = 29. Benign lesions: Melanocytic nevi: N = 217; seborrheic keratosis: N = 43; solar lentigo: N = 37; lichen planus-like keratosis: N = 21, others: N = 7.</p> <p><u>Inclusion criteria:</u> All pigmented lesions biopsied or excised during a 30-month period. <i>Patients included are only those who received resection. This changes the spectrum of disease as it excludes patients with lesions that were not considered concerning enough to warrant resection.</i></p> <p><u>Exclusion criteria:</u> Poor image quality (N = 3).</p> <p><u>Clinical setting:</u> Primary care skin cancer practice in Queensland, Australia</p>	
Are there concerns that the included patients and setting do not match the review question?		Unclear concern
INDEX TEST		
A. Risk of bias		
Index test	<p>For each lesion: A triplet of high-resolution digital images consisting of two clinical images (overview and close-up) followed by one dermatoscopic image. The clinical images were taken with Canon EOS digital single lens reflex cameras. The close-up was taken using a macro lens (60-mm f2.8 macro, Canon) with diffuse illumination at a constant reproduction ratio determined by a custom-fabricated spacer. The degree of magnification of the close-up images was similar to that of the dermatoscopy images. Dermatoscopic images were nonpolarising, preferentially using the Dermlite Fluid device (3 Gen, San Juan, Capistrano, Ca); alternatively Dermlite Foto (custom nonpolarised; 3 Gen) and Heine Delta 20 devices (Heines, Optotechnic GmbH< Herrsching, Germany) were used for large and inaccessible lesions, respectively. Dermatoscopic photographs were taken with Canon EOS single lens reflex cameras. Images were presented to the assessors as powerpoint slides. After inspection of the images, the assessor was required to give a diagnosis (criteria not reported, so presumably based on qualitative criteria). Dermatoscopic images were also screened for asymmetry of structure and colour (“chaos”) and for clues to malignancy. Asymmetry of colour and structure were defined according to the basic principles of pattern analysis as revised by Kittler (2007, Dermatopathology: Practical & Conceptual, 13:1). Clues to malignancy included: Eccentric structureless zone (any colour except skin colour), gray or blue structures, peripheral black dots or clods, segmental radial lines or pseudopods, polymorphous vessels, white lines, thick reticular or branched lines, and parallel lines on ridges (acral lesions). <i>Not further information regarding the specific cut-off criteria for malignancy reported. The reporting of the results suggests that the test performance is based on best possible scenario.</i></p>	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes

Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histopathology
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low concern
NOTES	The results are presented for all malignancies combined. The 2-by-2 table could not be extracted and the results could not be separated into the different malignancies

Walter (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective series of suspicious pigmented lesions
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 643 patients, mean age (SD) = 44.5 (16.7) years; 230 males / 413 females with N = 788 lesions:</p> <p><u>Inclusion criteria:</u> Patients aged ≥ 18 years presenting to one of the 15 participating general practices with a suspicious (any lesion presented by a patient, or opportunistically seen by a family doctor or practice nurse, that could not immediately be diagnosed as benign and about which the patient could not be reassured) pigmented lesion from March 2008 to May 2010.</p> <p><u>Exclusion criteria:</u> Patients who were unable to give informed consent or were considered inappropriate to include by their family doctor.</p> <p><u>Clinical setting:</u> UK primary care.</p>

Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Clinical assessment (clinical history and naked eye examination) followed by SIAscopy/MoleMate system (assessing clinician had completed a 2-hour training CD-ROM to identify relevant SIAscopic features of various pigmented skin lesions) .
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Expert opinion by a histologist or dermatologist or review by two other dermatology experts of the recorded clinical history and examination, a digital photograph, and MoleMate images where available with or without follow up 3-6 months later.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	Data are missing for 22/788 lesions
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes Tests: No
Could the patient flow have introduced bias?	Low risk
NOTES	Analysis was on a per-lesion basis rather than a per-patient basis. TP = 18, FN = 0, FP = 211, TN = 537.

Cost-effectiveness evidence

Information sources and eligibility criteria

The following databases were searched for economic evidence relevant to the PICO: MEDLINE, EMBASE, COCHRANE, NHS EED and HEED. Studies conducted in OECD countries other than the UK were considered.

Studies were selected for inclusion in the evidence review if the following criteria were met:

- Both cost and health consequences of interventions reported (i.e. true cost-effectiveness analyses)
- Conducted in an OECD country
- Incremental results are reported or enough information is presented to allow incremental results to be derived
- Studies that matched the population, interventions, comparators and outcomes specified in PICO
- Studies that meet the applicability and quality criteria set out by NICE, including relevance to the NICE reference case and UK NHS

Note that studies that measured effectiveness using quality of life based outcomes (e.g. QALYs) were desirable but, where this evidence was unavailable, studies using alternative effectiveness measures (e.g. life years) were considered.

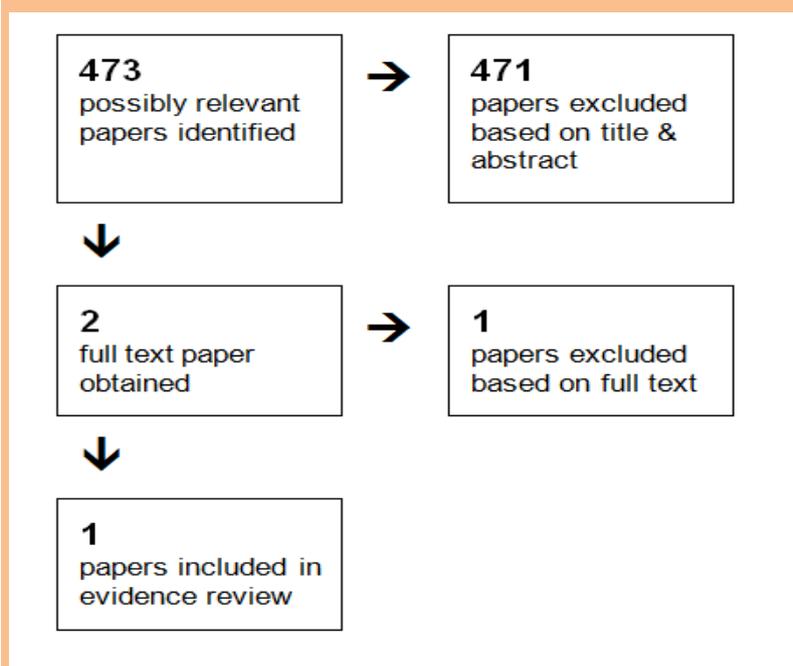
Selection of studies

The literature search results were screened by checking the article's title and abstract for relevance to the review question. The full articles of non-excluded studies were then attained for appraisal and compared against the inclusion criteria specified above.

Results

The diagram below summarises the search and sifting process for this topic.

Figure: Summary of evidence search and sifting process for this topic



It can be seen that, in total, 473 possibly relevant papers were identified. Of these, 471 papers were excluded at the initial sifting stage based on the title and abstract while two full papers were obtained for appraisal. One of these papers was excluded based on the full text as they were not applicable to the PICO or did not include an incremental analysis of both costs and health effects. Therefore, only one paper was included in the systematic review of the economic evidence for this topic; Wilson et al. 2012. Mowatt et al. 2010 was a comprehensive report conducted as part of the NIHR HTA programme. The study included was a cost-effectiveness analysis comparing standard care (clinical history, naked eye examination and completion of a seven point checklist) with standard care plus the addition of the Molemate system (SIAscopy scanner integrated with a diagnostic algorithm) for the diagnosis of potentially suspicious lesions.

Quality and applicability of included study

Wilson et al. 2012 was deemed to be directly applicable to the decision problem that we are evaluating since it considers relevant comparators in the UK primary care setting and takes a NHS and PSS perspective. Results were presented in terms of cost per QALY gained. No serious limitations were identified with the analysis, which was generally of a very high standard.

Table: Methodological quality and applicability of the included study

Methodological quality	Applicability	
	Directly applicable	Partially applicable
Minor limitations	Wilson et al. 2012	

Methodological quality	Applicability	
Potentially serious limitations		
Very serious limitations		

Modified GRADE table

The primary results of the analysis by Wilson et al. 2012 are summarised in the modified GRADE table below.

Modified GRADE table showing the included evidence (Wilson et al. 2012) on the cost-effectiveness of adding the molemate system to standard care in patients presenting in primary care with suspected melanoma.

Study	Population	Comparators	Costs	Effects	Incr costs	Incr effects	ICER	Uncertainty	Applicability and limitations
Wilson et al. 2012 UK study considering NHS and PSS perspective. Cost-utility analysis (CUA).	Patients presenting in primary care with at least one suspicious pigmented lesion.	Standard Care: Lesions assessed by lead clinician following NICE guidelines including clinical history, naked eye examination and completion of 7 point checklist.	£1115	15.098 QALYs	Reference			<p>Threshold Sensitivity Analysis</p> <p>The maximum cost per Molemate scan which would result in an ICER less than £30,000 was found to be £290 per consultation.</p> <p>Deterministic Sensitivity Analysis</p> <p>Use of East of England cancer registry data rather than trial data resulted in an ICER of £3,172 per QALY</p> <p>Probabilistic Sensitivity Analysis</p> <p>66.1% of iterations led to an ICER below £30,000 per QALY. The molemate system was dominant in 19.6% and dominated in 7.9% of iterations.</p>	<p>Directly Applicable</p> <p>Analysis conducted from a UK Health Service perspective.</p> <p>Results reported as incremental cost per QALY.</p> <p>Minor Limitations</p> <p>Further one-way sensitivity analysis could have been conducted.</p>
		Standard Care (as above) plus the addition of the Molemate system (SIAscopy scanner integrated with a diagnostic algorithm)	£1133	15.108 QALYs	£18	0.01 QALYs	£1896 per QALY		
Comments:									

Evidence statement

Wilson et al (2012) compared the cost-effectiveness of the Molemate system (SIAscopy scanner integrated with a diagnostic algorithm) in addition to usual care (clinical history, naked eye examination and completion of a seven point checklist) in comparison to usual care alone for the diagnosis of potentially suspicious lesions. The authors found that the addition of the Molemate system would increase lifetime costs by £18 and yield an additional 0.01 QALYs per patient. The resulting ICER of £1,896 per QALY falls well below the NICE threshold of £20,000 per QALY and so the base case results suggest that Molemate is a cost-effective addition to usual care.

The addition of the Molemate scan also appears to be cost-effective in an alternative analysis in which East of England cancer registry data were used rather than the trial data with an ICER of £3,172 per QALY. Furthermore, a threshold analysis showed that the cost of adding the Molemate scan would have to exceed £290 for it to no longer be considered cost-effective at a threshold of £30,000 per QALY. The true cost of adding the Molemate scan is unlikely to be as high as this and so this too appears to be a strong result.

The probabilistic sensitivity analysis showed that, at a threshold of £20,000 per QALY, the addition of the Molemate scan was cost-effective in 60.3% of iterations. This suggests that there is considerable uncertainty, which the authors attribute to uncertainty in the sensitivity and specificity of Molemate versus usual care and the risk of disease progression in undiagnosed melanoma.

While these results appear favourable, further consideration needs to be given to the key effects that are driving the result. The results were primarily driven by the differences in diagnostic accuracy between the two strategies, which were informed by RCT evidence showing that Molemate had higher sensitivity and lower specificity than usual care. However, only the lower specificity result was found to be statistically significant. Indeed, the conclusion drawn from the trial was that Molemate did not add to best application of NICE guidelines in terms of appropriateness of referral.

Furthermore, the implications of the diagnostic accuracy data used in the model is that both appropriate and inappropriate referrals would be increased by using the Molemate system (driven by better sensitivity and poorer specificity, respectively). Therefore, the results of the model essentially suggest that benefits of picking up more cancer through appropriate referral outweigh the costs of making more inappropriate referrals. In other words, a policy of 'over-referring' may be cost-effective.

This interpretation has implications for the cost-effectiveness of the Molemate system itself as it could be argued that the Molemate system is not actually required to achieve such a policy. Being less strict as primary care gatekeepers would very likely lead to similarly cost-effective outcomes without the need for the additional spending on the Molemate system. Indeed, it could be further argued that it would be counter-intuitive to spend money on a system that has only been proven to decrease specificity in comparison to current best practice.

References

Included Studies

- Emery, J. D., Hunter, J., Hall, P. N., Watson, A. J., Moncrieff, M. & Walter, F. M. (2010) Accuracy of SIAscopy for pigmented skin lesions encountered in primary care: development and validation of a new diagnostic algorithm. *BMC Dermatology*, 10: 9.
- Menzies, S. W., Emery, J., Staples, M., Davies, S., McAvoy, B., Fletcher, J., Shahid, K. R., Reid, G., Avramidis, M., Ward, A. M., Burton, R. C. & Elwood, J. M. (2009) Impact of dermoscopy and short-term sequential digital dermoscopy imaging for the management of pigmented lesions in primary care: a sequential intervention trial. *British Journal of Dermatology*, 161: 1270-1277.
- Rosendahl, C., Tschandl, P., Cameron, A. & Kittler, H. (2011) Diagnostic accuracy of dermatoscopy for melanocytic and nonmelanocytic pigmented lesions. *Journal of the American Academy of Dermatology*, 64: 1068-1073.
- Walter, F.M., Morris, H.C., Humphrys, E., Hall, P.N., Prevost, A.T., Burrows, N., Bradshaw, L., Wilson, E.C., Norris, P., Walls, J., Johnson, M., Kinmonth, A.L., Emery, J.D. (2012). Effect of adding a diagnostic aid to best practice to manage suspicious pigmented lesions in primary care: randomised controlled trial. *BMJ*, 345: e4110.

Excluded Studies

- (2009) New tools aid in diagnosing and detecting skin cancer in earliest stages. *Dermatology Nursing*, 21: 222-223.
Narrative review
- Aberg, P., Birgersson, U., Elsner, P., Mohr, P. & Ollmar, S. (2011) Electrical impedance spectroscopy and the diagnostic accuracy for malignant melanoma. *Experimental Dermatology*, 20: 648-652.
Not in PICO
- Achar, S. (1996) Principles of skin biopsies for the family physician. [Review] [14 refs]. *American Family Physician*, 54: 2411-2418.
Narrative review
- Ackerman, A. B. (1988) A "changing mole" is not the best clue to clinical detection of an "early" malignant melanoma. *Archives of Dermatological Research*, 280: Suppl-4.
Not in PICO
- Aharon, O., Abdulhalim, I., Arnon, O., Rosenberg, L., Dyomin, V. & Silberstein, E. (2011) Differential optical spectropolarimetric imaging system assisted by liquid crystal devices for skin imaging. *Journal of Biomedical Optics*, 16: 086008.
Narrative review
- Ahmed, M. M., Moore, B. A. & Schmalbach, C. E. (2014) Utility of Head and Neck Cutaneous Squamous Cell Carcinoma Sentinel Node Biopsy: A Systematic Review. *Otolaryngology-Head and Neck Surgery*, 150: 180-187.
Not in PICO
- Alendar, F., Drljevic, I., Drljevic, K. & Alendar, T. (2009) Early detection of melanoma skin cancer. *Bosnian Journal of Basic Medical Sciences*, 9: 77-80.
Not in PICO
- Alexandrescu, D. T., Kauffman, C. L., Jatcoe, T. A., Hartmann, D. P., Vener, T., Wang, H., Derecho, C., Rajpurohit, Y., Wang, Y. & Palma, J. F. (2010) Melanoma-specific marker expression in skin biopsy tissues as a tool to facilitate melanoma diagnosis. *Journal of Investigative Dermatology*, 130: 1887-1892.
Not in PICO
- Allon, I., Allon, D. M., Gal, G., Anavi, Y., Chaushu, G. & Kaplan, I. (2013) Re-evaluation of common paradigms regarding the clinical appearance of oral mucosal malignancies. *Journal of Oral Pathology and Medicine*, 42: 670-675.
Not in PICO

- Amin, K., Edmonds, K., Fleming, A. & Powell, B. (2011) Subungual malignant melanoma--re-learning the lesson. *BMJ Case Reports*, 2011, 2011.
Not in PICO
- Andersen, W. K. & Silvers, D. N. (1991) 'Melanoma? It can't be melanoma!' A subset of melanomas that defies clinical recognition. *JAMA*, 266: 3463-3465.
Not in PICO
- Anderson, A., Love, R. & Chan, J. (2012) Is sentinel node biopsy the standard of care in melanoma management? The opinions and practices of Australian specialists. *Australasian Journal of Dermatology*, 53: 93-97.
Not in PICO
- Antonio, J. R., Soubhia, R. M., D'Avila, S. C., Caldas, A. C., Tridico, L. A. & Alves, F. T. (2013) Correlation between dermoscopic and histopathological diagnoses of atypical nevi in a dermatology outpatient clinic of the Medical School of Sao Jose do Rio Preto, SP, Brazil. *Anais Brasileiros de Dermatologia*, 88: 199-203.
Not in PICO
- Apalla, Z., Lallas, A., Argenziano, G., Ricci, C., Piana, S., Moscarella, E., Longo, C. & Zalaudek, I. (2013) The light and the dark of dermoscopy in the early diagnosis of melanoma: Facts and controversies. *Clinics in Dermatology*, 31: 671-676.
Narrative review
- Argenziano, G., Puig, S., Zalaudek, I., Sera, F., Corona, R., Alsina, M., Barbato, F., Carrera, C., Ferrara, G., Guilabert, A., Massi, D., Moreno-Romero, J. A., Munoz-Santos, C., Petrillo, G., Segura, S., Soyer, H. P., Zanchini, R. & Malvehy, J. (2006) Dermoscopy improves accuracy of primary care physicians to triage lesions suggestive of skin cancer. *Journal of Clinical Oncology*, 24: 1877-1882.
Not in PICO (reference standard is expert opinion, not follow up and histopathology)
- Argenziano, G., Albertini, G., Castagnetti, F., De Pace, B., Di Lernia, V., Longo, C., Pellacani, G., Piana, S., Ricci, C. & Zalaudek, I. (2012) Early diagnosis of melanoma: what is the impact of dermoscopy? *Dermatologic Therapy*, 25: 403-409.
Narrative review
- Argenziano, G., Cerroni, L., Zalaudek, I., Staibano, S., Hofmann-Wellenhof, R., Arpaia, N., Bakos, R. M., Balme, B., Bandic, J., Bandelloni, R., Brunasso, A. M. G., Cabo, H., Calcara, D. A., Carlos-Ortega, B., Carvalho, A. C., Casas, G., Dong, H. T., Ferrara, G., Filotico, R., Gomez, G., Halpern, A., Iardi, G., Ishiko, A., Kandiloglu, G., Kawasaki, H., Kobayashi, K., Koga, H., Kovalyshyn, I., Langford, D., Liu, X., Marghoob, A. A., Mascolo, M., Massone, C., Mazzoni, L., Menzies, S., Minagawa, A., Nugnes, L., Ozdemir, F., Pellacani, G., Seidenari, S., Siamas, K., Stanganelli, I., Stoecker, W. V., Tanaka, M., Thomas, L., Tschandl, P. & Kittler, H. (2012) Accuracy in melanoma detection: A 10-year multicenter survey. *Journal of the American Academy of Dermatology*, 67: 54-U274.
Not in PICO
- Argenziano, G., Giacomel, J., Abramavicus, A., Pellacani, G., Longo, C., De Pace, B., Albertini, G., Cristofolini, M. & Zalaudek, I. (2012) Improving triage and management of patients with skin cancer: challenges and considerations for the future. *Expert Review of Anticancer Therapy*, 12: 609-621.
Narrative review
- Ascierto, P. A., Palmieri, G., Botti, G., Satriano, R. A., Stanganelli, I., Bono, R., Testori, A., Bosco, L., Daponte, A., Caraco, C., Chiofalo, M. G., Melucci, M. T., Calignano, R., Tatangelo, F., Cochran, A. J., Castello, G. & Melanoma Cooperative Group (2003) Early diagnosis of malignant melanoma: Proposal of a working formulation for the management of cutaneous pigmented lesions from the Melanoma Cooperative Group. *International Journal of Oncology*, 22: 1209-1215.
Not in PICO
- Augsburger, J. J. & Shields, J. A. (1984) Fine needle aspiration biopsy of solid intraocular tumors: indications, instrumentation and techniques. *Ophthalmic Surgery*, 15: 34-40.
Not in PICO

- Azimi, P., Mohmmadi, H. R. & Refieezadeh, M. (2012) Primary pineal melanoma presenting with leptomeningeal spreading in a 22-year-old woman: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 6: 165.
Not in PICO
- Baade, P. D., Del Mar, C. B., Lowe, J. B., Stanton, W. R. & Balanda, K. P. (2005) Clinical diagnosis and management of suspicious pigmented skin lesions--a survey of GPs. *Australian Family Physician*, 34: 79-83.
Not in PICO
- Baade, P. D., Youl, P. H., English, D. R., Mark, E. J. & Aitken, J. F. (2007) Clinical pathways to diagnose melanoma: a population-based study. *Melanoma Research*, 17: 243-249.
Not in PICO
- Baade, P. D., Youl, P. H., Janda, M., Whiteman, D. C., Del Mar, C. B. & Aitken, J. F. (2008) Factors associated with the number of lesions excised for each skin cancer: a study of primary care physicians in Queensland, Australia. *Archives of Dermatology*, 144: 1468-1476.
Not in PICO
- Bafounta, M. L., Beauchet, A., Aegerter, P. & Saiag, P. (2001) Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma: results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests (DARE structured abstract). *Archives of Dermatology*, 137: 1343-1350.
Not in PICO (secondary care)
- Baldwin, B. T., Cherpelis, B. S. & Fenske, N. A. (2010) Discussing Sentinel Lymph Node Biopsy With Your Melanoma Patients. *Journal of Drugs in Dermatology*, 9: 790-792.
Not in PICO
- Balois, T. & Amar, M. B. (2014) Morphology of melanocytic lesions in situ. *Science Reporter*, 4: 3622.
Not in PICO
- Bichakjian, C. K., Halpern, A. C., Johnson, T. M., Foote, H. A., Grichnik, J. M., Swetter, S. M., Tsao, H., Barbosa, V. H., Chuang, T. Y., Duvic, M., Ho, V. C., Sober, A. J., Beutner, K. R., Bhushan, R., Smith, B. W. & American Academy of Dermatology (2011) Guidelines of care for the management of primary cutaneous melanoma. American Academy of Dermatology. *Journal of the American Academy of Dermatology*, 65: 1032-1047.
Guideline
- Bishop, J. N., Bataille, V., Gavin, A., Lens, M., Marsden, J., Mathews, T. & Wheelhouse, C. (2007) The prevention, diagnosis, referral and management of melanoma of the skin: concise guidelines. [Review] [9 refs]. *Clinical Medicine*, 7: 283-290.
Guideline
- Blum, A. (1994) [Diagnostic dermoscopic algorithms]. [Review] [30 refs] [German]. *Hautarzt*, 56: 81-93.
Narrative review
- Boiko, P. E. & Piepkorn, M. W. (1994) Reliability of skin biopsy pathology. *Journal of the American Board of Family Practice*, 7: 371-374.
Not in PICO
- Boiko, P. E., Koepsell, T. D., Larson, E. B. & Wagner, E. H. (1996) Skin cancer diagnosis in a primary care setting. *Journal of the American Academy of Dermatology*, 34: 608-611.
Not in PICO
- Bomm, L., Benez, M. D., Maceira, J. M., Succi, I. C. & Scotelaro, M. F. (2013) Biopsy guided by dermoscopy in cutaneous pigmented lesion - Case report. *Anais Brasileiros de Dermatologia*, 88: 125-127.
Not in PICO
- Bonfa, R., Bonamigo, R. R., Bonfa, R., Duro, K. M., Furian, R. D. & Zelmanowicz, A. M. (2011) Early diagnosis of cutaneous melanoma: an observation in southern Brazil. *Anais Brasileiros de*

Dermatologia, 86: 215-221.
Not in PICO

Bordeaux, J. S., Lu, K. Q. & Cooper, K. D. (2007) Melanoma: prevention and early detection. [Review] [73 refs]. *Seminars in Oncology*, 34: 460-466.
Narrative review

Bourdeaud'hui, F. & del, M., V (2011) [Managing moles in general practice]. [French]. *Revue Medicale de Bruxelles*, 32: 205-209.
Narrative review

Bowns, I. R., Collins, K., Walters, S. J. & McDonagh, A. J. (2006) Telemedicine in dermatology: a randomised controlled trial. *Health Technology Assessment (Winchester, England)*, 10: iii-iv.
Not in PICO

Braun, R. P., Rabinovitz, H., Oliviero, M., Kopf, A. W., Saurat, J. H. & Thomas, L. (2002) [Dermatoscopy of pigmented lesions]. [Review] [112 refs] [French]. *Annales de Dermatologie et de Venereologie*, 129: 187-202.
Narrative review

Braun, R. P., Gaide, O., Le Gal, F. A., Saurat, J. H. & Marghoob, A. A. (2007) [Follow-up of melanoma lesions]. [Review] [5 refs] [French]. *Revue Medicale Suisse*, 3: 1119-1123.
Narrative review

Breitbart, E. W., Mohsenian, F., Roser, M., Schiers, C., Wiebecke, G. F., Reimitz, P. E. & Hohne, K. H. (1989) [Clinical recognition of early forms of malignant melanoma]. [German]. *Onkologie*, 12: 264-268.
Not in PICO

Brenner, S. & Tamir, E. (2002) Early detection of melanoma: the best strategy for a favorable prognosis. [Review] [74 refs]. *Clinics in Dermatology*, 20: 203-211.
Narrative review

Bricknell, M. C. (1993) Skin biopsies of pigmented skin lesions performed by general practitioners and hospital specialists. *British Journal of General Practice*, 43: 199-201.
Not in PICO

Bristow, I. R. & Bowling, J. (2009) Dermoscopy as a technique for the early identification of foot melanoma. *Journal of Foot and Ankle Research*, 2.
Narrative review

Brochez, L., Verhaeghe, E., Grosshans, E., Haneke, E., Pierard, G., Ruiters, D. & Naeyaert, J. M. (2002) Inter-observer variation in the histopathological diagnosis of clinically suspicious pigmented skin lesions. *Journal of Pathology*, 196: 459-466.
Not in PICO

Brown, M. D. (2010) Office management of melanoma patients. [Review]. *Seminars in Cutaneous Medicine & Surgery*, 29: 232-237.
Narrative review

Brown, S. J. & Lawrence, C. M. (2006) The management of skin malignancy: to what extent should we rely on clinical diagnosis? *British Journal of Dermatology*, 155: 100-103.
Not in PICO

Brundel, K. H. (1990) [Skin cancer in general practice]. [German]. *Dermatosen in Beruf und Umwelt.Occupational & Environmental Dermatoses*, 38: 54-57.
Not in PICO

Buckley, D. & McMonagle, C. (2014) Melanoma in primary care. The role of the general practitioner. *Irish Journal of Medical Science*, 183: 363-368.
Not in PICO

Buckley, D. & McMonagle, C. (2014) - Melanoma in primary care. The role of the general practitioner. - *Irish Journal of Medical Science*, 183: 363-368.
Duplicate

- Buis, P. A. J., Chorus, R. M. H. & van Diest, P. J. (2005) Value of histopathologic analysis of skin excisions by GPs. *British Journal of General Practice*, 55: 458-460.
Not in PICO
- Buljan, M., Situm, M., Bolanca, Z., Zivkovic, M. V. & Mihic, L. L. (2010) Multiple primary melanoma: epidemiological and prognostic implications; analysis of 36 cases. *Collegium Antropologicum*, 34: Suppl-4.
Not in PICO
- Burroni, M., Wollina, U., Torricelli, R., Gilardi, S., Dell'Eva, G., Helm, C., Bardey, W., Nami, N., Nobile, F., Ceccarini, M., Pomponi, A., Alessandro, B. & Rubegni, P. (2011) Impact of digital dermoscopy analysis on the decision to follow up or to excise a pigmented skin lesion: a multicentre study. *Skin Research & Technology*, 17: 451-460.
Not in PICO (secondary care)
- Carli, P., De, G., V, Nardini, P., Mannone, F., Palli, D. & Giannotti, B. (2002) Melanoma detection rate and concordance between self-skin examination and clinical evaluation in patients attending a pigmented lesion clinic in Italy. *British Journal of Dermatology*, 146: 261-266.
Not in PICO
- Carli, P., De Giorgi, V., Argenziano, G., Palli, D. & Giannotti, B. (2002) Pre-operative diagnosis of pigmented skin lesions: in vivo dermoscopy performs better than dermoscopy on photographic images. *Journal of the European Academy of Dermatology and Venereology*, 16: 339-346.
Not in PICO
- Carli, P., De, G., V, Betti, R., Vergani, R., Catricala, C., Mariani, G., Simonacci, M., Bettacchi, A., Bottoni, U., Lo, S. G., Mulas, P. & Giannotti, B. (2003) Relationship between cause of referral and diagnostic outcome in pigmented lesion clinics: a multicentre survey of the Italian Multidisciplinary Group on Melanoma (GIPMe). *Melanoma Research*, 13: 207-211.
Not in PICO
- Carlson, J. A., Mu, X. C., Slominski, A., Weismann, K., Crowson, A. N., Malfetano, J., Prieto, V. G. & Mihm, M. C., Jr. (2002) Melanocytic proliferations associated with lichen sclerosus. *Archives of Dermatology*, 138: 77-87.
Not in PICO
- Carlson, J. A., Ross, J. S. & Slominski, A. J. (2009) New techniques in dermatopathology that help to diagnose and prognosticate melanoma. *Clinics in Dermatology*, 27: 75-102.
Narrative review
- Castelli, F. (1993) [Cutaneous melanoma at the Turin Melanoma Center. Correlations of anamnestic data, histopathologic aspects and clinical picture in 306 stage-I patients (1990-1991)]. [Italian]. *Minerva Medica*, 84: 615-620.
Not in PICO
- Chamberlain, A. & Ng, J. (2009) Cutaneous melanoma--atypical variants and presentations. [Review] [25 refs]. *Australian Family Physician*, 38: 476-482.
Narrative review
- Chattopadhyay, M. & Ha, T. (2013) How to examine a patient with suspected skin cancer. *Medicine (United Kingdom)*, 41: 400-401.
Narrative review
- Chen, S. C., Bravata, D. M., Weil, E. & Olkin, I. (2001) A comparison of dermatologists' and primary care physicians' accuracy in diagnosing melanoma - A systematic review. *Archives of Dermatology*, 137: 1627-1634.
Not in PICO
- Chen, S. C., Pennie, M. L., Kolm, P., Warshaw, E. M., Weisberg, E. L., Brown, K. M., Ming, M. E. & Weintraub, W. S. (2006) Diagnosing and managing cutaneous pigmented lesions: Primary care physicians versus dermatologists. *Journal of General Internal Medicine*, 21: 678-682.
Not in PICO

- Cheng, H., Oakley, A. & Rademaker, M. (2013) Please see this child with ? melanoma. *Australasian Journal of Dermatology*, 54: 35.
Not in PICO
- Cheng, H., Oakley, A. & Rademaker, M. (2014) - Change in a child's naevus prompts referral to a dermatology service. - *Journal of Primary Health Care*, 6: 123-128.
Not in PICO
- Chiu, V., Won, E., Malik, M. & Weinstock, M. A. (2006) The use of mole-mapping diagrams to increase skin self-examination accuracy. *Journal of the American Academy of Dermatology*, 55: 245-250.
Not in PICO
- Ciocan, D., Barbe, C., Aubin, F., Granel-Brocard, F., Lipsker, D., Velten, M., Dalac, S., Truchetet, F., Michel, C., Mitschler, A., Arnoult, G., Buemi, A., Dalle, S., Bernard, P., Woronoff, A. S. & Grange, F. (2013) Distinctive features of melanoma and its management in elderly patients: a population-based study in France. *JAMA Dermatology*, 149: 1150-1157.
Not in PICO
- Ciocan, D., Barbe, C., Aubin, F., Granel-Brocard, F., Lipsker, D., Velten, M., Dalac, S., Truchetet, F., Michel, C., Mitschler, A., Arnoult, G., Buemi, A., Dalle, S., Bernard, P., Woronoff, A. S. & Grange, F. (2013) Distinctive Features of Melanoma and Its Management in Elderly Patients A Population-Based Study in France. *JAMA Dermatology*, 149: 1150-1157.
Not in PICO
- Civantos, F., Zitsch, R. & Bared, A. (2007) Sentinel node biopsy in oral squamous cell carcinoma. [Review] [49 refs]. *Journal of Surgical Oncology*, 96: 330-336.
Not in PICO
- Cockerell, C. J., Howell, J. B. & Balch, C. M. (1993) Think melanoma. [Review] [28 refs][Erratum appears in South Med J 1994 Feb;87(2):168]. *Southern Medical Journal*, 86: 1325-1333.
Narrative review
- Cooke, K., McNoe, B. & Spears, G. (1993) General practice consultations involving pigmented naevi presented for assessment of malignancy. *New Zealand Medical Journal*, 106: 493-495.
Not in PICO
- Cooper, S. M. & Wojnarowska, F. (2002) The accuracy of clinical diagnosis of suspected premalignant and malignant skin lesions in renal transplant recipients. *Clinical & Experimental Dermatology*, 27: 436-438.
Not in PICO
- Corbo, M. D., Vender, R. & Wismer, J. (2012) Comparison of Dermatologists' and Nondermatologists' Diagnostic Accuracy for Malignant Melanoma. *Journal of Cutaneous Medicine and Surgery*, 16: 272-280.
Not in PICO
- Crocetti, E., Caldarella, A., Massi, D., Sacchetti, C., Amunni, G. & Borgognoni, L. (2013) Indicators of the standard of care for melanoma: Tuscany data. *Melanoma Research*, 23: 283-289.
Not in PICO
- Czerniak, B., Woyke, S., Domagala, W. & Krzysztofik, Z. (1983) Fine needle aspiration cytology of intraocular malignant melanoma. *Acta Cytologica*, 27: 157-165.
Not in PICO
- Dalal, A., Moss, R. H., Stanley, R. J., Stoecker, W. V., Gupta, K., Calcara, D. A., Xu, J., Shrestha, B., Drugge, R., Malters, J. M. & Perry, L. A. (2011) Concentric decile segmentation of white and hypopigmented areas in dermoscopy images of skin lesions allows discrimination of malignant melanoma. *Computerized Medical Imaging & Graphics*, 35: 148-154.
Narrative review
- Damato, B. (2001) Detection of uveal melanoma by optometrists in the United Kingdom. *Ophthalmic & Physiological Optics*, 21: 268-271.
Not in PICO

- de Gannes, G. C., Ip, J. L., Martinka, M., Crawford, R. I. & Rivers, J. K. (2004) Early detection of skin cancer by family physicians: a pilot project. *Journal of Cutaneous Medicine & Surgery*, 8: 103-109.
Not in PICO
- De Giorgi, V., Grazzini, M., Rossari, S., Gori, A., Alfaioli, B., Papi, F., Savarese, I., Cervadoro, E. & Lotti, T. (2011) Adding dermatoscopy to naked eye examination of equivocal melanocytic skin lesions: effect on intention to excise by general dermatologists. *Clinical and Experimental Dermatology*, 36: 255-259.
Not in PICO
- De Giorgi, V., Gori, A., Alfaioli, B., Rossari, S., Grazzini, M., Pata, M. A., Moretti, S. & Lotti, T. Early diagnosis for melanoma: Is open access to skin cancer clinics really significant? A prospective study. [References]. *Preventive Medicine: An International Journal Devoted to Practice and Theory* 51[3-4], 334-335. 2010.
Not in PICO
- de Queiroz Fuscaldi, L. A., Bucard, A. M., Alvarez, C. D. & Barcaui, C. B. (2011) Epidermolysis bullosa nevi: report of a case and review of the literature. *Case Reports Dermatology*, 3: 235-239.
Not in PICO
- De, G., V., Grazzini, M., Rossari, S., Gori, A., Papi, F., Scarfi, F., Savarese, I. & Gandini, S. (2012) Is skin self-examination for cutaneous melanoma detection still adequate? A retrospective study. *Dermatology*, 225: 31-36.
Not in PICO
- Debniak, T. (2007) Some molecular and clinical aspects of genetic predisposition to malignant melanoma and tumours of various site of origin. *Hereditary Cancer in Clinical Practice*, 5: 97-116.
Not in PICO
- Del Mar, C. B. & Lowe, J. B. (1997) The skin cancer workload in Australian general practice. *Australian Family Physician*, 26: Suppl-7.
Not in PICO
- Del Mar, C. B., Green, A. C. & Battistutta, D. (1997) Patterns of excision and referral from primary care of melanocytic lesions. *Melanoma Research*, 7: 496-499.
Not in PICO
- Demierre, M. F., Chung, C., Miller, D. R. & Geller, A. C. (2005) Early detection of thick melanomas in the United States: beware of the nodular subtype. *Archives of Dermatology*, 141: 745-750.
Not in PICO
- Dhawan, A. P. (1985) Early detection of cutaneous malignant melanoma by three-dimensional nevoscopy. *Computer Methods & Programs in Biomedicine*, 21: 59-68.
Narrative review
- Divito, S. J. & Ferris, L. K. (2010) Advances and short comings in the early diagnosis of melanoma. *Melanoma Research*, 20: 450-458.
Narrative review
- Dixon, A. J. & Hall, R. S. (2005) Managing skin cancer--23 golden rules. [Review] [0 refs]. *Australian Family Physician*, 34: 669-671.
Narrative review
- Dolianitis, C., Kelly, J., Wolfe, R. & Simpson, P. (2005) Comparative performance of 4 dermoscopic algorithms by nonexperts for the diagnosis of melanocytic lesions. *Archives of Dermatology*, 141: 1008-1014.
Not in PICO
- Dove, S., Smith, M., Phillips, E. & Levell, N. (2010) Routine recording of dermoscopic images as an aid to diagnosis. *Journal of Visual Communication in Medicine*, 33: 150-152.
Narrative review
- Duff, C. G., Melsom, D., Rigby, H. S., Kenealy, J. M. & Townsend, P. L. (2001) A 6 year prospective analysis of the diagnosis of malignant melanoma in a pigmented-lesion clinic: even the experts

- miss malignant melanomas, but not often. *British Journal of Plastic Surgery*, 54: 317-321.
Not in PICO
- Dummer, W., Doehnel, K. A. & Remy, W. (1993) [Videomicroscopy in differential diagnosis of skin tumors and secondary prevention of malignant melanoma]. [German]. *Hautarzt*, 44: 772-776.
Not in PICO
- Durbec, F., Vitry, F., Granel-Brocard, F., Lipsker, D., Aubin, F., Hedelin, G., Dalac, S., Truchetet, F., Michel, C., Batard, M. L., Domissy-Baury, B., Halna, J. M., Schmutz, J. L., Delvincourt, C., Reuter, G., Dalle, S., Bernard, P., Danzon, A. & Grange, F. (2010) The role of circumstances of diagnosis and access to dermatological care in early diagnosis of cutaneous melanoma: a population-based study in France. *Archives of Dermatology*, 146: 240-246.
Not in PICO
- Durrani, A. J., Moir, G. C., Diaz-Cano, S. J. & Cerio, R. (2003) Malignant melanoma in an 8-year-old Caribbean girl: diagnostic criteria and utility of sentinel lymph node biopsy. *British Journal of Dermatology*, 148: 569-572.
Not in PICO
- Edlich, R. F., Becker, D. G., Long, W. B. & Masterson, T. M. (2004) Excisional biopsy of skin tumors. [Review] [25 refs]. *Journal of Long-Term Effects of Medical Implants*, 14: 201-214.
Narrative review
- Edman, R. L. & Wolfe, J. T. (2000) Prevention and early detection of malignant melanoma. *American Family Physician*, 62: 2277-2284.
Narrative review
- Eichhorn, R., Wessler, G., Scholz, M., Leupold, D., Stankovic, G., Buder, S., Stucker, M. & Hoffmann, K. (2009) Early diagnosis of melanotic melanoma based on laser-induced melanin fluorescence. *Journal of Biomedical Optics*, 14: 034033-034Jun.
Narrative review
- Elder, D. E. (2006) Pathology of melanoma. [Review] [48 refs]. *Clinical Cancer Research*, 12: t-2311s.
Narrative review
- Emery, J. (2011) Melanoma Improving diagnosis in general practice. *Australian Family Physician*, 40: 991.
Narrative review
- Esdaile, B., Mahmud, I., Palmer, A. & Bowling, J. (2014) Diagnosing melanoma: how do we assess how good we are? *Clinical and Experimental Dermatology*, 39: 129-134.
Not in PICO
- Foley, C. C., Corby, P. & Barnes, L. (1111) A dermatology outpatient waiting list initiative. *Irish Medical Journal*, 106: -August.
Not in PICO
- Fox, G. N. (2008) Dermoscopy: An invaluable tool for evaluating skin lesions. *American Family Physician*, 78: 704-+.
Narrative review
- Friedman, T., Klein, D., Hadad, E., Westreich, M. & Shalom, A. (1111) [Diagnostic accuracy of skin lesions excised by a plastic surgeon]. [Hebrew]. *Harefuah*, 147: 305-308.
Not in PICO
- Gannes, G. C., Ip, J. L., Martinka, M., Crawford, R. I. & Rivers, J. K. (2004) Early detection of skin cancer by family physicians: a pilot project. *Journal of Cutaneous Medicine and Surgery*, 8: 103-109.
Not in PICO
- Garbe, C., Eigentler, T. K., Bauer, J., Blodorn-Schlicht, N., Fend, F., Hantschke, M., Kurschat, P., Kutzner, H., Metze, D., Pressler, H., Reusch, M., Rocken, M., Stadler, R., Tronnier, M., Yazdi, A. & Metzler, G. (2011) Histopathological diagnostics of malignant melanoma in accordance with the recent AJCC classification 2009: Review of the literature and recommendations for general

- practice. *Journal der Deutschen Dermatologischen Gesellschaft*, 9: 690-699.
Not in PICO
- Gazzani, P., Rothwell, J., Kasparis, C. & Gee, B. (2013) Progress towards integrating a melanoma diagnostic index into a U.K. dermatology department quality dashboard. *British Journal of Dermatology*, 169: 46-47.
Not in PICO
- Geisse, J. K. (1994) Biopsy techniques for pigmented lesions of the skin. [Review] [43 refs]. *Pathology*, 2: 181-193.
Narrative review
- Gerbert, B., Bronstone, A., Maurer, T., Hofmann, R. & Berger, T. (2000) Decision support software to help primary care physicians triage skin cancer - A pilot study. *Archives of Dermatology*, 136: 187-192.
Not in PICO
- Giacomel, J. & Zalaudek, I. (2013) Pink Lesions. *Dermatologic Clinics*, 31: 649-678.
Narrative review
- Giard, R. W. & Neumann, H. A. (2004) [Diagnosis of pigmented skin lesions: how to recognize a malignant melanoma]. [Review] [24 refs] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 148: 2261-2267.
Narrative review
- Gilde, K. (2006) [Malignant tumors of the skin]. [Review] [25 refs] [Hungarian]. *Orvosi Hetilap*, 147: 2321-2330.
Narrative review
- Gonzalez, S., Swindells, K., Rajadhyaksha, M. & Torres, A. (2003) Changing paradigms in dermatology: Confocal microscopy in clinical and surgical dermatology. *Clinics in Dermatology*, 21: 359-369.
Narrative review
- Goodson, A. G. & Grossman, D. (2009) Strategies for early melanoma detection: Approaches to the patient with nevi. *Journal of the American Academy of Dermatology*, 60: 719-735.
Narrative review
- Goppner, D. & Leverkus, M. (2011) Prognostic parameters for the primary care of melanoma patients: what is really risky in melanoma? *Journal of Skin Cancer*, 2011: 521947.
Narrative review
- Grange, F., Maubec, E., Barbe, C., Kassouma, J., Vitry, F., Johanet, H., Granel-Brocard, F., Boitier, F., Girod, A., Couturaud, B., Saez, P., Albert, S., Le, C. A., Descamps, V. & Avril, M. F. (2011) Sentinel lymph node biopsy or nodal observation in melanoma: a prospective study of patient choices. *Dermatologic Surgery*, 37: 199-206.
Not in PICO
- Grange, F., Barbe, C., Mas, L., Granel-Brocard, F., Lipsker, D., Aubin, F., Velten, M., Dalac, S., Truchetet, F., Michel, C., Mitschler, A., Arnoult, G., Buemi, A., Dalle, S., Reuter, G., Bernard, P., Woronoff, A. S. & Arnold, F. (2012) The role of general practitioners in diagnosis of cutaneous melanoma: a population-based study in France. *British Journal of Dermatology*, 167: 1351-1359.
Not in PICO
- Gray, R. J., Pockaj, B. A., Vega, M. L., Connolly, S. M., DiCaudo, D. J., Kile, T. A. & Buchel, E. W. (2006) Diagnosis and treatment of malignant melanoma of the foot. *Foot & Ankle International*, 27: 696-705.
Not in PICO
- Green, J., Murchie, P. & Lee, A. J. (2013) Does patients' place of residence affect the type of physician performing primary excision of cutaneous melanoma in northern Scotland? *Journal of Rural Health*, 29: Suppl-42.
Not in PICO

- Griffiths, W. A. (2010) Improving melanoma diagnosis in primary care--a tele-dermatoscopy project. *Journal of Telemedicine & Telecare*, 16: 185-186.
Not in PICO
- Grimaldi, L., Silvestri, A., Brandi, C., Nisi, G., Brafa, A., Calabro, M., Campa, A. & D'Aniello, C. (2009) Digital epiluminescence dermoscopy for pigmented cutaneous lesions, primary care physicians, and telediagnosis: a useful tool? *Journal of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*, 62: 1054-1058.
Not in PICO
- Guillod, J. (1999) [Clinical differential diagnosis of pigmented skin changes and contribution of epiluminescence microscopy]. [German]. *Therapeutische Umschau*, 56: 312-317.
Narrative review
- Guitera-Rovel, P. & Vestergaard, M. E. (2008) Diagnosis tools for cutaneous melanoma. *Annales de Dermatologie et de Venereologie*, 135: 828-834.
Narrative review
- Guitera, P., Haydu, L. E., Menzies, S. W., Scolyer, R. A., Hong, A., Fogarty, G. B., Gallardo, F. & Segura, S. (2014) - Surveillance for treatment failure of lentigo maligna with dermoscopy and in vivo confocal microscopy: new descriptors. - *British Journal of Dermatology*, 170: 1305-1312.
Not in PICO
- Gunther, V., Alkatout, I., Lez, C., Altarac, S., Fures, R., Cupic, H., Persec, Z., Hrgovic, Z. & Mundhenke, C. (2012) Malignant melanoma of the urethra: a rare histologic subdivision of vulvar cancer with a poor prognosis. *Case Reports in Obstetrics and Gynecology*, 2012: 385175.
Not in PICO
- Gupta, M., Aggarwal, A., Ahuja, R., Pachauri, A. & Kumar, P. (2013) Significance of early detection of oral malignant melanoma: Some reasonable facts. *Clinical Cancer Investigation Journal*, 2: 178-180.
Narrative review
- Hajar-Serviansky, T., Gutierrez-Mendoza, D., Galvan, I. L., Lammoglia-Ordiales, L., Mosqueda-Taylor, A., Hernandez-Cazares, M. L. & Toussaint-Caire, S. (2012) A case of oral mucosal melanoma. Clinical and dermoscopic correlation. *Journal of Dermatological Case Reports*, 6: 1-4.
Not in PICO
- Hald, M., Christensen, B., Lock-Andersen, J. & Jemec, G. B. (2004) [Referrals for malignant melanoma. Opportunities for quality assurance and development]. [Danish]. *Ugeskrift for Laeger*, 166: 163-165.
Not in PICO
- Haliasos, E. C., Kerner, M., Jaimes, N., Zalaudek, I., Malvey, J., Lanschuetzer, C. M., Hinter, H., Hofmann-Wellenhof, R., Braun, R. P. & Marghoob, A. A. (2013) Dermoscopy for the pediatric dermatologist, part ii: dermoscopy of genetic syndromes with cutaneous manifestations and pediatric vascular lesions. *Pediatric Dermatology*, 30: 172-181.
Narrative review
- Halpern, A. C. & Lieb, J. A. (2007) Early melanoma diagnosis: a success story that leaves room for improvement. *Current Opinion in Oncology*, 19: 109-115.
Narrative review
- Hamm, H. & Hoyer, P. H. (2011) Skin tumors in childhood. [Review]. *Deutsches Arzteblatt International*, 108: 347-353.
Narrative review
- Harbour, J. W. & Chao, D. L. (2014) A Molecular Revolution in Uveal Melanoma Implications for Patient Care and Targeted Therapy. *Ophthalmology*, 121: 1281-1288.
Narrative review
- Haw, W. Y., Fraser, S., Affleck, A. & Holme, A. (2014) Skin cancer excision performance in primary and secondary care in Scotland. *British Journal of Dermatology*, 171: 25.
Not in PICO

- Heal, C. F., Raasch, B. A., Buettner, P. G. & Weedon, D. (2008) Accuracy of clinical diagnosis of skin lesions. *British Journal of Dermatology*, 159: 661-668.
Not in PICO
- Hengge, U. R. & Meurer, M. (2005) [Pigmented lesions of the genital mucosa]. [Review] [83 refs] [German]. *Hautarzt*, 56: 540-549.
Narrative review
- Hennrikus, D., Girgis, A., Redman, S. & Sanson-Fisher, R. W. (1991) A community study of delay in presenting with signs of melanoma to medical practitioners. *Archives of Dermatology*, 127: 356-361.
Not in PICO
- Herd, R. M., Hunter, J. A., McLaren, K. M., Chetty, U., Watson, A. C. & Gollock, J. M. (1992) Excision biopsy of malignant melanoma by general practitioners in south east Scotland 1982-91. *BMJ*, 305: 1476-1478.
Not in PICO
- Hermes, H. M., Sahu, J., Schwartz, L. R. & Lee, J. B. (2014) - Clinical and histologic characteristics of clinically unsuspected melanomas. - *Clinics in Dermatology*, 32: 324-330.
Not in PICO
- Herschorn, A. (2012) Dermoscopy for melanoma detection in family practice (Provisional abstract). *Database of Abstracts of Reviews of Effects.*, 740-745.
Semi systematic review, no new studies
- High, W. A. (2008) Malpractice in dermatopathology - Principles, risk mitigation, and opportunities for improved care for the histologic diagnosis of melanoma and pigmented lesions. *Clinics in Laboratory Medicine*, 28: 261-+.
Narrative review
- Holme, S. A. (2003) GPs have role in early detection of melanoma. [Review]. *Practitioner*, 257: 27-30.
Narrative review
- Hornung, R. L., Hansen, L. A., Sharp, L. K., Poorsattar, S. P. & Lipsky, M. S. (2007) Skin cancer prevention in the primary care setting: assessment using a standardized patient. *Pediatric Dermatology*, 24: 108-112.
Not in PICO
- Horsch, A., Stolz, W., Neiss, A., Abmayr, W., Pompl, R., Bernklau, A., Bunk, W., Dersch, D. R., Glassl, A., Schiffner, R. & Morfill, G. (1997) Improving early recognition of malignant melanomas by digital image analysis in dermatoscopy. *Studies in Health Technology & Informatics*, 43: t-5.
Narrative review
- Husemann, R., Tolg, S., Von Seelen, W., Altmeyer, P., Frosch, P. J., Stucker, M., Hoffmann, K. & el-Gammal, S. (1997) Computerised diagnosis of skin cancer using neural networks. *Skin Cancer and Uv Radiation*, 1052-1063.
Not in PICO
- Ishihara, Y., Saida, T., Miyazaki, A., Koga, H., Taniguchi, A., Tsuchida, T., Toyama, M. & Ohara, K. (2006) Early acral melanoma in situ: correlation between the parallel ridge pattern on dermoscopy and microscopic features. *American Journal of Dermatopathology*, 28: 21-27.
Not in PICO
- Jackson, A. M., Morgan, D. R. & Ellison, R. (2000) Diagnosis of malignant melanoma by general practitioners and hospital specialists. *Postgraduate Medical Journal*, 76: 295-298.
Not in PICO
- Jin, L., Arai, E., Anzai, S., Kimura, T., Tsuchida, T., Nagata, K. & Shimizu, M. (2010) Reassessment of histopathology and dermoscopy findings in 145 Japanese cases of melanocytic nevus of the sole: toward a pathological diagnosis of early-stage malignant melanoma in situ. *Pathology International*, 60: 65-70.
Not in PICO

- Jolliffe, V. M., Harris, D. W. & Whittaker, S. J. (2001) Can we safely diagnose pigmented lesions from stored video images? A diagnostic comparison between clinical examination and stored video images of pigmented lesions removed for histology. *Clinical & Experimental Dermatology*, 26: 84-87.
Not in PICO (secondary care)
- Jones, T. P., Boiko, P. E. & Piepkorn, M. W. (1996) Skin biopsy indications in primary care practice: a population-based study. *Journal of the American Board of Family Practice*, 9: 397-404.
Not in PICO
- Kahn, E., Sossong, S., Goh, A., Carpenter, D. & Goldstein, S. (2013) Evaluation of Skin Cancer in Northern California Kaiser Permanente's Store-and-Forward Teledermatology Referral Program. *Telemedicine and E-Health*, 19: 780-785.
Not in PICO
- Kaiser, S., Vassell, R., Pinckney, R. G., Holmes, T. E. & James, T. A. (2014) - Clinical impact of biopsy method on the quality of surgical management in melanoma. - *Journal of Surgical Oncology*, 109: 775-779.
Not in PICO
- Kaminska-Winciorek, G. & Spiewak, R. (2011) [Basic dermoscopy of melanocytic lesions for beginners]. [Review] [Polish]. *Postepy Higieny i Medycyny do Swiadczalnej (Online)*, 65: 501-508.
Not in PICO
- Kaminska-Winciorek, G. & Spiewak, R. (2013) [Dermoscopy on subungual melanoma]. [Polish]. *Postepy Higieny i Medycyny do Swiadczalnej (Online)*, 67: 380-387.
Narrative review
- Karakousis, C. P., Rizos, S. & Driscoll, D. L. (1994) Residual nodal disease after excisional biopsy of a palpable, positive node in melanoma. *American Journal of Surgery*, 168: 69-70.
Not in PICO
- Kester, B. S., Wayne, J. D., Ross, M. I., Bentrem, D. J., Merkow, R. P. & Bilimoria, K. Y. (2013) An Opportunity to Ensure High-Quality Melanoma Care Through the Use of a Preoperative Treatment Algorithm. *Annals of Surgical Oncology*, 20: 3976-3983.
Not in PICO
- Khorshid, S. M., Pinney, E. & Bishop, J. A. (1998) Melanoma excision by general practitioners in north-east Thames region, England. *British Journal of Dermatology*, 138: 412-417.
Not in PICO
- King, R., Hayzen, B. A., Page, R. N., Googe, P. B., Zeagler, D. & Mihm, M. C., Jr. (2009) Recurrent nevus phenomenon: a clinicopathologic study of 357 cases and histologic comparison with melanoma with regression. *Modern Pathology*, 22: 611-617.
Not in PICO
- Kirkwood, J. M., Jukic, D. M., Averbuck, B. J. & Sender, L. S. (2009) Melanoma in pediatric, adolescent, and young adult patients. [Review] [111 refs]. *Seminars in Oncology*, 36: 419-431.
Narrative review
- Kitchener, S., McMaster, S. & Nasveld, P. (2009) Dermoscopy in primary care for detection of melanoma. *International Journal of Dermatology*, 48: 1397-1398.
Letter
- Klein, D., Westreich, M. & Shalom, A. (2012) Accuracy of malignant melanoma detection in the community. *Acta Dermatovenerologica Croatica*, 20: 165-169.
Not in PICO
- Kolm, I., Hofbauer, G. & Braun, R. P. (2010) [Early diagnosis of skin cancer]. [Review] [German]. *Therapeutische Umschau*, 67: 439-446.
Narrative review
- Kretschmer, L. & Hilgers, R. (2006) Research supports the view that sentinel node biopsy is the standard of care in high-risk primary melanoma. *Journal of Clinical Oncology*, 24: 2965-2966.
Not in PICO

- Kundu, R. V. & Patterson, S. (2013) Dermatologic conditions in skin of color: part I. Special considerations for common skin disorders.[Summary for patients in Am Fam Physician. 2013 Jun 15;87(12):Online; PMID: 23939576]. *American Family Physician*, 87: 850-856.
Narrative review
- Lallas, A., Zalaudek, I., Apalla, Z., Longo, C., Moscarella, E., Piana, S., Reggiani, C. & Argenziano, G. (2013) Management Rules to Detect Melanoma. *Dermatology*, 226: 52-60.
Narrative review
- Lathlean, S. (1999) Skin cancer in general practice in South Australia. A five year study. *Australian Family Physician*, 28: Suppl-31.
Not in PICO
- LeBoit, P. E. (2009) What sentinel node biopsy in patients with melanoma (or patients whose doctors worry that they could have melanoma) might and might not do. [Review] [12 refs]. *Clinics in Dermatology*, 27: 588-593.
Narrative review
- Lee, K. C., Jayarajan, R. & Daruwalla, M. (2013) Skin cancer diagnosis hit or miss? the leicester experience. *International Journal of Surgery*, 11: 683.
Not in PICO
- Lee, S., Lee, H. J., Oh, S. H., Im, M., Lee, J. H., Seo, Y. J. & Lee, Y. (2011) The Appearance of a Candidate Site for a Primary Melanoma: A 5 Year-gap with a Melanoma of an Unknown Site. *Annals of Dermatology*, 23: 2-8.
Not in PICO
- Li, Z. G. & Qin, X. J. (2014) - Primary anorectal melanoma on FDG PET/CT. - *Clinical Nuclear Medicine*, 39: 762-764.
Not in PICO
- Liew, Y., De, B. D. & Sansom, J. (2014) Rapid clinical review of patients assessed by a teledermatology service: Analysis of pathways and outcomes. *British Journal of Dermatology*, 171: 138.
Not in PICO
- Lin, M. J. & Kelly, J. W. (2013) When is it melanoima? An update on diagnosis and management. *Medicine Today*, 14: 44-53.
Narrative review
- Lin, M. J., Mar, V., McLean, C., Wolfe, R. & Kelly, J. W. (2014) Diagnostic accuracy of malignant melanoma according to subtype. *Australasian Journal of Dermatology*, 55: 35-42.
Not in PICO
- Lin, M. J., Mar, V., McLean, C., Wolfe, R. & Kelly, J. W. (2014) - Diagnostic accuracy of malignant melanoma according to subtype. - *Australasian Journal of Dermatology*, 55: 35-42.
Not in PICO
- Lindelof, B., Hedblad, M. A. & Sigurgeirsson, B. (1998) Melanocytic naevus or malignant melanoma? A large-scale epidemiological study of diagnostic accuracy. *Acta Dermato-Venereologica*, 78: 284-288.
Not in PICO
- Liu, Z., Sun, J., Smith, L., Smith, M. & Warr, R. (2012) Distribution quantification on dermoscopy images for computer-assisted diagnosis of cutaneous melanomas. [Review]. *Medical & Biological Engineering & Computing*, 50: 503-513.
Not in PICO
- Lourari, S., Paul, C., Gouraud, P. A., Tavitian, S., Viraben, R., Leccia, M. T., Saiag, P., Lebbe, C. & Meyer, N. (2012) Sentinel lymph node biopsy for melanoma is becoming a consensus: a national survey of French centres involved in melanoma care in 2008. *Journal of the European Academy of Dermatology and Venereology*, 26: 1230-1235.
Not in PICO
- Lowy, A., Willis, D. & Abrams, K. (1997) Is histological examination of tissue removed by general practitioners always necessary? Before and after comparison of detection rates of serious skin

- lesions. *BMJ*, 315: 406-408.
Not in PICO
- Lukacs, L. & Peter, S. (1982) Early recognition of cutaneous malignant melanomas. *Acta Chirurgica Academiae Scientiarum Hungaricae*, 23: 183-191.
Narrative review
- Luttrell, M. J., McClenahan, P., Hofmann-Wellenhof, R., Fink-Puches, R. & Soyer, H. P. (2012) Laypersons' sensitivity for melanoma identification is higher with dermoscopy images than clinical photographs. *British Journal of Dermatology*, 167: 1037-1041.
Not in PICO
- MacDonald, A., Berty, C. & Holmes, S. (2006) An audit of the management of melanoma patients at Glasgow Royal Infirmary 1998-2003. *Scottish Medical Journal*, 51: 30-33.
Not in PICO
- MacKie, R. M., Fleming, C., McMahon, A. D. & Jarrett, P. (2002) The use of the dermatoscope to identify early melanoma using the three-colour test. *British Journal of Dermatology*, 146: 481-484.
Not in PICO
- MacNeill, K. N., Ghazarian, D., McCready, D. & Rotstein, L. (2005) Sentinel lymph node biopsy for cutaneous melanoma of the head and neck. *Annals of Surgical Oncology*, 12: 726-732.
Not in PICO
- Macy-Roberts, E. & Ackerman, A. B. (1982) A critique of techniques for biopsy of clinically suspected malignant melanomas. *American Journal of Dermatopathology*, 4: 391-398.
Not in PICO
- Magro, C. M., Crowson, A. N. & Mihm, M. C. (2006) Unusual variants of malignant melanoma. [Review] [204 refs]. *Modern Pathology*, 19: Suppl-70.
Narrative review
- Malik, A., Bansil, S., Junglee, N., Sutton, J., Gasem, J. & Ahmed, W. (2011) Synchronous primary oesophageal malignant melanoma and sigmoid adenocarcinoma. *BMJ Case Reports*, 2011, 2011.
Not in PICO
- Malvey, J. & Puig, S. (2004) Dermoscopic patterns of benign volar melanocytic lesions in patients with atypical mole syndrome. *Archives of Dermatology*, 140: 538-544.
Not in PICO
- Manca, G., Romanini, A., Rubello, D., Mazzarri, S., Boni, G., Chiacchio, S., Tredici, M., Duce, V., Tardelli, E., Volterrani, D. & Mariani, G. (2014) - A critical reappraisal of false negative sentinel lymph node biopsy in melanoma. - *The Quarterly Journal of Nuclear Medicine & Molecular Imaging*, 58: 105-113.
Not in PICO
- Marghoob, A. A., Usatine, R. P. & Jaimes, N. (2013) Dermoscopy for the family physician. [Review]. *American Family Physician*, 88: 441-450.
Narrative review
- Marghoob, A. A., Usatine, R. P. & Jaimes, N. (2013) Dermoscopy for the Family Physician. *American Family Physician*, 88: 441-450.
Narrative review
- Marsden, J. R., Newton-Bishop, J. A., Burrows, L., Cook, M., Corrie, P. G., Cox, N. H., Gore, M. E., Lorigan, P., Mackie, R., Nathan, P., Peach, H., Powell, B., Walker, C. & British Association of Dermatologists (BAD) Clinical Standards Unit (2010) Revised UK guidelines for the management of cutaneous melanoma 2010. *Journal of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*, 63: 1401-1419.
Guideline
- May, C., Giles, L. & Gupta, G. (2008) Prospective observational comparative study assessing the role of store and forward teledermatology triage in skin cancer. *Clinical & Experimental Dermatology*,

33: 736-739.

Not in PICO

Mayer, J. (1997) Systematic review of the diagnostic accuracy of dermoscopy in detecting malignant melanoma. [Review] [25 refs]. *Medical Journal of Australia*, 167: 206-210.

Not in PICO (secondary care)

McCannel, T. A. (2013) Fine-needle aspiration biopsy in the management of choroidal melanoma. *Current Opinion in Ophthalmology*, 24: 262-266.

Narrative review

McCourt, C., Dolan, O. & Gormley, G. (2014) Malignant melanoma: A pictorial review. *Ulster Medical Journal*, 83: 103-110.

Not in PICO

McWhirter, J. E. & Hoffman-Goetz, L. (2013) Visual images for patient skin self-examination and melanoma detection: a systematic review of published studies. [Review]. *Journal of the American Academy of Dermatology*, 69: 47-55.

Not in PICO

Medalie, N. S. & Ackerman, A. B. (2003) Sentinel lymph node biopsy has no benefit for patients with primary cutaneous melanoma metastatic to a lymph node: An assertion based on comprehensive, critical analysis - Part II. *American Journal of Dermatopathology*, 25: 473-484.

Not in PICO

Mehra, M., Stitson, R., Natkunarajah, J., George, S., Harland, C. C. & Abdul-Wahab, A. (2008) Skin cancer biopsies in primary care: neither BAD nor NICE. *British Journal of Dermatology*, 159: 56.

Not in PICO

Menzies, S. W., Bischof, L., Talbot, H., Gutenev, A., Avramidis, M., Wong, L., Lo, S. K., Mackellar, G., Skladnev, V., McCarthy, W., Kelly, J., Cranney, B., Lye, P., Rabinovitz, H., Oliviero, M., Blum, A., Varol, A., De'Ambrosio, B., McCleod, R., Koga, H., Grin, C., Braun, R. & Johr, R. (2005) The performance of SolarScan: an automated dermoscopy image analysis instrument for the diagnosis of primary melanoma. [Erratum appears in Arch Dermatol. 2006 May;142(5):558 Note: Virol, Alexandra [corrected to Varol, Alexandra]]. *Archives of Dermatology*, 141: 1388-1396.

Not in PICO (secondary care)

Menzies, S. W. (2006) Technologies for the diagnosis of primary melanoma of the skin. *Medical Journal of Australia*, 185: 533-534.

Narrative review

Menzies, S. W. & Zalaudek, I. (2006) Why perform dermoscopy? The evidence for its role in the routine management of pigmented skin lesions. *Archives of Dermatology*, 142: 1211-1212.

Narrative review

Menzies, S. W. (2007) Dermoscopy not yet shown to increase sensitivity of melanoma diagnosis in real practice - Reply. *Archives of Dermatology*, 143: 665-666.

Letter

Menzies, S. W., Moloney, F. J., Byth, K., Avramidis, M., Argenziano, G., Zalaudek, I., Braun, R. P., Malvey, J., Puig, S., Rabinovitz, H. S., Oliviero, M., Cabo, H., Bono, R., Pizzichetta, M. A., Claeson, M., Gaffney, D. C., Soyer, H. P., Stanganelli, I., Scolyer, R. A., Guitera, P., Kelly, J., McCurdy, O., Llambrich, A., Marghoob, A. A., Zaballos, P., Kirchesch, H. M., Piccolo, D., Bowling, J., Thomas, L., Terstappen, K., Tanaka, M., Pellacani, G., Pagnanelli, G., Ghigliotti, G., Ortega, B. C., Crafter, G., Ortiz, A. M., Tromme, I., Karaarslan, I. K., Ozdemir, F., Tam, A., Landi, C., Norton, P., Kacar, N., Rudnicka, L., Slowinska, M., Simionescu, O., Di, S. A., Coates, E. & Kreusch, J. (2013) Dermoscopic evaluation of nodular melanoma. *JAMA Dermatology*, 149: 699-709.

Not in PICO

Menzies, S. W. (2013) Evidence-Based Dermoscopy. *Dermatologic Clinics*, 31: 521-524.

Narrative review

Menzies, S. W., Moloney, F. J., Byth, K., Avramidis, M., Argenziano, G., Zalaudek, I., Braun, R. P., Malvey, J., Puig, S., Rabinovitz, H. S., Oliviero, M., Cabo, H., Bono, R., Pizzichetta, M. A., Claeson,

- M., Gaffney, D. C., Soyer, H. P., Stanganelli, I., Scolyer, R. A., Guitera, P., Kelly, J., McCurdy, O., Llambrich, A., Marghoob, A. A., Zaballos, P., Kirchesch, H. M., Piccolo, D., Bowling, J., Thomas, L., Terstappen, K., Tanaka, M., Pellacani, G., Pagnanelli, G., Ghigliotti, G., Ortega, B. C., Crafter, G., Perusquia Ortiz, A. M., Tromme, I., Karaarslan, I. K., Ozdemir, F., Tam, A., Landi, C., Norton, P., Kacar, N., Rudnicka, L., Slowinska, M., Simionescu, O., Di, S. A., Coates, E. & Kreusch, J. (2013) Dermoscopic evaluation of nodular melanoma. *JAMA Dermatology*, 149: 699-709.
Not in PICO
- Menzies, S. W. (2013) Evidence-Based Dermoscopy. *Dermatologic Clinics*, 31: 521-+.
Narrative review
- Messmer, E. M., Mackert, M. J., Zapp, D. M. & Kampik, A. (2006) In vivo confocal microscopy of pigmented conjunctival tumors. *Graefes Archive for Clinical & Experimental Ophthalmology*, 244: 1437-1445.
Not in PICO
- Metzger, S., Ellwanger, U., Stroebel, W., Schiebel, U., Rassner, G. & Fierlbeck, G. (1998) Extent and consequences of physician delay in the diagnosis of acral melanoma. *Melanoma Research*, 8: 181-186.
Not in PICO
- Midena, E. & Parrozzani, R. (2012) Biopsies in uveal melanoma. [Review]. *Developments in Ophthalmology*, 49: 81-95.
Narrative review
- Mihic-Probst, D. & Beer, M. (2013) [Insights into melanoma from a pathologist's perspective]. [Review] [German]. *Praxis*, 102: 219-224.
Narrative review
- Moffatt, C. R., Green, A. C. & Whiteman, D. C. (2006) Diagnostic accuracy in skin cancer clinics: the Australian experience. *International Journal of Dermatology*, 45: 656-660.
Not in PICO
- Mondragon, G. & Nygaard, F. (1981) Routine and special procedures for processing biopsy specimens of lesions suspected to be malignant melanomas. *American Journal of Dermatopathology*, 3: 265-272.
Not in PICO
- Monshizadeh, L., Hanikeri, M., Beer, T. W. & Heenan, P. J. (2012) A critical review of melanoma pathology reports for patients referred to the Western Australian Melanoma Advisory Service. *Pathology*, 44: 441-447.
Not in PICO
- Moore, P., Hundley, J., Hundley, J., Levine, E. A., Williford, P., Sanguenza, O., McCoy, T. & Shen, P. (2009) Does Shave Biopsy Accurately Predict the Final Breslow Depth of Primary Cutaneous Melanoma? *American Surgeon*, 75: 369-373.
Not in PICO
- Moreno-Ramirez, D., Ferrandiz, L., Nieto-Garcia, A., Carrasco, R., Moreno-Alvarez, P., Galdeano, R., Bidegain, E., Rios-Martin, J. J. & Camacho, F. M. (2007) Store-and-forward teledermatology in skin cancer triage: experience and evaluation of 2009 teleconsultations.[Erratum appears in Arch Dermatol. 2007 Jul;143(7):886]. *Archives of Dermatology*, 143: 479-484.
Not in PICO
- Moreno, G., Tran, H., Chia, A. L., Lim, A. & Shumack, S. (2007) Prospective study to assess general practitioners' dermatological diagnostic skills in a referral setting. *Australasian Journal of Dermatology*, 48: 77-82.
Not in PICO
- Morrison, A., O'Loughlin, S. & Powell, F. C. (2001) Suspected skin malignancy: a comparison of diagnoses of family practitioners and dermatologists in 493 patients. *International Journal of Dermatology*, 40: 104-107.
Not in PICO

- Morton, C. A., Downie, F., Auld, S., Smith, B., van der Pol, M., Baughan, P., Wells, J. & Wootton, R. (2011) Community photo-triage for skin cancer referrals: an aid to service delivery. *Clinical & Experimental Dermatology*, 36: 248-254.
Not in PICO
- Morton, D. L., Cochran, A. J., Thompson, J. F., Elashoff, R., Essner, R., Glass, E. C., Mozzillo, N., Nieweg, O. E., Roses, D. F., Hoekstra, H. J., Karakousis, C. P., Reintgen, D. S., Coventry, B. J. & Wang, H. J. (2005) Sentinel node biopsy for early-stage melanoma - Accuracy and morbidity in MSLT-I, an international multicenter trial. *Annals of Surgery*, 242: 302-313.
Not in PICO
- Moulin, C., Poulalhon, N., Duru, G., Debarbieux, S., Dalle, S. & Thomas, L. (2013) Dermoscopy use by French private practice dermatologists: a nationwide survey. *British Journal of Dermatology*, 168: 74-79.
Not in PICO
- Mowbray, M. & Yoo, J. (2014) - Diagnostic biopsy of melanoma: primary or secondary care? - *British Journal of General Practice*, 64: 14.
Letter
- Mowbray, M. & Yoo, J. (2014) Diagnostic biopsy of melanoma: primary or secondary care? *British Journal of General Practice*, 64: 14.
Duplicate
- Mozzillo, N., Pennacchioli, E., Gandini, S., Caraco, C., Crispo, A., Botti, G., Lastoria, S., Barberis, M., Verrecchia, F. & Testori, A. (2013) Sentinel Node Biopsy in Thin and Thick Melanoma. *Annals of Surgical Oncology*, 20: 2780-2786.
Not in PICO
- Murchie, P., Sinclair, E. & Lee, A. J. (2011) Primary excision of cutaneous melanoma: does the location of excision matter. *British Journal of General Practice*, 61: 131-134.
Not in PICO
- Murchie, P., Raja, E. A., Lee, A. J. & Campbell, N. C. (2013) Mortality and morbidity after initial diagnostic excision biopsy of cutaneous melanoma in primary versus secondary care. *British Journal of General Practice*, 63: e563-e572.
Not in PICO
- Murchie, P., Raja, E. A., Lee, A. J. & Campbell, N. C. (2013) Mortality and morbidity after initial diagnostic excision biopsy of cutaneous melanoma in primary versus secondary care. *British Journal of General Practice*, 63: E563-E572.
Not in PICO
- Murchie, P., Raja, E. A., Lee, A. J. & Campbell, N. C. (2014) Diagnostic biopsy of melanoma: primary or secondary care? Response. *British Journal of General Practice*, 64: 14.
Not in PICO
- Nami, N., Rubegni, P., Massone, C., Fimiani, M. & Hofmann-Wellenhof, R. (2011) New trends in dermoscopy. *Giornale Italiano di Dermatologia e Venereologia*, 146: 333-339.
Narrative review
- Nathansohn, N., Orenstein, A., Trau, H., Liran, A. & Schachter, J. (2007) Pigmented lesions clinic for early detection of melanoma: preliminary results. *Israel Medical Association Journal: Imaj*, 9: 708-712.
Not in PICO
- Negrier, S., Fervers, B., Bailly, C., Beckendorf, V., Cupissolv, D., Dore, J. F., Dorval, T., Garbay, J. R. & Vilmer, C. (2000) Standards, Options and Recommendations (SOR): clinical practice guidelines for diagnosis, treatment and follow-up of cutaneous melanoma. *Bulletin du Cancer*, 87: 173-182.
Guideline
- Newell, E. L., Shaw, L. & Bragonier, R. (2014) Rising referrals for suspected paediatric melanoma via the 2-week rule referral system. *British Journal of Dermatology*, 170: e15.
Not in PICO

- Newell, E. L., Shaw, L. & Bragonier, R. (2014) Rising referrals for suspected paediatric melanoma via the 2-week rule referral system. *British Journal of Dermatology*, 170: e15.
Not in PICO
- Ng, J. C., Swain, S., Dowling, J. P., Wolfe, R., Simpson, P. & Kelly, J. W. (2010) The impact of partial biopsy on histopathologic diagnosis of cutaneous melanoma: experience of an Australian tertiary referral service. *Archives of Dermatology*, 146: 234-239.
Not in PICO
- Ng, P. C., Barzilai, D. A., Ismail, S. A., Averitte, R. L., Jr. & Gilliam, A. C. (2003) Evaluating invasive cutaneous melanoma: is the initial biopsy representative of the final depth? *Journal of the American Academy of Dermatology*, 48: 420-424.
Not in PICO
- Niebling, M. G., Haydu, L. E., Karim, R. Z., Thompson, J. F. & Scolyer, R. A. (2014) - Pathology review significantly affects diagnosis and treatment of melanoma patients: an analysis of 5011 patients treated at a melanoma treatment center. - *Annals of Surgical Oncology*, 21: 2245-2251.
Not in PICO
- Nielsen, P. S., Lindebjerg, J., Rasmussen, J., Starklint, H., Waldstrom, M. & Nielsen, B. (2010) Virtual microscopy: an evaluation of its validity and diagnostic performance in routine histologic diagnosis of skin tumors. *Human Pathology*, 41: 1770-1776.
Not in PICO
- Nurnberg, D. (2005) [Ultrasound of adrenal gland tumours and indications for fine needle biopsy (uFNB)]. [Review] [116 refs] [German]. *Ultraschall in der Medizin*, 26: 458-469.
Narrative review
- Osborne, J. E. & Hutchinson, P. E. (2001) Clinical correlates of Breslow thickness of malignant melanoma. *British Journal of Dermatology*, 144: 476-483.
Not in PICO
- Osborne, J. E., Chave, T. A. & Hutchinson, P. E. (2003) Comparison of diagnostic accuracy for cutaneous malignant melanoma between general dermatology, plastic surgery and pigmented lesion clinics. *British Journal of Dermatology*, 148: 252-258.
Not in PICO
- Parkinson, R. W. (11111) Shave biopsies--simple and useful. *Postgraduate Medicine*, 84: 161-163.
Narrative review
- Penel, N., Valentin, F., Giscard, S., Vanseymortier, L. & Beuscart, R. (2007) General practitioners assessment of a structured report on medical decision making by a regional multidisciplinary cancer committee. *Bulletin du Cancer*, 94: E23-E26.
Not in PICO
- Pereda, C., Traves, V., Requena, C., Serra-Guillen, C., Llombart, B., Sanmartin, O., Guillen, C. & Nagore, E. (2013) Clinical presentation of acral lentiginous melanoma: a descriptive study. *Actas Dermo-Sifiliograficas*, 104: 220-226.
Not in PICO
- Pereda, C., Traves, V., Requena, C., Serra-Guillen, C., Llombart, B., Sanmartin, O., Guillen, C. & Nagore, E. (2013) Clinical presentation of acral lentiginous melanoma: a descriptive study. *Actas Dermo-Sifiliograficas*, 104: 220-226.
Not in PICO
- Pereira, R. D., Martin, A. A., Tierra-Criollo, C. J. & Santos, I. D. A. O. (2004) Diagnosis of squamous cell carcinoma of human skin by Raman spectroscopy. *Optical Biopsy V*, 5326: 106-112.
Not in PICO
- Perkins, P. J. (1992) Malignant melanoma: mole watching and the adolescent. *Professional Nurse*, 7: 678-680.
Narrative review

- Perniciaro, C. (1997) Dermatopathologic variants of malignant melanoma. [Review] [38 refs]. *Mayo Clinic Proceedings*, 72: 273-279.
Narrative review
- Perrinaud, A., Gaide, O., French, L. E., Saurat, J. H., Marghoob, A. A. & Braun, R. P. (2007) Can automated dermoscopy image analysis instruments provide added benefit for the dermatologist? A study comparing the results of three systems. *British Journal of Dermatology*, 157: 926-933.
Not in PICO (secondary care)
- Petousis, V., Finger, P. T. & Milman, T. (2011) Anterior segment tumor biopsy using an aspiration cutter technique: clinical experience. *American Journal of Ophthalmology*, 152: 771-775.
Not in PICO
- Pflugfelder, A., Weide, B., Eigentler, T. K., Forschner, A., Leiter, U., Held, L., Meier, F. & Garbe, C. (2010) Incisional biopsy and melanoma prognosis: Facts and controversies. *Clinics in Dermatology*, 28: 316-318.
Narrative review
- Pflugfelder, A., Kochs, C., Blum, A., Capellaro, M., Czeschik, C., Dettenborn, T., Dill, D., Dippel, E., Eigentler, T., Feyer, P., Follmann, M., Frerich, B., Ganten, M.-K., Gartner, J., Gutzmer, R., Hassel, J., Hauschild, A., Hohenberger, P., Hubner, J., Kaatz, M., Kleeberg, U. R., Kolbl, O., Kortmann, R.-D., Krause-Bergmann, A., Kurschat, P., Leiter, U., Link, H., Loquai, C., Loser, C., MacKensen, A., Meier, F., Mohr, P., Mohrle, M., Nashan, D., Reske, S., Rose, C., Sander, C., Satzger, I., Schiller, M., Schlemmer, H.-P., Strittmatter, G., Sunderkotter, C., Swoboda, L., Trefzer, U., Voltz, R., Vordermark, D., Weichenthal, M., Werner, A., Wesselmann, S., Weyergraf, A. J., Wick, W., Garbe, C. & Schadendorf, D. (2013) S3-Guideline "diagnosis, therapy and follow-up of melanoma" - Short version. [German, English]. *JDDG - Journal of the German Society of Dermatology*, 11: 593-602.
Guideline
- Phillips, C., Newsome, A., Jennifer, D., Lindsey, F., Green, H. & McLean, T. (2014) Anatomy of a skin biopsy: A retrospective analysis of outpatient biopsy results from 2000 to 2010. *Journal of the American Academy of Dermatology*, 70: AB36.
Not in PICO (setting)
- Pickett, H. (2011) Shave and punch biopsy for skin lesions. *American Family Physician*, 84: 995-1002.
Narrative review
- Pluddemann, A., Heneghan, C., Thompson, M., Wolstenholme, J. & Price, C. P. (2011) Dermoscopy for the diagnosis of melanoma: primary care diagnostic technology update. *British Journal of General Practice*, 61: 416-417.
Narrative review
- Pockney, P., Primrose, J., George, S., Jayatilleke, N., Leppard, B., Smith, H., Little, P., Kneebone, R. & Lowy, A. (2009) Recognition of skin malignancy by general practitioners: observational study using data from a population-based randomised controlled trial. *British Journal of Cancer*, 100: 24-27.
Not in PICO (secondary care, clinical diagnosis v histology)
- Poelmann, T. A., van der Heide, W. K. & Berendsen, A. J. (2012) [Skin tumours underexposed in general practice]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 156: A5279.
Narrative review
- Poulsen, A. G., Larsen, F. G., Weismann, K., Petersen, C. S., Ravnborg, L. R., Heidenheim, M., Lauritzen, T. E., Held, E. & Osterlind, A. L. (1999) [Investigation of malignant melanoma in an "open house" setting]. [Danish]. *Ugeskrift for Laeger*, 161: 1758-1761.
Not in PICO
- Raasch, B. A. (1999) Suspicious skin lesions and their management. *Australian Family Physician*, 28: 466-471.
Not in PICO (no verification of cancer/non-cancer diagnosis)

- Rademaker, M. & Thorburn, M. (2010) Pathology referrals for skin lesions--are we giving the pathologist sufficient clinical information? *New Zealand Medical Journal*, 123: 53-58.
Not in PICO
- Rajpara, S. M., Botello, A. P., Townend, J. & Ormerod, A. D. (2009) Systematic review of dermoscopy and digital dermoscopy/artificial intelligence for the diagnosis of melanoma (DARE structured abstract). *British Journal of Dermatology*, 161: 591-604.
Not in PICO (secondary care)
- Ramcharan, M., Evans, M. W., Jr., Ndetan, H. & Beddard, J. (2011) Knowledge, perceptions, and practices of chiropractic interns in the early detection of atypical moles. *Journal of Chiropractic Medicine*, 10: 77-85.
Not in PICO
- Rampen, F. H. & Rumke, P. (1987) [The changing pattern of referrals in relation to melanoma of the skin?]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 131: 997-999.
Not in PICO
- Reusch, M., Schaefer, I., Siebert, J., Kornek, T. & Augustin, M. (2013) Histological and epidemiological characteristics of cutaneous malignant melanoma in routine ambulatory care in germany. *JDDG - Journal of the German Society of Dermatology*, 11: 38-39.
Not in PICO
- Riker, A. I. (2001) Utility of fine-needle aspiration biopsy for prospective analysis of patients undergoing therapy for metastatic melanoma. *Methods in Molecular Medicine*, 61: 287-299.
Not in PICO
- Rivers, J. K. & Wulkan, S. (2010) The case for early detection of melanoma. [Review] [53 refs]. *Journal of Cutaneous Medicine & Surgery*, 14: 24-29.
Narrative review
- Roaten, J. B., Partrick, D. A., Pearlman, N., Gonzalez, R. J., Gonzalez, R. & McCarter, M. D. (2005) Sentinel lymph node biopsy for melanoma and other melanocytic tumors in adolescents. *Journal of Pediatric Surgery*, 40: 232-235.
Not in PICO
- Roberts, A. A. & Cochran, A. J. (2004) Pathologic analysis of sentinel lymph nodes in melanoma patients: Current and future trends. *Journal of Surgical Oncology*, 85: 152-161.
Narrative review
- Roberts, D. L., Anstey, A. V., Barlow, R. J., Cox, N. H., Newton Bishop, J. A., Corrie, P. G., Evans, J., Gore, M. E., Hall, P. N., Kirkham, N., British Association of Dermatologists & Melanoma Study Group (2002) U.K. guidelines for the management of cutaneous melanoma. *British Journal of Dermatology*, 146: 7-17.
Guideline
- Robison, S., Kljakovic, M. & Barry, P. (2012) Choosing to biopsy or refer suspicious melanocytic lesions in general practice. *BMC Family Practice*, 13: 78.
Not in PICO
- Roldan-Marin, R., Puig, S. & Malvehy, J. (2012) Dermoscopic criteria and melanocytic lesions. [Review]. *Giornale Italiano di Dermatologia e Venereologia*, 147: 149-159.
Narrative review
- Rolfe, H. M. (2012) Accuracy in skin cancer diagnosis: A retrospective study of an Australian public hospital dermatology department. *Australasian Journal of Dermatology*, 53: 112-117.
Not in PICO
- Romani, A., Baldeschi, L., Genovesi-Ebert, F., Gremigni, E., Ragone, M. C., Rizzo, S. & Nardi, M. (1998) Sensitivity and specificity of ultrasonography, fluorescein videoangiography, indocyanine green videoangiography, magnetic resonance and radioimmunosintigraphy in the diagnosis of primary choroidal malignant melanoma. *Ophthalmologica*, 212: Suppl-6.
Not in PICO

- Ropcke, D. M., Lorenzen, J. A. & Jorgensen, P. H. (2012) [Leiomyosarcoma of the great saphenous vein]. [Danish]. *Ugeskrift for Laeger*, 174: 1384-1385.
Not in PICO
- Rosendahl, C., Hansen, C., Cameron, A., Bourne, P., Wilson, T., Cook, B., Baker, M., Keir, J., Dicker, T., Reid, M., Williamson, R., Weedon, D., Soyer, H. P., Youl, P. H. & Wilkinson, D. (2011) Measuring performance in skin cancer practice: the SCARD initiative. *International Journal of Dermatology*, 50: 44-51.
Not in PICO
- Rosendahl, C., Williams, G., Eley, D., Wilson, T., Canning, G., Keir, J., McColl, I. & Wilkinson, D. (2012) The impact of subspecialization and dermatoscopy use on accuracy of melanoma diagnosis among primary care doctors in Australia. *Journal of the American Academy of Dermatology*, 67: 846-852.
Not in PICO
- Rosendahl, C., Cameron, A., McColl, I. & Wilkinson, D. (2012) Dermatoscopy in routine practice - 'chaos and clues'. *Australian Family Physician*, 41: 482-487.
Narrative review
- Rosendahl, C., Hishon, M., Cameron, A., Barksdale, S., Weedon, D. & Kittler, H. (2014) - Nodular melanoma: five consecutive cases in a general practice with polarized and non-polarized dermatoscopy and dermatopathology. - *Dermatology Practical & Conceptual*, 4: 69-75.
Not in PICO
- Roses, D. F. (1982) Proper biopsy of a lesion suspect of being a malignant melanoma. *American Journal of Dermatopathology*, 4: 475-476.
Narrative review
- Ross, M. I. & Gershenwald, J. E. (2013) Sentinel lymph node biopsy for melanoma: A critical update for dermatologists after two decades of experience. *Clinics in Dermatology*, 31: 298-310.
Narrative review
- Ruggieri, M., Iannetti, P., Polizzi, A., La, M., I, Spalice, A., Giliberto, O., Platania, N., Gabriele, A. L., Albanese, V. & Pavone, L. (2005) Earliest clinical manifestations and natural history of neurofibromatosis type 2 (NF2) in childhood: a study of 24 patients. *Neuropediatrics*, 36: 21-34.
Not in PICO
- Sahin, M. T., Ozturkcan, S., Ermertcan, A. T. & Gunes, A. T. (2004) A comparison of dermoscopic features among lentigo senilis/initial seborrheic keratosis, seborrheic keratosis, lentigo maligna and lentigo maligna melanoma on the face. *Journal of Dermatology*, 31: 884-889.
Not in PICO
- Salerni, G., Lovatto, L., Carrera, C., Puig, S. & Malvehy, J. (2011) Melanomas detected in a follow-up program compared with melanomas referred to a melanoma unit. *Archives of Dermatology*, 147: 549-555.
Not in PICO
- Salopek, T. G., Slade, J., Marghoob, A. A., Rigel, D. S., Kopf, A. W., Bart, R. S. & Friedman, R. J. (1995) Management of cutaneous malignant melanoma by dermatologists of the American Academy of Dermatology. I. Survey of biopsy practices of pigmented lesions suspected as melanoma. *Journal of the American Academy of Dermatology*, 33: 441-450.
Not in PICO
- Satzger, I., Klein, M., Loser, C., Reske, S., Kapp, A. & Gutzmer, R. (2010) Sentinel node biopsy in malignant melanoma. *Onkologe*, 16: 1140-+.
Narrative review
- Schade, A. T., Raymond, A. C. & Amirfeyz, R. (2013) If it is not healing, do worry about it! *BMJ Case Reports*, 2013, 2013.
Not in PICO

- Schmid-Wendtner, M. H., Baumert, J., Stange, J. & Volkenandt, M. (2002) Delay in the diagnosis of cutaneous melanoma: an analysis of 233 patients. *Melanoma Research*, 12: 389-394.
Not in PICO
- Schmoeckel, C., Wagner-Grosser, G. & Braun-Falco, O. (1985) [Clinical diagnosis of early malignant melanomas]. [German]. *Hautarzt*, 36: 558-562.
Not in PICO
- Schopf, T. & Funk, J. (2012) [Nevus or malignant melanoma?]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 132: 511.
Narrative review
- Sellheyer, K. & Bergfeld, W. F. (2005) A retrospective biopsy study of the clinical diagnostic accuracy of common skin diseases by different specialties compared with dermatology. *Journal of the American Academy of Dermatology*, 52: 823-830.
Not in PICO
- Sergieva, S. B. & Virtcheva-Genkova, A. (1997) Radioimmunosciintigraphy in patients with ocular melanoma. *Clinical Nuclear Medicine*, 22: 25-29.
Not in PICO
- Setala, L., Kemppainen, T., Virolainen, S. & Narkio, M. (2012) [Punch biopsy in the diagnosis of skin tumors]. [Review] [Finnish]. *Duodecim*, 128: 81-87.
Narrative review
- Shapiro, M., James, W. D., Kessler, R., Lazorik, F. C., Katz, K. A., Tam, J., Nieves, D. S. & Miller, J. J. (2004) Comparison of skin biopsy triage decisions in 49 patients with pigmented lesions and skin neoplasms: store-and-forward teledermatology vs face-to-face dermatology. *Archives of Dermatology*, 140: 525-528.
Not in PICO
- Shariff, Z., Roshan, A., Williams, A. M. & Platt, A. J. (2010) 2-Week wait referrals in suspected skin cancer: does an instructional module for general practitioners improve diagnostic accuracy? *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 8: 247-251.
Not in PICO
- Shenenberger, D. W. (2012) Cutaneous malignant melanoma: a primary care perspective. [Review][Summary for patients in Am Fam Physician. 2012 Jan 15;85(2):169; PMID: 22335217]. *American Family Physician*, 85: 161-168.
Narrative review
- Sheth, N., Sarker, S. J., Harries, M., Healy, C., Russell-Jones, R. & Acland, K. (2010) Predictors of patient satisfaction with initial diagnosis and management of malignant melanoma. *Clinical & Experimental Dermatology*, 35: 599-602.
Not in PICO
- Shields, J. A., Shields, C. L., Ehya, H., Eagle, R. C., Jr. & De, P. P. (1993) Fine-needle aspiration biopsy of suspected intraocular tumors. The 1992 Urwick Lecture. *Ophthalmology*, 100: 1677-1684.
Not in PICO
- Shoo, B. A., Sagebiel, R. W. & Kashani-Sabet, M. (2010) Discordance in the histopathologic diagnosis of melanoma at a melanoma referral center. *Journal of the American Academy of Dermatology*, 62: 751-756.
Not in PICO
- Shorrock, K. (1993) Use of histopathology services by general practitioners: recent changes in referral practice. *Journal of Clinical Pathology*, 46: 989-992.
Not in PICO
- Shrestha, B., Bishop, J., Kam, K., Chen, X., Moss, R. H., Stoecker, W. V., Umbaugh, S., Stanley, R. J., Celebi, M. E., Marghoob, A. A., Argenziano, G. & Soyer, H. P. (2010) Detection of atypical texture features in early malignant melanoma. *Skin Research & Technology*, 16: 60-65.
Not in PICO

- Simionescu, O., Costache, M. & Testori, A. (2006) Cutaneous melanoma: digital dermoscopy-essential tool for positive diagnosis. *Journal of Cellular & Molecular Medicine*, 10: 991-994.
Narrative review
- Soares, T. F., Laman, S. D., Yiannias, J. A., Connolly, S. M., Lim, K. K., Wu, Q. & Swanson, D. L. (2009) Factors leading to the biopsy of 1547 pigmented lesions at Mayo Clinic, Scottsdale, Arizona, in 2005. *International Journal of Dermatology*, 48: 1053-1056.
Not in PICO
- Sober, A. J., Chuang, T. Y., Duvic, M., Farmer, E. R., Grichnik, J. M., Halpern, A. C., Ho, V., Holloway, V., Hood, A. F., Johnson, T. M., Lowery, B. J. & Guidelines/Outcomes Committee (2001) Guidelines of care for primary cutaneous melanoma. *Journal of the American Academy of Dermatology*, 45: 579-586.
Guideline
- Stanganelli, I., Seidenari, S., Serafini, M., Pellacani, G. & Bucchi, L. (1999) Diagnosis of pigmented skin lesions by epiluminescence microscopy: determinants of accuracy improvement in a nationwide training programme for practical dermatologists. *Public Health*, 113: 237-242.
Not in PICO
- Stefano, Z., Cesare, B., Claudio, C., Fausto, C., Aldo, B. & Natale, C. (1992) Melanocytic neoplasia of the sole: diagnosis and therapeutic approach. *Journal of Dermatology*, 19: 280-284.
Not in PICO
- Stolz, W., Semmelmayr, U., Johow, K. & Burgdorf, W. H. (2003) Principles of dermatoscopy of pigmented skin lesions. [Review] [32 refs]. *Seminars in Cutaneous Medicine & Surgery*, 22: 9-20.
Narrative review
- Takata, M. & Saida, T. (2005) Early cancers of the skin: clinical, histopathological, and molecular characteristics. [Review] [44 refs]. *International Journal of Clinical Oncology*, 10: 391-397.
Narrative review
- Tan, E., Oakley, A., Soyer, H. P., Haskett, M., Marghoob, A., Jameson, M. & Rademaker, M. (2010) Interobserver variability of teledermoscopy: an international study. *British Journal of Dermatology*, 163: 1276-1281.
Not in PICO
- ten Koppel, P. G., Vuyk, H. D. & Neumann, H. A. (2005) [The feasibility of the razor-blade shave technique in the diagnosis and treatment of benign and malignant skin lesions on the face]. [Review] [26 refs] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 149: 1561-1567.
Narrative review
- Terushkin, V. & Halpern, A. C. (2009) Melanoma Early Detection. *Hematology-Oncology Clinics of North America*, 23: 481-+.
Narrative review
- Terushkin, V., Braga, J. C., Dusza, S. W., Scope, A., Busam, K., Marghoob, A. A., Gill, M. & Halpern, A. C. (2010) Agreement on the clinical diagnosis and management of cutaneous squamous neoplasms. *Dermatologic Surgery*, 36: 1514-1520.
Not in PICO
- Thomas, J. M. (2006) Research supports the view that sentinel node biopsy is the standard of care in high-risk primary melanoma - Reply. *Journal of Clinical Oncology*, 24: 2966-2967.
Not in PICO
- Thomas, S., Meng, Y. X., Patel, V. G. & Strayhorn, G. (2012) A rare form of melanoma masquerading as a diabetic foot ulcer: a case report. *Case Reports in Endocrinology Print*, 2012: 502806.
Not in PICO
- Thrasivoulou, C., Virich, G., Krenacs, T., Korom, I. & Becker, D. L. (2011) Optical delineation of human malignant melanoma using second harmonic imaging of collagen. *Biomedical Optics Express*, 2: 1282-1295.
Not in PICO

- Tlougan, B. E., Orlow, S. J. & Schaffer, J. V. (2013) Spitz nevi: beliefs, behaviors, and experiences of pediatric dermatologists. *JAMA Dermatology*, 149: 283-291.
 Not in PICO
- Topar, G. & Zelger, B. (2007) Assessment of value of the sentinel lymph node biopsy in melanoma in children and adolescents and applicability of subcutaneous infusion anesthesia. *Journal of Pediatric Surgery*, 42: 1716-1720.
 Not in PICO
- Tran, K. T., Wright, N. A. & Cockerell, C. J. (2008) Biopsy of the pigmented lesion--when and how. [Review] [174 refs]. *Journal of the American Academy of Dermatology*, 59: 852-871.
 Narrative review
- Tyler, I., Rivers, J. K., Shoveller, J. A. & Blum, A. (2005) Melanoma detection in British Columbia, Canada. *Journal of the American Academy of Dermatology*, 52: 48-54.
 Not in PICO
- Ulrich, M., Lange-Asschenfeldt, S. & Gonzalez, S. (2012) In vivo reflectance confocal microscopy for early diagnosis of nonmelanoma skin cancer. *Actas Dermo-Sifiliograficas*, 103: 784-789.
 Narrative review
- Urbancek, S., Simekova, P. & Tomkova, J. (2013) Misdiagnosis of melanoma: A 5 years analysis. *JDDG - Journal of the German Society of Dermatology*, 11: 31.
 Not in PICO
- Uren, R. F. (2006) Sentinel lymph node biopsy in melanoma. [Review] [44 refs]. *Journal of Nuclear Medicine*, 47: 191-195.
 Not in PICO
- van der Heijden, J. P., Thijssing, L., Witkamp, L., Spuls, P. I. & de Keizer, N. F. (2013) Accuracy and reliability of teledermatology with images taken by general practitioners during everyday practice. *Journal of Telemedicine and Telecare*, 19: 320-325.
 Not in PICO
- van der Rhee, J. I., Bergman, W. & Kukutsch, N. A. (2010) The impact of dermoscopy on the management of pigmented lesions in everyday clinical practice of general dermatologists: a prospective study. *British Journal of Dermatology*, 162: 563-567.
 Not in PICO
- van der Rhee, J. I., Bergman, W. & Kukutsch, N. A. (2011) Impact of Dermoscopy on the Management of High-risk Patients From Melanoma Families: A Prospective Study. *Acta Dermato-Venereologica*, 91: 428-431.
 Not in PICO
- Venkata, R. B. (2010) Desmoplastic melanoma presenting as pyogenic granuloma: report of a case with review of literature. *Indian Journal of Dermatology*, 55: 284-289.
 Not in PICO
- Vestergaard, M. E., Macaskill, P., Holt, P. E. & Menzies, S. W. (2008) Dermoscopy compared with naked eye examination for the diagnosis of primary melanoma: a meta-analysis of studies performed in a clinical setting. *British Journal of Dermatology*, 159: 669-676.
 Systematic review, no new studies identified. Relevant studies will be include separately.
- Vikey, A. K. & Vikey, D. (2012) Primary malignant melanoma, of head and neck: a comprehensive review of literature. [Review]. *Oral Oncology*, 48: 399-403.
 Narrative review
- Viola, K. V., Tolpinrud, W. L., Gross, C. P., Kirsner, R. S., Imaeda, S. & Federman, D. G. (2011) Outcomes of referral to dermatology for suspicious lesions: implications for teledermatology. *Archives of Dermatology*, 147: 556-560.
 Not in PICO
- Vogt, H., Schmidt, M., Bares, R., Brenner, W., Grunwald, F., Kopp, J., Reiners, C., Schober, O., Schumichen, C., Schicha, H., Sciuk, J., Sudbrock, F. & Wengenmair, H. (2010) [Procedure guideline

- for sentinel lymph node diagnosis]. [German]. *Nuclear-Medizin*, 49: 167-172.
Not in PICO
- Voigt, H. & Classen, R. (2002) Computer vision and digital imaging technology in melanoma detection. [Review] [234 refs]. *Seminars in Oncology*, 29: 308-327.
Narrative review
- Voit, C., Mayer, T., Proebstle, T. M., Weber, L., Kron, M., Krupienski, M., Zeelen, U., Sterry, W. & Schoengen, A. (2000) Ultrasound-guided fine-needle aspiration cytology in the early detection of melanoma metastases. *Cancer*, 90: 186-193.
Not in PICO
- Voit, C., Schoengen, A., Schwurzer-Voit, M., Weber, L., Ulrich, J., Sterry, W. & Proebstle, T. M. (2002) The role of ultrasound in detection and management of regional disease in melanoma patients. [Review] [58 refs]. *Seminars in Oncology*, 29: 353-360.
Not in PICO
- Voit, C. A., Gooskens, S. L., Siegel, P., Schaefer, G., Schoengen, A., Rowert, J., van Akkooi, A. C. & Eggermont, A. M. (2014) - Ultrasound-guided fine needle aspiration cytology as an addendum to sentinel lymph node biopsy can perfect the staging strategy in melanoma patients. - *European Journal of Cancer*, 50: 2280-2288.
Not in PICO
- Waller, J. M. & Zedek, D. C. (2010) How informative are dermatopathology requisition forms completed by dermatologists? A review of the clinical information provided for 100 consecutive melanocytic lesions. *Journal of the American Academy of Dermatology*, 62: 257-261.
Not in PICO
- Walter, F. M., Humphrys, E., Tso, S., Johnson, M. & Cohn, S. (2010) Patient understanding of moles and skin cancer, and factors influencing presentation in primary care: a qualitative study. *BMC Family Practice*, 11: 62.
Not in PICO
- Walter, F. M., Morris, H. C., Humphrys, E., Hall, P. N., Kinmonth, A. L., Prevost, A. T., Wilson, E. C., Burrows, N., Norris, P., Johnson, M. & Emery, J. (2010) Protocol for the MoleMate UK Trial: a randomised controlled trial of the MoleMate system in the management of pigmented skin lesions in primary care [ISRCTN 79932379]. *BMC Family Practice*, 11: 36.
Protocol
- Walter, F. M., Prevost, A. T., Vasconcelos, J., Hall, P. N., Burrows, N. P., Morris, H. C., Kinmonth, A. L. & Emery, J. D. (2013) Using the 7-point checklist as a diagnostic aid for pigmented skin lesions in general practice: A diagnostic validation study. *British Journal of General Practice*, 63: e345-e353.
Not in PICO
- Wang, S. Q., Kopf, A. W., Koenig, K., Polsky, D., Nudel, K. & Bart, R. S. (2004) Detection of melanomas in patients followed up with total cutaneous examinations, total cutaneous photography, and dermoscopy. *Journal of the American Academy of Dermatology*, 50: 15-20.
Not in PICO
- Warsaw, E. M., Lederle, F. A., Grill, J. P., Gravely, A. A., Bangerter, A. K., Fortier, L. A., Bohjanen, K. A., Chen, K., Lee, P. K., Rabinovitz, H. S., Johr, R. H., Kaye, V. N., Bowers, S., Wenner, R., Askari, S. K., Kedrowski, D. A. & Nelson, D. B. (2009) Accuracy of teledermatology for pigmented neoplasms.[Erratum appears in J Am Acad Dermatol. 2010 Feb;62(2):319]. *Journal of the American Academy of Dermatology*, 61: 753-765.
Not in PICO
- Watson, T., Walter, F. M., Wood, A., Morris, H., Hall, P., Karner, S. & Emery, J. (2009) Learning a novel technique to identify possible melanomas: are Australian general practitioners better than their U.K. colleagues? *Asia Pacific Family Medicine*, 8: 3.
Not in PICO
- Webb, J. B. & Khanna, A. (2006) Can we rely on a general practitioner's referral letter to a skin lesion clinic to prioritize appointments and does it make a difference to the patient's prognosis? *Annals*

- of the Royal College of Surgeons of England, 88: 40-45.
Not in PICO
- Weidner, F. (1980) [Malignant melanomas of the skin. Early diagnosis and differential diagnosis.-- conclusion]. [German]. *Fortschritte der Medizin*, 98: 1449-1452.
Narrative review
- Welch, H. G., Woloshin, S. & Schwartz, L. M. (2005) Skin biopsy rates and incidence of melanoma: population based ecological study. *BMJ*, 331: 481.
Not in PICO
- Wells, K. E., Rapaport, D. P., Cruse, C. W., Payne, W., Albertini, J., Berman, C., Lyman, G. H. & Reintgen, D. S. (1997) Sentinel lymph node biopsy in melanoma of the head and neck. *Plastic and Reconstructive Surgery*, 100: 591-594.
Not in PICO
- Westerhoff, K., McCarthy, W. H. & Menzies, S. W. (2000) Increase in the sensitivity for melanoma diagnosis by primary care physicians using skin surface microscopy. *British Journal of Dermatology*, 143: 1016-1020.
Not in PICO
- Wharton, J. M., Carlson, J. A. & Mihm, M. C., Jr. (1999) Desmoplastic malignant melanoma: diagnosis of early clinical lesions. *Human Pathology*, 30: 537-542.
Not in PICO
- Whitaker, D. (1991) Skin cancer: diagnosis and management. *Iowa Medicine*, 81: 211-214.
Narrative review
- Whitaker, D. K. (2004) Guideline on the management of melanoma. *Samj South African Medical Journal*, 94: 699-708.
Guideline
- White, J. W., Jr. (1985) Evaluating cancer metastatic to the skin. *Geriatrics*, 40: 67-73.
Narrative review
- Whited, J. D. & Grichnik, J. M. (1998) Does this patient have a mole or a melanoma? *Jama-Journal of the American Medical Association*, 279: 696-701.
Not in PICO
- Wilkes, D. (2010) The use of dermoscopy in medical photography for the early detection of skin cancer. *Journal of Visual Communication in Medicine*, 33: 169-173.
Narrative review
- Wilkinson, D., Askew, D. A. & Dixon, A. (2006) Skin cancer clinics in Australia: workload profile and performance indicators from an analysis of billing data. *Medical Journal of Australia*, 184: 162-164.
Not in PICO
- Wilson, E. C., Emery, J. D., Kinmonth, A. L., Prevost, A. T., Morris, H. C., Humphrys, E., Hall, P. N., Burrows, N., Bradshaw, L., Walls, J., Norris, P., Johnson, M. & Walter, F. M. (2013) The cost-effectiveness of a novel SIAscopic diagnostic aid for the management of pigmented skin lesions in primary care: a decision-analytic model. *Value in Health*, 16: 356-366.
Same data as Walter (2012) already included.
- Wilson, E. C., Emery, J. D., Louise, K. A., Toby, P. A., Morris, H. C., Humphrys, E., Hall, P. N., Burrows, N., Bradshaw, L., Walls, J., Norris, P., Johnson, M. & Walter, F. M. (2013) The Cost-Effectiveness of a Novel SIAscopic Diagnostic Aid for the Management of Pigmented Skin Lesions in Primary Care: A Decision-Analytic Model. *Value in Health*, 16: 356-366.
Not in PICO
- Wilson, E. C. F., Emery, J. D., Kinmonth, A. L., Prevost, A. T., Morris, H. C., Humphrys, E., Hall, P. N., Burrows, N., Bradshaw, L., Walls, J., Norris, P., Johnson, M. & Walter, F. M. (2013) The Cost-Effectiveness of a Novel SIAscopic Diagnostic Aid for the Management of Pigmented Skin Lesions in Primary Care: A Decision-Analytic Model. *Value in Health*, 16: 356-366.
Not in PICO

- Wilson, M. A. & Nathanson, K. L. (2012) Molecular testing in melanoma. [Review]. *Cancer Journal*, 18: 117-123.
Not in PICO
- Wilson, R. L., Yentzer, B. A., Isom, S. P., Feldman, S. R. & Fleischer, A. B. (2012) How good are US dermatologists at discriminating skin cancers? A number-needed-to-treat analysis. *Journal of Dermatological Treatment*, 23: 65-69.
Not in PICO
- Wolchok, J. D. & Saenger, Y. M. (2007) Current topics in melanoma. *Current Opinion in Oncology*, 19: 116-120.
Not in PICO
- Wolf, O. & Shalom, A. (1111) [Dermoscopy--a glimpse into the skin]. [Review] [Hebrew]. *Harefuah*, 149: 519-523.
Narrative review
- Wood, A., Morris, H., Emery, J., Hall, P. N., Cotton, S., Prevost, A. T. & Walter, F. M. (2008) Evaluation of the MoleMate training program for assessment of suspicious pigmented lesions in primary care. *Informatics in Primary Care*, 16: 41-50.
Not in PICO
- Woodman, S. E., Lazar, A. J., Aldape, K. D. & Davies, M. A. (2012) New strategies in melanoma: molecular testing in advanced disease. [Review]. *Clinical Cancer Research*, 18: 1195-1200.
Narrative review
- Wray, E. V., Brant, B., Hussain, F. & Muller, F. M. (2013) A new model of teledermoscopy combining service and education. *British Journal of Dermatology*, 169: 139.
Not in PICO
- Wright, B. E., Scheri, R. P., Ye, X., Faries, M. B., Turner, R. R., Essner, R. & Morton, D. L. (2008) Importance of sentinel lymph node biopsy in patients with thin melanoma. *Archives of Surgery*, 143: 892-899.
Not in PICO
- Yang, J. C., Sherry, R. M. & Rosenberg, S. A. (2014) Why is sentinel lymph node biopsy 'standard of care' for melanoma? *Nature Reviews Clinical Oncology*, 11: 245-246.
Not in PICO
- Youl, P. H., Baade, P. D., Janda, M., Del Mar, C. B., Whiteman, D. C. & Aitken, J. F. (2007) Diagnosing skin cancer in primary care: how do mainstream general practitioners compare with primary care skin cancer clinic doctors? *Medical Journal of Australia*, 187: 215-220.
Not in PICO
- Youl, P. H., Janda, M., Aitken, J. F., Del Mar, C. B., Whiteman, D. C. & Baade, P. D. (2011) Body-site distribution of skin cancer, pre-malignant and common benign pigmented lesions excised in general practice. *British Journal of Dermatology*, 165: 35-43.
Not in PICO
- Zager, J. S., Hochwald, S. N., Marzban, S. S., Francois, R., Law, K. M., Davis, A. H., Messina, J. L., Vincek, V., Mitchell, C., Church, A., Copeland, E. M., Sondak, V. K. & Grobmyer, S. R. (2011) Shave Biopsy Is a Safe and Accurate Method for the Initial Evaluation of Melanoma. *Journal of the American College of Surgeons*, 212: 454-460.
Not in PICO
- Zhang, J., Chang, C. I., Miller, S. J. & Kang, K. A. (2000) A feasibility study of multispectral image analysis of skin tumors. *Biomedical Instrumentation & Technology*, 34: 275-282.
Not in PICO
- Zortea, M., Schopf, T. R., Thon, K., Geilhufe, M., Hindberg, K., Kirchesch, H., Mollersen, K., Schulz, J., Skrovseth, S. O. & Godtlielsen, F. (2014) Performance of a dermoscopy-based computer vision system for the diagnosis of pigmented skin lesions compared with visual evaluation by experienced dermatologists. *Artificial Intelligence in Medicine*, 60: 13-26.
Not in PICO

Zortea, M., Schopf, T. R., Thon, K., Geilhufe, M., Hindberg, K., Kirchesch, H., Mollersen, K., Schulz, J., Skrovseth, S. O. & Godtlielsen, F. (2014) Performance of a dermoscopy-based computer vision system for the diagnosis of pigmented skin lesions compared with visual evaluation by experienced dermatologists. *Artificial Intelligence in Medicine*, 60: 13-26.

Not in PICO

Wilson ECF, Emery JD, Kinmonth AL et al 'The Cost-Effectiveness of a Novel SIAscopic Diagnostic Aid for the Management of Pigmented Skin Lesions in Primary Care: A Decision-Analytical Model' *Value in Health* 16.2 (2012): p356-366.

SQUAMOUS CELL CARCINOMA

Review question:

What is the risk of squamous cell carcinoma in patients presenting in primary care with symptom(s)?

Results

Literature search

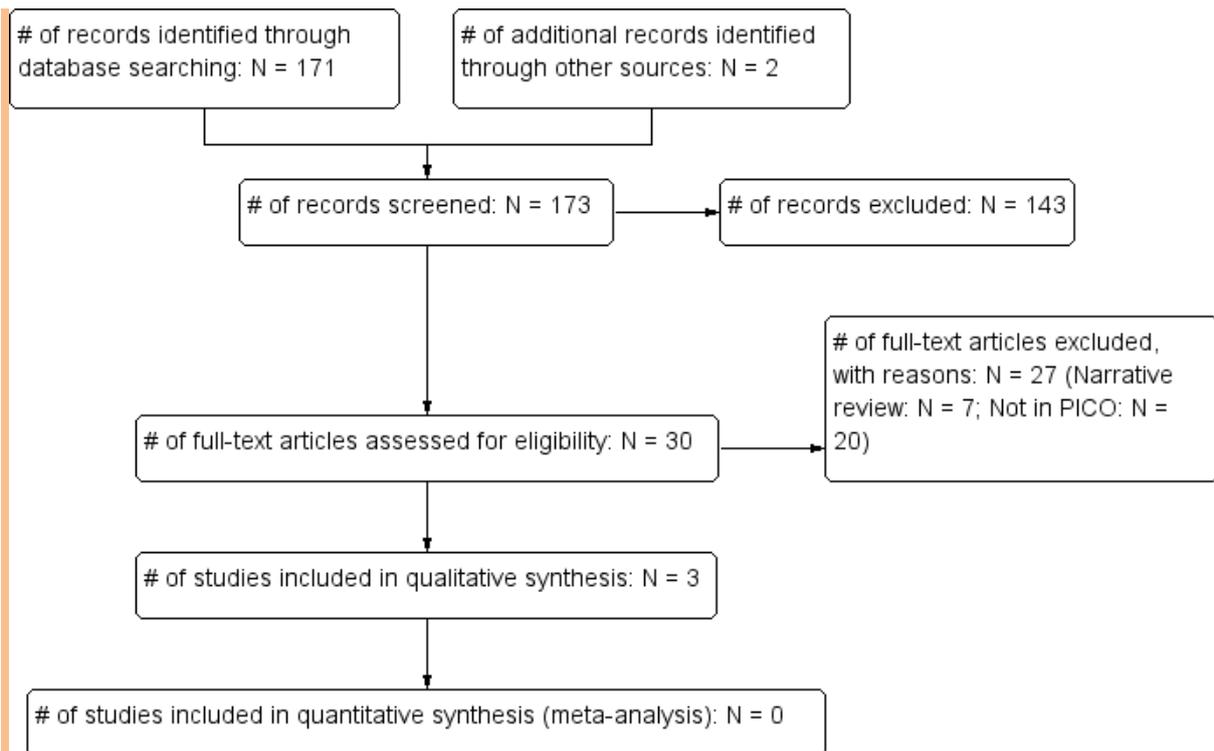
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	501	66	09/01/2013
<i>Premedline</i>	All-2012	66	5	09/01/2013
<i>Embase</i>	All-2012	2129	76	15/01/2013
<i>Cochrane Library</i>	All-2012	201	3	16/01/2013
<i>Psychinfo</i>	All-2012	4	1	09/01/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	569	36	16/01/2013
<i>Biomed Central</i>	All-2012	287	3	21/01/2013

Total References retrieved (after de-duplication): 151

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-11/08/2014	78	4	11/08/2014
<i>Premedline</i>	2013-11/08/2014	13	3	11/08/2014
<i>Embase</i>	2013-11/08/2014	123	6	11/08/2014
<i>Cochrane Library</i>	2013-11/08/2014	48	0	11/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-11/08/2014	89	7	11/08/2014

Total References retrieved (after de-duplication): 20



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main bias risks and applicability concerns that the studies are subject to relate to (1) the patient sampling method not clearly being consecutive or random, (2) the extent to which the study setting matches UK primary care, (3) the quality of the reference standard, which may not always reliably diagnose the symptoms, and (4) the fact that the reference standard did not in all cases match that of the current question, namely histology.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Emery (2010)	?	+	?	+	?	+	?
Rosendahl (2012)	?	+	+	+	?	+	+
Walter (2012)	?	+	?	+	+	+	?

	High		Unclear		Low
--	------	--	---------	--	-----

Study results

Table 1: Squamous cell carcinoma of the skin: Study results.

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI) Prevalence
Emery (2010) Patient-based analysis	Pigmented lesion	All included patients	0 (0-0.6) 0/858
		England sample	0 (0-1.2) 0/389
		Australia sample	0 (0-1) 0/469
Walter (2012) Lesion, not patient,-based analysis	Suspicious pigmented lesions	All included patients	0.06 (0.003-0.4) 1/1573
Rosendahl (2012) Lesion, not patient,-based analysis	Non-pigmented raised skin lesions	All included patients	SCC total: 41.26 (34.5-48.3) 85/206
			SCC: 15.53 (11-21.4) 32/206
			Keratoacanthoma: 14.08 (9.8-19.8) 29/206
			Bowen disease: 11.65 (7.8-17) 24/206
		Females	SCC and KA: 31.81 (21.2-44.6) 21/66
		Males	SCC and KA: 28.57 (21.4-36.9) 40/140
	Non-pigmented raised skin lesions on head and neck	Patients with specific symptom	SCC and KA: 23.33 (15.3-33.7) 21/90
	Non-pigmented raised skin lesions on trunk	Patients with specific symptom	SCC and KA: 14.29 (6.4-27.9) 7/49
	Non-pigmented raised skin lesions on upper extremities	Patients with specific symptom	SCC and KA: 45.16 (27.8-63.7) 14/31
	Non-pigmented raised skin lesions on lower extremities	Patients with specific symptom	SCC and KA: 52.78 (35.7-69.2) 19/36
Non-pigmented raised skin lesions with monomorphic vascular pattern	Patients with specific symptom	SCC and KA: 26.47 (19.5-34.8) 36/136	
Non-pigmented raised skin lesions with polymorphic vascular	Patients with specific symptom	SCC and KA: 31.71 (18.6-48.2) 13/41	

pattern		
Non-pigmented raised skin lesions with vessels absent	Patients with specific symptom	SCC and KA: 39.29 (22.1-59.3) 11/28
Non-pigmented raised skin lesions with vessel morphologic findings: Dots	Patients with specific symptom	SCC and KA: 0 (0-95) 0/1
Non-pigmented raised skin lesions with vessel morphologic findings: Coils	Patients with specific symptom	SCC and KA: 40 (30.1-49.8) 44/110
Non-pigmented raised skin lesions with vessel morphologic findings: Serpentine	Patients with specific symptom	SCC and KA: 9.76 (4.6-18.8) 8/82
Non-pigmented raised skin lesions with vessel morphologic findings: Looped	Patients with specific symptom	SCC and KA: 41.67 (22.8-63.1) 10/24
Non-pigmented raised skin lesions with vessel arrangement: No arrangement	Patients with specific symptom	SCC and KA: 36.7 (27.8-46.5) 40/109
Non-pigmented raised skin lesions with vessel arrangement: Radial	Patients with specific symptom	SCC and KA: 41.18 (19.4-66.5) 7/17
Non-pigmented raised skin lesions with vessel arrangement: Centered	Patients with specific symptom	SCC and KA: 0 (0-30.1) 0/12
Non-pigmented raised skin lesions with vessel arrangement: Branched	Patients with specific symptom	SCC and KA: 0 (0-12.3) 0/35
Non-pigmented raised skin lesions with vessel arrangement: Branched and radial	Patients with specific symptom	SCC and KA: 2/2 (TP = 2, FP = 0)
Non-pigmented raised skin lesions with vessel arrangement: Others	Patients with specific symptom	SCC and KA: 100 (19.8-100) 0/2
Non-pigmented raised skin lesions and keratin	Patients with specific symptom	SCC and KA: 52.17 (41.6-62.6) 48/92
Non-pigmented raised skin lesions and ulceration	Patients with specific symptom	SCC and KA: 27.27 (13.9-45.8) 9/33
Non-pigmented raised skin lesions with white structures: White clods	Patients with specific symptom	SCC and KA: 20 (5.3-48.6) 3/15
Non-pigmented raised skin lesions with white	Patients with	SCC and KA: 47.06 (3.2-61.4)

	structures: White structureless zones	specific symptom	24/51
	Non-pigmented raised skin lesions with white structures: White circles	Patients with specific symptom	SCC and KA: 58.7 (43.3-72.7) 27/46
	Non-pigmented raised skin lesions with white structures: White lines	Patients with specific symptom	SCC and KA: 6.67 (0.3-34) 1/15
	Non-pigmented raised skin lesions with white structures: White dots (milia)	Patients with specific symptom	SCC and KA: 16.67 (0.9-63.5) 1/6
	Non-pigmented raised skin lesions with white structures: Blood spots	Patients with specific symptom	SCC and KA: 45.61 (32.6-59.2) 26/57
	Non-pigmented raised skin lesions with white structures: Scale	Patients with specific symptom	SCC and KA: 40 (28.7-52.4) 28/70

KA = keratoacanthoma; TP = true positives; FP = false positives

Evidence statement(s):

Pigmented skin lesions (2 studies, N = 2784 *lesions*) presenting in a primary care setting do not seem to confer a risk of squamous cell carcinoma (1 case observed in total). The studies were associated with 3-4 bias and applicability concerns (See also Table 1).

Non-pigmented raised skin lesions (1 study, N = 206 *lesions*) presenting in a primary care setting are associated with a positive predictive value of 41.26% for squamous cell carcinoma. The study was associated with 2 bias and applicability concerns (See also Table 1).

Evidence tables

Emery (2010)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective series of pigmented lesions recruited from England (6 general practices covering urban, suburban and rural areas with a registered population of 52913) and Australia (3 primary care skin cancer clinics operated by GPs from a metropolitan area)
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	England: N = 389 patients, mean age = 44.9 years, 68.6% females with, interpretable images from N = 630 lesions. 0/630 lesions were squamous cell carcinoma, 0/630 lesions were basal cell carcinoma, 5/630 lesions were melanoma, and 0/630 lesions were lentigo maligna (melanoma). Australia: N = 469 patients, mean age = 50 years, 48% females, with

	<p>interpretable images from N = 581 lesions. 0/581 lesions were squamous cell carcinoma, 22/581 lesions were basal cell carcinoma, 7/581 lesions were melanoma, and 4/581 lesions were lentigo maligna (melanoma).</p> <p><u>Inclusion criteria:</u> England: Patients aged > 18 years were recruited into the study by their GP if they presented with concerns about a pigmented skin lesion between January 2005 and January 2006. Australia: Patients aged > 18 years were recruited into the study by their GP if they presented with concerns about a pigmented skin lesion between April 2008 and January 2009. Additional lesions were also included when a pigmented skin lesion was identified as potentially suspicious during their clinical examination</p> <p><u>Exclusion criteria:</u> None reported. <u>Clinical setting:</u> Primary care, UK, and primary care skin cancer practice, Queensland Australia.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Pigmented skin lesions that concerned patients, which were evaluated using macroscopic clinical photographs, dermoscopic images and SIAscan.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histopathology or in-person clinical review of the lesion by one expert, including the 7-point melanoma checklist and digital dermoscopy or clinical diagnosis made on the basis of the 7-point melanoma checklist, photographic and dermoscopy images
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes

Could the patient flow have introduced bias?	Low risk
NOTES	

Rosendahl (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective unselected consecutive series of raised non-pigmented lesions
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 186 patients, mean (SD) age = 65 (13) years, 32.8% females with N = 206 lesions. 32/206 lesions were squamous cell carcinoma (SCC), 29/206 lesions were keratoacanthoma (SCC), 24/206 lesions were Bowen disease (SCC), and 56/ 206 lesions were basal cell carcinoma.</p> <p><u>Inclusion criteria:</u> Patients presenting with non-pigmented raised lesions treated from March 1 through December 31 2011. All the lesions were excised or biopsied. It is unclear if there were any patients presenting with non-pigmented raised lesions not biopsied/excised who were not included.</p> <p><u>Exclusion criteria:</u> None reported.</p> <p><u>Clinical setting:</u> Private primary care skin cancer practice, Queensland Australia.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Non-pigmented raised skin lesions (not further defined, but see subgroup analyses) evaluated using dermoscopic images
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histopathology
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined	Low concern

by the reference standard does not match the question?		
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients are accounted for in the results	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk
NOTES	Analysis was on a per-lesion basis rather than a per-patient basis; some patients may have had more than one lesion diagnosed as skin cancer though it is not possible to ascertain the actual numbers from the data provided.	

Walter (2012)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective series of suspicious pigmented lesions	
Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?		Unclear risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 1293 patients, mean age (SD) = 44.6 (16.8) years; 465 males / 828 females with N = 1573 lesions, of which 1 was squamous cell carcinoma, 10 basal cell carcinomas, and 36 melanomas.</p> <p><u>Inclusion criteria:</u> Patients aged ≥ 18 years presenting to one of the 15 participating general practices with a suspicious (any lesion presented by a patient, or opportunistically seen by a family doctor or practice nurse, that could not immediately be diagnosed as benign and about which the patient could not be reassured) pigmented lesion from March 2008 to May 2010.</p> <p><u>Exclusion criteria:</u> Patients who were unable to give informed consent or were considered inappropriate to include by their family doctor.</p> <p><u>Clinical setting:</u> UK primary care.</p>	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	Suspicious (any lesion presented by a patient, or opportunistically seen by a family doctor or practice nurse, that could not immediately be diagnosed as benign and about which the patient could not be reassured) pigmented lesion	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		

A. risk of bias	
Reference standard(s)	Expert opinion by a histologist or dermatologist or review by two other dermatology experts of the recorded clinical history and examination, a digital photograph, and MoleMate images where available with or without follow up 3-6 months later.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes Tests: No
Could the patient flow have introduced bias?	Low risk
NOTES	Analysis was on a per-lesion basis rather than a per-patient basis.

References

Included Studies

Emery, J.D., Hunter, J., Hall, P.N., Watson, A.J., Moncrieff, M., Walter, F.M. (2010). Accuracy of SIAscopy for pigmented skin lesions encountered in primary care: development and validation of a new diagnostic algorithm. *BMJ Dermatology*, 10:9.

Rosendahl, C. (2012) Dermoscopy of squamous cell carcinoma and keratoacanthoma. *Archives of Dermatology*, 148: 1386-1392.

Walter, F.M., Morris, H.C., Humphrys, E., Hall, P.N., Prevost, A.T., Burrows, N., Bradshaw, L., Wilson, E.C., Norris, P., Walls, J., Johnson, M., Kinmonth, A.L., Emery, J.D. (2012). Effect of adding a diagnostic aid to best practice to manage suspicious pigmented lesions in primary care: randomised controlled trial. *BMJ*, 345: e4110.

Excluded Studies

Abbas, A., Yang, G. & Fakih, M. (2010) Management of Anal Cancer in 2010 Part 1: Overview, Screening, and Diagnosis. *Oncology-New York*, 24: 364-369.
Narrative review

ADAMS, W. M., HENDRIX, J. H., Jr., ADAMS, W. M. & HENDRIX, J. H. J. (1952) Facial lesions of interest to the general practitioner and the plastic surgeon. *Southern Medical Journal*, 45: 689-695.
Narrative review

Aitken, J. F., Janda, M., Elwood, M., Youl, P. H., Ring, I. T., Lowe, J. B., Aitken, J. F., Janda, M., Elwood, M., Youl, P. H., Ring, I. T. & Lowe, J. B. (2006) Clinical outcomes from skin screening clinics within a community-based melanoma screening program. *Journal of the American Academy of Dermatology*, 54: 105-114.

Not in PICO

- Alam, M. & Ratner, D. (2001) Primary care: Cutaneous squamous-cell carcinoma. *New England Journal of Medicine*, 344: 975-983.
Narrative review
- Albert, M. R. W. (2003) Keratinocyte carcinoma. *Ca-A Cancer Journal for Clinicians*, 53: 292-302.
Narrative review
- Aldridge, R. B., Naysmith, L., Ooi, E. T., Murray, C. S. & Rees, J. L. (1111) The importance of a full clinical examination: Assessment of index lesions referred to a skin cancer clinic without a total body skin examination would miss one in three melanomas. *Acta Dermato-Venereologica*, 93: 2013.
Not in PICO
- Alho, O. P., Teppo, H., Mantyselka, P. & Kantola, S. (2006) Head and neck cancer in primary care: presenting symptoms and the effect of delayed diagnosis of cancer cases. *CMAJ.*, 174: 779-784.
Not in PICO (cancer patients from one population, symptomatic patients from another population)
- Allon, I., Allon, D. M., Anavi, Y. & Kaplan, I. (2013) The significance of surface ulceration as a sign of malignancy in exophytic oral mucosal lesions: myth or fact? *Head and neck pathology*, 7: 149-154.
Not in PICO
- Almeida, L. P. C. (2011) Spectrum of presentations of disseminated warts among immunodeficient patients in a specialized dermatology outpatient unit care. *Journal of Clinical Immunology*, Conference: September.
Not in PICO
- Askari, S. K., Schram, S. E., Wenner, R. A., Bowers, S., Liu, A., Bangerter, A. K. & Warshaw, E. M. (2007) Evaluation of prospectively collected presenting signs/symptoms of biopsy-proven melanoma, basal cell carcinoma, squamous cell carcinoma, and seborrheic keratosis in an elderly male population. *Journal of the American Academy of Dermatology*, 56: 739-747.
Not in PICO
- Awan, B. A., Alzanbagi, H., Samargandi, O. A. & Ammar, H. (2014) Scalp squamous cell carcinoma in xeroderma pigmentosum. *North American Journal of Medical Sciences*, 6: 105-106.
Not in PICO
- Badertscher, N. (2011) MinSKIN Does a multifaceted intervention improve the competence in the diagnosis of skin cancer by general practitioners? Study protocol for a randomised controlled trial. *Trials*, 12: 17-19.
Protocol
- Badoual, C., Righini, C., Barry, B., Bertolus, C., Naderi, S., Moriniere, S., de, R. D., Badoual, C., Righini, C., Barry, B., Bertolus, C., Naderi, S., Moriniere, S. & de Raucourt, D. (2012) Pre-therapeutic histological and cytological assessment in head and neck squamous cell carcinomas. French Society of Otorhinolaryngology Guidelines - 2012. *European annals of otorhinolaryngology, head & neck diseases*, 129: 319-326.
Guidelines
- Balkrishnan, R., Cayce, K. A., Kulkarni, A. S., Orsagh, T., Gallagher, J. R., Richmond, D., Feldman, S. R., Balkrishnan, R., Cayce, K. A., Kulkarni, A. S., Orsagh, T., Gallagher, J. R., Richmond, D. & Feldman, S. R. (2006) Predictors of treatment choices and associated outcomes in actinic keratoses: results from a national physician survey study. *Journal of Dermatological Treatment*, 17: 162-166.
Not in PICO
- Balogh, K. (2012) Skin cancer 'filtered screening' by dermatologists: the 2-week wait system. *British Journal of Dermatology*, Conference: July.
Not in PICO

- Bataille, V. (2011) A teledermatology pilot study in Hertfordshire: Triage of 2-week-wait referrals. *British Journal of Dermatology*, Conference: July.
Not in PICO
- Benninger, M. S. & Benninger, M. S. (1992) Presentation and evaluation of patients with epidermoid head and neck cancers. [Review] [31 refs]. *Henry Ford Hospital Medical Journal*, 40: 144-148.
Narrative review
- Bentley, J. M., Barankin, B., Lauzon, G. J., Bentley, J. M., Barankin, B. & Lauzon, G. J. (2003) Paying more than lip service to lip lesions. [Review] [26 refs]. *Canadian Family Physician*, 49: 1111-1116.
Narrative review
- Behrens, A., May, A., Manner, H., Pohl, J. & Ell, C. (2013) Esophageal precancerous lesions: Early diagnosis, treatment, and preservation of quality of life. [German]. *Internist*, 54: 683-690.
Narrative review
- Bigot, P., Longvert, C., Bigot, P. & Longvert, C. (2011) [Penile dermatological lesions: how to identify premalignant lesions?]. [French]. *Progres En Urologie*, 21 Suppl 2: S50-S52.
Narrative review
- Bonsall, J. M., Hughes, R., Mosunjac, M., Harrison, D., Samady, H., Bonsall, J. M., Hughes, R., Mosunjac, M., Harrison, D. & Samady, H. (2010) A rare case of squamous cell carcinoma of the bladder presenting as a metastatic right ventricular mass. *Case Reports in Medicine*, 2010: 789609.
Not in PICO
- Bradley, P. J. & Bradley, P. T. (2010) Searching for metachronous tumours in patients with head and neck cancer: the ideal protocol! *Current Opinion in Otolaryngology & Head and Neck Surgery*, 18: 124-133.
Narrative review
- Brocklehurst, P., Rafiq, R., Lowe, D. & Rogers, S. (2012) Analysis of the impact of deprivation on urgent suspected head and neck cancer referrals in the Mersey region between January 2004 to December 2006. *British Journal of Oral & Maxillofacial Surgery*, 50: 215-220.
Not in PICO
- Bruce, A. J., Brodland, D. G., Bruce, A. J. & Brodland, D. G. (2000) Overview of skin cancer detection and prevention for the primary care physician. [Review] [34 refs]. *Mayo Clinic Proceedings*, 75: 491-500.
Narrative review
- Brundel, K.-H. (1990) Skin cancer in general practice. *Dermatosen in Beruf und Umwelt*, 38: 54-57.
Not in PICO
- Buis, P. A. J. (2005) Value of histopathologic analysis of skin excisions by GPs. *British Journal of General Practice*, 55: 458-460.
Not in PICO
- Burghout, K., Sigurdsson, V. & Toonstra, J. (2013) Non-melanoma skin cancer. [Dutch]. *Huisarts en Wetenschap*, 56: 174-178.
Narrative review
- Butani, A. (2005) Premalignant and early squamous cell carcinoma. *Clinics in Plastic Surgery*, 32: 223-235.
Narrative review
- Carvalho, A. L., Pintos, J., Schlecht, N. F., Oliveira, B. V., Fava, A. S., Curado, M. P., Kowalski, L. P. & Franco, E. L. (2002) Predictive factors for diagnosis of advanced-stage squamous cell carcinoma of the head and neck. *Archives of Otolaryngology-Head & Neck Surgery*, 128: 313-318.
Not in PICO
- Cassarino, D. S., DeRienzo, D. P. & Barr, R. J. (2006) Cutaneous squamous cell carcinoma: a comprehensive clinicopathologic classification - Part two. *Journal of Cutaneous Pathology*, 33:

261-279.

Narrative review

Chaidemenos, G. (2010) Inability of dermoscopy to differentiate early-stage squamous cell carcinoma from keratoacanthoma. *Melanoma Research*, Conference: June.

Not in PICO

Chan, K. H. N. (2006) Warty growth of the penis - Genital wart? *Hong Kong Practitioner*, 28: 225-227.

Not in PICO

Chattopadhyay, M. & Ha, T. (2013) How to examine a patient with suspected skin cancer. *Medicine (United Kingdom)*, 41: 400-401.

Narrative review

Cohen, J. L. & Cohen, J. L. (2010) Actinic keratosis treatment as a key component of preventive strategies for nonmelanoma skin cancer. *The Journal of Clinical & Aesthetic Dermatology*, 3: 39-44.

Narrative review

Collins, S. L. (1995) Avoiding delay and misdiagnosis of head and neck cancer: rare tumors with common symptoms. *Comprehensive Therapy*, 21: 59-67.

Narrative review

Corey, K. (2012) An analysis of terminology used by primary care physicians to describe concerning lesions referred to an urgent dermatology clinic. *Journal of Investigative Dermatology*, Conference: May.

Not in PICO

Correa, G. T., Bandeira, G. A., Cavalcanti, B. G., Santos, F. B., Rodrigues Neto, J. F., Guimaraes, A. L., Haikal, D. S. & De Paula, A. M. (2012) Analysis of ECOG performance status in head and neck squamous cell carcinoma patients: association with sociodemographical and clinical factors, and overall survival. *Supportive Care in Cancer*, 20: 2679-2685.

Not in PICO

Cox, N. H. & Cox, N. H. (2004) Evaluation of the U.K. 2-week referral rule for skin cancer. *British Journal of Dermatology*, 150: 291-298.

Not in PICO

Cox, N. H., Madan, V., Sanders, T., Cox, N. H., Madan, V. & Sanders, T. (2008) The U.K. skin cancer 'two-week rule' proforma: assessment of potential modifications to improve referral accuracy. *British Journal of Dermatology*, 158: 1293-1298.

Not in PICO

Das, S. (2005) Imaging of lumps and bumps in the nose: a review of sinonasal tumours. *Cancer imaging : the official publication of the International Cancer Imaging Society*, 5: 2005.

Narrative review

de Leeuw, J., van der Beek, N., Neugebauer, W. D., Bjerring, P. & Neumann, H. A. M. (2009) Fluorescence Detection and Diagnosis of Non-Melanoma Skin Cancer at an Early Stage. *Lasers in Surgery and Medicine*, 41: 96-103.

Not in PICO

Deal, A. M., Patel, M. R., Thorp, B. D., Cannon, T. Y., Shores, C. G. & Zanation, A. M. (2012) Liver function tests: inadequate screening modality for detection of liver metastasis in head and neck carcinoma. *Otolaryngology - Head and Neck Surgery*, 146: 88-91.

Not in PICO

Delaney, E. K. D. (2012) Excising squamous cell carcinomas: Comparing the performance of GPs, hospital skin specialists and other hospital specialists. *Family Practice*, 29: 541-546.

Not in PICO

Dewan, P. (2010) Are NICE skin cancer guidelines being followed in primary care? A re-audit to review changes in practice in an inner city setting. *British Journal of Dermatology*, Conference: July.

Not in PICO

- Dolan, R. W., Vaughan, C. W. & Fuleihan, N. (1998) Symptoms in early head and neck cancer: an inadequate indicator. *Otolaryngology - Head and Neck Surgery*, 119: 463-467.
Not in PICO
- Eekhof, J. A. (2013) [Actinic keratosis: the art of doing nothing]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 157: A5363.
Narrative review
- Eggesbo, H. B. & Eggesbo, H. B. (2012) Imaging of sinonasal tumours. [Review]. *Cancer Imaging*, 12: 136-152.
Narrative review
- Eide, M. J., Weinstock, M. A., Dufresne, R. G., Neelagaru, S., Risica, P., Burkholder, G. J., Upegui, D., Phillips, K. A., Armstrong, B. K. & Robinson-Bostom, L. (2005) Relationship of treatment delay with surgical defect size from keratinocyte carcinoma (basal cell carcinoma and squamous cell carcinoma of the skin). *Journal of Investigative Dermatology*, 124: 308-314.
Not in PICO
- Englert, C. (2012) A review of actinic keratosis for the nurse practitioner: Diagnosis, treatment, and clinical pearls. *Journal of the American Academy of Nurse Practitioners*, 24: 290-296.
Narrative review
- Epstein, J. B., Guneri, P., Boyacioglu, H. & Abt, E. (2013) The limitations of the clinical oral examination in detecting dysplastic oral lesions and oral squamous cell carcinoma.[Reprint of J Am Dent Assoc. 2012 Dec;143(12):1332-42; PMID: 23204089]. *Texas Dental Journal*, 130: 410-424.
Not in PICO
- Ferreira, P., Rodrigues, M., Ledo, S., Senra, R., Costa, S., V, Rocha, M. & Paiva, C. (2013) Back pain as the first manifestation of a cavum tumor. *European Journal of Internal Medicine*, 24: e149.
Not in PICO
- Firnhaber, J. M. (2012) Diagnosis and treatment of basal cell and squamous cell carcinoma. *American Family Physician*, 86: 161-168.
Narrative review
- Firooz, A. (2007) Pigmented Bowen's disease of the finger mimicking malignant melanoma. *Archives of Iranian Medicine*, 10: 255-257.
Not in PICO
- FitzGerald, K. L., Buttner, P. G., Donovan, S. A., FitzGerald, K. L., Buttner, P. G. & Donovan, S. A. (2006) Nonpigmented skin lesions - how many are nonmelanoma skin cancer? *Australian Family Physician*, 35: 555-557.
Not in PICO (only excised lesions, not examined lesions)
- Foley, C. (2012) A dermatology outpatient waiting list initiative. *British Journal of Dermatology*, Conference: e33-e34.
Not in PICO
- Fontes, K. B., Cunha, K. S., Rodrigues, F. R., Silva, L. E. & Dias, E. P. (2013) Concordance between cytopathology and incisional biopsy in the diagnosis of oral squamous cell carcinoma. *Brazilian oral research*, 27: 122-127.
Not in PICO
- Forsea, A. M., Carstea, E. M., Ghervase, L., Giurcaneanu, C., Pavelescu, G., Forsea, A. M., Carstea, E. M., Ghervase, L., Giurcaneanu, C. & Pavelescu, G. (2010) Clinical application of optical coherence tomography for the imaging of non-melanocytic cutaneous tumors: a pilot multi-modal study.[Erratum appears in J Med Life. 2011 Jan-Mar;4(1):7 p following 123]. *Journal of Medicine & Life*, 3: 381-389.
Not in PICO
- Forti, R. L., Medwell, S. J., Aboulafia, D. M., Surawicz, C. M., Spach, D. H., Forti, R. L., Medwell, S. J., Aboulafia, D. M., Surawicz, C. M. & Spach, D. H. (1995) Clinical presentation of minimally invasive and in situ squamous cell carcinoma of the anus in homosexual men. *Clinical*

- Infectious Diseases*, 21: 603-607.
Not in PICO
- Friedrich, R. E. (2010) Delay in Diagnosis and Referral Patterns of 646 Patients with Oral and Maxillofacial Cancer: A Report from a Single Institution in Hamburg, Germany. *Anticancer Research*, 30: 1833-1836.
Not in PICO
- Garbe, C. (2008) Early detection and primary prevention of skin cancer. *Onkologie*, 14: 156-163.
Narrative review
- Genden, E. M., Rinaldo, A., Bradley, P. J., Lowry, J., Suarez, C., Shaha, A. R., Scully, C. & Ferlito, A. (2006) Referral guidelines for suspected cancer of the head and neck. *Auris Nasus Larynx*, 33: 1-5.
Narrative review
- Giacomel, J. & Zalaudek, I. (2013) Pink Lesions. *Dermatologic Clinics*, 31: 649-678.
Narrative review
- Gilde, K. (2006) The importance of malignant skin tumors. *Orvosi Hetilap*, 147: 2321-2330.
Narrative review
- Gilde, K. & Gilde, K. (2006) [Malignant tumors of the skin]. [Review] [25 refs] [Hungarian]. *Orvosi Hetilap*, 147: 2321-2330.
Narrative review
- Golberg, O. (2011) Seasonal variation in 2-week-wait skin cancer referrals is not mirrored by changes in incidence of skin cancer: A message for service provision. *British Journal of Dermatology*, Conference: July.
Not in PICO
- Goy, J., Hall, S. F., Feldman-Stewart, D. & Groome, P. A. (2009) Diagnostic Delay and Disease Stage in Head Neck Cancer: A Systematic Review. *Laryngoscope*, 119: 889-898.
Not in PICO
- Graells, J., Espinola, A., Barrio, C., Munoz, M. D., Roman, A., Parellada, N., Graells, J., Espinola, A., Barrio, C., Munoz, M. D., Roman, A. & Parellada, N. (2007) [Minor cutaneous ambulatory surgery and cryotherapy. Comparative study between a dermatologist and family physicians]. [Spanish]. *Actas Dermo-Sifiliograficas*, 98: 171-177.
Not in PICO
- Graves, J. (2006) Derm Access: A new triage system to rapidly identify suspicious skin lesions. *Dermatologic Surgery*, 32: 1486-1490.
Not in PICO
- Gunson, T. (2009) Audit of histopathology request forms for cutaneous lesions comparing a large dermatology department with regional general practices. *British Journal of Dermatology*, Conference: July.
Not in PICO
- Haliasos, E. C., Kerner, M., Jaimes, N., Zalaudek, I., Malvey, J., Lanschuetzer, C. M., Hinter, H., Hofmann-Wellenhof, R., Braun, R. P. & Marghoob, A. A. (2013) Dermoscopy for the pediatric dermatologist, part ii: dermoscopy of genetic syndromes with cutaneous manifestations and pediatric vascular lesions. [Review]. *Pediatric Dermatology*, 30: 172-181.
Narrative review
- Halpern, A. C., Hanson, L. J., Halpern, A. C. & Hanson, L. J. (2004) Awareness of, knowledge of and attitudes to nonmelanoma skin cancer (NMSC) and actinic keratosis (AK) among physicians. *International Journal of Dermatology*, 43: 638-642.
Not in PICO
- Hansen, C. (2009) Factors contributing to incomplete excision of nonmelanoma skin cancer by Australian general practitioners. *Archives of Dermatology*, 145: 1253-1260.
Not in PICO

- Haw, W. Y., Fraser, S., Affleck, A. & Holme, A. (2014) Skin cancer excision performance in primary and secondary care in Scotland. *British Journal of Dermatology*, 171: 25.
Not in PICO
- Haws, M. J. N. (1997) Management of nonmelanoma skin tumors of the hand. *Clinics in Plastic Surgery*, 24: 779-795.
Narrative review
- Heal, C., Buettner, P., Raasch, B., Browning, S., Heal, C., Buettner, P., Raasch, B. & Browning, S. (2006) Minor skin excisions in general practice in North Queensland. *Australian Family Physician*, 35: 825-828.
Not in PICO (only excised lesions, not examined lesions; no information about symptoms/lesion features)
- Helfand, M., Gorman, A. K., Mahon, S., Chan, B. K. & Swanson, N. (2001) Actinic keratoses (Structured abstract). *Health Technology Assessment Database*, 71.
Narrative review
- Hill, G. M., Sowden, J. M., Lister, R. K., Logan, R. A. & Finlay, A. Y. (2010) Dermatology outpatient case-mix survey for all Welsh Trusts, 2007. *British Journal of Dermatology*, 162: 152-158.
Not in PICO
- Ho, K.-Y. (2008) Early recognition of nasopharyngeal cancer in adults with only otitis media with effusion. *Journal of Otolaryngology - Head and Neck Surgery*, 37: 362-365.
Not in PICO
- Hobson, J. C. M. (2008) Outcomes for patients referred urgently with suspected head and neck cancer. *Journal of Laryngology and Otology*, 122: 1241-1244.
Not in PICO
- Hochman, M., Lang, P., Hochman, M. & Lang, P. (1999) Skin cancer of the head and neck. [Review] [75 refs]. *Medical Clinics of North America*, 83: 261-282.
Narrative review
- Holmang, S. (2007) Squamous Cell Carcinoma of the Renal Pelvis and Ureter: Incidence, Symptoms, Treatment and Outcome. *Journal of Urology*, 178: 51-56.
Not in PICO
- Jacobs, C. D., Goffinet, D. R. & Fee, W. E., Jr. (1990) Head and neck squamous cancers. *Current Problems in Cancer*, 14: 1-72.
Narrative review
- Jensen, A. O., Bautz, A., Olesen, A. B., Karagas, M. R., Sorensen, H. T. & Friis, S. (2008) Mortality in Danish patients with nonmelanoma skin cancer, 1978-2001. *British Journal of Dermatology*, 159: 419-425.
Not in PICO
- Jerant, A. F. J. (2000) Early detection and treatment of skin cancer. *American Family Physician*, 62: 357-376+381.
Narrative review
- Joly, P., Bastuji-Garin, S., Frances, C., Lebbe, C., Aubin, F., Penso-Assathiany, D., D'incan, M., Avril, M. F., Lair, G., Barete, S. & Euvrard, S. (2010) Squamous Cell Carcinomas Are Associated With Verrucokeratotic Cutaneous Lesions But Not With Common Warts in Organ-Transplant Patients. A Case-Control Study. *Transplantation*, 89: 1224-1230.
Not in PICO
- Kahn, E., Sossong, S., Goh, A., Carpenter, D. & Goldstein, S. (2013) Evaluation of Skin Cancer in Northern California Kaiser Permanente's Store-and-Forward Teledermatology Referral Program. *Telemedicine and E-Health*, 19: 780-785.
Not in PICO
- Kamyab-Hesari, K., Seirafi, H., Naraghi, Z. S., Shahshahani, M. M., Rahbar, Z., Damavandi, M. R., Naraghi, M. M., Rezvani, M. & Aghazadeh, N. (2014) Diagnostic accuracy of punch biopsy in subtyping basal cell carcinoma. *Journal of the European Academy of Dermatology and*

- Venereology*, 28: 250-253.
Not in PICO
- Kennedy, A. M., Aziz, A., Khalid, S. & Hurman, D. (2012) Do GP referral guidelines really work? Audit of an electronic urgent referral system for suspected head and neck cancer. *European Archives of Oto-Rhino-Laryngology*, 269: 1509-1512.
Not in PICO
- Khorasgani, M. G. P. (2010) Dermatological surgery in the community: Are the guidelines being followed? *British Journal of Dermatology*, Conference: July.
Not in PICO
- Khorshid, S. M. R. (275) Recognising and treating. Premalignant skin conditions. *The Practitioner*, 242: 270-275.
Narrative review
- Kleinpenning, M. M., Wolberink, E. W., Smits, T., Blokk, W. A., van De Kerkhof, P. C., van Erp, P. E., Gerritsen, R. M., Kleinpenning, M. M., Wolberink, E. W., Smits, T., Blokk, W. A. M., van De Kerkhof, P. C. M., van Erp, P. E. J. & Gerritsen, R. M. J. P. (2010) Fluorescence diagnosis in actinic keratosis and squamous cell carcinoma. *Photodermatology, Photoimmunology & Photomedicine*, 26: 297-302.
Not in PICO
- Kok, L. P., V (2000) General practitioners use digital cameras and internet for telepathology of skin lesions. *Electronic Journal of Pathology and Histology*, 6: 7-19.
Not in PICO
- Kowal-Vern, A. (2005) Burn scar neoplasms: A literature review and statistical analysis. *Burns*, 31: 403-413.
Not in PICO
- Kundu, R. V. & Patterson, S. (2013) Dermatologic conditions in skin of color: part I. Special considerations for common skin disorders.[Summary for patients in Am Fam Physician. 2013 Jun 15;87(12):Online; PMID: 23939576]. *American Family Physician*, 87: 850-856.
Narrative review
- Kutcher, M. J., Rubenstein, D., Kutcher, M. J. & Rubenstein, D. (1995) Fifteen inches from cancer: early recognition of facial lesions by the dentist. [Review] [10 refs]. *Compendium of Continuing Education in Dentistry*, 25: 939-946.
Narrative review
- Lahiri, K. (1954) Skin diseases in general practice. *Indian Med, Forum* 5: 219-222.
Narrative review
- Lai, W.-Y. (1111) An elderly man with a painful scaly nodule. *Hong Kong Practitioner*, 35: September.
Not in PICO
- Lathlean, S. & Lathlean, S. (1999) Skin cancer in general practice in South Australia. A five year study. *Australian Family Physician*, 28 Suppl 1: S28-S31.
Not in PICO (only excised lesions, not examined lesions; no information about symptoms/lesion features)
- Laukkanen, A., Rummukainen, J., Kivinen, P., Lappalainen, K., Laukkanen, A., Rummukainen, J., Kivinen, P. & Lappalainen, K. (2006) [Skin squamous cell carcinoma and its precancerous conditions]. [Review] [25 refs] [Finnish]. *Duodecim*, 122: 71-79.
Narrative review
- Leggett, P. (2004) A randomized controlled trial using instant photography to diagnose and manage dermatology referrals. *Family Practice*, 21: 54-56.
Not in PICO
- Leiter, U. (2012) Secondary prevention of skin cancer. *Onkologe*, 18: 237-242.
Narrative review
- Lin, Y.-C., Perng, C.-L., Chang, Y.-M., Li, Y.-F., Tsai, Y.-M., Wu, G.-J. & Lin, C.-K. (2013) Coexistent squamous cell carcinoma and adenoid basal carcinoma in the uterine cervix and infection with

- human papillomavirus (HPV 31). *Taiwanese Journal of Obstetrics and Gynecology*, 52: 407-410.
Not in PICO
- Lober, C. W., Fenske, N. A., Lober, C. W. & Fenske, N. A. (1991) Basal cell, squamous cell, and sebaceous gland carcinomas of the periorbital region. [Review] [54 refs]. *Journal of the American Academy of Dermatology*, 25: 685-690.
Narrative review
- Long, M. D. (2012) Cutaneous malignancies in patients with inflammatory bowel disease. *Gastroenterology and Hepatology*, 8: 467-471.
Narrative review
- Loveland-Jones, C. E., Wang, F., Bankhead, R. R., Huang, Y., Reilly, K. J., Loveland-Jones, C. E., Wang, F., Bankhead, R. R., Huang, Y. & Reilly, K. J. (2010) Squamous cell carcinoma of the nipple following radiation therapy for ductal carcinoma in situ: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 4: 186.
Not in PICO
- MacLean, A. B., Jones, R. W., Scurry, J. & Neill, S. (2009) Vulvar Cancer and the Need for Awareness of Precursor Lesions. *Journal of Lower Genital Tract Disease*, 13: 115-117.
Narrative review
- Marghoob, A. A. & Marghoob, A. A. (146) Basal and squamous cell carcinomas. What every primary care physician should know. [Review] [20 refs]. *Postgraduate Medicine*, 102: 139-146.
Narrative review
- Marghoob, A. A., Usatine, R. P. & Jaimes, N. (2013) Dermoscopy for the family physician. [Review]. *American Family Physician*, 88: 441-450.
Narrative review
- Marks, R. & Marks, R. (2006) Who benefits from calling a solar keratosis a squamous cell carcinoma? *British Journal of Dermatology*, 155: 23-26.
Not in PICO
- Martinez, J. C. & Otley, C. C. (2001) The management of melanoma and nonmelanoma skin cancer: A review for the primary care physician. *Mayo Clinic Proceedings*, 76: 1253-1265.
Narrative review
- May, C., Giles, L., Gupta, G., May, C., Giles, L. & Gupta, G. (2008) Prospective observational comparative study assessing the role of store and forward teledermatology triage in skin cancer. *Clinical & Experimental Dermatology*, 33: 736-739.
Not in PICO
- Maybury, C. M., Craythorne, E. & Martin, B. (2013) An ulcerated nodule on the nose. *BMJ Case Reports*, 2013, 2013.
Not in PICO
- McKie, C., Ahmad, U. A., Fellows, S., Meikle, D., Stafford, F. W., Thomson, P. J., Welch, A. R. & Paleri, V. (2008) The 2-week rule for suspected head and neck cancer in the United Kingdom: referral patterns, diagnostic efficacy of the guidelines and compliance. *Oral Oncology*, 44: 851-856.
Not in PICO
- McNulty-Brown, E. (2012) An audit of all excisions undertaken by general practitioners in a rural community between March 2009 and March 2010. *British Journal of Dermatology*, Conference: July.
Not in PICO
- Medeiros, F. (2005) Early vulvar squamous neoplasia: Advances in classification, diagnosis, and differential diagnosis. *Advances in Anatomic Pathology*, 12: 20-26.
Narrative review
- Mencia Gutierrez, E. (2001) Basal cell and squamous cell carcinomas of the eyelid in adults under 50 years of age: 13 cases. *Archivos de la Sociedad Espanola de Oftalmologia*, 76: 643-648.
Not in PICO

- Malveyh, J., Puig, S., Rabinovitz, H. S., Oliviero, M., Cabo, H., Bono, R., Pizzichetta, M. A., Claeson, M., Gaffney, D. C., Soyer, H. P., Stanganelli, I., Scolyer, R. A., Guitera, P., Kelly, J., McCurdy, O., Llambrich, A., Marghoob, A. A., Zaballos, P., Kirchesch, H. M., Piccolo, D., Bowling, J., Thomas, L., Terstappen, K., Tanaka, M., Pellacani, G., Pagnanelli, G., Ghigliotti, G., Ortega, B. C., Crafter, G., Ortiz, A. M., Tromme, I., Karaarslan, I. K., Ozdemir, F., Tam, A., Landi, C., Norton, P., Kacar, N., Rudnicka, L., Slowinska, M., Simionescu, O., Di, S. A., Coates, E. & Kreusch, J. (2013) Dermoscopic evaluation of nodular melanoma. *JAMA Dermatology*, 149: 699-709.
Not in PICO
- Moffatt, C. R., Green, A. C., Whiteman, D. C., Moffatt, C. R. M., Green, A. C. & Whiteman, D. C. (2006) Diagnostic accuracy in skin cancer clinics: the Australian experience. *International Journal of Dermatology*, 45: 656-660.
Not in PICO
- Molina, R. & Bosch, X. (2012) Utility of serum tumor markers as an aid in the differential diagnosis of patients with clinical suspicion of cancer and in patients with cancer of unknown primary site. *Tumor Biology*, 33: 463-474.
Not in PICO
- Montero Perez, F. J., Munoz, A. M., Calvo-Rubio, B. M., Fernandez Roldan, J. C., Montero Perez, F. J., Munoz Alamo, M., Calvo-Rubio Burgos, M. & Fernandez Roldan, J. C. (1989) [Importance of skin cancer (non-melanoma): a study of 89 cases]. [Spanish]. *Atencion Primaria*, 6: 660-664.
Not in PICO
- Moran, B. & McDonald, I. (2010) Full skin examination is essential in the assessment of dermatology patients: An audit of 494 patients. *British Journal of Dermatology*, Conference: July.
Not in PICO
- Moran, B. & McDonald, I. (2011) Complete skin examination is essential in the assessment of dermatology patients: Findings from 483 patients. *British Journal of Dermatology*, 165: 1124-1126.
Not in PICO
- Morrison, A., O'Loughlin, S., Powell, F. C., Morrison, A., O'Loughlin, S. & Powell, F. C. (2001) Suspected skin malignancy: a comparison of diagnoses of family practitioners and dermatologists in 493 patients. *International Journal of Dermatology*, 40: 104-107.
Not in PICO
- Morteza, A. S., Salama, S. & Alowami, S. (2013) Lymphoepithelioma-like carcinoma of the skin: case report and approach to surgical pathology sign out. *Rare Tumors*, 5: e47.
Not in PICO
- Morton, C. A., Birnie, A. J. & Eedy, D. J. (2014) British Association of Dermatologists' guidelines for the management of squamous cell carcinoma in situ (Bowen's disease) 2014. *British Journal of Dermatology*, 170: 245-260.
Guideline
- Nordenvall, C., Nyren, O. & Ye, W. (2006) Elevated anal squamous cell carcinoma risk associated with benign inflammatory anal lesions. *Gut*, 55: 703-707.
Not in PICO
- Nthumba, P. M. & Nthumba, P. M. (2010) Marjolin's ulcers in sub-Saharan Africa. [Review]. *World Journal of Surgery*, 34: 2272-2277.
Not in PICO
- O'Hagan, A. (2010) Teledermatology triage for suspected skin cancers: An audit of service quality and effectiveness in a Northern Irish dermatology centre. *British Journal of Dermatology*, Conference: July.
Not in PICO
- Obata, H. (2005) Incidence of benign and malignant lesions of eyelid and conjunctival tumors. *Nippon Ganka Gakkai zasshi*, 109: 573-579.
Not in PICO

- Offidani, A., Simonetti, O., Bernardini, M. L., Alpagut, A., Cellini, A., Bossi, G., Offidani, A., Simonetti, O., Bernardini, M. L., Alpagut, A., Cellini, A. & Bossi, G. (2002) General practitioners' accuracy in diagnosing skin cancers. *Dermatology*, 205: 127-130.
Not in PICO
- Osthus, A. A., Aarstad, A. K., Olofsson, J. & Aarstad, H. J. (2013) Prediction of Survival by Pretreatment Health-Related Quality-of-Life Scores in a Prospective Cohort of Patients With Head and Neck Squamous Cell Carcinoma. *JAMA Otolaryngology - Head and Neck Surgery*, 139: 14-20.
Not in PICO
- Pallagatti, S., Sheikh, S., Aggarwal, A., Gupta, D., Singh, R., Handa, R., Kaur, S. & Mago, J. (2013) Toluidine blue staining as an adjunctive tool for early diagnosis of dysplastic changes in the oral mucosa. *Journal of Clinical & Experimental Dentistry*, 5: e187-e191.
Not in PICO
- Palmer, V. M. & Wilson, P. R. (2013) Incompletely excised basal cell carcinoma: residual tumor rates at Mohs re-excision. *Dermatologic Surgery*, 39: 706-718.
Not in PICO
- Patel, L. M., Lambert, P. J., Gagna, C. E., Maghari, A. & Lambert, W. C. (2011) Cutaneous signs of systemic disease. *Clinics in Dermatology*, 29: 511-522.
Narrative review
- Peris, K., Neri, L., Pinton, P. C., Catricala, C., Pellacani, G., Pimpinelli, N. & Peserico, A. (2014) Physicians' opinions and clinical practice patterns for actinic keratosis management in Italy. *Giornale Italiano di Dermatologia e Venereologia*, 149: 185-192.
Not in PICO
- Peris, K., Neri, L., Fagnoli, M. C. & Pellacani, G. (2014) Physicians' concerns towards prescription adherence and treatment effectiveness in the clinical management of actinic keratosis. *Giornale Italiano di Dermatologia e Venereologia*, 149: 193-198.
Not in PICO
- Perrotto, J., Glick, B., Perrotto, J. & Glick, B. (2006) Lower extremity malignancies masquerading as ulcers. *Ostomy Wound Management*, 52: 46-52.
Narrative review
- Plate, A. M., Steiner, G., Posner, M. A., Plate, A. M., Steiner, G. & Posner, M. A. (2006) Malignant tumors of the hand and wrist. *Journal of the American Academy of Orthopaedic Surgeons*, 14: 680-692.
Narrative review
- Qi Qi, C. & Ajit Singh, V. (2012) Palm oil thorn-induced squamous cell carcinoma with underlying burns scar. *BMJ Case Reports*, 2012.
Not in PICO
- Raasch, B. A. & Raasch, B. A. (1999) Suspicious skin lesions and their management. *Australian Family Physician*, 28: 466-471.
Not in PICO (no verification of cancer/non-cancer diagnosis)
- Raj, G. & Gupta, G. (1111) The need for full body skin examination on patients referred to dermatology with a lesion. *British Journal of Dermatology.Conference: 93rd Annual Meeting of the British Association of Dermatologists Liverpool United Kingdom.Conference Start: 20130709 Conference End: 20130711.Conference Publication: (var.pagings)*, 169: July.
Not in PICO
- Ramani, C., Shah, N. & Nathan, R. S. (2014) - Verrucous carcinoma of the esophagus: A case report and literature review. - *World Journal of Clinical Cases*, 2: 284-288.
Not in PICO
- Renzi, C., Mastroeni, S., Mannooranparampil, T. J., Passarelli, F., Caggiati, A., Potenza, C. & Pasquini, P. (2010) Delay in diagnosis and treatment of squamous cell carcinoma of the skin. *Acta*

Dermato-Venereologica, 90: 595-601.

Not in PICO

Renzi, C., Mastroeni, S., Passarelli, F., Mannooranparampil, T. J., Caggiati, A., Potenza, C. & Pasquini, P. (2010) Factors associated with large cutaneous squamous cell carcinomas. *Journal of the American Academy of Dermatology*, 63: 404-411.

Not in PICO

Renzi, C., Mastroeni, S. & Mannooranparampil, T. J. (2011) Timely diagnosis of cutaneous squamous cell carcinoma: The GP's role. *Family Practice*, 28: 277-279.

Not in PICO

Rice, S. A. S. (2012) Are we relying too heavily on dermoscopy? *British Journal of Dermatology*, Conference: July.

Not in PICO

Richert, B., Lecerf, P., Caucanas, M. & Andre, J. (2013) Nail tumors. *Clinics in Dermatology*, 31: 602-617.

Narrative review

Robinson, M. (2012) The pathology of virus-related carcinomas of the upper aerodigestive tract. *Journal of Pathology*, Conference: September.

Narrative review

Roozeboom, M. H., Mosterd, K., Winnepeninckx, V. J., Nelemans, P. J. & Kelleners-Smeets, N. W. (2013) Agreement between histological subtype on punch biopsy and surgical excision in primary basal cell carcinoma. *Journal of the European Academy of Dermatology & Venereology*, 27: 894-898.

Not in PICO

Rosendahl, C., Tschandl, P., Cameron, A., Kittler, H., Rosendahl, C., Tschandl, P., Cameron, A. & Kittler, H. (2011) Diagnostic accuracy of dermoscopy for melanocytic and nonmelanocytic pigmented lesions. *Journal of the American Academy of Dermatology*, 64: 1068-1073.

Not in PICO (only excised lesions, not examined lesions)

Rousset, J., Abgral, R., Chinellato, S., Garetier, M., Barberot, C., Valette, G., Potard, G., Le, B. T. & Salaun, P. Y. (2013) Early recurrence or submucosal residual of laryngeal squamous cell carcinoma: diagnosis by CT-guided endolaryngeal core biopsy on a transcutaneous approach. *Head & Neck*, 35: E202-E204.

Not in PICO

Rowert-Huber, J. (2007) Erratum: Actinic keratosis is an early in situ squamous cell carcinoma: A proposal for reclassification (*British Journal of Dermatology* (2007) 156, SUPPL., (S13-S17)). *British Journal of Dermatology*, 157: 431.

Not in PICO

Rowert-Huber, J. (2007) Actinic keratosis is an early in situ squamous cell carcinoma: A proposal for reclassification. *British Journal of Dermatology*, 156: 8-12.

Narrative review

Ruskiewicz, J. & Ruskiewicz, J. (1998) Skin cancer and actinic keratoses. *Journal of the American Optometric Association*, 69: 229-235.

Not in PICO

Sanyal, S., Holme, A. & Kemmett, D. (2013) How are patients with actinic keratoses managed in primary care? *British Journal of Dermatology*, 169: 45.

Not in PICO

Sharma, A., Alfa-Wali, M., Rodriguez-Justo, M. & Polychronis, A. (2013) Squamous cell carcinoma of pancreas: an unusual site of relapse from early-stage lung cancer: 12-month postsurgery. *BMJ Case Reports*, 2013, 2013.

Not in PICO

Schofield, J. (2011) The costs of diagnosing and treating skin cancer using the 2-week-wait referral process. *British Journal of Dermatology*, Conference: July.

Not in PICO

- See, A. (2005) Operational teledermatology in Broken Hill, rural Australia. *Australasian Journal of Dermatology*, 46: 144-149.
Not in PICO
- Selim, M. A., Hoang, M. P., Selim, M. A. & Hoang, M. P. (2010) A histologic review of vulvar inflammatory dermatoses and intraepithelial neoplasm. [Review]. *Dermatologic Clinics*, 28: 649-667.
Narrative review
- Shapiro, M., James, W. D., Kessler, R., Lazorik, F. C., Katz, K. A., Tam, J., Nieves, D. S., Miller, J. J., Shapiro, M., James, W. D., Kessler, R., Lazorik, F. C., Katz, K. A., Tam, J., Nieves, D. S. & Miller, J. J. (2004) Comparison of skin biopsy triage decisions in 49 patients with pigmented lesions and skin neoplasms: store-and-forward teledermatology vs face-to-face dermatology. *Archives of Dermatology*, 140: 525-528.
Not in PICO
- Shariff, Z., Roshan, A., Williams, A. M., Platt, A. J., Shariff, Z., Roshan, A., Williams, A. M. & Platt, A. J. (2010) 2-Week wait referrals in suspected skin cancer: does an instructional module for general practitioners improve diagnostic accuracy? *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 8: 247-251.
Not in PICO
- Singh, T. & Schenberg, M. (2013) Delayed diagnosis of oral squamous cell carcinoma following dental treatment. *Annals of the Royal College of Surgeons of England*, 95: 369-373.
Not in PICO
- Socha, A. & Niedzielska, I. (2013) Exophytic tumours of skin of the head - Case study and review of the literature. *Dental and Medical Problems*, 50: 229-237.
Not in PICO
- Spencer, R. J., Young, R. H., Goodman, A., Spencer, R. J., Young, R. H. & Goodman, A. (2011) The risk of squamous cell carcinoma in persistent vulvar ulcers. *Menopause*, 18: 1067-1071.
Not in PICO
- Strayer, S. M. & Reynolds, P. (2003) Diagnosing skin malignancy: Assessment of predictive clinical criteria and risk factors. *Journal of Family Practice*, 52: 210-218.
Narrative review
- Stulberg, D. L., Crandell, B., Fawcett, R. S., Stulberg, D. L., Crandell, B. & Fawcett, R. S. (2004) Diagnosis and treatment of basal cell and squamous cell carcinomas. *American Family Physician*, 70: 1481-1488.
Narrative review
- Sukur, Y. E., Gozukucuk, M. & Berker, B. (2010) Hypercalcemia associated with early recurrence of vulvar cancer. *Archives of Gynecology and Obstetrics*, 281: 117-118.
Not in PICO
- Tangjaturonrasme, N., Rerknimitr, R., Pittayanon, R., Wisedopas, N. & Kullavanijaya, P. (2013) The difference in detection rates during surveillance endoscopy for early squamous cell neoplasia of the esophagus between patients with previous nasopharyngeal cancer and patients with other ent related squamous cell cancers pornphan thienchanachaiya1. *Gastrointestinal Endoscopy*, 77: AB339-AB340.
Not in PICO
- Tate, B. (2007) Checking pigmented skin lesions. *Medicine Today*, 8: 38-46.
Narrative review
- Teppo, H., Koivunen, P., Hyrynkangas, K., Alho, O. P., Teppo, H., Koivunen, P., Hyrynkangas, K. & Alho, O. P. (2003) Diagnostic delays in laryngeal carcinoma: professional diagnostic delay is a strong independent predictor of survival. *Head & Neck*, 25: 389-394.
Not in PICO
- Terrill, P. J., Fairbanks, S., Bailey, M., Terrill, P. J., Fairbanks, S. & Bailey, M. (2009) Is there just one lesion? The need for whole body skin examination in patients presenting with non-

- melanocytic skin cancer. *ANZ Journal of Surgery*, 79: 707-712.
Not in PICO
- Terushkin, V. (2010) Agreement on the clinical diagnosis and management of cutaneous squamous neoplasms. *Dermatologic Surgery*, 36: 1514-1520.
Not in PICO
- Tochigi, T., Shuto, K., Staito, H., Kono, T. & Matsubara, H. (2013) Early esophageal squamous cell cancer by high-barium esophagography using flat panel X-ray detector in comparison with histological findings. *European Journal of Cancer*, 49: S252-S253.
Not in PICO
- Tolpinrud, W. L., Viola, K. V., Kirsner, R. S., Gross, C. P., Imaeda, S., Federman, D. G., Tolpinrud, W. L., Viola, K. V., Kirsner, R. S., Gross, C. P., Imaeda, S. & Federman, D. G. (2011) Nondermatologists' use of predictive terms for a potentially malignant lesion. *Southern Medical Journal*, 104: 477-481.
Not in PICO
- Tromp, D. M., Brouha, X. D., Hordijk, G. J., Winnubst, J. A. & de Leeuw, J. R. (2005) Patient factors associated with delay in primary care among patients with head and neck carcinoma: a case-series analysis. *Family Practice*, 22: 554-559.
Not in PICO
- Tully, A. S. T. (2012) Evaluation of nail abnormalities. *American Family Physician*, 85: 779-787.
Narrative review
- Turan, E., Yurt, N., Yesilova, Y. & Turkcu, G. (2013) Early-onset basal cell carcinoma. *Turkish Journal of Pediatrics*, 55: 354-356.
Not in PICO
- van Rijsingen, M. C. J., van Bon, B., van der Wilt, G. J., Lagro-Janssen, A. L. M. & Gerritsen, M. J. P. (2014) The current and future role of general practitioners in skin cancer care: an assessment of 268 general practitioners. *British Journal of Dermatology*, 170: 1366-1368.
Not in PICO
- Vargo, N. (2003) Basal cell and squamous cell carcinoma. *Seminars in Oncology Nursing*, 19: 12-21.
Narrative review
- Vermaak, P. V. & Manushakian, J. (2013) Rapidly enlarging skin lesion on the lip. *BMJ Case Reports*, 2013, 2013.
Not in PICO
- Voisard, J.-J. & Lazareth, I. (2001) Leg ulcers and cancer. *Journal des Maladies Vasculaires*, 26: 85-91.
Not in PICO
- Vowles, R. H., Ghiacy, S., Jefferis, A. F., Vowles, R. H., Ghiacy, S. & Jefferis, A. F. (1998) A clinic for the rapid processing of patients with neck masses. *Journal of Laryngology & Otology*, 112: 1061-1064.
Not in PICO
- Waldmann, A., Nolte, S., Geller, A. C., Katalinic, A., Weinstock, M. A., Volkmer, B., Greinert, R., Breitbart, E. W., Waldmann, A., Nolte, S., Geller, A. C., Katalinic, A., Weinstock, M. A., Volkmer, B., Greinert, R. & Breitbart, E. W. (2012) Frequency of excisions and yields of malignant skin tumors in a population-based screening intervention of 360,288 whole-body examinations. *Archives of Dermatology*, 148: 903-910.
Not in PICO
- Warshaw, E. M. G. (2010) Accuracy of teledermatology/teledermoscopy and clinic-based dermatology for specific categories of skin neoplasms. *Journal of the American Academy of Dermatology*, 63: 348-352.
Not in PICO
- Watkins, J. & Watkins, J. (2010) Dermatology and the community nurse: actinic (solar) keratosis. [Review] [13 refs]. *British Journal of Community Nursing*, 15: 6-1.
Narrative review

White, G. M., Zhou, H. C. & Burchette, R. J. (2013) Biopsy followed by immediate curettage and electrodesiccation of suspected basal cell carcinomas at the first visit. *JAMA Dermatology*, 149: 980-981.
Not in PICO

Wietfeldt, E. D., Thiele, J., Wietfeldt, E. D. & Thiele, J. (2009) Malignancies of the anal margin and perianal skin. *Clinics in Colon & Rectal Surgery*, 22: 127-135.
Narrative review

Wolberink, E. A. W., Pasch, M. C., Zeiler, M., Van Erp, P. E. J. & Gerritsen, M. J. P. (2013) High discordance between punch biopsy and excision in establishing basal cell carcinoma subtype: Analysis of 500 cases. *Journal of the European Academy of Dermatology and Venereology*, 27: 985-989.
Not in PICO

Wolpoe, M. E. G. (2006) Squamous cell carcinoma of the sinonasal cavity arising as a second primary in individuals with head and neck cancer. *Laryngoscope*, 116: 696-699.
Not in PICO

Woolley, S. D. & Hughes, C. (2013) A young military pilot presents with a periocular Basal Cell Carcinoma: A case report. *Travel Medicine and Infectious Disease*, 11: 435-437.
Not in PICO

Wray, E. V., Brant, B., Hussain, F. & Muller, F. M. (2013) A new model of teledermoscopy combining service and education. *British Journal of Dermatology*, 169: 139.
Not in PICO

Wustrow, J., Rudert, H., Diercks, M. & Beigel, A. (1989) Squamous cell carcinoma and undifferentiated carcinoma of the inner nose and the paranasal sinuses. *Strahlentherapie und Onkologie*, 165: 468-473.
Not in PICO

Yamamoto, E., Shibuya, H., Yoshimura, R. & Miura, M. (2002) Site specific dependency of second primary cancer in early stage head and neck squamous cell carcinoma. *Cancer*, 94: 2007-2014.
Not in PICO

Youl, P. H., Janda, M., Aitken, J. F., Del Mar, C. B., Whiteman, D. C., Baade, P. D., Youl, P. H., Janda, M., Aitken, J. F., Del Mar, C. B., Whiteman, D. C. & Baade, P. D. (2011) Body-site distribution of skin cancer, pre-malignant and common benign pigmented lesions excised in general practice. *British Journal of Dermatology*, 165: 35-43.
Not in PICO as results only reported for excised lesions (N = 11116, GPs and skin cancer clinic doctors), not examined lesions (N = 28755, GPs and skin cancer clinic doctors).

Zalaudek, I., Kreusch, J., Giacomel, J., Ferrara, G., Catricala, C. & Argenziano, G. (2010) How to diagnose nonpigmented skin tumors: A review of vascular structures seen with dermoscopy Part II. Nonmelanocytic skin tumors. *Journal of the American Academy of Dermatology*, 63: 377-386.
Narrative review

Review question:

Which investigations of symptoms of suspected squamous cell carcinoma should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	2206	141	07/02/2013
Premedline	1980-2013	85	9	07/02/2013

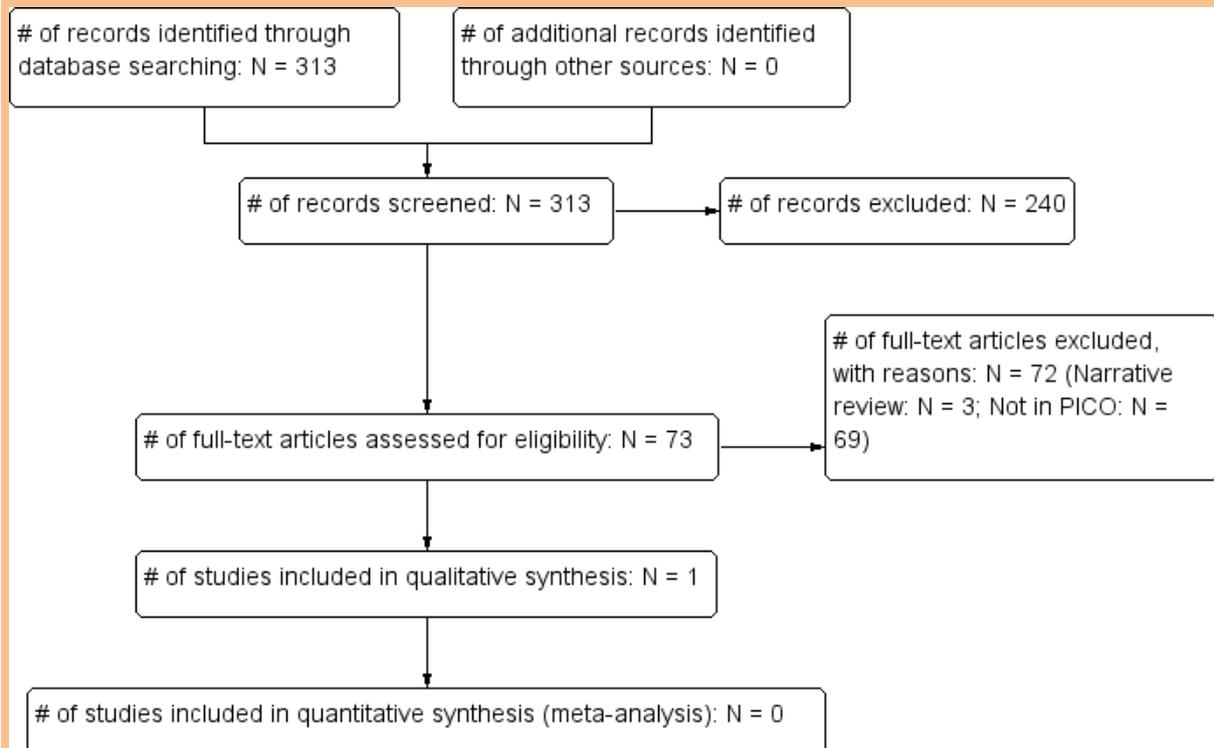
<i>Embase</i>	1980-2013	2263	146	08/02/2013
<i>Cochrane Library</i>	1980-2013	37	1	07/02/2013
<i>Psychinfo</i>	1980-2013	3	0	07/02/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	309	63	07/02/2013
<i>Biomed Central</i>	1980-2013	1026	4	07/02/2013

Total number of studies identified after de-duplication: 290

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-11/08/2014	87	7	11/08/2014
<i>Premedline</i>	2013-11/08/2014	123	6	11/08/2014
<i>Embase</i>	2013-11/08/2014	181	16	11/08/2014
<i>Cochrane Library</i>	2013-11/08/2014	55	0	11/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-11/08/2014	53	2	11/08/2014

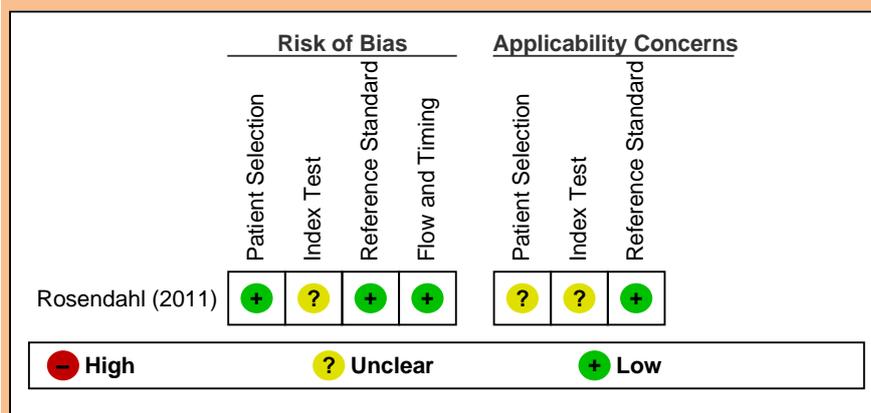
Total References retrieved (after de-duplication): 23



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issues to note are that the study population may not be directly representative of an unselected symptomatic population of patients presenting to the UK-based GP, that the index test does not specify the criteria for malignancy which may limit its external validity, and that the results

presented are based on a best case scenario, and are therefore likely to be inflated, and only available for skin malignancy as a whole and not for squamous cell carcinoma separately.



Study results

Table 1: Squamous cell carcinoma of the skin: Study results.

Study	Intervention	Prevalence	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	False negativity rate
Rosendahl (2011)	Clinical images and dermatoscopy	138 malignancies/463 lesions	82.6% (NR)	80% (NR)	NR (NR)	17.4% (NR)

NR = Not reported

No evidence was identified pertaining to the diagnostic accuracy of excision biopsy of the lesion in patients with suspected squamous cell cancer where the clinical responsibility was retained by primary care.

Evidence statement(s):

Dermatoscopy and clinical images (1 study, N = 463 lesions/389 patients) performed in symptomatic patients presenting in a primary care setting is associated with a best-case sensitivity of 82.6%, specificity of 80%, and false negativity rate of 17.4% for skin malignancy. The study was associated with 1 bias and 2 applicability concerns (See also Table 1)..

Evidence tables

Rosendahl (2011)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Consecutive series of lesions submitted for histology from the primary care skin cancer clinic of one of the authors.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Probably
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 463 pigmented lesions from 389 patients, mean (SD) age = 57 (17) years, 32.6% females. Lesion location: Trunk: N = 241; extremities: N = 128; head and face: N = 82; palms and soles: N = 10. Histopathologically, 246 pigmented lesions turned out to be melanocytic and 217 were of non-melanocytic origin.</p> <p>Final diagnoses: Malignant lesions: Basal cell carcinoma: N = 72; squamous cell carcinoma: N = 37; melanoma: N = 29. Benign lesions: Melanocytic nevi: N = 217; seborrheic keratosis: N = 43; solar lentigo: N = 37; lichen planus-like keratosis: N = 21, others: N = 7.</p> <p><u>Inclusion criteria:</u> All pigmented lesions biopsied or excised during a 30-month period. <i>Patients included are only those who received resection. This changes the spectrum of disease as it excludes patients with lesions that were not considered concerning enough to warrant resection.</i></p> <p><u>Exclusion criteria:</u> Poor image quality (N = 3).</p> <p><u>Clinical setting:</u> Primary care skin cancer practice in Queensland, Australia</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	<p>For each lesion: A triplet of high-resolution digital images consisting of two clinical images (overview and close-up) followed by one dermatoscopic image. The clinical images were taken with Canon EOS digital single lens reflex cameras. The close-up was taken using a macro lens (60-mm f2.8 macro, Canon) with diffuse illumination at a constant reproduction ratio determined by a custom-fabricated spacer. The degree of magnification of the close-up images was similar to that of the dermatoscopy images. Dermatoscopic images were nonpolarising, preferentially using the Dermlite Fluid device (3 Gen, San Juan, Capistrano, Ca); alternatively Dermlite Foto (custom nonpolarised; 3 Gen) and Heine Delta 20 devices (Heines, Optotechnic GmbH< Herrsching, Germany) were used for large and inaccessible lesions, respectively. Dermatoscopic photographs were taken with Canon EOS single lens reflex cameras. Images were presented to the assessors as powerpoint slides. After inspection of the images, the assessor was required to give a diagnosis (criteria not reported, so presumably based on qualitative criteria). Dermatoscopic images were also screened for asymmetry of structure and colour (“chaos”) and for clues to malignancy. Asymmetry of colour and structure were defined according to the basic principles of pattern analysis as revised by Kittler (2007, Dermatopathology: Practical & Conceptual, 13:1). Clues to malignancy included: Eccentric structureless zone (any colour except skin colour), gray or blue structures, peripheral black dots or clods, segmental radial lines or pseudopods, polymorphous vessels, white lines, thick reticular or branched lines, and parallel lines on ridges (acral lesions). <i>Not further information regarding the specific cut-off criteria for malignancy reported. The reporting of the results suggests that the test performance is based on best possible scenario.</i></p>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test	Unclear risk

have introduced bias?		
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Histopathology	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	The results are presented for all malignancies combined. The 2-by-2 table could not be extracted and the results could not be separated into the different malignancies	

References

Included Studies

Rosendahl C, Tschandl P, Med C, Cameron A, Kittler H. Diagnostic accuracy of dermatoscopy for melanocytic and nonmelanocytic pigmented lesions. *Journal of the American Academy of Dermatology* 2011;64(6):1068-73.

Excluded Studies

Abbas Q, Celebi ME, Garcia IF, Rashid M. Lesion border detection in dermoscopy images using dynamic programming. *Skin Research and Technology* 2011;17(1):91-100.

Exclusion Reason: Not in PICO

Adinarayan M, Krishnamurthy SP. Clinicopathological evaluation of nonmelanoma skin cancer. *Indian Journal of Dermatology* 2011;56(6):670-2.

Exclusion Reason: Narrative Review

Ahmed R, Soldin M. Incomplete excision rate of basal cell carcinoma: A 2-year retrospective clinical audit. *European Journal of Surgical Oncology* 2011;37(11):984.

Exclusion Reason: Not in PICO

Ahmad K, Siah T, Langtry JAA. Recurrent and incompletely excised nonmelanoma skin cancers referred for Mohs micrographic surgery. *British Journal of Dermatology* 2012;167:56.

Exclusion Reason: Not in PICO

- Ahmed, M. M., Moore, B. A. & Schmalbach, C. E. (2014) Utility of Head and Neck Cutaneous Squamous Cell Carcinoma Sentinel Node Biopsy: A Systematic Review. *Otolaryngology-Head and Neck Surgery*, 150: 180-187.
Exclusion Reason: Not in PICO
- Aitken JF, Janda M, Elwood M, Youl PH, Ring IT, Lowe JB. Clinical outcomes from skin screening clinics within a community-based melanoma screening program. *Journal of the American Academy of Dermatology* 2006;54(1):105-14.
Exclusion Reason: Not in PICO
- Alendar F, Drljevic I, Drljevic K, Alendar T. Early detection of melanoma skin cancer. *Bosnian Journal of Basic Medical Sciences* 2009;9(1):77-80.
Exclusion Reason: Not in PICO
- Albert MR, Weinstock MA. Keratinocyte carcinoma. [Review] [74 refs]. *CA: A Cancer Journal for Clinicians* 2003;53(5):292-302.
Exclusion Reason: Narrative Review
- Aldridge, R. B., Naysmith, L., Ooi, E. T., Murray, C. S. & Rees, J. L. (1111) The importance of a full clinical examination: Assessment of index lesions referred to a skin cancer clinic without a total body skin examination would miss one in three melanomas. *Acta Dermato-Venereologica*, 93: 2013.
Exclusion Reason: Not in PICO
- Allon, I., Allon, D. M., Anavi, Y. & Kaplan, I. (2013) The significance of surface ulceration as a sign of malignancy in exophytic oral mucosal lesions: myth or fact? *Head and neck pathology*, 7: 149-154.
Exclusion Reason: Not in PICO
- Alsharqi A, Wilson N, De Mozzi P. Basal cell carcinomas excision margins: Primary vs. secondary care. *British Journal of Dermatology* 2010;163:101.
Exclusion Reason: Narrative Review
- Alsharqi A, Wilson N. Will the introduction of new NICE guidelines change the management of basal cell carcinomas in the community? *British Journal of Dermatology* 2011;165:108.
Exclusion Reason: Narrative Review
- Altamura D, Menzies SW, Argenziano G, Zalaudek I, Soyer HP, Sera F, et al. Dermatoscopy of basal cell carcinoma: morphologic variability of global and local features and accuracy of diagnosis. *Journal of the American Academy of Dermatology* 2010;62(1):67-75.
Exclusion Reason: Not in PICO
- Angit C, Sharpe GR. Regional audit on squamous cell carcinoma excision margin. *Journal of the American Academy of Dermatology* 2011;64(2 SUPPL. 1):AB124.
Exclusion Reason: Not in PICO
- Anthony S, Vlachou C, Murdoch M, Tatnall F, Batta K, Brown V. Audit of 2-week-wait referrals: how does tertiary referral influence management? *British Journal of Dermatology* 2010;163:112-3.
Exclusion Reason: Not in PICO
- Anthony S, Ogden E, Blanshard M, Schofield JK. Basal cell carcinomas: Impact of national guidance on local specialist dermatology Department is likely to be manageable. *British Journal of Dermatology* 2009;161:64-5.
Exclusion Reason: Not in PICO
- Arits AHMM, Schlangen MHJ, Nelemans PJ, Kelleners-Smeets NWJ. Trends in the incidence of basal cell carcinoma by histopathological subtype. *Journal of the European Academy of Dermatology and Venereology* 2011;25(5):565-9.
Exclusion Reason: Not in PICO
- Arlt A, Luckhaupt H, Hildmann H. Diagnosis of recurrent squamous cell carcinomas with the tumor marker SCC-antigen. [German]. *Laryngo- Rhino- Otologie* 2000;79(4):207-12.
Exclusion Reason: Not in PICO

Astner S, Dietterle S, Otberg N, Rowert-Huber HJ, Stockfleth E, Lademann J. Clinical applicability of in vivo fluorescence confocal microscopy for noninvasive diagnosis and therapeutic monitoring of nonmelanoma skin cancer. *Journal of Biomedical Optics* 2008;13(1):014003-Feb.
Exclusion Reason: Not in PICO

Attili SK, Lesar A, McNeill A, Camacho-Lopez M, Moseley H, Ibbotson S, et al. An open pilot study of ambulatory photodynamic therapy using a wearable low-irradiance organic light-emitting diode light source in the treatment of nonmelanoma skin cancer. *British Journal of Dermatology* 2009;161(1):170-3.
Exclusion Reason: Not in PICO

Asuquo ME, Ebughe G. Major dermatological malignancies encountered in the University of Calabar Teaching Hospital, Calabar, southern Nigeria. *International Journal of Dermatology* 2012;51:32-6.
Exclusion Reason: Not in PICO

Baade PD, Youl PH, Janda M, Whiteman DC, Del Mar CB, Aitken JF. Factors associated with the number of lesions excised for each skin cancer: a study of primary care physicians in Queensland, Australia. *Archives of Dermatology* 2008;144(11):1468-76.
Exclusion Reason: Not in PICO

Bakis S, Irwig L, Wood G, Wong D. Exfoliative cytology as a diagnostic test for basal cell carcinoma: a meta-analysis. *British Journal of Dermatology* 2004;150(5):829-36.
Exclusion Reason: Not in PICO

Balogh K, Trehan P, Bashir S, Higgins E, Morris-Jones R. Skin cancer 'filtered screening' by dermatologists: the 2-week wait system. *British Journal of Dermatology* 2012;167:63.
Exclusion Reason: Not in PICO

Barry J, Oon SF, Watson R, Barnes L. The management of basal cell carcinomas. *Irish Medical Journal* 2006;99(6):179-81.
Exclusion Reason: Not in PICO

Bastiaens MT, Struyk L, Tjong AHung SP, Gruis N, ter Huurne J, Westendorp RG, et al. Cutaneous squamous cell carcinoma and p53 codon 72 polymorphism: a need for screening? *Molecular Carcinogenesis* 2001;30(1):56-61.
Exclusion Reason: Not in PICO

Bataille V, Hargest E, Brown V, Blackwell V, Dawe S, Cooper A, et al. A teledermatology pilot study in Hertfordshire: Triage of 2-week-wait referrals. *British Journal of Dermatology* 2011;165:137-8.
Exclusion Reason: Not in PICO

Beby F, Kodjikian L, Roche O, Bouvier R, Donat D, Guerillon F, et al. [Conjunctival tumors in children. A histopathologic study of 42 cases]. [French]. *Journal Francais d Ophthalmologie* 2005;28(8):817-23.
Exclusion Reason: Not in PICO

Behrens, A., May, A., Manner, H., Pohl, J. & Ell, C. (2013) Esophageal precancerous lesions: Early diagnosis, treatment, and preservation of quality of life. [German]. *Internist*, 54: 683-690.
Exclusion Reason: Narrative review

Bernard P, Derancourt C, Arnoult-Coudoux E, Picot R, Delvincourt C. Skin cancer diagnosis by dermatologists in the region of Champagne-Ardenne: A prospective study. *Annales de Dermatologie et de Venereologie* 2001;128(8-9):883-7.
Exclusion Reason: Not in PICO

Bhatti AZ, Asif S, Alwan M. Factors affecting incomplete excision of nonmelanoma skin cancers in New Zealand. *Annals of Plastic Surgery* 2006;57(5):513-6.
Exclusion Reason: Not in PICO

Bhatnagar A, Mohamad S, Sandramouli S. 'Fast-tracking' cancer referrals: application for periocular basal cell carcinoma. *Eye* 2006;20(4):428-30.
Exclusion Reason: Not in PICO

Blakeslee D, Vaughan CW, Shapshay SM. Excisional biopsy in the selective management of T1 glottic cancer: A three-year follow-up study. *Laryngoscope* 1984;94(4):488-94.

Exclusion Reason: Not in PICO
Blum A, Bauer J, Rassner G, Garbe C. Early detection of skin cancer. [German]. *Onkologie* 2002;8(10):1064-71.
Exclusion Reason: Narrative Review
Boiko PE, Koepsell TD, Larson EB, Wagner EH. Skin cancer diagnosis in a primary care setting. *Journal of the American Academy of Dermatology* 1996;34(4):608-11.
Exclusion Reason: Narrative Review
Bolac C, Cordel N, Deschamps L, Renier M, Quist D, Derancourt C. Diagnosis of skin cancer by dermatologists in the French West Indies: A prospective study. *Annales de Dermatologie et de Venereologie* 2011;138(1):11-6.
Exclusion Reason: Not in PICO
Bollschiweiler E, Ell C. Squamous cell carcinoma and adenocarcinoma of the esophagus. Differences in epidemiology, tumor biology, diagnostic procedures, and prevention. [German]. *Onkologie* 2004;10(11):1168-78.
Exclusion Reason: Narrative Review
Borgulya M, Kurz CM, Knoll T, Velten T, Vieth M, Ell C, et al. Diagnosis of early barrett's neoplasia and esophageal squamous cell neoplasia by electrical bio-impedance spectroscopy in human tissue. *Gastrointestinal Endoscopy* 2012;75(4 SUPPL. 1):AB127.
Exclusion Reason: Not in PICO
Bostock-Ling N. Excising basal cell carcinoma in general practice. *Australian Family Physician* 2006;35(7):558-60.
Exclusion Reason: Narrative Review
Bowns IR, Collins K, Walters SJ, McDonagh AJ. Telemedicine in dermatology: a randomised controlled trial. *Health Technology Assessment (Winchester, England)* 2006;10(43):iii-v.
Exclusion Reason: Not in PICO
Bower CP, Lear JT, de Berker DA. Basal cell carcinoma follow-up practices by dermatologists: a national survey. *British Journal of Dermatology* 2001;145(6):949-56.
Exclusion Reason: Not in PICO
Bradley N, Topham E. A service-evaluation of recurrence following curettage and cautery treatment of well-differentiated primary cutaneous squamous cell carcinoma. *British Journal of Dermatology* 2012;167:59.
Exclusion Reason: Not in PICO
Brewster DH, Bhatti LA, Inglis JH, Nairn ER, Doherty VR. Recent trends in incidence of nonmelanoma skin cancers in the East of Scotland, 1992-2003. *British Journal of Dermatology* 2007;156(6):1295-300.
Exclusion Reason: Not in PICO
Bristow Ivan, Bowling Jonathan. Dermoscopy as a technique for the early identification of foot melanoma. *Journal of Foot and Ankle Research* 2009;2(1):14.
Exclusion Reason: Not in PICO
Brown SJ, Lawrence CM. The management of skin malignancy: to what extent should we rely on clinical diagnosis? *British Journal of Dermatology* 2006;155(1):100-3.
Exclusion Reason: Narrative Review
Brundel K-H. Skin cancer in general practice. [German]. *Dermatosen in Beruf und Umwelt* 1990;38(2):54-7.
Exclusion Reason: Not in PICO
Buis PAJ, Chorus RMH, van Diest PJ. Value of histopathologic analysis of skin excisions by GPs. *British Journal of General Practice* 2005;55(515):458-60.
Exclusion Reason: Not in PICO
Burghout, K., Sigurdsson, V. & Toonstra, J. (2013) Non-melanoma skin cancer. [Dutch]. *Huisarts en Wetenschap*, 56: 174-178.
Exclusion Reason: Narrative review

Butani A, Arbesfeld DM, Schwartz RA. Premalignant and early squamous cell carcinoma. *Clinics in Plastic Surgery* 2005;32(2):223-+.
Exclusion Reason: Not in PICO

Carducci M, Bozzetti M, Foscolo AM, Betti R. Margin detection using digital dermatoscopy improves the performance of traditional surgical excision of basal cell carcinomas of the head and neck. *Dermatologic Surgery* 2011;37(2):280-5.
Exclusion Reason: Not in PICO

Carli P, Chiarugi A, De Giorgi V. Examination of lesions (including dermoscopy) without contact with the patient is associated with improper management in about 30% of equivocal melanomas. *Dermatologic Surgery* 2005;31(2):169-72.
Exclusion Reason: Not in PICO

Carter EJ, Whittam LR, Buckley DA. Failure of adherence to NICE guidelines for skin cancer surgery in general practice. *British Journal of Dermatology* 2009;161:63.
Exclusion Reason: Not in PICO

Carter J, Evans C, Ghebre R, Glubka B, Downs L. Superficially invasive squamous cell carcinoma of the vulva: Is radical excision necessary? *Gynecologic Oncology* 2012;125:S83.
Exclusion Reason: Not in PICO

Chaidemenos G, Apalla Z, Trigoni A, Koussidou T, Karakatsanis G. Inability of dermoscopy to differentiate early-stage squamous cell carcinoma from keratoacanthoma. *Melanoma Research* 2010;20:e66.
Exclusion Reason: N=2

Chambers M, Esdaile B, De Vos S, Bowling J, Cassell O, Turner R, et al. The oxfordshire community dermatology service. *British Journal of Dermatology* 2012;167:97.
Exclusion Reason: Not in PICO

Chan LS, Scholes NJ, Jones M. Skin excisions: not so simple for the regionally based general surgical trainee. *Australian Journal of Rural Health* 2011;19(4):205-10.
Exclusion Reason: Not in PICO

Chattopadhyay, M. & Ha, T. (2013) How to examine a patient with suspected skin cancer. *Medicine (United Kingdom)*, 41: 400-401.
Exclusion Reason: Narrative review

Cheah PL, Liam CK, Yap SF, Looi LM. Squamous cell carcinoma antigen as an adjunct tumour marker in primary carcinoma of the lung. *Journal of Clinical Pathology* 1994;47(6):535-7.
Exclusion Reason: Not in PICO

Chen P, Patel DC. Evaluation of surgical excision of non-melanoma skin cancers - A retrospective study. *Australasian Journal of Dermatology* 2011;52(4):A9.
Exclusion Reason: Not in PICO

Cheng B, Joe Stanley R, Stoecker WV, Osterwise CT, Stricklin SM, Hinton KA, et al. Automatic dirt trail analysis in dermoscopy images. *Skin Research & Technology* 2013;19(1):e20-6.
Exclusion Reason: Not in PICO

Cheng A, Bennett A, Pogrel MA, Schmidt BL. Should tumor depth measured from an incisional biopsy be used to guide the decision to perform an elective neck dissection? *Journal of Oral and Maxillofacial Surgery* 2012;70(9 SUPPL. 2):e-1.
Exclusion Reason: Not in PICO

Chiesa F, Sala L, Costa L, Moglia D, Mauri M, Podrecca S, et al. Excision of oral leukoplakias by CO2 laser on an out-patient basis: a useful procedure for prevention and early detection of oral carcinomas. *Tumori* 1986;72(3):307-12.
Exclusion Reason: Not in PICO

Chong SLP, Ferguson L, Lateo S. Skin cancer surgery in primary care: Results of an audit and re-audit. *British Journal of Dermatology* 2012;167:39.
Exclusion Reason: Not in PICO

Choy B, Bandla S, Xia Y, Tan D, Pennathur A, Luketich JD, et al. Clinicopathologic characteristics of high expression of Bmi-1 in esophageal adenocarcinoma and squamous cell carcinoma. *BMC Gastroenterology* 2012;12:146.
Exclusion Reason: Not in PICO

Chren MM, Sahay AP, Sands LP, Maddock L, Lindquist K, Bertenthal D, et al. Variation in care for nonmelanoma skin cancer in a private practice and a veterans affairs clinic. *Medical Care* 2004;42(10):1019-26.
Exclusion Reason: Not in PICO

Civantos F Jr, Zitsch R, Bared A, Amin A. Sentinel node biopsy for squamous cell carcinoma of the head and neck. [Review] [64 refs]. *Journal of Surgical Oncology* 2008;97(8):683-90.
Exclusion Reason: Narrative Review

Clarke P. Nonmelanoma skin cancers - treatment options. *Australian Family Physician* 2012;41(7):476-80.
Exclusion Reason: Narrative Review

Cleary RK, Schaldenbrand JD, Fowler JJ, Schuler JM, Lampman RM. Treatment options for perianal Bowen's disease: survey of American Society of Colon and Rectal Surgeons Members. *American Surgeon* 2000;66(7):686-8.
Exclusion Reason: Not in PICO

Cooper SM, Wojnarowska F. The accuracy of clinical diagnosis of suspected premalignant and malignant skin lesions in renal transplant recipients. *Clinical & Experimental Dermatology* 2002;27(6):436-8.
Exclusion Reason: Not in PICO

Cortinas Saenz M, Saenz Guirado S, Gamez Moreno J, Iglesias Cerrillo JA, Pardo Martinez A, Martinez Gomez L. Analysis of results, quality indicators, and postsurgical complications in an outpatient dermatological surgery program. *Actas Dermo-Sifiliograficas* 2012;103(1):36-43.
Exclusion Reason: Not in PICO

Corwin P, Munn E, Nicholls D. A study of general practitioners' skin surgery in Canterbury. *New Zealand Medical Journal* 1997;110(1047):253-5.
Exclusion Reason: Not in PICO

Costa S, De Nuzzo M, Rubino A, Rambelli V, Marinelli M, Santini D, et al. Independent determinants of inaccuracy of colposcopically directed punch biopsy of the cervix. *Gynecologic Oncology* 2003;90(1):57-63.
Exclusion Reason: Not in PICO

Cox NH. Basal cell carcinoma in young adults. *British Journal of Dermatology* 1992;127(1):26-9.
Exclusion Reason: Not in PICO

Cox NH, Wagstaff R, Popple AW. Using clinicopathological analysis of general practitioner skin surgery to determine educational requirements and guidelines. *BMJ* 1992;304(6819):93-6.
Exclusion Reason: Not in PICO

Cuellar F, Vilalta A, Puig S, Palou J, Zaballos P, Malveyh J. Dermoscopy of early recurrent basal cell carcinoma. *Archives of Dermatology* 2008;144(9):1254.
Exclusion Reason: N=3

de Hullu JA, Hollema H, Piers DA, Verheijen RH, van Diest PJ, Mourits MJ, et al. Sentinel lymph node procedure is highly accurate in squamous cell carcinoma of the vulva. *Journal of Clinical Oncology* 2000;18(15):2811-6.
Exclusion Reason: Not in PICO

De Berker DAR, Poirier V, Takwale A. Follow-up preferences for patients with basal cell carcinoma: The basis for modelling clinical practice and commissioning. *British Journal of Dermatology* 2010;163:112.
Exclusion Reason: Not in PICO

de Giorgi V, Alfaioli B, Papi F, Janowska A, Grazzini M, Lotti T, et al. Dermoscopy in Pigmented Squamous Cell Carcinoma. *Journal of Cutaneous Medicine and Surgery* 2009;13(6):326-9.

Exclusion Reason: N=1
 Delaney EK, Duckworth L, Thompson WD, Lee AJ, Murchie P. Excising squamous cell carcinomas: comparing the performance of GPs, hospital skin specialists and other hospital specialists. *Family Practice* 2012;29(5):541-6.
 Exclusion Reason: Not in PICO

Demir H, Isken T, Kus E, Tan YZ, Isgoren S, Gorur GD, et al. Sentinel lymph node biopsy with a gamma probe in patients with high-risk cutaneous squamous cell carcinoma: follow-up results of sentinel lymph node-negative patients. *Nuclear Medicine Communications* 2011;32(12):1216-22.
 Exclusion Reason: Not in PICO

Dewan P, Panagou E, Ajen S, Bewley AP, Sahota A, Gibbon K. Are NICE skin cancer guidelines being followed in primary care? A re-audit to review changes in practice in an inner city setting. *British Journal of Dermatology* 2010;163:65.
 Exclusion Reason: Not in PICO

Dixon AJ, Hall RS. Managing skin cancer--23 golden rules. [Review] [0 refs]. *Australian Family Physician* 2005;34(8):669-71.
 Exclusion Reason: Narrative Review

Dixon A. Rare skin cancers in general practice. *Australian Family Physician* 2007;36(3):141-3.
 Exclusion Reason: N=1

Dua J, Clayton R. A comparison of skin cancer excision rates between general practitioners and dermatologists in West Berkshire, South East England. *British Journal of Dermatology* 2012;167:60-1.
 Exclusion Reason: Not in PICO

Durdu M, Baba M, Seckin D. Dermatoscopy versus Tzanck smear test: A comparison of the value of two tests in the diagnosis of pigmented skin lesions. *Journal of the American Academy of Dermatology* 2011;65(5):972-82.
 Exclusion Reason: Not in PICO

Eekhof, J. A. (2013) [Actinic keratosis: the art of doing nothing]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 157: A5363.
 Exclusion Reason: Narrative review

Ehrig T, Cockerell C, Piacquadio D, Dromgoole S. Actinic keratoses and the incidence of occult squamous cell carcinoma: a clinical-histopathologic correlation. *Dermatologic Surgery* 2006;32(10):1261-5.
 Exclusion Reason: Not in PICO

Emery JD, Hunter J, Hall PN, Watson AJ, Moncrieff M, Walter FM. Accuracy of SIAscopy for pigmented skin lesions encountered in primary care: Development and validation of a new diagnostic algorithm. *BMC Dermatology* 2010;10.
 Exclusion Reason: Not in PICO

Epstein JB, Scully C. Assessing the patient at risk for oral squamous cell carcinoma. [Review] [87 refs]. *Special Care in Dentistry* 1997;17(4):120-8.
 Exclusion Reason: Narrative review

Epstein JB, Guneri P, Boyacioglu H, Abt E. The limitations of the clinical oral examination in detecting dysplastic oral lesions and oral squamous cell carcinoma. *Journal of the American Dental Association* 2012;143(12):1332-42.
 Exclusion Reason: Not in PICO

Epstein JB, Silverman S, Epstein JD, Lonky SA, Bride MA. Analysis of oral lesion biopsies identified and evaluated by visual examination, chemiluminescence and toluidine blue. *Oral Oncology* 2008;44(6):538-44.
 Exclusion Reason: Not in PICO

Epstein JB, Gorsky M, Cabay RJ, Day T, Gonsalves W. Screening for and diagnosis of oral premalignant lesions and oropharyngeal squamous cell carcinoma - Role of primary care physicians. *Canadian Family Physician* 2008;54(6):870-5.

Exclusion Reason: Not in PICO

Epstein, J. B., Guneri, P., Boyacioglu, H. & Abt, E. (2013) The limitations of the clinical oral examination in detecting dysplastic oral lesions and oral squamous cell carcinoma.[Reprint of J Am Dent Assoc. 2012 Dec;143(12):1332-42; PMID: 23204089]. *Texas Dental Journal*, 130: 410-424.

Exclusion Reason: Not in PICO

Felton J, Mellerio JE. Cutaneous squamous cell carcinomas in epidermolysis bullosa: A 20-year retrospective study. *British Journal of Dermatology* 2012;167:55-6.

Exclusion Reason: Not in PICO

Ferrandiz L, Ruiz-de-Casas A, Trakatelli M, de Vries E, Ulrich M, Aquilina S, et al. Assessing physicians' preferences on skin cancer treatment in Europe. *British Journal of Dermatology* 2012;167:Suppl-35.

Exclusion Reason: Not in PICO

Ferreira, P., Rodrigues, M., Ledo, S., Senra, R., Costa, S., V, Rocha, M. & Paiva, C. (2013) Back pain as the first manifestation of a cavum tumor. *European Journal of Internal Medicine*, 24: e149.

Exclusion Reason: Not in PICO

Firnhaber JM. Diagnosis and treatment of Basal cell and squamous cell carcinoma. [Review]. *American Family Physician* 2012;86(2):161-8.

Exclusion Reason: Narrative Review

FitzGerald KL, Buttner PG, Donovan SA. Nonpigmented skin lesions - how many are nonmelanoma skin cancer? *Australian Family Physician* 2006;35(7):555-7.

Exclusion Reason: Not in PICO

Fleischer AB, Feldman SR, Barlow JO, Zheng BY, Hahn HB, Chuang TY, et al. The specialty of the treating physician affects the likelihood of tumor-free resection margins for basal cell carcinoma: Results from a multi-institutional retrospective study. *Journal of the American Academy of Dermatology* 2001;44(2):224-30.

Exclusion Reason: Not in PICO

Fontes, K. B., Cunha, K. S., Rodrigues, F. R., Silva, L. E. & Dias, E. P. (2013) Concordance between cytopathology and incisional biopsy in the diagnosis of oral squamous cell carcinoma. *Brazilian oral research*, 27: 122-127.

Exclusion Reason: Not in PICO

Freitag CP, Barros SG, Krueh CD, Putten AC, Dietz J, Gruber AC, et al. Esophageal dysplasias are detected by endoscopy with Lugol in patients at risk for squamous cell carcinoma in southern Brazil. *Diseases of the Esophagus* 1999;12(3):191-5.

Exclusion Reason: Not in PICO

French Society of Dermatology. Guideline for the diagnosis and treatment of cutaneous squamous cell carcinoma and precursor lesions. *Annales de Dermatologie et de Venereologie* 2009;136:Suppl-86.

Exclusion Reason: Guidelines

Friedman T, Klein D, Hadad E, Westreich M, Shalom A. [Diagnostic accuracy of skin lesions excised by a plastic surgeon]. [Hebrew]. *Harefuah* 75;147(4):305-8.

Exclusion Reason: Not in PICO

Fujishiro M, Yahagi N, Kakushima N, Kodashima S, Muraki Y, Ono S, et al. Endoscopic submucosal dissection of esophageal squamous cell neoplasms. *Clinical Gastroenterology & Hepatology* 2006;4(6):688-94.

Exclusion Reason: Not in PICO

Gait R, Milligan A, Burd RM, Fletcher A. A review of procedures carried out on basal cell carcinomas by Primary care physicians. *British Journal of Dermatology* 2009;161:64.

Exclusion Reason: Not in PICO

- Gao L, Lin WH, Gong ZJ, Liu Y, Liu YM, Zhu MH. [Fine needle aspiration cytology of eyelid sebaceous gland carcinoma and its differential diagnosis]. [Chinese]. *Chung-Hua Ping Li Hsueh Tsa Chih - Chinese Journal of Pathology* 2004;33(1):36-9.
Exclusion Reason: Not in PICO
- Garcia-Solano J, Lopez-Avila A, Acosta J, Montalbana S, Sanchez-Sanchez C, Benito A, et al. Non-melanoma skin cancer with positive surgical and histological margins. Comparative study among the departments involved in their surgical excision. [Spanish]. *Actas Dermo-Sifilograficas* 2004;95(6):358-61.
Exclusion Reason: Not in PICO
- Garner KL, Rodney WM. Basal and squamous cell carcinoma. [Review] [21 refs]. *Primary Care; Clinics in Office Practice* 2000;27(2):447-58.
Exclusion Reason: Narrative Review
- Gerbert B, Bronstone A, Maurer T, Hofmann R, Berger T. Decision support software to help primary care physicians triage skin cancer - A pilot study. *Archives of Dermatology* 2000;136(2):187-92.
Exclusion Reason: Not in PICO
- Giacomel, J. & Zalaudek, I. (2013) Pink Lesions. *Dermatologic Clinics*, 31: 649-678.
Exclusion Reason: Narrative review
- Gilde K. [Malignant tumors of the skin]. [Review] [25 refs] [Hungarian]. *Orvosi Hetilap* 2006;147(48):2321-30.
Exclusion Reason: Narrative Review
- Girardi F, Pickel H, Joura EA, Breitenecker G, Gitsch G, Graf AH, et al. [Guidelines for diagnosis and therapy of intraepithelial neoplasia and early invasive carcinoma of the female lower genital system (cervix uteri, vagina, vulva) established by the AGK (Colposcopy Work Group in the OGGG [Austrian Society of Gynecology and Obstetrics])]. [German]. *Gynakologisch-Geburtshilfliche Rundschau* 2001;41(3):197-200.
Exclusion Reason: Guidelines
- Golberg O, Alexandroff AB, Burd RM. Seasonal variation in 2-week-wait skin cancer referrals is not mirrored by changes in incidence of skin cancer: A message for service provision. *British Journal of Dermatology* 2011;165:20-1.
Exclusion Reason: Not in PICO
- Goldberg LH, Rubin HA. Management of basal cell carcinoma. Which option is best? *Postgraduate Medicine* 1961;85(1):57-8.
Exclusion Reason: Narrative Review
- Goldstone SE, Winkler B, Ufford LJ, Alt E, Palefsky JM. High prevalence of anal squamous intraepithelial lesions and squamous-cell carcinoma in men who have sex with men as seen in a surgical practice. *Diseases of the Colon & Rectum* 2001;44(5):690-8.
Exclusion Reason: Not in PICO
- Gonsalves WC, Chi AC, Neville BW. Common oral lesions: Part II. Masses and neoplasia. *American Family Physician* 2007;75(4):509-12.
Exclusion Reason: Narrative Review
- Goulding JMR, Levine S, Blizard RA, Deroide F, Swale VJ. Dermatological surgery: a comparison of activity and outcomes in primary and secondary care. *British Journal of Dermatology* 2009;161(1):110-4.
Exclusion Reason: Not in PICO
- Graves J, Fleischman MH, Goldstein GD. Derm Access: A new triage system to rapidly identify suspicious skin lesions. *Dermatologic Surgery* 2006;32(12):1486-90.
Exclusion Reason: Not in PICO
- Griffiths RW, Suvarna SK, Stone J. Do basal cell carcinomas recur after complete conventional surgical excision? *British Journal of Plastic Surgery* 2005;58(6):795-805.
Exclusion Reason: Not in PICO

Gross EA. Nonmelanoma skin cancer: Clues to early detection, keys to effective treatment. *Consultant* 1999;39(3):829-39.
Exclusion Reason: Narrative Review

Gudi V, Ormerod AD, Dawn G, Green C, MacKie RM, Douglas WS, et al. Management of basal cell carcinoma by surveyed dermatologists in Scotland. *Clinical & Experimental Dermatology* 2006;31(5):648-52.
Exclusion Reason: Not in PICO

Gurudutt VV, Genden EM. Cutaneous squamous cell carcinoma of the head and neck. *Journal of Skin Cancer* 2011;2011:502723.
Exclusion Reason: Not in PICO

Guther S, Ramrath K, Dyll-Smith D, Landthaler M, Stolz W. Development of a targeted risk-group model for skin cancer screening based on more than 100,000 total skin examinations. *Journal of the European Academy of Dermatology & Venereology* 2012;26(1):86-94.
Exclusion Reason: Not in PICO

Haliasos, E. C., Kerner, M., Jaimes, N., Zalaudek, I., Malvey, J., Lanschuetzer, C. M., Hinter, H., Hofmann-Wellenhof, R., Braun, R. P. & Marghoob, A. A. (2013) Dermoscopy for the pediatric dermatologist, part ii: dermoscopy of genetic syndromes with cutaneous manifestations and pediatric vascular lesions. [Review]. *Pediatric Dermatology*, 30: 172-181.
Exclusion Reason: Narrative review

Halpern SM, Shall L. Establishment of a primary care-based teledermatology service in Kent. *British Journal of Dermatology* 2011;165:136-7.
Exclusion Reason: Not in PICO

Hamm H, Hoger PH. Skin tumors in childhood. [Review]. *Deutsches Arzteblatt International* 2011;108(20):347-53.
Exclusion Reason: Narrative Review

Han MW, Lee B-J, Jang YJ, Chung Y-S. Clinical value of office-based endoscopic incisional biopsy in diagnosis of nasal cavity masses. *Otolaryngology - Head and Neck Surgery* 2010;143(3):341-7.
Exclusion Reason: Not in PICO

Hansen C, Wilkinson D, Hansen M, Soyer HP. Factors contributing to incomplete excision of nonmelanoma skin cancer by Australian general practitioners. *Archives of Dermatology* 2009;145(11):1253-60.
Exclusion Reason: Not in PICO

Haw, W. Y., Fraser, S., Affleck, A. & Holme, A. (2014) Skin cancer excision performance in primary and secondary care in Scotland. *British Journal of Dermatology*, 171: 25.
Exclusion Reason: Not in PICO

Hayashi T, Muto M, Hayashi R, Minashi K, Yano T, Kishimoto S, et al. Usefulness of narrow-band imaging for detecting the primary tumor site in patients with primary unknown cervical lymph node metastasis. *Japanese Journal of Clinical Oncology* 2010;40(6):537-41.
Exclusion Reason: Not in PICO

Heal CF, Raasch BA, Buettner PG, Weedon D. Accuracy of clinical diagnosis of skin lesions. *British Journal of Dermatology* 2008;159(3):661-8.
Exclusion Reason: Not in PICO

Heal C, Buettner P, Raasch B, Browning S. Minor skin excisions in general practice in North Queensland. *Australian Family Physician* 2006;35(10):825-8.
Exclusion Reason: Not in PICO

Hermes, H. M., Sahu, J., Schwartz, L. R. & Lee, J. B. (2014) - Clinical and histologic characteristics of clinically unsuspected melanomas. - *Clinics in Dermatology*, 32: 324-330.
Exclusion Reason: Not in PICO

Hernandez-Martin A, Arias-Palomo D, Barahona E, Hidalgo C, Munoz C, Garcia-Higuera I. [Analysis of surgical treatment for nonmelanoma skin cancer performed by dermatologists in a public hospital: clinical-pathological correlation, use of hospital resources, and waiting list time from

diagnosis]. [Spanish][Erratum appears in *Actas Dermosifiliogr.* 2008 Mar;99(2):170]. *Actas Dermosifiliograficas* 2007;98(10):694-701.
 Exclusion Reason: Not in PICO

Hjortdal O, Naess A, Berner A. Squamous cell carcinomas of the lower lip. *Journal of Cranio-Maxillo-Facial Surgery* 1995;23(1):34-7.
 Exclusion Reason: Narrative Review

Holmkvist KA, Rogers GS, Dahl PR. Incidence of residual basal cell carcinoma in patients who appear tumor free after biopsy. *Journal of the American Academy of Dermatology* 1999;41(4):600-5.
 Exclusion Reason: Not in PICO

Humphreys TR. Skin cancer: Recognition and management. *Clinical Cornerstone* 2001;4(1):23-9.
 Exclusion Reason: Narrative Review

Ishihara R, Inoue T, Hanaoka N, Takeuchi Y, Tsujii Y, Kanzaki H, et al. Autofluorescence imaging endoscopy for screening of esophageal squamous mucosal high-grade neoplasia: a phase II study. *Journal of Gastroenterology & Hepatology* 2012;27(1):86-90.
 Exclusion Reason: Not in PICO

Ismail N, D'Adhemar C, Kirby B, Collins P, Sheahan K, Lally A. An audit of basal cell carcinoma in St Vincent's University Hospital. *British Journal of Dermatology* 2012;167(6):e34-5.
 Exclusion Reason: Not in PICO

Jainkittivong A, Swadison S, Thangpitsityotin M, Langlais RP. Oral squamous cell carcinoma: a clinicopathological study of 342 Thai cases. *Journal of Contemporary Dental Practice [Electronic Resource]* 2009;10(5):E033-40.
 Exclusion Reason: Not in PICO

Janda, M., Youl, P., Neale, R., Aitken, J., Whiteman, D., Gordon, L. & Baade, P. (2014) - Clinical skin examination outcomes after a video-based behavioral intervention: analysis from a randomized clinical trial. - *JAMA Dermatology*, 150: 372-379.
 Exclusion Reason: Population not in PICO

Jeong W-J, Paik JH, Cho S-W, Sung M-W, Kim KH, Ahn S-H. Excisional biopsy for management of lateral tongue leukoplakia. *Journal of Oral Pathology and Medicine* 2012;41(5):384-8.
 Exclusion Reason: Not in PICO

Jerant AF, Johnson JT, Sheridan CD, Caffrey TJ. Early detection and treatment of skin cancer. [Review] [32 refs]. *American Family Physician* 375;62(2):357-68.
 Exclusion Reason: Narrative Review

Johnson SJ, Wadehra V. How predictive is a cervical smear suggesting invasive squamous cell carcinoma? *Cytopathology* 2001;12(3):144-50.
 Exclusion Reason: Not in PICO

Jung JE, Rah DK, Kim YO. Effects of preoperative biopsies on recurrence in head and neck skin cancer. *Archives of Plastic Surgery* 2012;39(5):518-21.
 Exclusion Reason: Not in PICO

Kahn, E., Sossong, S., Goh, A., Carpenter, D. & Goldstein, S. (2013) Evaluation of Skin Cancer in Northern California Kaiser Permanente's Store-and-Forward Teledermatology Referral Program. *Telemedicine and E-Health*, 19: 780-785.
 Exclusion Reason: Not in PICO

Kamyab-Hesari, K., Seirafi, H., Naraghi, Z. S., Shahshahani, M. M., Rahbar, Z., Damavandi, M. R., Naraghi, M. M., Rezvani, M. & Aghazadeh, N. (2014) Diagnostic accuracy of punch biopsy in subtyping basal cell carcinoma. *Journal of the European Academy of Dermatology and Venereology*, 28: 250-253.
 Exclusion Reason: Not in PICO

Karagozoglu KH, Castelijns J, Bloemena E, de Bree R, van der Waal L. [An enlarged lymph node in the neck; what to do?]. [Dutch]. *Nederlands Tijdschrift Voor Tandheelkunde* 2011;118(5):267-71.
 Exclusion Reason: Narrative Review

Kersten RC, Ewing-Chow D, Kulwin DR, Gallon M. Accuracy of clinical diagnosis of cutaneous eyelid lesions. *Ophthalmology* 1997;104(3):479-84.
Exclusion Reason: Not in PICO

Khalid S, Spicer A, Gee B, Carr R. The impact of Improved Outcome Guidance (IOG) for skin cancer: A comparative re-audit of excision rates of basal cell carcinomas by general practitioners in South Warwickshire. *British Journal of Dermatology* 2009;161:109.
Exclusion Reason: Not in PICO

Khorasgani MG, Simpson R, Burd RM. How effective is the skin cancer referral pathway? *British Journal of Dermatology* 2011;165:109.
Exclusion Reason: Not in PICO

Kibarian MA, Hruza GJ. Nonmelanoma skin cancer. Risks, treatment options, and tips on prevention. *Postgraduate Medicine* 1945;98(6):39-40.
Exclusion Reason: Narrative Review

Koch FP, Kunkel M, Biesterfeld S, Wagner W. Diagnostic efficiency of differentiating small cancerous and precancerous lesions using mucosal brush smears of the oral cavity--a prospective and blinded study. *Clinical Oral Investigations* 2011;15(5):763-9.
Exclusion Reason: Not in PICO

Koerner KR. Evaluation and treatment by general dentists of oral soft-tissue lesions. *Dentistry Today* 2006;25(7):90-5.
Exclusion Reason: Narrative Review

Kolm I, Hofbauer G, Braun RP. [Early diagnosis of skin cancer]. [Review] [German]. *Therapeutische Umschau* 2010;67(9):439-46.
Exclusion Reason: Narrative Review

Kok LP, Van Drunen R, Boon ME, Beck S, Van Coevorden RS. General practitioners use digital cameras and internet for telepathology of skin lesions. *Electronic Journal of Pathology and Histology* 2000;6(3):7-19.
Exclusion Reason: Narrative Review

Kopf AW, Salopek TG, Slade J, Marghoob AA, Bart RS. Techniques of cutaneous examination for the detection of skin cancer. *Cancer* 1995;75(2:Suppl):Suppl-90.
Exclusion Reason: Narrative Review

Krol S, Keijser LMT, Van Der Rhee HJ, Welvaart K. Screening for skin cancer in The Netherlands. *Acta Dermato-Venereologica* 1991;71(4):317-21.
Exclusion Reason: Not in PICO

Kundu, R. V. & Patterson, S. (2013) Dermatologic conditions in skin of color: part I. Special considerations for common skin disorders.[Summary for patients in *Am Fam Physician*. 2013 Jun 15;87(12):Online; PMID: 23939576]. *American Family Physician*, 87: 850-856.
Exclusion Reason: Narrative review

Kunte C, Konz B. Current recommendations in the treatment of basal cell carcinoma and squamous cell carcinoma of the skin. *Hautarzt* 2007;58(5):419-26.
Exclusion Reason: Narrative Review

Kusukawa J, Kameyama T, Nakamura Y. Evaluation of excisional biopsy for stage I and II squamous cell carcinoma of the oral cavity. *International Journal of Clinical Oncology* 1998;3(5):317-22.
Exclusion Reason: Not in PICO

Lacava V, Salesi N, Ferrone L, Veri A, Lembo R, Masi MC, et al. [Importance of dermatologic screening within the frame work of a general cancer prevention program]. [Italian]. *Minerva Medica* 2001;92(2):85-8.
Exclusion Reason: Not in PICO

Lai, W.-Y. (1111) An elderly man with a painful scaly nodule. *Hong Kong Practitioner*, 35: September.
Exclusion Reason: Not in PICO

Lathlean S. Skin cancer in general practice in South Australia. A five year study. *Australian Family Physician* 1999;28:Suppl-31.

Exclusion Reason: Not in PICO
Laukkanen A, Rummukainen J, Kivinen P, Lappalainen K. [Skin squamous cell carcinoma and its precancerous conditions]. [Review] [25 refs] [Finnish]. *Duodecim* 2006;122(1):71-9.
Exclusion Reason: Narrative Review

Lee C, Kang KH, Koh Y, Chang J, Chung HS, Park SK, et al. Characteristics of lung cancer in Korea, 1997. *Lung Cancer* 2000;30(1):15-22.
Exclusion Reason: Not in PICO

Liebman TN, Wang SQ. Detection of early basal cell carcinoma with dermoscopy in a patient with psoriasis. *Dermatology Online Journal* 2011;17(2):12.
Exclusion Reason: N=1

Lim D, Oakley AMM, Rademaker M. Better, sooner, more convenient: A successful teledermoscopy service. *Australasian Journal of Dermatology* 2012;53(1):22-5.
Exclusion Reason: Narrative Review

Lin, Y.-C., Perng, C.-L., Chang, Y.-M., Li, Y.-F., Tsai, Y.-M., Wu, G.-J. & Lin, C.-K. (2013) Coexistent squamous cell carcinoma and adenoid basal carcinoma in the uterine cervix and infection with human papillomavirus (HPV 31). *Taiwanese Journal of Obstetrics and Gynecology*, 52: 407-410.
Exclusion Reason: Not in PICO

Lober CW, Fenske NA. Basal cell, squamous cell, and sebaceous gland carcinomas of the periorbital region. [Review] [54 refs]. *Journal of the American Academy of Dermatology* 1991;25(4):685-90.
Exclusion Reason: Narrative Review

Lohmann CM, Solomon AR. Clinicopathologic variants of cutaneous squamous cell carcinoma. [Review] [82 refs]. *Advances in Anatomic Pathology* 2001;8(1):27-36.
Exclusion Reason: Narrative Review

Lopes LL, Alchorne ADD, Pereira GC, Lopes LRS, de Carvalho TC. Histological and immunohistochemical evaluation of basal cell carcinoma following curettage and electrodesiccation. *International Journal of Dermatology* 2008;47(6):610-4.
Exclusion Reason: Not in PICO

Luckey L. Seeding of head and neck cancer during placement of percutaneous gastrostomy tube. *American Journal of Gastroenterology* 2012;107:S279.
Exclusion Reason: Not in PICO

Lynget E, Hunskar S. [Skin neoplasms in general practice]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening* 2001;121(19):2281-3.
Exclusion Reason: Not in PICO

Maguire-Eisen M. Risk assessment and early detection of skin cancers. [Review] [69 refs]. *Seminars in Oncology Nursing* 2003;19(1):43-51.
Exclusion Reason: Narrative Review

Malberger E, Tillinger R, Lichtig C. Diagnosis of basal-cell carcinoma with aspiration cytology. *Acta Cytologica* 1984;28(3):301-4.
Exclusion Reason: Narrative Review

Malvey J, Puig S, Marti-Laborda RM. Dermoscopy of skin lesions in two patients with xeroderma pigmentosum. *British Journal of Dermatology* 2005;152(2):271-8.
Exclusion Reason: Not in PICO

Marchonda PJ, Krause LK, Jensen JD, Dellavalle RP. A North American perspective on dermoscopy: benefits, limitations, and grey zones. *Giornale Italiano di Dermatologia e Venereologia* 2010;145(1):89-97.
Exclusion Reason: Narrative Review

Marghoob AA. Basal and squamous cell carcinomas: What every primary care physician should know. *Postgraduate Medicine* 1997;102(2):139-59.
Exclusion Reason: Narrative Review

- Marghoob, A. A., Usatine, R. P. & Jaimes, N. (2013) Dermoscopy for the family physician. [Review]. *American Family Physician*, 88: 441-450.
Exclusion Reason: Narrative review
- Martinez JC, Otley CC. The management of melanoma and nonmelanoma skin cancer: A review for the primary care physician. *Mayo Clinic Proceedings* 2001;76(12):1253-65.
Exclusion Reason: Narrative Review
- Maybury, C. M., Craythorne, E. & Martin, B. (2013) An ulcerated nodule on the nose. *BMJ Case Reports*, 2013, 2013.
Exclusion Reason: Not in PICO
- McGuire JF, Ge NN, Dyson S. Nonmelanoma skin cancer of the head and neck I: histopathology and clinical behavior. *American Journal of Otolaryngology* 2009;30(2):121-33.
Exclusion Reason: Narrative Review
- McNulty-Brown E, Veysey E. An audit of all excisions undertaken by general practitioners in a rural community between March 2009 and March 2010. *British Journal of Dermatology* 2012;167:91-2.
Exclusion Reason: Not in PICO
- Medeiros F, Nascimento AF, Crum CP. Early vulvar squamous neoplasia: advances in classification, diagnosis, and differential diagnosis. [Review] [32 refs]. *Advances in Anatomic Pathology* 2005;12(1):20-6.
Exclusion Reason: Narrative Review
- Mehrotra R, Gupta DK. Exciting new advances in oral cancer diagnosis: avenues to early detection. [Review]. *Head & neck oncology* 2011;3:33.
Exclusion Reason: Narrative Review
- Mencia Gutierrez E, Herrero Lluch MJ, Gutierrez Diaz E, Galvez Ruiz A. [Basal cell and squamous cell carcinomas of the eyelid in adults under 50 years of age: 13 cases]. [Spanish]. *Archivos de la Sociedad Espanola de Oftalmologia* 2001;76(11):643-8.
Exclusion Reason: Not in PICO
- Menzies SW, Emery J, Staples M, Davies S, McAvoy B, Fletcher J, et al. Impact of dermoscopy and short-term sequential digital dermoscopy imaging for the management of pigmented lesions in primary care: a sequential intervention trial. *British Journal of Dermatology* 2009;161(6):1270-7.
Exclusion Reason: Not in PICO
- Menzies SW. Using dermoscopy to diagnose pigmented skin lesions. *Medicine Today* 2004;5(4):63-71.
Exclusion Reason: Narrative Review
- Menzies, S. W., Moloney, F. J., Byth, K., Avramidis, M., Argenziano, G., Zalaudek, I., Braun, R. P., Malvey, J., Puig, S., Rabinovitz, H. S., Oliviero, M., Cabo, H., Bono, R., Pizzichetta, M. A., Claesson, M., Gaffney, D. C., Soyer, H. P., Stanganelli, I., Scolyer, R. A., Guitera, P., Kelly, J., McCurdy, O., Llambrich, A., Marghoob, A. A., Zaballos, P., Kirchesch, H. M., Piccolo, D., Bowling, J., Thomas, L., Terstappen, K., Tanaka, M., Pellacani, G., Pagnanelli, G., Ghigliotti, G., Ortega, B. C., Crafter, G., Ortiz, A. M., Tromme, I., Karaarslan, I. K., Ozdemir, F., Tam, A., Landi, C., Norton, P., Kacar, N., Rudnicka, L., Slowinska, M., Simionescu, O., Di, S. A., Coates, E. & Kreusch, J. (2013) Dermoscopic evaluation of nodular melanoma. *JAMA Dermatology*, 149: 699-709.
Exclusion Reason: Not in PICO
- Milicic-Juhas V, Peric M, Pajtler M, Prvulovic I, Curzik D. Pap test--with or without vaginal smear? *Collegium Antropologicum* 2010;34(1):69-74.
Exclusion Reason: Not in PICO
- Miller SJ. II. Biopsy techniques for suspected nonmelanoma skin cancers. *Dermatologic Surgery* 2000;26(1):91.
Exclusion Reason: Narrative Review
- Moffatt CR, Green AC, Whiteman DC. Diagnostic accuracy in skin cancer clinics: the Australian experience. *International Journal of Dermatology* 2006;45(6):656-60.

Exclusion Reason: Not in PICO: Clinical versus histological diagnosis (not biopsy or dermatoscopy versus histology or follow up)

Mojca I, Kaczmarzyk T, Zaleska M, Stypulkowska J, Zapala-Pospiech A, Sadecki D. Value of the ViziLite Plus System as a diagnostic aid in the early detection of oral cancer/premalignant epithelial lesions. *Journal of Craniofacial Surgery* 2012;23(2):e162-4.
Exclusion Reason: Not in PICO

Monnier P, Savary M. Epidermoid cancer of the upper respiratory and digestive tracts. [French]. *Schweizerische medizinische Wochenschrift* 1986;116(51):1817-23.
Exclusion Reason: Narrative Review

Moreno G, Tran H, Chia ALK, Lim A, Shumack S. Prospective study to assess general practitioners' dermatological diagnostic skills in a referral setting. *Australasian Journal of Dermatology* 2007;48(2):77-82.
Exclusion Reason: Not in PICO

Morrison A, O'Loughlin S, Powell FC. Suspected skin malignancy: a comparison of diagnoses of family practitioners and dermatologists in 493 patients. *International Journal of Dermatology* 2001;40(2):104-7.
Exclusion Reason: Not in PICO

Morteza, A. S., Salama, S. & Alowami, S. (2013) Lymphoepithelioma-like carcinoma of the skin: case report and approach to surgical pathology sign out. *Rare Tumors*, 5: e47.
Exclusion Reason: Not in PICO

Morton CA, Downie F, Auld S, Smith B, Pol M, Baughan P, et al. Community photo-triage for skin cancer referrals: an aid to service delivery (Structured abstract). *Clinical and Experimental Dermatology* 2011;36:248-54.
Exclusion Reason: Not in PICO

Motley RJ, Gould DJ, Douglas WS, Simpson NB. Treatment of basal cell carcinoma by dermatologists in the United Kingdom. British Association of Dermatologists Audit Subcommittee and the British Society for Dermatological Surgery. *British Journal of Dermatology* 1995;132(3):437-40.
Exclusion Reason: Not in PICO

Muldoon TJ, Burgess SA, Chen BR, Ratner D, Hillman EMC. Analysis of skin lesions using laminar optical tomography. *Biomedical Optics Express* 2012;3(7):1701-12.
Exclusion Reason: Narrative Review

Mullen JT, Feng L, Xing Y, Mansfield PF, Gershenwald JE, Lee JE, et al. Invasive squamous cell carcinoma of the skin: Defining a high-risk group. *Annals of Surgical Oncology* 2006;13(7):902-9.
Exclusion Reason: Not in PICO

Murchie P, Delaney EK, Thompson WD, Lee AJ. Excising basal cell carcinomas: comparing the performance of general practitioners, hospital skin specialists and other hospital specialists. *Clinical & Experimental Dermatology* 2008;33(5):565-71.
Exclusion Reason: Not in PICO

Musiatowicz B, Dzieciol J, Sulkowska M, Polakow J, Baltaziak M. Fine needle aspiration biopsy cytology of pulmonary tumors. *Roczniki Akademii Medycznej W Bialymstoku* 1997;42:Suppl-13.
Exclusion Reason: Not in PICO

Myers M, Gurwood AS. Periocular malignancies and primary eye care. [Review] [22 refs]. *Optometry (St.Louis, Mo.)* 2001;72(11):705-12.
Exclusion Reason: Narrative Review

Nagami Y, Machida H, Tominaga K, Nakatani M, Kameda N, Sugimori S, et al. Accurate detection and diagnosis of esophageal squamous cancer by tandem conventional endoscopy with narrow-band imaging and iodine staining: A prospective study. *Gastrointestinal Endoscopy* 2010;71(5):AB252-3.
Exclusion Reason: Not in PICO

Navone R, Pentenero M, Gandolfo S. Liquid-based cytology in oral cavity squamous cell cancer. [Review]. *Current Opinion in Otolaryngology & Head & Neck Surgery* 2011;19(2):77-81.

Exclusion Reason: Narrative Review
 Nguyen TH, Ho DQ. Nonmelanoma skin cancer. *Current treatment options in oncology* 2002;3(3):193-203.

Exclusion Reason: Narrative Review
 Niederkorn A, Gabler G, Argenziano G, Muir J, Zalaudek I, Soyer HP, et al. The user-generated web-based dermoscopy image archive of the international dermoscopy society: A contribution to E-learning and exchange of knowledge. *Dermatology* 2011;222(2):131-7.

Exclusion Reason: Not in PICO
 Ogden E, Schofield J. Two-week wait skin cancer referral outcomes: Differences in management between plastic surgery and dermatology. *British Journal of Dermatology* 2010;163:60-1.

Exclusion Reason: Not in PICO
 Paderni C, Compilato D, Lo Muzio L, Campisi G. Direct visualization of oral-cavity tissue fluorescence and toluidine blue staining: New adjunctive aids for oral medicine practitioners in early oral cancer diagnosis and potentially malignant disorders follow-up? *Oral Diseases* 2010;16(6):535-6.

Exclusion Reason: Not in PICO
 Palamaras I, Hamill M, Sethi G, Wilkinson D, Lamba H. The usefulness of a diagnostic biopsy clinic in a genitourinary medicine setting: recent experience and a review of the literature. *Journal of the European Academy of Dermatology and Venereology* 2006;20(8):905-10.

Exclusion Reason: Not in PICO
 Palanivel JA, Macbeth AE, Dootson G, Graham R, Mahmood K, Garioch J. An audit of incomplete excision rates of basal cell carcinoma from four U.K. teaching hospitals. *British Journal of Dermatology* 2011;165:106.

Exclusion Reason: Not in PICO
 Palka KT, Slebos RJ, Chung CH. Update on molecular diagnostic tests in head and neck cancer. [Review] [100 refs]. *Seminars in Oncology* 2008;35(3):198-210.

Exclusion Reason: Narrative Review
 Pallagatti, S., Sheikh, S., Aggarwal, A., Gupta, D., Singh, R., Handa, R., Kaur, S. & Mago, J. (2013) Toluidine blue staining as an adjunctive tool for early diagnosis of dysplastic changes in the oral mucosa. *Journal of Clinical & Experimental Dentistry*, 5: e187-e191.

Exclusion Reason: Not in PICO
 Palmer, V. M. & Wilson, P. R. (2013) Incompletely excised basal cell carcinoma: residual tumor rates at Mohs re-excision. *Dermatologic Surgery*, 39: 706-718.

Exclusion Reason: Not in PICO
 Pariser DM, Phillips PK. Basal cell carcinoma: When to treat it yourself, and when to refer. *Geriatrics* 1994;49(3):39-42+44.

Exclusion Reason: Narrative Review
 Parkinson RW. Shave biopsies--simple and useful. *Postgraduate Medicine* 166;84(8):161-70.

Exclusion Reason: Narrative Review
 Pech O, Rabenstein T, Manner H, Petrone MC, Pohl J, Vieth M, et al. Confocal laser endomicroscopy for in vivo diagnosis of early squamous cell carcinoma in the esophagus. *Clinical Gastroenterology & Hepatology* 2008;6(1):89-94.

Exclusion Reason: Not in PICO
 Pereira RD, Martin AA, Tierra-Criollo CJ, Santos IDAO. Diagnosis of squamous cell carcinoma of human skin by Raman spectroscopy. *Optical Biopsy V* 2004;5326:106-12.

Exclusion Reason: Not in PICO
 Phillips, C., Newsome, A., Jennifer, D., Lindsey, F., Green, H. & McLean, T. (2014) Anatomy of a skin biopsy: A retrospective analysis of outpatient biopsy results from 2000 to 2010. *Journal of the American Academy of Dermatology*, 70: AB36.

Exclusion Reason: Not in PICO

Piccolo D, Smolle J, Argenziano G, Wolf IH, Braun R, Cerroni L, et al. Teledermoscopy--results of a multicentre study on 43 pigmented skin lesions. *Journal of Telemedicine & Telecare* 2000;6(3):132-7.
Exclusion Reason: Not in PICO

Pignatelli I, Poirier V, De Berker DAR, Verne J. Audit of completeness of cancer registration for basal cell carcinoma and its impact on use for quality assurance. *British Journal of Dermatology* 2010;163:58.
Exclusion Reason: Not in PICO

Pignatelli I, Poirier V, De Berker DAR, Verne J. Completeness of basal cell carcinoma excisions in an english region. *British Journal of Dermatology* 2010;163:69-70.
Exclusion Reason: Not in PICO

Poirier V, Osinowo A, Takwale A, De Berker DAR, Verne J. Basal cell carcinoma follow-up in the South West, Hampshire and Isle of Wight. *British Journal of Dermatology* 2012;167:61.
Exclusion Reason: Not in PICO

Pop Stefanija N, Blanken R, Vodegel RM. The positive predictive value of clinical diagnosis of basal cell carcinoma. [Dutch]. *Nederlands Tijdschrift voor Dermatologie en Venereologie* 2006;16(6):237-40.
Exclusion Reason: Not in PICO

Popadic, M. (2014) Statistical evaluation of dermoscopic features in basal cell carcinomas. *Dermatologic Surgery*, 40: 718-724.
Exclusion Reason: Not in PICO

Poulsen AG, Larsen FG, Weismann K, Petersen CS, Ravnborg LR, Heidenheim M, et al. [Investigation of malignant melanoma in an "open house" setting]. [Danish]. *Ugeskrift for Laeger* 1999;161(12):1758-61.
Exclusion Reason: Not in PICO

Prout MN, Sidari JN, Witzburg RA, Grillone GA, Vaughan CW. Head and neck cancer screening among 4611 tobacco users older than forty years. *Otolaryngology - Head & Neck Surgery* 1997;116(2):201-8.
Exclusion Reason: Not in PICO

Quereux G, Lequeux Y, Cary M, Jumbou O, Nguyen JM, Dreno B. Feasibility and effectiveness of a melanoma targeted screening strategy. *Melanoma Research* 2011;21:e1-2.
Exclusion Reason: Not in PICO

Raasch B, Maclennan R, Wronski I, Robertson I. Body site specific incidence of basal and squamous cell carcinoma in an exposed population, Townsville, Australia. *Mutation Research* 1998;422(1):101-6.
Exclusion Reason: Not in PICO

Raasch BA. Suspicious skin lesions and their management. *Australian Family Physician* 1999;28(5):466-71.
Exclusion Reason: Not in PICO: Clinical versus histological diagnosis (not biopsy or dermatoscopy versus histology or follow up)

Rademaker M, Thorburn M. Pathology referrals for skin lesions - Are we giving the pathologist sufficient clinical information? *New Zealand Medical Journal* 2010;123(1325):53-8.
Exclusion Reason: Not in PICO

Radziszewski J, Kowalewska M, Jedrzejczak T, Kozlowicz-Gudzinska I, Nasierowska-Guttmejer A, Bidzinski M, et al. The accuracy of the sentinel lymph node concept in early stage squamous cell vulvar carcinoma. *Gynecologic Oncology* 2010;116(3):473-7.
Exclusion Reason: Not in PICO

Rahman F, Tippu SR, Khandelwal S, Girish KL, Manjunath BC, Bhargava A. A study to evaluate the efficacy of toluidine blue and cytology in detecting oral cancer and dysplastic lesions. *Quintessence International* 2012;43(1):51-9.
Exclusion Reason: Not in PICO

Raj, G. & Gupta, G. (1111) The need for full body skin examination on patients referred to dermatology with a lesion. *British Journal of Dermatology. Conference: 93rd Annual Meeting of the British Association of Dermatologists Liverpool United Kingdom. Conference Start: 20130709 Conference End: 20130711. Conference Publication: (var.pagings)*, 169: July.
Exclusion Reason: Not in PICO

Rajaram N, Tunnell J, Reichenberg J. Pilot clinical study for noninvasive diagnosis of nonmelanoma skin cancer. *Journal of the American Academy of Dermatology* 2011;64(2 SUPPL. 1):AB76.
Exclusion Reason: Not in PICO

Reed SF, Britt RC, Novosel TJ, Collins JN, Weireter LJ, Britt LD. Screening human immunodeficiency virus-positive men for anal intraepithelial neoplasia. *American Surgeon* 2012;78(8):901-3.
Exclusion Reason: Not in PICO

Reynolds PL, Strayer SM. Treatment of skin malignancies. [Review] [33 refs]. *Journal of Family Practice* 2003;52(6):456-64.
Exclusion Reason: Narrative Review

Rezze GG, De Sa BCS, Neves RI. Dermoscopy: The pattern analysis. *Anais Brasileiros de Dermatologia* 2006;81(3):261-8.
Exclusion Reason: Narrative Review

Rice SA, Swale VJ, Cerio R. Are we relying too heavily on dermoscopy? *British Journal of Dermatology* 2012;167:105.
Exclusion Reason: Narrative review

Richert, B., Lecerf, P., Caucanas, M. & Andre, J. (2013) Nail tumors. *Clinics in Dermatology*, 31: 602-617.
Exclusion Reason: Narrative review

Robison Sean, Kljakovic Marjan, Barry Peter. Choosing to biopsy or refer suspicious melanocytic lesions in general practice. *BMC Family Practice* 2012;13(1):78.
Exclusion Reason: Not in PICO

Roozeboom, M. H., Mosterd, K., Winnepenninckx, V. J., Nelemans, P. J. & Kelleners-Smeets, N. W. (2013) Agreement between histological subtype on punch biopsy and surgical excision in primary basal cell carcinoma. *Journal of the European Academy of Dermatology & Venereology*, 27: 894-898.
Exclusion Reason: Not in PICO

Rose LC. Recognizing neoplastic skin lesions: a photo guide. [Review] [18 refs]. *American Family Physician* 887;58(4):873-84.
Exclusion Reason: Narrative Review

Rosen R. Managing nonmelanoma skin cancer. *Modern Medicine of Australia* 1999;42(2):74-85.
Exclusion Reason: Narrative Review

Rosendahl C, Cameron A, Argenziano G, Zalaudek I, Tschandl P, Kittler H. Dermoscopy of Squamous Cell Carcinoma and Keratoacanthoma. *Archives of Dermatology* 2012;148(12):1386-92.
Exclusion Reason: Not in PICO

Rosendahl C, Hansen C, Cameron A, Bourne P, Wilson T, Cook B, et al. Measuring performance in skin cancer practice: the SCARD initiative. *International Journal of Dermatology* 2011;50(1):44-51.
Exclusion Reason: Not in PICO

Rosendahl C, Tschandl P, Cameron A, Kittler H. Diagnostic accuracy of dermoscopy for melanocytic and nonmelanocytic pigmented lesions. *Journal of the American Academy of Dermatology* 2011;64(6):1068-73.
Exclusion Reason: Duplicate

Rousset, J., Abgral, R., Chinellato, S., Garetier, M., Barberot, C., Valette, G., Potard, G., Le, B. T. & Salaun, P. Y. (2013) Early recurrence or submucosal residual of laryngeal squamous cell carcinoma: diagnosis by CT-guided endolaryngeal core biopsy on a transcutaneous approach. *Head & Neck*, 35: E202-E204.
Exclusion Reason: Not in PICO

Rudkin AK, Dodd T, Muecke JS. The differential diagnosis of localised amelanotic limbal lesions: a review of 162 consecutive excisions. *British Journal of Ophthalmology* 2011;95(3):350-4.
Exclusion Reason: Not in PICO

Russell EB, Carrington PR, Smoller BR. Basal cell carcinoma: a comparison of shave biopsy versus punch biopsy techniques in subtype diagnosis. *Journal of the American Academy of Dermatology* 1999;41(1):69-71.
Exclusion Reason: Not in PICO

Ryu IS, Choi SH, Kim do H, Han MW, Roh JL, Kim SY, et al. Detection of the primary lesion in patients with cervical metastases from unknown primary tumors with narrow band imaging endoscopy: preliminary report. *Head & Neck* 2013;35(1):10-4.
Exclusion Reason: Not in PICO

Sabir F, Aziz M, Afroz N, Amin SS. Clinical and cyto-histopathological evaluation of skin lesions with special reference to bullous lesions. *Indian Journal of Pathology and Microbiology* 2010;53(1):41-6.
Exclusion Reason: Narrative Review

Saldanha G, Fletcher A, Slater DN. Basal cell carcinoma: a dermatopathological and molecular biological update. *British Journal of Dermatology* 2003;148(2):195-202.
Exclusion Reason: Narrative Review

Sandison A. Common head and neck cases in our consultation referrals: diagnostic dilemmas in inverted papilloma. [Review] [13 refs]. *Head and neck pathology* 2009;3(3):260-2
Exclusion Reason: Narrative Review

Santi EG, Inoue H, Sato H, Maselli R, Ikeda H, Yoshida A, et al. Endoscopic treatment for esophageal achalasia with early squamous cell carcinoma: POEM plus ESD. *Journal of Gastroenterology and Hepatology* 2012;27:317-8.
Exclusion Reason: Not in PICO

Sanyal, S., Holme, A. & Kemmett, D. (2013) How are patients with actinic keratoses managed in primary care? *British Journal of Dermatology*, 169: 45.
Exclusion Reason: Not in PICO

Schlemper RJ, Dawsey SM, Itabashi M, Iwashita A, Kato Y, Koike M, et al. Differences in diagnostic criteria for esophageal squamous cell carcinoma between Japanese and Western pathologists. *Cancer* 2000;88(5):996-1006.
Exclusion Reason: Not in PICO

Schofield J, Hepburn N, Scharrer K, Hussain K. The costs of diagnosing and treating skin cancer using the 2-week-wait referral process. *British Journal of Dermatology* 2011;165:22-3.
Exclusion Reason: Not in PICO

Schroeder BM, American Cancer Society. ACS updates guideline for the early detection of cervical neoplasia and cancer. American Cancer Society. *American Family Physician* 2003;67(9):2011-6.
Exclusion Reason: Not in PICO

Schwartzberg JB, Elgart GW, Romanelli P, Fangchao M, Federman DG, Kirsner RS. Accuracy and predictors of basal cell carcinoma diagnosis. *Dermatologic Surgery* 2005;31(5):534-7.
Exclusion Reason: Not in PICO

Scully C, Newman L, Bagan JV. The role of the dental team in preventing and diagnosing cancer: 3. oral cancer diagnosis and screening. *Dental Update* 331;32(6):326-8.
Exclusion Reason: Not in PICO

Sendagorta E, Herranz P, Guadalajara H, Zamora FX. [Early detection of anal intraepithelial neoplasia in high-risk patients]. [Review] [Spanish]. *Actas Dermo-Sifiliograficas* 2011;102(10):757-65.
Exclusion Reason: Narrative Review

Senel E. Dermatoscopy of non-melanocytic skin tumors. *Indian Journal of Dermatology Venereology & Leprology* 2011;77(1):16-21.
Exclusion Reason: Narrative Review

Shariff Z, Roshan A, Williams AM, Platt AJ. 2-Week wait referrals in suspected skin cancer: does an instructional module for general practitioners improve diagnostic accuracy? *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland* 2010;8(5):247-51.
Exclusion Reason: Not in PICO

Sharma, A., Alfa-Wali, M., Rodriguez-Justo, M. & Polychronis, A. (2013) Squamous cell carcinoma of pancreas: an unusual site of relapse from early-stage lung cancer: 12-month postsurgery. *BMJ Case Reports*, 2013, 2013.
Exclusion Reason: Not in PICO

Shimizu Y, Omori T, Yokoyama A, Yoshida T, Hirota J, Ono Y, et al. Endoscopic diagnosis of early squamous neoplasia of the esophagus with iodine staining: high-grade intra-epithelial neoplasia turns pink within a few minutes. *Journal of Gastroenterology & Hepatology* 2008;23(4):546-50.
Exclusion Reason: Not in PICO

Shitara, D., Ishioka, P., Alonso-Pinedo, Y., Palacios-Bejarano, L., Carrera, C., Malveyh, J. & Puig, S. (2014) Shiny White Streaks: A Sign of Malignancy at Dermoscopy of Pigmented Skin Lesions. *Acta Dermato-Venereologica*, 94: 132-137.
Exclusion Reason: Setting not in PICO

Shum WY, Hsieh TC, Yeh JJ, Chen JH, Su CC, Liang JA, et al. Clinical usefulness of dual-time FDG PET-CT in assessment of esophageal squamous cell carcinoma. *European Journal of Radiology* 2012;81(5):1024-8.
Exclusion Reason: Not in PICO

Singh, T. & Schenberg, M. (2013) Delayed diagnosis of oral squamous cell carcinoma following dental treatment. *Annals of the Royal College of Surgeons of England*, 95: 369-373.
Exclusion Reason: Not in PICO

Skiljevic D, Stojkovic-Filipovic J, Nikolic M, Medenica L. Early-onset basal cell carcinoma. *Melanoma Research* 2010;20:e68.
Exclusion Reason: N=1

Smithers BM, Fahey PP, Corish T, Gotley DC, Falk GL, Smith GS, et al. Symptoms, investigations and management of patients with cancer of the oesophagus and gastro-oesophageal junction in Australia. *Medical Journal of Australia* 2010;193(10):572-7.
Exclusion Reason: Not in PICO

Sober AJ. Diagnosis and management of skin cancer. *Cancer* 1983;51(12:Suppl):Suppl-52.
Exclusion Reason: Not in PICO

Socha, A. & Niedzielska, I. (2013) Exophytic tumours of skin of the head - Case study and review of the literature. *Dental and Medical Problems*, 50: 229-237.
Exclusion Reason: Not in PICO

Speel E-J, Leusink FKJ, Van Hooff SR, Kummer JA, van Diest PJ, Koole R, et al. Multi-center validation of a lymph node metastasis gene-expression signature for head and neck squamous cell carcinomas. *Cancer Research* 2011;71(8 SUPPL. 1).
Exclusion Reason: Not in PICO

Spencer JM, Tannenbaum A, Sloan L, Amonette RA. Does inflammation contribute to the eradication of basal cell carcinoma following curettage and electrodesiccation? *Dermatologic Surgery* 1997;23(8):625-30.
Exclusion Reason: Not in PICO

Spencer RJ, Young RH, Goodman A. The risk of squamous cell carcinoma in persistent vulvar ulcers. *Menopause* 2011;18(10):1067-71.
Exclusion Reason: Not in PICO

Stegman SJ. Basal cell carcinoma and squamous cell carcinoma. Recognition and treatment. [Review] [28 refs]. *Medical Clinics of North America* 1986;70(1):95-107.
Exclusion Reason: Narrative Review

Stell PM, Wood GD, Scott MH. Early oral cancer: treatment by biopsy excision. *British Journal of Oral Surgery* 1982;20(4):234-8.

Exclusion Reason: Not in PICO
 Stockfleth E. Non melanoma skin cancer - Early excision is still the standard in therapy. [German]. *Klinikerarzt* 2002;31(5):122-5.
 Exclusion Reason: Narrative Review

Stoekli SJ, Broglie MA. Sentinel node biopsy for early oral carcinoma. *Current Opinion in Otolaryngology & Head and Neck Surgery* 2012;20(2):103-8.
 Exclusion Reason: Narrative Review

Stolte M. [The new "Vienna Classification" for epithelial neoplasia of the gastrointestinal tract. Pros or cons?]. [Review] [34 refs] [German]. *Pathologie* 2001;22(1):4-12.
 Exclusion Reason: Narrative Review

Streeton CL, Gospodarevskaya E, Harris A. Treatment of basal cell carcinomas by general practitioners in Australia. *International Journal of Dermatology* 2006;45(4):345-51.
 Exclusion Reason: Not in PICO

Stulberg DL, Crandell B, Fawcett RS. Diagnosis and treatment of basal cell and squamous cell carcinomas. *American Family Physician* 2004;70(8):1481-8.
 Exclusion Reason: Narrative Review

Szalai K, Hatvani Z, Harsing J, Somlai B, Karpati S. High frequency ultrasonography in the diagnosis of cutaneous pigmented lesions and melanoma reduce the possibilities of diagnostic pitfalls. *Melanoma Research* 2011;21:e4-5.
 Exclusion Reason: Narrative Review

Talbot S, Hitchcock B. Incomplete primary excision of cutaneous basal and squamous cell carcinomas in the Bay of Plenty. *New Zealand Medical Journal* 2004;117(1192):U848.
 Exclusion Reason: Not in PICO

Tan E, Yung A, Jameson M, Oakley A, Rademaker M. Successful triage of patients referred to a skin lesion clinic using teledermoscopy (IMAGE IT trial). *British Journal of Dermatology* 2010;162(4):803-11.
 Exclusion Reason: Not in PICO

Tandon Y, Brodell RT. Local reactions to imiquimod in the treatment of basal cell carcinoma. *Dermatology Online Journal* 2012;18(9):1.
 Exclusion Reason: Not in PICO

Tangjaturonrasme, N., Rerknimitr, R., Pittayanon, R., Wisedopas, N. & Kullavanijaya, P. (2013) The difference in detection rates during surveillance endoscopy for early squamous cell neoplasia of the esophagus between patients with previous nasopharyngeal cancer and patients with other ent related squamous cell cancers pornphan thienchanachaiya1. *Gastrointestinal Endoscopy*, 77: AB339-AB340.
 Exclusion Reason: Not in PICO

Tannapfel A, Weber A. Tumor markers in squamous cell carcinoma of the head and neck: clinical effectiveness and prognostic value. *European Archives of Oto-Rhino-Laryngology* 2001;258(2):83-8.
 Exclusion Reason: Narrative Review

Teoh YL, Halpern SM, Shall L. Factors associated with incomplete excision of basal cell carcinomas. *British Journal of Dermatology* 2010;163:55-6.
 Exclusion Reason: Not in PICO

TerKonda SP, Perdakis G. Non-melanotic skin tumors of the upper extremity. [Review] [50 refs]. *Hand Clinics* 104;20(3):293-301.
 Exclusion Reason: Narrative Review

Terrill PJ, Fairbanks S, Bailey M. Is there just one lesion? The need for whole body skin examination in patients presenting with non-melanocytic skin cancer. *ANZ Journal of Surgery* 2009;79(10):707-12.
 Exclusion Reason: Not in PICO

Terstappen K, Larko O, Wennberg AM. Pigmented basal cell carcinoma - Comparing the diagnostic methods of SIAscopy and dermoscopy. *Acta Dermato-Venereologica* 2007;87(3):238-42.
Exclusion Reason: Narrative Review

Terushkin V, Braga JC, Dusza SW, Scope A, Busam K, Marghoob AA, et al. Agreement on the Clinical Diagnosis and Management of Cutaneous Squamous Neoplasms. *Dermatologic Surgery* 2010;36(10):1514-20.
Exclusion Reason: Not in PICO

Thienchanachaiya P, Rerknimitr R, Pittayanon R, Wisedopas N, Tangjaturonrasme N, Kullavanijaya P. Preliminary study of FICE for detection of early esophageal neoplasm in patients with history of ENT related squamous cell cancers. *Journal of Gastroenterology and Hepatology* 2012;27:319-20.
Exclusion Reason: Not in PICO

Thissen MR, Neumann HA, Berretty PJ, Ideler AH. [The treatment of basal cell carcinoma patients by dermatologists in Netherland]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde* 1998;142(27):1563-7.
Exclusion Reason: Not in PICO

Tochigi, T., Shuto, K., Staito, H., Kono, T. & Matsubara, H. (2013) Early esophageal squamous cell cancer by high-barium esophagography using flat panel X-ray detector in comparison with histological findings. *European Journal of Cancer*, 49: S252-S253.
Exclusion Reason: Not in PICO

Tomas S. Difficult to diagnose skin cancer The 'aggressive' BCC. *Australian Family Physician* 2009;38(7):492-7.
Exclusion Reason: Narrative Review

Trotter MJ, Bruecks AK. Interpretation of Skin Biopsies by General Pathologists: Diagnostic Discrepancy Rate Measured by Blinded Review. *Archives of Pathology and Laboratory Medicine* 2003;127(11):1489-92.
Exclusion Reason: Not in PICO

Turan, E., Yurt, N., Yesilova, Y. & Turkcu, G. (2013) Early-onset basal cell carcinoma. *Turkish Journal of Pediatrics*, 55: 354-356.
Exclusion Reason: Not in PICO

Ulrich M, Lange-Asschenfeldt S, Gonzalez S. In vivo reflectance confocal microscopy for early diagnosis of nonmelanoma skin cancer. *Actas Dermo-Sifiliograficas* 2012;103(9):784-9.
Exclusion Reason: Narrative Review

Vacher-Lavenu MC. [Histology and cytology of cervical cancers]. [Review] [24 refs] [French]. *Revue du Praticien* 2001;51(13):1417-23.
Exclusion Reason: Narrative Review

Vargo N. Basal cell and squamous cell carcinoma. [Review] [46 refs]. *Seminars in Oncology Nursing* 2003;19(1):12-21.
Exclusion Reason: Narrative Review

Vermaak, P. V. & Manushakian, J. (2013) Rapidly enlarging skin lesion on the lip. *BMJ Case Reports*, 2013, 2013.
Exclusion Reason: Not in PICO

Viglizzo G, Rongioletti F. Clinical, dermoscopic and pathologic correlation of pigmentary lesions observed in a dermoscopy service in the year 2003. [Italian, English]. *Giornale Italiano di Dermatologia e Venereologia* 2004;139(4):339-44.
Exclusion Reason: Not in PICO

Viola KV, Tolpinrud WL, Gross CP, Kirsner RS, Imaeda S, Federman DG. Outcomes of referral to dermatology for suspicious lesions: implications for teledermatology. *Archives of Dermatology* 2011;147(5):556-60.
Exclusion Reason: Not in PICO

Wade S, Gonzalez ML, Basra M. An audit of the diagnostic accuracy and complete excision rate for skin cancers in primary and secondary care in the Cardiff area. *British Journal of Dermatology* 2011;165:105.
Exclusion Reason: Not in PICO

Wagoner J, Keehn C, Morgan MB. CD-10 immunostaining differentiates superficial basal cell carcinoma from cutaneous squamous cell carcinoma. *American Journal of Dermatopathology* 2007;29(6):555-8.
Exclusion Reason: Narrative Review

Wan A, Savage NW. Biopsy and diagnostic histopathology in dental practice in Brisbane: usage patterns and perceptions of usefulness. *Australian Dental Journal* 2010;55(2):162-9.
Exclusion Reason: Not in PICO

Watson Tony, Walter Fiona, Wood Annabel, Morris Helen, Hall Per, Karner Simone, et al. Learning a novel technique to identify possible melanomas: are Australian general practitioners better than their U.K. colleagues? *Asia Pacific Family Medicine* 2009;8(1):3.
Exclusion Reason: Narrative Review

Wetzig T, Woitek M, Eichhorn K, Simon JC, Paasch U. Surgical Excision of Basal Cell Carcinoma with Complete Margin Control: Outcome at 5-Year Follow-Up. *Dermatology* 2010;220(4):363-9.
Exclusion Reason: Not in PICO

White, G. M., Zhou, H. C. & Burchette, R. J. (2013) Biopsy followed by immediate curettage and electrodesiccation of suspected basal cell carcinomas at the first visit. *JAMA Dermatology*, 149: 980-981.
Exclusion Reason: Not in PICO

Whitesides LM, Ferreira LR, Ord RA. Audit of clinical information and diagnoses supplied to the pathologist following biopsy of oral squamous cell carcinomas. *MSDA Journal* 1995;38(2):63-5.
Exclusion Reason: Narrative Review

Wilkinson D, Askew DA, Dixon A. Skin cancer clinics in Australia: workload profile and performance indicators from an analysis of billing data. *Medical Journal of Australia* 2006;184(4):162-4.
Exclusion Reason: Not in PICO

Williams RB, Burdge AH, Lewis Jones S. Skin biopsy in general practice. *British Medical Journal* 1991;303(6811):1179-80.
Exclusion Reason: Not in PICO

Wilson RL, Yentzer BA, Isom SP, Feldman SR, Fleischer AB Jr. How good are US dermatologists at discriminating skin cancers? A number-needed-to-treat analysis. *Journal of Dermatological Treatment* 2012;23(1):65-9.
Exclusion Reason: Not in PICO

Winzenburg SM, Niehans GA, George E, Daly K, Adams GL. Basaloid squamous carcinoma: a clinical comparison of two histologic types with poorly differentiated squamous cell carcinoma. *Otolaryngology - Head & Neck Surgery* 1998;119(5):471-5.
Exclusion Reason: Not in PICO

Wlodarczyk J. [Application of Lugol solution in the gastroesophageal reflux disease]. [Polish]. *Przegląd Lekarski* 2007;64(9):549-51
Won S-S, Jung D-S, Kim H-S, Kwon K-S, Hee S-S. Clinicopathologic features of postlaser basal cell carcinoma: Does it differ from primary basal cell carcinoma? *Journal of the American Academy of Dermatology* 2010;62(3 SUPPL. 1):AB146.
Exclusion Reason: Not in PICO

Wolberink, E. A. W., Pasch, M. C., Zeiler, M., Van Erp, P. E. J. & Gerritsen, M. J. P. (2013) High discordance between punch biopsy and excision in establishing basal cell carcinoma subtype: Analysis of 500 cases. *Journal of the European Academy of Dermatology and Venereology*, 27: 985-989.
Exclusion Reason: Not in PICO

Wong KY, Gilleard O, Price R. Non-melanoma skin cancer incomplete excision rates of different grades of plastic surgeons and the implications for service provision. *European Journal of Surgical Oncology* 2012;38(11):1121.
Exclusion Reason: Not in PICO

Woolley, S. D. & Hughes, C. (2013) A young military pilot presents with a periocular Basal Cell Carcinoma: A case report. *Travel Medicine and Infectious Disease*, 11: 435-437.
Exclusion Reason: Not in PICO

Wray, E. V., Brant, B., Hussain, F. & Muller, F. M. (2013) A new model of teledermoscopy combining service and education. *British Journal of Dermatology*, 169: 139.
Exclusion Reason: Not in PICO

Wright VC. When to suspect squamous cancer at colposcopy. [Review] [22 refs]. *Nurse Practitioner* 1959;26(9):50-6.
Exclusion Reason: Narrative Review

Wustrow J, Rudert H, Diercks M, Beigel A. Squamous cell carcinoma and undifferentiated carcinoma of the inner nose and the paranasal sinuses. [German]. *Strahlentherapie und Onkologie* 1989;165(6):468-73.
Exclusion Reason: Not in PICO

Yamazaki N. [Squamous cell carcinoma]. [Review] [9 refs] [Japanese]. *Gan to Kagaku Ryoho* [Japanese Journal of Cancer & Chemotherapy] 2006;33(10):1392-7.
Exclusion Reason: Narrative Review

Youl PH, Baade PD, Janda M, Del Mar CB, Whiteman DC, Aitken JF. Diagnosing skin cancer in primary care: how do mainstream general practitioners compare with primary care skin cancer clinic doctors? *Medical Journal of Australia* 2007;187(4):215-20.
Exclusion Reason: Not in PICO: Clinical versus histological diagnosis (not biopsy or dermatoscopy versus histology or follow up)

Youl PH, Janda M, Aitken JF, Del Mar CB, Whiteman DC, Baade PD. Body-site distribution of skin cancer, pre-malignant and common benign pigmented lesions excised in general practice. *British Journal of Dermatology* 2011;165(1):35-43
Exclusion Reason: Not in PICO

Zalaudek I, Argenziano G, Soyer HP, Corona R, Sera F, Blum A, et al. Three-point checklist of dermoscopy: an open internet study. *British Journal of Dermatology* 2006;154(3):431-7.
Exclusion Reason: Not in PICO

Zedek DC, Smith ET Jr, Hitchcock MG, Feldman SR, Shelton BJ, White WL. Cutaneous lupus erythematosus simulating squamous neoplasia: the clinicopathologic conundrum and histopathologic pitfalls. *Journal of the American Academy of Dermatology* 2007;56(6):1013-20.
Exclusion Reason: Not in PICO

Zheng W, Soo KC, Sivanandan R, Olivo M. Detection of squamous cell carcinomas and pre-cancerous lesions in the oral cavity by quantification of 5-aminolevulinic acid induced fluorescence endoscopic images. *Lasers in Surgery & Medicine* 2002;31(3):151-7.
Exclusion Reason: Not in PICO

Zhou XH. Primary squamous cell carcinoma of the thyroid. *European Journal of Surgical Oncology* 2002;28(1):42-5.
Exclusion Reason: N=2

BASAL CELL CARCINOMA

Review question:

What is the risk of basal cell carcinoma in patients presenting in primary care with symptom(s)?

Results

Literature search

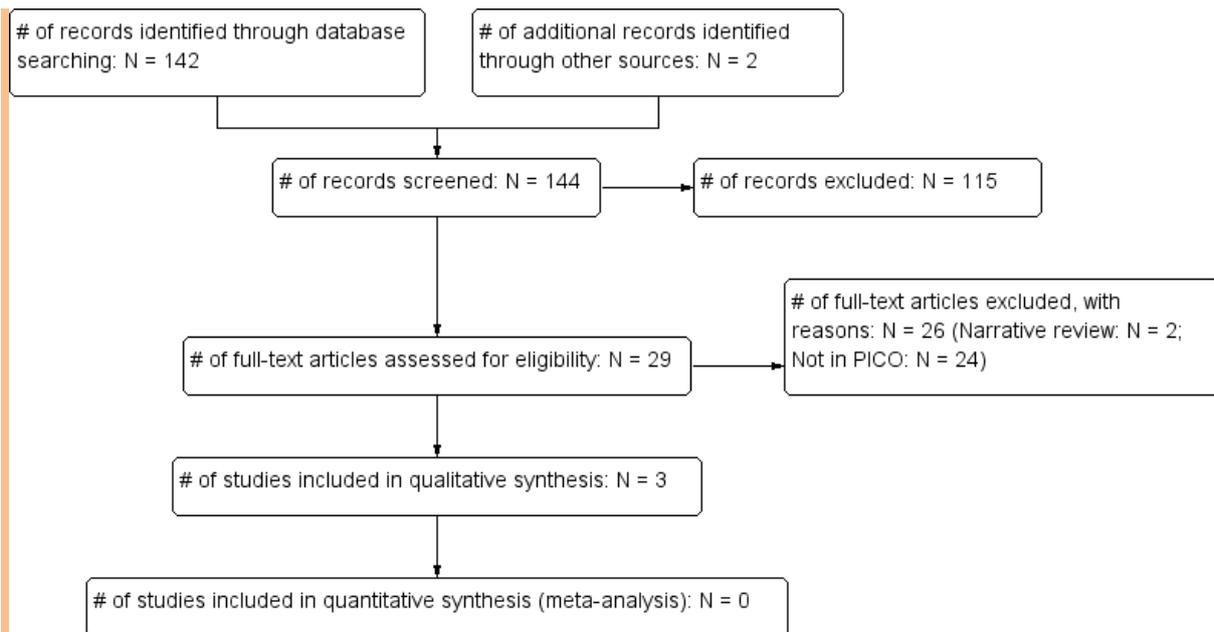
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	501	66	09/01/2013
<i>Premedline</i>	All-2012	66	5	09/01/2013
<i>Embase</i>	All-2012	2129	76	15/01/2013
<i>Cochrane Library</i>	All-2012	201	3	16/01/2013
<i>Psychinfo</i>	All-2012	4	1	09/01/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	569	36	16/01/2013
<i>Biomed Central</i>	All-2012	287	3	21/01/2013

Total References retrieved (after de-duplication): 127

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-11/08/2014	17	2	11/08/2014
<i>Premedline</i>	2013-11/08/2014	26	2	11/08/2014
<i>Embase</i>	2013-11/08/2014	101	15	11/08/2014
<i>Cochrane Library</i>	2013-11/08/2014	63	0	11/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-11/08/2014	114	0	11/08/2014

Total References retrieved (after de-duplication): 15



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main bias risks and applicability concerns that the studies are subject to relate to (1) the patient sampling method not clearly being consecutive or random, (2) the extent to which the study setting matches UK primary care, (3) the quality of the reference standard, which may not always reliably diagnose the symptoms, and (4) the fact that the reference standard did not in all cases match that of the current question, namely histology.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Emery (2010)	?	+	?	+	?	+	?
Rosendahl (2012)	?	+	+	+	?	+	+
Walter (2012)	?	+	?	+	+	+	?

- High
 ? Unclear
 + Low

Study results

Table 1: Basal cell carcinoma: Study results

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI) Prevalence

Emery (2010) Lesion, not patient,- based analysis	Pigmented lesion	All included patients	1.82 (1.2-2.8) 22/1211
		England sample	0/630 (0-0.8)
		Australia sample	3.79 (2.4-5.8) 22/581
Walter (2012) Lesion, not patient,- based analysis	Suspicious pigmented lesions	All included patients	0.64 (0.3-1.2) 10/1573
Rosendahl (2010) Lesion, not patient,- based analysis	Non-pigmented raised lesion	All included patients	27.18 (21.3-33.9) 56/206

Evidence statement(s):

Pigmented skin lesions (2 studies, N = 2784 *lesions*) presenting in a primary care setting are associated with positive predictive value of 0.64-1.82% for basal cell carcinoma. The studies were associated with 3-4 bias and applicability concerns (see also Table 1).

Non-pigmented skin lesions (1 study, N = 206 *lesions*) presenting in a primary care setting are associated with a positive predictive value of 27.18% for basal cell carcinoma. The study was associated with 2 bias and applicability concerns (see also Table 1).

Evidence tables

Emery (2010)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective series of pigmented lesions recruited from England (6 general practices covering urban, suburban and rural areas with a registered population of 52913) and Australia (3 primary care skin cancer clinics operated by GPs from a metropolitan area)
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	England: N = 389 patients, mean age = 44.9 years, 68.6% females with, interpretable images from N = 630 lesions. 0/630 lesions were squamous cell carcinoma, 0/630 lesions were basal cell carcinoma, 5/630 lesions were melanoma, and 0/630 lesions were lentigo maligna (melanoma). Australia: N = 469 patients, mean age = 50 years, 48% females, with interpretable images from N = 581 lesions. 0/581 lesions were squamous cell carcinoma, 22/581 lesions were basal cell carcinoma, 7/581 lesions were melanoma, and 4/581 lesions were lentigo maligna (melanoma). <u>Inclusion criteria:</u>

	<p>England: Patients aged > 18 years were recruited into the study by their GP if they presented with concerns about a pigmented skin lesion between January 2005 and January 2006.</p> <p>Australia: Patients aged > 18 years were recruited into the study by their GP if they presented with concerns about a pigmented skin lesion between April 2008 and January 2009. Additional lesions were also included when a pigmented skin lesion was identified as potentially suspicious during their clinical examination</p> <p><u>Exclusion criteria:</u> None reported.</p> <p><u>Clinical setting:</u> Primary care, UK, and primary care skin cancer practice, Queensland Australia.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Pigmented skin lesions that concerned patients, which were evaluated using macroscopic clinical photographs, dermoscopic images and SIAscan.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histopathology or in-person clinical review of the lesion by one expert, including the 7-point melanoma checklist and digital dermoscopy or clinical diagnosis made on the basis of the 7-point melanoma checklist, photographic and dermoscopy images
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Analysis was on a per lesion basis rather than a per patient basis

Rosendahl (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective unselected consecutive series of raised non-pigmented lesions
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 186 patients, mean (SD) age = 65 (13) years, 32.8% females with N = 206 lesions. 32/206 lesions were squamous cell carcinoma (SCC), 29/206 lesions were keratoacanthoma (SCC), 24/206 lesions were Bowen disease (SCC), and 56/ 206 lesions were basal cell carcinoma.</p> <p><u>Inclusion criteria:</u> Patients presenting with non-pigmented raised lesions treated from March 1 through December 31 2011. All the lesions were excised or biopsied. It is unclear if there were any patients presenting with non-pigmented raised lesions not biopsied/excised who were not included.</p> <p><u>Exclusion criteria:</u> None reported.</p> <p><u>Clinical setting:</u> Private primary care skin cancer practice, Queensland Australia.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Non-pigmented raised skin lesions (not further defined, but see subgroup analyses) evaluated using dermoscopic images
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histopathology
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Analysis was on a per lesion basis rather than a per patient basis; some patients may have had more than one lesion diagnosed as skin cancer though it is not possible to ascertain the actual numbers from the data provided.

Walter (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective series of suspicious pigmented lesions
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1293 patients, mean age (SD) = 44.6 (16.8) years; 465 males / 828 females with N = 1573 lesions, of which 1 was squamous cell carcinoma, 10 basal cell carcinomas, and 36 melanomas. <u>Inclusion criteria:</u> Patients aged ≥ 18 years presenting to one of the 15 participating general practices with a suspicious (any lesion presented buy a patient, or opportunistically seen by a family doctor or practice nurse, that could not immediately be diagnosed as benign and about which the patient could not be reassured) pigmented lesion from March 2008 to May 2010. <u>Exclusion criteria:</u> Patients who were unable to give informed consent or were considere3d inappropriate to include by their family doctor. <u>Clinical setting:</u> UK primary care.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Suspicious (any lesion presented buy a patient, or opportunistically seen by a family doctor or practice nurse, that could not immediately be diagnosed as benign and about which the patient could not be reassured) pigmented lesion
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Expert opinion by a histologist or dermatologist or review by two other dermatology experts of the recorded clinical history and examination, a digital photograph, and MoleMate images where available with or without

	follow up 3-6 months later.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for in the results
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes Tests: No
Could the patient flow have introduced bias?	Low risk
NOTES	Analysis was on a per lesion basis rather than a per patient basis.

References

Included Studies

Emery, J.D., Hunter, J., Hall, P.N., Watson, A.J., Moncrieff, M., Walter, F.M. (2010). Accuracy of SIAscopy for pigmented skin lesions encountered in primary care: development and validation of a new diagnostic algorithm. *BMJ Dermatology*, 10:9.

Rosendahl, C. (2012) Dermoscopy of squamous cell carcinoma and keratoacanthoma. *Archives of Dermatology*, 148: 1386-1392.

Walter, F.M., Morris, H.C., Humphrys, E., Hall, P.N., Prevost, A.T., Burrows, N., Bradshaw, L., Wilson, E.C., Norris, P., Walls, J., Johnson, M., Kinmonth, A.L., Emery, J.D. (2012). Effect of adding a diagnostic aid to best practice to manage suspicious pigmented lesions in primary care: randomised controlled trial. *BMJ*, 345: e4110.

Excluded Studies

Abuzahra, F., Parren, L. J., Frank, J., Abuzahra, F., Parren, L. J. M. T., and Frank, J. Multiple familial and pigmented basal cell carcinomas in early childhood - Bazex-Dupre-Christol syndrome. *Journal of the European Academy of Dermatology & Venereology* 26[1], 117-121. 2012. Netherlands.
Reason Single Case

Agarwal S. Out patient waiting time for common skin conditions - Do general practitioners and dermatologists have the same priorities? A questionnaire-based survey. *Clinical and Experimental Dermatology* 26[1], 13-15. 2001. United Kingdom.
Reason Not relevant to PICO

Ahmad, I., Das Gupta, A. R., Ahmad, I., and Das Gupta, A. R. Epidemiology of basal cell carcinoma and squamous cell carcinoma of the pinna. *Journal of Laryngology & Otology* 115[2], 85-86. 2001. England.
Reason Comparison not relevant to PICO

Alam, M., Goldberg, L. H., Silapun, S., Gardner, E. S., Strom, S. S., Rademaker, A. W., and Margolis, D. J. Delayed treatment and continued growth of nonmelanoma skin cancer. *Journal of the American Academy of Dermatology* 64[5], 839-848. 2011.
Reason Not relevant to PICO

- Aldridge, R. B. F. Do laypersons have intrinsic pattern recognition abilities that could be harnessed to allow the accurate and early diagnosis of skin cancers? *British Journal of Dermatology Conference*[var.pagings], 949-950. 2010.
Reason Not relevant to PICO
- Aldridge, R. B., Naysmith, L., Ooi, E. T., Murray, C. S. & Rees, J. L. (1111) The importance of a full clinical examination: Assessment of index lesions referred to a skin cancer clinic without a total body skin examination would miss one in three melanomas. *Acta Dermato-Venereologica*, 93: 2013.
Reason Not in PICO
- Allon, I., Allon, D. M., Anavi, Y. & Kaplan, I. (2013) The significance of surface ulceration as a sign of malignancy in exophytic oral mucosal lesions: myth or fact? *Head and neck pathology*, 7: 149-154.
Reason Not in PICO
- Argenziano, G., Puig, S., Zalaudek, I., Sera, F., Corona, R., Alsina, M., Barbato, F., Carrera, C., Ferrara, G., Guilabert, A., Massi, D., Moreno-Romero, J. A., Munoz-Santos, C., Petrillo, G., Segura, S., Soyer, H. P., Zanchini, R., and Malvehy, J. Dermoscopy improves accuracy of primary care physicians to triage lesions suggestive of skin cancer. *Journal of Clinical Oncology* 24[12], 1877-1882. 20-4-2006.
Reason Not relevant to PICO
- Askari, S. K., Schram, S. E., Wenner, R. A., Bowers, S., Liu, A., Bangerter, A. K., and Warshaw, E. M. Evaluation of prospectively collected presenting signs/symptoms of biopsy-proven melanoma, basal cell carcinoma, squamous cell carcinoma, and seborrheic keratosis in an elderly male population. *Journal of the American Academy of Dermatology* 56[5], 739-747. 2007.
Reason Not relevant to PICO
- Baade, P. D., Youl, P. H., Janda, M., Whiteman, D. C., Del Mar, C. B., Aitken, J. F., Baade, Peter D., Youl, Philippa H., Janda, Monika, Whiteman, David C., Del Mar, Christopher B., and Aitken, Joanne F. Factors associated with the number of lesions excised for each skin cancer: a study of primary care physicians in Queensland, Australia. *Archives of Dermatology* 144[11], 1468-1476. 2008. United States.
Reason Not relevant to PICO
- Bataille, V. A teledermatology pilot study in Hertfordshire: Triage of 2-week-wait referrals. *British Journal of Dermatology Conference*[var.pagings], July. 2011.
Reason Not relevant to PICO
- Behrens, A., May, A., Manner, H., Pohl, J. & Ell, C. (2013) Esophageal precancerous lesions: Early diagnosis, treatment, and preservation of quality of life. [German]. *Internist*, 54: 683-690.
Reason Narrative review
- Bekkenk, M. W. H. Basal cell carcinoma and squamous cell carcinoma arising from a sebaceous nevus in young patients. *Nederlands Tijdschrift voor Dermatologie en Venereologie* 17[9], 345-346. 2007. Netherlands.
Reason Narrative review
- Berman, B. Basal cell carcinoma and actinic keratoses: Patients' perceptions of their disease and current treatments. *International Journal of Dermatology* 40[9], 573-576. 2001. United Kingdom.
Reason Not relevant to PICO
- Bernard, P. Skin cancer diagnosis by dermatologists in the region of Champagne-Ardenne: A prospective study. *Annales de Dermatologie et de Venereologie* 128[8-9], 883-887. 2001. France.
Reason Not relevant to PICO
- Bhatnagar, A., Mohamad, S., and Sandramouli, S. 'Fast-tracking' cancer referrals: application for periocular basal cell carcinoma. *Eye (London)* 20[4], 428-430. 2006.
Reason Not relevant to PICO

Bitar, G. J., Herman, C. K., Dahman, M. I., and Hoard, M. A. Basal cell nevus syndrome: Guidelines for early detection. *American Family Physician* 65[12], 2501-2504. 2002.
Reason Not relevant to PICO

Breglia, M. D., Oliva, P., Breglia, Michael D., and Oliva, Patricia. Basal cell carcinoma presenting as symptomatic iron deficiency anaemia. *BMJ Case Reports* 2011, 2011. 2011. England.
Reason Case report

Bruce, A. J., Brodland, D. G., Bruce, A. J., and Brodland, D. G. Overview of skin cancer detection and prevention for the primary care physician. [Review] [34 refs]. *Mayo Clinic Proceedings* 75[5], 491-500. 2000. UNITED STATES.
Reason Narrative Review

Brundel, K. H. and Brundel, K. H. [Skin cancer in general practice]. [German]. *Dermatosen in Beruf und Umwelt Occupational & Environmental Dermatoses*. 38[2], 54-57. 1990. GERMANY, WEST.
Reason Not relevant to PICO

Buis, P.A.J. et al (2005) Value of histopathologic analysis of skin lesions by GPs *British Journal of General Practice* 55;458-460
Reason Not in PICO

Burghout, K., Sigurdsson, V. & Toonstra, J. (2013) Non-melanoma skin cancer. [Dutch]. *Huisarts en Wetenschap*, 56: 174-178.
Reason Narrative review

Carli, P., Chiarugi, A., De, Giorgi, V, Carli, Paolo, Chiarugi, Alessandra, and De Giorgi, Vincenzo. Examination of lesions (including dermoscopy) without contact with the patient is associated with improper management in about 30% of equivocal melanomas. *Dermatologic Surgery* 31[2], 169-172. 2005. United States.
Reason Not relevant to PICO

Carlsson, L. Common cancer-related symptoms among GP patients: Opportunistic screening in primary health care. *Scandinavian Journal of Primary Health Care* 19[3], 199-203. 2001. Norway.
Reason No relevant data

Carter, E. J. W. Failure of adherence to NICE guidelines for skin cancer surgery in general practice. *British Journal of Dermatology Conference*[var.pagings], July. 2009.
Reason Not relevant to PICO

Castori, M., Morrone, A., Kanitakis, J., Grammatico, P., Castori, Marco, Morrone, Aldo, Kanitakis, Jean, and Grammatico, Paola. Genetic skin diseases predisposing to basal cell carcinoma. [Review]. *European Journal of Dermatology* 22[3], 299-309. 2012. France.
Reason Narrative Review

Ceylan, C. A case of basal cell carcinoma arising in epidermal nevus. *International Journal of Dermatology* 41[12], 926-927. 2002. United Kingdom.
Reason Narrative Review

Charman, C., Whitley, H. & Bogucki, P. (2014) Teledermatology using 'Choose and Book': A review of 1000 patient referrals. *British Journal of Dermatology*, 171: 138.
Reason Not in PICO

Chattopadhyay, M. & Ha, T. (2013) How to examine a patient with suspected skin cancer. *Medicine (United Kingdom)*, 41: 400-401.
Reason Narrative review

Chiscop, I., Popescu, E., Mihai, C., Budacu, C., Chiscop, Iulia, Popescu, Eugenia, Mihai, Constantin, and Budacu, Cristian. [Cutaneous carcinoma of the face. Clinical and histopathological forms. Retrospective study of 308 cases]. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi* 115[2], 560-566. 2011. Romania.
Reason Not relevant to PICO

- Coates, E. An observational study of skin disease in rural Australian general practice. *Australasian Journal of Dermatology Conference*[var.pagings], October. 2011.
Reason Not relevant to PICO
- Corey, K. An analysis of terminology used by primary care physicians to describe concerning lesions referred to an urgent dermatology clinic. *Journal of Investigative Dermatology Conference*[var.pagings], May. 2012.
Reason Not relevant to PICO
- Cox, N. H. and Cox, N. H. Basal cell carcinoma in young adults. *British Journal of Dermatology* 127[1], 26-29. 1992. ENGLAND.
Reason Narrative Review
- de Antonio Garcia, M. P., Borbujo, Martinez J., Juez, Juez A., Olmos, Carrasco O., Castell Alcala, M. V., Casado, Jimenez M., de Antonio Garcia, M. P., Borbujo Martinez, J., Juez Juez, A., Olmos Carrasco, O., Castell Alcala, M. V., and Casado Jimenez, M. [Pigmented basocellular epithelioma. Presentation of 7 cases]. [Spanish]. *Atencion Primaria* 9[8], 439-442. 15-5-1992. SPAIN.
Reason Not relevant to PICO
- De Stefano, A. Features of biopsy in diagnosis of metatypical basal cell carcinoma (Basosquamous Carcinoma) of head and neck. *Otolaryngologia Polska* 66[6], 419-423. 2012. Poland.
Reason Narrative Review
- Dewan, P. Are NICE skin cancer guidelines being followed in primary care? A re-audit to review changes in practice in an inner city setting. *British Journal of Dermatology Conference*[var.pagings], July. 2010.
Reason Not relevant to PICO
- Eekhof, J. A. (2013) [Actinic keratosis: the art of doing nothing]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 157: A5363.
Reason Narrative review
- Ehlers, G. Clinic data on basal cell epithelioma in connection with statistical investigations. *Zeitschrift fur Haut- und Geschlechtskrankheiten* 41[6], 226-238. 1966.
Reason Narrative Review
- Emery, J. D. H. Accuracy of SIAscopy for pigmented skin lesions encountered in primary care: Development and validation of a new diagnostic algorithm. *BMC Dermatology* 10 , 2010. Article Number, 9. 2009. United Kingdom.
Reason Relevant for tests
- Epstein, J. B., Guneri, P., Boyacioglu, H. & Abt, E. (2013) The limitations of the clinical oral examination in detecting dysplastic oral lesions and oral squamous cell carcinoma.[Reprint of J Am Dent Assoc. 2012 Dec;143(12):1332-42; PMID: 23204089]. *Texas Dental Journal*, 130: 410-424.
Reason Not in PICO
- Federman, D. G., Concato, J., Caralis, P. V., Hunkele, G. E., and Kirsner, R. S. Screening for skin cancer in primary care settings. *Archives of Dermatology* 133[11], 1423-1425. 1997.
Reason Not relevant to PICO
- Federman, D. G., Kravetz, J. D., Tobin, D. G., Ma, F., and Kirsner, R. S. Full-body skin examinations: the patient's perspective. *Archives of Dermatology* 140[5], 530-534. 2004.
Reason Not relevant to PICO
- Ferreira, P., Rodrigues, M., Ledo, S., Senra, R., Costa, S., V, Rocha, M. & Paiva, C. (2013) Back pain as the first manifestation of a cavum tumor. *European Journal of Internal Medicine*, 24: e149.
Reason Not in PICO
- Firnhaber, J. M. Diagnosis and treatment of basal cell and squamous cell carcinoma. *American Family Physician* 86[2], 161-168. 2012. United States.
Reason Narrative Review

- FitzGerald, K. L., Buttner, P. G., Donovan, S. A., FitzGerald, K. L., Buttner, P. G. & Donovan, S. A. (2006) Nonpigmented skin lesions - how many are nonmelanoma skin cancer? *Australian Family Physician*, 35: 555-557.
Reason Not in PICO (only excised lesions, not examined lesions)
- Fontes, K. B., Cunha, K. S., Rodrigues, F. R., Silva, L. E. & Dias, E. P. (2013) Concordance between cytopathology and incisional biopsy in the diagnosis of oral squamous cell carcinoma. *Brazilian oral research*, 27: 122-127.
Reason Not in PICO
- Gait, R. A review of procedures carried out on basal cell carcinomas by Primary care physicians. *British Journal of Dermatology Conference*[var.pagings], July. 2009.
Reason Population not relevant to PICO
- Gajdatsy, A. Common and clinically important eyelid lesions. *Medicine Today* 13[5], 71-74. 2012. Australia.
Reason Narrative Review
- Gallo, M. Relevance of early diagnosis of nevoid basal cell carcinoma syndrome (Gorlin's syndrome). *Rivista Italiana di Chirurgia Plastica* 28[3], 265-272. 1996. Italy.
Reason Narrative Review
- Garcia, L., Nagore, E., Llombart, B., Sanmartin, O., Botella-Estrada, R., Requena, C., Jorda, E., and Guillen, C. Basal cell carcinoma of the nasolabial fold: an apparently 'benign' tumour that often needs complex surgery. *Journal of the European Academy of Dermatology & Venereology* 20[8], 926-930. 2006.
Reason Not relevant to PICO
- Gerbert, B., Maurer, T., Berger, T., Pantilat, S., McPhee, S. J., Wolff, M., Bronstone, A., and Caspers, N. Primary care physicians as gatekeepers in managed care. Primary care physicians' and dermatologists' skills at secondary prevention of skin cancer. *Archives of Dermatology* 132[9], 1030-1038. 1996.
Not relevant to PICO
- Giacomel, J. & Zalaudek, I. (2013) Pink Lesions. *Dermatologic Clinics*, 31: 649-678.
Reason Narrative review
- Gilde, K. The importance of malignant skin tumors. *Orvosi Hetilap* 147[48], 2321-2330. 2006. Hungary.
Reason Narrative Review
- Gordon, P. M., Cox, N. H., Paterson, W. D., Lawrence, C. M., Gordon, P. M., Cox, N. H., Paterson, W. D., and Lawrence, C. M. Basal cell carcinoma: are early appointments justifiable? *British Journal of Dermatology* 142[3], 446-448. 2000. ENGLAND.
Reason Not relevant to PICO
- Graves, J. Derm Access: A new triage system to rapidly identify suspicious skin lesions. *Dermatologic Surgery* 32[12], 1486-1490. 2006. United Kingdom.
Reason Not relevant to PICO
- Green, W. H., Wang, S. Q., and Cagnetta, A. B. Total-Body Cutaneous Examination, Total-Body Photography, and Dermoscopy in the Care of a Patient With Xeroderma Pigmentosum and Multiple Melanomas. *Archives of Dermatology* 145[8], 910-915. 2009.
Reason Single Case
- Grimaldi, L. Digital epiluminescence dermoscopy for pigmented cutaneous lesions, primary care physicians, and telediagnosis: a useful tool? *Journal of Plastic, Reconstructive and Aesthetic Surgery* 62[8], 1054-1058. 2009. United Kingdom.
Reason Not relevant to PICO
- Gupta, A., Stacey, S. & Amisshah-Arthur, K. N. (2014) Eyelid lumps and lesions. *BMJ (Online)*, 348.
Reason Narrative review
- Haliasos, E. C., Kerner, M., Jaimes, N., Zalaudek, I., Malveyh, J., Lanschuetzer, C. M., Hinter, H., Hofmann-Wellenhof, R., Braun, R. P. & Marghoob, A. A. (2013) Dermoscopy for the pediatric

dermatologist, part ii: dermoscopy of genetic syndromes with cutaneous manifestations and pediatric vascular lesions. [Review]. *Pediatric Dermatology*, 30: 172-181.

Reason Narrative review

Halpern, A. C., Hanson, L. J., Halpern, Allan C., and Hanson, Laura J. Awareness of, knowledge of and attitudes to nonmelanoma skin cancer (NMSC) and actinic keratosis (AK) among physicians. *International Journal of Dermatology* 43[9], 638-642. 2004. United States.

Reason Not relevant to PICO

Halpern, S. M. S. Establishment of a primary care-based teledermatology service in Kent. *British Journal of Dermatology Conference*[var.pagings], July. 2011.

Reason Not relevant to PICO

Hansen, C., Wilkinson, D., Hansen, M., Soyer, H. P., Hansen, Craig, Wilkinson, David, Hansen, Mary, and Soyer, H. Peter. Factors contributing to incomplete excision of nonmelanoma skin cancer by Australian general practitioners. *Archives of Dermatology* 145[11], 1253-1260. 2009. United States.

Reason Not relevant to PICO

Heal, C. and Raasch, B. Diagnosing skin cancer in primary care: how do main-stream general practitioners compare with primary care skin cancer clinic doctors? *Medical Journal of Australia* 188[2], 125. 21-1-2008.

Reason Narrative Review

Heal, C., Buettner, P., Raasch, B., Browning, S., Heal, C., Buettner, P., Raasch, B. & Browning, S. (2006) Minor skin excisions in general practice in North Queensland. *Australian Family Physician*, 35: 825-828.

Reason Not in PICO (only excised lesions, not examined lesions; no information about symptoms/lesion features)

Hochman, M., Lang, P., Hochman, M., and Lang, P. Skin cancer of the head and neck. [Review] [75 refs]. *Medical Clinics of North America* 83[1], 261-282. 10-9-0010. UNITED STATES.

Reason Narrative Review

Jacobs, R. J., Phillips, G., Jacobs, Robert J., and Phillips, Geraint. Basal cell carcinoma mistaken for actinic keratosis. *Clinical & Experimental Optometry* 89[3], 171-175. 2006. Australia.

Reason Single Case/Narrative Review

Jolliffe, V. M., Harris, D. W., Morris, R., Wallacet, P., Whittaker, S. J., Jolliffe, V. M., Harris, D. W., Morris, R., Wallacet, P., and Whittaker, S. J. Can we use video images to triage pigmented lesions? *British Journal of Dermatology* 145[6], 904-910. 2001. England.

Reason Not relevant to PICO

Kahn, E., Sossong, S., Goh, A., Carpenter, D. & Goldstein, S. (2013) Evaluation of Skin Cancer in Northern California Kaiser Permanente's Store-and-Forward Teledermatology Referral Program. *Telemedicine and E-Health*, 19: 780-785.

Reason Not in PICO

Kamyab-Hesari, K., Seirafi, H., Naraghi, Z. S., Shahshahani, M. M., Rahbar, Z., Damavandi, M. R., Naraghi, M. M., Rezvani, M. & Aghazadeh, N. (2014) Diagnostic accuracy of punch biopsy in subtyping basal cell carcinoma. *Journal of the European Academy of Dermatology and Venereology*, 28: 250-253.

Reason Not in PICO

Keir, J. Re: Diagnosing skin cancer in primary care: how do main-stream general practitioners compare with primary care skin cancer clinic doctors? *Medical Journal of Australia* 188[2], 125-126. 21-1-2008.

Reason Narrative Review

Khorasgani, M. G. P. Dermatological surgery in the community: Are the guidelines being followed? *British Journal of Dermatology Conference*[var.pagings], July. 2010.

Reason Not relevant to PICO

- Kiwilsza, M. and Sporniak-Tutak, K. Gorlin-Goltz syndrome--a medical condition requiring a multidisciplinary approach. *Medical Science Monitor* 18[9], RA145-RA153. 2012.
Reason Narrative Review
- Kok, L. P., V. General practitioners use digital cameras and internet for telepathology of skin lesions. *Electronic Journal of Pathology and Histology* 6[3], 7-19. 2000. Germany.
Reason Narrative Review
- Kundu, R. V. & Patterson, S. (2013) Dermatologic conditions in skin of color: part I. Special considerations for common skin disorders.[Summary for patients in *Am Fam Physician*. 2013 Jun 15;87(12):Online; PMID: 23939576]. *American Family Physician*, 87: 850-856.
Reason Narrative review
- Kutcher, M. J. R. Fifteen inches from cancer: early recognition of facial lesions by the dentist. *Compendium of continuing education in dentistry (Jamesburg, N J.*[12], 939-942. 10-10-0106. United States.
Reason Not relevant to PICO
- Lai, W.-Y. (1111) An elderly man with a painful scaly nodule. *Hong Kong Practitioner*, 35: September.
Reason Not in PICO
- Lathlean, S. & Lathlean, S. (1999) Skin cancer in general practice in South Australia. A five year study. *Australian Family Physician*, 28 Suppl 1: S28-S31.
Reason Not in PICO (only excised lesions, not examined lesions; no information about symptoms/lesion features)
- Leber, K., Perron, V. D., and Sinni-McKeehen, B. Common skin cancers in the United States: A practical guide for diagnosis and treatment. *Nurse Practitioner Forum-Current Topics and Communications* 10[2], 106-116. 1999.
Reason Narrative Review
- Leggett, P. A randomized controlled trial using instant photography to diagnose and manage dermatology referrals. *Family Practice* 21[1], 54-56. 2004. United Kingdom.
Reason Not relevant to PICO
- Lester, J. & Weinstock, M. A. (2014) Telerriage for provision of dermatologic care: A pilot program in the Department of Veterans Affairs. *Journal of Cutaneous Medicine and Surgery*, 18: 170-173.
Reason Not in PICO
- Liebman, T. N., Wang, S. Q., Liebman, Tracey N., and Wang, Steven Q. Detection of early basal cell carcinoma with dermoscopy in a patient with psoriasis. *Dermatology Online Journal* 17[2], 12. 2011. United States.
Reason Single Case
- Liew, Y., De, B. D. & Sansom, J. (2014) Rapid clinical review of patients assessed by a teledermatology service: Analysis of pathways and outcomes. *British Journal of Dermatology*, 171: 138.
Reason Not in PICO
- Lin, Y.-C., Perng, C.-L., Chang, Y.-M., Li, Y.-F., Tsai, Y.-M., Wu, G.-J. & Lin, C.-K. (2013) Coexistent squamous cell carcinoma and adenoid basal carcinoma in the uterine cervix and infection with human papillomavirus (HPV 31). *Taiwanese Journal of Obstetrics and Gynecology*, 52: 407-410.
Reason Not in PICO
- Ljubenic, M., Ljubenic, D., Binic, I., Jovanovic, D., Stanojevic, M., Ljubenic, M., Ljubenic, D., Binic, I., Jovanovic, D., and Stanojevic, M. Gorlin-Goltz syndrome. *Acta Dermatovenerologica Alpina, Panonica et Adriatica* 16[4], 166-169. 2007. Slovenia.
Reason Single Case
- Lo, Muzio L., Nocini, P., Bucci, P., Pannone, G., Consolo, U., Procaccini, M., Lo Muzio, L., Nocini, P., Bucci, P., Pannone, G., Consolo, U., and Procaccini, M. Early diagnosis of nevoid basal cell carcinoma syndrome. *Journal of the American Dental Association* 130[5], 669-674. 1999. UNITED STATES.
Reason Not relevant to PICO
- Lober, C. W., Fenske, N. A., Lober, C. W., and Fenske, N. A. Basal cell, squamous cell, and sebaceous gland carcinomas of the periorbital region. [Review] [54 refs]. *Journal of the American*

Academy of Dermatology 25[4], 685-690. 1991. UNITED STATES.
Reason Narrative Review

Lyngset, E., Hunskar, S., Lyngset, E., and Hunskar, S. [Skin neoplasms in general practice]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening* 121[19], 2281-2283. 20-8-2001. Norway.
Reason Population not relevant to PICO

Mantese, S. A. O. Basal cell Carcinoma - Analysis of 300 cases observed in Uberlandia - MG, Brazil. *Anais Brasileiros de Dermatologia* 81[2], 136-142. 2006. Brazil.
Reason Not relevant to PICO

Marghoob, A. A. and Marghoob, A. A. Basal and squamous cell carcinomas. What every primary care physician should know. [Review] [20 refs]. *Postgraduate Medicine* 102[2], 139-142. 15-4-0146. UNITED STATES.
Reason Narrative Review

Marghoob, A. A., Usatine, R. P. & Jaimes, N. (2013) Dermoscopy for the family physician. [Review]. *American Family Physician*, 88: 441-450.
Reason Narrative review

Martinez, J. C., Otley, C. C., Martinez, J. C., and Otley, C. C. The management of melanoma and nonmelanoma skin cancer: a review for the primary care physician. [Review] [54 refs]. *Mayo Clinic Proceedings* 76[12], 1253-1265. 2001. United States.
Reason Narrative Review

Maybury, C. M., Craythorne, E. & Martin, B. (2013) An ulcerated nodule on the nose. *BMJ Case Reports*, 2013, 2013.
Reason Not in PICO

McGregor, J. C. and McGregor, J. C. Skin cancer referrals--could prioritization be a reasonable approach in the new millennium? *Scottish Medical Journal* 45[3], 77-78. 2000. SCOTLAND.
Reason Narrative Review

McLaughlin S.Tobin. The role of digital photography and electronic referral in the triage of patients with suspected skin cancer [6]. *British Journal of Dermatology* 154[1], 188-190. 2006. United Kingdom.
Reason Not relevant to PICO

McNulty-Brown E.Veysey. An audit of all excisions undertaken by general practitioners in a rural community between March 2009 and March 2010. *British Journal of Dermatology Conference*[var.pagings], July. 2012.
Reason Not relevant to PICO

Menzies, S. W. Using dermoscopy to diagnose pigmented skin lesions. *Medicine Today* 5[4], 63-71. 2004. Australia.
Reason Narrative Review

Menzies, S. W., Emery, J., Staples, M., Davies, S., McAvoy, B., Fletcher, J., Shahid, K. R., Reid, G., Avramidis, M., Ward, A. M., Burton, R. C., Elwood, J. M., Menzies, S. W., Emery, J., Staples, M., Davies, S., McAvoy, B., Fletcher, J., Shahid, K. R., Reid, G., Avramidis, M., Ward, A. M., Burton, R. C., and Elwood, J. M. Impact of dermoscopy and short-term sequential digital dermoscopy imaging for the management of pigmented lesions in primary care: a sequential intervention trial. *British Journal of Dermatology* 161[6], 1270-1277. 2009. England.
Reason Not relevant to PICO

Menzies, S. W., Moloney, F. J., Byth, K., Avramidis, M., Argenziano, G., Zalaudek, I., Braun, R. P., Malvey, J., Puig, S., Rabinovitz, H. S., Oliviero, M., Cabo, H., Bono, R., Pizzichetta, M. A., Claeson, M., Gaffney, D. C., Soyer, H. P., Stanganelli, I., Scolyer, R. A., Guitera, P., Kelly, J., McCurdy, O., Llambrich, A., Marghoob, A. A., Zaballos, P., Kirchesch, H. M., Piccolo, D., Bowling, J., Thomas, L., Terstappen, K., Tanaka, M., Pellacani, G., Pagnanelli, G., Ghigliotti, G., Ortega, B. C., Crafter, G., Ortiz, A. M., Tromme, I., Karaarslan, I. K., Ozdemir, F., Tam, A., Landi, C., Norton, P., Kacar, N., Rudnicka, L., Slowinska, M., Simionescu, O., Di, S. A., Coates, E. & Kreuzsch, J. (2013) Dermoscopic evaluation of nodular melanoma. *JAMA Dermatology*, 149:

699-709.

Reason Not in PICO

Mitchell, G. Farndon. Genetic predisposition to cancer: The consequences of a delayed diagnosis of Gorlin syndrome. *Clinical Oncology* 17[8], 650-654. 2005. United Kingdom.

Reason Single Case

Moffatt, C. R. M. Diagnostic accuracy in skin cancer clinics: The Australian experience. *International Journal of Dermatology* 45[6], 656-660. 2006. United Kingdom.

Reason Not relevant to PICO

Montero Perez, F. J. M. Importance of skin cancer (non-melanoma): a study of 89 cases. *Atencion primaria / Sociedad Espanola de Medicina de Familia y Comunitaria* 6[9], 660-664. 1989. Spain.

Reason Outcomes not relevant to PICO

Moreno, G. Tran. Prospective study to assess general practitioners' dermatological diagnostic skills in a referral setting. *Australasian Journal of Dermatology* 48[2], 77-82. 2007. Australia.

Reason Not relevant to PICO

Morteza, A. S., Salama, S. & Alowami, S. (2013) Lymphoepithelioma-like carcinoma of the skin: case report and approach to surgical pathology sign out. *Rare Tumors*, 5: e47.

Reason Not in PICO

Naik, N. S., Brodell, R. T., and Fatteh, S. When to suspect superficial basal cell carcinoma. *Postgraduate Medicine* 104[5], 157-158. 1998.

Reason Single Case

Nakjang, Y. and Kullavanijaya, P. Basal cell carcinoma: seven years' experience at the Institute of Dermatology in Bangkok. *Journal of Dermatology* 21[9], 660-663. 1994.

Reason Population not relevant to PICO

Oakley, A. M. A. Diagnostic accuracy of teledermatology: results of a preliminary study in New Zealand. *The New Zealand medical journal* 110[1038], 51-53. 1997. New Zealand.

Reason Not relevant to PICO

Obata, H. Aoki. Incidence of benign and malignant lesions of eyelid and conjunctival tumors. *Nippon Ganka Gakkai zasshi* 109[9], 573-579. 2005. Japan.

Reason Not relevant to PICO

Offidani, A., Simonetti, O., Bernardini, M. L., Alpagut, A., Cellini, A., Bossi, G., Offidani, Annamaria, Simonetti, Oriana, Bernardini, Maria Luisa, Alpagut, Ayhan, Cellini, Andreina, and Bossi, Guido. General practitioners' accuracy in diagnosing skin cancers. *Dermatology* 205[2], 127-130. 2002. Switzerland.

Reason Not relevant to PICO

Ojeda, R. M. and Graells, J. [Effectiveness of primary care physicians and dermatologists in the diagnosis of skin cancer: a comparative study in the same geographic area][Spanish]. *Actas Dermosifiliograficas* 102[1], 48-52. 2011.

Reason Not relevant to PICO

Pallagatti, S., Sheikh, S., Aggarwal, A., Gupta, D., Singh, R., Handa, R., Kaur, S. & Mago, J. (2013) Toluidine blue staining as an adjunctive tool for early diagnosis of dysplastic changes in the oral mucosa. *Journal of Clinical & Experimental Dentistry*, 5: e187-e191.

Reason Not in PICO

Palmer, V. M. & Wilson, P. R. (2013) Incompletely excised basal cell carcinoma: residual tumor rates at Mohs re-excision. *Dermatologic Surgery*, 39: 706-718.

Reason Not in PICO

Pan, Y. Chamberlain. Dermatoscopy aids in the diagnosis of the solitary red scaly patch or plaque-features distinguishing superficial basal cell carcinoma, intraepidermal carcinoma, and psoriasis. *Journal of the American Academy of Dermatology* 59[2], 268-274. 2008. United States.

Reason Population not relevant to PICO

- Pariser, D. M., Phillips, P. K., Pariser, D. M., and Phillips, P. K. Basal cell carcinoma: when to treat it yourself, and when to refer. [Review] [5 refs]. *Geriatrics* 49[3], 39-44. 1994. UNITED STATES.
Reason Narrative Review
- Piccolo, D. Smolle. Teledermoscopy--results of a multicentre study on 43 pigmented skin lesions. *Journal of Telemedicine and Telecare* 6[3], 132-137. 2000. United Kingdom.
Reason Not relevant to PICO
- Porta, N., San, Juan J., Grasa, M. P., Simal, E., Ara, M., Querol, M. A., Porta, N., San Juan, J., Grasa, M. P., Simal, E., Ara, M., and Querol, M. Ara. [Diagnostic agreement between primary care physicians and dermatologists in the health area of a referral hospital]. [Spanish]. *Actas Dermo-Sifiliograficas* 99[3], 207-212. 2008. Spain.
Reason Not relevant to PICO
- Price, H. N., Zaenglein, A. L., Price, Harper N., and Zaenglein, Andrea L. Diagnosis and management of benign lumps and bumps in childhood. [Review] [34 refs]. *Current Opinion in Pediatrics* 19[4], 420-424. 2007. United States.
Reason Narrative Review
- Raasch, B. A. and Raasch, B. A. Suspicious skin lesions and their management. *Australian Family Physician* 28[5], 466-471. 1999. AUSTRALIA.
Reason Not relevant to PICO
- Rademaker, M. Thorburn. Pathology referrals for skin lesions - Are we giving the pathologist sufficient clinical information? *New Zealand Medical Journal* 123[1325], 53-58. 2010. New Zealand.
Reason Not relevant to PICO
- Raj, G. & Gupta, G. (1111) The need for full body skin examination on patients referred to dermatology with a lesion. *British Journal of Dermatology.Conference: 93rd Annual Meeting of the British Association of Dermatologists Liverpool United Kingdom.Conference Start: 20130709 Conference End: 20130711.Conference Publication: (var.pagings)*, 169: July.
Reason Not in PICO
- Richert, B., Lecerf, P., Caucanas, M. & Andre, J. (2013) Nail tumors. *Clinics in Dermatology*, 31: 602-617.
Reason Narrative review
- Rodriguez, Caravaca G., Garcia-Cruces, Mendez J., Hobson, S., Rodriguez, Caravaca F., Villar Del, Campo M., Gonzalez, Mosquera M., Rodriguez Caravaca, G., Garcia-Cruces Mendez, J., Hobson, S., Rodriguez Caravaca, F., Villar Del Campo, M., and Gonzalez Mosquera, M. [Validity of the clinical diagnosis of the basal cell carcinoma in primary health care]. [Spanish]. *Atencion Primaria* 28[6], 391-395. 15-10-2001. Spain.
Reason Not relevant to PICO
- Rodriguez, Caravaca G., Villar Del, Campo M., Gonzalez, Mosquera M., Garcia-Cruces, Mendez J., Lopez, Bran E., Pombo, Liria N., Rodriguez Caravaca, G., Villar Del Campo, M., Gonzalez Mosquera, M., Garcia-Cruces Mendez, J., Lopez Bran, E., and Pombo Liria, N. [Diagnostic agreement between primary and hospital care in the assessment of basal cell carcinoma]. [Spanish]. *Gaceta Sanitaria* 15[3], 255-258. 2001. Spain.
Reason Setting not relevant to PICO
- Roozeboom, M. H., Mosterd, K., Winnepeninckx, V. J., Nelemans, P. J. & Kelleners-Smeets, N. W. (2013) Agreement between histological subtype on punch biopsy and surgical excision in primary basal cell carcinoma. *Journal of the European Academy of Dermatology & Venereology*, 27: 894-898.
Reason Not in PICO
- Rosendahl, C., Tschandl, P., Cameron, A., Kittler, H., Rosendahl, C., Tschandl, P., Cameron, A. & Kittler, H. (2011) Diagnostic accuracy of dermatoscopy for melanocytic and nonmelanocytic pigmented lesions. *Journal of the American Academy of Dermatology*, 64: 1068-1073.
Reason Not in PICO (only excised lesions, not examined lesions)

- Rosendahl, C., Hansen, C., Cameron, A., Bourne, P., Wilson, T., Cook, B., Baker, M., Keir, J., Dicker, T., Reid, M., Williamson, R., Weedon, D., Soyer, H. P., Youl, P. H., and Wilkinson, D. Measuring performance in skin cancer practice: the SCARD initiative. *International Journal of Dermatology* 50[1], 44-51. 2011.
Reason Not relevant to PICO
- Rousset, J., Abgral, R., Chinellato, S., Garetier, M., Barberot, C., Valette, G., Potard, G., Le, B. T. & Salaun, P. Y. (2013) Early recurrence or submucosal residual of laryngeal squamous cell carcinoma: diagnosis by CT-guided endolaryngeal core biopsy on a transcutaneous approach. *Head & Neck*, 35: E202-E204.
Reason Not in PICO
- Ruskiewicz, J. and Ruskiewicz, J. Skin cancer and actinic keratoses. *Journal of the American Optometric Association* 69[4], 229-235. 1998. UNITED STATES.
Reason Narrative Review
- Sambandan, P. G. G. Infiltrative basal cell carcinomas presenting as actinic keratosis: Implications for clinical practice. *Dermatologic Surgery* 34[1], 9-13. 2008. United Kingdom.
Reason Narrative Review
- Sanyal, S., Holme, A. & Kemmett, D. (2013) How are patients with actinic keratoses managed in primary care? *British Journal of Dermatology*, 169: 45.
Reason Not in PICO
- Schlien, H. P., Niemeyer, K., Habel, G., and Happle, R. [Keratocysts in adolescent patients--early symptoms in the diagnosis of basal cell nevus syndrome?][German]. *Deutsche Zahnärztliche Zeitschrift* 40[6], 521-524. 1985.
Reason Awaiting arrival of paper
- Schofield, J. Hepburn. The costs of diagnosing and treating skin cancer using the 2-week-wait referral process. *British Journal of Dermatology Conference*[var.pagings], July. 2011.
Reason Health Economics
- See, A. Lim. Operational teledermatology in Broken Hill, rural Australia. *Australasian Journal of Dermatology* 46[3], 144-149. 2005. Australia.
Reason Narrative Review
- Shapiro, M., James, W. D., Kessler, R., Lazorik, F. C., Katz, K. A., Tam, J., Nieves, D. S., Miller, J. J., Shapiro, Michael, James, William D., Kessler, Rex, Lazorik, Francis C., Katz, Kenneth A., Tam, John, Nieves, David S., and Miller, Jeffrey J. Comparison of skin biopsy triage decisions in 49 patients with pigmented lesions and skin neoplasms: store-and-forward teledermatology vs face-to-face dermatology. *Archives of Dermatology* 140[5], 525-528. 2004. United States.
Reason Not relevant to PICO
- Sharma, A., Alfa-Wali, M., Rodriguez-Justo, M. & Polychronis, A. (2013) Squamous cell carcinoma of pancreas: an unusual site of relapse from early-stage lung cancer: 12-month postsurgery. *BMJ Case Reports*, 2013, 2013.
Reason Not in PICO
- Shlyankevich, J., Kimball, A., Corey, K. & Kardos, M. (2014) Diagnostic accuracy of referring providers sending patients to dermatology urgent care clinic for suspected skin cancers. *Journal of the American Academy of Dermatology*, 70: AB81.
Reason Not in PICO
- Singh, T. & Schenberg, M. (2013) Delayed diagnosis of oral squamous cell carcinoma following dental treatment. *Annals of the Royal College of Surgeons of England*, 95: 369-373.
Reason Not in PICO
- Socha, A. & Niedzielska, I. (2013) Exophytic tumours of skin of the head - Case study and review of the literature. *Dental and Medical Problems*, 50: 229-237.
Reason Not in PICO
- Steel, B. J. (2014) - Skin cancer - an overview for dentists. - *British Dental Journal*, 216: 575-581.
Reason Narrative review

- Steiner, A. Pehamberger. In vivo epiluminescence microscopy of pigmented skin lesions. II. Diagnosis of small pigmented skin lesions and early detection of malignant melanoma. *Journal of the American Academy of Dermatology* 17[4], 584-591. 1987. United States.
Reason Outcomes not relevant to PICO
- Steinmann, A. Liebl. Prevention and Early Detection of Cancer of the Skin. *Gesundheitswesen, Supplement* 66[1], S37-S42. 2004. Germany.
Reason Narrative Review
- Streeton, C. L. G. Treatment of basal cell carcinomas by general practitioners in Australia. *International Journal of Dermatology* 45[4], 345-351. 2006. United Kingdom.
Reason Narrative Review
- Stulberg, D. L., Crandell, B., Fawcett, R. S., Stulberg, Daniel L., Crandell, Blain, and Fawcett, Robert S. Diagnosis and treatment of basal cell and squamous cell carcinomas. *American Family Physician* 70[8], 1481-1488. 15-10-2004. United States.
Reason Narrative Review
- Takahashi, H. and Takahashi, H. Non-ulcerative basal cell carcinoma arising on the genitalia. *Journal of Dermatology* 27[12], 798-801. 2000. Japan.
Reason N=2
- Tan, E., Yung, A., Jameson, M., Oakley, A., Rademaker, M., Tan, E., Yung, A., Jameson, M., Oakley, A., and Rademaker, M. Successful triage of patients referred to a skin lesion clinic using teledermoscopy (IMAGE IT trial). *British Journal of Dermatology* 162[4], 803-811. 2010. England.
Reason Not relevant to PICO
- Tangjaturonrasme, N., Rerknimitr, R., Pittayanon, R., Wisedopas, N. & Kullavanijaya, P. (2013) The difference in detection rates during surveillance endoscopy for early squamous cell neoplasia of the esophagus between patients with previous nasopharyngeal cancer and patients with other ent related squamous cell cancers pornphan thienchanachaiya1. *Gastrointestinal Endoscopy*, 77: AB339-AB340.
Reason Not in PICO
- Tate, B. Checking pigmented skin lesions. *Medicine Today* 8[3], 38-46. 2007. Australia.
Reason Narrative Review
- Terrill, P. J. F. Is there just one lesion? the need for whole body skin examination in patients presenting with non-melanocytic skin cancer. *ANZ Journal of Surgery* 79[10], 707-712. 2009. Australia.
Reason Population not relevant to PICO
- Tochigi, T., Shuto, K., Staito, H., Kono, T. & Matsubara, H. (2013) Early esophageal squamous cell cancer by high-barium esophagography using flat panel X-ray detector in comparison with histological findings. *European Journal of Cancer*, 49: S252-S253.
Reason Not in PICO
- Tolpinrud, W. L., Viola, K. V., Kirsner, R. S., Gross, C. P., Imaeda, S., Federman, D. G., Tolpinrud, Whitney L., Viola, Kate V., Kirsner, Robert Scott, Gross, Cary P., Imaeda, Suguru, and Federman, Daniel G. Nondermatologists' use of predictive terms for a potentially malignant lesion. *Southern Medical Journal* 104[7], 477-481. 2011. United States.
Reason Outcomes not relevant to PICO
- Treiber, N., Huber, M. A., Scharffetter-Kochanek, K. & Schneider, L. A. (2014) - [Early detection of skin cancer]. [German]. - *MMW Fortschritte der Medizin*, 156: 37-40.
Reason Narrative review
- Turan, E., Yurt, N., Yesilova, Y. & Turkcu, G. (2013) Early-onset basal cell carcinoma. *Turkish Journal of Pediatrics*, 55: 354-356.
Reason Not in PICO

- Turner, T. Pigmented lesions - A plan for management in general practice. *Medical Journal of Australia* 159[11-12], 809-814. 1993. Australia.
Reason Narrative Review
- Twist, M. Rate of incomplete excision of basal cell carcinomas by General Practitioners with Special Interest. *British Journal of Dermatology* 161[1], 187. 2009.
Reason Not relevant to PICO
- Ubriani, R. Grossman. Facial Papules as a Marker of Internal Malignancy. *Medical Clinics of North America* 93[6], 1305-1331. 2009. United States.
Reason Narrative Review
- Uslu, M. Karaman. A case of nevoid basal cell carcinoma syndrome. *Turkderm Deri Hastaliklari ve Frengi Arsivi* 40[4], 136-138. 2006. Turkey.
Reason Single Case
- van Rijsingen, M. C., Van, B. B., Van Der Wilt, G. J., Lagro-Janssen, A. L. & Gerritsen, M. J. (2014) - The current and future role of general practitioners in skin cancer care: an assessment of 268 general practitioners. - *British Journal of Dermatology*, 170: 1366-1368.
Reason Not in PICO
- Van Rijsingen, M. C. J., Hanssen, S. C. A., Groenewoud, J. M. M., Van Der Wilt, G. J. & Gerritsen, M.-J. (2014) Referrals by general practitioners for suspicious skin lesions: The urgency of training. *Acta Dermato-Venereologica*, 94: 138-141.
Reason Not in PICO
- Vermaak, P. V. & Manushakian, J. (2013) Rapidly enlarging skin lesion on the lip. *BMJ Case Reports*, 2013, 2013.
Reason Not in PICO
- Viglizzo, G. Rongioletti. Clinical, dermoscopic and pathologic correlation of pigmentary lesions observed in a dermoscopy service in the year 2003. *Giornale Italiano di Dermatologia e Venereologia* 139[4], 339-344. 2004. Italy.
Reason Setting not relevant to PICO
- Walker, M. S. R. Treatment patterns and clinical characteristics of patients with advanced basal cell carcinoma (ABCC) in the community oncology setting. *Journal of the American Academy of Dermatology Conference*[var.pagings], AB159. 2012.
Reason Not relevant to PICO
- Warshaw, E. M., Lederle, F. A., Grill, J. P., Gravely, A. A., Bangerter, A. K., Fortier, L. A., Bohjanen, K. A., Chen, K., Lee, P. K., Rabinovitz, H. S., Johr, R. H., Kaye, V. N., Bowers, S., Wenner, R., Askari, S. K., Kedrowski, D. A., Nelson, D. B., Warshaw, Erin M., Lederle, Frank A., Grill, Joseph P., Gravely, Amy A., Bangerter, Ann K., Fortier, Lawrence A., Bohjanen, Kimberly A., Chen, Karen, Lee, Peter K., Rabinovitz, Harold S., Johr, Robert H., Kaye, Valda N., Bowers, Sacharitha, Wenner, Rachel, Askari, Sharone K., Kedrowski, Deborah A., and Nelson, David B. Accuracy of teledermatology for pigmented neoplasms.[Erratum appears in *J Am Acad Dermatol*. 2010 Feb;62(2):319]. *Journal of the American Academy of Dermatology* 61[5], 753-765. 2009. United States.
Reason Not relevant to PICO
- Watkins, J. and Watkins, Jean. Dermatology and the community nurse: actinic (solar) keratosis. [Review] [13 refs]. *British journal of community nursing* 15[1], 6-1. 2010. England.
Reason Narrative Review
- Westbrook, R. H. G. Diagnostic accuracy for skin cancer: Comparison of general practitioner with dermatologist and dermatopathologist [1]. *Journal of Dermatological Treatment* 17[1], 57-58. 2006. United Kingdom.
Reason Narrative Review
- White, G. M., Zhou, H. C. & Burchette, R. J. (2013) Biopsy followed by immediate curettage and electrodesiccation of suspected basal cell carcinomas at the first visit. *JAMA Dermatology*,

149: 980-981.

Reason Not in PICO

Whited, J. D., Hall, R. P., Simel, D. L., and Horner, R. D. Primary care clinicians' performance for detecting actinic keratoses and skin cancer. *Archives of Internal Medicine* 157[9], 985-990. 1997.

Reason Not relevant to PICO

Wietfeldt, E. D., Thiele, J., Wietfeldt, E Dawn, and Thiele, James. Malignancies of the anal margin and perianal skin. *Clinics in Colon & Rectal Surgery* 22[2], 127-135. 2009. United States.

Reason Narrative Review

Winzenburg, S. M., Niehans, G. A., George, E., Daly, K., Adams, G. L., Winzenburg, S. M., Niehans, G. A., George, E., Daly, K., and Adams, G. L. Basaloid squamous carcinoma: a clinical comparison of two histologic types with poorly differentiated squamous cell carcinoma. *Otolaryngology - Head & Neck Surgery* 119[5], 471-475. 1998. UNITED STATES.

Reason Not relevant to PICO

Wolberink, E. A. W., Pasch, M. C., Zeiler, M., Van Erp, P. E. J. & Gerritsen, M. J. P. (2013) High discordance between punch biopsy and excision in establishing basal cell carcinoma subtype: Analysis of 500 cases. *Journal of the European Academy of Dermatology and Venereology*, 27: 985-989.

Reason Not in PICO

Woolley, S. D. & Hughes, C. (2013) A young military pilot presents with a periocular Basal Cell Carcinoma: A case report. *Travel Medicine and Infectious Disease*, 11: 435-437.

Reason Not in PICO

Wray, E. V., Brant, B., Hussain, F. & Muller, F. M. (2013) A new model of teledermoscopy combining service and education. *British Journal of Dermatology*, 169: 139.

Reason Not in PICO

Youl, P. H., Janda, M., Aitken, J. F., Del Mar, C. B., Whiteman, D. C., Baade, P. D., Youl, P. H., Janda, M., Aitken, J. F., Del Mar, C. B., Whiteman, D. C. & Baade, P. D. (2011) Body-site distribution of skin cancer, pre-malignant and common benign pigmented lesions excised in general practice. *British Journal of Dermatology*, 165: 35-43.

Reason Same data as Youl (20067), which is not in PICO as results only reported for excised lesions (N = 11116, GPs and skin cancer clinic doctors), not examined lesions (N = 28755, GPs and skin cancer clinic doctors).

Youl, P.H. et. Al. (2007) Diagnosing skin cancer in primary care: how do mainstream general practioners compare with primary care skin cancer clinic doctors? *Medical Journal of Australia* 187;215-220

Reason Not in PICO as results only reported for excised lesions (N = 11116, GPs and skin cancer clinic doctors), not examined lesions (N = 28755, GPs and skin cancer clinic doctors).

Zalaudek, I., Kreuzsch, J., Giacomel, J., Ferrara, G., Catricala, C., and Argenziano, G. How to diagnose nonpigmented skin tumors: A review of vascular structures seen with dermoscopy Part II. Nonmelanocytic skin tumors. *Journal of the American Academy of Dermatology* 63[3], 377-386. 2010.

Reason Narrative Review

Zucker, J. L. The eyelids: Some common disorders seen in everyday practice. *Geriatrics* 64[4], 14-19+28. 2009. United States.

Reason Narrative Review

Review question:

Which investigations of symptoms of suspected basal cell carcinoma should be done with clinical responsibility retained by primary care?

Results

Literature search

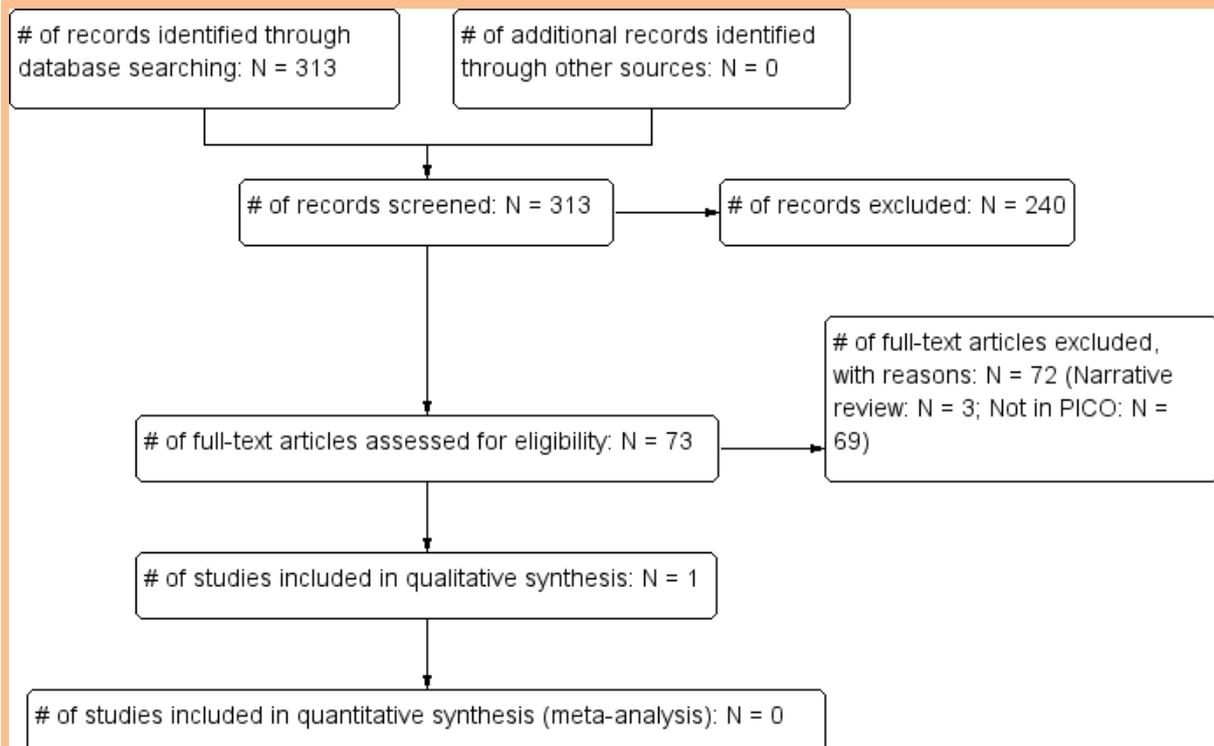
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	2206	141	07/02/2013
<i>Premedline</i>	1980-2013	85	9	07/02/2013
<i>Embase</i>	1980-2013	2263	146	08/02/2013
<i>Cochrane Library</i>	1980-2013	37	1	07/02/2013
<i>Psychinfo</i>	1980-2013	3	0	07/02/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	309	63	07/02/2013
<i>Biomed Central</i>	1980-2013	1026	4	07/02/2013

Total number of studies identified after de-duplication: 290

Update Search

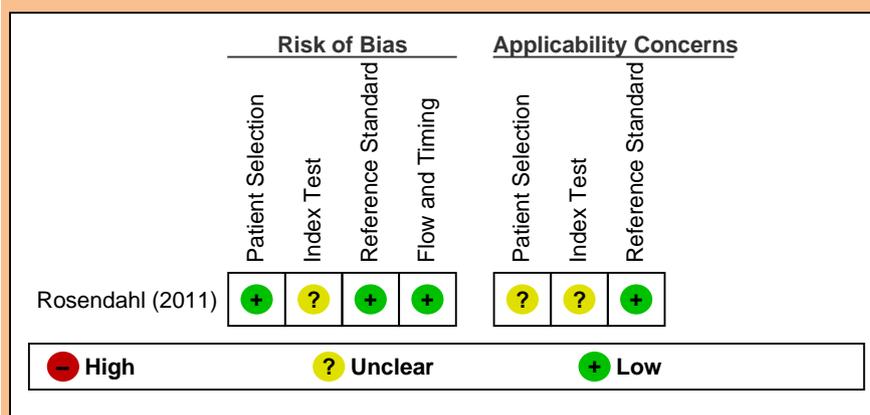
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-11/08/2014	87	7	11/08/2014
<i>Premedline</i>	2013-11/08/2014	123	6	11/08/2014
<i>Embase</i>	2013-11/08/2014	181	16	11/08/2014
<i>Cochrane Library</i>	2013-11/08/2014	55	0	11/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-11/08/2014	53	2	11/08/2014

Total References retrieved (after de-duplication): 23



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issues to note are that the study population may not be directly representative of an unselected symptomatic population of patients presenting to the UK-based GP, that the index test does not specify the criteria for malignancy which may limit its external validity, and that the results presented are based on a best case scenario, and are therefore likely to be inflated, and only available for skin malignancy as a whole and not for basal cell carcinoma separately.



Study results

Table 1: Basal cell carcinoma: Study results

Study	Intervention	Prevalence	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	False negativity rate
Rosendahl (2011)	Clinical images and dermatoscopy	138 malignancies/463 lesions	82.6% (NR)	80% (NR)	NR (NR)	17.4% (NR)

NR = not reported

No evidence was identified pertaining to the diagnostic accuracy of excision biopsy of the lesion in patients with suspected basal cell cancer where the clinical responsibility was retained by primary care.

Evidence statement(s):

Dermatoscopy and clinical images (1 study, N = 463 lesions/389 patients) performed in symptomatic patients presenting in a primary care setting is associated with a best-case sensitivity of 82.6%, specificity of 80%, and false negativity rate of 17.4% for basal cell carcinoma. The study was associated with 1 bias and 2 applicability concerns (see also Table 1).

Evidence tables

Rosendahl (2011)

PATIENT SELECTION

A. risk of bias	
Patient sampling	Consecutive series of lesions submitted for histology from the primary care skin cancer clinic of one of the authors.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Probably
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 463 pigmented lesions from 389 patients, mean (SD) age = 57 (17) years, 32.6% females. Lesion location: Trunk: N = 241; extremities: N = 128; head and face: N = 82; palms and soles: N = 10. Histopathologically, 246 pigmented lesions turned out to be melanocytic and 217 were of non-melanocytic origin.</p> <p>Final diagnoses: Malignant lesions: Basal cell carcinoma: N = 72; squamous cell carcinoma: N = 37; melanoma: N = 29. Benign lesions: Melanocytic nevi: N = 217; seborrheic keratosis: N = 43; solar lentigo: N = 37; lichen planus-like keratosis: N = 21, others: N = 7.</p> <p><u>Inclusion criteria:</u> All pigmented lesions biopsied or excised during a 30-month period. <i>Patients included are only those who received resection. This changes the spectrum of disease as it excludes patients with lesions that were not considered concerning enough to warrant resection.</i></p> <p><u>Exclusion criteria:</u> Poor image quality (N = 3).</p> <p><u>Clinical setting:</u> Primary care skin cancer practice in Queensland, Australia</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	<p>For each lesion: A triplet of high-resolution digital images consisting of two clinical images (overview and close-up) followed by one dermatoscopic image. The clinical images were taken with Canon EOS digital single lens reflex cameras. The close-up was taken using a macro lens (60-mm f2.8 macro, Canon) with diffuse illumination at a constant reproduction ratio determined by a custom-fabricated spacer. The degree of magnification of the close-up images was similar to that of the dermatoscopy images.</p> <p>Dermatoscopic images were nonpolarising, preferentially using the DermLite Fluid device (3 Gen, San Juan, Capistrano, Ca); alternatively DermLite Foto (custom nonpolarised; 3 Gen) and Heine Delta 20 devices (Heines, Optotechnic GmbH< Herrsching, Germany) were used for large and inaccessible lesions, respectively. Dermatoscopic photographs were taken with Canon EOS single lens reflex cameras. Images were presented to the assessors as powerpoint slides. After inspection of the images, the assessor was required to give a diagnosis (criteria not reported, so presumably based on qualitative criteria). Dermatoscopic images were also screened for asymmetry of structure and colour (“chaos”) and for clues to malignancy. Asymmetry of colour and structure were defined according to the basic principles of pattern analysis as revised by Kittler (2007, Dermatopathology: Practical & Conceptual, 13:1). Clues to malignancy included: Eccentric structureless zone (any colour except skin colour), gray or blue structures, peripheral black dots or clods, segmental radial lines or pseudopods,</p>

	polymorphous vessels, white lines, thick reticular or branched lines, and parallel lines on ridges (acral lesions). <i>Not further information regarding the specific cut-off criteria for malignancy reported. The reporting of the results suggests that the test performance is based on best possible scenario.</i>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histopathology
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	The results are presented for all malignancies combined. The 2-by-2 table could not be extracted and the results could not be separated into the different malignancies

References

Included Studies

Rosendahl C, Tschandl P, Med C, Cameron A, Kittler H. Diagnostic accuracy of dermatoscopy for melanocytic and nonmelanocytic pigmented lesions. *Journal of the American Academy of Dermatology* 2011;64(6):1068-73.

Excluded Studies

Abbas Q, Celebi ME, Garcia IF, Rashid M. Lesion border detection in dermoscopy images using dynamic programming. *Skin Research and Technology* 2011;17(1):91-100.

Exclusion Reason: Not in PICO

Adinarayan M, Krishnamurthy SP. Clinicopathological evaluation of nonmelanoma skin cancer. *Indian Journal of Dermatology* 2011;56(6):670-2.

Exclusion Reason: Narrative Review

Ahmed R, Soldin M. Incomplete excision rate of basal cell carcinoma: A 2-year retrospective clinical audit. *European Journal of Surgical Oncology* 2011;37(11):984.
Exclusion Reason: Not in PICO

Ahmad K, Siah T, Langtry JAA. Recurrent and incompletely excised nonmelanoma skin cancers referred for Mohs micrographic surgery. *British Journal of Dermatology* 2012;167:56.
Exclusion Reason: Not in PICO

Ahmed, M. M., Moore, B. A. & Schmalbach, C. E. (2014) Utility of Head and Neck Cutaneous Squamous Cell Carcinoma Sentinel Node Biopsy: A Systematic Review. *Otolaryngology-Head and Neck Surgery*, 150: 180-187.
Exclusion Reason: Not in PICO

Aitken JF, Janda M, Elwood M, Youl PH, Ring IT, Lowe JB. Clinical outcomes from skin screening clinics within a community-based melanoma screening program. *Journal of the American Academy of Dermatology* 2006;54(1):105-14.
Exclusion Reason: Not in PICO

Alendar F, Drljevic I, Drljevic K, Alendar T. Early detection of melanoma skin cancer. *Bosnian Journal of Basic Medical Sciences* 2009;9(1):77-80.
Exclusion Reason: Not in PICO

Albert MR, Weinstock MA. Keratinocyte carcinoma. [Review] [74 refs]. *CA: A Cancer Journal for Clinicians* 2003;53(5):292-302.
Exclusion Reason: Narrative Review

Aldridge, R. B., Naysmith, L., Ooi, E. T., Murray, C. S. & Rees, J. L. (1111) The importance of a full clinical examination: Assessment of index lesions referred to a skin cancer clinic without a total body skin examination would miss one in three melanomas. *Acta Dermato-Venereologica*, 93: 2013.
Exclusion Reason: Not in PICO

Allon, I., Allon, D. M., Anavi, Y. & Kaplan, I. (2013) The significance of surface ulceration as a sign of malignancy in exophytic oral mucosal lesions: myth or fact? *Head and neck pathology*, 7: 149-154.
Exclusion Reason: Not in PICO

Alsharqi A, Wilson N, De Mozzi P. Basal cell carcinomas excision margins: Primary vs. secondary care. *British Journal of Dermatology* 2010;163:101.
Exclusion Reason: Narrative Review

Alsharqi A, Wilson N. Will the introduction of new NICE guidelines change the management of basal cell carcinomas in the community? *British Journal of Dermatology* 2011;165:108.
Exclusion Reason: Narrative Review

Altamura D, Menzies SW, Argenziano G, Zalaudek I, Soyer HP, Sera F, et al. Dermatoscopy of basal cell carcinoma: morphologic variability of global and local features and accuracy of diagnosis. *Journal of the American Academy of Dermatology* 2010;62(1):67-75.
Exclusion Reason: Not in PICO

Angit C, Sharpe GR. Regional audit on squamous cell carcinoma excision margin. *Journal of the American Academy of Dermatology* 2011;64(2 SUPPL. 1):AB124.
Exclusion Reason: Not in PICO

Anthony S, Vlachou C, Murdoch M, Tatnall F, Batta K, Brown V. Audit of 2-week-wait referrals: how does tertiary referral influence management? *British Journal of Dermatology* 2010;163:112-3.
Exclusion Reason: Not in PICO

Anthony S, Ogden E, Blanshard M, Schofield JK. Basal cell carcinomas: Impact of national guidance on local specialist dermatology Department is likely to be manageable. *British Journal of Dermatology* 2009;161:64-5.
Exclusion Reason: Not in PICO

Arits AHMM, Schlangen MHJ, Nelemans PJ, Kelleners-Smeets NWJ. Trends in the incidence of basal cell carcinoma by histopathological subtype. *Journal of the European Academy of Dermatology and Venereology* 2011;25(5):565-9.
Exclusion Reason: Not in PICO

Arlt A, Luckhaupt H, Hildmann H. Diagnosis of recurrent squamous cell carcinomas with the tumor marker SCC-antigen. [German]. *Laryngo- Rhino- Otologie* 2000;79(4):207-12.
Exclusion Reason: Not in PICO

Astner S, Dietterle S, Otberg N, Rowert-Huber HJ, Stockfleth E, Lademann J. Clinical applicability of in vivo fluorescence confocal microscopy for noninvasive diagnosis and therapeutic monitoring of nonmelanoma skin cancer. *Journal of Biomedical Optics* 2008;13(1):014003-Feb.
Exclusion Reason: Not in PICO

Attili SK, Lesar A, McNeill A, Camacho-Lopez M, Moseley H, Ibbotson S, et al. An open pilot study of ambulatory photodynamic therapy using a wearable low-irradiance organic light-emitting diode light source in the treatment of nonmelanoma skin cancer. *British Journal of Dermatology* 2009;161(1):170-3.
Exclusion Reason: Not in PICO

Asuquo ME, Ebughe G. Major dermatological malignancies encountered in the University of Calabar Teaching Hospital, Calabar, southern Nigeria. *International Journal of Dermatology* 2012;51:32-6.
Exclusion Reason: Not in PICO

Baade PD, Youl PH, Janda M, Whiteman DC, Del Mar CB, Aitken JF. Factors associated with the number of lesions excised for each skin cancer: a study of primary care physicians in Queensland, Australia. *Archives of Dermatology* 2008;144(11):1468-76.
Exclusion Reason: Not in PICO

Bakis S, Irwig L, Wood G, Wong D. Exfoliative cytology as a diagnostic test for basal cell carcinoma: a meta-analysis. *British Journal of Dermatology* 2004;150(5):829-36.
Exclusion Reason: Not in PICO

Balogh K, Trehan P, Bashir S, Higgins E, Morris-Jones R. Skin cancer 'filtered screening' by dermatologists: the 2-week wait system. *British Journal of Dermatology* 2012;167:63.
Exclusion Reason: Not in PICO

Barry J, Oon SF, Watson R, Barnes L. The management of basal cell carcinomas. *Irish Medical Journal* 2006;99(6):179-81.
Exclusion Reason: Not in PICO

Bastiaens MT, Struyk L, Tjong AHung SP, Gruis N, ter Huurne J, Westendorp RG, et al. Cutaneous squamous cell carcinoma and p53 codon 72 polymorphism: a need for screening? *Molecular Carcinogenesis* 2001;30(1):56-61.
Exclusion Reason: Not in PICO

Bataille V, Hargest E, Brown V, Blackwell V, Dawe S, Cooper A, et al. A teledermatology pilot study in Hertfordshire: Triage of 2-week-wait referrals. *British Journal of Dermatology* 2011;165:137-8.
Exclusion Reason: Not in PICO

Beby F, Kodjikian L, Roche O, Bouvier R, Donate D, Guerillon F, et al. [Conjunctival tumors in children. A histopathologic study of 42 cases]. [French]. *Journal Francais d Ophthalmologie* 2005;28(8):817-23.
Exclusion Reason: Not in PICO

Behrens, A., May, A., Manner, H., Pohl, J. & Ell, C. (2013) Esophageal precancerous lesions: Early diagnosis, treatment, and preservation of quality of life. [German]. *Internist*, 54: 683-690.
Exclusion Reason: Narrative review

Bernard P, Derancourt C, Arnoult-Coudoux E, Picot R, Delvincourt C. Skin cancer diagnosis by dermatologists in the region of Champagne-Ardenne: A prospective study. *Annales de Dermatologie et de Venereologie* 2001;128(8-9):883-7.
Exclusion Reason: Not in PICO

Bhatti AZ, Asif S, Alwan M. Factors affecting incomplete excision of nonmelanoma skin cancers in New Zealand. *Annals of Plastic Surgery* 2006;57(5):513-6.
Exclusion Reason: Not in PICO

Bhatnagar A, Mohamad S, Sandramouli S. 'Fast-tracking' cancer referrals: application for periocular basal cell carcinoma. *Eye* 2006;20(4):428-30.
Exclusion Reason: Not in PICO

Blakeslee D, Vaughan CW, Shapshay SM. Excisional biopsy in the selective management of T1 glottic cancer: A three-year follow-up study. *Laryngoscope* 1984;94(4):488-94.
Exclusion Reason: Not in PICO

Blum A, Bauer J, Rassner G, Garbe C. Early detection of skin cancer. [German]. *Onkologie* 2002;8(10):1064-71.
Exclusion Reason: Narrative Review

Boiko PE, Koepsell TD, Larson EB, Wagner EH. Skin cancer diagnosis in a primary care setting. *Journal of the American Academy of Dermatology* 1996;34(4):608-11.
Exclusion Reason: Narrative Review

Bolac C, Cordel N, Deschamps L, Renier M, Quist D, Derancourt C. Diagnosis of skin cancer by dermatologists in the French West Indies: A prospective study. *Annales de Dermatologie et de Venereologie* 2011;138(1):11-6.
Exclusion Reason: Not in PICO

Bollschweiler E, Ell C. Squamous cell carcinoma and adenocarcinoma of the esophagus. Differences in epidemiology, tumor biology, diagnostic procedures, and prevention. [German]. *Onkologie* 2004;10(11):1168-78.
Exclusion Reason: Narrative Review

Borgulya M, Kurz CM, Knoll T, Velten T, Vieth M, Ell C, et al. Diagnosis of early barrett's neoplasia and esophageal squamous cell neoplasia by electrical bio-impedance spectroscopy in human tissue. *Gastrointestinal Endoscopy* 2012;75(4 SUPPL. 1):AB127.
Exclusion Reason: Not in PICO

Bostock-Ling N. Excising basal cell carcinoma in general practice. *Australian Family Physician* 2006;35(7):558-60.
Exclusion Reason: Narrative Review

Bowns IR, Collins K, Walters SJ, McDonagh AJ. Telemedicine in dermatology: a randomised controlled trial. *Health Technology Assessment (Winchester, England)* 2006;10(43):iii-v.
Exclusion Reason: Not in PICO

Bower CP, Lear JT, de Berker DA. Basal cell carcinoma follow-up practices by dermatologists: a national survey. *British Journal of Dermatology* 2001;145(6):949-56.
Exclusion Reason: Not in PICO

Bradley N, Topham E. A service-evaluation of recurrence following curettage and cautery treatment of well-differentiated primary cutaneous squamous cell carcinoma. *British Journal of Dermatology* 2012;167:59.
Exclusion Reason: Not in PICO

Brewster DH, Bhatti LA, Inglis JH, Nairn ER, Doherty VR. Recent trends in incidence of nonmelanoma skin cancers in the East of Scotland, 1992-2003. *British Journal of Dermatology* 2007;156(6):1295-300.
Exclusion Reason: Not in PICO

Bristow Ivan, Bowling Jonathan. Dermoscopy as a technique for the early identification of foot melanoma. *Journal of Foot and Ankle Research* 2009;2(1):14.
Exclusion Reason: Not in PICO

Brown SJ, Lawrence CM. The management of skin malignancy: to what extent should we rely on clinical diagnosis? *British Journal of Dermatology* 2006;155(1):100-3.
Exclusion Reason: Narrative Review

Brundel K-H. Skin cancer in general practice. [German]. *Dermatosen in Beruf und Umwelt* 1990;38(2):54-7.
 Exclusion Reason: Not in PICO

Buis PAJ, Chorus RMH, van Diest PJ. Value of histopathologic analysis of skin excisions by GPs. *British Journal of General Practice* 2005;55(515):458-60.
 Exclusion Reason: Not in PICO

Burghout, K., Sigurdsson, V. & Toonstra, J. (2013) Non-melanoma skin cancer. [Dutch]. *Huisarts en Wetenschap*, 56: 174-178.
 Exclusion Reason: Narrative review

Butani A, Arbesfeld DM, Schwartz RA. Premalignant and early squamous cell carcinoma. *Clinics in Plastic Surgery* 2005;32(2):223-+.
 Exclusion Reason: Not in PICO

Carducci M, Bozzetti M, Foscolo AM, Betti R. Margin detection using digital dermatoscopy improves the performance of traditional surgical excision of basal cell carcinomas of the head and neck. *Dermatologic Surgery* 2011;37(2):280-5.
 Exclusion Reason: Not in PICO

Carli P, Chiarugi A, De Giorgi V. Examination of lesions (including dermoscopy) without contact with the patient is associated with improper management in about 30% of equivocal melanomas. *Dermatologic Surgery* 2005;31(2):169-72.
 Exclusion Reason: Not in PICO

Carter EJ, Whittam LR, Buckley DA. Failure of adherence to NICE guidelines for skin cancer surgery in general practice. *British Journal of Dermatology* 2009;161:63.
 Exclusion Reason: Not in PICO

Carter J, Evans C, Ghebre R, Glubka B, Downs L. Superficially invasive squamous cell carcinoma of the vulva: Is radical excision necessary? *Gynecologic Oncology* 2012;125:S83.
 Exclusion Reason: Not in PICO

Chaidemenos G, Apalla Z, Trigoni A, Koussidou T, Karakatsanis G. Inability of dermoscopy to differentiate early-stage squamous cell carcinoma from keratoacanthoma. *Melanoma Research* 2010;20:e66.
 Exclusion Reason: N=2

Chambers M, Esdaile B, De Vos S, Bowling J, Cassell O, Turner R, et al. The oxfordshire community dermatology service. *British Journal of Dermatology* 2012;167:97.
 Exclusion Reason: Not in PICO

Chan LS, Scholes NJ, Jones M. Skin excisions: not so simple for the regionally based general surgical trainee. *Australian Journal of Rural Health* 2011;19(4):205-10.
 Exclusion Reason: Not in PICO

Chattopadhyay, M. & Ha, T. (2013) How to examine a patient with suspected skin cancer. *Medicine (United Kingdom)*, 41: 400-401.
 Exclusion Reason: Narrative review

Cheah PL, Liam CK, Yap SF, Looi LM. Squamous cell carcinoma antigen as an adjunct tumour marker in primary carcinoma of the lung. *Journal of Clinical Pathology* 1994;47(6):535-7.
 Exclusion Reason: Not in PICO

Chen P, Patel DC. Evaluation of surgical excision of non-melanoma skin cancers - A retrospective study. *Australasian Journal of Dermatology* 2011;52(4):A9.
 Exclusion Reason: Not in PICO

Cheng B, Joe Stanley R, Stoecker WV, Osterwise CT, Stricklin SM, Hinton KA, et al. Automatic dirt trail analysis in dermoscopy images. *Skin Research & Technology* 2013;19(1):e20-6.
 Exclusion Reason: Not in PICO

Cheng A, Bennett A, Pogrel MA, Schmidt BL. Should tumor depth measured from an incisional biopsy be used to guide the decision to perform an elective neck dissection? *Journal of Oral and Maxillofacial Surgery* 2012;70(9 SUPPL. 2):e-1.

Exclusion Reason: Not in PICO

Chiesa F, Sala L, Costa L, Moglia D, Mauri M, Podrecca S, et al. Excision of oral leukoplakias by CO2 laser on an out-patient basis: a useful procedure for prevention and early detection of oral carcinomas. *Tumori* 1986;72(3):307-12.

Exclusion Reason: Not in PICO

Chong SLP, Ferguson L, Lateo S. Skin cancer surgery in primary care: Results of an audit and re-audit. *British Journal of Dermatology* 2012;167:39.

Exclusion Reason: Not in PICO

Choy B, Bandla S, Xia Y, Tan D, Pennathur A, Luketich JD, et al. Clinicopathologic characteristics of high expression of Bmi-1 in esophageal adenocarcinoma and squamous cell carcinoma. *BMC Gastroenterology* 2012;12:146.

Exclusion Reason: Not in PICO

Chren MM, Sahay AP, Sands LP, Maddock L, Lindquist K, Bertenthal D, et al. Variation in care for nonmelanoma skin cancer in a private practice and a veterans affairs clinic. *Medical Care* 2004;42(10):1019-26.

Exclusion Reason: Not in PICO

Civantos F Jr, Zitsch R, Bared A, Amin A. Sentinel node biopsy for squamous cell carcinoma of the head and neck. [Review] [64 refs]. *Journal of Surgical Oncology* 2008;97(8):683-90.

Exclusion Reason: Narrative Review

Clarke P. Nonmelanoma skin cancers - treatment options. *Australian Family Physician* 2012;41(7):476-80.

Exclusion Reason: Narrative Review

Cleary RK, Schaldenbrand JD, Fowler JJ, Schuler JM, Lampman RM. Treatment options for perianal Bowen's disease: survey of American Society of Colon and Rectal Surgeons Members. *American Surgeon* 2000;66(7):686-8.

Exclusion Reason: Not in PICO

Cooper SM, Wojnarowska F. The accuracy of clinical diagnosis of suspected premalignant and malignant skin lesions in renal transplant recipients. *Clinical & Experimental Dermatology* 2002;27(6):436-8.

Exclusion Reason: Not in PICO

Cortinas Saenz M, Saenz Guirado S, Gamez Moreno J, Iglesias Cerrillo JA, Pardo Martinez A, Martinez Gomez L. Analysis of results, quality indicators, and postsurgical complications in an outpatient dermatological surgery program. *Actas Dermo-Sifiliograficas* 2012;103(1):36-43.

Exclusion Reason: Not in PICO

Corwin P, Munn E, Nicholls D. A study of general practitioners' skin surgery in Canterbury. *New Zealand Medical Journal* 1997;110(1047):253-5.

Exclusion Reason: Not in PICO

Costa S, De Nuzzo M, Rubino A, Rambelli V, Marinelli M, Santini D, et al. Independent determinants of inaccuracy of colposcopically directed punch biopsy of the cervix. *Gynecologic Oncology* 2003;90(1):57-63.

Exclusion Reason: Not in PICO

Cox NH. Basal cell carcinoma in young adults. *British Journal of Dermatology* 1992;127(1):26-9.

Exclusion Reason: Not in PICO

Cox NH, Wagstaff R, Popple AW. Using clinicopathological analysis of general practitioner skin surgery to determine educational requirements and guidelines. *BMJ* 1992;304(6819):93-6.

Exclusion Reason: Not in PICO

Cuellar F, Vilalta A, Puig S, Palou J, Zaballos P, Malveyh J. Dermoscopy of early recurrent basal cell carcinoma. *Archives of Dermatology* 2008;144(9):1254.

Exclusion Reason: N=3

de Hullu JA, Hollema H, Piers DA, Verheijen RH, van Diest PJ, Mourits MJ, et al. Sentinel lymph node procedure is highly accurate in squamous cell carcinoma of the vulva. *Journal of Clinical Oncology* 2000;18(15):2811-6.
Exclusion Reason: Not in PICO

De Berker DAR, Poirier V, Takwale A. Follow-up preferences for patients with basal cell carcinoma: The basis for modelling clinical practice and commissioning. *British Journal of Dermatology* 2010;163:112.
Exclusion Reason: Not in PICO

de Giorgi V, Alfaioli B, Papi F, Janowska A, Grazzini M, Lotti T, et al. Dermoscopy in Pigmented Squamous Cell Carcinoma. *Journal of Cutaneous Medicine and Surgery* 2009;13(6):326-9.
Exclusion Reason: N=1

Delaney EK, Duckworth L, Thompson WD, Lee AJ, Murchie P. Excising squamous cell carcinomas: comparing the performance of GPs, hospital skin specialists and other hospital specialists. *Family Practice* 2012;29(5):541-6.
Exclusion Reason: Not in PICO

Demir H, Isken T, Kus E, Tan YZ, Isgoren S, Gorur GD, et al. Sentinel lymph node biopsy with a gamma probe in patients with high-risk cutaneous squamous cell carcinoma: follow-up results of sentinel lymph node-negative patients. *Nuclear Medicine Communications* 2011;32(12):1216-22.
Exclusion Reason: Not in PICO

Dewan P, Panagou E, Ajen S, Bewley AP, Sahota A, Gibbon K. Are NICE skin cancer guidelines being followed in primary care? A re-audit to review changes in practice in an inner city setting. *British Journal of Dermatology* 2010;163:65.
Exclusion Reason: Not in PICO

Dixon AJ, Hall RS. Managing skin cancer--23 golden rules. [Review] [0 refs]. *Australian Family Physician* 2005;34(8):669-71.
Exclusion Reason: Narrative Review

Dixon A. Rare skin cancers in general practice. *Australian Family Physician* 2007;36(3):141-3.
Exclusion Reason: N=1

Dua J, Clayton R. A comparison of skin cancer excision rates between general practitioners and dermatologists in West Berkshire, South East England. *British Journal of Dermatology* 2012;167:60-1.
Exclusion Reason: Not in PICO

Durdu M, Baba M, Seckin D. Dermoscopy versus Tzanck smear test: A comparison of the value of two tests in the diagnosis of pigmented skin lesions. *Journal of the American Academy of Dermatology* 2011;65(5):972-82.
Exclusion Reason: Not in PICO

Eekhof, J. A. (2013) [Actinic keratosis: the art of doing nothing]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 157: A5363.
Exclusion Reason: Narrative review

Ehrig T, Cockerell C, Piacquadio D, Dromgoole S. Actinic keratoses and the incidence of occult squamous cell carcinoma: a clinical-histopathologic correlation. *Dermatologic Surgery* 2006;32(10):1261-5.
Exclusion Reason: Not in PICO

Emery JD, Hunter J, Hall PN, Watson AJ, Moncrieff M, Walter FM. Accuracy of SIAscopy for pigmented skin lesions encountered in primary care: Development and validation of a new diagnostic algorithm. *BMC Dermatology* 2010;10.
Exclusion Reason: Not in PICO

Epstein JB, Scully C. Assessing the patient at risk for oral squamous cell carcinoma. [Review] [87 refs]. *Special Care in Dentistry* 1997;17(4):120-8.
Exclusion Reason: Narrative review

Epstein JB, Guneri P, Boyacioglu H, Abt E. The limitations of the clinical oral examination in detecting dysplastic oral lesions and oral squamous cell carcinoma. *Journal of the American Dental Association* 2012;143(12):1332-42.
Exclusion Reason: Not in PICO

Epstein JB, Silverman S, Epstein JD, Lonky SA, Bride MA. Analysis of oral lesion biopsies identified and evaluated by visual examination, chemiluminescence and toluidine blue. *Oral Oncology* 2008;44(6):538-44.
Exclusion Reason: Not in PICO

Epstein JB, Gorsky M, Cabay RJ, Day T, Gonsalves W. Screening for and diagnosis of oral premalignant lesions and oropharyngeal squamous cell carcinoma - Role of primary care physicians. *Canadian Family Physician* 2008;54(6):870-5.
Exclusion Reason: Not in PICO

Epstein, J. B., Guneri, P., Boyacioglu, H. & Abt, E. (2013) The limitations of the clinical oral examination in detecting dysplastic oral lesions and oral squamous cell carcinoma. [Reprint of *J Am Dent Assoc.* 2012 Dec;143(12):1332-42; PMID: 23204089]. *Texas Dental Journal*, 130: 410-424.
Exclusion Reason: Not in PICO

Felton J, Mellerio JE. Cutaneous squamous cell carcinomas in epidermolysis bullosa: A 20-year retrospective study. *British Journal of Dermatology* 2012;167:55-6.
Exclusion Reason: Not in PICO

Ferrandiz L, Ruiz-de-Casas A, Trakatelli M, de Vries E, Ulrich M, Aquilina S, et al. Assessing physicians' preferences on skin cancer treatment in Europe. *British Journal of Dermatology* 2012;167:Suppl-35.
Exclusion Reason: Not in PICO

Ferreira, P., Rodrigues, M., Ledo, S., Senra, R., Costa, S., V, Rocha, M. & Paiva, C. (2013) Back pain as the first manifestation of a cavum tumor. *European Journal of Internal Medicine*, 24: e149.
Exclusion Reason: Not in PICO

Firnhaber JM. Diagnosis and treatment of Basal cell and squamous cell carcinoma. [Review]. *American Family Physician* 2012;86(2):161-8.
Exclusion Reason: Narrative Review

FitzGerald KL, Buttner PG, Donovan SA. Nonpigmented skin lesions - how many are nonmelanoma skin cancer? *Australian Family Physician* 2006;35(7):555-7.
Exclusion Reason: Not in PICO

Fleischer AB, Feldman SR, Barlow JO, Zheng BY, Hahn HB, Chuang TY, et al. The specialty of the treating physician affects the likelihood of tumor-free resection margins for basal cell carcinoma: Results from a multi-institutional retrospective study. *Journal of the American Academy of Dermatology* 2001;44(2):224-30.
Exclusion Reason: Not in PICO

Fontes, K. B., Cunha, K. S., Rodrigues, F. R., Silva, L. E. & Dias, E. P. (2013) Concordance between cytopathology and incisional biopsy in the diagnosis of oral squamous cell carcinoma. *Brazilian oral research*, 27: 122-127.
Exclusion Reason: Not in PICO

Freitag CP, Barros SG, Krueh CD, Putten AC, Dietz J, Gruber AC, et al. Esophageal dysplasias are detected by endoscopy with Lugol in patients at risk for squamous cell carcinoma in southern Brazil. *Diseases of the Esophagus* 1999;12(3):191-5.
Exclusion Reason: Not in PICO

French Society of Dermatology. Guideline for the diagnosis and treatment of cutaneous squamous cell carcinoma and precursor lesions. *Annales de Dermatologie et de Venereologie* 2009;136:Suppl-86.
Exclusion Reason: Guidelines

Friedman T, Klein D, Hadad E, Westreich M, Shalom A. [Diagnostic accuracy of skin lesions excised by a plastic surgeon]. [Hebrew]. Harefuah 75;147(4):305-8.
Exclusion Reason: Not in PICO

Fujishiro M, Yahagi N, Kakushima N, Kodashima S, Muraki Y, Ono S, et al. Endoscopic submucosal dissection of esophageal squamous cell neoplasms. *Clinical Gastroenterology & Hepatology* 2006;4(6):688-94.
Exclusion Reason: Not in PICO

Gait R, Milligan A, Burd RM, Fletcher A. A review of procedures carried out on basal cell carcinomas by Primary care physicians. *British Journal of Dermatology* 2009;161:64.
Exclusion Reason: Not in PICO

Gao L, Lin WH, Gong ZJ, Liu Y, Liu YM, Zhu MH. [Fine needle aspiration cytology of eyelid sebaceous gland carcinoma and its differential diagnosis]. [Chinese]. *Chung-Hua Ping Li Hsueh Tsa Chih - Chinese Journal of Pathology* 2004;33(1):36-9.
Exclusion Reason: Not in PICO

Garcia-Solano J, Lopez-Avila A, Acosta J, Montalbana S, Sanchez-Sanchez C, Benito A, et al. Non-melanoma skin cancer with positive surgical and histological margins. Comparative study among the departments involved in their surgical excision. [Spanish]. *Actas Dermo-Sifiliograficas* 2004;95(6):358-61.
Exclusion Reason: Not in PICO

Garner KL, Rodney WM. Basal and squamous cell carcinoma. [Review] [21 refs]. *Primary Care; Clinics in Office Practice* 2000;27(2):447-58.
Exclusion Reason: Narrative Review

Gerbert B, Bronstone A, Maurer T, Hofmann R, Berger T. Decision support software to help primary care physicians triage skin cancer - A pilot study. *Archives of Dermatology* 2000;136(2):187-92.
Exclusion Reason: Not in PICO

Giacomel, J. & Zalaudek, I. (2013) Pink Lesions. *Dermatologic Clinics*, 31: 649-678.
Exclusion Reason: Narrative review

Gilde K. [Malignant tumors of the skin]. [Review] [25 refs] [Hungarian]. *Orvosi Hetilap* 2006;147(48):2321-30.
Exclusion Reason: Narrative Review

Girardi F, Pickel H, Joura EA, Breitenecker G, Gitsch G, Graf AH, et al. [Guidelines for diagnosis and therapy of intraepithelial neoplasia and early invasive carcinoma of the female lower genital system (cervix uteri, vagina, vulva) established by the AGK (Colposcopy Work Group in the OGGG [Austrian Society of Gynecology and Obstetrics])]. [German]. *Gynakologisch-Geburtshilfliche Rundschau* 2001;41(3):197-200.
Exclusion Reason: Guidelines

Golberg O, Alexandroff AB, Burd RM. Seasonal variation in 2-week-wait skin cancer referrals is not mirrored by changes in incidence of skin cancer: A message for service provision. *British Journal of Dermatology* 2011;165:20-1.
Exclusion Reason: Not in PICO

Goldberg LH, Rubin HA. Management of basal cell carcinoma. Which option is best? *Postgraduate Medicine* 1961;85(1):57-8.
Exclusion Reason: Narrative Review

Goldstone SE, Winkler B, Ufford LJ, Alt E, Palefsky JM. High prevalence of anal squamous intraepithelial lesions and squamous-cell carcinoma in men who have sex with men as seen in a surgical practice. *Diseases of the Colon & Rectum* 2001;44(5):690-8.
Exclusion Reason: Not in PICO

Gonsalves WC, Chi AC, Neville BW. Common oral lesions: Part II. Masses and neoplasia. *American Family Physician* 2007;75(4):509-12.
Exclusion Reason: Narrative Review

Goulding JMR, Levine S, Blizard RA, Deroide F, Swale VJ. Dermatological surgery: a comparison of activity and outcomes in primary and secondary care. *British Journal of Dermatology* 2009;161(1):110-4.
Exclusion Reason: Not in PICO

Graves J, Fleischman MH, Goldstein GD. Derm Access: A new triage system to rapidly identify suspicious skin lesions. *Dermatologic Surgery* 2006;32(12):1486-90.
Exclusion Reason: Not in PICO

Griffiths RW, Suvarna SK, Stone J. Do basal cell carcinomas recur after complete conventional surgical excision? *British Journal of Plastic Surgery* 2005;58(6):795-805.
Exclusion Reason: Not in PICO

Gross EA. Nonmelanoma skin cancer: Clues to early detection, keys to effective treatment. *Consultant* 1999;39(3):829-39.
Exclusion Reason: Narrative Review

Gudi V, Ormerod AD, Dawn G, Green C, MacKie RM, Douglas WS, et al. Management of basal cell carcinoma by surveyed dermatologists in Scotland. *Clinical & Experimental Dermatology* 2006;31(5):648-52.
Exclusion Reason: Not in PICO

Gurudutt VV, Genden EM. Cutaneous squamous cell carcinoma of the head and neck. *Journal of Skin Cancer* 2011;2011:502723.
Exclusion Reason: Not in PICO

Guther S, Ramrath K, Dyll-Smith D, Landthaler M, Stolz W. Development of a targeted risk-group model for skin cancer screening based on more than 100,000 total skin examinations. *Journal of the European Academy of Dermatology & Venereology* 2012;26(1):86-94.
Exclusion Reason: Not in PICO

Haliasos, E. C., Kerner, M., Jaimes, N., Zalaudek, I., Malvehy, J., Lanschuetzer, C. M., Hinter, H., Hofmann-Wellenhof, R., Braun, R. P. & Marghoob, A. A. (2013) Dermoscopy for the pediatric dermatologist, part ii: dermoscopy of genetic syndromes with cutaneous manifestations and pediatric vascular lesions. [Review]. *Pediatric Dermatology*, 30: 172-181.
Exclusion Reason: Narrative review

Halpern SM, Shall L. Establishment of a primary care-based teledermatology service in Kent. *British Journal of Dermatology* 2011;165:136-7.
Exclusion Reason: Not in PICO

Hamm H, Hoger PH. Skin tumors in childhood. [Review]. *Deutsches Arzteblatt International* 2011;108(20):347-53.
Exclusion Reason: Narrative Review

Han MW, Lee B-J, Jang YJ, Chung Y-S. Clinical value of office-based endoscopic incisional biopsy in diagnosis of nasal cavity masses. *Otolaryngology - Head and Neck Surgery* 2010;143(3):341-7.
Exclusion Reason: Not in PICO

Hansen C, Wilkinson D, Hansen M, Soyer HP. Factors contributing to incomplete excision of nonmelanoma skin cancer by Australian general practitioners. *Archives of Dermatology* 2009;145(11):1253-60.
Exclusion Reason: Not in PICO

Haw, W. Y., Fraser, S., Affleck, A. & Holme, A. (2014) Skin cancer excision performance in primary and secondary care in Scotland. *British Journal of Dermatology*, 171: 25.
Exclusion Reason: Not in PICO

Hayashi T, Muto M, Hayashi R, Minashi K, Yano T, Kishimoto S, et al. Usefulness of narrow-band imaging for detecting the primary tumor site in patients with primary unknown cervical lymph node metastasis. *Japanese Journal of Clinical Oncology* 2010;40(6):537-41.
Exclusion Reason: Not in PICO

Heal CF, Raasch BA, Buettner PG, Weedon D. Accuracy of clinical diagnosis of skin lesions. *British Journal of Dermatology* 2008;159(3):661-8.

Exclusion Reason: Not in PICO
 Heal C, Buettner P, Raasch B, Browning S. Minor skin excisions in general practice in North Queensland. *Australian Family Physician* 2006;35(10):825-8.
 Exclusion Reason: Not in PICO
 Hermes, H. M., Sahu, J., Schwartz, L. R. & Lee, J. B. (2014) - Clinical and histologic characteristics of clinically unsuspected melanomas. - *Clinics in Dermatology*, 32: 324-330.
 Exclusion Reason: Not in PICO
 Hernandez-Martin A, Arias-Palomo D, Barahona E, Hidalgo C, Munoz C, Garcia-Higuera I. [Analysis of surgical treatment for nonmelanoma skin cancer performed by dermatologists in a public hospital: clinical-pathological correlation, use of hospital resources, and waiting list time from diagnosis]. [Spanish][Erratum appears in *Actas Dermosifiliogr*. 2008 Mar;99(2):170]. *Actas Dermosifiliograficas* 2007;98(10):694-701.
 Exclusion Reason: Not in PICO
 Hjortdal O, Naess A, Berner A. Squamous cell carcinomas of the lower lip. *Journal of Cranio-Maxillo-Facial Surgery* 1995;23(1):34-7.
 Exclusion Reason: Narrative Review
 Holmkvist KA, Rogers GS, Dahl PR. Incidence of residual basal cell carcinoma in patients who appear tumor free after biopsy. *Journal of the American Academy of Dermatology* 1999;41(4):600-5.
 Exclusion Reason: Not in PICO
 Humphreys TR. Skin cancer: Recognition and management. *Clinical Cornerstone* 2001;4(1):23-9.
 Exclusion Reason: Narrative Review
 Ishihara R, Inoue T, Hanaoka N, Takeuchi Y, Tsujii Y, Kanzaki H, et al. Autofluorescence imaging endoscopy for screening of esophageal squamous mucosal high-grade neoplasia: a phase II study. *Journal of Gastroenterology & Hepatology* 2012;27(1):86-90.
 Exclusion Reason: Not in PICO
 Ismail N, D'Adhemar C, Kirby B, Collins P, Sheahan K, Lally A. An audit of basal cell carcinoma in St Vincent's University Hospital. *British Journal of Dermatology* 2012;167(6):e34-5.
 Exclusion Reason: Not in PICO
 Jankittivong A, Swasdison S, Thangpitsityotin M, Langlais RP. Oral squamous cell carcinoma: a clinicopathological study of 342 Thai cases. *Journal of Contemporary Dental Practice [Electronic Resource]* 2009;10(5):E033-40.
 Exclusion Reason: Not in PICO
 Janda, M., Youl, P., Neale, R., Aitken, J., Whiteman, D., Gordon, L. & Baade, P. (2014) - Clinical skin examination outcomes after a video-based behavioral intervention: analysis from a randomized clinical trial. - *JAMA Dermatology*, 150: 372-379.
 Exclusion Reason: Population not in PICO
 Jeong W-J, Paik JH, Cho S-W, Sung M-W, Kim KH, Ahn S-H. Excisional biopsy for management of lateral tongue leukoplakia. *Journal of Oral Pathology and Medicine* 2012;41(5):384-8.
 Exclusion Reason: Not in PICO
 Jerant AF, Johnson JT, Sheridan CD, Caffrey TJ. Early detection and treatment of skin cancer. [Review] [32 refs]. *American Family Physician* 375;62(2):357-68.
 Exclusion Reason: Narrative Review
 Johnson SJ, Wadehra V. How predictive is a cervical smear suggesting invasive squamous cell carcinoma? *Cytopathology* 2001;12(3):144-50.
 Exclusion Reason: Not in PICO
 Jung JE, Rah DK, Kim YO. Effects of preoperative biopsies on recurrence in head and neck skin cancer. *Archives of Plastic Surgery* 2012;39(5):518-21.
 Exclusion Reason: Not in PICO
 Kahn, E., Sossong, S., Goh, A., Carpenter, D. & Goldstein, S. (2013) Evaluation of Skin Cancer in Northern California Kaiser Permanente's Store-and-Forward Teledermatology Referral Program.

Telemedicine and E-Health, 19: 780-785.

Exclusion Reason: Not in PICO

Kamyab-Hesari, K., Seirafi, H., Naraghi, Z. S., Shahshahani, M. M., Rahbar, Z., Damavandi, M. R., Naraghi, M. M., Rezvani, M. & Aghazadeh, N. (2014) Diagnostic accuracy of punch biopsy in subtyping basal cell carcinoma. *Journal of the European Academy of Dermatology and Venereology*, 28: 250-253.

Exclusion Reason: Not in PICO

Karagozoglu KH, Castelijns J, Bloemena E, de Bree R, van der Waal L. [An enlarged lymph node in the neck; what to do?]. [Dutch]. *Nederlands Tijdschrift Voor Tandheelkunde* 2011;118(5):267-71.

Exclusion Reason: Narrative Review

Kersten RC, Ewing-Chow D, Kulwin DR, Gallon M. Accuracy of clinical diagnosis of cutaneous eyelid lesions. *Ophthalmology* 1997;104(3):479-84.

Exclusion Reason: Not in PICO

Khalid S, Spicer A, Gee B, Carr R. The impact of Improved Outcome Guidance (IOG) for skin cancer: A comparative re-audit of excision rates of basal cell carcinomas by general practitioners in South Warwickshire. *British Journal of Dermatology* 2009;161:109.

Exclusion Reason: Not in PICO

Khorasgani MG, Simpson R, Burd RM. How effective is the skin cancer referral pathway? *British Journal of Dermatology* 2011;165:109.

Exclusion Reason: Not in PICO

Kibarian MA, Hruza GJ. Nonmelanoma skin cancer. Risks, treatment options, and tips on prevention. *Postgraduate Medicine* 1945;98(6):39-40.

Exclusion Reason: Narrative Review

Koch FP, Kunkel M, Biesterfeld S, Wagner W. Diagnostic efficiency of differentiating small cancerous and precancerous lesions using mucosal brush smears of the oral cavity--a prospective and blinded study. *Clinical Oral Investigations* 2011;15(5):763-9.

Exclusion Reason: Not in PICO

Koerner KR. Evaluation and treatment by general dentists of oral soft-tissue lesions. *Dentistry Today* 2006;25(7):90-5.

Exclusion Reason: Narrative Review

Kolm I, Hofbauer G, Braun RP. [Early diagnosis of skin cancer]. [Review] [German]. *Therapeutische Umschau* 2010;67(9):439-46.

Exclusion Reason: Narrative Review

Kok LP, Van Drunen R, Boon ME, Beck S, Van Coevorden RS. General practitioners use digital cameras and internet for telepathology of skin lesions. *Electronic Journal of Pathology and Histology* 2000;6(3):7-19.

Exclusion Reason: Narrative Review

Kopf AW, Salopek TG, Slade J, Marghoob AA, Bart RS. Techniques of cutaneous examination for the detection of skin cancer. *Cancer* 1995;75(2:Suppl):Suppl-90.

Exclusion Reason: Narrative Review

Krol S, Keijser LMT, Van Der Rhee HJ, Welvaart K. Screening for skin cancer in The Netherlands. *Acta Dermato-Venereologica* 1991;71(4):317-21.

Exclusion Reason: Not in PICO

Kundu, R. V. & Patterson, S. (2013) Dermatologic conditions in skin of color: part I. Special considerations for common skin disorders.[Summary for patients in *Am Fam Physician*. 2013 Jun 15;87(12):Online; PMID: 23939576]. *American Family Physician*, 87: 850-856.

Exclusion Reason: Narrative review

Kunte C, Konz B. Current recommendations in the treatment of basal cell carcinoma and squamous cell carcinoma of the skin. *Hautarzt* 2007;58(5):419-26.

Exclusion Reason: Narrative Review

Kusukawa J, Kameyama T, Nakamura Y. Evaluation of excisional biopsy for stage I and II squamous cell carcinoma of the oral cavity. *International Journal of Clinical Oncology* 1998;3(5):317-22.
Exclusion Reason: Not in PICO

Lacava V, Salesi N, Ferrone L, Veri A, Lembo R, Masi MC, et al. [Importance of dermatologic screening within the frame work of a general cancer prevention program]. [Italian]. *Minerva Medica* 2001;92(2):85-8.
Exclusion Reason: Not in PICO

Lai, W.-Y. (1111) An elderly man with a painful scaly nodule. *Hong Kong Practitioner*, 35: September.
Exclusion Reason: Not in PICO

Lathlean S. Skin cancer in general practice in South Australia. A five year study. *Australian Family Physician* 1999;28:Suppl-31.
Exclusion Reason: Not in PICO

Laukkanen A, Rummukainen J, Kivinen P, Lappalainen K. [Skin squamous cell carcinoma and its precancerous conditions]. [Review] [25 refs] [Finnish]. *Duodecim* 2006;122(1):71-9.
Exclusion Reason: Narrative Review

Lee C, Kang KH, Koh Y, Chang J, Chung HS, Park SK, et al. Characteristics of lung cancer in Korea, 1997. *Lung Cancer* 2000;30(1):15-22.
Exclusion Reason: Not in PICO

Liebman TN, Wang SQ. Detection of early basal cell carcinoma with dermoscopy in a patient with psoriasis. *Dermatology Online Journal* 2011;17(2):12.
Exclusion Reason: N=1

Lim D, Oakley AMM, Rademaker M. Better, sooner, more convenient: A successful teledermoscopy service. *Australasian Journal of Dermatology* 2012;53(1):22-5.
Exclusion Reason: Narrative Review

Lin, Y.-C., Perng, C.-L., Chang, Y.-M., Li, Y.-F., Tsai, Y.-M., Wu, G.-J. & Lin, C.-K. (2013) Coexistent squamous cell carcinoma and adenoid basal carcinoma in the uterine cervix and infection with human papillomavirus (HPV 31). *Taiwanese Journal of Obstetrics and Gynecology*, 52: 407-410.
Exclusion Reason: Not in PICO

Lober CW, Fenske NA. Basal cell, squamous cell, and sebaceous gland carcinomas of the periorbital region. [Review] [54 refs]. *Journal of the American Academy of Dermatology* 1991;25(4):685-90.
Exclusion Reason: Narrative Review

Lohmann CM, Solomon AR. Clinicopathologic variants of cutaneous squamous cell carcinoma. [Review] [82 refs]. *Advances in Anatomic Pathology* 2001;8(1):27-36.
Exclusion Reason: Narrative Review

Lopes LL, Alchorne ADD, Pereira GC, Lopes LRS, de Carvalho TC. Histological and immunohistochemical evaluation of basal cell carcinoma following curettage and electrodesiccation. *International Journal of Dermatology* 2008;47(6):610-4.
Exclusion Reason: Not in PICO

Luckey L. Seeding of head and neck cancer during placement of percutaneous gastrostomy tube. *American Journal of Gastroenterology* 2012;107:S279.
Exclusion Reason: Not in PICO

Lynget E, Hunskar S. [Skin neoplasms in general practice]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening* 2001;121(19):2281-3.
Exclusion Reason: Not in PICO

Maguire-Eisen M. Risk assessment and early detection of skin cancers. [Review] [69 refs]. *Seminars in Oncology Nursing* 2003;19(1):43-51.
Exclusion Reason: Narrative Review

Malberger E, Tillinger R, Lichtig C. Diagnosis of basal-cell carcinoma with aspiration cytology. *Acta Cytologica* 1984;28(3):301-4.
Exclusion Reason: Narrative Review

Malvey J, Puig S, Marti-Laborda RM. Dermoscopy of skin lesions in two patients with xeroderma pigmentosum. *British Journal of Dermatology* 2005;152(2):271-8.
Exclusion Reason: Not in PICO

Marchonda PJ, Krause LK, Jensen JD, Dellavalle RP. A North American perspective on dermoscopy: benefits, limitations, and grey zones. *Giornale Italiano di Dermatologia e Venereologia* 2010;145(1):89-97.
Exclusion Reason: Narrative Review

Marghoob AA. Basal and squamous cell carcinomas: What every primary care physician should know. *Postgraduate Medicine* 1997;102(2):139-59.
Exclusion Reason: Narrative Review

Marghoob, A. A., Usatine, R. P. & Jaimes, N. (2013) Dermoscopy for the family physician. [Review]. *American Family Physician*, 88: 441-450.
Exclusion Reason: Narrative review

Martinez JC, Otley CC. The management of melanoma and nonmelanoma skin cancer: A review for the primary care physician. *Mayo Clinic Proceedings* 2001;76(12):1253-65.
Exclusion Reason: Narrative Review

Maybury, C. M., Craythorne, E. & Martin, B. (2013) An ulcerated nodule on the nose. *BMJ Case Reports*, 2013, 2013.
Exclusion Reason: Not in PICO

McGuire JF, Ge NN, Dyson S. Nonmelanoma skin cancer of the head and neck I: histopathology and clinical behavior. *American Journal of Otolaryngology* 2009;30(2):121-33.
Exclusion Reason: Narrative Review

McNulty-Brown E, Veysey E. An audit of all excisions undertaken by general practitioners in a rural community between March 2009 and March 2010. *British Journal of Dermatology* 2012;167:91-2.
Exclusion Reason: Not in PICO

Medeiros F, Nascimento AF, Crum CP. Early vulvar squamous neoplasia: advances in classification, diagnosis, and differential diagnosis. [Review] [32 refs]. *Advances in Anatomic Pathology* 2005;12(1):20-6.
Exclusion Reason: Narrative Review

Mehrotra R, Gupta DK. Exciting new advances in oral cancer diagnosis: avenues to early detection. [Review]. *Head & neck oncology* 2011;3:33.
Exclusion Reason: Narrative Review

Mencia Gutierrez E, Herrero Lluch MJ, Gutierrez Diaz E, Galvez Ruiz A. [Basal cell and squamous cell carcinomas of the eyelid in adults under 50 years of age: 13 cases]. [Spanish]. *Archivos de la Sociedad Espanola de Oftalmologia* 2001;76(11):643-8.
Exclusion Reason: Not in PICO

Menzies SW, Emery J, Staples M, Davies S, McAvoy B, Fletcher J, et al. Impact of dermoscopy and short-term sequential digital dermoscopy imaging for the management of pigmented lesions in primary care: a sequential intervention trial. *British Journal of Dermatology* 2009;161(6):1270-7.
Exclusion Reason: Not in PICO

Menzies SW. Using dermoscopy to diagnose pigmented skin lesions. *Medicine Today* 2004;5(4):63-71.
Exclusion Reason: Narrative Review

Menzies, S. W., Moloney, F. J., Byth, K., Avramidis, M., Argenziano, G., Zalaudek, I., Braun, R. P., Malvey, J., Puig, S., Rabinovitz, H. S., Oliviero, M., Cabo, H., Bono, R., Pizzichetta, M. A., Claesson, M., Gaffney, D. C., Soyer, H. P., Stanganelli, I., Scolyer, R. A., Guitera, P., Kelly, J., McCurdy, O., Llambrich, A., Marghoob, A. A., Zaballos, P., Kirchesch, H. M., Piccolo, D., Bowling, J., Thomas, L., Terstappen, K., Tanaka, M., Pellacani, G., Pagnanelli, G., Ghigliotti, G., Ortega, B. C., Crafter, G., Ortiz, A. M., Tromme, I., Karaarslan, I. K., Ozdemir, F., Tam, A., Landi, C., Norton, P., Kacar, N., Rudnicka, L., Slowinska, M., Simionescu, O., Di, S. A., Coates, E. & Kreusch, J. (2013) Dermoscopic

evaluation of nodular melanoma. *JAMA Dermatology*, 149: 699-709.
 Exclusion Reason: Not in PICO

Milicic-Juhas V, Peric M, Pajtler M, Prvulovic I, Curzik D. Pap test--with or without vaginal smear? *Collegium Antropologicum* 2010;34(1):69-74.
 Exclusion Reason: Not in PICO

Miller SJ. II. Biopsy techniques for suspected nonmelanoma skin cancers. *Dermatologic Surgery* 2000;26(1):91.
 Exclusion Reason: Narrative Review

Moffatt CR, Green AC, Whiteman DC. Diagnostic accuracy in skin cancer clinics: the Australian experience. *International Journal of Dermatology* 2006;45(6):656-60.
 Exclusion Reason: Not in PICO: Clinical versus histological diagnosis (not biopsy or dermatoscopy versus histology or follow up)

Mojca I, Kaczmarzyk T, Zaleska M, Stypulkowska J, Zapala-Pospiech A, Sadecki D. Value of the ViziLite Plus System as a diagnostic aid in the early detection of oral cancer/premalignant epithelial lesions. *Journal of Craniofacial Surgery* 2012;23(2):e162-4.
 Exclusion Reason: Not in PICO

Monnier P, Savary M. Epidermoid cancer of the upper respiratory and digestive tracts. [French]. *Schweizerische medizinische Wochenschrift* 1986;116(51):1817-23.
 Exclusion Reason: Narrative Review

Moreno G, Tran H, Chia ALK, Lim A, Shumack S. Prospective study to assess general practitioners' dermatological diagnostic skills in a referral setting. *Australasian Journal of Dermatology* 2007;48(2):77-82.
 Exclusion Reason: Not in PICO

Morrison A, O'Loughlin S, Powell FC. Suspected skin malignancy: a comparison of diagnoses of family practitioners and dermatologists in 493 patients. *International Journal of Dermatology* 2001;40(2):104-7.
 Exclusion Reason: Not in PICO

Morteza, A. S., Salama, S. & Alowami, S. (2013) Lymphoepithelioma-like carcinoma of the skin: case report and approach to surgical pathology sign out. *Rare Tumors*, 5: e47.
 Exclusion Reason: Not in PICO

Morton CA, Downie F, Auld S, Smith B, Pol M, Baughan P, et al. Community photo-triage for skin cancer referrals: an aid to service delivery (Structured abstract). *Clinical and Experimental Dermatology* 2011;36:248-54.
 Exclusion Reason: Not in PICO

Motley RJ, Gould DJ, Douglas WS, Simpson NB. Treatment of basal cell carcinoma by dermatologists in the United Kingdom. British Association of Dermatologists Audit Subcommittee and the British Society for Dermatological Surgery. *British Journal of Dermatology* 1995;132(3):437-40.
 Exclusion Reason: Not in PICO

Muldoon TJ, Burgess SA, Chen BR, Ratner D, Hillman EMC. Analysis of skin lesions using laminar optical tomography. *Biomedical Optics Express* 2012;3(7):1701-12.
 Exclusion Reason: Narrative Review

Mullen JT, Feng L, Xing Y, Mansfield PF, Gershenwald JE, Lee JE, et al. Invasive squamous cell carcinoma of the skin: Defining a high-risk group. *Annals of Surgical Oncology* 2006;13(7):902-9.
 Exclusion Reason: Not in PICO

Murchie P, Delaney EK, Thompson WD, Lee AJ. Excising basal cell carcinomas: comparing the performance of general practitioners, hospital skin specialists and other hospital specialists. *Clinical & Experimental Dermatology* 2008;33(5):565-71.
 Exclusion Reason: Not in PICO

Musiatowicz B, Dzieciol J, Sulowska M, Polakow J, Baltaziak M. Fine needle aspiration biopsy cytology of pulmonary tumors. *Roczniki Akademii Medycznej W Bialymstoku* 1997;42:Suppl-13.
 Exclusion Reason: Not in PICO

Myers M, Gurwood AS. Periocular malignancies and primary eye care. [Review] [22 refs]. *Optometry (St.Louis, Mo.)* 2001;72(11):705-12.
Exclusion Reason: Narrative Review

Nagami Y, Machida H, Tominaga K, Nakatani M, Kameda N, Sugimori S, et al. Accurate detection and diagnosis of esophageal squamous cancer by tandem conventional endoscopy with narrow-band imaging and iodine staining: A prospective study. *Gastrointestinal Endoscopy* 2010;71(5):AB252-3.
Exclusion Reason: Not in PICO

Navone R, Pentenero M, Gandolfo S. Liquid-based cytology in oral cavity squamous cell cancer. [Review]. *Current Opinion in Otolaryngology & Head & Neck Surgery* 2011;19(2):77-81.
Exclusion Reason: Narrative Review

Nguyen TH, Ho DQ. Nonmelanoma skin cancer. Current treatment options in oncology 2002;3(3):193-203.
Exclusion Reason: Narrative Review

Niederhorn A, Gabler G, Argenziano G, Muir J, Zalaudek I, Soyer HP, et al. The user-generated web-based dermoscopy image archive of the international dermoscopy society: A contribution to E-learning and exchange of knowledge. *Dermatology* 2011;222(2):131-7.
Exclusion Reason: Not in PICO

Ogden E, Schofield J. Two-week wait skin cancer referral outcomes: Differences in management between plastic surgery and dermatology. *British Journal of Dermatology* 2010;163:60-1.
Exclusion Reason: Not in PICO

Paderni C, Compilato D, Lo Muzio L, Campisi G. Direct visualization of oral-cavity tissue fluorescence and toluidine blue staining: New adjunctive aids for oral medicine practitioners in early oral cancer diagnosis and potentially malignant disorders follow-up? *Oral Diseases* 2010;16(6):535-6.
Exclusion Reason: Not in PICO

Palamaras I, Hamill M, Sethi G, Wilkinson D, Lamba H. The usefulness of a diagnostic biopsy clinic in a genitourinary medicine setting: recent experience and a review of the literature. *Journal of the European Academy of Dermatology and Venereology* 2006;20(8):905-10.
Exclusion Reason: Not in PICO

Palanivel JA, Macbeth AE, Dootson G, Graham R, Mahmood K, Garioch J. An audit of incomplete excision rates of basal cell carcinoma from four U.K. teaching hospitals. *British Journal of Dermatology* 2011;165:106.
Exclusion Reason: Not in PICO

Palka KT, Slebos RJ, Chung CH. Update on molecular diagnostic tests in head and neck cancer. [Review] [100 refs]. *Seminars in Oncology* 2008;35(3):198-210.
Exclusion Reason: Narrative Review

Pallagatti, S., Sheikh, S., Aggarwal, A., Gupta, D., Singh, R., Handa, R., Kaur, S. & Mago, J. (2013) Toluidine blue staining as an adjunctive tool for early diagnosis of dysplastic changes in the oral mucosa. *Journal of Clinical & Experimental Dentistry*, 5: e187-e191.
Exclusion Reason: Not in PICO

Palmer, V. M. & Wilson, P. R. (2013) Incompletely excised basal cell carcinoma: residual tumor rates at Mohs re-excision. *Dermatologic Surgery*, 39: 706-718.
Exclusion Reason: Not in PICO

Pariser DM, Phillips PK. Basal cell carcinoma: When to treat it yourself, and when to refer. *Geriatrics* 1994;49(3):39-42+44.
Exclusion Reason: Narrative Review

Parkinson RW. Shave biopsies--simple and useful. *Postgraduate Medicine* 1966;84(8):161-70.
Exclusion Reason: Narrative Review

Pech O, Rabenstein T, Manner H, Petrone MC, Pohl J, Vieth M, et al. Confocal laser endomicroscopy for in vivo diagnosis of early squamous cell carcinoma in the esophagus. *Clinical Gastroenterology & Hepatology* 2008;6(1):89-94.

Exclusion Reason: Not in PICO

Pereira RD, Martin AA, Tierra-Criollo CJ, Santos IDAO. Diagnosis of squamous cell carcinoma of human skin by Raman spectroscopy. *Optical Biopsy V* 2004;5326:106-12.

Exclusion Reason: Not in PICO

Phillips, C., Newsome, A., Jennifer, D., Lindsey, F., Green, H. & McLean, T. (2014) Anatomy of a skin biopsy: A retrospective analysis of outpatient biopsy results from 2000 to 2010. *Journal of the American Academy of Dermatology*, 70: AB36.

Exclusion Reason: Not in PICO

Piccolo D, Smolle J, Argenziano G, Wolf IH, Braun R, Cerroni L, et al. Teledermoscopy--results of a multicentre study on 43 pigmented skin lesions. *Journal of Telemedicine & Telecare* 2000;6(3):132-7.

Exclusion Reason: Not in PICO

Pignatelli I, Poirier V, De Berker DAR, Verne J. Audit of completeness of cancer registration for basal cell carcinoma and its impact on use for quality assurance. *British Journal of Dermatology* 2010;163:58.

Exclusion Reason: Not in PICO

Pignatelli I, Poirier V, De Berker DAR, Verne J. Completeness of basal cell carcinoma excisions in an english region. *British Journal of Dermatology* 2010;163:69-70.

Exclusion Reason: Not in PICO

Poirier V, Osinowo A, Takwale A, De Berker DAR, Verne J. Basal cell carcinoma follow-up in the South West, Hampshire and Isle of Wight. *British Journal of Dermatology* 2012;167:61.

Exclusion Reason: Not in PICO

Pop Stefanija N, Blanken R, Vodegel RM. The positive predictive value of clinical diagnosis of basal cell carcinoma. [Dutch]. *Nederlands Tijdschrift voor Dermatologie en Venereologie* 2006;16(6):237-40.

Exclusion Reason: Not in PICO

Popadic, M. (2014) Statistical evaluation of dermoscopic features in basal cell carcinomas. *Dermatologic Surgery*, 40: 718-724.

Exclusion Reason: Not in PICO

Poulsen AG, Larsen FG, Weismann K, Petersen CS, Ravnborg LR, Heidenheim M, et al. [Investigation of malignant melanoma in an "open house" setting]. [Danish]. *Ugeskrift for Laeger* 1999;161(12):1758-61.

Exclusion Reason: Not in PICO

Prout MN, Sidari JN, Witzburg RA, Grillone GA, Vaughan CW. Head and neck cancer screening among 4611 tobacco users older than forty years. *Otolaryngology - Head & Neck Surgery* 1997;116(2):201-8.

Exclusion Reason: Not in PICO

Quereux G, Lequeux Y, Cary M, Jumbou O, Nguyen JM, Dreno B. Feasibility and effectiveness of a melanoma targeted screening strategy. *Melanoma Research* 2011;21:e1-2.

Exclusion Reason: Not in PICO

Raasch B, Maclennan R, Wronski I, Robertson I. Body site specific incidence of basal and squamous cell carcinoma in an exposed population, Townsville, Australia. *Mutation Research* 1998;422(1):101-6.

Exclusion Reason: Not in PICO

Raasch BA. Suspicious skin lesions and their management. *Australian Family Physician* 1999;28(5):466-71.

Exclusion Reason: Not in PICO: Clinical versus histological diagnosis (not biopsy or dermatoscopy versus histology or follow up)

Rademaker M, Thorburn M. Pathology referrals for skin lesions - Are we giving the pathologist sufficient clinical information? *New Zealand Medical Journal* 2010;123(1325):53-8.

Exclusion Reason: Not in PICO

Radziszewski J, Kowalewska M, Jedrzejczak T, Kozlowicz-Gudzinska I, Nasierowska-Guttmejer A, Bidzinski M, et al. The accuracy of the sentinel lymph node concept in early stage squamous cell vulvar carcinoma. *Gynecologic Oncology* 2010;116(3):473-7.
Exclusion Reason: Not in PICO

Rahman F, Tippu SR, Khandelwal S, Girish KL, Manjunath BC, Bhargava A. A study to evaluate the efficacy of toluidine blue and cytology in detecting oral cancer and dysplastic lesions. *Quintessence International* 2012;43(1):51-9.
Exclusion Reason: Not in PICO

Raj, G. & Gupta, G. (1111) The need for full body skin examination on patients referred to dermatology with a lesion. *British Journal of Dermatology. Conference: 93rd Annual Meeting of the British Association of Dermatologists Liverpool United Kingdom. Conference Start: 20130709 Conference End: 20130711. Conference Publication: (var.pagings)*, 169: July.
Exclusion Reason: Not in PICO

Rajaram N, Tunnell J, Reichenberg J. Pilot clinical study for noninvasive diagnosis of nonmelanoma skin cancer. *Journal of the American Academy of Dermatology* 2011;64(2 SUPPL. 1):AB76.
Exclusion Reason: Not in PICO

Reed SF, Britt RC, Novosel TJ, Collins JN, Weireter LJ, Britt LD. Screening human immunodeficiency virus-positive men for anal intraepithelial neoplasia. *American Surgeon* 2012;78(8):901-3.
Exclusion Reason: Not in PICO

Reynolds PL, Strayer SM. Treatment of skin malignancies. [Review] [33 refs]. *Journal of Family Practice* 2003;52(6):456-64.
Exclusion Reason: Narrative Review

Rezze GG, De Sa BCS, Neves RI. Dermoscopy: The pattern analysis. *Anais Brasileiros de Dermatologia* 2006;81(3):261-8.
Exclusion Reason: Narrative Review

Rice SA, Swale VJ, Cerio R. Are we relying too heavily on dermoscopy? *British Journal of Dermatology* 2012;167:105.
Exclusion Reason: Narrative review

Richert, B., Lecerf, P., Caucanas, M. & Andre, J. (2013) Nail tumors. *Clinics in Dermatology*, 31: 602-617.
Exclusion Reason: Narrative review

Robison Sean, Kljakovic Marjan, Barry Peter. Choosing to biopsy or refer suspicious melanocytic lesions in general practice. *BMC Family Practice* 2012;13(1):78.
Exclusion Reason: Not in PICO

Roozeboom, M. H., Mosterd, K., Winnepenninckx, V. J., Nelemans, P. J. & Kelleners-Smeets, N. W. (2013) Agreement between histological subtype on punch biopsy and surgical excision in primary basal cell carcinoma. *Journal of the European Academy of Dermatology & Venereology*, 27: 894-898.
Exclusion Reason: Not in PICO

Rose LC. Recognizing neoplastic skin lesions: a photo guide. [Review] [18 refs]. *American Family Physician* 887;58(4):873-84.
Exclusion Reason: Narrative Review

Rosen R. Managing nonmelanoma skin cancer. *Modern Medicine of Australia* 1999;42(2):74-85.
Exclusion Reason: Narrative Review

Rosendahl C, Cameron A, Argenziano G, Zalaudek I, Tschandl P, Kittler H. Dermoscopy of Squamous Cell Carcinoma and Keratoacanthoma. *Archives of Dermatology* 2012;148(12):1386-92.
Exclusion Reason: Not in PICO

Rosendahl C, Hansen C, Cameron A, Bourne P, Wilson T, Cook B, et al. Measuring performance in skin cancer practice: the SCARD initiative. *International Journal of Dermatology* 2011;50(1):44-51.
Exclusion Reason: Not in PICO

Rosendahl C, Tschandl P, Cameron A, Kittler H. Diagnostic accuracy of dermatoscopy for melanocytic and nonmelanocytic pigmented lesions. *Journal of the American Academy of Dermatology* 2011;64(6):1068-73.
Exclusion Reason: Duplicate

Rousset, J., Abgral, R., Chinellato, S., Garetier, M., Barberot, C., Valette, G., Potard, G., Le, B. T. & Salaun, P. Y. (2013) Early recurrence or submucosal residual of laryngeal squamous cell carcinoma: diagnosis by CT-guided endolaryngeal core biopsy on a transcutaneous approach. *Head & Neck*, 35: E202-E204.
Exclusion Reason: Not in PICO

Rudkin AK, Dodd T, Muecke JS. The differential diagnosis of localised amelanotic limbal lesions: a review of 162 consecutive excisions. *British Journal of Ophthalmology* 2011;95(3):350-4.
Exclusion Reason: Not in PICO

Russell EB, Carrington PR, Smoller BR. Basal cell carcinoma: a comparison of shave biopsy versus punch biopsy techniques in subtype diagnosis. *Journal of the American Academy of Dermatology* 1999;41(1):69-71.
Exclusion Reason: Not in PICO

Ryu IS, Choi SH, Kim do H, Han MW, Roh JL, Kim SY, et al. Detection of the primary lesion in patients with cervical metastases from unknown primary tumors with narrow band imaging endoscopy: preliminary report. *Head & Neck* 2013;35(1):10-4.
Exclusion Reason: Not in PICO

Sabir F, Aziz M, Afroz N, Amin SS. Clinical and cyto-histopathological evaluation of skin lesions with special reference to bullous lesions. *Indian Journal of Pathology and Microbiology* 2010;53(1):41-6.
Exclusion Reason: Narrative Review

Saldanha G, Fletcher A, Slater DN. Basal cell carcinoma: a dermatopathological and molecular biological update. *British Journal of Dermatology* 2003;148(2):195-202.
Exclusion Reason: Narrative Review

Sandison A. Common head and neck cases in our consultation referrals: diagnostic dilemmas in inverted papilloma. [Review] [13 refs]. *Head and neck pathology* 2009;3(3):260-2
Exclusion Reason: Narrative Review

Santi EG, Inoue H, Sato H, Maselli R, Ikeda H, Yoshida A, et al. Endoscopic treatment for esophageal achalasia with early squamous cell carcinoma: POEM plus ESD. *Journal of Gastroenterology and Hepatology* 2012;27:317-8.
Exclusion Reason: Not in PICO

Sanyal, S., Holme, A. & Kemmett, D. (2013) How are patients with actinic keratoses managed in primary care? *British Journal of Dermatology*, 169: 45.
Exclusion Reason: Not in PICO

Schlemper RJ, Dawsey SM, Itabashi M, Iwashita A, Kato Y, Koike M, et al. Differences in diagnostic criteria for esophageal squamous cell carcinoma between Japanese and Western pathologists. *Cancer* 2000;88(5):996-1006.
Exclusion Reason: Not in PICO

Schofield J, Hepburn N, Scharrer K, Hussain K. The costs of diagnosing and treating skin cancer using the 2-week-wait referral process. *British Journal of Dermatology* 2011;165:22-3.
Exclusion Reason: Not in PICO

Schroeder BM, American Cancer Society. ACS updates guideline for the early detection of cervical neoplasia and cancer. American Cancer Society. *American Family Physician* 2003;67(9):2011-6.
Exclusion Reason: Not in PICO

Schwartzberg JB, Elgart GW, Romanelli P, Fangchao M, Federman DG, Kirsner RS. Accuracy and predictors of basal cell carcinoma diagnosis. *Dermatologic Surgery* 2005;31(5):534-7.
Exclusion Reason: Not in PICO

- Scully C, Newman L, Bagan JV. The role of the dental team in preventing and diagnosing cancer: 3. oral cancer diagnosis and screening. *Dental Update* 331;32(6):326-8.
Exclusion Reason: Not in PICO
- Sendagorta E, Herranz P, Guadalajara H, Zamora FX. [Early detection of anal intraepithelial neoplasia in high-risk patients]. [Review] [Spanish]. *Actas Dermo-Sifiliograficas* 2011;102(10):757-65.
Exclusion Reason: Narrative Review
- Senel E. Dermatoscopy of non-melanocytic skin tumors. *Indian Journal of Dermatology Venereology & Leprology* 2011;77(1):16-21.
Exclusion Reason: Narrative Review
- Shariff Z, Roshan A, Williams AM, Platt AJ. 2-Week wait referrals in suspected skin cancer: does an instructional module for general practitioners improve diagnostic accuracy? *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland* 2010;8(5):247-51.
Exclusion Reason: Not in PICO
- Sharma, A., Alfa-Wali, M., Rodriguez-Justo, M. & Polychronis, A. (2013) Squamous cell carcinoma of pancreas: an unusual site of relapse from early-stage lung cancer: 12-month postsurgery. *BMJ Case Reports*, 2013, 2013.
Exclusion Reason: Not in PICO
- Shimizu Y, Omori T, Yokoyama A, Yoshida T, Hirota J, Ono Y, et al. Endoscopic diagnosis of early squamous neoplasia of the esophagus with iodine staining: high-grade intra-epithelial neoplasia turns pink within a few minutes. *Journal of Gastroenterology & Hepatology* 2008;23(4):546-50.
Exclusion Reason: Not in PICO
- Shitara, D., Ishioka, P., Alonso-Pinedo, Y., Palacios-Bejarano, L., Carrera, C., Malveyh, J. & Puig, S. (2014) Shiny White Streaks: A Sign of Malignancy at Dermoscopy of Pigmented Skin Lesions. *Acta Dermato-Venereologica*, 94: 132-137.
Exclusion Reason: Setting not in PICO
- Shum WY, Hsieh TC, Yeh JJ, Chen JH, Su CC, Liang JA, et al. Clinical usefulness of dual-time FDG PET-CT in assessment of esophageal squamous cell carcinoma. *European Journal of Radiology* 2012;81(5):1024-8.
Exclusion Reason: Not in PICO
- Singh, T. & Schenberg, M. (2013) Delayed diagnosis of oral squamous cell carcinoma following dental treatment. *Annals of the Royal College of Surgeons of England*, 95: 369-373.
Exclusion Reason: Not in PICO
- Skiljevic D, Stojkovic-Filipovic J, Nikolic M, Medenica L. Early-onset basal cell carcinoma. *Melanoma Research* 2010;20:e68.
Exclusion Reason: N=1
- Smithers BM, Fahey PP, Corish T, Gotley DC, Falk GL, Smith GS, et al. Symptoms, investigations and management of patients with cancer of the oesophagus and gastro-oesophageal junction in Australia. *Medical Journal of Australia* 2010;193(10):572-7.
Exclusion Reason: Not in PICO
- Sober AJ. Diagnosis and management of skin cancer. *Cancer* 1983;51(12:Suppl):Suppl-52.
Exclusion Reason: Not in PICO
- Socha, A. & Niedzielska, I. (2013) Exophytic tumours of skin of the head - Case study and review of the literature. *Dental and Medical Problems*, 50: 229-237.
Exclusion Reason: Not in PICO
- Speel E-J, Leusink FKJ, Van Hooff SR, Kummer JA, van Diest PJ, Koole R, et al. Multi-center validation of a lymph node metastasis gene-expression signature for head and neck squamous cell carcinomas. *Cancer Research* 2011;71(8 SUPPL. 1).
Exclusion Reason: Not in PICO
- Spencer JM, Tannenbaum A, Sloan L, Amonette RA. Does inflammation contribute to the eradication of basal cell carcinoma following curettage and electrodesiccation? *Dermatologic Surgery* 1997;23(8):625-30.

Exclusion Reason: Not in PICO
 Spencer RJ, Young RH, Goodman A. The risk of squamous cell carcinoma in persistent vulvar ulcers. *Menopause* 2011;18(10):1067-71.
 Exclusion Reason: Not in PICO
 Stegman SJ. Basal cell carcinoma and squamous cell carcinoma. Recognition and treatment. [Review] [28 refs]. *Medical Clinics of North America* 1986;70(1):95-107.
 Exclusion Reason: Narrative Review
 Stell PM, Wood GD, Scott MH. Early oral cancer: treatment by biopsy excision. *British Journal of Oral Surgery* 1982;20(4):234-8.
 Exclusion Reason: Not in PICO
 Stockfleth E. Non melanoma skin cancer - Early excision is still the standard in therapy. [German]. *Klinikerarzt* 2002;31(5):122-5.
 Exclusion Reason: Narrative Reivew
 Stoeckli SJ, Broglie MA. Sentinel node biopsy for early oral carcinoma. *Current Opinion in Otolaryngology & Head and Neck Surgery* 2012;20(2):103-8.
 Exclusion Reason: Narrative Review
 Stolte M. [The new "Vienna Classification" for epithelial neoplasia of the gastrointestinal tract. Pros or cons?]. [Review] [34 refs] [German]. *Pathologe* 2001;22(1):4-12.
 Exclusion Reason: Narrative Review
 Streeton CL, Gospodarevskaya E, Harris A. Treatment of basal cell carcinomas by general practitioners in Australia. *International Journal of Dermatology* 2006;45(4):345-51.
 Exclusion Reason: Not in PICO
 Stulberg DL, Crandell B, Fawcett RS. Diagnosis and treatment of basal cell and squamous cell carcinomas. *American Family Physician* 2004;70(8):1481-8.
 Exclusion Reason: Narrative Review
 Szalai K, Hatvani Z, Harsing J, Somlai B, Karpati S. High frequency ultrasonography in the diagnosis of cutaneous pigmented lesions and melanoma reduce the possibilities of diagnostic pitfalls. *Melanoma Research* 2011;21:e4-5.
 Exclusion Reason: Narrative Review
 Talbot S, Hitchcock B. Incomplete primary excision of cutaneous basal and squamous cell carcinomas in the Bay of Plenty. *New Zealand Medical Journal* 2004;117(1192):U848.
 Exclusion Reason: Not in PICO
 Tan E, Yung A, Jameson M, Oakley A, Rademaker M. Successful triage of patients referred to a skin lesion clinic using teledermoscopy (IMAGE IT trial). *British Journal of Dermatology* 2010;162(4):803-11.
 Exclusion Reason: Not in PICO
 Tandon Y, Brodell RT. Local reactions to imiquimod in the treatment of basal cell carcinoma. *Dermatology Online Journal* 2012;18(9):1.
 Exclusion Reason: Not in PICO
 Tangjaturonrasme, N., Rerknimitr, R., Pittayanon, R., Wisedopas, N. & Kullavanijaya, P. (2013) The difference in detection rates during surveillance endoscopy for early squamous cell neoplasia of the esophagus between patients with previous nasopharyngeal cancer and patients with other ent related squamous cell cancers pornphan thienchanachaiya1. *Gastrointestinal Endoscopy*, 77: AB339-AB340.
 Exclusion Reason: Not in PICO
 Tannapfel A, Weber A. Tumor markers in squamous cell carcinoma of the head and neck: clinical effectiveness and prognostic value. *European Archives of Oto-Rhino-Laryngology* 2001;258(2):83-8.
 Exclusion Reason: Narrative Review
 Teoh YL, Halpern SM, Shall L. Factors associated with incomplete excision of basal cell carcinomas. *British Journal of Dermatology* 2010;163:55-6.

Exclusion Reason: Not in PICO
 TerKonda SP, Perdakis G. Non-melanotic skin tumors of the upper extremity. [Review] [50 refs]. *Hand Clinics* 104;20(3):293-301.
 Exclusion Reason: Narrative Review

Terrill PJ, Fairbanks S, Bailey M. Is there just one lesion? The need for whole body skin examination in patients presenting with non-melanocytic skin cancer. *ANZ Journal of Surgery* 2009;79(10):707-12.
 Exclusion Reason: Not in PICO

Terstappen K, Larko O, Wennberg AM. Pigmented basal cell carcinoma - Comparing the diagnostic methods of SIAscopy and dermoscopy. *Acta Dermato-Venereologica* 2007;87(3):238-42.
 Exclusion Reason: Narrative Review

Terushkin V, Braga JC, Dusza SW, Scope A, Busam K, Marghoob AA, et al. Agreement on the Clinical Diagnosis and Management of Cutaneous Squamous Neoplasms. *Dermatologic Surgery* 2010;36(10):1514-20.
 Exclusion Reason: Not in PICO

Thienchanachaiya P, Rerknimitr R, Pittayanon R, Wisedopas N, Tangjaturonrasme N, Kullavanijaya P. Preliminary study of FICE for detection of early esophageal neoplasm in patients with history of ENT related squamous cell cancers. *Journal of Gastroenterology and Hepatology* 2012;27:319-20.
 Exclusion Reason: Not in PICO

Thissen MR, Neumann HA, Berretty PJ, Ideler AH. [The treatment of basal cell carcinoma patients by dermatologists in Netherland]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde* 1998;142(27):1563-7.
 Exclusion Reason: Not in PICO

Tochigi, T., Shuto, K., Staito, H., Kono, T. & Matsubara, H. (2013) Early esophageal squamous cell cancer by high-barium esophagography using flat panel X-ray detector in comparison with histological findings. *European Journal of Cancer*, 49: S252-S253.
 Exclusion Reason: Not in PICO

Tomas S. Difficult to diagnose skin cancer The 'aggressive' BCC. *Australian Family Physician* 2009;38(7):492-7.
 Exclusion Reason: Narrative Review

Trotter MJ, Bruecks AK. Interpretation of Skin Biopsies by General Pathologists: Diagnostic Discrepancy Rate Measured by Blinded Review. *Archives of Pathology and Laboratory Medicine* 2003;127(11):1489-92.
 Exclusion Reason: Not in PICO

Turan, E., Yurt, N., Yesilova, Y. & Turkcu, G. (2013) Early-onset basal cell carcinoma. *Turkish Journal of Pediatrics*, 55: 354-356.
 Exclusion Reason: Not in PICO

Ulrich M, Lange-Asschenfeldt S, Gonzalez S. In vivo reflectance confocal microscopy for early diagnosis of nonmelanoma skin cancer. *Actas Dermo-Sifiliograficas* 2012;103(9):784-9.
 Exclusion Reason: Narrative Review

Vacher-Lavenu MC. [Histology and cytology of cervical cancers]. [Review] [24 refs] [French]. *Revue du Praticien* 2001;51(13):1417-23.
 Exclusion Reason: Narrative Review

Vargo N. Basal cell and squamous cell carcinoma. [Review] [46 refs]. *Seminars in Oncology Nursing* 2003;19(1):12-21.
 Exclusion Reason: Narrative Review

Vermaak, P. V. & Manushakian, J. (2013) Rapidly enlarging skin lesion on the lip. *BMJ Case Reports*, 2013, 2013.
 Exclusion Reason: Not in PICO

Viglizzo G, Rongioletti F. Clinical, dermoscopic and pathologic correlation of pigmentary lesions observed in a dermoscopy service in the year 2003. [Italian, English]. *Giornale Italiano di Dermatologia e Venereologia* 2004;139(4):339-44.
Exclusion Reason: Not in PICO

Viola KV, Tolpinrud WL, Gross CP, Kirsner RS, Imaeda S, Federman DG. Outcomes of referral to dermatology for suspicious lesions: implications for teledermatology. *Archives of Dermatology* 2011;147(5):556-60.
Exclusion Reason: Not in PICO

Wade S, Gonzalez ML, Basra M. An audit of the diagnostic accuracy and complete excision rate for skin cancers in primary and secondary care in the Cardiff area. *British Journal of Dermatology* 2011;165:105.
Exclusion Reason: Not in PICO

Wagoner J, Keehn C, Morgan MB. CD-10 immunostaining differentiates superficial basal cell carcinoma from cutaneous squamous cell carcinoma. *American Journal of Dermatopathology* 2007;29(6):555-8.
Exclusion Reason: Narrative Review

Wan A, Savage NW. Biopsy and diagnostic histopathology in dental practice in Brisbane: usage patterns and perceptions of usefulness. *Australian Dental Journal* 2010;55(2):162-9.
Exclusion Reason: Not in PICO

Watson Tony, Walter Fiona, Wood Annabel, Morris Helen, Hall Per, Karner Simone, et al. Learning a novel technique to identify possible melanomas: are Australian general practitioners better than their U.K. colleagues? *Asia Pacific Family Medicine* 2009;8(1):3.
Exclusion Reason: Narrative Review

Wetzig T, Woitek M, Eichhorn K, Simon JC, Paasch U. Surgical Excision of Basal Cell Carcinoma with Complete Margin Control: Outcome at 5-Year Follow-Up. *Dermatology* 2010;220(4):363-9.
Exclusion Reason: Not in PICO

White, G. M., Zhou, H. C. & Burchette, R. J. (2013) Biopsy followed by immediate curettage and electrodesiccation of suspected basal cell carcinomas at the first visit. *JAMA Dermatology*, 149: 980-981.
Exclusion Reason: Not in PICO

Whitesides LM, Ferreira LR, Ord RA. Audit of clinical information and diagnoses supplied to the pathologist following biopsy of oral squamous cell carcinomas. *MSDA Journal* 1995;38(2):63-5.
Exclusion Reason: Narrative Review

Wilkinson D, Askew DA, Dixon A. Skin cancer clinics in Australia: workload profile and performance indicators from an analysis of billing data. *Medical Journal of Australia* 2006;184(4):162-4.
Exclusion Reason: Not in PICO

Williams RB, Burdge AH, Lewis Jones S. Skin biopsy in general practice. *British Medical Journal* 1991;303(6811):1179-80.
Exclusion Reason: Not in PICO

Wilson RL, Yentzer BA, Isom SP, Feldman SR, Fleischer AB Jr. How good are US dermatologists at discriminating skin cancers? A number-needed-to-treat analysis. *Journal of Dermatological Treatment* 2012;23(1):65-9.
Exclusion Reason: Not in PICO

Winzenburg SM, Niehans GA, George E, Daly K, Adams GL. Basaloid squamous carcinoma: a clinical comparison of two histologic types with poorly differentiated squamous cell carcinoma. *Otolaryngology - Head & Neck Surgery* 1998;119(5):471-5.
Exclusion Reason: Not in PICO

Wlodarczyk J. [Application of Lugol solution in the gastroesophageal reflux disease]. [Polish]. *Przegląd Lekarski* 2007;64(9):549-51
Won S-S, Jung D-S, Kim H-S, Kwon K-S, Hee S-S. Clinicopathologic features of postlaser basal cell carcinoma: Does it differ from primary basal cell carcinoma? *Journal of the American Academy of Dermatology* 2010;62(3 SUPPL. 1):AB146.

Exclusion Reason: Not in PICO

Wolberink, E. A. W., Pasch, M. C., Zeiler, M., Van Erp, P. E. J. & Gerritsen, M. J. P. (2013) High discordance between punch biopsy and excision in establishing basal cell carcinoma subtype: Analysis of 500 cases. *Journal of the European Academy of Dermatology and Venereology*, 27: 985-989.

Exclusion Reason: Not in PICO

Wong KY, Gilleard O, Price R. Non-melanoma skin cancer incomplete excision rates of different grades of plastic surgeons and the implications for service provision. *European Journal of Surgical Oncology* 2012;38(11):1121.

Exclusion Reason: Not in PICO

Woolley, S. D. & Hughes, C. (2013) A young military pilot presents with a periocular Basal Cell Carcinoma: A case report. *Travel Medicine and Infectious Disease*, 11: 435-437.

Exclusion Reason: Not in PICO

Wray, E. V., Brant, B., Hussain, F. & Muller, F. M. (2013) A new model of teledermoscopy combining service and education. *British Journal of Dermatology*, 169: 139.

Exclusion Reason: Not in PICO

Wright VC. When to suspect squamous cancer at colposcopy. [Review] [22 refs]. *Nurse Practitioner* 1959;26(9):50-6.

Exclusion Reason: Narrative Review

Wustrow J, Rudert H, Diercks M, Beigel A. Squamous cell carcinoma and undifferentiated carcinoma of the inner nose and the paranasal sinuses. [German]. *Strahlentherapie und Onkologie* 1989;165(6):468-73.

Exclusion Reason: Not in PICO

Yamazaki N. [Squamous cell carcinoma]. [Review] [9 refs] [Japanese]. *Gan to Kagaku Ryoho* [Japanese Journal of Cancer & Chemotherapy] 2006;33(10):1392-7.

Exclusion Reason: Narrative Review

Youl PH, Baade PD, Janda M, Del Mar CB, Whiteman DC, Aitken JF. Diagnosing skin cancer in primary care: how do mainstream general practitioners compare with primary care skin cancer clinic doctors? *Medical Journal of Australia* 2007;187(4):215-20.

Exclusion Reason: Not in PICO: Clinical versus histological diagnosis (not biopsy or dermatoscopy versus histology or follow up)

Youl PH, Janda M, Aitken JF, Del Mar CB, Whiteman DC, Baade PD. Body-site distribution of skin cancer, pre-malignant and common benign pigmented lesions excised in general practice. *British Journal of Dermatology* 2011;165(1):35-43

Exclusion Reason: Not in PICO

Zalaudek I, Argenziano G, Soyer HP, Corona R, Sera F, Blum A, et al. Three-point checklist of dermoscopy: an open internet study. *British Journal of Dermatology* 2006;154(3):431-7.

Exclusion Reason: Not in PICO

Zedek DC, Smith ET Jr, Hitchcock MG, Feldman SR, Shelton BJ, White WL. Cutaneous lupus erythematosus simulating squamous neoplasia: the clinicopathologic conundrum and histopathologic pitfalls. *Journal of the American Academy of Dermatology* 2007;56(6):1013-20.

Exclusion Reason: Not in PICO

Zheng W, Soo KC, Sivanandan R, Olivo M. Detection of squamous cell carcinomas and pre-cancerous lesions in the oral cavity by quantification of 5-aminolevulinic acid induced fluorescence endoscopic images. *Lasers in Surgery & Medicine* 2002;31(3):151-7.

Exclusion Reason: Not in PICO

Zhou XH. Primary squamous cell carcinoma of the thyroid. *European Journal of Surgical Oncology* 2002;28(1):42-5.

Exclusion Reason: N=2

HEAD AND NECK CANCERS

LARYNGEAL CANCER

Review question:

What is the risk of laryngeal cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

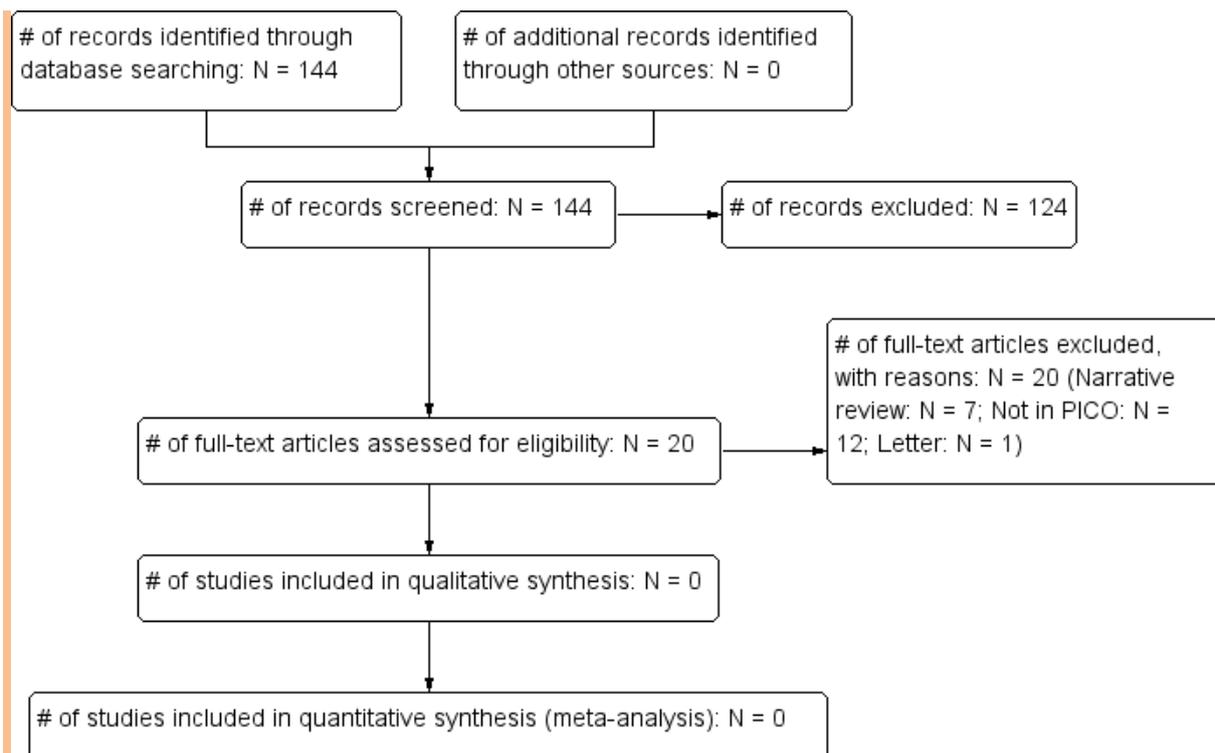
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	1085	97	08/10/2012
<i>Premedline</i>	All-2012	19	1	08/10/2012
<i>Embase</i>	All-2012	1352	75	08/10/2012
<i>Cochrane Library</i>	All-2012	89	0	10/10/2012
<i>Psychinfo</i>	All-2012	6	0	08/10/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	149	10	10/10/2012
<i>Biomed Central</i>	All-2012	200	3	08/10/2012

Total References retrieved (after de-duplication): 137

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	10/2012-26/08/2014	66	3	26/08/2014
<i>Premedline</i>	10/2012-26/08/2014	74	3	26/08/2014
<i>Embase</i>	10/2012-26/08/2014	262	5	26/08/2014
<i>Cochrane Library</i>	10/2012-26/08/2014	45	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	10/2012-26/08/2014	26	2	26/08/2014

Total References retrieved (after de-duplication): 7



Study results

No evidence was identified.

References

Included studies

None

Excluded studies (with excl reason)

- (1207) Society of Surgical Oncology Practice Guidelines. Laryngeal cancer surgical practice guidelines. *Oncology (Williston Park)*, 11: 1201-1203.
Guideline
- (1991) Early pharyngolaryngeal carcinomas with palpable nodes. French Head and Neck Study Group (GETTEC). *American Journal of Surgery*, 162: 377-380.
Not in PICO
- Ah-See, K. (2008) The evidence for different management strategies for laryngeal cancer: summaries of systematic reviews commissioned for an educational meeting. [Review] [13 refs]. *Clinical Otolaryngology*, 33: 90-93.
Not in PICO
- Alho, O.-P., Teppo, H., Mantyselka, P. & Kantola, S. (2006) Head and neck cancer in primary care: Presenting symptoms and the effect of delayed diagnosis of cancer cases. *CMAJ*, 174: 779-784.
Study design not in PICO: Symptom prevalence study (with no case/no case verification) + cancer patient study
- Ameille, J., Ruffie, P. & Bergeret, A. (2004) [Asbestos-related occupational cancers]. [French]. *Revue du Praticien*, 54: 1649-1659.
Narrative review
- Arens, C. (2004) [Early diagnosis of laryngeal cancer]. [German]. *Laryngo-Rhino-Otologie*, 83: 768-770.
Narrative review

- Arias, F., Villafranca, E., Duenas, M. T. & Vera, R. (2001) Prognostic factors in carcinomas of the head and neck. [Spanish]. *Anales del Sistema Sanitario de Navarra*, 24: 73-81.
Narrative review
- Assimakopoulos, D. & Patrikakos, G. (2002) The role of gastroesophageal reflux in the pathogenesis of laryngeal carcinoma. [Review] [77 refs]. *American Journal of Otolaryngology*, 23: 351-357.
Narrative review
- Babu, S., B, S., M, G. & Salih, S. (2011) A rare presentation of Pulmonary Lymphangitic Carcinomatosis in cancer of lip: case report. *World Journal of Surgical Oncology*, 9: 77.
Not in PICO
- Back, G. & Sood, S. (2005) The management of early laryngeal cancer: options for patients and therapists. [Review] [51 refs]. *Current Opinion in Otolaryngology & Head & Neck Surgery*, 13: 85-91.
Narrative review
- Bahar, G., Nageris, B. I., Spitzer, T., Popovtzer, A., Mharshak, G. & Feinmesser, R. (1929) [Subglottic carcinoma]. [Review] [33 refs] [Hebrew]. *Harefuah*, 141: 914-918.
Narrative review
- Bajaj, Y., Uppal, S., Sharma, R. K., Grace, A. R. H., Howard, D. M., Nicolaidis, A. R. & Coatesworth, A. P. (2011) Evaluation of voice and quality of life after transoral endoscopic laser resection of early glottic carcinoma. *Journal of Laryngology and Otology*, 125: 706-713.
Not in PICO
- Banfield, G., Tandon, P. & Solomons, N. (2000) Hoarse voice: an early symptom of many conditions. [Review] [3 refs]. *Practitioner*, 244: 267-271.
Narrative review
- Barnett, R. J., Ceasar, S. C. & Wisdom, G. S. (2001) Laryngoceles and saccular cyst. *The Journal of the Louisiana State Medical Society : official organ of the Louisiana State Medical Society*, 153: 170-173.
Not in PICO
- Barra, S., Mattotti, M., Bertos, G. & Barzan, L. (1992) [The program for early diagnosis of the upper respiratory tract and digestive system neoplasms offered to alcoholics in the region of Friuli-Venice Giulia]. [Italian]. *Acta Otorhinolaryngologica Italica*, 12: 337-344.
Not in PICO
- Baughan, P., Keatings, J. & O'Neill, B. (2011) Urgent suspected cancer referrals from general practice: audit of compliance with guidelines and referral outcomes. *British Journal of General Practice*, 61: e700-e706.
Not in PICO
- Betlejewski, S. & Betlejewski, A. (2008) Cancer or syphilis laryngis, politics or diagnostic failure - Problems of Emperor Frederick's III disease. [Polish]. *Otolaryngologia Polska*, 62: 803-809.
Narrative review
- Bibby, J. R., Cotton, S. M., Perry, A. & Corry, J. F. (2008) Voice outcomes after radiotherapy treatment for early glottic cancer: assessment using multidimensional tools. *Head & Neck*, 30: 600-610.
Not in PICO
- Bjorck, G., Johansson, S., Milerad, J., Katz-Salamon, M., Hertegard, S. & Kuylenstierna, R. (2000) [Fiberoptic endoscopy confirms the cause of upper respiratory obstruction in small children. The most common causes to referrals are sleep apnea syndrome and inspiratory stridor]. [Swedish]. *Lakartidningen*, 97: 2446-2450.
Not in PICO
- Blair, R. L. & McKerrow, W. S. (1994) The Scottish Otolaryngology Audit--laryngeal cancer audit. *Journal of Laryngology & Otology*, 108: 332-335.
Narrative review

- Bova, R. & McGuinness, J. (2007) Hoarseness: A guide to voice disorders. *Medicine Today*, 8: 38-45.
Narrative review
- Bradley, P. J. (1986) Dysphonia. *British Journal of Hospital Medicine*, 35: 331-334.
Narrative review
- Brenner, B., Marshak, G., Rakowsky, E., Shvero, J., Sulkes, A. & Gutman, H. (2001) Laryngeal carcinoma--epidemiological and clinical features: experience of the Rabin Medical Center in Israel. *Oncology Reports*, 8: 141-144.
Not in PICO
- Brouha, X. D., Tromp, D. M., de Leeuw, J. R., Hordijk, G. J. & Winnubst, J. A. (2005) Laryngeal cancer patients: analysis of patient delay at different tumor stages. *Head & Neck*, 27: 289-295.
Not in PICO
- Brouha, X. D., Tromp, D. M., Koole, R., Hordijk, G. J., Winnubst, J. A. & de Leeuw, J. R. (2007) Professional delay in head and neck cancer patients: analysis of the diagnostic pathway. *Oral Oncology*, 43: 551-556.
Not in PICO
- Brunton, S. & McGuigan, J. (2005) Diagnostic challenges: Differentiating nighttime GERD. *Journal of Family Practice*, 54: 1073-1078.
Narrative review
- Bulman, C. H. (1998) A ten year audit of the management of cancers of the larynx and pharynx. *Journal of Laryngology and Otology*, 112: 948-953.
Not in PICO/narrative review
- Cammarota, G., Galli, J., Agostino, S., De, C. E., Rigante, M., Cianci, R., Cesaro, P., Nista, E. C., Candelli, M., Gasbarrini, A. & Gasbarrini, G. (2006) Accuracy of laryngeal examination during upper gastrointestinal endoscopy for premalignancy screening: prospective study in patients with and without reflux symptoms. *Endoscopy*, 38: 376-381.
Not in PICO
- Carvalho, A. L., Pintos, J., Schlecht, N. F., Oliveira, B. V., Fava, A. S., Curado, M. P., Kowalski, L. P. & Franco, E. L. (2002) Predictive factors for diagnosis of advanced-stage squamous cell carcinoma of the head and neck. *Archives of Otolaryngology - Head and Neck Surgery*, 128: 313-318.
Not in PICO
- Chan, T. V. (2010) The patient with sore throat. [Review] [44 refs]. *Medical Clinics of North America*, 94: 923-943.
Narrative review
- Chen, A. Y., Frankowski, R., Bishop-Leone, J., Hebert, T., Leyk, S., Lewin, J. & Goepfert, H. (2001) The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer - The M. D. Anderson dysphagia inventory. *Archives of Otolaryngology-Head & Neck Surgery*, 127: 870-876.
Not in PICO
- Chen, J.-J. (2007) Laryngeal lesions in patients with chronic cough and normal chest radiographs and auscultation. *Tzu Chi Medical Journal*, 19: 145-151+182.
Not in PICO
- Chodynicky, S. & Pyd, M. (1985) [Use of questionnaires in the early diagnosis of precancerous conditions and cancer of the larynx]. [Polish]. *Polski Tygodnik Lekarski*, 40: 1089-1091.
Not in PICO (screening)
- Christopoulos, T. A., Papageorgakopoulou, N., Theocharis, D. A., Aletras, A. J., Tsiganos, C. P., Papadas, T. A., Mastronikolis, N. S., Goumas, P. & Vynios, D. H. (2004) Diagnostic and classification value of metalloproteinases in squamous human laryngeal carcinoma. *International Journal of Oncology*, 25: 481-485.
Not in PICO
- Crossen, I. C., de, B. R., Rinkel, R. N., Eerenstein, S. E., Rietveld, D. H., Doornaert, P., Buter, J., Langendijk, J. A., Leemans, C. R. & Verdonck-de Leeuw, I. M. (2012) Computerized monitoring of

- patient-reported speech and swallowing problems in head and neck cancer patients in clinical practice. *Supportive Care in Cancer*, 20: 2925-2931.
Not in PICO
- Cohen, S. M., Kim, J., Roy, N., Asche, C. & Courey, M. (2012) Prevalence and causes of dysphonia in a large treatment-seeking population. *Laryngoscope*, 122: 343-348.
Not in PICO
- Cohen, S. M., Kim, J., Roy, N. & Courey, M. (2014) Factors influencing referral of patients with voice disorders from primary care to otolaryngology. *Laryngoscope*, 124: 214-220.
Not in PICO
- Cohen, S. M., Dinan, M. A., Roy, N., Kim, J. & Courey, M. (2014) Diagnosis Change in Voice-Disordered Patients Evaluated by Primary Care and/or Otolaryngology: A Longitudinal Study. *Otolaryngology - Head & Neck Surgery*, 150: 95-102.
Not in PICO
- Corey, G. A., Hocutt, J. E., Jr. & Rodney, W. M. (1988) Preliminary study of rhinolaryngoscopy by family physicians. *Family Medicine*, 20: 262-265.
Not in PICO
- Cotulbea, S., Marin, I., Golumba, R., Barbos, R., Valean, M. & Anghel, I. (1986) [Early diagnosis of laryngeal cancer in patients in the area of the Timisoara ENT Clinic]. [Romanian]. *Revista de Chirurgie Oncologie Radiologie ORL Oftalmologie Stomatologie - Oto-Rino-Laringologia*, 31: 137-141.
Not in PICO (referred patients; with cancer)
- Crozier, E. & Sumer, B. D. (2010) Head and Neck Cancer. *Medical Clinics of North America*, 94: 1031-+.
Narrative review
- Dammer, R., Bonkowski, V., Kutz, R., Friesenecker, J. & Schusselbauer, T. (1999) [Early detection of multiple tumors in primary diagnosis of oral carcinomas using panendoscopy]. [German]. *Mund-, Kiefer- und Gesichtschirurgie*, 3: 61-66.
Not in PICO
- de, B. R. (2011) [Early detection of laryngeal carcinoma: limited improvement possible]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 155: A3045.
Narrative review
- De, V. A. & Vicini, C. (2013) Narrow-band imaging in the early detection of laryngeal cancer: A prospective study. *European Archives of Oto-Rhino-Laryngology*, 270: 389.
Not in PICO
- Dean, S. S. (2014) Otolaryngology head and neck surgery. A review of malignancies. *Australian Family Physician*, 23: 2130-2131.
Narrative review
- Dechaphunkul, T. (2011) Epidemiology, risk factors, and overall survival rate of laryngeal cancer in Songklanagarind Hospital. *Journal of the Medical Association of Thailand*, 94: 355-360.
Not in PICO
- DeSanto, L. W. & Olsen, K. D. (1994) Early glottic cancer. [Review] [32 refs]. *American Journal of Otolaryngology*, 15: 242-249.
Not in PICO/narrative review
- Diouf, R., Diop, E. M., Ndiaye, I. C., Tall, A., Kasse, A. A. & Diop, L. S. (1990) Limitations on the practice of head-and-neck oncology in Africa. The example of laryngeal cancers. [French]. *Dakar Medical*, 35: 252-259.
Not in PICO
- Djambazov, K., Djambazov, B., Traikova, N. & Semerdjieva, M. (2005) Factors delaying the diagnosis of Laryngeal carcinoma. [Bulgarian]. *General Medicine*, 7: 15-18.
Not in PICO

- Dostalova, S., Smahel, Z. & Sonka, K. (1998) Craniofacial abnormalities in sleep apnoea syndrome. *Acta Chirurgiae Plasticae*, 40: 49-53.
Not in PICO
- Eckert, D., Bloom, H. J. & Ross, L. S. (1982) A review of oral cancer screening and detection in the metropolitan Detroit cancer control program. *Progress in Clinical & Biological Research*, 83: 195-206.
Not in PICO
- Eckley, C. A., Anelli, W. & Duprat, A. C. (2008) Auditory voice-perception analysis sensitivity and specificity in the screening of laryngeal disorders. *Revista Brasileira de Otorrinolaringologia*, 74: 168-171.
Not in PICO
- Esser, D., Anke, S., Roessner, A. & Freigang, B. (2000) [Second carcinomas in cancers of the mouth cavity, pharynx and larynx. Clinical, histopathologic and cell kinetic findings]. [German]. *Laryngo-Rhino- Otologie*, 79: 478-482.
Not in PICO
- Fasunla, A. J. & Lasisi, O. A. (2009) Diagnostic challenges of laryngeal papillomatosis and its implications among children in developing country. *International Journal of Pediatric Otorhinolaryngology*, 73: 593-595.
Not in PICO
- Ferlito, A. (1995) The natural history of early vocal cord cancer. *Acta Oto-Laryngologica*, 115: 345-347.
Narrative review
- Ferlito, A., Carbone, A., Rinaldo, A., Ferlito, A., DeSanto, L. W., D'Angelo, L., Barnes, L. & Devaney, K. O. (1996) "Early" cancer of the larynx: the concept as defined by clinicians, pathologists, and biologists. [Review] [18 refs]. *Annals of Otolaryngology, Rhinology & Laryngology*, 105: 245-250.
Narrative review
- Fischinger, J. & Mlacak, B. (1997) The usefulness of screening in the early detection of laryngeal cancer. *Acta Oto-Laryngologica Supplement*, 527: 150-151.
Not in PICO
- Ford, S., Gollins, S., Hobson, P. & Vyas, S. (2009) Structural displacements during the swallow in patients with early laryngeal cancers and other early primary cancers of the head and neck. *Dysphagia*, 24: 127-136.
Not in PICO
- Garas, J. & McGuirt, W. F., Sr. (2006) Squamous cell carcinoma of the subglottis. *American Journal of Otolaryngology*, 27: 1-4.
Not in PICO
- Goon, P., Stanley, M., Ebmeyer, J., Steinstrasser, L., Upile, T., Jerjes, W., Bernal-Sprekelsen, M., Gorner, M. & Sudhoff, H. (2009) HPV & head and neck cancer: a descriptive update. *Head & Neck Oncology*, 1: 36.
Narrative review
- Gorsky, M. & Dayan, D. (1995) Referral delay in diagnosis of oro/oropharyngeal cancer in Israel. *European Journal of Cancer. Part B, Oral Oncology*, 31B: 166-168.
Not in PICO
- Guo, T., Sun, J. W., Lv, Q. P. & Li, X. G. (2008) Allelic imbalance on chromosomes 3p, 9p and 17p in malignant progression of laryngeal mucosa. *Journal of Laryngology and Otology*, 122: 72-77.
Not in PICO
- Hagen, P., Lyons, G. D. & Nuss, D. W. (1996) Dysphonia in the elderly: diagnosis and management of age-related voice changes. *Southern Medical Journal*, 89: 204-207.
Not in PICO

- Hamzany, Y., Hadar, T., Feinmesser, R., Guttman, D. & Shvero, J. (2008) Laryngeal carcinoma in nonsmoking patients. *Annals of Otolaryngology, Rhinology & Laryngology*, 117: 564-568.
Not in PICO
- Hanson, J., Bruchmuller, W. & Nischwitz, A. S. (1989) [Precancerous diseases and the early recognition of pharyngeal and laryngeal carcinomas]. [German]. *Archiv fur Geschwulstforschung*, 59: 99-105.
Narrative review
- Healy, G. B. (1984) Neoplasia of the pediatric larynx. *Otolaryngologic Clinics of North America*, 17: 69-74.
Narrative review
- Herrera-Gomez, A., Villavicencio-Valencia, V., Rascon-Ortiz, M. & Luna-Ortiz, K. (2009) Demographic data of laryngeal cancer at the Instituto Nacional de Cancerologia in Mexico City. *Cirugia y Cirujanos*, 77: 353-357.
Not in PICO
- Hoare, T. J., Thomson, H. G. & Proops, D. W. (1993) Detection of laryngeal cancer--the case for early specialist assessment. *Journal of the Royal Society of Medicine*, 86: 390-392.
Not in PICO
- Hordijk, G. J., Kaanders, J. H. & Nederlandse Werkgroep Hoofd-Halstumoren (NWHHT) (2001) [CBO guideline 'larynx carcinoma']. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 145: 998-1002.
Narrative review
- Jaworowska, E., Serrano-Fernandez, P., Tarnowska, C., Brzosko, M., Flicinski, J., Masojc, B., Matyjasik, J., Scott, R. J., Narod, S. A. & Lubinski, J. (2008) Familial association of laryngeal, lung, stomach and early-onset breast cancer. *Breast Cancer Research and Treatment*, 112: 359-361.
Not in PICO
- Johnson, J. T., Newman, R. K. & Olson, J. E. (1980) Persistent hoarseness: an aggressive approach for early detection of laryngeal cancer. *Postgraduate Medicine*, 67: 122-126.
Narrative review
- Jovanovic, M. B. (2008) [Diagnosis of laryngeal carcinoma]. [Review] [52 refs] [Serbian]. *Medicinski Pregled*, 61: 591-595.
Narrative review
- Kaanders, J. H. A. M. & Hordijk, G. J. (2002) Carcinoma of the larynx: the Dutch national guideline for diagnostics, treatment, supportive care and rehabilitation. *Radiotherapy and Oncology*, 63: 299-307.
Guideline
- Kawakubo, J., Okikura, K. & Aika, Y. (1988) [Detection rate of laryngeal cancer in thorough medical check up performed by all Japan National Health Insurance Association of Engineering & Construction]. [Japanese]. *Nippon Jibiinkoka Gakkai Kaiho [Journal of the Oto-Rhino-Laryngological Society of Japan]*, 91: 553-560.
Not in PICO (population)
- Koscielny, S., Wagner, C. & Beleites, E. (1999) [Interval between initial symptoms and first treatment in patients with head-neck tumors]. [German]. *HNO*, 47: 551-555.
Not in PICO
- Koscielny, S., Wagner, C. & Beleites, E. (1999) Investigation of the time interval between the onset of symptoms and the beginning of therapy in patients with head and neck cancer. [German]. *HNO*, 47: 551-555.
Not in PICO
- Koskinen, W. J., Brondbo, K., Mellin, D. H., Luostarinen, T., Hakulinen, T., Leivo, I., Molijn, A., Quint, W. G., Roysland, T., Munck-Wikland, E., Makitie, A. A., Pyykko, I., Dillner, J., Vaheri, A. & Aaltonen, L. M. (2007) Alcohol, smoking and human papillomavirus in laryngeal carcinoma: a Nordic prospective multicenter study. *Journal of Cancer Research & Clinical Oncology*, 133: 673-678.
Not in PICO

- Kosztyla-Hojna, B. & Rogowski, M. (2003) [Usefulness of video-laryngo-stroboscopy in the diagnosis of laryngeal pathology]. [Polish]. *Polski Merkurusz Lekarski*, 14: 413-416.
Narrative review
- Laccourreya, O., Weinstein, G., Chabardes, E., Housset, M., Laccourreya, H. & Brasnu, D. (1992) T1 squamous cell carcinoma of the arytenoid. *Laryngoscope*, 102: 896-900.
Not in PICO
- Lai, Y.-H., Chen, M.-H. & Chang, S.-Y. (2009) Communication status, quality of life and their relationships in head and neck cancer patients with surgery in Taiwan. *Supportive Care in Cancer*, 17: 1012-1013.
Not in PICO
- Leithauser, D. (1997) [Hoarseness often minimized by patients. Preventive examination of the larynx gets too little regard]. [German]. *Fortschritte der Medizin*, 115: 38-39.
Narrative review
- Lore, J. M., Jr. (1991) Controversies in the diagnosis and treatment of early carcinoma of the larynx. [Review] [9 refs]. *Seminars in Surgical Oncology*, 7: 31-37.
Narrative review
- Luft, A. & Pons, Y. (2011) [Signs of upper airways digestive tract cancers and the general practitioner. Study of the practices by a Script Test Concordance]. [French]. *Revue de Laryngologie Otologie Rhinologie*, 132: 131-136.
Not in PICO
- Lydiatt, D. D. (2002) Medical malpractice and cancer of the larynx. *Laryngoscope*, 112: 445-448.
Not in PICO
- Lyons, B. (1999) ENT malignancies. What the GP needs to know. [Review] [9 refs]. *Australian Family Physician*, 28: 209-215.
Narrative review
- Mau, T. (2010) Diagnostic evaluation and management of hoarseness. *Medical Clinics of North America*, 94: 945-960.
Narrative review
- McDonald, S., Haie, C., Rubin, P., Nelson, D. & Divers, L. D. (1989) Second malignant tumors in patients with laryngeal carcinoma: diagnosis, treatment, and prevention. [Review] [45 refs]. *International Journal of Radiation Oncology, Biology, Physics*, 17: 457-465.
Not in PICO
- Meyer-Breiting, E. (1990) [Considerations and studies of the classification of glottis cancers]. [German]. *Laryngo- Rhino- Otologie*, 69: 6-12.
Narrative review
- Michnay-Becker, A. (1993) [Recommendations for the physician's patient education consultation with laryngeal and pharyngeal cancer patients]. [German]. *HNO*, 41: A17.
Not in PICO
- Mikic, A., Petrovic, Z., Djukic, V., Dimitrijevic, M., Stankovic, P., Pendjer, I. & Dudvarski, Z. (2004) [Surgery treatment of laryngeal carcinoma T1]. [Serbian]. *Acta Chirurgica Iugoslavica*, 51: 21-25.
Not in PICO
- Minnis, N. L. (2002) A practical approach to managing hoarseness. *Medicine Today*, 3: 36-42.
Narrative review
- Mlacak, B. & Fischinger, J. (1997) The role of general practitioner in the detection of epithelial hyperplastic lesions and carcinoma of the larynx. *Acta Oto-Laryngologica Supplement*, 527: 152-154.
Not in PICO - no method/result section detailing the population
- Moore, P. L., Kim, D., Selby, G. & Proops, D. W. (2004) Detection of laryngeal carcinoma and epithelial hyperplastic laryngeal lesions via a rapid-access dysphonia clinic. *Journal of Laryngology & Otology*, 118: 633-636.
Not in PICO

- Morton, R. P. (1982) A profile of laryngeal cancer in Auckland 1965-1979. *New Zealand Medical Journal*, 95: 652-655.
Narrative review
- Muller, R. (1995) [Hoarseness]. [German]. *Therapeutische Umschau*, 52: 759-762.
Narrative review
- Myssiorek, D., Rinaldo, A., Barnes, L. & Ferlito, A. (2004) Laryngeal paraganglioma: an updated critical review. [Review] [57 refs]. *Acta Oto-Laryngologica*, 124: 995-999.
Narrative review
- Nedio, S. & Marcos, A. S. (2011) The world voice day as a public health program-rippling the idea. *European Archives of Oto-Rhino-Laryngology*, 268: 773.
Narrative review
- Ni, X. G., He, S., Xu, Z. G., Gao, L., Lu, N., Yuan, Z., Lai, S. Q., Zhang, Y. M., Yi, J. L., Wang, X. L., Zhang, L., Li, X. Y. & Wang, G. Q. (2011) Endoscopic diagnosis of laryngeal cancer and precancerous lesions by narrow band imaging. *Journal of Laryngology & Otology*, 125: 288-296.
Not in PICO
- Oburra, H. O. (1998) Late presentation of laryngeal and nasopharyngeal cancer in Kenyatta National Hospital. *East African Medical Journal*, 75: 223-226.
Not in PICO
- Okawa, T., Yamada, K. & Kita, M. (1988) Early cancer in the head and neck. [Japanese]. *Gan no rinsho*, Japan: 1295-1302.
Narrative review
- Omori, K. (2011) Diagnosis of voice disorders. *Japan Medical Association Journal*, 54: 248-253.
Narrative review
- Orvidas, L. J., Olsen, K. D., Lewis, J. E. & Suman, V. J. (1998) Verrucous carcinoma of the larynx: a review of 53 patients. *Head & Neck*, 20: 197-203.
Not in PICO
- Paleri, V., Mackenzie, K., Wight, R. G., Mehanna, H., Pracy, P., Bradley, P. J. & ENT-UK Head and Neck Group (2009) Management of laryngeal dysplasia in the United Kingdom: a web-based questionnaire survey of current practice. *Clinical Otolaryngology*, 34: 385-389.
Not in PICO
- Prout, M. N., Sidari, J. N., Witzburg, R. A., Grillone, G. A. & Vaughan, C. W. (1997) Head and neck cancer screening among 4611 tobacco users older than forty years. *Otolaryngology - Head & Neck Surgery*, 116: 201-208.
Not in PICO
- Rafferty, A., Greensmith, M., Robinson, S. & Jose, J. (2012) Laryngeal cancer social marketing project. *Clinical Otolaryngology*, 37: 46.
Not in PICO
- Reiter, R. & Brosch, S. (2009) [Chronic laryngitis--associated factors and voice assessment]. [German]. *Laryngo- Rhino- Otologie*, 88: 181-185.
Not in PICO
- Resouly, A., Hope, A. & Thomas, S. (2001) A rapid access husky voice clinic: useful in diagnosing laryngeal pathology. *Journal of Laryngology & Otology*, 115: 978-980.
Not in PICO
- Reulbach, T. R., Belafsky, P. C., Blalock, P. D., Koufman, J. A. & Postma, G. N. (2001) Occult laryngeal pathology in a community-based cohort. *Otolaryngology - Head & Neck Surgery*, 124: 448-450.
Not in PICO
- Righini, C. A., Karkas, A., Morel, N., Soriano, E. & Reyt, E. (2008) [Risk factors for cancers of the oral cavity, pharynx (cavity excluded) and larynx]. [Review] [76 refs] [French]. *Presse Medicale*, 37: 1229-1240.
Not in PICO

- Rodrigo, J. P., Garcia-Carracedo, D., Gonzalez, M. V., Mancebo, G., Fresno, M. F. & Garcia-Pedrero, J. (2010) Podoplanin expression in the development and progression of laryngeal squamous cell carcinomas. *Molecular Cancer*, 9: 48.
Not in PICO
- Rogachikova, T. A., Abakumova, L. I. & Denisova, I. I. (1990) [Determination of groups at risk for laryngeal tumors]. [Russian]. *Voprosy Onkologii*, 36: 1466-1469.
Not in PICO
- Rousset, J., Abgral, R., Chinellato, S., Garetier, M., Barberot, C., Valette, G., Potard, G., Le, B. T. & Salaun, P. Y. (2013) Early recurrence or submucosal residual of laryngeal squamous cell carcinoma: diagnosis by CT-guided endolaryngeal core biopsy on a transcutaneous approach. *Head & Neck*, 35: E202-E204.
Not in PICO
- Rua, S., Comino, A., Fruttero, A., Cera, G., Semeria, C., Lanzillotta, L. & Boffetta, P. (1991) Relationship between histologic features, DNA flow cytometry, and clinical behavior of squamous cell carcinomas of the larynx. *Cancer*, 67: 141-149.
Not in PICO
- Sahin, M., Kirazli, T., Ozturk, K. & Ogut, M. F. (2013) [A presentation of a practical algorithm which can be used in the management of vocal cord nodules, polyps and intraepithelial neoplasias]. [Turkish]. *Kulak Burun Bogaz Ihtisas Dergisi/Journal of Ear, Nose & Throat: Kbb*, 23: 96-103.
Not in PICO
- Sato, T. (1987) [High-risk factors in the development of head and neck cancers]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 14: 2626-2631.
Narrative review
- Savic, D., Djeric, D., Jesic, S. & Bankovic, S. (1987) [Early diagnosis of malignant tumors of the glottis]. [Serbian]. *Srpski Arhiv Za Celokupno Lekarstvo*, 115: 323-332.
In Serbian without an English abstract. Looks like a narrative review
- Seoane, J., Takkouche, B., Varela-Centelles, P., Tomas, I. & Seoane-Romero, J. M. (2012) Impact of delay in diagnosis on survival to head and neck carcinomas: a systematic review with meta-analysis. *Clinical Otolaryngology*, 37: 99-106.
Not in PICO
- Sereg-Bahar, M., Jerin, A. & Hocevar-Boltezar, I. (2013) The role of gastroesophageal reflux in pathogenesis of benign and malignant laryngeal lesions. *European Archives of Oto-Rhino-Laryngology*, 270: 398.
Not in PICO
- Sharma, S. J., Linke, J. J., Kroll, T., Klussmann, J.-P., Guntinas-Lichius, O. & Wittekindt, C. (2013) Current practice of tumour endoscopy in German ENT-clinics. [German]. *Laryngo-Rhino-Otologie*, 92: 166-169.
Not in PICO
- Shinozaki, N., Sakamoto, A., Kasai, N., Uchida, M. & Sakurai, K. (1983) Multiple primary malignancies associated with thyroid cancer. [Japanese]. *Gan no rinsho*, Japan: 1385-1391.
Not in PICO
- Singh, H. & Chauhan, A. (2011) Primary small cell carcinoma of the larynx: report of a rare tumor. *Case Reports in Oncological Medicine*, 2011: 978676.
Not in PICO
- Siupsinskiene, N., Vaitkus, S., Grebliauskaite, M., Engelmanaite, L. & Sumskiene, J. (2008) Quality of life and voice in patients treated for early laryngeal cancer. *Medicina (Kaunas, Lithuania)*, 44: 288-295.
Not in PICO
- Smart, C. R. (1993) Screening for cancer of the aerodigestive tract. [Review] [6 refs]. *Cancer*, 72: Suppl-5.
Narrative review

- Smith, M. D., Fleming, J., Lew-Gor, S., Simcock, R., Weighill, J. & Harries, M. L. (2012) 4-Year demographic study of laryngeal carcinoma. *Otolaryngology - Head and Neck Surgery (United States)*, 147: 144.
Not in PICO
- Smulders, Y., De Bondt, B. J., Lacko, M., Hodge, J. & Kross, K. (2009) Laryngeal tuberculosis presenting as a supraglottic carcinoma: a case report and review of the literature. *Journal of Medical Case Reports*, 3: 9288.
Not in PICO
- Splete, H. (2009) Primary care physicians can expose laryngeal Ca. *Oncology Report*, 31.
Letter
- Steiner, W., Jaumann, M. P. & Pesch, H. J. (1980) [Early detection of laryngeal cancer (author's transl)]. [German]. *Therapeutische Umschau*, 37: 1087-1091.
Narrative review
- Steiner, W. (1982) Aspects of clinical differential diagnosis and therapy of early laryngeal cancer (microcarcinoma). *Clinics in Oncology*, 1: 489-493.
Not in PICO
- Steiner, W. (1982) Early detection of cancer in the upper aerodigestive tract and its prophylaxis. [German]. *Munchener Medizinische Wochenschrift*, 124: 22-30.
Narrative review
- Stephen, J. K., Chen, K. M., Shah, V., Havard, S., Lu, M., Schweitzer, V. P., Gardner, G. & Worsham, M. J. (2012) Human papillomavirus outcomes in an access-to-care laryngeal cancer cohort. *Otolaryngology - Head & Neck Surgery*, 146: 730-738.
Not in PICO
- Stiefelhagen, P. (2010) [Clinical assessment of a "voice disorder" with simple measures. In chronic hoarseness laryngoscopy is essential]. [German]. *MMW Fortschritte der Medizin*, 152: 25.
Narrative review
- Szlezak, L. & Przybora, L. A. (1983) Early cancer of the vocal cords: Clinical and pathological progression and results of treatment. [French]. *Annales d'Oto-Laryngologie et de Chirurgie Cervico-Faciale*, 100: 115-124.
Not in PICO
- Tan, I. B., Roodenburg, J. L., Copper, M. P., Coebergh, J. W. & van, d. W., I (2001) [Early diagnosis and prevention of malignant tumors in the head and neck region]. [Review] [8 refs] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 145: 567-572.
Narrative review
- Teppo, H., Koivunen, P., Hyrynkangas, K. & Alho, O. P. (2003) Diagnostic delays in laryngeal carcinoma: professional diagnostic delay is a strong independent predictor of survival. *Head & Neck*, 25: 389-394.
Not in PICO
- Teppo, H., Hyrynkangas, K., Koivunen, P., Jokinen, K. & Alho, O. P. (2005) Impact of patient and professional diagnostic delays on the risk of recurrence in laryngeal carcinoma. *Clinical Otolaryngology*, 30: 157-163.
Not in PICO
- Teppo, H. & Alho, O. P. (2009) Comorbidity and diagnostic delay in cancer of the larynx, tongue and pharynx. *Oral Oncology*, 45: 692-695.
Not in PICO
- Thirumaran, M., Sundar, R., Sutcliffe, I. M. & Currie, D. C. (2009) Is investigation of patients with haemoptysis and normal chest radiograph justified? *Thorax*, 64: 854-856.
Not in PICO
- Thompson, L. W. (1989) Head and neck cancer: early detection. [Review] [25 refs]. *Seminars in Surgical Oncology*, 5: 168-175.
Narrative review

van, A. M., Heule-Dieleman, H. A., de Boer, M. F., Kaanders, J. H., Baatenburg de Jong, R. J., Kremer, B., Leemans, C. R., Marres, H. A., Manni, J. J., Langendijk, J. A., Levendag, P. C., Tjho-Heslinga, R. E., de Jong, J. M., Uyl-de Groot, C. A. & Knegt, P. P. (2005) Evaluating adherence to the Dutch guideline for diagnosis, treatment and follow-up of laryngeal carcinomas. *Radiotherapy & Oncology*, 74: 337-344.

Not in PICO

Vecerina, V. S., Kovac, D., Seiwert, S. & Manojlovic, S. (1997) Correlation between instability of fundamental voice frequency and malignant infiltration of vocal fold nerve endings. *Acta Oto-Laryngologica Supplement*, 527: 131-133.

Not in PICO

Vlachtsis, K., Naoum, V., Karasmanis, I. & Nikolaou, A. (2011) Inflammatory myofibroblastic tumor of the larynx. *European Archives of Oto-Rhino-Laryngology*, 268: 799.

Not in PICO

Vracko-Tusevljak, M. & Kambic, V. (1989) [The significance of psychological factors in the early diagnosis of laryngeal and hypopharyngeal tumors]. [German]. *Laryngo- Rhino- Otologie*, 68: 118-121.

Not in PICO

Wenig, B. M., Hyams, V. J. & Heffner, D. K. (1988) Moderately differentiated neuroendocrine carcinoma of the larynx. A clinicopathologic study of 54 cases. [Review] [103 refs]. *Cancer*, 62: 2658-2676.

Not in PICO

Wilkins, T., Gillies, R. A., Getz, A., Zimmerman, D. & Kang, L. (2010) Nasolaryngoscopy in a family medicine clinic: indications, findings, and economics. *Journal of the American Board of Family Medicine: JABFM*, 23: 591-597.

Not in PICO

Wunsch, F., V (2004) The epidemiology of laryngeal cancer in Brazil. [Review] [89 refs]. *Sao Paulo Medical Journal = Revista Paulista de Medicina*, 122: 188-194.

Narrative review

Ya, S. (1985) Diagnosis of laryngeal cancer in tuberculous patients. [Russian]. *Problemy Tuberkuleza*, 63: 10-13.

Not in PICO

Yoshino, K., Endo, M., Ishikawa, N. & Takahashi, Y. (1995) Diagnosis and treatment of metachronous cancers in the esophagus and the head and neck region. *Journal of Surgical Oncology*, 58: 246-251.

Not in PICO

Review question:

Which investigations of symptoms of suspected laryngeal cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	210	47	10/04/2013
Premedline	1980-2013	10	2	10/04/2013
Embase	1980-2013	348	47	10/04/2013
Cochrane Library	1980-2013	2	0	10/04/2013
Psychinfo	1980-2013	0	0	10/04/2013

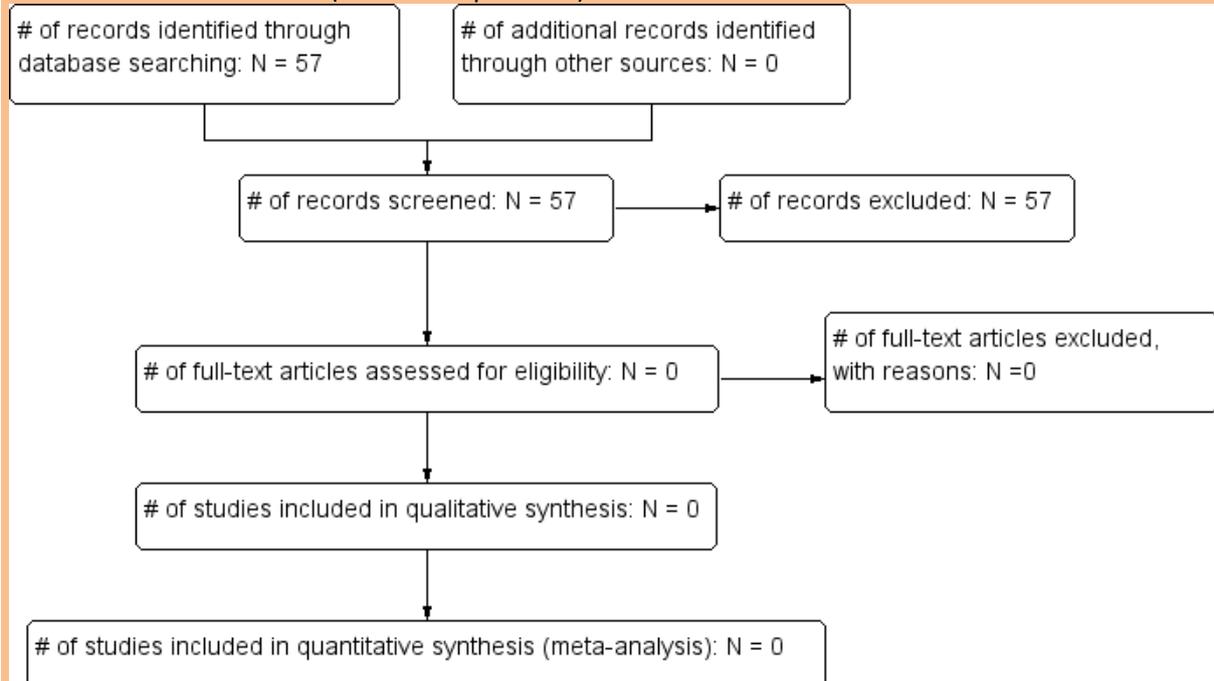
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	20	2	10/04/2013
--	-----------	----	---	------------

Total References retrieved (after de-duplication): 53

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	4/2013-26/08/2014	3	0	26/08/2014
Premedline	4/2013-26/08/2014	15	2	26/08/2014
Embase	4/2013-26/08/2014	28	3	26/08/2014
Cochrane Library	4/2013-26/08/2014	5	0	26/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	4/2013-26/08/2014	3	0	26/08/2014

Total References retrieved (after de-duplication): 4



Study results

No evidence was identified pertaining to the diagnostic accuracy of chest x-ray in patients with suspected laryngeal cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

- Arens, C., Glanz, H., Dreyer, T. & Malzahn, K. (2003) Compact endoscopy of the larynx. *Annals of Otolaryngology, Rhinology & Laryngology*, 112: 113-119.
Not in PICO
- Arens, C., Glanz, H., Wonckhaus, J., Hersemeyer, K. & Kraft, M. (2007) Histologic assessment of epithelial thickness in early laryngeal cancer or precursor lesions and its impact on endoscopic imaging. *European Archives of Oto-Rhino-Laryngology*, 264: 645-649.
Not in PICO
- Banko, B., Dukic, V., Milovanovic, J., Kovac, J. D., Artiko, V. & Maksimovic, R. (2011) Diagnostic significance of magnetic resonance imaging in preoperative evaluation of patients with laryngeal tumors. *European Archives of Oto-Rhino-Laryngology*, 268: 1617-1623.
Not in PICO
- Bongers, V., Hobbelen, M. G., van Rijk, P. P. & Hordijk, G. J. (2002) Cost-effectiveness of dual-head 18F-fluorodeoxyglucose PET for the detection of recurrent laryngeal cancer. *Cancer Biotherapy & Radiopharmaceuticals*, 17: 303-306.
Not in PICO
- Brandt, R. H. & Weidner, I. (1984) [Early diagnosis of laryngeal cancer by endoscopy and histology in the risk group dispensary]. [German]. *Zeitschrift fur Arztliche Fortbildung (Jena)*, 78: 763-766.
Not in PICO
- Brouwer, J., Bodar, E. J., de Bree, R., Langendijk, J. A., Castelijns, J. A., Hoekstra, O. S. & Leemans, C. R. (2004) Detecting recurrent laryngeal carcinoma after radiotherapy: room for improvement. *European Archives of Oto-Rhino-Laryngology*, 261: 417-422.
Not in PICO
- Brouwers, J., de Bree, R., Comans, E. F. I., Akarriou, M., Langendijk, J. A., Castelijns, J. A., Hoekstra, O. S. & Leemans, C. R. (2008) Improved detection of recurrent laryngeal tumor after radiotherapy using (18)FDG-PET as initial method. *Radiotherapy and Oncology*, 87: 217-220.
Not in PICO
- Cetinkaya, E., Veyseller, B., Yildirim, Y. S., Aksoy, F., Ozgul, M. A., Gencoglu, A. & Altin, S. (2011) Value of autofluorescence bronchoscopy in patients with laryngeal cancer. *Journal of Laryngology & Otology*, 125: 181-187.
Not in PICO
- Chang, J., Fang, T. J., Yung, K., van, Z. A., Miller, T., Al-Jurf, S., Schneider, S. & Courey, M. (2012) Clinical and histologic predictors of voice and disease outcome in patients with early glottic cancer. *Laryngoscope*, 122: 2240-2247.
Not in PICO
- Cnossen, I. C., de, B. R., Rinkel, R. N., Eerenstein, S. E., Rietveld, D. H., Doornaert, P., Buter, J., Langendijk, J. A., Leemans, C. R. & Verdonck-de Leeuw, I. M. (2012) Computerized monitoring of patient-reported speech and swallowing problems in head and neck cancer patients in clinical practice. *Supportive Care in Cancer*, 20: 2925-2931.
Not in PICO
- Cobben, D. C., van der Laan, B. F., Maas, B., Vaalburg, W., Suurmeijer, A. J., Hoekstra, H. J., Jager, P. L. & Elsinga, P. H. (2004) 18F-FLT PET for visualization of laryngeal cancer: comparison with 18F-FDG PET. *Journal of Nuclear Medicine*, 45: 226-231.
Not in PICO
- Cohen, S. M., Kim, J., Roy, N. & Courey, M. (2014) Factors influencing referral of patients with voice disorders from primary care to otolaryngology. *Laryngoscope*, 124: 214-220.
Not in PICO
- Cohen, S. M., Dinan, M. A., Roy, N., Kim, J. & Courey, M. (2014) Diagnosis Change in Voice-Disordered Patients Evaluated by Primary Care and/or Otolaryngology: A Longitudinal Study. *Otolaryngology - Head & Neck Surgery*, 150: 95-102.
Not in PICO

- Conrad, R., Pauleit, D., Layer, G., Kandyba, J., Kohlbecher, R., Hortling, N., Baselides, P. & Schild, H. (1999) [Spiral CT of the head-neck area: the advantages of the early arterial phase in the detection of squamous-cell carcinomas]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 171: 15-19.
Not in PICO
- Croce, A., de, V. M., Primerano, G., Gallo, A., Rendina, E. A. & Venuta, F. (1989) [Early diagnosis of pulmonary tumors in patients treated for laryngeal cancer]. [Review] [46 refs] [Italian]. *Acta Otorhinolaryngologica Italica*, 9: 139-147.
Not in PICO
- Dammer, R., Bonkowski, V., Kutz, R., Friesenecker, J. & Schusselbauer, T. (1999) [Early detection of multiple tumors in primary diagnosis of oral carcinomas using panendoscopy]. [German]. *Mund-, Kiefer- und Gesichtschirurgie*, 3: 61-66.
Not in PICO
- De, V. A. & Vicini, C. (2013) Narrow-band imaging in the early detection of laryngeal cancer: A prospective study. *European Archives of Oto-Rhino-Laryngology*, 270: 389.
Not in PICO
- de Bree, R., van der Putten, L., Hoekstra, O. S., Kuik, D. J., Groot, C. A. U. D., van Tinteren, H., Leemans, C. R. & Boers, M. (2007) A randomized trial of PET scanning to improve diagnostic yield of direct laryngoscopy in patients with suspicion of recurrent laryngeal carcinoma after radiotherapy. *Contemporary Clinical Trials*, 28: 705-712.
Not in PICO
- Dequanter, D., Lothaire, P., Zouaoui, K. & Brohee, D. (2012) Epidemiology and clinical characteristics of larynx and hypopharynx carcinoma: a comparative study in the Hainaut and review of the literature. *Acta Chirurgica Belgica*, 112: 423-425.
Not in PICO
- DeSanto, L. W. (1982) The options in early laryngeal carcinoma. [Review] [10 refs]. *New England Journal of Medicine*, 306: 910-912.
Not in PICO
- Dullerud, R., Johansen, J. G., Dahl, T. & Faye-Lund, H. (1992) Influence of CT on tumor classification of laryngeal carcinomas. *Acta Radiologica*, 33: 314-318.
Not in PICO
- Engelen, A. M., Stalpers, L. J., Manni, J. J., Ruijs, J. H. & van Daal, W. A. (1992) Yearly chest radiography in the early detection of lung cancer following laryngeal cancer. [Review] [30 refs]. *European Archives of Oto-Rhino-Laryngology*, 249: 364-369.
Not in PICO
- Fasunla, A. J. & Lasisi, O. A. (2009) Diagnostic challenges of laryngeal papillomatosis and its implications among children in developing country. *International Journal of Pediatric Otorhinolaryngology*, 73: 593-595.
Not in PICO
- Gaafar, H., Hussein, M. & el-Assi, H. (1989) Cytopathology in cancer of larynx. *Orl; Journal of Oto-Rhino-Laryngology & its Related Specialties*, 51: 216-220.
Not in PICO
- Garcia Callejo, F. J., Dualde, B. D., Benlloch, R. E., Montoro Elena, M. J., Hernandorena, G. M. & Marco, A. J. (2008) [Use of imaging criteria to identify cervical metastases using CT scans in head and neck tumours]. [Spanish]. *Acta Otorrinolaringologica Espanola*, 59: 257-262.
Not in PICO
- Gugatschka, M., Kiesler, K., Beham, A., Rechenmacher, J. & Friedrich, G. (2008) Hyperplastic epithelial lesions of the vocal folds: combined use of exfoliative cytology and laryngostroboscopy in differential diagnosis. *European Archives of Oto-Rhino-Laryngology*, 265: 797-801.
Not in PICO

- Hanson, J., Bruchmuller, W. & Nischwitz, A. S. (1989) [Precancerous diseases and the early recognition of pharyngeal and laryngeal carcinomas]. [German]. *Archiv fur Geschwulstforschung*, 59: 99-105.
Narrative review
- Hoare, T. J., Thomson, H. G. & Proops, D. W. (1993) Detection of Laryngeal-Cancer - the Case for Early Specialist Assessment. *Journal of the Royal Society of Medicine*, 86: 390-392.
Not in PICO
- Huang, Z., Xiao, W. & Li, G. (2002) [Evaluating the clinical applications of CTVL in laryngeal carcinomas]. [Chinese]. *Lin Chuang Erh Pi Yen Hou Ko Tsa Chih Journal of Clinical Otorhinolaryngology*, 16: 104-105.
Not in PICO
- Jarmuz, M., Szyfter, K., Grenman, R., Golusinski, W. & Szyfter, W. (2000) [Usefulness of chromosome alteration analysis in cell lines derived from laryngeal tumors for evaluation of laryngeal neoplasms]. [Polish]. *Otolaryngologia Polska*, 54: 567-572.
Not in PICO
- Kraft, M., Luerssen, K., Lubatschowski, H., Woenckhaus, J., Schoberlein, S., Glanz, H. & Arens, C. (2008) [Mucosal lesions in the larynx: predictive value of new imaging modalities for a histological diagnosis]. [German]. *HNO*, 56: 609-613.
Not in PICO
- Lell, M. M., Greess, H., Hothorn, T., Janka, R., Bautz, W. A. & Baum, U. (2004) Multiplanar functional imaging of the larynx and hypopharynx with multislice spiral CT. *European Radiology*, 14: 2198-2205.
Not in PICO
- Lewin, J. S., Gillenwater, A. M., Garrett, J. D., Bishop-Leone, J. K., Nguyen, D. D., Callender, D. L., Ayers, G. D. & Myers, J. N. (2003) Characterization of laryngopharyngeal reflux in patients with premalignant or early carcinomas of the larynx. *Cancer*, 97: 1010-1014.
Not in PICO
- Li, Y., Arens, C. & Glanz, H. (2005) [Autofluorescence endoscopy for diagnosing early laryngeal cancer and its precursor lesions]. [Chinese]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi = Chinese Journal of Otorhinolaryngology Head & Neck Surgery*, 40: 696-700.
Not in PICO
- Lim, S. (2014). Are we performing more laryngeal biopsies, and if so, why? A decade of results. *Journal of Laryngology and Otology*, 28, 3.
Not in PICO
- Lowe, V. J., Kim, H., Boyd, J. H., Eisenbeis, J. F., Dunphy, F. R. & Fletcher, J. W. (1999) Primary and recurrent early stage laryngeal cancer: preliminary results of 2-[fluorine 18]fluoro-2-deoxy-D-glucose PET imaging. *Radiology*, 212: 799-802.
Not in PICO
- Lydiatt, D. D. (2002) Medical malpractice and cancer of the larynx. *Laryngoscope*, 112: 445-448.
Not in PICO
- Mancuso, A. A., Tamakawa, Y. & Hanafee, W. N. (1980) CT of the fixed vocal cord. *AJR. American Journal of Roentgenology*, 135: 7529-7534.
Not in PICO
- Mashkova, T. A., Ovsiannikov, I. & Panchenko, I. G. (2010) [Potential of fibrolaryngoscopy for the improvement of diagnosis of laryngeal diseases]. [Russian]. *Vestnik Otorinolaringologii*.(5):28-9, 2010., 28-29.
Not in PICO
- Mehlmann, M., Betz, C. S., Stepp, H., Arbogast, S., Baumgartner, R., Grevers, G. & Leunig, A. (1999) Fluorescence staining of laryngeal neoplasms after topical application of 5-aminolevulinic acid: preliminary results. *Lasers in Surgery & Medicine*, 25: 414-420.
Not in PICO

- Naidu, H., Noordzij, J. P., Samim, A., Jalisi, S. & Grillone, G. A. (2012) Comparison of efficacy, safety, and cost-effectiveness of in-office cup forcep biopsies versus operating room biopsies for laryngopharyngeal tumors. *Journal of Voice*, 26: 604-606.
Not in PICO
- Ni, X. G., He, S., Xu, Z. G., Lu, N., Gao, L., Yuan, Z., Zhang, Y. M., Lai, S. Q., Yi, J. L., Wang, X. L., Zhang, L., Li, X. Y. & Wang, G. Q. (2010) [Application of narrow band imaging endoscopy in the diagnosis of laryngeal cancer]. [Chinese]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi = Chinese Journal of Otorhinolaryngology Head & Neck Surgery*, 45: 143-147.
Not in PICO
- Ni, X. G., He, S., Xu, Z. G., Gao, L., Lu, N., Yuan, Z., Lai, S. Q., Zhang, Y. M., Yi, J. L., Wang, X. L., Zhang, L., Li, X. Y. & Wang, G. Q. (2011) Endoscopic diagnosis of laryngeal cancer and precancerous lesions by narrow band imaging. *Journal of Laryngology & Otology*, 125: 288-296.
Not in PICO
- Nix, P. A. & Salvage, D. (2004) Neoplastic invasion of laryngeal cartilage: the significance of cartilage sclerosis on computed tomography images. *Clinical Otolaryngology & Allied Sciences*, 29: 372-375.
Not in PICO
- Paczona, R., Temam, S., Janot, F., Marandas, P. & Luboinski, B. (2003) Autofluorescence videoendoscopy for photodiagnosis of head and neck squamous cell carcinoma. *European Archives of Oto-Rhino-Laryngology*, 260: 544-548.
Not in PICO
- Pan, C. T., Lee, L. A., Fang, T. J., Li, H. Y., Liao, C. T. & Chen, I. H. (2013) NBI flexible laryngoscopy targeted tissue sampling in head and neck cancer patients with difficult airways. *European Archives of Oto-Rhino-Laryngology*, 270: 263-269.
Not in PICO
- Rafferty, A., Greensmith, M., Robinson, S. & Jose, J. (2012) Laryngeal cancer social marketing project. *Clinical Otolaryngology*, 37: 46.
Not in PICO
- Ramirez-Anguiano, J., Lara-Sanchez, H., Martinez-Banos, D. & Martinez-Benitez, B. (2012) Extramedullary plasmacytoma of the larynx: a case report of subglottic localization. *Case Reports in Otolaryngology Print*, 2012: 437264.
Not in PICO
- Reiter, R. & Brosch, S. (2009) [Chronic laryngitis--associated factors and voice assessment]. [German]. *Laryngo- Rhino- Otologie*, 88: 181-185.
Not in PICO
- Rodrigo, J. P., Garcia-Carracedo, D., Gonzalez, M. V., Mancebo, G., Fresno, M. F. & Garcia-Pedrero, J. (2010) Podoplanin expression in the development and progression of laryngeal squamous cell carcinomas. *Molecular Cancer*, 9: 48.
Not in PICO
- Rousset, J., Abgral, R., Chinellato, S., Garetier, M., Barberot, C., Valette, G., Potard, G., Le, B. T. & Salaun, P. Y. (2013) Early recurrence or submucosal residual of laryngeal squamous cell carcinoma: diagnosis by CT-guided endolaryngeal core biopsy on a transcutaneous approach. *Head & Neck*, 35: E202-E204.
Not in PICO
- Sahin, M., Kirazli, T., Ozturk, K. & Ogut, M. F. (2013) [A presentation of a practical algorithm which can be used in the management of vocal cord nodules, polyps and intraepithelial neoplasias]. [Turkish]. *Kulak Burun Bogaz Ihtisas Dergisi/Journal of Ear, Nose & Throat: Kbb*, 23: 96-103.
Not in PICO
- Sereg-Bahar, M., Jerin, A. & Hocevar-Boltezar, I. (2013) The role of gastroesophageal reflux in pathogenesis of benign and malignant laryngeal lesions. *European Archives of Oto-Rhino-*

- Laryngology*, 270: 398.
Not in PICO
- Sharma, S. J., Linke, J. J., Kroll, T., Klussmann, J.-P., Guntinas-Lichius, O. & Wittekindt, C. (2013) Current practice of tumour endoscopy in German ENT-clinics. [German]. *Laryngo- Rhino- Otologie*, 92: 166-169.
Not in PICO
- Smith, M. D., Fleming, J., Lew-Gor, S., Simcock, R., Weighill, J. & Harries, M. L. (2012) 4-Year demographic study of laryngeal carcinoma. *Otolaryngology - Head and Neck Surgery (United States)*, 147: 144.
Not in PICO
- Stoeckli, S. J. & Broglie, M. A. (2012) Sentinel node biopsy for early oral carcinoma. *Current Opinion in Otolaryngology & Head and Neck Surgery*, 20: 103-108.
Not in PICO
- Stone, N., Stavroulaki, P., Kendall, C., Birchall, M. & Barr, H. (2000) Raman spectroscopy for early detection of laryngeal malignancy: preliminary results. *Laryngoscope*, 110: t-63.
Not in PICO
- Szmeja, Z., Wierzbicka, M. & Kordylewska, M. (1999) The value of ultrasound examination in preoperative neck assessment and in early diagnosis of nodal recurrences in the follow-up of patients operated for laryngeal cancer. *European Archives of Oto-Rhino-Laryngology*, 256: 415-417.
Not in PICO
- Ustundag, E., Kaur, A. C., Boyaci, Z., Keskin, G. & Aydin, O. (2006) Combined use of histopathology with touch smear cytology in biopsies of the larynx. *European Archives of Oto-Rhino-Laryngology*, 263: 866-871.
Not in PICO
- van Agthoven, M., Heule-Dieleman, H. A. G., de Boer, M. F., Kaanders, J. H. A. M., de Jong, R. J. B., Kremer, B., Leemans, C. R., Marres, H. A. M., Manni, J. J., Langendijk, J. A., Levendag, P. C., Tjho-Heslinga, R. E., de Jong, J. M. A., Uyl-de Groot, C. A. & Knegt, P. P. (2005) Evaluating adherence to the Dutch guideline for diagnosis, treatment and follow-up of laryngeal carcinomas. *Radiotherapy and Oncology*, 74: 337-344.
Not in PICO
- Warnecke, A., Averbeck, T., Leinung, M., Soudah, B., Wenzel, G. I., Kreipe, H. H., Lenarz, T. & Stover, T. (2010) Contact endoscopy for the evaluation of the pharyngeal and laryngeal mucosa. *Laryngoscope*, 120: 253-258.
Not in PICO
- Zan, E., Yousem, D. M. & Aygun, N. (2011) Asymmetric mineralization of the arytenoid cartilages in patients without laryngeal cancer. *Ajnr: American Journal of Neuroradiology*, 32: 1113-1118.
Not in PICO
- Zargi, M., Smid, L., Fajdiga, I., Bubnic, B., Lenarcic, J. & Oblak, P. (1997) Detection and localization of early laryngeal cancer with laser-induced fluorescence: preliminary report. *European Archives of Oto-Rhino-Laryngology*, 254: Suppl-6.
Not in PICO
- Zargi, M., Fajdiga, I. & Smid, L. (2000) Autofluorescence imaging in the diagnosis of laryngeal cancer. *European Archives of Oto-Rhino-Laryngology*, 257: 17-23.
Not in PICO

ORAL CANCER

Review question:

What is the risk of oral cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

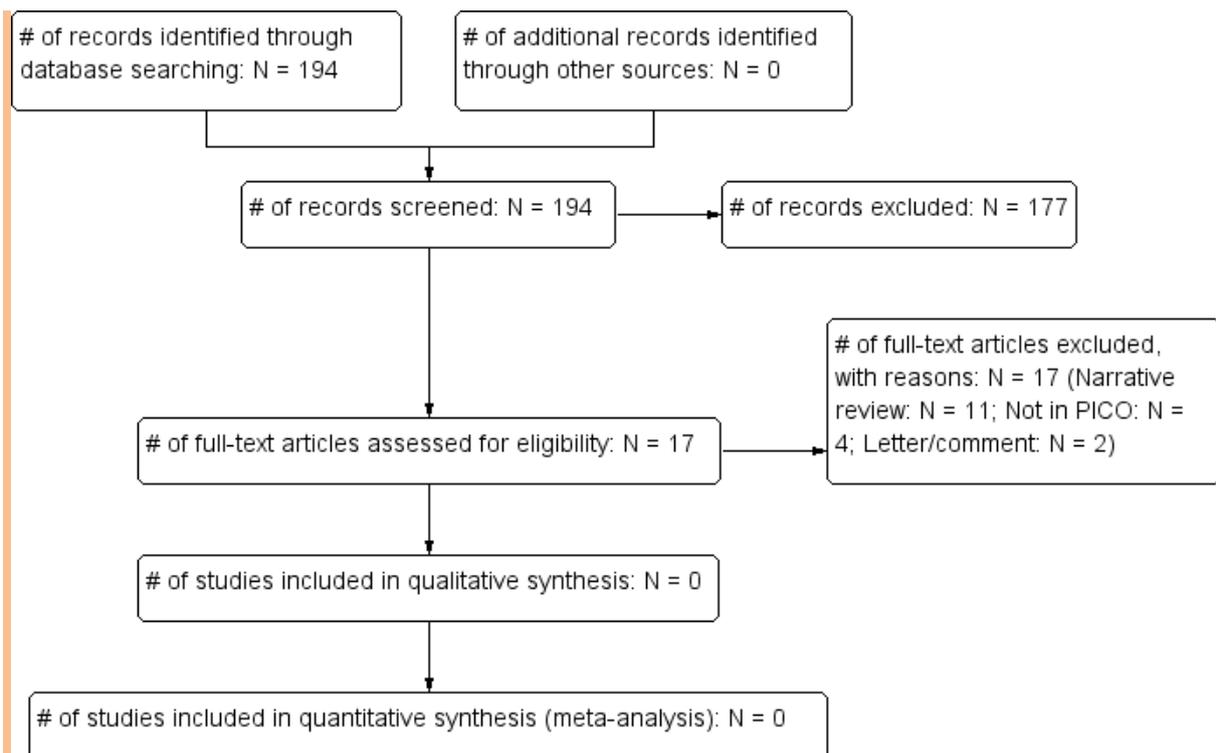
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	766	43	15/04/2013
<i>Premedline</i>	1980-2013	31	9	15/04/2013
<i>Embase</i>	1980-2013	1551	118	16/04/2013
<i>Cochrane Library</i>	1980-2013	137	9	17/04/2013
<i>Psychinfo</i>	1980-2013	4	0	17/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	594	70	17/04/2013

Total References retrieved (after de-duplication): 184

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-20/08/2014	23	4	20/08/2014
<i>Premedline</i>	4/2013-20/08/2014	25	4	20/08/2014
<i>Embase</i>	4/2013-20/08/2014	85	2	20/08/2014
<i>Cochrane Library</i>	4/2013-20/08/2014	279	0	20/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	4/2013-20/08/2014	57	1	20/08/2014

Total References retrieved (after de-duplication): 10



Study results

No evidence was identified.

References

Included studies

None

Excluded studies (with excl reason)

(1995) Early diagnosis and prevention of oral cancer and precancer: report of Symposium III.

Advances in Dental Research, 9: 134-137.

Narrative review

Abdelghany, A., Nolan, A., Freeman, R., Abdelghany, A., Nolan, A. & Freeman, R. (2011) Treating patients with dry mouth: general dental practitioners' knowledge, attitudes and clinical management. *British Dental Journal*, 211: E21.

Not in PICO

Abdul-Hussein, N., Mekaeil, R. & Walker, D. M. (2001) Referral attendance pattern and risk factors for oral cancer. *Journal of Dental Research*, 80: 979.

Not in PICO

Alho, O.-P. (2006) Head and neck cancer in primary care: Presenting symptoms and the effect of delayed diagnosis of cancer cases. *CMAJ*, 174: 779-784.

Study design not in PICO: Symptom prevalence study (with no case/no case verification) + cancer patient study

Allison, P. (2003) Information on oral cancer encourages primary-care patients to accept oral cancer screening and reduces associated anxiety. *Evidence-Based Dentistry*, 4: 68-69.

Not in PICO

- Allon, I., Allon, D. M., Gal, G., Anavi, Y., Chaushu, G. & Kaplan, I. (2013) Re-evaluation of common paradigms regarding the clinical appearance of oral mucosal malignancies. *Journal of Oral Pathology & Medicine*, 42: 670-675.
Not in PICO
- Alvi, A. (1996) Oral cancer: How to recognize the danger signs. *Postgraduate Medicine*, 99: 149-156.
Narrative review
- Applebaum, E. (2009) Oral cancer knowledge, attitudes and practices: a survey of dentists and primary care physicians in Massachusetts. *Journal of the American Dental Association (1939)*, 140: 461-467.
Not in PICO
- Arishiya Thapasum, F. (2011) Primary care clinicians' knowledge of oral cancer: A study of oral and general physicians in Kuala Muda & Kota Setar Districts, Malaysia. *Oral Oncology*, Conference: July.
Not in PICO
- Awojobi, O., Scott, S. E. & Newton, T. (2012) Patients' perceptions of oral cancer screening in dental practice: a cross-sectional study. *Bmc Oral Health*, 12.
Not in PICO
- Barucchi, A. M. B. (1987) Aspects of various lesions in the early diagnosis of oral carcinoma. *Giornale di Stomatologia e di Ortognatodonzia*, 6: 29-35.
Narrative review
- Bassi, K. K., Srivastava, A., Seenu, V., Kumar, R., Parshad, R., Chumber, S., Gupta, S. D. & Bahadur, S. (2013) The first and second echelon sentinel lymph node evaluation in oral cancer. *Indian Journal of Surgery*, 75: 377-382.
Not in PICO
- Bateman, C. (2002) Oral cancer - An underestimated killer. *South African Medical Journal*, 92: 410-412.
Narrative review
- Beck-Mannagetta, J. (2009) Squamous cell carcinoma and potentially malignant disorders of the oral mucosa. *Hautarzt*, 60: 859-865.
Narrative review
- Bierne, P. (2007) Recall intervals for oral health in primary care patients. *Cochrane Database of Systematic Reviews*.
Not in PICO
- Bentley, J. M., Barankin, B., Lauzon, G. J., Bentley, J. M., Barankin, B. & Lauzon, G. J. (2003) Paying more than lip service to lip lesions. [Review] [26 refs]. *Canadian Family Physician*, 49: 1111-1116.
Not in PICO
- Blanchaert, J. (2002) Oral and oral pharyngeal cancer: an update on incidence and epidemiology, identification, advances in treatment, and outcomes. *Compendium of continuing education in dentistry (Jamesburg, N, J.): 25-29*.
Narrative review
- Bleyer, A. (2009) CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology*, 36: 207-212.
Narrative review
- Borhan-Mojabi, K., Moradi, A. & Yazdabadi, A. (2012) Evaluating the degree of knowledge on oral cancer among general practitioners and dentists in Qazvin. *Journal of Evaluation in Clinical Practice*, 18: 498-501.
Not in PICO
- Borowski, B., Margainaud, J. P., Borowski, B. & Margainaud, J. P. (1990) [Early diagnosis of cancers of the mouth]. [French]. *Revue d Odonto-Stomatologie*, 19: 291-297.
Narrative review

- Bradley, P. J. & McGurk, M. (2013) Incidence of salivary gland neoplasms in a defined UK population. *British Journal of Oral & Maxillofacial Surgery*, 51: 399-403.
Not in PICO
- Brocklehurst, P., Kujan, O., Glenny, A.-M., Oliver, R., Sloan, P., Ogden, G. & Shepherd, S. (2010) Screening programmes for the early detection and prevention of oral cancer. *Cochrane database of systematic reviews (Online)*, 11.
Not in PICO
- Brocklehurst, P. R., Baker, S. R. & Speight, P. M. (2010) Oral cancer screening: what have we learnt and what is there still to achieve? *Future Oncology*, 6: 299-304.
Narrative review
- Brocklehurst, P. R., Baker, S. R. & Speight, P. M. (2010) A qualitative study examining the experience of primary care dentists in the detection and management of potentially malignant lesions. 1. Factors influencing detection and the decision to refer. *British Dental Journal*, 208: 72-73.
Not in PICO
- Brocklehurst, P. R. B. (2009) Factors affecting the referral of potentially malignant lesions from primary dental care: a pilot study in South Yorkshire. *Primary dental care : journal of the Faculty of General Dental Practitioners (UK)*, 16: 13-18.
Not in PICO
- Brocklehurst, P. R. B. (2010) Factors which determine the referral of potentially malignant disorders by primary care dentists. *Journal of Dentistry*, 38: 569-578.
Not in PICO
- Brouha, X. D., Tromp, D. M., Hordijk, G. J., Winnubst, J. A., de Leeuw, J. R., Brouha, X. D. R., Tromp, D. M., Hordijk, G. J., Winnubst, J. A. M. & de Leeuw, J. R. (2005) Oral and pharyngeal cancer: analysis of patient delay at different tumor stages. *Head & Neck*, 27: 939-945.
Not in PICO
- Brouha, X. D. R. (2007) Professional delay in head and neck cancer patients: Analysis of the diagnostic pathway. *Oral Oncology*, 43: 551-556.
Not in PICO
- Brzak, B. L., Mravak-Stipetiv, M., Canjuga, I., Baricevic, M., Balicevic, D., Sikora, M. & Filipovic-Zore, I. (2012) The Frequency and Malignant Transformation Rate of Oral Lichen Planus and Leukoplakia - A Retrospective Study. *Collegium Antropologicum*, 36: 773-777.
Not in PICO
- Burgess, L., Hamburger, J., White, D. A. & Morris, A. J. (2003) Patients referred with suspected oral malignancy - General dental practitioners' approaches. *Journal of Dental Research*, 82: 587.
Not in PICO
- Campos, A. E. (1988) Early detection of oral cancer. *Factor Odontologico*, 15: 13-15.
Nowhere available, but I think it is a narrative review
- Casiglia, J., Woo, S. B., Casiglia, J. & Woo, S. B. (2001) A comprehensive review of oral cancer. [Review] [101 refs]. *General Dentistry*, 49: 72-82.
Narrative review
- Cianfriglia, F. M. (1991) Diagnostic delay in neoplasms of the oral cavity. *Minerva Stomatologica*, 40: 717-728.
Not in PICO
- Cnossen, I. C., de B., Rinkel, R. N., Eerenstein, S. E., Rietveld, D. H., Doornaert, P., Buter, J., Langendijk, J. A., Leemans, C. R., Verdonck-de Leeuw, I. M., Cnossen, I. C., de Bree, R., Rinkel, R. N. P. M., Eerenstein, S. E. J., Rietveld, D. H. F., Doornaert, P., Buter, J., Langendijk, J. A., Leemans, C. R. & Verdonck-de Leeuw, I. M. (2012) Computerized monitoring of patient-reported speech and swallowing problems in head and neck cancer patients in clinical practice. *Supportive Care in Cancer*, 20: 2925-2931.
Not in PICO

- Cowan, C. G. G. (1995) Prevention and detection of oral cancer: the views of primary care dentists in Northern Ireland. *British Dental Journal*, 179: 338-342.
Not in PICO
- Dave, B. (2013) Why do GPs fail to recognise oral cancer? The argument for an oral cancer checklist. *British Dental Journal*, 214: 223-225.
Narrative review
- Dave, B. (2013) Why do GPs fail to recognise oral cancer? The argument for an oral cancer checklist. *British Dental Journal*, 214: 223-225.
Narrative review
- Dedhia, R. C., Smith, K. J., Johnson, J. T. & Roberts, M. (2011) The Cost-Effectiveness of Community-Based Screening for Oral Cancer in High-Risk Males in the United States: A Markov Decision Analysis Approach. *Laryngoscope*, 121: 952-960.
Not in PICO
- Demko, C. A., Sawyer, D., Slivka, M., Smith, D., Wotman, S., Demko, C. A., Sawyer, D., Slivka, M., Smith, D. & Wotman, S. (2009) Prevalence of oral lesions in the dental office. *General Dentistry*, 57: 504-509.
Not in PICO
- Dequanter, D., Shahla, M., Paulus, P. & Lothaire, P. (2013) Long term results of sentinel lymph node biopsy in early oral squamous cell carcinoma. *Oncotargets and therapy*, 6: 799-802.
Not in PICO
- Desouky, A. F. (2012) Incidental finding of parotid neoplasia-a report of two cases. *Oral Diseases*, Conference: September.
Not in PICO
- Dimitroulis, G. R. (1992) Referral patterns of patients with oral squamous cell carcinoma, Australia. *European Journal of Cancer Part B: Oral Oncology*, 28: 23-27.
Not in PICO
- dos Santos, L. C. O., Batista, O. D. & Cangussu, M. C. T. (2010) Characterization of oral cancer diagnostic delay in the state of Alagoas. *Brazilian Journal of Otorhinolaryngology*, 76: 416-422.
Not in PICO
- Douglass, A. B. M. (2008) Promoting oral health: The family physician's role. *American Family Physician*, 78: 814-815.
Editorial
- Dreyer, W. P., de, W. J., Dreyer, W. P. & de Waal, J. (2010) Oral medicine case book 29. Early squamous cell carcinoma of the gingiva and erosive lichen planus of the buccal tissues. *SADJ*, 65: 326-327.
Not in PICO
- Eisen, D., V (1991) Oral melanoma and other pigmented lesions of the oral cavity. *Journal of the American Academy of Dermatology*, 24: 527-537.
Narrative review
- Elango, K. J. A. (2011) Mouth self-examination to improve oral cancer awareness and early detection in a high-risk population. *Oral Oncology*, 47: 620-624.
Not in PICO
- Elkhoury, J. (2004) Undifferentiated malignant neoplasm involving the interdental gingiva: A case report. *Journal of Periodontology*, 75: 1295-1299.
Not in PICO
- Epstein, J. B. G. (2008) Screening for and diagnosis of oral premalignant lesions and oropharyngeal squamous cell carcinoma: Role of primary care physicians. *Canadian Family Physician*, 54: 870-875.
Narrative review

- Farah, C. S. & McCullough, M. J. (2008) Oral cancer awareness for the general practitioner: new approaches to patient care. *Australian Dental Journal*, 53: 2-10.
Narrative review
- Field, E. A. M. (1995) Oral mucosal screening as an integral part of routine dental care. *British Dental Journal*, 179: 262-266.
Not in PICO
- Foroughi, R., Seyedmajidi, M., Bijani, A. & Omid, D. M. (2013) Comparison of clinical diagnosis and histopathological report of referred biopsies to oral and maxillofacial pathology department of dental school of Babol, Iran (2003-2010). *Journal of Babol University of Medical Sciences*, 15: 71-77.
Not in PICO
- Fowler, G. G. R. (1980) Intraoral cancer in Victoria. *Medical Journal of Australia*, 2: 20-22.
Not in PICO
- Franklin, C. D. J. (2006) A survey of oral and maxillofacial pathology specimens submitted by general dental practitioners over a 30-year period. *British Dental Journal*, 200: 447-450.
Not in PICO
- Friedrich, R. E. & Friedrich, R. E. (2010) Delay in diagnosis and referral patterns of 646 patients with oral and maxillofacial cancer: a report from a single institution in Hamburg, Germany. *Anticancer Research*, 30: 1833-1836.
Not in PICO
- Garg, P. (2012) "Catch them before it becomes too late"-oral cancer detection. Report of two cases and review of diagnostic AIDS in cancer detection. *International Journal of Preventive Medicine*, 3: 737-741.
Not in PICO
- Genden, E. M., Rinaldo, A., Bradley, P. J., Lowry, J., Suarez, C., Shaha, A. R., Scully, C. & Ferlito, A. (2006) Referral guidelines for suspected cancer of the head and neck. *Auris Nasus Larynx*, 33: 1-5.
Narrative review
- Gillenwater, A. M., Chambers, M. S., Gillenwater, A. M. & Chambers, M. S. (2006) Diagnosis of premalignant lesions and early cancers of the oral cavity. *Texas Dental Journal*, 123: 512-520.
Narrative review
- Gjurcheski, J. (2012) Understanding the role of general dentists in the process of screening and early diagnosis of oral premalignant and malignant lesions - brief literature review. *Macedonian Journal of Medical Sciences*, 5: 462-471.
Narrative review
- Gomez, I. (2010) Is early diagnosis of oral cancer a feasible objective? Who is to blame for diagnostic delay? *Oral Diseases*, 16: 333-342.
Narrative review
- Gonsalves, W. C. C. (2007) Common oral lesions: Part II. Masses and neoplasia. *American Family Physician*, 75: 509-512.
Narrative review
- Gorsky, M. (1995) Referral delay in diagnosis of oro/oropharyngeal cancer in Israel. *European Journal of Cancer Part B: Oral Oncology*, 31: 166-168.
Not in PICO
- Grant, E. (2010) The experiences of young oral cancer patients in Scotland: Symptom recognition and delays in seeking professional help. *British Dental Journal*, 208: 465-471.
Not in PICO
- Greenwood, M. & Lowry, R. J. (2001) Primary care clinicians' knowledge of oral cancer: a study of dentists and doctors in the North East of England. *British Dental Journal*, 191: 510-512.
Not in PICO
- Groome, P. A., Rohland, S. L., Hall, S. F., Irish, J., Mackillop, W. J., O'Sullivan, B., Groome, P. A., Rohland, S. L., Hall, S. F., Irish, J., Mackillop, W. J. & O'Sullivan, B. (2011) A population-based study

- of factors associated with early versus late stage oral cavity cancer diagnoses. *Oral Oncology*, 47: 642-647.
Not in PICO
- Hanken, H., Kraatz, J., Smeets, R., Heiland, M., Assaf, A. T., Blessmann, M., Eichhorn, W., Clauditz, T. S., Grobe, A., Kolk, A. & Rana, M. (2013) The detection of oral pre- malignant lesions with an autofluorescence based imaging system (VELscope) - a single blinded clinical evaluation.[Erratum appears in *Head Face Med.* 2013;9:26 Note: Assaf, Alexandre Thomas [added]]. *Head & Face Medicine*, 9: 23.
Not in PICO
- Heiner, H. (1983) Early detection of tumors in the oral cavity. *Stomatologie der DDR*, 33: 438-445.
Narrative review
- Hirshberg, A., Calderon, S., Kaplan, I., Hirshberg, A., Calderon, S. & Kaplan, I. (1989) [Update review on prevention and early diagnosis in oral cancer]. [Review] [69 refs] [Hebrew]. *Refuat Hapeh Vehashinayim*, 19: 38-48.
Narrative review
- Hodgson, T. A., Buchanan, J. A., Garg, A., Ilyas, S. E., Porter, S. R., Hodgson, T. A., Buchanan, J. A. G., Garg, A., Ilyas, S. E. & Porter, S. R. (2006) An audit of the UK national cancer referral guidelines for suspected oral mucosal malignancy. *British Dental Journal*, 201: 643-647.
Not in PICO
- Hollows, P. (2000) Delays in the referral and treatment of oral squamous cell carcinoma. *British Dental Journal*, 188: 262-265.
Not in PICO
- Holmes, L., desVignes-Kendrick, M., Slomka, J., Mahabir, S., Beeravolu, S. & Emani, S. R. (2009) Is dental care utilization associated with oral cavity cancer in a large sample of community-based United States residents? *Community Dentistry and Oral Epidemiology*, 37: 134-142.
Not in PICO
- Horowitz, A. M., Drury, T. F. & Canto, M. T. (2000) Practices of Maryland dentists: oral cancer prevention and early detection - baseline data from 1995. *Oral Diseases*, 6: 282-288.
Not in PICO
- Horowitz, A. M., Drury, T. F., Goodman, H. S. & Yellowitz, J. A. (2000) Oral pharyngeal cancer prevention and early detection - Dentists' opinions and practices. *Journal of the American Dental Association*, 131: 453-462.
Not in PICO
- Horowitz, A. M., Siriphant, P., Sheikh, A. & Child, W. L. (2001) Perspectives of Maryland dentists on oral cancer. *Journal of the American Dental Association*, 132: 65-72.
Not in PICO
- Hsieh, R., Yen, M.-F., Chen, H.-H. & Zavras, A. (2013) Metabolic syndrome and development of oral neoplasms. *American Journal of Epidemiology*, 177: S60.
Not in PICO
- Hueston, W. J. & Kaur, D. (2013) Upper respiratory conditions: oral cancers. *Fp Essentials*, 415: 22-26.
Narrative review
- Huff, K. (2009) Sensitivity of direct tissue fluorescence visualization in screening for oral premalignant lesions in general practice. *General Dentistry*, 57: 34-38.
Not in PICO
- Humphris, G. M., Ireland, R. S. & Field, E. A. (2001) Randomised trial of the psychological effect of information about oral cancer in primary care settings. *Oral Oncology*, 37: 548-552.
Not in PICO
- Humphris, G. M. & Field, E. A. (2004) An oral cancer information leaflet for smokers in primary care: results from two randomised controlled trials. *Community Dentistry and Oral Epidemiology*, 32:

143-149.

Not in PICO

Hyde, N., Hopper, C., Hyde, N. & Hopper, C. (760) Oral cancer: the importance of early referral. [Review] [5 refs]. *Practitioner*, 243: 753-758.

Narrative review

Jaikittivong, A. (2009) Oral squamous cell carcinoma: a clinicopathological study of 342 Thai cases. *The journal of contemporary dental practice*, 10: E033-E040.

Not in PICO

Jin, X., Zeng, X., Jin, X. & Zeng, X. (822) Images in emergency medicine. Woman with white patches on tongue. Malignant transformation of oral leukoplakia. *Annals of Emergency Medicine*, 60: 815.

Not in PICO

Jones, D. L. & Rankin, K. V. (2013) Oral cancer: FAQ.[Reprint of Tex Dent J. 2013 May;130(5):438-43; PMID: 23923466]. *Journal of Michigan Dental Association*, 95: 32-35.

Narrative review

Jovanovic, A. (1992) Delay in diagnosis of oral squamous cell carcinoma; a report from The Netherlands. *European Journal of Cancer Part B: Oral Oncology*, 28: 37-38.

Not in PICO

Jurca, M. (1983) Observation of the oral mucosa for early diagnosis of malignant disease. *Zobozdravstveni Vestnik*, 38: 131-138.

Narrative review

Kantola, S. (2001) Detection of tongue cancer in primary care. *British Journal of General Practice*, 51: 106-111.

Not in PICO

Kao, S.-Y. (2009) Detection and Screening of Oral Cancer and Pre-cancerous Lesions. *Journal of the Chinese Medical Association*, 72: 227-233.

Narrative review

Koerner, K. R. (2006) Evaluation and treatment by general dentists of oral soft-tissue lesions. *Dentistry Today*, 25: 90-95.

Narrative review

Kokalj, V. N., Cizmarevic, B., Zagorac, A., Zagradisnik, B. & Lanisnik, B. (2014) An evaluation of SOX2 and hTERT gene amplifications as screening markers in oral and oropharyngeal squamous cell carcinomas. *Molecular Cytogenetics*, 7: 5.

Not in PICO

Kominek, P., Vitek, P., Urban, O., Zelenik, K., Halamka, M., Feltl, D., Cvek, J. & Matousek, P. (2013) Chromoendoscopy to detect early synchronous second primary esophageal carcinoma in patients with squamous cell carcinomas of the head and neck? *Gastroenterology research & practice*, 2013: 236264.

Not in PICO

Kondori, I., Mottin, R. W., Laskin, D. M., Kondori, I., Mottin, R. W. & Laskin, D. M. (2011) Accuracy of dentists in the clinical diagnosis of oral lesions. *Quintessence International*, 42: 575-577.

Not in PICO

Kowalski, I. S. G., Souza, C. P. & Kowalski, L. P. (2002) Factors delaying the diagnosis and lateness of referral as determinants of advanced stage oral cancer. *International Journal of Cancer*, 81.

Not in PICO

Lam, D. K., Schmidt, B. L., Lam, D. K. & Schmidt, B. L. (2011) Orofacial pain onset predicts transition to head and neck cancer. *Pain*, 152: 1206-1209.

Not in PICO

Langevin, S. M., Michaud, D. S., Eliot, M., Peters, E. S., McClean, M. D. & Kelsey, K. T. (2012) Regular dental visits are associated with earlier stage at diagnosis for oral and pharyngeal cancer. *Cancer Causes & Control*, 23: 1821-1829.

Not in PICO

- Laudenbach, J. M. (2013) Oral medicine update: oral cancer--screening, lesions and related infections. *Journal of the California Dental Association*, 41: 326-328.
Narrative review
- Lazarchik, D. A. F. (1996) Oral screening exam for the primary care physician. *Primary Care Update for Ob/Gyns*, 3: 108-113.
Narrative review
- Lee, K. H. P. (2009) Oral white lesions: Pitfalls of diagnosis. *Medical Journal of Australia*, 190: 274-277.
Narrative review
- Lehew, C., Epstein, J. B., Kaste, L. M. & Choi, Y. K. (2010) Assessing oral cancer early detection: clarifying dentists' practices. *Journal of Public Health Dentistry*, 70: 93-100.
Not in PICO
- Leocata, P. (2007) A screening program for the early detection and prevention of oral cancer. *Journal of Plastic Dermatology*, 3: 71-75.
Not in PICO
- Levi, J. (2005) Squamous cell carcinoma presenting as an endodontic-periodontic lesion. *Journal of Periodontology*, 76: 1798-1804.
Not in PICO
- Lim, K., Moles, D. R., Downer, M. C. & Speight, P. M. (2003) Opportunistic screening for oral cancer and precancer in general dental practice: results of a demonstration study. *British Dental Journal*, 194: 497-502.
Not in PICO
- Liu, W. (2012) Oral cancer development in patients with leukoplakia - clinicopathological factors affecting outcome. *PLoS ONE*, 7.
Not in PICO
- Llewellyn, C. D., Johnson, N. W. & Warnakulasuriya, S. (2004) Factors associated with delay in presentation among younger patients with oral cancer. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics*, 97: 707-713.
Not in PICO
- Lopez-Jornet, P. (2008) Influence of years of professional experience in relation to the diagnostic skill of general dental practitioners (GDPs) in identifying oral cancer and precancerous lesions. *International Dental Journal*, 58: 127-133.
Not in PICO
- Lopez-Jornet, P., Camacho-Alonso, F. & Molina-Minano, F. (2010) Knowledge and attitudes about oral cancer among dentists in Spain. *Journal of Evaluation in Clinical Practice*, 16: 129-133.
Not in PICO
- Lyons, B. (1999) ENT malignancies. What the GP needs to know. *Australian Family Physician*, 28: 209-215.
Narrative review
- M S, Shetty, P., Decruz, A. M. & Pai, P. (2013) The Self-Reported Knowledge, Attitude and the Practices Regarding the Early Detection of Oral Cancer and Precancerous Lesions among the Practising Dentists of Dakshina Kannada-A Pilot Study. *Journal of Clinical and Diagnostic Research JCDR*, 7: 1491-1494.
Not in PICO
- Mashberg, A. (1989) Appearance, site of occurrence, and physical and clinical characteristics of oral carcinoma in Torino, Italy. *Cancer*, 63: 2522-2527.
Not in PICO
- Mashberg, A. (2000) Diagnosis of early oral and oropharyngeal squamous carcinoma: Obstacles and their amelioration. *Oral Oncology*, 36: 253-255.
Narrative review

- Mccann, M. F., Macpherson, L. M. D., Binnie, V. I. & Stephen, K. W. (2000) A survey of Scottish primary care dental practitioners' oral cancer-related practices and training requirements. *Community Dental Health*, 17: 24-30.
Not in PICO
- McCullough, M. J., Prasad, G. & Farah, C. S. (2010) Oral mucosal malignancy and potentially malignant lesions: an update on the epidemiology, risk factors, diagnosis and management. *Australian Dental Journal*, 55: 61-65.
Narrative review
- McCunniff, M. D., Barker, G. J., Barker, B. E. & Williams, K. (2000) Health professionals' baseline knowledge of oral/pharyngeal cancers. *Journal of Cancer Education*, 15: 79-81.
Not in PICO
- McGurk, M. (2010) The reality of identifying early oral cancer in the general dental practice. *British Dental Journal*, 208: 347-351.
Narrative review
- McIntyre, G. T., Oliver, R. J., McIntyre, G. T. & Oliver, R. J. (1999) Update on precancerous lesions. *Dental Update*, 26: 382-386.
Narrative review
- McLeod, N. M. H. (2005) Oral cancer: Delays in referral and diagnosis persist. *British Dental Journal*, 198: 681-684.
Not in PICO
- Mehanna, H. (2012) Salivary gland swellings. *BMJ (Online)*, 345.
Narrative review
- Messadi, D. V. (2013) Diagnostic aids for detection of oral precancerous conditions. [Review]. *International Journal of Oral Science*, 5: 59-65.
Narrative review
- Mishra, R. & Mishra, R. (2012) Biomarkers of oral premalignant epithelial lesions for clinical application. [Review]. *Oral Oncology*, 48: 578-584.
Narrative review
- Morelato, R. A. H. (2007) Diagnostic delay of oral squamous cell carcinoma in two diagnosis centers in Cordoba Argentina. *Journal of Oral Pathology and Medicine*, 36: 405-408.
Not in PICO
- Morse, D. E., V (2011) Perspectives of San Juan healthcare practitioners on the detection deficit in oral premalignant and early cancers in Puerto Rico: a qualitative research study. *BMC public health*, 11: 2011.
Not in PICO
- Munde, A. D., Karle, R. R., Wankhede, P. K., Shaikh, S. S. & Kulkurni, M. (2013) Demographic and clinical profile of oral lichen planus: A retrospective study. *Contemporary Clinical Dentistry*, 4: 181-185.
Not in PICO
- Nair, D. R., Pruthy, R., Pawar, U., Chaturvedi, P., Nair, D. R., Pruthy, R., Pawar, U. & Chaturvedi, P. (2012) Oral cancer: Premalignant conditions and screening--an update. [Review]. *Journal of Cancer Research & Therapeutics*, 8 Suppl 1: S57-S66.
Narrative review
- Ni Riordain, R. (2009) Oral cancer - Current knowledge, practices and implications for training among an Irish general medical practitioner cohort. *Oral Oncology*, 45: 958-962.
Not in PICO
- Nicotera, G., Di Stasio, S. M., Angelillo, I. F., Nicotera, G., Di Stasio, S. M. & Angelillo, I. F. (2004) Knowledge and behaviors of primary care physicians on oral cancer in Italy. *Oral Oncology*, 40: 490-495.
Not in PICO

- Noorman van der Dussen, M. F. (1994) Oral cancer. The importance of early diagnosis and role of the dentist. *Revue Belge de Medecine Dentaire*, Belgisch tijdschrift voor tandheelkunde. 49: 35-49.
Narrative review
- Obradovic, R., Kesic, L., Mihailovic, D., Radicevic, G., Obradovic, R., Kesic, L., Mihailovic, D. & Radicevic, G. (2009) Malignant transformation of oral lichen planus. A case report. *West Indian Medical Journal*, 58: 490-492.
Not in PICO
- Ogden, G., Lewthwaite, R. & Shepherd, S. D. (2013) Early detection of oral cancer: how do I ensure I don't miss a tumour? *Dental Update*, 40: 462-465.
Narrative review
- Onizawa, K. (2003) Factors associated with diagnostic delay of oral squamous cell carcinoma. *Oral Oncology*, 39: 781-788.
Not in PICO
- Pakfetrat, A. (2010) Oral cancer knowledge among patients referred to Mashhad Dental School, Iran. *Archives of Iranian Medicine*, 13: 543-548.
Not in PICO
- Paleri, V. (2010) Evaluation of oral ulceration in primary care. *BMJ (Online)*, 340: 1234-1239.
Narrative review
- Patel, M. (196) Importance of quality in referral letters sent for potentially malignant oral, head and neck lesions. *Dental Update*, 38: 192-194.
Not in PICO
- Petti, S. & Scully, C. (2007) Oral cancer knowledge and awareness: Primary and secondary effects of an information leaflet. *Oral Oncology*, 43: 408-415.
Not in PICO
- Pitchers, M. (2006) Delay in referral of oropharyngeal squamous cell carcinoma to secondary care correlates with a more advanced stage at presentation, and is associated with poorer survival. *British Journal of Cancer*, 94: 955-958.
Not in PICO
- Poh, C. F., MacAulay, C. E., Laronde, D. M., Williams, P. M., Zhang, L., Rosin, M. P., Poh, C. F., MacAulay, C. E., Laronde, D. M., Williams, P. M., Zhang, L. & Rosin, M. P. (2011) Squamous cell carcinoma and precursor lesions: diagnosis and screening in a technical era. [Review]. *Periodontology 2000*, 57: 73-88.
Narrative review
- Raubenheimer, E. J. (1989) Clinical manifestations of oral precancer and cancer. *The Journal of the Dental Association of South Africa = Die Tydskrif van die Tandheelkundige Vereniging van Suid-Afrika*, Suppl 1: Mar.
Narrative review
- Reamy, B. V. D. (2010) Common tongue conditions in primary care. *American Family Physician*, 81: 627-634.
Narrative review
- Reid, B. C. & Rozier, R. G. (2006) Continuity of care and early diagnosis of head and neck cancer. *Oral Oncology*, 42: 510-516.
Not in PICO
- Reychler, H., Weynand, B., Reychler, H. & Weynand, B. (2010) [Screening and diagnosis of precancerous oral mucosa lesions]. [Review] [French]. *Revue de Stomatologie et de Chirurgie Maxillo-Faciale*, 111: 203-207.
Narrative review
- Robinson, P. N. & Mickelson, A. R. (2006) Diagnosis of oral cavity cancers. *Otolaryngologic Clinics of North America*, 39: 295-+.
Narrative review

- Rodrigues, V. C., Moss, S. M., Tuomainen, H., Rodrigues, V. C., Moss, S. M. & Tuomainen, H. (1998) Oral cancer in the UK: to screen or not to screen. [Review] [142 refs]. *Oral Oncology*, 34: 454-465.
Narrative review
- Rogers, S. N., V (2011) Reasons for delayed presentation in oral and oropharyngeal cancer: The patients perspective. *British Journal of Oral and Maxillofacial Surgery*, 49: 349-353.
Not in PICO
- Rogers, S. N. G. (2008) A survey of general dental practitioners in Merseyside regarding urgent appointments and suspected cancer referrals. *Primary dental care : journal of the Faculty of General Dental Practitioners (UK)*, 15: 25-30.
Not in PICO
- Rosillo, G. M., Sanchez Lopez, J. D., Perez, A. A., Rosales Varo, A. P., Rosillo Galindo, M., Sanchez Lopez, J. D., Perez Abela, A. & Rosales Varo, A. P. (1999) [Premalignant lesions of the oral cavity in primary care]. [Spanish]. *Atencion Primaria*, 23: 445-446.
Letter
- Ryba, F., Rice, S. & Hutchison, I. L. (2010) Numb chin syndrome: an ominous clinical sign. *British Dental Journal*, 208: 283-285.
Not in PICO
- Sardella, A., Demarosi, F., Lodi, G., Canegallo, L., Rimondini, L., Carrassi, A., Sardella, A., Demarosi, F., Lodi, G., Canegallo, L., Rimondini, L. & Carrassi, A. (2007) Accuracy of referrals to a specialist oral medicine unit by general medical and dental practitioners and the educational implications. *Journal of Dental Education*, 71: 487-491.
Not in PICO
- Sartori, L. C. & Frazao, P. (2012) Accuracy of Screening for Potentially Malignant Disorders of the Oral Mucosa by Dentists in Primary Care. *Oral Health & Preventive Dentistry*, 10: 53-58.
Not in PICO
- Schnetler, J. F. C. (1992) Oral cancer diagnosis and delays in referral. *British Journal of Oral and Maxillofacial Surgery*, 30: 210-213.
Not in PICO
- Scott S. (2008) Patient delay for potentially malignant oral symptoms. *European Journal of Oral Sciences*, 116: 141-147.
Not in PICO
- Scott, S. E., McGurk, M. & Grunfeld, E. A. (2007) The process of symptom appraisal: Cognitive and emotional responses to detecting potentially malignant oral symptoms. *Journal of Psychosomatic Research*, 62: 621-630.
Not in PICO
- Scott, S. E., Weinman, J. & Grunfeld, E. A. (2011) Developing ways to encourage early detection and presentation of oral cancer: What do high-risk individuals think? *Psychology & Health*, 26: 1392-1405.
Not in PICO
- Scott, S. E. G. (2006) Patient's delay in oral cancer: A systematic review. *Community Dentistry and Oral Epidemiology*, 34: 337-343.
Not in PICO
- Scott, S. E. G. (2009) Barriers and triggers to seeking help for potentially malignant oral symptoms: Implications for interventions. *Journal of Public Health Dentistry*, 69: 34-40.
Not in PICO
- Scott, S. E. K. (2012) A randomised controlled trial of a pilot intervention to encourage early presentation of oral cancer in high risk groups. *Patient Education and Counseling*, 88: 241-248.
Not in PICO
- Scully, C. (331) The role of the dental team in preventing and diagnosing cancer: 3. oral cancer diagnosis and screening. *Dental Update*, 32: 326-328.
Narrative review

- Scully, C. (1986) Sources and patterns of referrals of oral cancer: role of general practitioners. *British Medical Journal*, 293: 599-601.
Not in PICO
- Scully, C., Felix, D. H., Scully, C. & Felix, D. H. (2005) Oral Medicine--update for the dental practitioner: oral white patches. *British Dental Journal*, 199: 565-572.
Narrative review
- Scully, C. & Felix, D. H. (2006) Oral Medicine - Update for the dental practitioner - Oral cancer. *British Dental Journal*, 200: 13-17.
Narrative review
- Scully, C. (2008) Oral cancer: Current and future diagnostic techniques. *American Journal of Dentistry*, 21: 199-209.
Narrative review
- Scully, C. & Kirby, J. (2014) - Statement on mouth cancer diagnosis and prevention. - *British Dental Journal*, 216: 37-38.
Narrative review
- Scully, C. & Kirby, J. (2014) Statement on mouth cancer diagnosis and prevention. *British Dental Journal*, 216: 37-38.
Narrative review
- Seifert, G. (1981) Precursor and early stages of cancer of the oral cavity. *Deutsches Arzteblatt*, 78: 327-332.
Narrative review
- Seoane-Romero, J. M., Vazquez-Mahia, I., Seoane, J., Varela-Centelles, P., Tomas, I., Lopez-Cedrun, J. L., Seoane-Romero, J. M., Vazquez-Mahia, I., Seoane, J., Varela-Centelles, P., Tomas, I. & Lopez-Cedrun, J. L. (2012) Factors related to late stage diagnosis of oral squamous cell carcinoma. *Medicina Oral, Patologia Oral y Cirugia Bucal*, 17: e35-e40.
Not in PICO
- Seoane, J., Warnakulasuriya, S., Varela-Centelles, P., Esparza, G. & Dios, P. D. (2006) Oral cancer: experiences and diagnostic abilities elicited by dentists in North-western Spain. *Oral Diseases*, 12: 487-492.
Not in PICO
- Seoane, J., Varela-Centelles, P. I., Walsh, T. F., Lopez-Cedrun, J. L. & Vazquez, I. (2006) Gingival squamous cell carcinoma: Diagnostic delay or rapid invasion? *Journal of Periodontology*, 77: 1229-1233.
Not in PICO
- Seoane, J., Corral-Lizana, C., Gonzalez-Mosquera, A., Cerero, R., Esparza, G., Sanz-Cuesta, T., Varela-Centelles, P., Seoane, J., Corral-Lizana, C., Gonzalez-Mosquera, A., Cerero, R., Esparza, G., Sanz-Cuesta, T. & Varela-Centelles, P. (2011) The use of clinical guidelines for referral of patients with lesions suspicious for oral cancer may ease early diagnosis and improve education of healthcare professionals. *Medicina Oral, Patologia Oral y Cirugia Bucal*, 16: e864-e869.
Not in PICO
- Seoane, J. (2012) Impact of delay in diagnosis on survival to head and neck carcinomas: A systematic review with meta-analysis. *Clinical Otolaryngology*, 37: 99-106.
Not in PICO
- Shetty, K. V. & Johnson, N. W. (1999) Knowledge, attitudes and beliefs of adult South Asians living in London regarding risk factors and signs for oral cancer. *Community Dental Health*, 16: 227-231.
Not in PICO
- Siar, C. H., Mah, M. C., Gill, P. P., Siar, C. H., Mah, M. C. & Gill, P. P. (2012) Prevalence of bilateral 'mirror-image' lesions in patients with oral potentially malignant epithelial lesions. *European Archives of Oto-Rhino-Laryngology*, 269: 999-1004.
Not in PICO

- Silverman, J. (1988) Early diagnosis of oral cancer. *Cancer*, 62: 1796-1799.
Narrative review
- Silverman, S. (1994) Oral cancer. *Seminars in Dermatology*, 13: 132-137.
Narrative review
- Singh, P. & Warnakulasuriya, S. (2006) The two-week wait cancer initiative on oral cancer; the predictive value of urgent referrals to an oral medicine unit. *British Dental Journal*, 201: 717-720.
Not in PICO
- Singh, T. & Schenberg, M. (2013) Delayed diagnosis of oral squamous cell carcinoma following dental treatment. *Annals of the Royal College of Surgeons of England*, 95: 369-373.
Not in PICO
- Siriphant, P., Drury, T. F., Horowitz, A. M. & Harris, R. M. (2001) Oral cancer knowledge and opinions among Maryland nurse practitioners. *Journal of Public Health Dentistry*, 61: 138-144.
Not in PICO
- Siriphant, P., Horowitz, A. M. & Child, W. L. (2001) Perspectives of Maryland adult and family practice nurse practitioners on oral cancer. *Journal of Public Health Dentistry*, 61: 145-149.
Not in PICO
- Sousa, F. B., - de Freitas e Silva MR, Fernandes, C. P., Silva, P. G. & Alves, A. P. (2014) - Oral cancer from a health promotion perspective: experience of a diagnosis network in Ceara. - *Pesquisa Odontologica Brasileira = Brazilian Oral Research*, 28 Spec, 2014..
Only 73/296 lesions were confirmed histologically. The others do not appear to have been followed up.
- Souza, L. M. M. (2011) Scheduling delay in suspected cases of oral cancer. *Revista Brasileira de Epidemiologia*, 14: 642-650.
Not in PICO
- Speight, P. M. P. (2006) The cost-effectiveness of screening for oral cancer in primary care. *Health Technology Assessment*, 10: 1-65.
Not in PICO
- Spitzer, W. J. (1990) Cancers: concerns and early diagnosis by the dentist. *Zahnarztliche Praxis*, 41: 365-367.
Narrative review
- St George, G., Welfare, R. D. & Lund, V. J. (2006) Referral speed. *British Dental Journal*, 200: 185-186.
Comment
- Steele, T. O., Meyers, A., Steele, T. O. & Meyers, A. (2011) Early detection of premalignant lesions and oral cancer. [Review]. *Otolaryngologic Clinics of North America*, 44: 221-229.
Narrative review
- Stoykova, M. (1999) Delayed diagnosis of cancer with emphasis on oral cavity cancers. *Folia Medica*, 41: 132-135.
Not in PICO
- Szpirglas, H. (1995) Detection of oral cancers and current conception of precancerous conditions. *La Revue du praticien*, 45: 831-837.
Narrative review
- Teppo, H. (2009) Comorbidity and diagnostic delay in cancer of the larynx, tongue and pharynx. *Oral Oncology*, 45: 692-695.
Not in PICO
- Tripathi, P. (2010) Adenoid cystic carcinoma of the palate: A case report with review of literature. *Journal of Cancer Science and Therapy*, 2: 160-162.
Not in PICO
- van den Berg, A. D. & Palmer, N. O. (2012) An investigation of West Sussex general dental practitioners' awareness, attitudes and adherence to NICE dental recall guidelines. *Primary Dental Care*, 19: 11-22.
Not in PICO

- van der Meij, E. H., Bezemer, P. D., van, d. W., I, van der Meij, E. H., Bezemer, P. D. & van der Waal, I. (2002) Cost-effectiveness of screening for the possible development of cancer in patients with oral lichen planus. [Review] [57 refs]. *Community Dentistry & Oral Epidemiology*, 30: 342-351.
Not in PICO
- van der Meij, E. H., Mast, H., van, d. W., I, van der Meij, E. H., Mast, H. & van der Waal, I. (2007) The possible premalignant character of oral lichen planus and oral lichenoid lesions: a prospective five-year follow-up study of 192 patients. [Review] [43 refs]. *Oral Oncology*, 43: 742-748.
Not in PICO
- van der Meij, E. H. (2008) Epidemiology, aetiology, and clinical aspects of oral cancer and premalignant lesions. *Nederlands Tijdschrift Voor Tandheelkunde*, 115: 186-191.
Narrative review
- Van Der Meij, E. H. S. (2005) "Classical" oral lichen planus is not premalignant. *Nederlands Tijdschrift voor Dermatologie en Venereologie*, 15: 334-338.
Narrative review
- van der Waal, I. (1996) Mouth neoplasms: a review. *Nederlands Tijdschrift Voor Tandheelkunde*, 103: 345-347.
Narrative review
- van der Waal, I. (2011) Early diagnosis in primary oral cancer: Is it possible? *Medicina Oral, Patologia Oral y Cirugia Bucal*, 16: 300-305.
Narrative review
- van Heerden, W. F. B. (2002) The role of the dentist in the prevention and early diagnosis of oral cancer. *SADJ : journal of the South African Dental Association = tydskrif van die Suid-Afrikaanse Tandheelkundige Vereniging*, 57: 22-24.
Narrative review
- van, d. W., I (2014) - Oral potentially malignant disorders: is malignant transformation predictable and preventable? - *Medicina Oral, Patologia Oral y Cirugia Bucal*, 19: e386-e390.
Narrative review
- Venta, I., Oikarinen, V. J., Soderholm, A. L., Lindqvist, C., Venta, I., Oikarinen, V. J., Soderholm, A. L. & Lindqvist, C. (1993) Third molars confusing the diagnosis of carcinoma. *Oral Surgery, Oral Medicine, Oral Pathology*, 75: 551-555.
Not in PICO
- von Arx, T., Koch, S. & Hardt, N. (2002) [Lesions of the mouth mucosa. An anamnestic and clinical study of 100 consecutive patients with mucosal lesions]. [German]. *Schweizer Monatsschrift fur Zahnmedizin*, 112: 326-329.
Not in PICO
- Warnakulasuriya, K. A. A. S., Ekanayake, A. N. I., Sivayoham, S., Stjernsward, J., Pindborg, J. J., Sobin, L. H. & Perera, K. S. G. P. (1984) Utilization of Primary Health-Care Workers for Early Detection of Oral-Cancer and Precancer Cases in Sri-Lanka. *Bulletin of the World Health Organization*, 62: 243-250.
Not in PICO (screening)
- Warnakulasuriya, K. A. A. S. & Nanayakkara, B. G. (1991) Reproducibility of An Oral-Cancer and Precancer Detection Program Using A Primary Health-Care Model in Sri-Lanka. *Cancer Detection and Prevention*, 15: 331-334.
Not in PICO
- Warnakulasuriya, S., Ekanayake, A., Stjernsward, J., Pindborg, J. J. & Sivayoham, S. (1988) Compliance Following Referral in the Early Detection of Oral-Cancer and Precancer in Sri-Lanka. *Community Dentistry and Oral Epidemiology*, 16: 326-329.
Not in PICO
- Warnakulasuriya, S., Gould, A., Leuci, S., Mignogna, M., Seoane-Leston, J. M., Diz-Dios, P., McAlister, C., McEvoy, P., Thermidou, I. & Rapidis, A. D. (2013) Leonardo da Vinci Partnership - A lifelong learning programme to raise awareness of dental and medical professionals within Europe for the

early detection of oral cancer - Phase 2. *Oral Oncology*, 49: S59.

Not in PICO

Waskowska, J. (2012) Verrucous carcinoma of the tongue - A rare case study. *Central European Journal of Medicine*, 7: 145-148.

Not in PICO

Williams, M. & Bethea, J. (2011) Patient awareness of oral cancer health advice in a dental access centre: a mixed methods study. *British Dental Journal*, 210.

Not in PICO

Williams, R. G. (1981) The early diagnosis of carcinoma of the mouth. *Annals of the Royal College of Surgeons of England*, 63: 423-425.

Not in PICO

Yeatts, D., Burns, J. C., Yeatts, D. & Burns, J. C. (1991) Common oral mucosal lesions in adults. [Review] [5 refs]. *American Family Physician*, 44: 2043-2050.

Narrative review

Yellowitz, J., Horowitz, A. M., Goodman, H. S., Canto, M. T. & Farooq, N. S. (1998) Knowledge, opinions and practices of general dentists regarding oral cancer: A pilot survey. *Journal of the American Dental Association*, 129: 579-583.

Not in PICO

Yellowitz, J. A. & Goodman, H. S. (1995) Assessing Physicians and Dentists Oral-Cancer Knowledge, Opinions and Practices. *Journal of the American Dental Association*, 126: 53-60.

Not in PICO

Yu, T. (2008) Delays in diagnosis of head and neck cancers. *Journal of the Canadian Dental Association*, 74: 61-61c.

Not in PICO

Zohoori, F. V., Shah, K., Mason, J. & Shucksmith, J. (2012) Identifying Factors to Improve Oral Cancer Screening Uptake: A Qualitative Study. *PLoS ONE*, 7.

Not in PICO

Review question:

Which investigations of symptoms of suspected oral cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-5/2013	499	116	09/05/2013
<i>Premedline</i>	1980-5/2013	47	20	09/05/2013
<i>Embase</i>	1980-5/2013	937	93	09/05/2013
<i>Cochrane Library</i>	1980-5/2013	194	3	09/05/2013
<i>Psychinfo</i>	1980-5/2013	2	0	09/05/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-5/2013	246	5	09/05/2013

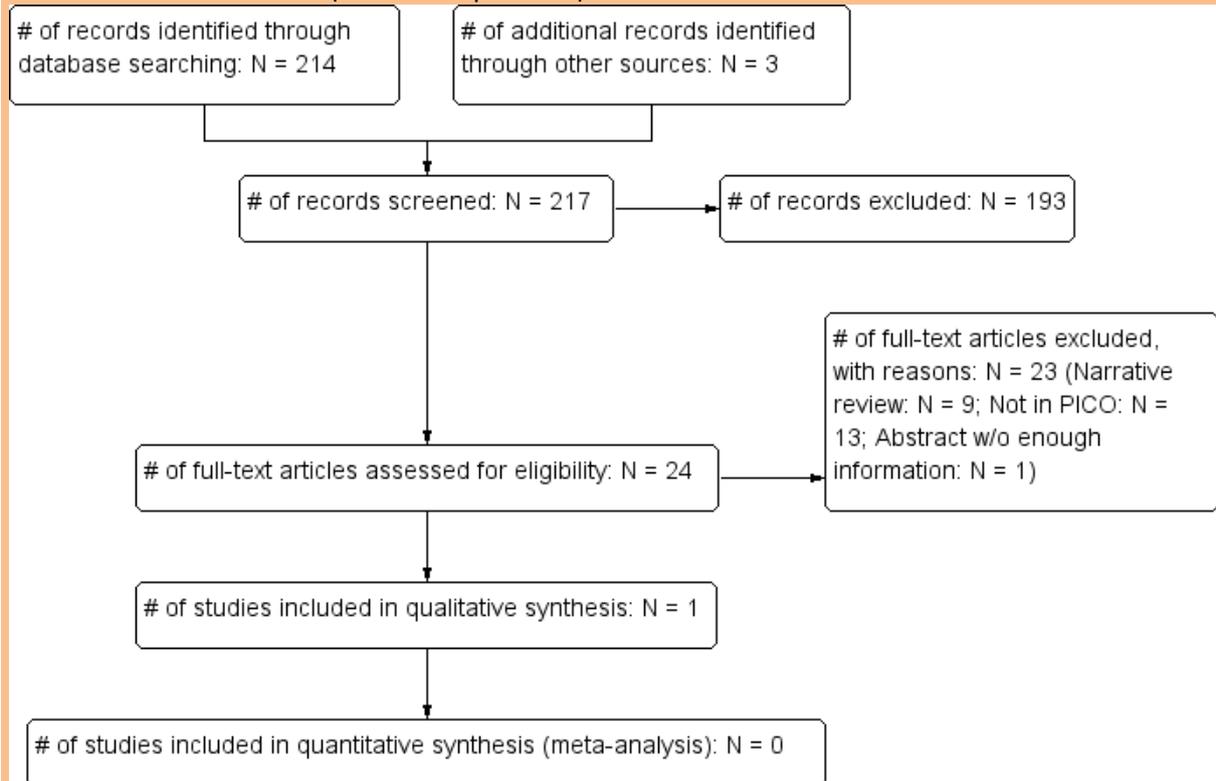
Total References retrieved (after de-duplication): 190

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-20/08/2014	23	0	20/08/2014

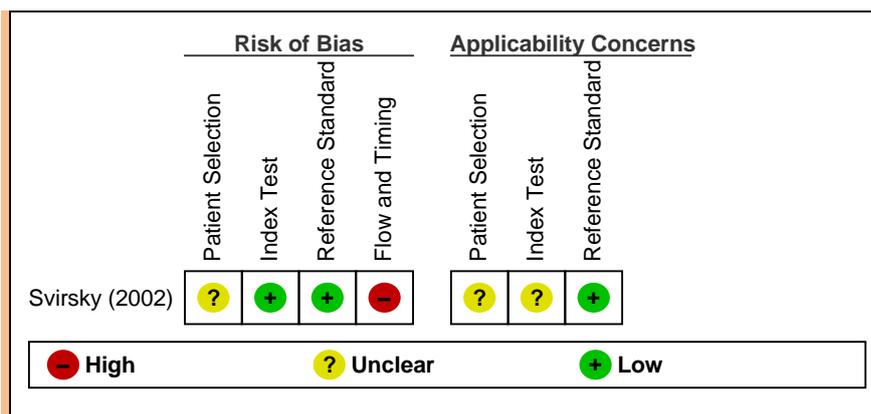
Premedline	5/2013-20/08/2014	75	20	20/08/2014
Embase	5/2013-20/08/2014	58	6	20/08/2014
Cochrane Library	5/2013-20/08/2014	98	0	20/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	5/2013-20/08/2014	11	1	20/08/2014

Total References retrieved (after de-duplication): 24



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included study in the figure below. The study was associated with a number of bias and validity issues. The following issues compromise the validity and applicability of this study, (1) it is unclear (and probably unlikely) that the patient population consists of consecutive or randomly recruited patients (and may therefore bias the results), (2) the study is conducted in the USA in an unclear setting and it is therefore not clearly transferable to UK-based primary care, and (3) the timespan between the index test and reference standard is unclear in all but one patient and the results are therefore compromised to an unknown extent.



Study results

Table 1: Oral cancer: Study results

Study	Test	Prevalence	Sensitivity (95% CI) %	Specificity (95% CI) %	Other results (95% CI)
Svirsky (2002)	Transepithelial oral brush biopsy with a computer-assisted method of analysis	15/298	93.3 (66-99.7)	19.1 (14.8-24.3)	<u>Malignancy:</u> TP = 14 FN = 1 TN = 54 FP = 229 Positive predictive value = 5.76 (3.3-9.7)% Negative predictive value = 98.18 (89-99.9)% False negativity rate = 6.7%
Svirsky (2002)	Transepithelial oral brush biopsy with a computer-assisted method of analysis	97/298	95.88 (89.2-98.7)%	25.37 (19.6-32.1)%	<u>Malignancy and dysplasia:</u> TP = 93 FN = 4 TN = 51 FP = 150 Positive predictive value = 38.27 (32.2-44.7) % Negative predictive value = 92.73 (81.6-97.6)% False negativity rate = 4.12%

TP = true positives, FP = false positives, TN = true negatives, FN = false negatives.

Evidence statement(s):

Transepithelial oral brush biopsy with a computer-assisted method of analysis (1 study, N = 298) is associated with a sensitivity of 93.3%, a specificity of 19.1%, a positive predictive value of 5.76%, and a false negativity rate of 6.7% for oral cancer. Transepithelial oral brush biopsy with a computer-assisted method of analysis (1 study, N = 298) is associated with a sensitivity of 95.88%, a specificity of 25.37%, a positive predictive value of 38.27%, and a false negativity rate of 4.12% for oral cancer/dysplasia. The study was associated with 4 bias or applicability concerns (see also Table 1).

Evidence tables

Svirsky (2002)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 298 (146 males/152 females), mean (range) age = 52 (18-89); location of surgical biopsy: Ventral/lateral tongue (N = 90), palate (N = 63), gingival (N = 65), buccal/alveolar mucosa (N = 43), floor of mouth (N = 8), unspecified/other (N = 29). <u>Inclusion criteria</u> : "This study analyzed scalpel biopsies with test requisition forms that either were accompanied by an oral brush biopsy report or contained the findings of an oral brush biopsy report. Only oral pathology laboratories were included." "A total of 298 patients with scalpel biopsies that were accompanied by prior brush biopsy results were identified in the authors' laboratories". <u>Exclusion criteria</u> : None reported. <u>Clinical setting</u> : Unclear, USA
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Transepithelial oral brush biopsy with a computer-assisted method of analysis (OralCDx, CDx Laboratories, NY).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Scalpel biopsy
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

FLOW AND TIMING	
A. risk of bias	
Flow and timing	Data are available for all the included patients, but for least one of the patients the brush and scalpel biopsies were obtained 8 months apart.
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	High risk
NOTES	

References

Included studies

Svirsky, J. A., Burns, J. C., Carpenter, W. M. & et.al. (2002) Comparison of computer-assisted brush biopsy results with follow up scalpel biopsy and histology. *Gen Dent*, 50: 500-503.

Excluded studies (with excl reason)

Reference List

(2002) Study: one in 10 dental professionals had oral lesions that required additional testing.

Dentistry Today, 21: 40.

Narrative review

(2008) Guideline for the early detection of oral cancer in British Columbia 2008. *Journal (Canadian Dental Association)*, 74: 245.

Guideline

(2010) High-tech oral cancer detection. Less invasive, less painful microchip technology could identify mouth cancers in the very early stages. *Duke Medicine Health News*, 16: 4-5.

Not in PICO

Ahmed, S. M., Mubeen & Jigna, V. R. (2009) Molecular biology: an early detector of oral cancers.

Annals of Diagnostic Pathology, 13: 140-145.

Narrative review

Ahn, S.-H., Jeong, W.-J., Sung, M.-W. & Kim, K.-H. (2011) Management of lateral tongue leukoplakia proven as benign in incisional biopsy. *Oral Oncology*, 47: S93-S94.

Not in PICO

Ajayi, B. A., Pugh, N. D., Carolan, G. & Woodcock, J. P. (1992) Salivary gland tumours: Is colour Doppler imaging of added value in their preoperative assessment? *European Journal of Surgical Oncology*, 18: 463-468.

Not in PICO

Akrish, S., Buchner, A. & Dayan, D. (1993) Oral cancer: diagnostic options as an aid to histology in order to predict patients at high risk for malignant transformation. *Refuat Hapeh Vehashinayim*, 21: 6-15.

Narrative review

Allegra, E., Lombardo, N., Puzzo, L. & Garozzo, A. (2009) The usefulness of toluidine staining as a diagnostic tool for precancerous and cancerous oropharyngeal and oral cavity lesions. [Italian].

Acta Otorhinolaryngologica Italica, 29: 187-190.

Not in PICO

Allon, I., Allon, D. M., Gal, G., Anavi, Y., Chaushu, G. & Kaplan, I. (2013) Re-evaluation of common paradigms regarding the clinical appearance of oral mucosal malignancies. *Journal of Oral*

- Pathology & Medicine*, 42: 670-675.
Not in PICO
- Allon, I., Allon, D. M., Anavi, Y. & Kaplan, I. (2013) The significance of surface ulceration as a sign of malignancy in exophytic oral mucosal lesions: myth or fact? *Head and neck pathology*, 7: 149-154.
Not in PICO
- Aradore, M., Tempia, V. G., Pentenero, M. & Gandolfo, S. (2012) Role of VELscope test in the assessment of oral mucosal lesions suspected to be oncologically relevant. [Italian]. *Dental Cadmos*, 80: 538-546.
Not in PICO (On the basis of the clinical diagnostic suspicion and state of dysplasia / carcinoma in 31/67 lesions, while the remaining 35/66 led to a clinical diagnosis of precancerous dysplasia probably without)
- Bahar, G., Dudkiewicz, M., Feinmesser, R., Joshua, B. Z., Braslavsky, D., Popovtzer, A., Galil, D. & Shpitzer, T. (2006) Acute parotitis as a complication of fine-needle aspiration in Warthin's tumor. A unique finding of a 3-year experience with parotid tumor aspiration. *Otolaryngology - Head & Neck Surgery*, 134: 646-649.
Not in PICO
- Bajaj, D. R., Khoso, N. A., Devrajani, B. R., Matlani, B. L. & Lohana, P. (2010) Oral lichen planus: A clinical study. *Journal of the College of Physicians and Surgeons Pakistan*, 20: 154-157.
Not in PICO
- Bakebua, B. P. (1987) Oral smear--early detection of oral malignant tumours. *Odonto-Stomatologie Tropicale*, 10: 45-50.
Not in PICO
- Balakrishnan, K., Castling, B., McMahon, J., Imrie, J., Feeley, K. M., Parker, A. J., Bull, P. D. & Johnston, A. (2005) Fine needle aspiration cytology in the management of a parotid mass: a two centre retrospective study. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 3: 67-72.
Not in PICO
- Bassi, K. K., Srivastava, A., Seenu, V., Kumar, R., Parshad, R., Chumber, S., Gupta, S. D. & Bahadur, S. (2013) The first and second echelon sentinel lymph node evaluation in oral cancer. *Indian Journal of Surgery*, 75: 377-382.
Not in PICO
- Bentley, R. H., Johnson, S. J. & Sloan, P. (2011) Audit of pre-operative fine needle aspiration cytology (FNAC) for suspected salivary neoplasms. *Cytopathology*, 22: ii.
Published as abstract only. Not enough information available, but I think it is "Not in PICO".
- Bhalla, R., Parker, D. C. & Tadros, T. S. (2006) Salivary duct carcinoma metastatic to inguinal lymph node: a case report of salivary duct carcinoma with distant metastasis diagnosed by fine-needle aspiration. *Diagnostic Cytopathology*, 34: 41-44.
Not in PICO
- Bocking, A., Sproll, C., Stocklein, N., Naujoks, C., Depprich, R., Kubler, N. R. & Handschel, J. (2011) Role of brush biopsy and DNA cytometry for prevention, diagnosis, therapy, and followup care of oral cancer. *Journal of Oncology Print*, 2011: 875959.
Narrative review
- Borgemeester, M. C., van den Brekel, M. W., van, T. H., Smeele, L. E., Pameijer, F. A., van Velthuysen, M. L. & Balm, A. J. (2008) Ultrasound-guided aspiration cytology for the assessment of the clinically NO neck: factors influencing its accuracy. *Head & Neck*, 30: 1505-1513.
Not in PICO
- Bradley, P. J. & McGurk, M. (2013) Incidence of salivary gland neoplasms in a defined UK population. *British Journal of Oral & Maxillofacial Surgery*, 51: 399-403.
Not in PICO

- Brennan, P. A., Davies, B., Poller, D., Mead, Z., Bayne, D., Puxeddu, R. & Oeppen, R. S. (2010) Fine needle aspiration cytology (FNAC) of salivary gland tumours: repeat aspiration provides further information in cases with an unclear initial cytological diagnosis. *British Journal of Oral & Maxillofacial Surgery*, 48: 26-29.
Not in PICO
- British Columbia Oral Cancer Prevention Program, B. C. A. & College of Dental Surgeons of British Columbia (2008) Guideline for the early detection of oral cancer in British Columbia 2008. *Journal (Canadian Dental Association)*, 74: 245.
Guideline
- Brogie, M. A., Haerle, S. K., Huber, G. F., Haile, S. R. & Stoeckli, S. J. (2013) Occult metastases detected by sentinel node biopsy in patients with early oral and oropharyngeal squamous cell carcinomas: Impact on survival. *Head and Neck*, 35: 660-666.
Not in PICO
- Brown, J. S., Griffith, J. F., Phelps, P. D. & Browne, R. M. (1994) A comparison of different imaging modalities and direct inspection after periosteal stripping in predicting the invasion of the mandible by oral squamous cell carcinoma. *British Journal of Oral & Maxillofacial Surgery*, 32: 347-359.
Not in PICO
- Canto, M. T., Horowitz, A. M., Drury, T. F. & Goodman, H. S. (2002) Maryland family physicians' knowledge, opinions and practices about oral cancer. *Oral Oncology*, 38: 416-424.
Not in PICO
- Carpenter, W. M. & Silverman S Jr (2001) Oral cancer: the role of the dentist in prevention and early detection. *Dentistry Today*, 20: 92-97.
Narrative review
- Casparis, S., Borm, J. M., Tomic, M. A., Burkhardt, A. & Locher, M. C. (2014) Transepithelial brush biopsy - Oral CDx - A noninvasive method for the early detection of precancerous and cancerous lesions. *Journal of Clinical and Diagnostic Research*, 8: 222-226.
Not in PICO (secondary care)
- Chaudhari, V. V., Dandekar, R., Mahajan, A. M. & Prakash, N. (2014) - Sediment cytology in diagnostic evaluation of oral neoplasms. - *Indian Journal of Dental Research*, 25: 147-149.
Not in PICO
- Chen, C. T., Wang, C. Y., Kuo, Y. S., Chiang, H. H., Chow, S. N., Hsiao, I. Y. & Chiang, C. P. (1996) Light-induced fluorescence spectroscopy: a potential diagnostic tool for oral neoplasia. *Proceedings of the National Science Council, Republic of China - Part B, Life Sciences*, 20: 123-130.
Narrative review
- Chiesa, F., Mauri, S., Grana, C., Tradati, N., Calabrese, L., Ansarin, M., Mazzarol, G. & Paganelli, G. (2000) Is there a role for sentinel node biopsy in early N0 tongue tumors? *Surgery*, 128: 16-21.
Not in PICO
- Civantos, F., Zitsch, R. & Bared, A. (2007) Sentinel node biopsy in oral squamous cell carcinoma. [Review] [49 refs]. *Journal of Surgical Oncology*, 96: 330-336.
Not in PICO
- Collins, B. M. (2002) The oral brush biopsy: an adjunct to early oral cancer detection. *Pennsylvania Dental Journal*, 69: 35-37.
Narrative review
- Cornfield, D., Liu, Z., Gorczyca, W. & Weisberger, J. (2003) The potential role of flow cytometry in the diagnosis of small cell carcinoma. *Archives of Pathology & Laboratory Medicine*, 127: 461-464.
Not in PICO
- Costa Fontes, K. B., Cunha, K. S., Rodrigues, F. R., Silva, L. E. & Dias, E. P. (2013) Concordance between cytopathology and incisional biopsy in the diagnosis of oral squamous cell carcinoma. *Pesquisa Odontologica Brasileira = Brazilian Oral Research*, 27: 122-127.
Not in PICO

- Cruz, I. B., Snijders, P. J., Meijer, C. J., Braakhuis, B. J., Snow, G. B., Walboomers, J. M. & van, d. W., I (1998) p53 expression above the basal cell layer in oral mucosa is an early event of malignant transformation and has predictive value for developing oral squamous cell carcinoma. *Journal of Pathology*, 184: 360-368.
Not in PICO
- Daneshbod, Y., Oryan, A., Davarmanesh, M., Shirian, S., Negahban, S., Aledavood, A., Davarpanah, M. A., Soleimanpoor, H. & Daneshbod, K. (2011) Clinical, histopathologic, and cytologic diagnosis of mucosal leishmaniasis and literature review. [Review]. *Archives of Pathology & Laboratory Medicine*, 135: 478-482.
Not in PICO
- Das, D. K. & Anim, J. T. (2005) Pleomorphic adenoma of salivary gland: to what extent does fine needle aspiration cytology reflect histopathological features? *Cytopathology*, 16: 65-70.
Not in PICO
- Dequanter, D., Shahla, M., Paulus, P. & Lothaire, P. (2013) Long term results of sentinel lymph node biopsy in early oral squamous cell carcinoma. *OncoTargets and therapy*, 6: 799-802.
Not in PICO
- Descamps, G., Duray, A., Rodriguez, A., Chantrain, G., Depuydt, C. E., Delvenne, P. & Saussez, S. (2012) Detection and quantification of human papillomavirus in benign and malignant parotid lesions. *Anticancer Research*, 32: 3929-3932.
Not in PICO
- Dhanalakshmi, M., Lakshmana, R. L., Krishnaswamy, M. U., Gopalakrishnan, K. R. & Aruna, P. (2009) Fine needle aspiration cytology and histopathology of salivary gland lesions: A correlative study in a rural teaching hospital. *Journal of Chinese Clinical Medicine*, 4: 674-680.
Not in PICO
- Divani, S., Exarhou, M., Theodorou, L.-N., Georgantzis, D. & Skoulakis, H. (2009) Advantages and difficulties of brush cytology in the identification of early oral cancer. *Archive of Oncology*, 17: 11-12.
Not in PICO
- Driemel, O., Murzik, U., Escher, N., Melle, C., Bleul, A., Dahse, R., Reichert, T. E., Ernst, G. & von, E. F. (2007) Protein profiling of oral brush biopsies: S100A8 and S100A9 can differentiate between normal, premalignant, and tumor cells. *Proteomics Clinical Applications*, 1: 486-493.
Not in PICO
- Elwood, J. M. & Gallagher, R. P. (1985) Factors influencing early diagnosis of cancer of the oral cavity. *CMAJ Canadian Medical Association Journal*, 133: 651-656.
Not in PICO
- Epstein, J. B., Scully, C. & Spinelli, J. (1992) Toluidine blue and Lugol's iodine application in the assessment of oral malignant disease and lesions at risk of malignancy. *Journal of Oral Pathology and Medicine*, 21: 160-163.
Not in PICO
- Epstein, J. B., Guneri, P., Boyacioglu, H. & Abt, E. (2012) The limitations of the clinical oral examination in detecting dysplastic oral lesions and oral squamous cell carcinoma. *Journal of the American Dental Association*, 143: 1332-1342.
Not in PICO
- Ergun, S., Ozel, S., Koray, M., Kurklu, E., Ak, G. & Tanyeri, H. (2009) Dentists' knowledge and opinions about oral mucosal lesions. *International Journal of Oral & Maxillofacial Surgery*, 38: 1283-1288.
Not in PICO
- Ethunandan, M., Davies, B., Pratt, C. A., Puxeddu, R. & Brennan, P. A. (2009) Primary epithelial submandibular salivary gland tumours--review of management in a district general hospital setting. *Oral Oncology*, 45: 173-176.
Not in PICO

- Florentine, B. D., Staymates, B., Rabadi, M., Barstis, J., Black, A. & Cancer Committee of the Henry Mayo Newhall Memorial Hospital (2006) The reliability of fine-needle aspiration biopsy as the initial diagnostic procedure for palpable masses: a 4-year experience of 730 patients from a community hospital-based outpatient aspiration biopsy clinic. *Cancer*, 107: 406-416.
Not in PICO (40% referrals from primary care practitioners; results not split by referral type)
- Folia, M., Kany, M., Fillola, G., Serrano, E. & Pessey, J. J. (2002) [Value of of fine-needle aspiration cytology and MRI in parotid gland masses]. [French]. *Revue de Laryngologie Otologie Rhinologie*, 123: 153-157.
Not in PICO
- Foroughi, R., Seyedmajidi, M., Bijani, A. & Omid, D. M. (2013) Comparison of clinical diagnosis and histopathological report of referred biopsies to oral and maxillofacial pathology department of dental school of Babol, Iran (2003-2010). *Journal of Babol University of Medical Sciences*, 15: 71-77.
Not in PICO
- Francisco, A. L. N., Correr, W. R., Kurachi, C., Pinto, C. A. L. & Kowalski, L. P. (2010) Fluorescence spectroscopy for early detection of oral cancer. *Histopathology*, 57: 133.
Not in PICO
- Francisco, A. L. N., Correr, W. R., Azevedo, L. H., Kern, V. G., Pinto, C. A. L., Kowalski, L. P. & Kurachi, C. (2014) Fluorescence spectroscopy for the detection of potentially malignant disorders and squamous cell carcinoma of the oral cavity. *Photodiagnosis and Photodynamic Therapy*, 11: 82-90.
Not in PICO
- Franklin, C. D. & Jones, A. V. (2006) A survey of oral and maxillofacial pathology specimens submitted by general dental practitioners over a 30-year period. *British Dental Journal*, 200: 447-450.
Not in PICO
- Freitas, V. S., dos Santos, J. N., Oliveira, M. C., Santos, P. P., Freitas, R. A. & de Souza, L. B. (2012) Intraoral granular cell tumors: clinicopathologic and immunohistochemical study. *Quintessence International*, 43: 135-142.
Not in PICO
- Frydrych, A. M., Parsons, R., Threlfall, T., Austin, N., Davies, G. R., Booth, D. & Slack-Smith, L. M. (2010) Oral cavity squamous cell carcinoma survival by biopsy type: a cancer registry study. *Australian Dental Journal*, 55: 378-384.
Not in PICO
- Gandolfo, S., Carbone, M., Carrozzo, M. & Scamuzzi, S. (1993) [Biopsy technics in oral oncology: excisional or incisional biopsy? A critical review of the literature and the authors' personal contribution]. [Review] [38 refs] [Italian]. *Minerva Stomatologica*, 42: 69-75.
Narrative review
- Gillenwater, A., Papadimitrakopoulou, V. & Richards-Kortum, R. (2006) Oral premalignancy: New methods of detection and treatment. *Current Oncology Reports*, 8: 146-154.
Narrative review
- Gillenwater, A. M. & Chambers, M. S. (2006) Diagnosis of premalignant lesions and early cancers of the oral cavity. *Texas Dental Journal*, 123: 512-520.
Narrative review
- Gilliam, K. (1986) Saving lives in the dental office. *Dentistry Today*, 23: 84.
Narrative review
- Giroux-Slavas, J. (2000) Missing the diagnosis of oral cancer: recognition & liability. *Pennsylvania Dental Journal*, 67: 34-35.
Narrative review
- Godballe, C., Schultz, J. H., Krogdahl, A., Moller-Grontved, A. & Johansen, J. (2003) Parotid carcinoma: impact of clinical factors on prognosis in a histologically revised series. *Laryngoscope*,

113: 1411-1417.

Not in PICO

Goerres, G. W., Schmid, D. T., Schuknecht, B. & Eyrich, G. K. (2005) Bone invasion in patients with oral cavity cancer: comparison of conventional CT with PET/CT and SPECT/CT.[Erratum appears in *Radiology*. 2006 Apr;239(1):303]. *Radiology*, 237: 281-287.

Not in PICO

Gonsalves, W. C., Chi, A. C. & Neville, B. W. (2007) Common oral lesions: Part II. Masses and neoplasia. *American Family Physician*, 75: 509-512.

Narrative review

Gray, M., Gold, L., Burls, A. & Elley, K. (2000) The effectiveness of toluidine blue dye as an adjunct to oral cancer screening in general dental practice (DARE structured abstract). *Database of Abstracts of Reviews of Effects.*, 40.

Not in PICO

Gupta, S., Shah, J. S., Parikh, S., Limbdiwala, P. & Goel, S. (2014) - Clinical correlative study on early detection of oral cancer and precancerous lesions by modified oral brush biopsy and cytology followed by histopathology. - *Journal of Cancer Research & Therapeutics*, 10: 232-238.

Not in PICO

Gynther, G. W., Rozell, B. & Heimdahl, A. (2000) Direct oral microscopy and its value in diagnosing mucosal lesions: a pilot study. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics*, 90: 164-170.

Not in PICO

Habermann, C. R., Gossrau, P., Graessner, J., Arndt, C., Cramer, M. C., Reitmeier, F., Jaehne, M. & Adam, G. (2005) Diffusion-weighted echo-planar MRI: a valuable tool for differentiating primary parotid gland tumors?.[Erratum appears in *Rofo*. 2005 Sep;177(9):1312]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 177: 940-945.

Not in PICO

Hamad, L. O., Vervoorts, A., Hennig, T. & Bayer, R. (2010) Ex vivo photodynamic diagnosis to detect malignant cells in oral brush biopsies. *Lasers in medical science*, 25: 293-301.

Not in PICO

Hanken, H., Kraatz, J., Smeets, R., Heiland, M., Assaf, A. T., Blessmann, M., Eichhorn, W., Clauditz, T. S., Grobe, A., Kolk, A. & Rana, M. (2013) The detection of oral pre-malignant lesions with an autofluorescence based imaging system (VELscope) - a single blinded clinical evaluation.[Erratum appears in *Head Face Med*. 2013;9:26 Note: Assaf, Alexandre Thomas [added]]. *Head & Face Medicine*, 9: 23.

Not in PICO

Haris, P. S., Balan, A., Jayasree, R. S. & Gupta, A. K. (2009) Autofluorescence spectroscopy for the in vivo evaluation of oral submucous fibrosis. *Photomedicine and Laser Surgery*, 27: 757-761.

Not in PICO

Hartig, G., Zhang, J., Voytovich, G. M., Newton, M., Chen, A., Collins, S. P. & Wu, S. Q. (2000) Fluorescent in situ hybridization evaluation of p53 gene deletions at a tumor interface of lingual carcinoma. *Laryngoscope*, 110: 1474-1478.

Not in PICO

Hasegawa, Y., Terada, A., Yatabe, Y., Hanai, N., Ozawa, T. & Hirakawa, H. (2011) Sentinel lymph node biopsy in early tongue cancer patients. *Oral Oncology*, 47: S16.

Not in PICO

Heller, K. S., Dubner, S., Chess, Q. & Attie, J. N. (1992) Value of fine needle aspiration biopsy of salivary gland masses in clinical decision-making. *American Journal of Surgery*, 164: 667-670.

Not in PICO

Hsieh, R., Yen, M.-F., Chen, H.-H. & Zavras, A. (2013) Metabolic syndrome and development of oral neoplasms. *American Journal of Epidemiology*, 177: S60.

Not in PICO

- Hueston, W. J. & Kaur, D. (2013) Upper respiratory conditions: oral cancers. *Fp Essentials*, 415: 22-26.
Narrative review
- Ikeda, M., Motoori, K., Hanazawa, T., Nagai, Y., Yamamoto, S., Ueda, T., Funatsu, H. & Ito, H. (2004) Warthin tumor of the parotid gland: diagnostic value of MR imaging with histopathologic correlation. *Ajnr: American Journal of Neuroradiology*, 25: 1256-1262.
Not in PICO
- Isaac, U., Isaac, J. S. & Memon, F. (2009) Presentation of histological types and common sites of oral cancers in lower Sindh. *Journal of the Liaquat University of Medical and Health Sciences*, 8: 210-213.
Not in PICO
- Iseli, T. A., Lin, M. J., Tsui, A., Guiney, A., Wiesenfeld, D. & Iseli, C. E. (2012) Are wider surgical margins needed for early oral tongue cancer? *Journal of Laryngology & Otology*, 126: 289-294.
Not in PICO
- Jainkittivong, A., Swadison, S., Thangpitsityotin, M. & Langlais, R. P. (2009) Oral squamous cell carcinoma: a clinicopathological study of 342 Thai cases. *The journal of contemporary dental practice*, 10: E033-E040.
Not in PICO
- James, K., Toner, M. & Stassen, L. F. (2011) Performing mucosal tissue biopsies in general dental practice. *Journal of the Irish Dental Association*, 57: 203-208.
Narrative review
- Jayanthi, J. L., Nisha, G. U., Manju, S., Philip, E. K., Jeemon, P., Baiju, K. V., Beena, V. T. & Subhash, N. (2011) Diffuse reflectance spectroscopy: diagnostic accuracy of a non-invasive screening technique for early detection of malignant changes in the oral cavity. *BMJ Open*, 1: e000071.
Not in PICO
- Jeong, W. J., Paik, J. H., Cho, S. W., Sung, M. W., Kim, K. H. & Ahn, S. H. (2012) Excisional biopsy for management of lateral tongue leukoplakia. *Journal of Oral Pathology & Medicine*, 41: 384-388.
Not in PICO
- Jiang, C. F., Wang, C. Y. & Chiang, C. P. (2004) Oral cancer detection in fluorescent image by color image fusion. *Conference Proceedings: ...Annual International Conference of the IEEE Engineering in Medicine & Biology Society*, 2: 1260-1262.
Narrative review
- Jones, D. L. & Rankin, K. V. (2013) Oral cancer: FAQ.[Reprint of *Tex Dent J*. 2013 May;130(5):438-43; PMID: 23923466]. *Journal of Michigan Dental Association*, 95: 32-35.
Narrative review
- Kahn, M. A., Lynch, D. P., Turner, J. E. & Mincer, H. H. (1998) The dos and don'ts of an oral mucosal biopsy performed by the general dentist. *The Journal of the Tennessee Dental Association*, 78: 28-31.
Narrative review
- Kammerer, P. W., Koch, F. P., Santoro, M., Babaryka, G., Biesterfeld, S., Brieger, J. & Kunkel, M. (2013) Prospective, blinded comparison of cytology and DNA-image cytometry of brush biopsies for early detection of oral malignancy. *Oral Oncology*, 49: 420-426.
Not in PICO
- Kannan, S., Thakkar, P. & Dcruz, A. K. (2011) Tuberculosis masquerading as oral malignancy. *Indian journal of medical and paediatric oncology : official journal of Indian Society of Medical & Paediatric Oncology*, 32: 180-182.
Not in PICO
- Kantola, S., Parikka, M., Jokinen, K., Hyrynkangas, K., Soini, Y., Alho, O. P. & Salo, T. (2000) Prognostic factors in tongue cancer - relative importance of demographic, clinical and histopathological factors. *British Journal of Cancer*, 83: 614-619.
Not in PICO

- Kaugars, G. E., Silverman, J., Ray, A. K., Page, D. G., Abbey, L. M., Burns, J. C. & Svirsky, J. A. (1998) The use of exfoliative cytology for the early diagnosis of oral cancers: Is there a role for it in education and private practice? *Journal of Cancer Education*, 13: 85-89.
Not in PICO
- Kawaratani, H., Tsujimoto, T., Yoshikawa, M., Kawanami, F., Shirai, Y., Yoshiji, H., Morita, K. & Fukui, H. (2013) Large cell neuroendocrine carcinoma presenting with neck swelling in the submandibular gland: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 7: 81.
Not in PICO
- Kerr, A. R. & Cruz, G. D. (2002) Oral cancer. Practical prevention and early detection for the dental team. *New York State Dental Journal*, 68: 44-54.
Narrative review
- Klijanienko, J. & Vielh, P. (1997) Fine-needle sampling of salivary gland lesions. IV. Review of 50 cases of mucoepidermoid carcinoma with histologic correlation. [Review] [41 refs]. *Diagnostic Cytopathology*, 17: 92-98.
Not in PICO
- Klijanienko, J., el-Naggar, A. K. & Vielh, P. (1999) Comparative cytologic and histologic study of fifteen salivary basal-cell tumors: differential diagnostic considerations. *Diagnostic Cytopathology*, 21: 30-34.
Not in PICO
- Koerner, K. R. (2006) Evaluation and treatment by general dentists of oral soft-tissue lesions. *Dentistry Today*, 25: 90-95.
Narrative review
- Kokalj, V. N., Cizmarevic, B., Zagorac, A., Zagradisnik, B. & Lanisnik, B. (2014) - An evaluation of SOX2 and hTERT gene amplifications as screening markers in oral and oropharyngeal squamous cell carcinomas. - *Molecular Cytogenetics*, 7: 5.
Not in PICO
- Kokalj, V. N., Cizmarevic, B., Zagorac, A., Zagradisnik, B. & Lanisnik, B. (2014) An evaluation of SOX2 and hTERT gene amplifications as screening markers in oral and oropharyngeal squamous cell carcinomas. *Molecular Cytogenetics*, 7: 5.
Not in PICO
- Kominek, P., Vitek, P., Urban, O., Zelenik, K., Halamka, M., Feltl, D., Cvek, J. & Matousek, P. (2013) Chromoendoscopy to detect early synchronous second primary esophageal carcinoma in patients with squamous cell carcinomas of the head and neck? *Gastroenterology research & practice*, 2013: 236264.
Not in PICO
- Kondori, I., Mottin, R. W. & Laskin, D. M. (2011) Accuracy of dentists in the clinical diagnosis of oral lesions. *Quintessence International*, 42: 575-577.
Not in PICO
- Kotecha, S., Bhatia, P. & Rout, P. G. (533) Diagnostic ultrasound in the head and neck region. *Dental Update*, 35: 529-530.
Narrative review
- Krahl, D., Altenburg, A. & Zouboulis, C. C. (2008) Reactive hyperplasias, precancerous and malignant lesions of the oral mucosa. [Review] [19 refs]. *Journal der Deutschen Dermatologischen Gesellschaft*, 6: 217-232.
Narrative review
- Kress, E., Schulz, H. G. & Neumann, T. (1993) [Diagnosis of diseases of the large salivary glands of the head by ultrasound, sialography and CT-sialography. A comparison of methods]. [German]. *HNO*, 41: 345-351.
Not in PICO

- Kusukawa, J., Kameyama, T. & Nakamura, Y. (1998) Evaluation of excisional biopsy for stage I and II squamous cell carcinoma of the oral cavity. *International Journal of Clinical Oncology*, 3: 317-322.
Not in PICO
- Laronde, D. M., Williams, P. M., Hislop, T. G., Poh, C., Ng, S., Zhang, L. & Rosin, M. P. (2014) - Decision making on detection and triage of oral mucosa lesions in community dental practices: screening decisions and referral. - *Community Dentistry & Oral Epidemiology*, 42: 375-384.
Not in PICO
- Laudenbach, J. M. (2013) Oral medicine update: oral cancer--screening, lesions and related infections. *Journal of the California Dental Association*, 41: 326-328.
Narrative review
- Lee, Y. Y., Wong, K. T., King, A. D. & Ahuja, A. T. (2008) Imaging of salivary gland tumours. [Review] [44 refs]. *European Journal of Radiology*, 66: 419-436.
Narrative review
- Leunig, A., Betz, C. S., Mehlmann, M., Stepp, H., Arbogast, S., Grevers, G. & Baumgartner, R. (2000) Detection of squamous cell carcinoma of the oral cavity by imaging 5-aminolevulinic acid-induced protoporphyrin IX fluorescence. *Laryngoscope*, 110: 78-83.
Not in PICO
- Litonjua, L. S. (1997) Algorithm for the management of oral pathologic lesions. *Journal of the Philippine Dental Association*, 49: 60-63.
Narrative review
- Liu Joseph, L. Y., Walsh, T., Kerr, A. R., Lingen, M., Brocklehurst, P., Ogden, G., Warnakulasuriya, S. & Scully, C. (2012) Diagnostic tests for oral cancer and potentially malignant disorders in patients presenting with clinically evident lesions. *Cochrane Database of Systematic Reviews*.
Protocol
- Liu, W., Shi, L. J., Wu, L., Feng, J. Q., Yang, X., Li, J., Zhou, Z. T. & Zhang, C. P. (2012) Oral cancer development in patients with leukoplakia--clinicopathological factors affecting outcome. *PLoS ONE [Electronic Resource]*, 7: e34773.
Not in PICO
- Liu, X., Bai, X. F. & Huang, S. H. (2012) [A diagnostic meta-analysis: sentinel lymph node biopsy for neck metastasis in patients with early oral squamous cell carcinoma]. [Chinese]. *Chung-Hua Kou Chiang i Hsueh Tsa Chih Chinese Journal of Stomatology*, 47: 350-353.
Not in PICO
- Logan, R. M. & Goss, A. N. (2010) Biopsy of the oral mucosa and use of histopathology services. *Australian Dental Journal*, 55: Suppl-13.
Narrative review
- Lopez, J. P., Velandrino, N. A., Martinez, B. Y. & Fernandez, S. M. (2007) Attitude towards oral biopsy among general dentists in Murcia. *Medicina Oral, Patologia Oral y Cirugia Bucal*, 12: E116-E121.
Not in PICO
- Lydiatt, D. D. (2002) Cancer of the oral cavity and medical malpractice. *Laryngoscope*, 112: 816-819.
Not in PICO
- M S, Shetty, P., Decruz, A. M. & Pai, P. (2013) The Self-Reported Knowledge, Attitude and the Practices Regarding the Early Detection of Oral Cancer and Precancerous Lesions among the Practising Dentists of Dakshina Kannada-A Pilot Study. *Journal of Clinical and Diagnostic Research JCDR*, 7: 1491-1494.
Not in PICO
- MacCarthy, D., Flint, S. R., Healy, C. & Stassen, L. F. (2011) Oral and neck examination for early detection of oral cancer--a practical guide. *Journal of the Irish Dental Association*, 57: 195-199.
Narrative review
- MacCarthy, D., Nunn, J., Healy, C. M., Stassen, L. F., Gorman, T., Martin, B., Toner, M., Clarke, M., Dougall, A., McLoughlin, J., Kelly, A., Waldron, C., O'Sullivan, M., Doyle, C. & Flint, S. (2012) Outcomes from the first mouth cancer awareness and clinical check-up day in the Dublin Dental

- University Hospital. *Journal of the Irish Dental Association*, 58: 101-108.
Not in PICO
- Mao, L. (2010) Identifying the premalignant lesion at high risk for progression to cancer. *Cancer Prevention Research*, 3.
Narrative review
- Maraki, D., Becker, J. & Boecking, A. (2004) Cytologic and DNA-cytometric very early diagnosis of oral cancer. *Journal of Oral Pathology & Medicine*, 33: 398-404.
Not in PICO
- Martinez-Conde, R., Aguirre, J. M., Burgos, J. J. & Rivera, J. M. (2001) Clinicopathological factors in early squamous cell carcinoma of the tongue and floor of the mouth, in Biscay (the Basque Country, Spain). [Spanish, English]. *Medicina Oral*, 6: 87-94.
Not in PICO
- Masthan, K. M. K., Aravindha, B. N., Dash, K. C. & Elumalai, M. (2012) Advanced diagnostic aids in oral cancer. *Asian Pacific Journal of Cancer Prevention*, 13: 3573-3576.
Narrative review
- Matsuzuka, T., Miura, T., Suzuki, M., Yokoyama, S., Matsui, T., Nomoto, Y., Kunii, M., Saijoh, S. & Omori, K. (2011) Sentinel node biopsy for deciding neck dissection for early-stage tongue cancer. *Japanese Journal of Head and Neck Cancer*, 37: 355-358.
Not in PICO
- Matthias, C., Mack, B., Berghaus, A. & Gires, O. (2008) Keratin 8 expression in head and neck epithelia. *BMC Cancer*, 8: 267.
Not in PICO
- Maurer, K., Eschrich, K., Schellenberger, W., Bertolini, J., Rupf, S. & Remmerbach, T. W. (2013) Oral brush biopsy analysis by MALDI-ToF Mass Spectrometry for early cancer diagnosis. *Oral Oncology*, 49: 152-156.
Not in PICO
- McIntosh, L., McCullough, M. J. & Farah, C. S. (2009) The assessment of diffused light illumination and acetic acid rinse (Microlux/DL) in the visualisation of oral mucosal lesions. *Oral Oncology*, 45: e227-e231.
Not in PICO
- Mehrotra, R., Gupta, A., Singh, M. & Ibrahim, R. (2006) Application of cytology and molecular biology in diagnosing premalignant or malignant oral lesions. *Molecular Cancer*, 5.
Narrative review
- Mehrotra, R., Mishra, S., Singh, M. & Singh, M. (2011) The efficacy of oral brush biopsy with computer-assisted analysis in identifying precancerous and cancerous lesions. *Head & neck oncology*, 3: 39.
Same as Mehrotra 2011
- Mehrotra, R. & Gupta, D. K. (2011) Exciting new advances in oral cancer diagnosis: avenues to early detection. [Review]. *Head & neck oncology*, 3: 33.
Narrative review
- Mehrotra, R., Mishra, S. & Singh, M. (2011) The efficacy of oral brush biopsy with computer-assisted analysis in identifying precancerous and cancerous lesions. *Head and Neck Oncology*, 3.
Not in PICO
- Mehrotra, R. & Gupta, D. K. (2011) Exciting new advances in oral cancer diagnosis: Avenues to early detection. *Head and Neck Oncology*, 3.
Narrative review
- Mercadante, V., Paderni, C. & Campisi, G. (2012) Novel non-invasive adjunctive techniques for early oral cancer diagnosis and oral lesions examination. [Review]. *Current Pharmaceutical Design*, 18: 5442-5451.
Narrative review

- Messadi, D. V. (2013) Diagnostic aids for detection of oral precancerous conditions. [Review]. *International Journal of Oral Science*, 5: 59-65.
Narrative review
- Mittal, N., Palaskar, S. & Shankari, M. (2012) Rose Bengal staining - diagnostic aid for potentially malignant and malignant disorders: a pilot study. *Indian Journal of Dental Research*, 23: 561-564.
Not in PICO
- Monroe, M. M. & Gross, N. D. (2012) Evidence-based practice: management of the clinical node-negative neck in early-stage oral cavity squamous cell carcinoma. [Review]. *Otolaryngologic Clinics of North America*, 45: 1181-1193.
Narrative review
- Monroe, M. M. & Lai, S. Y. (2014) - Sentinel lymph node biopsy for oral cancer: supporting evidence and recent novel developments. - *Current Oncology Reports*, 16: 385.
Not in PICO
- Mordas, A., Blozelyte-Plesniene, L., Cepulis, V., Venius, J., Liutkeviciute-Navickiene, J. & Rutkovskiene, L. (2011) Intra-arterial fluorescence diagnostics of oral cancer. *European Journal of Cancer*, 47: S573.
Not in PICO
- Morelato, R. A., Herrera, M. C., Fernandez, E. N., Corball, A. G. & Lopez de Blanc, S. A. (2007) Diagnostic delay of oral squamous cell carcinoma in two diagnosis centers in Cordoba Argentina. *Journal of Oral Pathology & Medicine*, 36: 405-408.
Not in PICO
- Mota-Ramirez, A., Silvestre, F. J. & Simo, J. M. (2007) Oral biopsy in dental practice. [Review] [24 refs]. *Medicina Oral, Patologia Oral y Cirugia Bucal*, 12: E504-E510.
Narrative review
- Munde, A. D., Karle, R. R., Wankhede, P. K., Shaikh, S. S. & Kulkurni, M. (2013) Demographic and clinical profile of oral lichen planus: A retrospective study. *Contemporary Clinical Dentistry*, 4: 181-185.
Not in PICO
- Murata, Y., Yamada, I., Umehara, I., Okada, N. & Shibuya, H. (1998) Diagnostic accuracy of technetium-99m-pertechnetate scintigraphy with lemon juice stimulation to evaluate Warthin's tumor. *Journal of Nuclear Medicine*, 39: 43-46.
Not in PICO
- Murti, P. R., Warnakulasuriya, K. A., Johnson, N. W., Bhonsle, R. B., Gupta, P. C., Daftary, D. K. & Mehta, F. S. (1998) p53 expression in oral precancer as a marker for malignant potential. *Journal of Oral Pathology & Medicine*, 27: 191-196.
Not in PICO
- Nagaraju, K., Prasad, S. & Ashok, L. (2010) Diagnostic efficiency of toluidine blue with Lugol's iodine in oral premalignant and malignant lesions. *Indian Journal of Dental Research*, 21: 218-223.
Not in PICO
- Naugler, C. (2008) Practice tips. Brush biopsy sampling of oral lesions. *Canadian Family Physician*, 54: 194.
Narrative review
- Nayyar, A. S. (2012) Novel biochemical markers: early detection and prevention of malignant transformation a pilot study. *Acta Medica Iranica*, 50: 597-602.
Not in PICO
- Ng, S.-H., Chan, S.-C., Liao, C.-T., Chang, J. T. C., Ko, S.-F., Wang, H.-M., Chin, S.-C., Lin, C.-Y., Huang, S.-F. & Yen, T.-C. (2008) Distant metastases and synchronous second primary tumors in patients with newly diagnosed oropharyngeal and hypopharyngeal carcinomas: Evaluation of 18F-FDG PET and extended-field multi-detector row CT. *Neuroradiology*, 50: 969-979.
Not in PICO

- Nicotera, G., Di Stasio, S. M. & Angelillo, I. F. (2004) Knowledge and behaviors of primary care physicians on oral cancer in Italy. *Oral Oncology*, 40: 490-495.
Not in PICO
- Noorman van der Dussen MF (1994) [Oral cancer. The importance of early diagnosis and role of the dentist]. [French]. *Revue Belge de Medecine Dentaire*, 49: 35-49.
Narrative review
- Ogden, G., Lewthwaite, R. & Shepherd, S. D. (2013) Early detection of oral cancer: how do I ensure I don't miss a tumour? *Dental Update*, 40: 462-465.
Narrative review
- Oka, K., Chikamatsu, K., Eura, M., Katsura, F., Yumoto, E. & Tokunaga, H. (2002) [Clinical significance of fine-needle aspiration biopsy in major salivary gland tumors]. [Japanese]. *Nippon Jibiinkoka Gakkai Kaiho [Journal of the Oto-Rhino-Laryngological Society of Japan]*, 105: 1109-1115.
Not in PICO
- Omitola, O. G., Ajayi, O. F., Banjo, A. A., Anunobi, C. C. & Arotiba, G. T. (2010) The sensitivity, specificity and accuracy of fine needle aspirational cytology in the diagnosis of oro-facial neoplasms at Lagos University Teaching Hospital, Nigeria. *Odonto-Stomatologie Tropicale*, 33: 21-25.
Not in PICO
- Paderni, C., Compilato, D., Lo, M. L. & Campisi, G. (2010) Direct visualization of oral-cavity tissue fluorescence and toluidine blue staining: New adjunctive aids for oral medicine practitioners in early oral cancer diagnosis and potentially malignant disorders follow-up? *Oral Diseases*, 16: 535-536.
Not in PICO (tests)
- Pallagatti, S., Sheikh, S., Puri, N., Gupta, D. & Singh, B. (2011) Colposcopy: a new ray in the diagnosis of oral lesions. [Review]. *Indian Journal of Dental Research*, 22: 810-815.
Narrative review
- Patton, L. L., Epstein, J. B. & Kerr, A. R. (1993) Adjunctive techniques for oral cancer examination and lesion diagnosis: a systematic review of the literature. [Review] [34 refs]. *Journal of the American Dental Association*, 139: 896-905.
Duplicate
- Patton, L. L., Elter, J. R., Southerland, J. H. & Strauss, R. P. (2005) Knowledge of oral cancer risk factors and diagnostic concepts among North Carolina dentists: Implications for diagnosis and referral. *Journal of the American Dental Association*, 136: 602-610.
Not in PICO
- Patton, L. L., Epstein, J. B. & Kerr, A. R. (2008) Adjunctive techniques for oral cancer examination and lesion diagnosis a systematic review of the literature. *Journal of the American Dental Association*, 139: 896-905.
Not in PICO, but included cytopathology papers checked for relevance
- Pektas, Z. O., Keskin, A., Gunhan, O. & Karslioglu, Y. (2006) Evaluation of nuclear morphometry and DNA ploidy status for detection of malignant and premalignant oral lesions: quantitative cytologic assessment and review of methods for cytomorphometric measurements. *Journal of Oral & Maxillofacial Surgery*, 64: 628-635.
Not in PICO
- Pentenero, M., Carrozzo, M., Pagano, M., Galliano, D., Broccoletti, R., Scully, C. & Gandolfo, S. (2003) Oral mucosal dysplastic lesions and early squamous cell carcinomas: underdiagnosis from incisional biopsy. *Oral Diseases*, 9: 68-72.
Not in PICO
- Pentenero, M., Marino, R., Valenta, G. T., Navone, R. & Gandolfo, S. (2014) Microbiopsy a novel sampling technique to early detect dysplastic/malignant alterations in oral mucosal lesions: practicability by general dentists. *Journal of Oral Pathology & Medicine*, 43: 435-440.
Not in PICO

- Pentenero, M., Marino, R., Tempia, V. G., Navone, R. & Gandolfo, S. (2014) - Microbiopsy a novel sampling technique to early detect dysplastic/malignant alterations in oral mucosal lesions: practicability by general dentists. - *Journal of Oral Pathology & Medicine*, 43: 435-440.
Duplicate
- Pentenero, M., Marino, R., Tempia, V. G., Navone, R. & Gandolfo, S. (2014) Microbiopsy a novel sampling technique to early detect dysplastic/malignant alterations in oral mucosal lesions: Practicability by general dentists. *Journal of Oral Pathology and Medicine*, 43: 435-440.
Duplicate
- Pillay, M., Vasudevan, D. M., Rao, C. P. & Vidya, M. (2003) p53 expression in oral cancer: observations of a South Indian study. *Journal of Experimental & Clinical Cancer Research*, 22: 447-451.
Not in PICO
- Poate, T. W., Buchanan, J. A., Hodgson, T. A. & et.al. (2004) An audit of the efficacy of the oral brush biopsy technique in a specialist oral medicine unit. *Oral Oncology*, 40: 829-834.
Not in PICO
- Poh, C. F., Ng, S., Berean, K. W., Williams, P. M., Rosin, M. P. & Zhang, L. (2008) Biopsy and histopathologic diagnosis of oral premalignant and malignant lesions. *Journal (Canadian Dental Association)*, 74: 283-288.
Narrative review
- Poulias, E., Melakopoulos, I. & Tosios, K. (2011) Metastatic breast carcinoma in the mandible presenting as a periodontal abscess: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 5: 265.
Not in PICO
- Rajput, D. V. & Tupkari, J. V. (2010) Early detection of oral cancer: PAP and AgNOR staining in brush biopsies. *Journal of Oral & Maxillofacial Pathology*, 14: 52-58.
Not in PICO
- Regezi, J. A., Zarbo, R. J., Regev, E., Pisanty, S., Silverman, S. & Gazit, D. (1995) p53 protein expression in sequential biopsies of oral dysplasias and in situ carcinomas. *Journal of Oral Pathology & Medicine*, 24: 18-22.
Not in PICO
- Remmerbach, T. W., Meyer-Ebrecht, D., Aach, T., Wurflinger, T., Bell, A. A., Schneider, T. E., Nietzke, N., Frerich, B. & Bocking, A. (2009) Toward a multimodal cell analysis of brush biopsies for the early detection of oral cancer. *Cancer*, 117: 228-235.
Not in PICO
- Richards, D. (2010) Does toluidine blue detect more oral cancer? *Evidence-Based Dentistry*, 11: 104-105.
Not in PICO
- Robinson, P. N. & Mickelson, A. R. (2006) Early Diagnosis of Oral Cavity Cancers. *Otolaryngologic Clinics of North America*, 39: 295-306.
Narrative review
- Rogers, S. N., Pabla, R., McSorley, A., Lowe, D., Brown, J. S. & Vaughan, E. D. (2007) An assessment of deprivation as a factor in the delays in presentation, diagnosis and treatment in patients with oral and oropharyngeal squamous cell carcinoma. *Oral Oncology*, 43: 648-655.
Not in PICO
- Sardella, A., Demarosi, F., Lodi, G., Canegallo, L., Rimondini, L. & Carrassi, A. (2007) Accuracy of referrals to a specialist oral medicine unit by general medical and dental practitioners and the educational implications. *Journal of Dental Education*, 71: 487-491.
Not in PICO
- Scala, M., Moresco, L., Comandini, D., Monteghirfo, S. & Tomei, D. (1997) [The role of the general practitioner and dentist in the early diagnosis of preneoplastic and neoplastic lesions of the oral

- cavity]. [Italian]. *Minerva Stomatologica*, 46: 133-137.
Narrative review
- Scheifele, C., Schmidt-Westhausen, A.-M., Dietrich, T. & Reichart, P. A. (2004) The sensitivity and specificity of the OralCDx technique: Evaluation of 103 cases. *Oral Oncology*, 40: 824-828.
Not in PICO
- Schmid-Meier, E. (1984) [Diagnostic possibilities in suspected tumor]. [German]. *Schweizerische Monatsschrift für Zahnmedizin*, 94: Spec-7.
Not in PICO
- Schoengen, A., Binder, T., Krause, H. R., Stussak, G. & Zeelen, U. (1995) [The value of fine needle aspiration cytology in suspected neoplastic salivary gland enlargement]. [German]. *HNO*, 43: 239-243.
Not in PICO
- Sciubba, J. J. (1999) Improving detection of precancerous and cancerous oral lesions. Computer-assisted analysis of the oral brush biopsy. U.S. Collaborative OralCDx Study Group. *Journal of the American Dental Association*, 130: 1445-1457.
Primary care, but result not reported for index test negative patients (618/945)
- Scully, C. (1993) Clinical diagnostic methods for the detection of premalignant and early malignant oral lesions. [Review] [51 refs]. *Community Dental Health*, 10: Suppl-52.
Narrative review
- Scully, C. & Ward-Booth, R. P. (1995) Detection and treatment of early cancers of the oral cavity. [Review] [111 refs]. *Critical Reviews in Oncology-Hematology*, 21: 63-75.
Narrative review
- Scully, C. & Kirby, J. (2014) Statement on mouth cancer diagnosis and prevention. *British Dental Journal*, 216: 37-38.
Narrative review
- Sen, E., Basut, O., Ozturk, I., Demir, U. L., Ozmen, O. A., Kasapoglu, F. & Durgut, O. (2012) [The role of sentinel lymph node biopsy in oral cavity cancer]. [Turkish]. *Kulak Burun Bogaz Ihtisas Dergisi/Journal of Ear, Nose & Throat: Kbb*, 22: 81-86.
Not in PICO
- Seoane, J., Varela-Centelles, P. I., Ramirez, J. R., Cameselle-Teijeiro, J. & Romero, M. A. (2004) Artefacts in oral incisional biopsies in general dental practice: a pathology audit. *Oral Diseases*, 10: 113-117.
Not in PICO
- Shah, S. K., Le, M. C. & Carpenter, W. M. (2009) Retrospective review of pediatric oral lesions from a dental school biopsy service. *Pediatric Dentistry*, 31: 14-19.
Not in PICO
- Silverman S Jr (2000) Diagnosing oral lesions. Interview by Phillip Bonner. *Dentistry Today*, 19: 80-87.
Interview
- Silverman, J., Migliorati, C. & Barbosa, J. (1984) Toluidine blue staining in the detection of oral precancerous and malignant lesions. *Oral Surgery Oral Medicine and Oral Pathology*, 57: 379-382.
Not in PICO
- Silverman, J. (2000) Diagnosing oral lesions. Interview by Phillip Bonner. *Dentistry Today*, 19: 80-87.
Interview
- Silverman, S. (1994) Oral cancer. *Seminars in Dermatology*, 13: 132-137.
Narrative review
- Singh, T. & Schenberg, M. (2013) Delayed diagnosis of oral squamous cell carcinoma following dental treatment. *Annals of the Royal College of Surgeons of England*, 95: 369-373.
Not in PICO
- Sousa, F. B., - de Freitas e Silva MR, Fernandes, C. P., Silva, P. G. & Alves, A. P. (2014) - Oral cancer from a health promotion perspective: experience of a diagnosis network in Ceara. - *Pesquisa*

- Odontologica Brasileira = Brazilian Oral Research*, 28 Spec, 2014..
Not in PICO
- Stanley, R. E. (1991) Parapharyngeal space tumours. *Annals of the Academy of Medicine, Singapore*, 20: 589-596.
Not in PICO
- Stell, P. M., Wood, G. D. & Scott, M. H. (1982) Early oral cancer: treatment by biopsy excision. *British Journal of Oral Surgery*, 20: 234-238.
Not in PICO
- Subhash, N., Mallia, J. R., Thomas, S. S., Mathews, A., Sebastian, P. & Madhavan, J. (2006) Oral cancer detection using diffuse reflectance spectral ratio R540/R575 of oxygenated hemoglobin bands. *Journal of Biomedical Optics*, 11: 014018-014Feb.
Narrative review
- Sudbo, J., Bryne, M., Johannessen, A. C., Kildal, W., Danielsen, H. E. & Reith, A. (2001) Comparison of histological grading and large-scale genomic status (DNA ploidy) as prognostic tools in oral dysplasia.[Retraction in *J Pathol*. 2007 Jan;211(1):109; PMID: 17136756]. *Journal of Pathology*, 194: 303-310.
Not in PICO
- Sugerman, P. B. & Savage, N. W. (2002) Oral lichen planus: causes, diagnosis and management. [Review] [40 refs]. *Australian Dental Journal*, 47: 290-297.
Narrative review
- Svistun, E., Alizadeh-Naderi, R., El-Naggar, A., Jacob, R., Gillenwater, A. & Richards-Kortum, R. (2004) Vision enhancement system for detection of oral cavity neoplasia based on autofluorescence. *Head & Neck*, 26: 205-215.
Not in PICO
- Terada, T. (2011) Hepatocellular carcinoma metastatic to the gingiva as a first manifestation of hepatocellular carcinoma. *Journal of Maxillofacial & Oral Surgery*, 10: 271-274.
Not in PICO
- Thapasum, F. A., Faraz, M. & Shamaz, M. (2011) Primary care clinicians' knowledge of oral cancer: A Study of oral and general physicians in Kuala Muda & Kota Setar Districts, Malaysia. *Oral Oncology*, 47: S108.
Not in PICO
- To, E. W., Tsang, W. M., Cheng, J., Lai, E., Pang, P., Ahuja, A. T. & Ying, M. (2003) Is neck ultrasound necessary for early stage oral tongue carcinoma with clinically N0 neck? *Dento-Maxillo-Facial Radiology*, 32: 156-159.
Not in PICO
- Uppal, N. & Baliga, M. (2014) - Necrotizing sialometaplasia: A rare lesion that mimics oral cancer clinically and histopathologically. - *Otolaryngologia Polska*, 68: 154-156.
Not in PICO
- Urquhart, A., Hutchins, L. G. & Berg, R. L. (2001) Preoperative computed tomography scans for parotid tumor evaluation. *Laryngoscope*, 111: t-8.
Not in PICO
- van Heerden, W. F. & Butow, K. W. (2002) The role of the dentist in the prevention and early diagnosis of oral cancer. *SADJ*, 57: 22-24.
Narrative review
- van, d. W., I (2005) [Research methods in dentistry 7. Diagnostic tests in oral diseases]. [Review] [6 refs] [Dutch]. *Nederlands Tijdschrift Voor Tandheelkunde*, 112: 3-6.
Narrative review
- Vashisht, N., Ravikiran, A., Samatha, Y., Rao, P. C., Naik, R. & Vashisht, D. (2014) - Chemiluminescence and Toluidine Blue as Diagnostic Tools for Detecting Early Stages of Oral Cancer: An invivo Study. - *Journal of Clinical and Diagnostic Research JCDR*, 8: ZC35-ZC38.
Not in PICO

- Vercellino, V., Gandolfo, S., Camoletto, D., Griffa, B. & Mori, C. (1985) Toluidine blue (tolonium chloride) in the early diagnosis of dysplasias and carcinomas of the oral mucosa. [Italian]. *Minerva Stomatologica*, 34: 257-261.
Narrative review
- Vigneswaran, N. & Williams, M. D. (2014) - Epidemiologic trends in head and neck cancer and aids in diagnosis. - *Oral & Maxillofacial Surgery Clinics of North America*, 26: 123-141.
Narrative review
- Vora, H. H., Trivedi, T. I., Shukla, S. N., Shah, N. G., Goswami, J. V. & Shah, P. M. (2006) p53 expression in leukoplakia and carcinoma of the tongue. *International Journal of Biological Markers*, 21: 74-80.
Not in PICO
- Wakui, T., Hakata, Y., Doi, Y., Asano, K., Kawamata, H. & Imai, Y. (2014) Investigation of sentinel lymph node biopsy using genetic analysis in squamous cell carcinoma of the tongue. *Dokkyo Journal of Medical Sciences*, 41: 129-136.
Not in PICO
- Wan, A. & Savage, N. W. (2010) Biopsy and diagnostic histopathology in dental practice in Brisbane: usage patterns and perceptions of usefulness. *Australian Dental Journal*, 55: 162-169.
Not in PICO
- Wang, H.-C., Zuo, C.-T., Hua, F.-C., Huang, Z.-M., Tan, H.-B., Zhao, J. & Guan, Y.-H. (2010) Efficacy of conventional whole-body 18F-FDG PET/CT in the incidental findings of parotid masses. *Annals of Nuclear Medicine*, 24: 571-577.
Not in PICO
- Wang, Y. C., Fang, K. H., Jung, S. M., Zheng, J. & Hao, S. P. (2010) Excisional biopsy with margin control for oral cancers. *Head & Neck*, 32: 1528-1533.
Not in PICO
- Warnakulasuriya, K. A. A. S. & Nanayakkara, B. G. (1991) Reproducibility of An Oral-Cancer and Precancer Detection Program Using A Primary Health-Care Model in Sri-Lanka. *Cancer Detection and Prevention*, 15: 331-334.
Not in PICO
- Warnakulasuriya, S., Gould, A., Leuci, S., Mignogna, M., Seoane-Leston, J. M., Diz-Dios, P., McAlister, C., McEvoy, P., Thermidou, I. & Rapidis, A. D. (2013) Leonardo da Vinci Partnership - A lifelong learning programme to raise awareness of dental and medical professionals within Europe for the early detection of oral cancer - Phase 2. *Oral Oncology*, 49: S59.
Not in PICO
- White, M. W., Rajadhyaksha, M., Gonzalez, S., Fabian, R. L. & Anderson, R. R. (1999) Noninvasive imaging of human oral mucosa in vivo by confocal reflectance microscopy. *Laryngoscope*, 109: 1709-1717.
Not in PICO
- Whitesides, L. M., Ferreira, L. R. & Ord, R. A. (1995) Audit of clinical information and diagnoses supplied to the pathologist following biopsy of oral squamous cell carcinomas. *MSDA Journal*, 38: 63-65.
Not in PICO
- Williams, H. K., Hey, A. A. & Browne, R. M. (1997) The use by general dental practitioners of an oral pathology diagnostic service over a 20-year period: the Birmingham Dental Hospital experience. *British Dental Journal*, 182: 424-429.
Not in PICO
- Williams, P. M., Poh, C. F., Hovan, A. J., Ng, S. & Rosin, M. P. (2008) Evaluation of a suspicious oral mucosal lesion. *Journal (Canadian Dental Association)*, 74: 275-280.
Narrative review

- Wong, D. S. & Li, G. K. (2000) The role of fine-needle aspiration cytology in the management of parotid tumors: a critical clinical appraisal. *Head & Neck*, 22: 469-473.
Not in PICO
- Wyss, E., Mueller-Garamvolgyi, E., Ghadjar, P., Rauch, D., Zbaren, P. & Arnold, A. (2013) Diagnosis and treatment outcomes for patients with lymphoma of the parotid gland. *Laryngoscope*, 123: 662-669.
Not in PICO
- Yamauchi, M., Shinozaki, K., Doi, M., Nitta, T. & Nishisaka, T. (2014) - A Case of Gingival Metastasis from Rectal Cancer in Which Immunohistochemistry and PET-CT Were Useful for the Diagnostic Procedure. - *Case Reports Oncology*, 7: 246-251.
Not in PICO
- Yang, Y., Li, Y. X., Yang, X., Jiang, L., Zhou, Z. J. & Zhu, Y. Q. (2013) Progress risk assessment of oral premalignant lesions with saliva miRNA analysis. *BMC Cancer*, 13: 129.
Not in PICO
- Yesilova, E., Akgunlu, F., Dolanmaz, D., Yasar, F. & Sener, S. (2007) Osteosarcoma: a case report. *European journal of dentistry*, 1: 60-63.
Not in PICO
- Yoshihara, T. (2002) Bilateral enlargement of the submandibular glands - Clinical and pathological appearance. [Japanese]. *Practica Oto-Rhino-Laryngologica*, 95: 555-561.
Narrative review
- Zenk, W., Dietel, W., Schleier, P. & Gunzel, S. (1999) [Visualizing carcinomas of the mouth cavity by stimulating synthesis of fluorescent protoporphyrin IX]. [German]. *Mund-, Kiefer- und Gesichtschirurgie*, 3: 205-209.
Not in PICO
- Zhang, S., Bao, R., Bagby, J. & Abreo, F. (2009) Fine needle aspiration of salivary glands: 5-Year experience from a single academic center. *Acta Cytologica*, 53: 375-382.
Not in PICO
- Zheng, W., Soo, K. C., Sivanandan, R. & Olivo, M. (2002) Detection of squamous cell carcinomas and pre-cancerous lesions in the oral cavity by quantification of 5-aminolevulinic acid induced fluorescence endoscopic images. *Lasers in Surgery & Medicine*, 31: 151-157.
Not in PICO
- Zheng, W., Olivo, M. & Soo, K. C. (2004) The use of digitized endoscopic imaging of 5-ALA-induced PPIX fluorescence to detect and diagnose oral premalignant and malignant lesions in vivo. *International Journal of Cancer*, 110: 295-300.
Not in PICO
- Zini, A., Czerninski, R. & Sgan-Cohen, H. D. (2010) Oral cancer over four decades: epidemiology, trends, histology, and survival by anatomical sites. *Journal of Oral Pathology & Medicine*, 39: 299-305.
Narrative review
- Zunt, S. L. (2001) Transepithelial Brush Biopsy: an adjunctive diagnostic procedure. *Journal of the Indiana Dental Association*, 80: 6-8.
Narrative review

THYROID CANCER

Review question:

What is the risk of thyroid cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

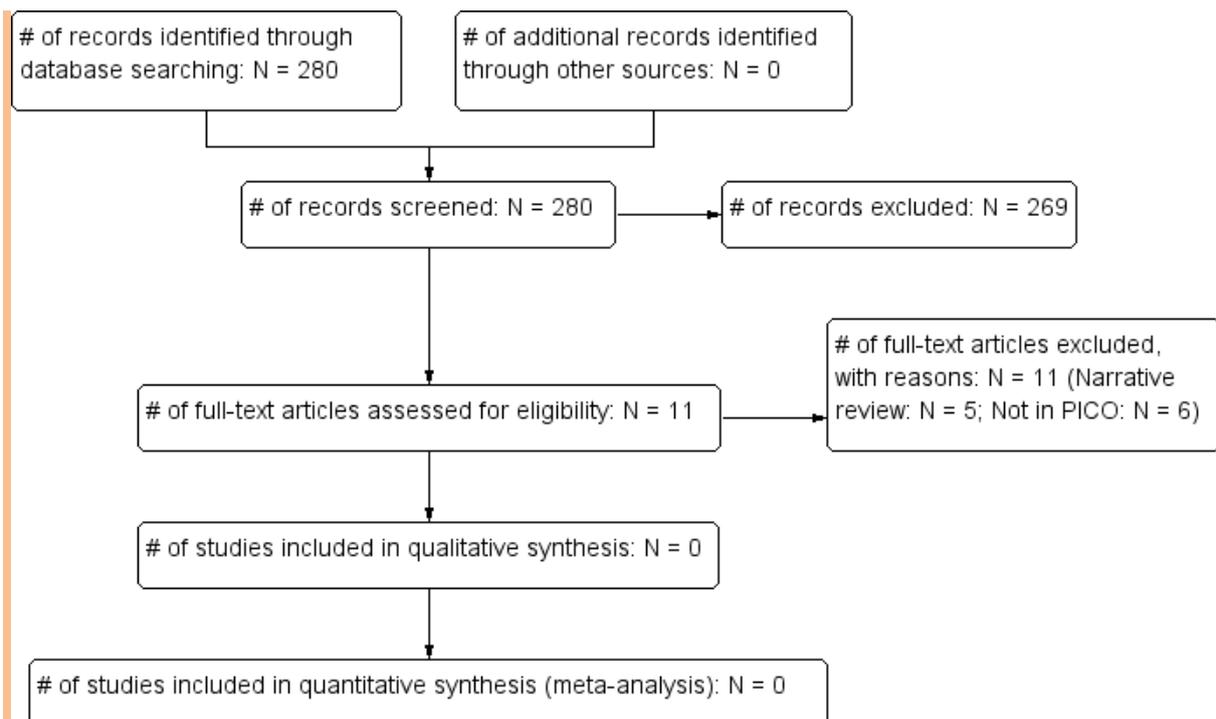
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	1325	162	03/10/2012
<i>Premedline</i>	All-2012	44	0	03/10/2012
<i>Embase</i>	All-2012	1696	137	04/10/2012
<i>Cochrane Library</i>	All-2012	147	1	01/10/2012
<i>Psychinfo</i>	All-2012	5	1	03/10/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	196	32	01/10/2012
<i>Biomed Central</i>	All-2012	460	4	01/10/2012

Total References retrieved (after de-duplication): 274

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	10/2012-27/08/2014	65	4	27/08/2014
<i>Premedline</i>	10/2012-27/08/2014	105	3	27/08/2014
<i>Embase</i>	10/2012-27/08/2014	126	2	27/08/2014
<i>Cochrane Library</i>	10/2012-27/08/2014	89	0	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	10/2012-27/08/2014	45	0	27/08/2014

Total References retrieved (after de-duplication): 6



Study results

No evidence was identified.

References

Included studies

None

Excluded studies (with excl reason)

(2003) Information from your family doctor. Thyroid nodules. *American Family Physician*, 67: 573-574.

Patient information leaflet

(2006) [Assess the patients' necks!]. [German]. *MMW Fortschritte der Medizin*, 148: 62-63.

Put down as Narrative review, but not seen. Not available unless we try using a world wide search, which I have decided not to as highly unlikely it will be relevant.

Ageev, I. S., Chizhikov, N. V., Paniushov, S. P., Tiumin, V. B., Grishaev, A. A. & Meniasheva, E. A.

(2005) [Thyroid cancer in male patients]. [Russian]. *Voprosy Onkologii*, 51: 717-718.

Not in PICO

Ainahi, A., Kebbou, M., Timinouni, M., Benabdeljalil, N. & Oufara, S. (2006) Treatment evaluation, follow-up and familial screening of medullary thyroid carcinoma by highly specific calcitonin measurements. *Indian Journal of Cancer*, 43: 75-79.

Not in PICO

Alexander, C. L., Izquierdo, R. E., Figge, J. & Horton, J. (1995) Diagnosis and management of thyroid cancer. *Cancer Control*, 2: 128-135.

Narrative review

Alfonso, E., Sanabria, A. & Castillo, M. (2011) Surgeons overestimate the risk of malignancy in thyroid nodules, evaluation of subjective estimates using a bayesian analysis. *Biomedica*, 31: 590-598.

Not in PICO

Allen, M., Sapinho, I., Raposo, L. & Torrinha, J. (2008) [Cyto-histological correlation of malignant thyroid nodules: clinical factors as predictors of malignancy]. [Portuguese]. *Acta Medica*

- Portuguesa*, 21: 135-140.
Not in PICO
- Amirova, N. M., Rodnikovskii, V. B. & Soldatov, I. P. (1989) The diagnosis of cancer and nodular formations of the thyroid by using a mathematical table. [Russian]. *Problemy Endokrinologii*, 35: 28-29.
Not in PICO
- Andry, G., Willemse, E., Digonnet, A., De, K. C., Vandeveld, L., Plat, L., Larsimont, D., Muylle, K. & Lemort, M. (2009) [Thyroid cancers]. [French][Erratum appears in Rev Med Brux. 2009 Sep-Oct;30(5):482]. *Revue Medicale de Bruxelles*, 30: 279-286.
Narrative review
- Arbelle, J. E., Shalom, S. I., Benbassat, C., Dickstein, G., Glasser, B. & Liel, Y. (836) [Summary of the Israeli Endocrine Society's consensus statement on the diagnosis, treatment and follow-up of well-differentiated thyroid cancer]. [27 refs] [Hebrew]. *Harefuah*, 147: 825-832.
Narrative review
- Arif, S., Blanes, A. & Diaz-Cano, S. J. (2002) Hashimoto's thyroiditis shares features with early papillary thyroid carcinoma. [Review] [32 refs]. *Histopathology*, 41: 357-362.
Narrative review
- Arora, N., Scognamiglio, T., Zhu, B. & Fahey, T. J., III (2008) Do benign thyroid nodules have malignant potential? An evidence-based review. [Review] [93 refs]. *World Journal of Surgery*, 32: 1237-1246.
Not in PICO
- Arslan, M. S., Topaloglu, O., Tural, E., Karbek, B., Ucan, B., Unsal, I. O., Gungunes, A., Ozkaya, E. C., Bozkurt, N. C., Ozbek, M., Cakal, E., Sahin, M. & Delibasi, T. (2012) Hyperprolactinemia: A risk factor of thyroid disease in patients with prolactinoma. *Endocrine Reviews*, 33.
Not in PICO
- Babcock, D. S. (372) Thyroid disease in the pediatric patient: emphasizing imaging with sonography. [Review] [26 refs]. *Pediatric Radiology*, 36: 299-308.
Narrative review
- Bae, J. S., Chae, B. J., Park, W. C., Kim, J. S., Kim, S. H., Jung, S. S. & Song, B. J. (2009) Incidental thyroid lesions detected by FDG-PET/CT: prevalence and risk of thyroid cancer. *World Journal of Surgical Oncology*, 7: 63.
Not in PICO
- Bartos, M., Pomorski, L. & Narebski, J. (2000) [The diagnosis and operative treatment of solitary thyroid nodule: a prospective study]. [Polish]. *Wiadomosci Lekarskie*, 53: 134-141.
Not in PICO
- Bennedbaek, F. N., Perrild, H. & Hegedus, L. (1999) Diagnosis and treatment of the solitary thyroid nodule. Results of a European survey. *Clinical Endocrinology*, 50: 357-363.
Not in PICO
- Berchtold, R., Studer, H. & Teuscher, J. (1982) Which diseases of the thyroid should be operated upon?. [German]. *Therapeutische Umschau*, 39: 768-775.
Not in PICO
- Bergholm, U., Adami, H. O., Bergstrom, R., Johansson, H., Lundell, G., Telenius-Berg, M. & Akerstrom, G. (1989) Clinical characteristics in sporadic and familial medullary thyroid carcinoma. A nationwide study of 249 patients in Sweden from 1959 through 1981. *Cancer*, 63: 1196-1204.
Not in PICO
- Beristain Hernandez, J. L., Servin, T. E., Sosa, C. A., Velazquez Garcia, J. A., Pozzo, B. R., Delgadillo, T. G., Serrano, G., I, Marquez, H. A., Bevia, P. F., Piscil Salazar, M. A., Ortiz De La Pena Salazar Ilarregui, Sanchez Gonzalez, F. J. & Espinoza, A. A. (2010) [Determination of the diagnostic accuracy of 99mTc sestamibi scanning in patients with thyroid nodule and a definitive histopathological report]. [Spanish]. *Endocrinologia y Nutricion*, 57: 460-466.
Not in PICO

- Besic, N., Sesek, M., Peric, B., Zgajnar, J. & Hocevar, M. (2008) Predictive factors of carcinoma in 327 patients with follicular neoplasm of the thyroid. *Medical Science Monitor*, 14: CR459-CR467.
Not in PICO
- Bleyer, A. (2009) CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology*, 36: 207-212.
Narrative review
- Bomeli, S. R., LeBeau, S. O. & Ferris, R. L. (2010) Evaluation of a thyroid nodule. [Review] [44 refs]. *Otolaryngologic Clinics of North America*, 43: 229-238.
Narrative review
- Brennan, M. & French, J. (2007) Thyroid lumps and bumps. *Australian Family Physician*, 36: 531-536.
Narrative review
- Brenner, W., Bohuslavizki, K. H., Klutmann, S. & Henze, E. (1997) Diagnostic value of currently available tumor markers in thyroid cancers. *Radiology and Oncology*, 31: 18-20.
Narrative review
- Brownlie, B., Mercer, P., Turner, J. & Allison, R. (2008) Thyroid malignancies: a New Zealand South Island thyroid clinic experience 1995-2006. *New Zealand Medical Journal*, 121: 36-45.
Not in PICO
- Brunese, L., Romeo, A., Iorio, S., Napolitano, G., Fucili, S., Zeppa, P., Vallone, G., Lombardi, G., Bellastella, A., Biondi, B. & Sodano, A. (2008) Thyroid B-flow twinkling sign: a new feature of papillary cancer. *European Journal of Endocrinology*, 159: 447-451.
Not in PICO
- Brunt, L. M. & Wells, S. A., Jr. (1983) The Multiple Endocrine Neoplasia syndromes. *Annales Chirurgiae et Gynaecologiae*, 72: 153-159.
Narrative review
- Bukhari, U., Sadiq, S., Memon, J. & Baig, F. (2009) Thyroid carcinoma in Pakistan: a retrospective review of 998 cases from an academic referral center. *Hematology/oncology & stem cell therapy*, 2: 345-348.
Not in PICO
- Cairncross, L. & Panieri, E. (2013) Pre-operative diagnosis of thyroid cancer: Clinical, radiological and pathological correlation. *South African Journal of Surgery*, 51: 46-49.
Not in PICO
- Cakir, M., Celik, E., Tuncer, F. B. & Tekin, A. (2013) A rare coexistence of thyroid lymphoma with papillary thyroid carcinoma. *Annals of African Medicine*, 12: 188-190.
Not in PICO
- Caplan, R. H., Wester, S. M., Lambert, P. J. & Rooney, B. L. (2000) Efficient evaluation of thyroid nodules by primary care providers and thyroid specialists. *American Journal of Managed Care*, 6: 1134-1140.
Not in PICO
- Caplan, R. H. (2001) Evaluation of palpable thyroid nodules: Are endocrinologists assessing patients efficiently? *Endocrinologist*, 11: 321-326.
Narrative review
- Carter, W. B., Tourtelot, J. B., Savell, J. G. & Lilienfeld, H. (2011) New treatments and shifting paradigms in differentiated thyroid cancer management. [Review]. *Cancer Control*, 18: 96-103.
Narrative review
- Caruso, D. R., O'Dorisio, T. M. & Mazzaferri, E. L. (1991) Multiple endocrine neoplasia. [Review] [26 refs]. *Current Opinion in Oncology*, 3: 103-108.
Narrative review
- Castro, M. R. & Gharib, H. (2000) Thyroid nodules and cancer. *Postgraduate Medicine*, 107: 113-124.
Narrative review

- Castro, M. R. & Gharib, H. (2005) Continuing controversies in the management of thyroid nodules. [Review] [79 refs]. *Annals of Internal Medicine*, 142: 926-931.
Narrative review
- Cattaneo, F., Burgi, U. & Mueller, B. (1999) [Goiter and nodular thyroid disease: clinical guidelines for diagnosis and treatment. (Waiting? Hormone therapy? Surgery? radioiodine?).] [Review] [42 refs] [German]. *Therapeutische Umschau*, 56: 356-363.
Narrative review
- Chabon, S. L. (505) Identification and evaluation of thyroid nodules. [Review] [8 refs]. *Lippincott's Primary Care Practice*, 1: 499-504.
Narrative review
- Chadha, N. K. & Forte, V. (2009) Pediatric head and neck malignancies. [Review] [41 refs]. *Current Opinion in Otolaryngology & Head & Neck Surgery*, 17: 471-476.
Narrative review
- Chang, Y. J., Mittal, V., Remine, S., Manyam, H., Sabir, M., Richardson, T. & Young, S. (2006) Correlation between clinical and histological findings in parathyroid tumors suspicious for carcinoma. *American Surgeon*, 72: 419-426.
Not in PICO
- Chen, H., Roberts, J. R., Ball, D. W., Eisele, D. W., Baylin, S. B., Udelsman, R. & Bulkley, G. B. (1998) Effective long-term palliation of symptomatic, incurable metastatic medullary thyroid cancer by operative resection. *Annals of Surgery*, 227: 887-895.
Not in PICO
- Cheung, K., Roman, S. A., Wang, T. S., Walker, H. D. & Sosa, J. A. (2008) Calcitonin measurement in the evaluation of thyroid nodules in the United States: a cost-effectiveness and decision analysis. *Journal of Clinical Endocrinology & Metabolism*, 93: 2173-2180.
Not in PICO
- Choi, Y. J., Park, Y. L. & Koh, J. H. (2008) Prevalence of thyroid cancer at a medical screening center: pathological features of screen-detected thyroid carcinomas. *Yonsei Medical Journal*, 49: 748-756.
Not in PICO
- Chow, S. M., Law, S. C. K., Au, S. K., Leung, T. W., Chan, P. T. M., Mendenhall, W. M. & Lau, W. H. (2002) Differentiated thyroid carcinoma: Comparison between papillary and follicular carcinoma in a single institute. *Head and Neck-Journal for the Sciences and Specialties of the Head and Neck*, 24: 670-677.
Not in PICO
- Chung, W. Y., Chang, H. S., Kim, E. K. & Park, C. S. (2001) Ultrasonographic mass screening for thyroid carcinoma: a study in women scheduled to undergo a breast examination. *Surgery Today*, 31: 763-767.
Not in PICO
- Clero, E., Doyon, F., Chungue, V., Rachedi, F., Boissin, J. L., Sebbag, J., Shan, L., Bost-Bezeaud, F., Petitdidier, P., Dewailly, E., Rubino, C. & de, V. F. (2012) Dietary iodine and thyroid cancer risk in French Polynesia: a case-control study. *Thyroid*, 22: 422-429.
Not in PICO
- Conzo, G., Troncone, G., Docimo, G., Pizza, A., Sciascia, V., Bellevicine, C., Napolitano, S., Della, P. C., Palazzo, A., Signoriello, G. & Santini, L. (2013) Cytologically undetermined thyroid's follicular lesions: surgical procedures and histological outcome in 472 cases. *Annali Italiani di Chirurgia*, 84: 251-256.
Not in PICO
- Corrias, A., Mussa, A., Baronio, F., Arrigo, T., Salerno, M., Segni, M., Vigone, M. C., Gastaldi, R., Zirilli, G., Tuli, G., Beccaria, L., Iughetti, L., Einaudi, S., Weber, G., De, L. F., Cassio, A. & Study Group for Thyroid Diseases of Italian Society for Pediatric Endocrinology and Diabetology (SIEDP/ISPED) (2010) Diagnostic features of thyroid nodules in pediatrics. *Archives of Pediatrics & Adolescent*

- Medicine*, 164: 714-719.
Not in PICO
- Costante, G. & Filetti, S. (2011) Early diagnosis of medullary thyroid carcinoma: is systematic calcitonin screening appropriate in patients with nodular thyroid disease? *The Oncologist*, 16: 49-52.
Narrative review
- D'Ugo, D., Persiani, R., Pende, V., D'Andrilli, A., De, C. E., Rausei, S. & Picciocchi, A. (2001) [Clinical role of the cytologic study of thyroid nodules]. [Italian]. *Annali Italiani di Chirurgia*, 72: 287-291.
Not in PICO
- Damante, G., Scaloni, A. & Tell, G. (2009) Thyroid tumors: novel insights from proteomic studies. [Review] [130 refs]. *Expert Review of Proteomics*, 6: 363-376.
Narrative review
- Damion, J. & Hybels, R. L. (106) The neck mass. 2. Inflammatory and neoplastic causes. *Postgraduate Medicine*, 81: 97-103.
Narrative review
- Danese, D., Centanni, M., Farsetti, A. & Andreoli, M. (1997) Diagnosis of thyroid carcinoma. [Review] [85 refs]. *Journal of Experimental & Clinical Cancer Research*, 16: 337-347.
Narrative review
- Dardas, M., Abboud, M., Salti, I., Sabri, A., Shoucair, M., Saleh, M., Azar, S., Rodriguez-Galindo, C. & Muwakkit, S. (2009) Thyroid Cancer in Lebanese Children and Adolescents: A 15-Year Experience at A Single Institution. *Pediatric Hematology and Oncology*, 26: 439-447.
Not in PICO
- Davies, L., Ouellette, M., Hunter, M. & Welch, H. G. (2010) The increasing incidence of small thyroid cancers: where are the cases coming from? *Laryngoscope*, 120: 2446-2451.
Not in PICO
- Deandrea, M., Ragazzoni, F., Motta, M., Torchio, B., Mormile, A., Garino, F., Magliona, G., Gamarra, E., Ramunni, M. J., Garberoglio, R. & Limone, P. P. (2010) Diagnostic value of a cytomorphological subclassification of follicular patterned thyroid lesions: a study of 927 consecutive cases with histological correlation. *Thyroid*, 20: 1077-1083.
Not in PICO
- Delisle, M.-J., Schwartz, C., Theobald, S., Maes, B., Vaudrey, C. & Pochart, J.-M. (1996) The thyroid carcinomas. Interest of a regional registry of 627 patients diagnosed, treated and followed by a multidisciplinary group. [French]. *Annales d'Endocrinologie*, 57: 41-49.
Not in PICO
- Delisle, M. J., Hannequin, P., Liehn, J. C., Gibold, C., Maes, B., Vaudrey, C., Pochart, J. M. & Morel, M. (1986) [Thyroid cancer in Champagne-Ardenne: 1967-1984. Epidemiologic findings in a regional register]. [French]. *Bulletin du Cancer*, 73: 165-170.
Not in PICO
- Delisle, M. J., Schwartz, C., Theobald, S., Maes, B., Vaudrey, C. & Pochart, J. M. (1996) Cancers of the thyroid. Value of a regional registry on 627 patients diagnosed, treated and followed by a multidisciplinary team. [French]. *Annales d'Endocrinologie*, 57: 41-49.
Not in PICO
- Demeter, J. G., De Jong, S. A., Lawrence, A. M. & Paloyan, E. (1991) Anaplastic thyroid carcinoma: Risk factors and outcome. *Surgery*, 110: 956-963.
Not in PICO
- Demidov, V. P., Voronetskii, I. B., Sergeev, S. A. & Babakulyeva, D. (1982) [Current diagnostic and treatment problems in thyroid cancer]. [Russian]. *Voprosy Onkologii*, 28: 70-77.
Not in PICO
- Desai, M. P. (1997) Disorders of thyroid gland in India. *Indian Journal of Pediatrics*, 64: 11-20.
Not in PICO

- Dietlein, M., Wegscheider, K., Vaupel, R., Schmidt, M. & Schicha, H. (2007) Management of multinodular goiter in Germany (Papillon 2005): do the approaches of thyroid specialists and primary care practitioners differ? *Nuclear-Medizin*, 46: 65-75.
Not in PICO
- Dietlein, M., Wegscheider, K., Vaupel, R., Schmidt, M. & Schicha, H. (2008) Survey of management of solitary thyroid nodules in Germany. *Nuclear-Medizin*, 47: 87-96.
Not in PICO
- Dionigi, G., Tanda, M. L., Piantanida, E., Boni, L., Rovera, F., Dionigi, R. & Bartalena, L. (2009) Time interval in diagnosis and treatment of papillary thyroid cancer: a descriptive, retrospective study. *American Journal of Surgery*, 197: 434-438.
Not in PICO
- Domanski, M. C., Ashktorab, S. & Bielamowicz, S. A. (2010) Primary care perceptions of otolaryngology. *Otolaryngology-Head and Neck Surgery*, 143: 337-340.
Not in PICO
- Dong, S., Lu, G. Z., Gao, Y. M., Zhang, H., Guo, X. H. & Gao, Y. (2008) [A clinical pathological study of thyroid nodules detected by physical examinations]. [Chinese]. *Chung-Hua Nei Ko Tsa Chih Chinese Journal of Internal Medicine*, 47: 189-192.
Not in PICO
- Dotzenrath, C., Goretzki, P. E., Cupisti, K., Simon, D., Witte, J., Yang, Q., Ohmann, C. & Roher, H. D. (2001) Is there any consensus in diagnostic and operative strategy with respect to medullary thyroid cancer? A questionnaire answered by 73 endocrine surgical units. *Langenbecks Archives of Surgery*, 386: 47-52.
Not in PICO
- Elahi, S., Manzoor-ul-Hassan, A., Syed, Z., Nazeer, L., Nagra, S. A. & Hyder, S. W. (2005) A study of goiter among female adolescents referred to Centre for Nuclear Medicine, Lahore. *Pakistan Journal of Medical Sciences*, 21: 56-62.
Not in PICO
- Elsaesser, H. (2005) 14 Years of thyroid disorders in general practice - What is left?. [German]. *Zeitschrift fur Allgemeinmedizin*, 81: 97-102.
Narrative review
- Ershova, G. I. (2004) Methods of improvement of diagnosis of thyroid cancer. [Russian]. *Khirurgiia*, 47-49.
Narrative review
- Esik, O., Szavcsur, P., Szakall S Jr, Bajzik, G., Repa, I., Dabasi, G., Fuzy, M., Szentirmay, Z., Perner, F., Kasler, M., Lengyel, Z. & Tron, L. (2001) Angiography effectively supports the diagnosis of hepatic metastases in medullary thyroid carcinoma. *Cancer*, 91: 2084-2095.
Not in PICO
- Esik, O., Tusnady, G., Tron, L., Boer, A., Szentirmay, Z., Szabolcs, I., Racz, K., Lengyel, E., Szekely, J. & Kasler, M. (2002) Markov model-based estimation of individual survival probability for medullary thyroid cancer patients. *Pathology and Oncology Research*, 8: 93-104.
Not in PICO
- Evans, T. C. (2003) Thyroid disease. *Primary Care - Clinics in Office Practice*, 30: 625-640.
Narrative review
- Faggiano, A., Del Prete, M., Marciello, F., Marotta, V., Ramundo, V. & Colao, A. (2011) Thyroid diseases in elderly. *Minerva Endocrinologica*, 36: 211-231.
Narrative review
- Feldmann, M. (1980) Thyroid investigations in general practice. [German]. *Zeitschrift fur Allgemeinmedizin*, 56: 1893-1896.
Not in PICO
- Filicori, F., Keutgen, X. M., Buitrago, D., AlDailami, H., Crowley, M., Fahey, T. J., III & Zarnegar, R. (2011) Risk stratification of indeterminate thyroid fine-needle aspiration biopsy specimens based

- on mutation analysis. *Surgery*, 150: 1085-1091.
Not in PICO
- Fromigue, J., De, B. T., Baudin, E., Dromain, C., Leboulleux, S. & Schlumberger, M. (2006) Review: Chemoembolization for liver metastases from medullary thyroid carcinoma. *Journal of Clinical Endocrinology and Metabolism*, 91: 2496-2499.
Not in PICO
- Fruth, K. & Mann, W. J. (2009) [Malignant thyroid neoplasms: a diagnostic challenge for ENT specialists]. [German]. *HNO*, 57: 257-261.
Not in PICO
- Fuhrer, D., Bockisch, A. & Schmid, K. W. (516) Euthyroid goiter with and without nodules--diagnosis and treatment. [Review]. *Deutsches Arzteblatt International*, 109: 506-515.
Narrative review
- Gallego, C., Gonzalez-Diaz, S., Del Carmen, Z. M., Arias-Cruz, A., Garcia-Calderin, D., Salas, K. Y. M., Calva, M. & Sansores, L. A. D. (2012) CVID: A common but still underdiagnosed disease. *World Allergy Organization Journal*, 5: S207-S208.
Not in PICO
- Gamboa-Dominguez, A., Lino-Silva, S., Candanedo-Gonzalez, F., Medina-Lopez, E., Acuna-Gonzalez, D., Jacinto-Cortes, I. & Gonzalez-Trevino, O. (2011) [Trends of thyroid pathology in a referral center: steady prevalence of papillary thyroid carcinoma but goiter increase in thyroidectomies]. [Spanish]. *Revista de Investigacion Clinica*, 63: 148-154.
Not in PICO
- Gavriloaia, G. V., Gavriloaia, M. R. & Novac, M. L. (2011) Bioacoustics response of small benign or malignant nodules. *Conference Proceedings: ...Annual International Conference of the IEEE Engineering in Medicine & Biology Society*, 2011: 7695-7698.
Not in PICO
- Gharib, H., McConahey, W. M., Tieg, R. D., Bergstralh, E. J., Goellner, J. R., Grant, C. S., van Heerden, J. A., Sizemore, G. W. & Hay, I. D. (1992) Medullary thyroid carcinoma: clinicopathologic features and long-term follow-up of 65 patients treated during 1946 through 1970. *Mayo Clinic Proceedings*, 67: 934-940.
Not in PICO
- Giammarile, F., Houzard, C., Bournaud, C., Hafdi, Z., Sassolas, G. & Borson-Chazot, F. (2004) Diagnostic management of suspected metastatic thyroid carcinoma: clinical value of octreotide scintigraphy in patients with negative high-dose radioiodine scans. *European Journal of Endocrinology*, 150: 277-283.
Not in PICO
- Gibbons, V., Conaglen, J. V., Lillis, S., Naras, V. & Lawrenson, R. (2008) Epidemiology of thyroid disease in Hamilton (New Zealand) general practice. *Australian and New Zealand Journal of Public Health*, 32: 421-423.
Not in PICO
- Giuffrida, D. & Gharib, H. (1995) Controversies in the Management of Cold, Hot, and Occult Thyroid-Nodules. *American Journal of Medicine*, 99: 642-650.
Narrative review
- Glastonbury, C. M., Davidson, H. C., Haller, J. R. & Harnsberger, H. R. (2000) The CT and MR imaging features of carcinoma arising in thyroglossal duct remnants. *American Journal of Neuroradiology*, 21: 770-774.
Not in PICO
- Glinioer, D. (2010) Consensus guidelines for the management of thyroid disorders associated with the pregnancy: An overview. *Endocrine Abstracts*, 20: S26.
Guideline/Not in PICO
- Goldstein, R. E., Nettekville, J. L., Burkey, B. & Johnson, J. E. (2002) Implications of follicular neoplasms, atypia, and lesions suspicious for malignancy diagnosed by fine-needle aspiration of

- thyroid nodules. *Annals of Surgery*, 235: 656-662.
Not in PICO
- Gomes, E. M. D., Vaisman, F., Vidal, A. P., Corbo, R., da Cruz, M. D. G., Teixeira, P. D. D., Buescu, A. & Vaisman, M. (2011) Frequency of thyroid carcinoma and thyroid autoimmunity in first-degree relatives of patients with papillary thyroid carcinoma - A single center experience. *Arquivos Brasileiros de Endocrinologia e Metabologia*, 55: 326-330.
Not in PICO
- Gomez Saez, J. M. & en nombre del grupo de Cancer de Tiroides de la Sociedad Espanola de Endocrinologia (2010) [Is our approach to thyroid nodules and differentiated thyroid carcinoma in agreement with the American guideline and European consensus?]. [Spanish]. *Endocrinologia y Nutricion*, 57: 357-363.
Not in PICO
- Gossain, V. V., Charnas, J., Carella, M. J., Rovner, D. R. & Calaca, W. M. (1998) Evaluation of "solitary" thyroid nodules in a community practice: a managed care approach. *American Journal of Managed Care*, 4: 679-684.
Not in PICO
- Guerrier, B., Berthet, J. P., Cartier, C., Dehesdin, D., Edet-Sanson, A., Le, C. G., Garrel, R., Kania, R., Makeieff, M., Page, C., Poiree, S., Potard, G., Prades, J. M., Righini, C., Roussel, F. & Toubert, M. E. (2012) French ENT Society (SFORL) practice guidelines for lymph-node management in adult differentiated thyroid carcinoma. *European Annals of Otorhinolaryngology, Head and Neck Diseases*, 129: 197-206.
Guideline
- Guliana, J. M., Modigliani, E., Guillausseau, P. J., Aubert, P., Milhaud, G., Moukhtar, M. S. & Calmettes, C. (1989) Detection and prognosis of medullary cancer of the thyroid gland. Influence of national multidisciplinary cooperation. [French]. *Presse medicale (Paris, France : 1983)*, 18: 521-524.
Not in PICO
- Haid, A., Zimmermann, G., Fritzsche, H., Kargl, M., De, M. R. & Gruber, U. (1989) Simultaneous occurrence of thyroid cancer and hyperthyroid goiter nodules in an endemic area. [German]. *Chirurg*, 60: 39-43.
Narrative review
- Hakala, T., Kholova, I., Sand, J., Saaristo, R. & Kellokumpu-Lehtinen, P. (2013) A core needle biopsy provides more malignancy-specific results than fine-needle aspiration biopsy in thyroid nodules suspicious for malignancy. *Journal of Clinical Pathology*, 66: 1046-1050.
Not in PICO
- Hamburger, J. I., Miller, J. M. & Kini, S. R. (1983) Lymphoma of the thyroid. *Annals of Internal Medicine*, 99: 685-693.
Not in PICO
- Hammond, I., Lentle, B. C. & Odell, P. F. (2010) The pursuit of impalpable thyroid nodules: are we using scarce resources wisely? *Canadian Association of Radiologists Journal*, 61: 98-101.
Narrative review
- Hands, K. E., Cervera, A. & Fowler, L. J. (2010) Enlarged benign-appearing cervical lymph nodes by ultrasonography are associated with increased likelihood of cancer somewhere within the thyroid in patients undergoing thyroid nodule evaluation. *Thyroid*, 20: 857-862.
Not in PICO
- Haq, M. & Harmer, C. (2004) Thyroid cancer: an overview. [Review] [28 refs]. *Nuclear Medicine Communications*, 25: 861-867.
Narrative review
- Harach, H. R. & Ceballos, G. A. (2008) Thyroid cancer, thyroiditis and dietary iodine: A review based on the salta, argentina model. *Endocrine Pathology*, 19: 209-220.
Narrative review

- Harris, P. E. (2002) The management of thyroid cancer in adults: a review of new guidelines. *Clinical Medicine*, 2: 144-146.
Guideline
- HAYES & -Inc (2013) BRAF p.Val600Glu testing in papillary thyroid carcinoma (Structured abstract). *Health Technology Assessment.Database.*
Not in PICO
- Hemminki, K., Sundquist, J. & Bermejo, J. L. (2008) Familial risks for cancer as the basis for evidence-based clinical referral and counseling. *The Oncologist*, 13: 239-247.
Not in PICO
- Hennemann, G. & Van Der Snoek, J. A. (1985) Consensus meeting on the diagnostic procedure in single thyroid nodule. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 129: 1878-1882.
Guideline/consensus statement
- Henry, J. F., Denizot, A., Puccini, M., Niccoli, P., Conte-Devolx, B. & de, M. C. (1996) Early diagnosis of sporadic medullary cancers of the thyroid: value of systematic assay of calcitonin. [French]. *Presse medicale (Paris, France : 1983)*, 25: 1583-1588.
Not in PICO
- Herraiz, M., Barbesino, G., Faquin, W., Chan-Smutko, G., Patel, D., Shannon, K. M., Daniels, G. H. & Chung, D. C. (2007) Prevalence of thyroid cancer in familial adenomatous polyposis syndrome and the role of screening ultrasound examinations. *Clinical Gastroenterology & Hepatology*, 5: 367-373.
Not in PICO
- Herrmann, B. L., Schmid, K. W., Goerges, R., Kemen, M. & Mann, K. (2010) Calcitonin screening and pentagastrin testing: Predictive value for the diagnosis of medullary carcinoma in nodular thyroid disease. *European Journal of Endocrinology*, 162: 1141-1145.
Not in PICO
- Hobbs, C. & Bova, R. (2010) Neck lumps: A guide to assessment and management. *Medicine Today*, 11: 26-34.
Narrative review
- Holzer, S., Reiners, C., Mann, K., Bamberg, M., Rothmund, M., Dudeck, J., Stewart, A. K. & Hundahl, S. A. (2000) Patterns of care for patients with primary differentiated carcinoma of the thyroid gland treated in Germany during 1996. *Cancer*, 89: 192-201.
Not in PICO
- Huang, T. W., Lai, J. H., Wu, M. Y., Chen, S. L., Wu, C. H. & Tam, K. W. (2013) Systematic review of clinical practice guidelines in the diagnosis and management of thyroid nodules and cancer. *BMC Medicine*, 11: 191.
Not in PICO
- Huong, J., Menezes, J. & Naqvi, S. (2012) Respiratory failure leading to an unexpected diagnosis of men syndrome. *Journal of Hospital Medicine*, 7: S216.
Not in PICO
- Huszno, B. (1987) Early diagnosis of cancer of the thyroid based on current clinical data. [Polish]. *Endokrynologia Polska*, 38: 49-107.
Not in PICO
- Ilyes, I. (2011) [Current questions of thyroid diseases in childhood]. [Review] [Hungarian]. *Orvosi Hetilap*, 152: 617-627.
Narrative review
- Irani, S., Rashidian, A., Yousefi-Nooraie, R. & Soltani, A. (2011) Evaluating clinical practice guidelines developed for the management of thyroid nodules and thyroid cancers and assessing the reliability and validity of the AGREE instrument. *Journal of Evaluation in Clinical Practice*, 17: 729-736.
Not in PICO

- Isaacs, J. D., Lundgren, C. I., Sidhu, S. B., Sywak, M. S., Edhouse, P. J. & Delbridge, L. W. (2008) The Delphian lymph node in thyroid cancer. *Annals of Surgery*, 247: 477-482.
Not in PICO
- Ito, K. (1989) [Definition, diagnosis and treatment of thyroid carcinoma at an early stage]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 47: 1147-1151.
Not in PICO/narrative review
- Izikson, L., English III, J. C. & Zirwas, M. J. (2006) The flushing patient: Differential diagnosis, workup, and treatment. *Journal of the American Academy of Dermatology*, 55: 193-208.
Narrative review
- Jett, J. R. (2010) Mediastinal tumors. *Respirology*, 15: 18.
Narrative review
- Joung, K. H., Park, J. Y., Kim, K. S. & Koo, B. S. (2014) Primary amyloid goiter mimicking rapid growing thyroid malignancy. *European Archives of Oto-Rhino-Laryngology*, 271: 417-420.
Not in PICO
- Kahn, C., Simonella, L., Sywak, M., Boyages, S., Ung, O. & O'Connell, D. (2012) Pathways to the diagnosis of thyroid cancer in New South Wales: a population-based cross-sectional study. *Cancer Causes & Control*, 23: 35-44.
Not in PICO
- Kalvachova, B. (2011) The thyroid gland in primary pediatric care. [Czech]. *Pediatric pro Praxi*, 12: 91-93.
Narrative review
- Kanakatti Shankar, R., Rutter, M., Chernausek, S., Samuels, P., Mo, J. & Rutter, M. (2012) Medullary thyroid cancer in a 9-week-old infant with familial MEN 2B: Implications for timing of prophylactic thyroidectomy. *International Journal of Pediatric Endocrinology*, 2012: 25.
Not in PICO
- Karges, W., Dralle, H., Raue, F., Mann, K., Reiners, C., Grussendorf, M., Hufner, M., Niederle, B. & Brabant, G. (2004) Calcitonin Measurement to Detect Medullary Thyroid Carcinoma in Nodular Goiter: German Evidence-Based Consensus Recommendation. *Experimental and Clinical Endocrinology and Diabetes*, 112: 52-58.
Consensus statement/guideline
- Karges, W. (2010) [Calcitonin determination for early diagnosis of medullary thyroid cancer]. [Review] [German]. *Chirurg*, 81: 620-626.
Narrative review
- Kassum, T. A., Goldstein, D. P., Rafferty, M. A., Rotstein, L. E. & Irish, J. C. (2007) Thyroid scintigraphy in the assessment of the solitary thyroid nodule: Differences in practice patterns between family physicians and specialists. *Journal of Otolaryngology*, 36: 49-53.
Not in PICO
- Khachatryan, A. S. (2011) [Problems of early clinical diagnosis of thyroid cancer]. [Russian]. *Georgian medical news*, 19-23.
Not in PICO
- Khachatryan, A. S. (2012) [Problem of early intra- and preoperative pathomorphologic diagnosis of thyroid cancer]. [Russian]. *Georgian Medical News*.(202):11-6, 2012 Jan., 11-16.
Not in PICO
- Khachatryan, A. (2012) [Background diseases in thyroid cancer]. [Russian]. *Georgian Medical News*.(203):7-11, 2012 Feb., 7-11.
Not in PICO
- Khairy, G. A. & Guraya, S. Y. (2004) Primary care evaluation of thyroid disease: Which clinical group needs urgent surgical referral? *Bahrain Medical Bulletin*, 26: 143-146.
Not in PICO
- Knox, M. A. (2013) Thyroid nodules. *American Family Physician*, 88: 193-196.
Narrative review

- Komminoth, P. (2010) Medullary carcinoma and familial non-medullary thyroid carcinoma: When do you suspect the thyroid tumor is familiar? *Virchows Archiv*, 457: 129.
Not in PICO
- Koulouri, O., Auldin, M. A., Agarwal, R., Kieffer, V., Robertson, C., Smith, J. F., Levy, M. J. & Howlett, T. A. (2011) Diagnosis and treatment of hypothyroidism in TSH deficiency compared to primary thyroid disease: pituitary patients are at risk of under-replacement with levothyroxine. *Clinical Endocrinology*, 74: 744-749.
Not in PICO
- Koutras, D. A. (2001) Thyroid nodules in children and adolescents: consequences in adult life. [Review] [29 refs]. *Journal of Pediatric Endocrinology*, 14: Suppl-7.
Not in PICO
- Kwak, J. Y., Kim, E. K., Kim, M. J. & Son, E. J. (2009) Significance of sonographic characterization for managing subcentimeter thyroid nodules. *Acta Radiologica*, 50: 917-923.
Not in PICO
- Kwak, J. Y. & Kim, E. K. (2013) Cancer: Indeterminate thyroid nodules--added testing, added value? *Nature Reviews Endocrinology*, 9: 321-323.
Not in PICO
- La, G. L., O'Malley, M., Milas, M., Burke, C., Kalady, M., Church, J. & Weiss, S. R. (2011) Uncovering the hidden risk of thyroid cancer in MYH-associated polyposis. *Familial Cancer*, 10: 719.
Not in PICO
- Lacey, N. A., Jones, A. & Clarke, S. E. (2001) Role of radionuclide imaging in hyperthyroid patients with no clinical suspicion of nodules. *British Journal of Radiology*, 74: 486-489.
Not in PICO
- Ladenson, P. W. (1996) Optimal laboratory testing for diagnosis and monitoring of thyroid nodules, goiter, and thyroid cancer. *Clinical Chemistry*, 42: 183-187.
Narrative review
- Langer, M., Maddeddu, G. & Dettori, G. (1980) The problem of cancer diagnosis in thyroid nodules. [German]. *Schweizerische Medizinische Wochenschrift*, 110: 1411-1414.
Not in PICO
- Leclere, J., Beckers, C., Cussac, J. F., Renan, C. A. & Vielh, P. (1993) Thyroid nodule. [French]. *Medecine Nucleaire*, 17: 191-201.
Narrative review
- Lee, J., Kee, H. N., Woung, Y. C., Soh, E.-Y. & Cheong, S. P. (2008) Clinicopathologic features and treatment outcomes in differentiated thyroid carcinoma patients with concurrent Graves' disease. *Journal of Korean Medical Science*, 23: 796-801.
Not in PICO
- Lee, N. C. & Norton, J. A. (2000) Multiple endocrine neoplasia type 2B--genetic basis and clinical expression. [Review] [59 refs]. *Surgical Oncology*, 9: 111-118.
Narrative review
- Lee, S. M. & Kwak, K. H. (2010) Risk Factors and a Predictive Model for Thyroid Cancer in Korean Women. *Cancer Nursing*, 33: 310-319.
Narrative review
- Leux, C. & Guenel, P. (2010) Risk factors of thyroid tumors: Role of environmental and occupational exposures to chemical pollutants. [French]. *Revue d'Epidemiologie et de Sante Publique*, 58: 359-367.
Narrative review
- Liang, H., Zhong, Y., Luo, Z., Huang, Y., Lin, H., Luo, M., Zhan, S., Xie, K., Ma, Y. & Li, Q. Q. (2010) Assessment of biomarkers for clinical diagnosis of papillary thyroid carcinoma with distant metastasis. *International Journal of Biological Markers*, 25: 38-45.
Narrative review

- Liang, H., Zhong, Y., Luo, Z., Huang, Y., Lin, H., Zhan, S., Xie, K. & Li, Q. Q. (2011) Diagnostic value of 16 cellular tumor markers for metastatic thyroid cancer: an immunohistochemical study. *Anticancer Research*, 31: 3433-3440.
Not in PICO
- Liel, Y. & Fraenkel, N. (2005) Brief report: Use and misuse of thyroid ultrasound in the initial workup of patients with suspected thyroid problems referred by primary care physicians to an endocrine clinic. *Journal of General Internal Medicine*, 20: 766-768.
Not in PICO
- Lin, J. D., Chao, T. C., Huang, B. Y., Chen, S. T., Chang, H. Y. & Hsueh, C. (2005) Thyroid cancer in the thyroid nodules evaluated by ultrasonography and fine-needle aspiration cytology. *Thyroid*, 15: 708-717.
Not in PICO
- Lin, K.-D., Lin, J.-D., Huang, M.-J., Huang, H.-S., Jeng, L.-B. & Ho, Y.-S. (1998) Acute suppurative thyroiditis and aggressive malignant thyroid tumors: Differences in clinical presentation. *Journal of Surgical Oncology*, 67: 28-32.
Not in PICO
- Lind, P., Igerc, I. & Kohlfurst, S. (2005) [Diagnosis, treatment and follow-up in the case of differentiated thyroid cancer]. [German]. *Wiener Medizinische Wochenschrift*, 155: 429-435.
Narrative review
- Listewnik, M. H., Birkenfeld, B., Chosia, M., Elbl, B., Niedzialkowska, K. & Sawrymowicz, M. (2010) The occurrence of malignant thyroid lesions in patients after radioiodine treatment due to benign thyroid diseases. *Endokrynologia Polska*, 61: 454-457.
Not in PICO
- Listewnik, M. H., Birkenfeld, B., Piwowarska-Bilska, H., Cichon-Bankowska, K., Iglinska-Wagner, L., Watrak, W., Smolira, W., Zorga, P., Niedzialkowska, K., Elbl, B. & Sawrymowicz, M. (2010) The application of SPECT/CT scintigraphy with MIBI-Tc99(m) in the diagnosis of thyroid nodules - a preliminary report. *Endokrynologia Polska*, 61: 422-426.
Not in PICO
- Listewnik, M. H., Birkenfeld, B., Chosia, M., Elbl, B., Piwowarska-Bilska, H., Zorga, P. & Niedzialkowska, K. (2011) Thyroid fine-needle aspiration biopsy: which lesions should be biopsied before 131I therapy? *Annales Academiae Medicae Stetinensis*, 57: 54-58.
Not in PICO
- Little, J. W. (2006) Thyroid disorders. Part III: neoplastic thyroid disease. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics*, 102: 275-280.
Narrative review
- Liu, W., Yang, J., Zhang, Y., Shao, K.-W. & Zhu, C.-S. (2010) The value of calcification in CT differentiating benign and malignant thyroid lesions. [Chinese]. *Chinese Journal of Radiology*, 44: 147-151.
Not in PICO
- Lowenstein, E. B. & Lowenstein, E. J. (2010) Cutaneous manifestations of endocrine neoplasia. *Giornale Italiano di Dermatologia e Venereologia*, 145: 229-244.
Narrative review
- Luger, A. (2005) [Schilddrüse und polyendokrinopathien]. [Review] [24 refs] [German]. *Wiener Medizinische Wochenschrift*, 155: 454-457.
Narrative review
- Lyshchik, A., Higashi, T., Asato, R., Tanaka, S., Ito, J., Hiraoka, M., Insana, M. F., Brill, A. B., Saga, T. & Togashi, K. (2007) Cervical lymph node metastases: Diagnosis at sonoelastography - Initial experience. *Radiology*, 243: 258-267.
Not in PICO

- Machens, A., Holzhausen, H. J. & Dralle, H. (2005) The prognostic value of primary tumor size in papillary and follicular thyroid carcinoma - A comparative analysis. *Cancer*, 103: 2269-2273.
Not in PICO
- Machens, A., Hauptmann, S. & Dralle, H. (2008) Referral bias in thyroid cancer surgery: direction and magnitude. *European Journal of Surgical Oncology*, 34: 556-562.
Not in PICO
- Machens, A. & Dralle, H. (2009) Age disparities in referrals to specialist surgical care for papillary thyroid cancer. *European Journal of Surgical Oncology*, 35: 1312-1317.
Not in PICO
- Malesevic, M., Mihailovic, J., Vojcic, J. & Popadic, S. (2003) [Early diagnosis, therapy, follow-up and survival in patients with thyroid malignancies]. [Serbian]. *Acta Chirurgica Iugoslavica*, 50: 177-183.
Not in PICO/narrative review
- Mallick, U. K., Ball, S., Fenwick, J. D., James, R. A., Johnson, S. J., Kendall-Taylor, P., Lennard, T. W. J., Lucraft, H. H., Proud, G., Perros, P., Weightman, D. R. & Douglas, F. (2000) Northern cancer network guidelines for management of thyroid cancer. *Clinical Oncology*, 12: 373-391.
Guideline
- Mallick, U. K. & Charalambous, H. (2004) Current issues in the management of differentiated thyroid cancer. [Review] [74 refs]. *Nuclear Medicine Communications*, 25: 873-881.
Not in PICO
- Mallory, S. B. (1995) Cowden syndrome (multiple hamartoma syndrome). [Review] [30 refs]. *Dermatologic Clinics*, 13: 27-31.
Narrative review
- Marcy, P. Y., Thariat, J., Bozec, A., Poissonnet, G., Benisvy, D. & Dassonville, O. (2009) Venous obstruction of thyroid malignancy origin: the Antoine Lacassagne Institute experience. *World Journal of Surgical Oncology*, 7: 40.
Not in PICO
- Marqusee, E., Benson, C. B., Frates, M. C., Doubilet, P. M., Larsen, P. R., Cibas, E. S. & Mandel, S. J. (2000) Usefulness of ultrasonography in the management of nodular thyroid disease. *Annals of Internal Medicine*, 133: 696-700.
Not in PICO
- Martinez, I., V, Perez, M. A., Roset, S. L., Sanchez de, T. J., Regas Bech de, C. J. & Marques, G. A. (1993) [Thyroid cancer in childhood: review of 7 cases]. [Spanish]. *Anales Espanoles de Pediatria*, 38: 229-231.
Not in PICO
- Massol, J., Pazart, L., Aho, S., Strauch, G., Leclere, J. & Durieux, P. (1993) [Management of the thyroid nodule. Preliminary results of a practice survey of 685 general practitioners and specialists]. [French]. *Annales d'Endocrinologie*, 54: 220-225.
Not in PICO
- Mauny, F., Grandmottet, M., Marquet, G., Floret, N., Crenn, D., Olivier-Koehret, M. & Viel, J.-F. (2002) Childhood thyroid cancer in the French region of Franche-Comte: Chernobyl impact not proven. [French]. *Environnement, Risques et Sante*, 1: 283-288.
Not in PICO
- Mazzaferri, E. L. (1999) An overview of the management of papillary and follicular thyroid carcinoma. [Review] [38 refs]. *Thyroid*, 9: 421-427.
Narrative review
- McTiernan, A., Weiss, N. S. & Daling, J. R. (1987) Incidence of thyroid cancer in women in relation to known or suspected risk factors for breast cancer. *Cancer Research*, 47: 292-295.
Not in PICO

- Mehanna, H. M., Jain, A., Morton, R. P., Watkinson, J. & Shaha, A. (2009) Investigating the thyroid nodule. [Review] [25 refs]. *BMJ*, 338: b733.
Narrative review
- Mehrotra, P. K., Mishra, A., Mishra, S. K., Agarwal, G., Agarwal, A. & Verma, A. K. (2011) Medullary thyroid cancer: clinico-pathological profile and outcome in a tertiary care center in North India. *World Journal of Surgery*, 35: 1273-1280.
Not in PICO
- Michikawa, T., Inoue, M., Shimazu, T., Sawada, N., Iwasaki, M., Sasazuki, S., Yamaji, T., Tsugane, S. & Japan Public Health Center-based Prospective Study Group (2012) Seaweed consumption and the risk of thyroid cancer in women: the Japan Public Health Center-based Prospective Study. *European Journal of Cancer Prevention*, 21: 254-260.
Not in PICO
- Moonim, M. T. (2012) Thyroid microcarcinoma - Definitions and significance. *Journal of Pathology*, 228: S4.
Narrative review
- Moser, E. (2005) Thyroid diseases in general practice - Impact of nuclear medicine diagnostics and therapy. [German]. *Zeitschrift für Allgemeinmedizin*, 81: 109-114.
Narrative review
- Mukasa, K., Noh, J. Y., Kunii, Y., Matsumoto, M., Sato, S., Yasuda, S., Suzuki, M., Ito, K. & Ito, K. (2011) Prevalence of malignant tumors and adenomatous lesions detected by ultrasonographic screening in patients with autoimmune thyroid diseases. *Thyroid*, 21: 37-41.
Not in PICO
- Mulla, Z. D. & Margo, C. E. (2000) Primary malignancies of the thyroid: Epidemiologic analysis of the Florida Cancer Data System registry. *Annals of Epidemiology*, 10: 24-30.
Not in PICO
- Naidoo, J., O'Briain, S., Sheehy, N., Vandenberghe, E., Gilham, C. & O'Mahony, D. (2011) Thyroid lymphoma presenting as a rapidly expanding neck mass. *Journal of Clinical Oncology*, 29.
Not in PICO
- Natale, F., Tedesco, M. A., Mocerino, R., Rinaldi, G., Tassinario, G., De, S., V, Gregorio, G. & Calabro, R. (2007) Feasibility, accuracy, and clinical relevance of a rapid thyroid evaluation during carotid duplex ultrasonography in hypertensive patients. *Journal of Clinical Hypertension*, 9: 518-521.
Not in PICO
- Nguyen, G.-K., Ginsberg, J., Crockford, P. M. & Villanueva, R. R. (1997) Hashimoto's thyroiditis: Cytodiagnostic accuracy and pitfalls. *Diagnostic Cytopathology*, 16: 531-536.
Not in PICO
- Nicolosi, A., Addis, E., Calo, P. G. & Tarquini, A. (1994) [Hyperthyroidism and cancer of the thyroid]. [Italian]. *Minerva Chirurgica*, 49: 491-495.
Not in PICO
- Nieder, C., Andratschke, N. H., Geinitz, H. & Grosu, A. L. (2012) Use of the Graded Prognostic Assessment (GPA) score in patients with brain metastases from primary tumours not represented in the diagnosis-specific GPA studies. *Strahlentherapie und Onkologie*, 188: 692-695.
Not in PICO
- Nys, P., Cordray, J.-P. & Merceron, R.-E. (2009) Etiologic discussion and clinical relevance of thyroid ultrasonography in subclinical hypothyroidism. A retrospective study in 1845 patients. *Annales d'Endocrinologie*, 70: 59-63.
Not in PICO (referred)
- Oberwittler, H., Nawroth, P. P., Ziegler, R. & Seibel, M. J. (1998) Clinical presentation of thyroid carcinomas. [German]. *Tumor Diagnostik und Therapie*, 19: 52-55.
Narrative review
- Oi, N. & Ohi, K. (2013) Comparison of the symptoms of menopause and symptoms of thyroid disease in Japanese women aged 35-59 years. *Climacteric*, 16: 555-560.

- Not in PICO (population/outcome [e.g., no distinction between benign & malignant thyroid tumours])
- OlaOlorun, D. A., Meier, D. E. & Tarpley, J. L. (2000) Operative management of thyroid abnormalities in a general medical practice hospital in sub-Saharan Africa. *Tropical Doctor*, 30: 221-223.
Not in PICO
- Omori, K. (2011) Diagnosis of voice disorders. *Japan Medical Association Journal*, 54: 248-253.
Narrative review
- Orlandi, F., Caraci, P., Mussa, A., Saggiorato, E., Pancani, G. & Angeli, A. (2001) Treatment of medullary thyroid carcinoma: an update. [Review] [143 refs]. *Endocrine-Related Cancer*, 8: 135-147.
Narrative review
- Ortiz, R., Hupart, K. H., Defesi, C. R. & Surks, M. I. (1998) Effect of early referral to an endocrinologist on efficiency and cost of evaluation and development of treatment plan in patients with thyroid nodules. *The Journal of clinical endocrinology and metabolism*, 83: 3803-3807.
Not in PICO
- Ott, J. J., Ullrich, A. & Miller, A. B. (2009) The importance of early symptom recognition in the context of early detection and cancer survival. *European Journal of Cancer*, 45: 2743-2748.
Narrative review
- Pacini, F., Burrioni, L., Ciuoli, C., Di, C. G. & Guarino, E. (2004) Management of thyroid nodules: a clinicopathological, evidence-based approach. [Review] [32 refs]. *European Journal of Nuclear Medicine & Molecular Imaging*, 31: 1443-1449.
Narrative review
- Panigrahi, B., Roman, S. A. & Sosa, J. A. (2010) Medullary thyroid cancer: are practice patterns in the United States discordant from American Thyroid Association guidelines? *Annals of Surgical Oncology*, 17: 1490-1498.
Not in PICO
- Parham, M., Aminorroaya, A. & Amini, M. (2009) Prevalence of palpable thyroid nodule in Isfahan, Iran, 2006: a population based study. *Experimental & Clinical Endocrinology & Diabetes*, 117: 209-213.
Not in PICO
- Park, K. W., Shin, J. H., Han, B. K., Ko, E. Y. & Chung, J. H. (2011) Inoperable symptomatic recurrent thyroid cancers: preliminary result of radiofrequency ablation. *Annals of Surgical Oncology*, 18: 2564-2568.
Not in PICO
- Paschke, R., Schmid, K. W., Gartner, R., Mann, K., Dralle, H. & Reiners, C. (2010) [Epidemiology, pathophysiology, guideline-adjusted diagnostics, and treatment of thyroid nodules]. [German]. *Medizinische Klinik*, 105: 80-87.
Narrative review
- Patel, N. & Vanderpump, M. (2005) Goitres and thyroid carcinoma. *Practitioner*, 249: 574-577.
Narrative review
- Petrone, L. R. (1996) A primary care approach to the adult patient with nodular thyroid disease. *Archives of Family Medicine*, 5: 92-100.
Narrative review
- Petronella, P., Scorzelli, M., Luise, R., Iannaci, G., Sapere, P., Ferretti, M., Costanzo, R. M. A., Freda, F., Canonico, S. & Rossiello, R. (2012) Primary thyroid angiosarcoma: an unusual localization. *World Journal of Surgical Oncology*, 10: 73.
Not in PICO
- Pichon, M. F., Basuyau, J. P., Gory-Delabaere, G., Eche, N., Daver, A., Blanc-Vincent, M. P., Riedinger, J. M., Deneux, L. & Bidart, J. M. (2001) Standards, Options and Recommendations for tumor markers in thyroid cancers. *Bulletin du Cancer*, 88: 775-792.
Guideline

- Polyzos, S. A., Kita, M. & Avramidis, A. (2007) Thyroid nodules - stepwise diagnosis and management. [Review] [227 refs]. *Hormones*, 6: 101-119.
Narrative review
- Popovtzer, A., Shpitzer, T., Bahar, G., Feinmesser, R. & Segal, K. (2006) Thyroid cancer in children: management and outcome experience of a referral center. *Otolaryngology - Head & Neck Surgery*, 135: 581-584.
Not in PICO
- Puigdevall, V., Serrano, L. & Lapuerta, L. (1997) Acute thyroïdal situations in primary care. [Spanish]. *Atencion Primaria*, 20: 148-152.
Narrative review
- Puthenparambil, J., Lechner, K. & Kornek, G. (2010) Autoimmune hemolytic anemia as a paraneoplastic phenomenon in solid tumors: A critical analysis of 52 cases reported in the literature. *Wiener Klinische Wochenschrift*, 122: 229-236.
Not in PICO
- Quadbeck, B. & Mann, K. (1998) Malignant struma - Diagnostics of thyroid cancer. [German]. *Tumor Diagnostik und Therapie*, 19: 56-59.
Narrative review
- Quadbeck, B., Pruellage, J., Roggenbuck, U., Hirche, H., Janssen, O. E., Mann, K. & Hoermann, R. (2002) Long-term follow-up of thyroid nodule growth. *Experimental & Clinical Endocrinology & Diabetes*, 110: 348-354.
Not in PICO
- Rahimi, M., Farshchian, N., Rezaee, E., Shahebrahimi, K. & Madani, H. (2013) To differentiate benign from malignant thyroid nodule comparison of sonography with FNAC findings. *Pakistan Journal of Medical Sciences*, 29: 77-80.
Not in PICO
- Raijmakers, P. G., Paul, M. A. & Lips, P. (2008) Sentinel node detection in patients with thyroid carcinoma: a meta-analysis. *World Journal of Surgery*, 32: 1961-1967.
Not in PICO
- Rakover, Y., Dharan, M. & Luboshitsky, R. (1994) Hirschsprung's disease associated with isolated familial medullary carcinoma of the thyroid. *Journal of Pediatric Endocrinology*, 7: 373-377.
Not in PICO
- Ramschak-Schwarzer, S., Langsteger, W., Wolf, G., Dimai, H. P. & Leb, G. (1997) Management of suspected malignant nodular goiter in pregnancy. [German]. *Acta Medica Austriaca*, 24: 146-147.
Narrative review
- Ranganathan, B., Thriyayi, S., Yap, B., Loughran, S. & Homer, J. J. (2012) Regional audit on thyroid cytology reporting. *Clinical Otolaryngology*, 37: 115.
Abstract only, not enough information available to ascertain relevance, but I don't think it is in PICO
- Re, M., Pepe, M., Orlando, G., Sorcini, G., Clemenzia, G., Canova, R., Falcone, M., Cancrini, A., Gallo, G. & Russo, G. (1989) Tumour markers in the early diagnosis of thyroid tumours. [Italian]. *Minerva Medica*, 80: 341-343.
Not in PICO
- Redlich, A., Boxberger, N., Kurt, W. S., Fruhwald, M., Rohrer, T. & Vorwerk, P. (2012) Sensitivity of fine-needle biopsy in detecting pediatric differentiated thyroid carcinoma. *Pediatric Blood & Cancer*, 59: 233-237.
Not in PICO
- Regional Thyroid Cancer Group (2000) Northern Cancer Network guidelines for management of thyroid cancer. [Review] [155 refs]. *Clinical Oncology (Royal College of Radiologists)*, 12: 373-391.
Guideline
- Reynolds, R. M., Weir, J., Stockton, D. L., Brewster, D. H., Sandeep, T. C. & Strachan, M. W. J. (2005) Changing trends in incidence and mortality of thyroid cancer in Scotland. *Clinical Endocrinology*,

- 62: 156-162.
Not in PICO
- Richards, M. L. (2009) Thyroid cancer genetics: multiple endocrine neoplasia type 2, non-medullary familial thyroid cancer, and familial syndromes associated with thyroid cancer. [Review] [58 refs]. *Surgical Oncology Clinics of North America*, 18: 39-52.
Narrative review
- Rifat, S. F. & Ruffin, M. T. (1994) Management of thyroid nodules. [Review] [36 refs]. *American Family Physician*, 50: 785-790.
Narrative review
- Rivkees, S. A., Mazzaferri, E. L., Verburg, F. A., Reiners, C., Luster, M., Breuer, C. K., Dinauer, C. A. & Udelsman, R. (2011) The Treatment of Differentiated Thyroid Cancer in Children: Emphasis on Surgical Approach and Radioactive Iodine Therapy. *Endocrine Reviews*, 32: 798-826.
Narrative review
- Ron, E., Lubin, E. & Modan, B. (1984) Screening for early detection of radiation-associated thyroid cancer: a pilot study. *Israel Journal of Medical Sciences*, 20: 1164-1168.
Not in PICO
- Ron, E., Curtis, R., Hoffman, D. A. & Flannery, J. T. (1984) Multiple primary breast and thyroid cancer. *British Journal of Cancer*, 49: 87-92.
Not in PICO
- Rosen, J. E. & Stone, M. D. (2006) Contemporary diagnostic approach to the thyroid nodule. *Journal of Surgical Oncology*, 94: 649-661.
Narrative review
- Rosenberg, H. K. (2009) Sonography of pediatric neck masses. *Ultrasound Quarterly*, 25: 111-127.
Narrative review
- Rousset, B., Ziercher, L. & Borson-Chazot, F. (2011) Molecular analyses of thyroid tumors for diagnosis of malignancy on fine-needle aspiration biopsies and for prognosis of invasiveness on surgical specimens. *Annales d'Endocrinologie*, 72: 125-128.
Not in PICO
- Rubinstein, W. S. (2010) Endocrine cancer predisposition syndromes: hereditary paraganglioma, multiple endocrine neoplasia type 1, multiple endocrine neoplasia type 2, and hereditary thyroid cancer. [Review]. *Hematology - Oncology Clinics of North America*, 24: 907-937.
Narrative review
- Rukhman, N. & Silverberg, A. (2011) Thyroid cancer in older men. [Review]. *Aging Male*, 14: 91-98.
Narrative review
- Sadetzki, S., Calderon-Margalit, R., Peretz, C., Novikov, I., Barchana, M. & Papa, M. Z. (2003) Second primary breast and thyroid cancers (Israel). *Cancer Causes and Control*, 14: 367-375.
Not in PICO
- Sahin, T. T., Yuksel, O., Girgin, G., Sipahi, H., Dikmen, K., Azili, C., Taneri, F. & Baydar, T. (2009) Is neopterin level a predictive and differential biomarker in patients with thyroid disorders? *Journal of Endocrinological Investigation*, 32: 147-149.
Not in PICO
- Saller, B., Moeller, L., Gorges, R., Janssen, O. E. & Mann, K. (2002) Role of conventional ultrasound and color Doppler sonography in the diagnosis of medullary thyroid carcinoma. *Experimental and Clinical Endocrinology and Diabetes*, 110: 403-407.
Not in PICO
- Sarac, F., Savas, S., Yalcin, M. A. & Akcicek, F. (2011) Thyroid nodules in patients with adrenal incidentaloma. *European Geriatric Medicine*, 2: S102.
Not in PICO
- Schmid, K. W. & Reiners, C. (2011) [When is thyroid fine-needle biopsy most effective?]. [German]. *Pathologe*, 32: 169-172.
Narrative review

- Schmidt, M. & Schicha, H. (2011) [Thyroid disorders]. [German]. *Versicherungsmedizin / herausgegeben von Verband der Lebensversicherungs-Unternehmen e, und*: 176-179.
Narrative review
- Schroder, S. & Bocker, W. (1983) [Early cancer of the thyroid. Subclassification of 268 differentiated thyroid cancers]. [German]. *Pathologe*, 4: 225-234.
Not in PICO
- Sebastian-Ochoa, N., Fernandez-Garcia, J. C., Mancha, D., I, Sebastian-Ochoa, A., Fernandez, G. D., Ortega Jimenez, M. V., Gallego, D. E. & Tinahones, M. F. (2011) [Clinical experience in a high-resolution thyroid nodule clinic]. [Spanish]. *Endocrinologia y Nutricion*, 58: 409-415.
Not in PICO
- Serra, M., Mendez, M. A., Davins, J., Borrell, M., Baxarias, J. & Rios, L. (1995) Thyroid pathology in a health center. [Spanish]. *Atencion primaria / Sociedad Espanola de Medicina de Familia y Comunitaria*, 15: 457-460.
Not in PICO
- Sherman, S. I. (2003) Thyroid carcinoma. *Lancet*, 361: 501-511.
Narrative review
- Shinozaki, N., Sakamoto, A., Kasai, N., Uchida, M. & Sakurai, K. (1983) [Multiple primary malignancies associated with thyroid cancer]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 29: 1385-1391.
Not in PICO
- Siegmund, T., Scholz, I. & Schumm-Draeger, P. M. (2004) [How to treat benign thyroid gland nodules]. [German]. *MMW Fortschritte der Medizin*, 146: 24-27.
Narrative review
- Silver, C. E., Brauer, R. J. & Schreiber, K. (1984) Cytologic evaluation of thyroid nodules: New criteria for surgery. *New York State Journal of Medicine*, 84: 109-112.
Narrative review
- Singer, P. A., Cooper, D. S., Daniels, G. H., Ladenson, P. W., Greenspan, F. S., Levy, E. G., Braverman, L. E., Clark, O. H., McDougall, I. R., Ain, K. V. & Dorfman, S. G. (1996) Treatment guidelines for patients with thyroid nodules and well-differentiated thyroid cancer. *Archives of Internal Medicine*, 156: 2165-2172.
Guideline
- Sipos, J. A. & Mazzaferri, E. L. (2008) The therapeutic management of differentiated thyroid cancer. *Expert Opinion on Pharmacotherapy*, 9: 2627-2637.
Narrative review
- Sippel, R. S., Kunnimalaiyaan, M. & Chen, H. (2008) Current management of medullary thyroid cancer. *The Oncologist*, 13: 539-547.
Narrative review
- Smellie, W. S. A., Vanderpump, M. P. J., Fraser, W. D., Bowley, R. & Shaw, N. (2008) Best practice in primary care pathology: Review 11. *Journal of Clinical Pathology*, 61: 410-418.
Narrative review
- Smith, L. H. & Oi, R. H. (1984) Detection of malignant ovarian neoplasms: a review of the literature. I. Detection of the patient at risk; clinical, radiological and cytological detection. [Review] [205 refs]. *Obstetrical & Gynecological Survey*, 39: 313-328.
Not in PICO
- Sogol, P. B., Sugawara, M., Gordon, H. E., Shellow, W. V., Hernandez, F. & Hershman, J. M. (1983) Cowden's disease: familial goiter and skin hamartomas. A report of three cases. *Western Journal of Medicine*, 139: 324-328.
Not in PICO
- Soh, E. Y. & Park, C. S. (1993) Diagnostic approach to thyroid carcinoma in Graves' disease. *Yonsei Medical Journal*, 34: 191-194.
Not in PICO

- Stevenson, J. C., Hillyard, C. J., Spanos, E., MacIntyre, I., Ackroyd, N., Lynn, J., Brown, M. J. & Stevenson, B. M. (1981) Sipple syndrome: marked variability of the disease within a family and implications for management. *Postgraduate Medical Journal*, 57: 104-108.
Not in PICO
- Stiefelbogen, P. (2001) [Thyroid gland diseases. The etiology of many symptoms]. [German]. *MMW Fortschritte der Medizin*, 143: Suppl-86.
Narrative review
- Stojadinovic, A., Peoples, G., Libutti, S., Henry, L., Eberhardt, J., Howard, R., Gur, D., Elster, E. & Nissan, A. (2009) Development of a clinical decision model for thyroid nodules. *BMC Surgery*, 9: 12.
Not in PICO
- Suehiro, F. (2006) Thyroid cancer detected by mass screening over a period of 16 years at a health care center in Japan. *Surgery Today*, 36: 947-953.
Not in PICO
- Sultana, N., March, Z. & Trousdale, R. (2012) Prevalence of thyroid cancer in minority patients with thyroid nodules at an urban inner city hospital. *Endocrine Reviews*, 33.
Not in PICO
- Svinaryov, M. & Aranovich, V. (2003) Iodine deficiency disorders in the Saratov province in Russia. *Journal of Endocrinological Investigation*, 26: Suppl-9.
Not in PICO
- Szybinski, P. & Nowak, W. (2001) [Thyroid carcinoma--contemporary diagnostic principles and treatment]. [Review] [22 refs] [Polish]. *Przegląd Lekarski*, 58: 809-813.
Narrative review
- Tamiolakis, D., Tsamis, I., Thomaidis, V., Lambropoulou, M., Alexiadis, G., Venizelos, I., Jivanakis, T. & Papadopoulos, N. (2007) Oral complaints caused from metastases to the mandible and maxilla. *Chirurgia (Bucharest, Romania : 1990)*, 102: 439-442.
Not in PICO
- Telander, R. L., Zimmerman, D., Sizemore, G. W., van Heerden, J. A. & Grant, C. S. (1989) Medullary carcinoma in children. Results of early detection and surgery. *Archives of Surgery*, 124: 841-843.
Not in PICO
- Terris, D. J., Anderson, S. K., Seybt, M. W. & Gourin, C. G. (2008) Findings from a public thyroid screening protocol: ultrasound and disease characteristics. *Orl; Journal of Oto-Rhino-Laryngology & its Related Specialties*, 70: 335-337.
Not in PICO
- Todd, C. H. (2009) Management of thyroid disorders in primary care: Challenges and controversies. *Postgraduate Medical Journal*, 85: 655-659.
Narrative review
- Tonjes, A. & Paschke, R. (573) [Diagnosis and therapy of thyroid nodules]. [Review] [22 refs] [German]. *Internist*, 46: 565-572.
Narrative review
- Tranquart, F., Bleuzen, A., Pierre-Renoult, P., Chabrolle, C., Sam, G. M. & Lecomte, P. (2008) [Elastosonography of thyroid lesions]. [French]. *Journal de Radiologie*, 89: t-9.
Not in PICO
- Tuttle, R. M. & Fagin, J. A. (100) Can risk-adapted treatment recommendations replace the 'one size fits all' approach for early-stage thyroid cancer patients? *Oncology (Williston Park)*, 23: 592.
Not in PICO
- Tuttle, R. M., Vaisman, F. & Tronko, M. D. (2011) Clinical presentation and clinical outcomes in Chernobyl-related paediatric thyroid cancers: what do we know now? What can we expect in the future?. [Review]. *Clinical Oncology (Royal College of Radiologists)*, 23: 268-275.
Narrative review

- Upile, T., Jerjes, W., Mahil, J., Tailor, H., Balakumar, R., Rao, A., Qureshi, Y., Bowman, I. & Mukhopadhyay, S. (2011) How to do it: the difficult thyroid. *Head & Neck Oncology*, 3: 54.
Narrative review
- Vaisman, F., Bulzico, D. A., Pessoa, C. H. C. N., Bordallo, M. A. N., de Mendonca, U. B. T., Dias, F. L., Coeli, C. M., Corbo, R. & Vaisman, M. (2011) Prognostic factors of a good response to initial therapy in children and adolescents with differentiated thyroid cancer. *Clinics*, 66: 281-286.
Not in PICO
- Valeri, R., Chatzis, O., Mygdakos, N., Sioutopoulou, D., Makrantonakis, P., Angel, I., Pazaitou, K. & Destouni, C. (2011) Occurrence of second primary malignancies in patients with thyroid cancer. *Cytopathology*, 22: 108.
Not in PICO
- Van den Brink, J. L., De Herder, W. W., Bonjer, H. J. & Poulblon, R. M. L. (2000) Palpable thyroid nodules; a diagnostic protocol for otolaryngologists. [Dutch]. *Nederlands Tijdschrift voor Keel-Neus- Oorheelkunde*, 6: 101-106.
Not in PICO
- Van den Bruel, A., Moreno-Reyes, R., Bex, M., Daumerie, C. & Glinoyer, D. (2008) Is the management of thyroid nodules and differentiated thyroid cancer in accordance with recent consensus guidelines? - Results of a national survey. *Clinical Endocrinology*, 68: 599-604.
Not in PICO
- van, L. J., Wessels, P., van, R. E., Boer, A. M., Wiersma, A., Goudswaard, A. N. & Nederlands, H. G. (2007) [Summary of the practice guideline 'Thyroid disorders' (first revision) from the Dutch College of General Practitioners]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 151: 2829-2832.
Guideline
- Vidal-Trecan, G. M., Pazart, L. H. & Massol, J. A. (1999) A method for guideline development: assessing practical feasibility and adaptation of thyroid nodule guidelines. *Journal of Evaluation in Clinical Practice*, 5: 189-198.
Not in PICO
- Vitale, G., Tagliaferri, P., Caraglia, M., Rampone, E., Ciccarelli, A., Bianco, A. R., Abbruzzese, A. & Lupoli, G. (2000) Slow release lanreotide in combination with interferon-alpha2b in the treatment of symptomatic advanced medullary thyroid carcinoma. *Journal of Clinical Endocrinology and Metabolism*, 85: 983-988.
Not in PICO
- von der Weid, N. X. (2008) Adult life after surviving lymphoma in childhood. [Review] [41 refs]. *Supportive Care in Cancer*, 16: 339-345.
Narrative review
- Voronetskii, I. B. & Varshavskii, I. (1989) [Standardization of diagnostic studies in thyroid diseases]. [Russian]. *Meditssinskaia Radiologija*, 34: 16-20.
Narrative review
- Wade, H. (1980) The treatment and preoperative diagnosis of differentiated thyroid carcinoma presenting as a clinically solitary nodule. *British Journal of Surgery*, 67: 728-731.
Narrative review
- Wakasugi-Sato, N., Wakasugi, T., Oda, M., Yamashita, Y., Yoshioka, I., Yamamoto, N., Habu, M., Kodama, M., Kokuryo, S., Ichimiya, H., Miyamoto, I., Tanaka, T., Kito, S., Matsumoto-Takeda, S., Ishikawa, A., Seta, Y., Matsuo, K., Takahashi, T., Tominaga, K. & Morimoto, Y. (2010) Clinical significance of ultrasonographic examination including detection of thyroid gland diseases when surveying cervical lymph nodes in subjects with oral squamous cell carcinoma. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics*, 109: e78-e85.
Not in PICO

Wanis, K., Oucharek, J. & Groot, G. (2013) Quality of thyroid referrals in Saskatchewan. *Quality in Primary Care*, 21: 247-252.
Not in PICO

Wasko, R., Michalek, K., Pacholska, J., Obrepalska-Stepelowska, A., Gozdicka-Jozefiak, A. & Sowinski, J. (2005) Clinical significance of the insulin-like growth factor I gene promoter (P1) polymorphism in thyroid nodular disease. *Neuroendocrinology Letters*, 26: 699-703.
Not in PICO

Watkinson, J. C. & British Thyroid Association (2004) The British Thyroid Association guidelines for the management of thyroid cancer in adults. *Nuclear Medicine Communications*, 25: 897-900.
Guideline

Watkinson, J. C., Franklyn, J. A. & Olliff, J. F. (2006) Detection and surgical treatment of cervical lymph nodes in differentiated thyroid cancer. *Thyroid*, 16: 187-194.
Narrative review

Weinrib, S. L., Lane, W. S. & Rappaport, J. M. (2012) Successful Management of Differentiated Thyroid Cancer in A Community-Based Endocrine Practice. *Endocrine Practice*, 18: 170-178.
Not in PICO

Weiss, R. E. & Lado-Abeal, J. (2002) Thyroid nodules: diagnosis and therapy. *Current Opinion in Oncology*, 14: 46-52.
Narrative review

Welkenhuysen, M. & Evers-Kiebooms, G. (2002) General practitioners and predictive genetic testing for late-onset diseases in Flanders: what are their opinions and do they want to be involved? *Community Genetics*, 5: 128-137.
Not in PICO

Wellhoner, P. (2011) Endocrine disorders and the gastrointestinal tract : What consequences are possible?. [German]. *Gastroenterologe*, 6: 285-291.
Narrative review

Wemeau, J. L. & Do, C. C. (2002) [Thyroid nodule, cancer and pregnancy]. [Review] [32 refs] [French]. *Annales d Endocrinologie*, 63: 438-442.
Narrative review

Wojciechowski, B. & Kusmann, J. (2013) Thyroid nodules as secondary finding. *Langenbeck's Archives of Surgery*, 398: 1019.
Not in PICO

Wu, S. Y. & Weiss, R. E. (2006) Radioiodine imaging in the primary care of thyroid disease. *Postgraduate Medicine*, 119: 70-77.
Narrative review

Wygoda, A., Wygoda, Z., Jarzab, B. & Skladowski, K. (2004) Parathyroid cancer - Differential diagnosis difficulties and therapeutic problems. [Polish]. *Nowotwory*, 54: 377-383.
Narrative review

Zhang, L., Wei, W. J., Ji, Q. H., Zhu, Y. X., Wang, Z. Y., Wang, Y., Huang, C. P., Shen, Q., Li, D. S. & Wu, Y. (2012) Risk Factors for Neck Nodal Metastasis in Papillary Thyroid Microcarcinoma: A Study of 1066 Patients. *Journal of Clinical Endocrinology & Metabolism*, 97: 1250-1257.
Not in PICO

Review question:

Which investigations of symptoms of suspected thyroid cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references	No of references	Finish date of
---------------	---------------	------------------	------------------	----------------

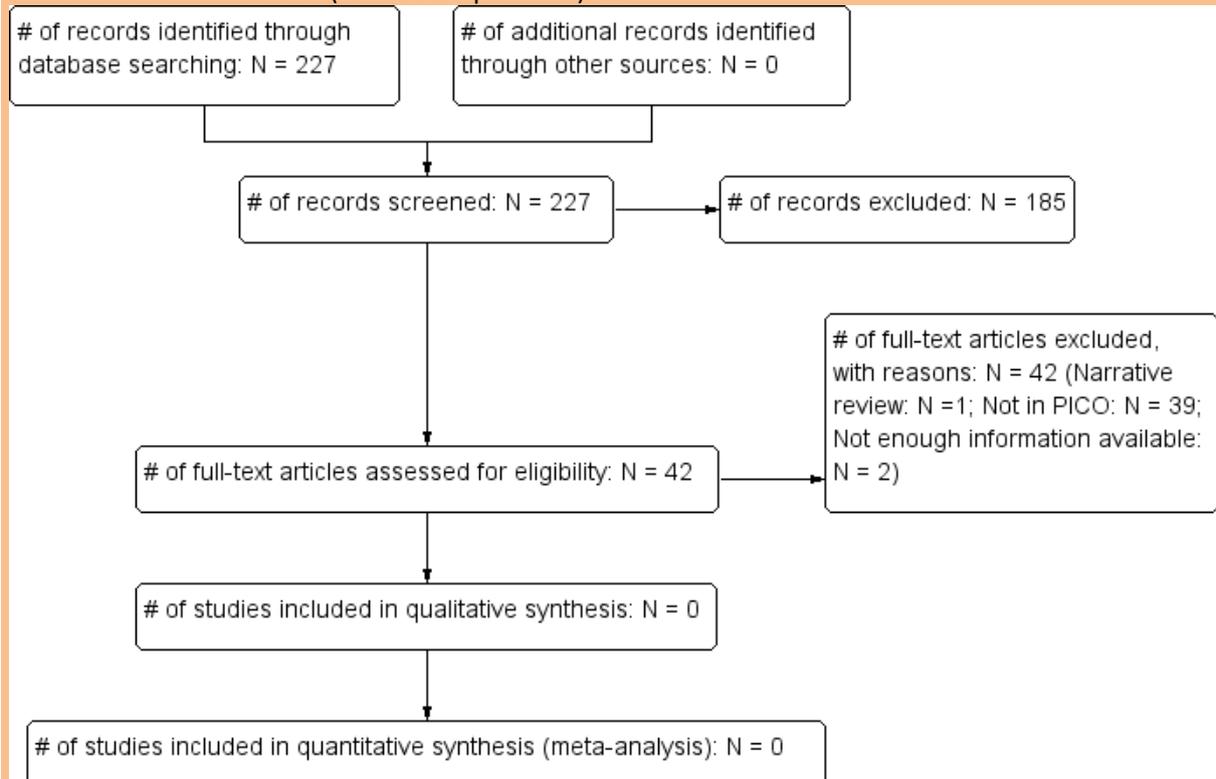
		found	retrieved	search
<i>Medline</i>	1980-2013	545	118	16/05/2013
<i>Premedline</i>	1980-2013	53	9	16/05/2013
<i>Embase</i>	1980-2013	770	150	17/05/2013
<i>Cochrane Library</i>	1980-2013	70	13	20/05/2013
<i>Psychinfo</i>	1980-2013	2	1	16/05/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	65	12	20/05/2013

Total References retrieved (after de-duplication): 205

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	5/2013-27/08/2014	16	5	27/08/2014
<i>Premedline</i>	5/2013-27/08/2014	48	10	27/08/2014
<i>Embase</i>	5/2013-27/08/2014	47	8	27/08/2014
<i>Cochrane Library</i>	5/2013-27/08/2014	3	1	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	5/2013-27/08/2014	13	1	27/08/2014

Total References retrieved (after de-duplication): 22



Study results

No evidence was identified pertaining to the diagnostic accuracy of ultrasound, thyroid function tests, or fine needle aspiration in patients with suspected thyroid cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Acharya, U. R., Faust, O., Sree, S. V., Molinari, F., Garberoglio, R. & Suri, J. S. (2011) Cost-effective and non-invasive automated benign & malignant thyroid lesion classification in 3D contrast-enhanced ultrasound using combination of wavelets and textures: A class of thyroscan algorithms. *Technology in Cancer Research and Treatment*, 10: 371-380.

Reference test not in PICO

Acharya, U. R., Faust, O., Sree, S. V., Molinari, F. & Suri, J. S. (2012) ThyroScreen system: high resolution ultrasound thyroid image characterization into benign and malignant classes using novel combination of texture and discrete wavelet transform. *Computer Methods & Programs in Biomedicine*, 107: 233-241.

Population not in PICO

Aksu, O., Koroglu, B. K., Ersoy, I. H., Koroglu, M., Ciris, M., Ersoy, S. & Tamer, M. N. (2014) Thyroid fine needle aspiration biopsy: Which method should be preferred in an endemic goiter region? *Acta Medica Mediterranea*, 30: 297-301.

Not in PICO (secondary care)

Al-Qasabi, Q. O. (1999) The role of fine needle aspiration biopsy and frozen section in the management of nodular thyroid lesions. *Saudi Medical Journal*, 20: 258-262.

Population not in PICO

Allen, M., Sapinho, I., Raposo, L. & Torrinha, J. (2008) [Cyto-histological correlation of malignant thyroid nodules: clinical factors as predictors of malignancy]. [Portuguese]. *Acta Medica Portuguesa*, 21: 135-140.

Population not in PICO

Alonso, N., Lucas, A., Salinas, I., Castella, E. & Sanmarti, A. (2003) Frozen section in a cytological diagnosis of thyroid follicular neoplasm. *Laryngoscope*, 113: 563-566.

Population not in PICO

Altavilla, G., Pascale, M. & Nenci, I. (1990) Fine needle aspiration cytology of thyroid gland diseases. *Acta Cytologica*, 34: 251-256.

Population not in PICO

Alter, C. A. & Moshang, T., Jr. (1991) Diagnostic dilemma. The goiter. [Review] [31 refs]. *Pediatric Clinics of North America*, 38: 567-578.

Narrative review

Anne, S., Teot, L. A. & Mandell, D. L. (2008) Fine needle aspiration biopsy: role in diagnosis of pediatric head and neck masses. *International Journal of Pediatric Otorhinolaryngology*, 72: 1547-1553.

Population not in PICO

Appetecchia, M., Bacaro, D., Brigida, R., Milardi, D., Bianchi, A. & Solivetti, F. (2006) Second generation ultrasonographic contrast agents in the diagnosis of neoplastic thyroid nodules. *Journal of Experimental & Clinical Cancer Research*, 25: 325-330.

Population not in PICO

Aron, M., Kapila, K. & Verma, K. (2006) Role of fine-needle aspiration cytology in the diagnosis of secondary tumors of the thyroid - twenty years' experience. *Diagnostic Cytopathology*, 34: 240-245.

Population not in PICO

Aversa, S., Pivano, G., Vergano, R., Mussa, A., Gonzatto, I., Ondolo, C. & Orlandi, F. (1999) [The accuracy of the fine needle aspiration biopsy in 1250 thyroid nodules]. [Italian]. *Acta*

Otorhinolaryngologica Italica, 19: 260-264.

Population not in PICO

Aversa, S., Pivano, G., Vergano, R., Mussa, A., Gonzatto, I., Ondolo, C. & Orlandi, F. (1999) The accuracy of the fine needle aspiration biopsy in 1250 thyroid nodules. [Italian]. *Acta otorhinolaryngologica Italica : organo ufficiale della Societa italiana di otorinolaringologia e chirurgia cervico-facciale*, 19: 260-264.

Duplicate

Avetis'ian, I. L., Iarovoi, A. O. & Gul'chii, N. V. (1999) Guided fine-needle biopsy of thyroid nodular formations in the early diagnosis of thyroid carcinoma. [Russian]. *Likars'ka sprava / Ministerstvo okhorony zdorov'ia Ukrainy*, 106-110.

Paper in Russian with English abstract. Unable to translate the whole paper, but from abstract appear to be in secondary care

Babcock, D. S. (372) Thyroid disease in the pediatric patient: emphasizing imaging with sonography. [Review] [26 refs]. *Pediatric Radiology*, 36: 299-308.

Narrative review

Bajaj, J., Morgenstern, N., Sugrue, C., Wasserman, J. & Wasserman, P. (2012) Clinical impact of second opinion in thyroid fine needle aspiration cytology (FNAC): A study of 922 interinstitutional consultations. *Diagnostic Cytopathology*, 40: 422-429.

Reference test not in PICO

Bal'ter, S. A., Paches, A. I., Anokhin, B. M., Mironova, G. T. & Chubarova, N. V. (1989) [Ultrasonic tomography in the diagnosis of diseases of the thyroid gland]. [Russian]. *Voprosy Onkologii*, 35: 920-924.

Narrative review

Bannas, P., Derlin, T., Groth, M., Apostolova, I., Adam, G., Mester, J. & Klutmann, S. (2012) Can (18)F-FDG-PET/CT be generally recommended in patients with differentiated thyroid carcinoma and elevated thyroglobulin levels but negative I-131 whole body scan? *Annals of Nuclear Medicine*, 26: 77-85.

Population not in PICO

Bartolazzi, A., Bellotti, C. & Sciacchitano, S. (2012) Methodology and technical requirements of the galectin-3 test for the preoperative characterization of thyroid nodules. *Applied Immunohistochemistry and Molecular Morphology*, 20: 2-7.

Narrative review

Bartos, M., Pomorski, L. & Narebski, J. (2000) The diagnosis and operative treatment of solitary thyroid nodule: a prospective study. [Polish]. *Wiadomosci lekarskie (Warsaw, Poland : 1960)*, 53: 134-141.

Population not in PICO

Basharat, R., Bukhari, M. H., Saeed, S. & Hamid, T. (2011) Comparison of fine needle aspiration cytology and thyroid scan in solitary thyroid nodule. *Pathology Research International*, 2011: 754041.

Population not in PICO

Baskin, H. J. (2004) New applications of thyroid and parathyroid ultrasound. [Review] [50 refs]. *Minerva Endocrinologica*, 29: 195-206.

Narrative review

Behnia, M. & Gharib, H. (1996) Primary care diagnosis of thyroid disease. *Hospital Practice*, 31: 121-134.

Narrative review

Block, M. A. (1987) Diagnosis and management of carcinoma of the thyroid. *Comprehensive Therapy*, 13: 48-56.

Narrative review

Boi, F., Lai, M. L., Deias, C., Piga, M., Serra, A., Uccheddu, A., Faa, G. & Mariotti, S. (2003) The usefulness of 99mTc-SestaMIBI scan in the diagnostic evaluation of thyroid nodules with

- oncocytic cytology. *European Journal of Endocrinology*, 149: 493-498.
Population not in PICO
- Boigon, M. & Moyer, D. (1977) Solitary thyroid nodules. Separating benign from malignant conditions. [Review] [14 refs]. *Postgraduate Medicine*, 98: 73-74.
Narrative review
- Brake, M. K., Bartlett, C., Hart, R. D., Trites, J. R. B. & Taylor, S. M. (2011) Complementary and alternative medicine use in the thyroid patients of a head and neck practice. *Otolaryngology - Head and Neck Surgery*, 145: 208-212.
Test not in PICO
- Bravis, V., Lingam, R., Haroon, M. & Devendra, D. (2009) Access to thyroid ultrasound: Audit of clinical efficiency & governance of the rapid access one-stop thyroid ultrasound FNA clinic. *Endocrine Abstracts*, 19: 395.
Reference test not in PICO
- Brennan, M. & French, J. (2007) Thyroid lumps and bumps. *Australian Family Physician*, 36: 531-536.
Narrative review
- Breslin, M., Lawrance, J. A., Desai, M., Ryder, W. D. & Allan, E. (2004) The role of ultrasound-guided fine-needle aspiration biopsy in the previously treated patient with thyroid cancer. *Clinical Otolaryngology & Allied Sciences*, 29: 146-148.
Population not in PICO
- Briggs, J. C., A'amar, O., Bigio, I., Rosen, J. E., Lee, S. L., Sharon, A. & Sauer-Budge, A. F. (2014) Integrated Device for in Vivo Fine Needle Aspiration Biopsy and Elastic Scattering Spectroscopy in Preoperative Thyroid Nodules. *Journal of Medical Devices-Transactions of the Asme*, 8.
Not in PICO
- Brougham, K., Nixon, F., Maurice, Y., Clark, A. H. & Srinivasan, V. (2011) A correlation review of diagnostic modalities for assessing thyroid nodules. *Journal of Pathology*, 224: S32.
Case series
- Brown, R. L., de Souza, J. A. & Cohen, E. E. W. (2011) Thyroid cancer: Burden of illness and management of disease. *Journal of Cancer*, 2: 193-199.
Narrative review
- Brunese, L., Romeo, A., Iorio, S., Napolitano, G., Fucili, S., Zeppa, P., Vallone, G., Lombardi, G., Bellastella, A., Biondi, B. & Sodano, A. (2008) Thyroid B-flow twinkling sign: a new feature of papillary cancer. *European Journal of Endocrinology / European Federation of Endocrine Societies*, 159: 447-451.
Population not in PICO
- Brychta, I., Dropco, I., Stencl, J. & Danis, D. (2002) Diagnostic reliability of aspiration biopsy and peroperative histology in thyroid gland carcinoma. [Slovak]. *Lekarsky Obzor*, 51: 173-175.
Population not in PICO
- Buitrago, R. F., Saenz de Santamaria, M. J. & Moreno, C. J. (1989) [Cytological diagnosis of thyroid nodules by fine needle aspiration. A study of 385 cases from primary care]. [Spanish]. *Atencion Primaria*, 6: 714-718.
Reference test not in PICO
- Cairncross, L. & Panieri, E. (2013) Pre-operative diagnosis of thyroid cancer: Clinical, radiological and pathological correlation. *South African Journal of Surgery*, 51: 46-49.
Not in PICO
- Cakir, M., Celik, E., Tuncer, F. B. & Tekin, A. (2013) A rare coexistence of thyroid lymphoma with papillary thyroid carcinoma. *Annals of African Medicine*, 12: 188-190.
Not in PICO
- Can, A. S. & Peker, K. (2008) Comparison of palpation-versus ultrasound-guided fine-needle aspiration biopsies in the evaluation of thyroid nodules. *BMC Research Notes*, 1: 12.
Population not in PICO

- Caplan, R. H., Wester, S. M., Lambert, P. J. & Rooney, B. L. (2000) Efficient evaluation of thyroid nodules by primary care providers and thyroid specialists. *American Journal of Managed Care*, 6: 1134-1140.
Reference test not in PICO
- Caplan, R. H. (2001) Evaluation of palpable thyroid nodules: Are endocrinologists assessing patients efficiently? *Endocrinologist*, 11: 321-326.
Test not in PICO
- Cappelli, C., Tironi, A., Mattanza, C., Cumetti, D., Agosti, B., Gandossi, E., Pirola, I., Martino, E., Cherubini, L., Micheletti, L., Castellano, M. & Agabiti, R. E. (2005) Cost-effectiveness of fine-needle-aspiration cytology of thyroid nodules with intranodular vascular pattern using two different needle types (Structured abstract). *Endocrine Pathology*, 16: 349-354.
Population not in PICO
- Cappelli, C., Castellano, M., Pirola, I., Gandossi, E., De, M. E., Cumetti, D., Agosti, B. & Rosei, E. A. (2006) Thyroid nodule shape suggests malignancy. *European Journal of Endocrinology*, 155: 27-31.
Population not in PICO
- Carpi, A., Ferrari, E., De, G. C., Sagripanti, A., Nicolini, A. & Di, C. G. (1994) The value of aspiration needle biopsy in evaluating thyroid nodules. *Thyroidology*, 6: 5-9.
Population not in PICO
- Carpi, A., Nicolini, A., Sagripanti, A., Righi, C., Menchini, F. F. & Di, C. G. (2000) Large-needle aspiration biopsy for the preoperative selection of palpable thyroid nodules diagnosed by fine-needle aspiration as a microfollicular nodule or suspected cancer. *American Journal of Clinical Pathology*, 113: 872-877.
Population not in PICO
- Carpi, A., Nicolini, A., Sagripanti, A., Menchini, F. F., Righi, C., Romani, R. & Di, C. G. (2002) Large-needle aspiration biopsy for the preoperative selection of follicular adenoma diagnosed by fine-needle aspiration as a microfollicular nodule or suspected cancer. *American Journal of Clinical Oncology: Cancer Clinical Trials*, 25: 209-212.
Population not in PICO
- Carpi, A., Rossi, G., Mechanick, J. I., Nicolini, A., Camici, M., Russo, M. A. & Di, C. G. (2011) Large needle aspiration biopsy histology for preoperative selection of Hurthle cell thyroid nodules. *Histopathology*, 59: 892-896.
Population not in PICO
- Castells, I., Pardo, N., Videla, S., Gimenez, G., Llargues, E., Simo, O., Recasens, M. A., Guirao, X., Mira, X., Serrano, A. & Sanmarti, A. (2013) [Healthcare impact of introduction of thyroid ultrasound in a thyroid nodule pathology unit]. [Spanish]. *Endocrinologia y Nutricion*, 60: 53-59.
Reference test not in PICO
- Castro, M. R. & Gharib, H. (2000) Thyroid nodules and cancer. *Postgraduate Medicine*, 107: 113-124.
Narrative review
- Castro, M. R. & Gharib, H. (2005) Continuing controversies in the management of thyroid nodules. [Review] [79 refs]. *Annals of Internal Medicine*, 142: 926-931.
Narrative review
- Cattaneo, F., Burgi, U. & Mueller, B. (1999) [Goiter and nodular thyroid disease: clinical guidelines for diagnosis and treatment. (Waiting? Hormone therapy? Surgery? radioiodine?)]. [Review] [42 refs] [German]. *Therapeutische Umschau*, 56: 356-363.
Narrative review
- Cavaliere, A., Colella, R., Puxeddu, E., Gambelunghe, G., Avenia, N., d'Ajello, M., Cartaginese, F., Vitali, R., Bellezza, G., Giansanti, M., Sidoni, A. & De, F. P. (2008) Fine needle aspiration cytology of thyroid nodules: conventional vs thin layer technique. *Journal of Endocrinological Investigation*, 31: 303-308.
Reference test not in PICO

- Cerutti, J. M. (2011) Employing genetic markers to improve diagnosis of thyroid tumor fine needle biopsy. *Current Genomics*, 12: 589-596.
Narrative review
- Chabon, S. L. (505) Identification and evaluation of thyroid nodules. [Review] [8 refs]. *Lippincott's Primary Care Practice*, 1: 499-504.
Narrative review
- Chammas, M. C., de Araujo Filho, V. J., Moyses, R. A., Brescia, M. D., Mulatti, G. C., Brandao, L. G., Cerri, G. G. & Ferraz, A. R. (2008) Predictive value for malignancy in the finding of microcalcifications on ultrasonography of thyroid nodules. *Head & Neck*, 30: 1206-1210.
Reference test not in PICO
- Chang, D. L. F., Leung, A. M., Braverman, L. E. & Pearce, E. N. (2011) Thyroid testing during pregnancy at an Academic Boston Area Medical Center. *Journal of Clinical Endocrinology and Metabolism*, 96: E1452-E1456.
Population not in PICO
- Chang, Y.-J., Mittal, V., Remine, S., Manyam, H., Sabir, M., Richardson, T. & Young, S. (2006) Correlation between clinical and histological findings in parathyroid tumors suspicious for carcinoma. *American Surgeon*, 72: 419-426.
Population not in PICO
- Choi, J. W., Lee, J. H., Baek, J. H., Choi, B. S., Jeong, K. S., Ryu, J. S., Kim, T. Y., Kim, W. B. & Shong, Y. K. (2010) Diagnostic accuracy of ultrasound and 18-F-FDG PET or PET/CT for patients with suspected recurrent papillary thyroid carcinoma. *Ultrasound in Medicine & Biology*, 36: 1608-1615.
Population not in PICO
- Cibas, E. S. (2010) Fine-needle aspiration in the work-up of thyroid nodules. [Review] [78 refs]. *Otolaryngologic Clinics of North America*, 43: 257-271.
Narrative review
- Cochand-Priollet, B., Vielh, P., Royer, B., Belleannee, G., Collet, J. F., Goubin-Versini, I., Leteurtre, E. & sous l'egide de la Societe francaise de cytologie clinique (2012) [Thyroid cytopathology: Bethesda System 2010]. [French]. *Annales de Pathologie*, 32: 177-183.
Narrative review
- Conti, P. S., Durski, J. M., Bacqai, F., Grafton, S. T. & Singer, P. A. (1999) Imaging of locally recurrent and metastatic thyroid cancer with positron emission tomography. *Thyroid*, 9: 797-804.
Population not in PICO
- Conzo, G., Troncone, G., Docimo, G., Pizza, A., Sciascia, V., Bellevicine, C., Napolitano, S., Della, P. C., Palazzo, A., Signoriello, G. & Santini, L. (2013) Cytologically undetermined thyroid's follicular lesions: surgical procedures and histological outcome in 472 cases. *Annali Italiani di Chirurgia*, 84: 251-256.
Not in PICO
- Corrias, A., Mussa, A., Baronio, F., Arrigo, T., Salerno, M., Segni, M., Vigone, M. C., Gastaldi, R., Zirilli, G., Tuli, G., Beccaria, L., Iughetti, L., Einaudi, S., Weber, G., De, L. F., Cassio, A. & Study Group for Thyroid Diseases of Italian Society for Pediatric Endocrinology and Diabetology (SIEDP/ISPED) (2010) Diagnostic features of thyroid nodules in pediatrics. *Archives of Pediatrics & Adolescent Medicine*, 164: 714-719.
Population not in PICO
- D'Ugo, D., Persiani, R., Pende, V., De, C. E., Rausei, S. & Picciocchi, A. (2000) The impact of the fine needle aspiration in the management of thyroid nodules. [Italian]. *Minerva Endocrinologica*, 25: 5-10.
Population not in PICO
- D'Ugo, D., Persiani, R., Pende, V., D'Andrilli, A., De, C. E., Rausei, S. & Picciocchi, A. (2001) [Clinical role of the cytologic study of thyroid nodules]. [Italian]. *Annali Italiani di Chirurgia*, 72: 287-291.
Population not in PICO

- Dan, H.-J., Wang, Y., Dan, H.-Y., Lu, B.-J., Li, T. & Hu, B. (2010) Diagnosis of small single solid thyroid nodule with real-time ultrasound elastography. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 26: 63-65.
Population not in PICO
- Daneman, D. & Daneman, A. (2005) Diagnostic imaging of the thyroid and adrenal glands in childhood. *Endocrinology and Metabolism Clinics of North America*, 34: 745-768.
Narrative review
- Deandrea, M., Mormile, A., Veglio, M., Motta, M., Pellerito, R., Gallone, G., Grassi, A., Torchio, B., Bradac, R., Garberoglio, R. & Fonzo, D. (2002) Fine-needle aspiration biopsy of the thyroid: Comparison between thyroid palpation and ultrasonography. *Endocrine Practice*, 8: 282-286.
Population not in PICO
- Demirci, H., Erdamar, H., Karakoc, A. & Arslan, M. (2010) Thyroid fine needle aspiration biopsy: is topical local anaesthesia beneficial? *International journal of clinical practice.*, 64: 25-28.
Reference test not in PICO
- Deshpande, H. A., Morgensztern, D. & Sosa, J. A. (2011) Medullary thyroid cancer in the past, present and future: From bench to bedside. *Expert Review of Endocrinology and Metabolism*, 6: 585-597.
Narrative review
- Dong, M. J., Liu, Z. F., Zhao, K., Ruan, L. X., Wang, G. L., Yang, S. Y., Sun, F. & Luo, X. G. (2009) Value of 18F-FDG-PET/PET-CT in differentiated thyroid carcinoma with radioiodine-negative whole-body scan: a meta-analysis (DARE structured abstract). *Nuclear Medicine Communications.*, 30: 639-650.
Test not in PICO
- Dong, S., Lu, G. Z., Gao, Y. M., Zhang, H., Guo, X. H. & Gao, Y. (2008) [A clinical pathological study of thyroid nodules detected by physical examinations]. [Chinese]. *Chung-Hua Nei Ko Tsa Chih Chinese Journal of Internal Medicine*, 47: 189-192.
Paper in Chinese with English abstract. Unable to translate the whole paper, but from abstract appear to be in secondary care
- Drozdz, V., Polyanskaya, O., Ostapenko, V., Demidchik, Y., Biko, I. & Reiners, C. (2002) Systematic ultrasound screening as a significant tool for early detection of thyroid carcinoma in Belarus. *Journal of pediatric endocrinology & metabolism : JPEM*, 15: 979-984.
Population not in PICO
- Dumitriu, L., Mogos, I. & Calin, E. (1984) Fine-needle aspiration biopsy of the thyroid correlated with clinical scintigraphic, echographic and pathologic data in nodular and diffuse goiter. *Endocrinologie*, 22: 261-268.
Population not in PICO
- Ershova, G. I. (2004) [Methods of improvement of diagnosis of thyroid cancer]. [Russian]. *Khirurgiia.*(12):47-9, 2004., 47-49.
Reference test not in PICO
- Faquin, W. C., Bongiovanni, M. & Sadow, P. M. (2011) Update in thyroid fine needle aspiration. *Endocrine Pathology*, 22: 178-183.
Narrative review
- Filatov, A. A., Svjatov, A. V. & Scerbakova, N. G. (1989) [The clinical value of ultrasonic study of the thyroid gland]. [German]. *Radiologia Diagnostica*, 30: 633-638.
Population not in PICO
- Fitz-Patrick, D., Navin, J. J. & Fukunaga, B. N. (1968) Fine-needle aspiration biopsy of thyroid nodules. A diagnostic method that minimizes the need for surgery. *Postgraduate Medicine*, 80: 62-65.
Narrative review
- Fleischer, B. & Borm, D. (1984) Early diagnosis and treatment of thyroid carcinoma. [German]. *Therapiewoche*, 34: 4568-4571.
Narrative review

- Florentine, B. D., Staymates, B., Rabadi, M., Barstis, J., Black, A. & Cancer Committee of the Henry Mayo Newhall Memorial Hospital (2006) The reliability of fine-needle aspiration biopsy as the initial diagnostic procedure for palpable masses: a 4-year experience of 730 patients from a community hospital-based outpatient aspiration biopsy clinic. *Cancer*, 107: 406-416.
Population not in PICO
- Flynn, K. (1996) Positron emission tomography: systematic review. PET as a diagnostic test in head and neck cancer (DARE structured abstract). *Database of Abstracts of Reviews of Effects.*, 18.
Test not in PICO
- Freeman, L. M. & Blafox, M. D. (2011) Letter from the editors: Controversies and changing concepts in thyroid cancer management. *Seminars in Nuclear Medicine*, 41: 81-82.
Letter from Editor
- Fruth, K. & Mann, W. J. (2009) [Malignant thyroid neoplasms: a diagnostic challenge for ENT specialists]. [German]. *HNO*, 57: 257-261.
Population not in PICO
- Fuhrer, D., Bockisch, A. & Schmid, K. W. (516) Euthyroid goiter with and without nodules--diagnosis and treatment. [Review]. *Deutsches Arzteblatt International*, 109: 506-515.
Narrative review
- Fukunari, N., Nagahama, M., Sugino, K., Mimura, T., Ito, K. & Ito, K. (2004) Clinical evaluation of color Doppler imaging for the differential diagnosis of thyroid follicular lesions. *World Journal of Surgery*, 28: 1261-1265.
Population not in PICO
- Furlan, J. C., Bedard, Y. C. & Rosen, I. B. (2005) Single versus sequential fine-needle aspiration biopsy in the management of thyroid nodular disease (Structured abstract). *Canadian Journal of Surgery*, 48: 12-18.
Reference test not in PICO
- Goldstein, R. E., Netterville, J. L., Burkey, B. & Johnson, J. E. (2002) Implications of follicular neoplasms, atypia, and lesions suspicious for malignancy diagnosed by fine-needle aspiration of thyroid nodules. *Annals of Surgery*, 235: 656-662.
Population not in PICO
- Gossain, V. V., Charnas, J., Carella, M. J., Rovner, D. R. & Calaca, W. M. (1998) Evaluation of "solitary" thyroid nodules in a community practice: a managed care approach. *American Journal of Managed Care*, 4: 679-684.
Reference test not in PICO
- Grob, F., Carrillo, D., Martinez-Aguayo, A., Zoroquain, P., Solar, A., Nicolaidis, I. & Gonzalez, H. (2014) - [Diagnostic yield of fine-needle aspiration cytology for the detection of thyroid cancer in pediatric patients]. [Spanish]. - *Revista Medica de Chile*, 142: 330-335.
Not in PICO
- Grunwald, F., Kalicke, T., Feine, U., Lietzenmayer, R., Scheidhauer, K., Dietlein, M., Schober, O., Lerch, H., Brandt-Mainz, K., Burchert, W., Hiltermann, G., Cremerius, U. & Biersack, H. J. (1999) Fluorine-18 fluorodeoxyglucose positron emission tomography in thyroid cancer: results of a multicentre study. *European Journal of Nuclear Medicine*, 26: 1547-1552.
Population not in PICO
- Grussendorf, M. (2001) Laboratory diagnostic of thyroid diseases in daily clinical practice. *Medizinische Welt*, 52: 24-27.
Narrative review
- Gu, M. (2014) The role of interventional cytopathologist in the cytologic diagnosis of thyroid nodules-an experience of a community FNA clinic of 1,424 nodules in 958 patients. *Laboratory Investigation*, 94: 104A.
Published as abstract only. Not enough information available to ascertain relevance.
- Gul, K., Ersoy, R., Dirikoc, A., Korukluoglu, B., Ersoy, P. E., Aydin, R., Ugras, S. N., Belenli, O. K. & Cakir, B. (2009) Ultrasonographic evaluation of thyroid nodules: Comparison of ultrasonographic,

- cytological, and histopathological findings. *Endocrine*, 36: 464-472.
Population not in PICO
- Gul, K., Aydin, C., Balkan, F., Erkan, A., Ersoy, R. & Cakir, B. (2010) Nondiagnostic fine needle aspiration biopsy results. *Endocrine Abstracts*, 20: 146.
Population not in PICO
- Gursoy, A., Anil, C. & Erismis, B. (2010) Fine needle aspiration biopsy of a thyroid nodule: A comparison of diagnostic performance of experienced and inexperienced physicians. *Endocrine Abstracts*, 22: 845.
Population not in PICO
- Hakala, T., Kholova, I., Sand, J., Saaristo, R. & Kellokumpu-Lehtinen, P. (2013) A core needle biopsy provides more malignancy-specific results than fine-needle aspiration biopsy in thyroid nodules suspicious for malignancy. *Journal of Clinical Pathology*, 66: 1046-1050.
Not in PICO
- Hamburger, J. I. (1988) Needle aspiration for thyroid nodules. Skip ultrasound--do initial assessment in the office. *Postgraduate Medicine*, 84: 61-66.
Population not in PICO
- Hamburger, J. I. & Husain, M. (1988) Semiquantitative criteria for fine-needle biopsy diagnosis: reduced false-negative diagnoses. *Diagnostic Cytopathology*, 4: 14-17.
Population not in PICO
- Hammond, I., Lentle, B. C. & Odell, P. F. (2010) The pursuit of impalpable thyroid nodules: are we using scarce resources wisely? *Canadian Association of Radiologists Journal*, 61: 98-101.
Narrative review
- Hammond, I. & Schweitzer, M. E. (2011) A resource allocation metric for thyroid biopsies. *JACR Journal of the American College of Radiology*, 8: 49-52.
Population not in PICO
- Harolds, J. A. (2011) New scrutiny of outpatient therapy with I-131. *Clinical Nuclear Medicine*, 36: 206-208.
Narrative review
- HAYES & -Inc (2013) BRAF p.Val600Glu testing in papillary thyroid carcinoma (Structured abstract). *Health Technology Assessment.Database..*
Not in PICO
- Higashi, T., Ito, K., Nishikawa, Y., Everhart, F. R., Jr., Ozaki, O., Manabe, Y., Suzuki, A., Yashiro, T., Hasegawa, M. & Mimura, T. (1988) Gallium-67 imaging in the evaluation of thyroid malignancy. *Clinical Nuclear Medicine*, 13: 792-799.
Test not in PICO
- Higashi, T., Kudo, T. & Kinuya, S. (2012) Radioactive iodine (131I) therapy for differentiated thyroid cancer in Japan: Current issues with historical review and future perspective. *Annals of Nuclear Medicine*, 26: 99-112.
Narrative review
- Ho, S., I, Depczynski, B., Lin, M., Clark, J. R., Wong, V., Lin, P. & Campbell, P. (2011) Positron emission tomography in non-medullary thyroid cancer. *ANZ Journal of Surgery*, 81: 116-124.
Narrative review
- Hoang, J. K., Raduazo, P., Yousem, D. M. & Eastwood, J. D. (2012) What to Do With Incidental Thyroid Nodules on Imaging? An Approach for the Radiologist. *Seminars in Ultrasound, CT and MRI*, 33: 150-157.
Narrative review
- Holan, J., Plank, J. & Uhrin, P. (1982) Results of thin-needle aspiration cytology combined with scintigraphy in nodular goiter. [Slovak]. *Bratislavske Lekarske Listy*, 77: 670-677.
Population not in PICO
- Hooft, L., Hoekstra, O. S., Deville, W., Lips, P., Teule, G. J., Boers, M. & Tulder, M. W. (2001) Diagnostic accuracy of 18F-fluorodeoxyglucose positron emission tomography in the follow-up of

- papillary or follicular thyroid cancer (DARE structured abstract). *Journal of Clinical Endocrinology and Metabolism*, 86: 3779-3786.
Test not in PICO
- Huang, I.-C., Chou, F.-F., Liu, R.-T., Tung, S.-C., Chen, J.-F., Kuo, M.-C., Hsieh, C.-J. & Wang, P.-W. (2012) Long-term outcomes of distant metastasis from differentiated thyroid carcinoma. *Clinical Endocrinology*, 76: 439-447.
Population not in PICO
- Huang, T. W., Lai, J. H., Wu, M. Y., Chen, S. L., Wu, C. H. & Tam, K. W. (2013) Systematic review of clinical practice guidelines in the diagnosis and management of thyroid nodules and cancer. *BMC Medicine*, 11: 191.
Not in PICO
- Iared, W., Shigueoka, D. C., Cristofoli, J. C., Andriolo, R., Atallah, A. N., Ajzen, S. A. & Valente, O. (2010) Use of color Doppler ultrasonography for the prediction of malignancy in follicular thyroid neoplasms: systematic review and meta-analysis (DARE structured abstract). *Journal of Ultrasound in Medicine*, 29: 419-425.
Population not in PICO
- Ito, K. (1989) [Definition, diagnosis and treatment of thyroid carcinoma at an early stage]. [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine*, 47: 1147-1151.
Narrative review
- Jargin, S. V. (2011) Validity of thyroid cancer incidence data following the chernobyl accident. *Health Physics*, 101: 754-757.
Narrative review
- Jaume, J. C. & Chen, H. (2011) Inadequate cytology of thyroid nodules. Repeat it or live with it. *Annals of Surgical Oncology*, 18: 1222-1223.
Narrative review
- Jiskra, J., Kubinyi, J. & Telicka, Z. (2012) Radioiodine 131I therapy of hyperthyroidism on an outpatient basis - Safe, effective and economic option. [Czech]. *Vnitřní Lekarství*, 58: 94-98.
Test not in PICO
- Joung, K. H., Park, J. Y., Kim, K. S. & Koo, B. S. (2014) Primary amyloid goiter mimicking rapid growing thyroid malignancy. *European Archives of Oto-Rhino-Laryngology*, 271: 417-420.
Not in PICO
- Kaczka, K., Celnik, A., Luks, B., Jasion, J. & Pomorski, L. (2012) Sentinel lymph node biopsy techniques in thyroid pathologies--a meta-analysis. *Endokrynologia Polska*, 63: 222-231.
Test not in PICO
- Karger, S., Engelhardt, C., Eszlinger, M., Tonjes, A., Herrmann, F., Muller, P., Schmidt, T., Weiss, C. L., Dralle, H., Lippitzsch, F., Tannapfel, A. & Fuhrer, D. (2006) Cytology and mRNA expression analysis of fine needle aspirates of thyroid nodules in an East German region with borderline iodine deficiency. *Hormone & Metabolic Research*, 38: 662-667.
Population not in PICO
- Kashiwagi, S., Onoda, N., Asano, Y., Watanabe, M., Morisaki, T., Aomatsu, N., Nakamura, M., Kawajiri, H., Takashima, T., Ohsawa, M., Ishikawa, T., Wakasa, K. & Hirakawa, K. (2012) [Needle biopsy using a Monopty Biopsy Instrument for the accurate diagnosis of thyroid cancer]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]*, 39: 2407-2409.
Population not in PICO
- Kassum, T. A., Goldstein, D. P., Rafferty, M. A., Rotstein, L. E. & Irish, J. C. (2007) Thyroid scintigraphy in the assessment of the solitary thyroid nodule: Differences in practice patterns between family physicians and specialists. *Journal of Otolaryngology*, 36: 49-53.
Population not in PICO
- Khairy, G. A. & Guraya, S. Y. (2004) Primary care evaluation of thyroid disease: Which clinical group needs urgent surgical referral? *Bahrain Medical Bulletin*, 26: 143-146.
Population not in PICO

- Khalid, A. N., Hollenbeak, C. S., Quraishi, S. A., Fan, C. Y. & Stack, B. C. (2006) The cost-effectiveness of iodine 131 scintigraphy, ultrasonography, and fine-needle aspiration biopsy in the initial diagnosis of solitary thyroid nodules (Structured abstract). *Archives of Otolaryngology, Head and Neck Surgery*, 132: 244-250.
Population not in PICO
- Khalid, A. N., Quraishi, S. A., Hollenbeak, C. S. & Stack, B. C. (2008) Fine-needle aspiration biopsy versus ultrasound-guided fine-needle aspiration biopsy: cost-effectiveness as a frontline diagnostic modality for solitary thyroid nodules (Structured abstract). *Head and Neck*, 30: 1035-1039.
Reference test not in PICO
- Kim, D.-L., Song, K.-H. & Kim, S. K. (2008) High prevalence of carcinoma in ultrasonography-guided fine needle aspiration cytology of thyroid nodules. *Endocrine Journal*, 55: 135-142.
Population not in PICO
- Klopper, J. P. & McDermott, M. T. (2007) Palpable pediatric thyroid abnormalities - diagnostic pitfalls necessitate a high index of clinical suspicion: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 1: 29.
Case series
- Knox, M. A. (2013) Thyroid nodules. *American Family Physician*, 88: 193-196.
Narrative review
- Ko, S. Y., Kim, E. K., Sung, J. M., Moon, H. J. & Kwak, J. Y. (2014) - Diagnostic performance of ultrasound and ultrasound elastography with respect to physician experience. - *Ultrasound in Medicine & Biology*, 40: 854-863.
Not in PICO
- Koutras, D. A. (2001) Thyroid nodules in children and adolescents: consequences in adult life. [Review] [29 refs]. *Journal of Pediatric Endocrinology*, 14: Suppl-7.
Narrative review
- Kovatcheva, R., Ivanova, R. S., Ivanova, R. B., Kanev, N., Sarafova, A. & Borissova, A.-M. (2004) Diagnostic value of echography, ultrasound-guided fine-needle biopsy and cytology in the early diagnosis of papillary thyroid cancer. [Bulgarian]. *Endokrinologiya*, 9: 42-48.
Population not in PICO
- Krawiecka-Jaworska, E. & Bujnowska-Fedak, M. M. (2009) The usefulness of ultrasound of the neck region, in particular the thyroid gland and lymph nodes, in general practice. [Polish]. *Family Medicine and Primary Care Review*, 11: 37-41.
Reference test not in PICO
- Kuz'michev, A. S. (1981) Thermography in the diagnosis of thyroid neoplasms. [Russian]. *Voprosy Onkologii*, 27: 33-37.
Population not in PICO
- Kwak, J. Y., Kim, E. K., Kim, M. J. & Son, E. J. (2009) Significance of sonographic characterization for managing subcentimeter thyroid nodules. *Acta Radiologica*, 50: 917-923.
Population not in PICO
- Kwak, J. Y. & Kim, E. K. (2013) Cancer: Indeterminate thyroid nodules--added testing, added value? *Nature Reviews Endocrinology*, 9: 321-323.
Not in PICO
- Labat-Moleur, F., Seigneurin, D., Breyton, M., Bachelot, I. & Sarrazin, R. (1995) Role and limitation of fine needle cytology of the thyroid. [French]. *Lyon Chirurgical*, 91: 117-119.
Narrative review
- Langer, M., Madeddu, G., Dettori, G., Tanda, F. & Solinas, A. M. (1980) [The problem of cancer diagnosis in thyroid nodules: a study in an endemic area for goiter in North Sardinia]. [German]. *Schweizerische Medizinische Wochenschrift. Journal Suisse de Medecine*, 110: 1411-1414.
Population not in PICO

- Leclere, J., Beckers, C., Cussac, J. F., Renan, C. A. & Vielh, P. (1993) Thyroid nodule. [French]. *Medecine Nucleaire*, 17: 191-201.
Narrative review
- Lee, J. K., Liu, R. S., Wu, S. Y., Huang, W. S. & Chou, M. C. (2006) Thallium-201 scan in evaluating thyroid nodules following equivocal fine-needle aspiration cytology. *Nuklearmedizin*, 45: 201-205.
Test not in PICO
- Leung, B. C. H. (2003) Management of thyroid nodules. *Hong Kong Practitioner*, 25: 611-615.
Narrative review
- Levy, M. J., Clain, J. E., Clayton, A., Halling, K. C., Kipp, B. R., Rajan, E., Roberts, L. R., Root, R. M., Sebo, T. J., Topazian, M. D., Wang, K. K., Wiersema, M. J. & Gores, G. J. (2007) Preliminary experience comparing routine cytology results with the composite results of digital image analysis and fluorescence in situ hybridization in patients undergoing EUS-guided FNA. *Gastrointestinal Endoscopy*, 66: 483-490.
Population not in PICO
- Li, H., Robinson, K. A., Anton, B., Saldanha, I. J. & Ladenson, P. W. (2011) Cost-effectiveness of a novel molecular test for cytologically indeterminate thyroid nodules. *Endocrine Reviews*, 32.
Population not in PICO
- Liang, H., Zhong, Y., Luo, Z., Huang, Y., Lin, H., Zhan, S., Xie, K. & Li, Q. Q. (2011) Diagnostic value of 16 cellular tumor markers for metastatic thyroid cancer: an immunohistochemical study. *Anticancer Research*, 31: 3433-3440.
Population not in PICO
- Liel, Y. & Fraenkel, N. (2005) Brief report: Use and misuse of thyroid ultrasound in the initial workup of patients with suspected thyroid problems referred by primary care physicians to an endocrine clinic. *Journal of General Internal Medicine*, 20: 766-768.
Population not in PICO
- Lin, J. D., Chao, T. C., Huang, B. Y., Chen, S. T., Chang, H. Y. & Hsueh, C. (2005) Thyroid cancer in the thyroid nodules evaluated by ultrasonography and fine-needle aspiration cytology. *Thyroid*, 15: 708-717.
Population not in PICO
- Lind, P. & Kohlfurst, S. (2006) Respective roles of thyroglobulin, radioiodine imaging, and positron emission tomography in the assessment of thyroid cancer. [Review] [82 refs]. *Seminars in Nuclear Medicine*, 36: 194-205.
Narrative review
- Listewnik, M. H., Birkenfeld, B., Piwowarska-Bilska, H., Cichon-Bankowska, K., Iglinska-Wagner, L., Watrak, W., Smolira, W., Zorga, P., Niedzialkowska, K., Elbl, B. & Sawrymowicz, M. (2010) The application of SPECT/CT scintigraphy with MIBI-Tc99(m) in the diagnosis of thyroid nodules - a preliminary report. *Endokrynologia Polska*, 61: 422-426.
Population not in PICO
- Listewnik, M. H., Birkenfeld, B., Chosia, M., Elbl, B., Piwowarska-Bilska, H., Zorga, P. & Niedzialkowska, K. (2011) Thyroid fine-needle aspiration biopsy: which lesions should be biopsied before 131I therapy? *Annales Academiae Medicae Stetinensis*, 57: 54-58.
Reference test not in PICO
- Little, J. W. (2006) Thyroid disorders. Part III: neoplastic thyroid disease. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*, 102: 275-280.
Narrative review
- Liu, F. H., Liou, M. J., Hsueh, C., Chao, T. C. & Lin, J. D. (2010) Thyroid follicular neoplasm: analysis by fine needle aspiration cytology, frozen section, and histopathology. *Diagnostic Cytopathology*, 38: 801-805.
Population not in PICO
- Maia, F. F., Matos, P. S., Pavin, E. J., Vassallo, J. & Zantut-Wittmann, D. E. (2011) Value of repeat ultrasound-guided fine-needle aspiration in thyroid nodule with a first benign cytologic result:

- impact of ultrasound to predict malignancy. *Endocrine*, 40: 290-296.
Population not in PICO
- Malesevic, M., Mihailovic, J., Vojcic, J. & Popadic, S. (2003) [Early diagnosis, therapy, follow-up and survival in patients with thyroid malignancies]. [Serbian]. *Acta Chirurgica Iugoslavica*, 50: 177-183.
Population not in PICO
- Marqusee, E., Benson, C. B., Frates, M. C., Doubilet, P. M., Larsen, P. R., Cibas, E. S. & Mandel, S. J. (2000) Usefulness of ultrasonography in the management of nodular thyroid disease. *Annals of Internal Medicine*, 133: 696-700.
Population not in PICO
- McShane, D. P., Freeman, J. L., Noyek, A. M. & Steinhardt, M. I. (1987) A review of conventional and CT imaging in the evaluation of thyroid malignancies.[Erratum appears in J Otolaryngol 1987 Jun;16(3):192]. *Journal of Otolaryngology*, 16: 4-9.
Narrative review
- Mehanna, H. M., Jain, A., Morton, R. P., Watkinson, J. & Shaha, A. (2009) Investigating the thyroid nodule. [Review] [25 refs]. *BMJ*, 338: b733.
Narrative review
- Meier, J. D. & Grimmer, J. F. (2014) - Evaluation and management of neck masses in children. [Review]. - *American Family Physician*, 89: 353-358.
Narrative review
- Meller, J. & Becker, W. (2002) The continuing importance of thyroid scintigraphy in the era of high-resolution ultrasound. [Review] [98 refs]. *European Journal of Nuclear Medicine & Molecular Imaging*, 29: Suppl-38.
Narrative review
- Mikosch, P., Gallowitsch, H. J., Kresnik, E., Jester, J., Wurtz, F. G., Kerschbaumer, K., Unterweger, O., Dinges, H. P. & Lind, P. (2000) Value of ultrasound-guided fine-needle aspiration biopsy of thyroid nodules in an endemic goitre area. *European Journal of Nuclear Medicine*, 27: 62-69.
Population not in PICO
- Miller, J. M., Kini, S. R. & Hamburger, J. I. (1985) The diagnosis of malignant follicular neoplasms of the thyroid by needle biopsy. *Cancer*, 55: 2812-2817.
Population not in PICO
- Mosci, C. & Iagaru, A. (2011) PET/CT imaging of thyroid cancer. [Review]. *Clinical Nuclear Medicine*, 36: e180-e185.
Narrative review
- Muddegowda, P. H., Lingegowda, J., Natesan, R. & Kurpad, R. (2011) Divide and rule: Cytodiagnosis of thyroid lesions using pattern analysis: A study of 233 cases. *Diagnostic Cytopathology*, 39: 888-895.
Population not in PICO
- Nabriski, D., Ness-Abramof, R., Brosh, T., Konen, O., Shapiro, M. S. & Shenkman, L. (2003) Clinical relevance of non-palpable thyroid nodules as assessed by ultrasound-guided fine needle aspiration biopsy. *Journal of Endocrinological Investigation*, 26: 61-64.
Reference test not in PICO
- Nacamulli, D., Nico, L., Barollo, S., Zambonin, L., Pennelli, G., Girelli, M. E., Casal, I. E., Pelizzo, M. R., Vianello, F., Negro, I., Watutantrige-Fernando, S., Mantero, F., Rugge, M. & Mian, C. (2012) Comparison of the diagnostic accuracy of combined elastosonography and BRAF analysis vs cytology and ultrasonography for thyroid nodule suspected of malignancy. *Clinical Endocrinology*, 77: 608-614.
Population not in PICO
- Oberwittler, H., Nawroth, P. P., Ziegler, R. & Seibel, M. J. (1998) Clinical presentation of thyroid carcinomas. [German]. *Tumor Diagnostik und Therapie*, 19: 52-55.
Narrative review

- Oi, N. & Ohi, K. (2013) Comparison of the symptoms of menopause and symptoms of thyroid disease in Japanese women aged 35-59 years. *Climacteric*, 16: 555-560.
Not in PICO (population/outcome [e.g., no distinction between benign & malignant thyroid tumours])
- Ongphiphadhanakul, B., Rajatanavin, R., Chiemchanya, S., Chailurkit, L., Kongsuksai, A. & Isarangkul Na Ayuthya, W. I. (1992) Systematic inclusion of clinical and laboratory data improves diagnostic accuracy of fine-needle aspiration biopsy in solitary thyroid nodules. *Acta Endocrinologica*, 126: 233-237.
Population not in PICO
- Ortiz, R., Hupart, K. H., DeFesi, C. R. & Surks, M. I. (1998) Effect of early referral to an endocrinologist on efficiency and cost of evaluation and development of treatment plan in patients with thyroid nodules. *Journal of Clinical Endocrinology & Metabolism*, 83: 3803-3807.
Population not in PICO
- Ota, H., Ito, Y., Matsuzuka, F., Kuma, S., Fukata, S., Morita, S., Kobayashi, K., Nakamura, Y., Kakudo, K., Amino, N. & Miyauchi, A. (2006) Usefulness of ultrasonography for diagnosis of malignant lymphoma of the thyroid. *Thyroid*, 16: 983-987.
Population not in PICO
- Paschke, R., Schmid, K. W., Gartner, R., Mann, K., Dralle, H. & Reiners, C. (2010) [Epidemiology, pathophysiology, guideline-adjusted diagnostics, and treatment of thyroid nodules]. [German]. *Medizinische Klinik*, 105: 80-87.
Narrative review
- Pelizzo, M. R., Merante, B., I, Toniato, A., Piotto, A., Bernante, P., Paggetta, C., De Salvo, G. L., Carpi, A., Rubello, D. & Casara, D. (2006) Sentinel node mapping and biopsy in thyroid cancer: a surgical perspective. *Biomedicine & Pharmacotherapy*, 60: 405-408.
Population not in PICO
- Perez, J. A., Pisano, R., Kinast, C., Valencia, V., Araneda, M. & Mera, M. E. (1991) [Needle aspiration cytology in euthyroid uninodular goiter]. [Spanish]. *Revista Medica de Chile*, 119: 158-163.
Population not in PICO
- Petrone, L. R. (1996) A primary care approach to the adult patient with nodular thyroid disease. [Review] [98 refs]. *Archives of Family Medicine*, 5: 92-100.
Narrative review
- Punthakee, X., Palme, C. E., Franklin, J. H., Zhang, I., Freeman, J. L. & Bedard, Y. C. (2005) Fine-needle aspiration biopsy findings suspicious for papillary thyroid carcinoma: a review of cytopathological criteria. *Laryngoscope*, 115: 433-436.
Population not in PICO
- Quon, A., Fischbein, N. J., McDougall, I. R., Le, Q. T., Loo, B. W., Jr., Pinto, H. & Kaplan, M. J. (2007) Clinical role of 18F-FDG PET/CT in the management of squamous cell carcinoma of the head and neck and thyroid carcinoma. [Review] [62 refs]. *Journal of Nuclear Medicine*, 48: Suppl-67S.
Narrative review
- Raber, W., Kmen, E., Kaserer, K., Waldhausl, W. & Vierhapper, H. (1997) [The "cold" nodule of the thyroid gland: 20 years experience with 2,071 patients and diagnostic limits of fine needle biopsy]. [German]. *Wiener Klinische Wochenschrift*, 109: 116-122.
Population not in PICO
- Raggiunti, B., Capone, F., Franchi, A., Fiore, G., Filippini, S., Colagrande, V., Di, N. M., Mangifesta, R. & Ballone, E. (2011) Ultrasound elastography: Can it provide valid information for differentiation of benign and malignant thyroid nodules? *Journal of Ultrasound*, 14: 136-141.
Population not in PICO
- Rahimi, M., Farshchian, N., Rezaee, E., Shahebrahimi, K. & Madani, H. (2013) To differentiate benign from malignant thyroid nodule comparison of sonography with FNAC findings. *Pakistan Journal of Medical Sciences*, 29: 77-80.
Not in PICO

- Raijmakers, P. G., Paul, M. A. & Lips, P. (2008) Sentinel node detection in patients with thyroid carcinoma: a meta-analysis. *World Journal of Surgery*, 32: 1961-1967.
Test not in PICO
- Ranganathan, B., Thriyayi, S., Yap, B., Loughran, S. & Homer, J. J. (2012) Regional audit on thyroid cytology reporting. *Clinical Otolaryngology*, 37: 115.
Abstract only, not enough information available to ascertain relevance, but I don't think it is in PICO
- Ravula, S., ZopfiConklin, A., Fung, P. C., Hirschowitz, S. L. & Sullivan, P. S. (2012) The benefits of a repeat FNA in follicular lesion of undetermined significance (FLUS) cases. *Laboratory Investigation*, 92: 103A.
Reference test not in PICO
- Redlich, A., Boxberger, N., Kurt, W. S., Fruhwald, M., Rohrer, T. & Vorwerk, P. (2012) Sensitivity of fine-needle biopsy in detecting pediatric differentiated thyroid carcinoma. *Pediatric Blood & Cancer*, 59: 233-237.
Population not in PICO
- Rifat, S. F. & Ruffin IV, M. T. (1994) Management of thyroid nodules. *American Family Physician*, 50: 785-790.
Narrative review
- Rizzo, M., Sindoni, A., Talamo, R. R., Bonaffini, O., Panetta, S., Scisca, C., Altavilla, G., Denaro, L., Rosano, A., Saraceno, G., Trimarchi, F. & Benvenga, S. (2013) Annual increase in the frequency of papillary thyroid carcinoma as diagnosed by fine-needle aspiration at a cytology unit in Sicily. *Hormones*, 12: 46-57.
Population not in PICO
- Rodriguez-Gil, Y., Perez-Barrios, A., Alberti-Masgrau, N., Garzon, A. & De, A. P. (2012) Fine-needle aspiration cytology diagnosis of metastatic nonhaematological neoplasms of the breast: A series of seven cases. *Diagnostic Cytopathology*, 40: 297-304.
Case series
- Rosario, P. W., Penna, G. C. & Calsolari, M. R. (2014) - Predictive factors of malignancy in thyroid nodules with repeatedly nondiagnostic cytology (Bethesda category I): value of ultrasonography. - *Hormone & Metabolic Research*, 46: 294-298.
Not in PICO
- Rosen, J. E. & Stone, M. D. (2006) Contemporary diagnostic approach to the thyroid nodule. *Journal of Surgical Oncology*, 94: 649-661.
Narrative review
- Rosenberg, H. K. (2009) Sonography of pediatric neck masses. *Ultrasound Quarterly*, 25: 111-127.
Narrative review
- Rossi, E. D., Morassi, F., Santeusano, G., Zannoni, G. F. & Fadda, G. (2010) Thyroid fine needle aspiration cytology processed by ThinPrep: an additional slide decreased the number of inadequate results. *Cytopathology*, 21: 97-102.
Reference test not in PICO
- Rousset, B., Ziercher, L. & Borson-Chazot, F. (2011) Molecular analyses of thyroid tumors for diagnosis of malignancy on fine-needle aspiration biopsies and for prognosis of invasiveness on surgical specimens. *Annales d'Endocrinologie*, 72: 125-128.
Population not in PICO
- Ruchala, M. & Szczepanek, E. (2008) Thyroid nodular disease. [Polish]. *Family Medicine and Primary Care Review*, 10: 1383-1392.
Narrative review
- Saller, B., Moeller, L., Gorges, R., Janssen, O. E. & Mann, K. (2002) Role of conventional ultrasound and color Doppler sonography in the diagnosis of medullary thyroid carcinoma. *Experimental and Clinical Endocrinology and Diabetes*, 110: 403-407.
Population not in PICO

- Scacchi, M., Andrioli, M., Carzaniga, C., Vitale, G., Moro, M., Poggi, L., Pecori, G. F., Fatti, L. M. & Cavagnini, F. (2009) Elastasonographic evaluation of thyroid nodules in acromegaly. *European Journal of Endocrinology*, 161: 607-613.
Reference test not in PICO
- Scheffler, P., Forest, V. I., Leboeuf, R., Florea, A. V., Tamilia, M., Sands, N. B., Hier, M. P., Mlynarek, A. M. & Payne, R. J. (2014) - Serum thyroglobulin improves the sensitivity of the McGill thyroid nodule score for well-differentiated thyroid cancer. - *Thyroid*, 24: 852-857.
Not in PICO
- Schmid, K. W., Lucciarini, P., Ladurner, D., Zechmann, W. & Hofstadter, F. (1987) Papillary carcinoma of the thyroid gland. Analysis of 94 cases with preoperative fine needle aspiration cytologic examination. *Acta Cytologica*, 31: 591-594.
Population not in PICO
- Schmid, K. W. & Reiners, C. (2011) [When is thyroid fine-needle biopsy most effective?]. [German]. *Pathologe*, 32: 169-172.
Narrative review
- Schueller-Weidekamm, C., Schueller, G., Kaserer, K., Scheuba, C., Ringl, H., Weber, M., Czerny, C. & Herneth, A. M. (2010) Diagnostic value of sonography, ultrasound-guided fine-needle aspiration cytology, and diffusion-weighted MRI in the characterization of cold thyroid nodules. *European Journal of Radiology*, 73: 538-544.
Population not in PICO
- Schwarzrock, R., Muller, S., Schober, O. & Hundeshagen, H. (1983) Ultrasonography in malignant thyroid disease. [German]. *Aktuelle Endokrinologie und Stoffwechsel*, 4: 107-120.
Reference test not in PICO
- Sebastian-Ochoa, N., Fernandez-Garcia, J. C., Mancha, D., I, Sebastian-Ochoa, A., Fernandez, G. D., Ortega Jimenez, M. V., Gallego, D. E. & Tinahones, M. F. (2011) [Clinical experience in a high-resolution thyroid nodule clinic]. [Spanish]. *Endocrinologia y Nutricion*, 58: 409-415.
Population not in PICO
- Seiberling, K. A., Dutra, J. C. & Gunn, J. (2008) Ultrasound-guided fine needle aspiration biopsy of thyroid nodules performed in the office. *The Laryngoscope*, 118: 228-231.
Population not in PICO
- Sellami, M., Tababi, S., Mamy, J., Zainine, R., Charfi, A., Beltaief, N., Sahtout, S. & Besbes, G. (2011) Interest of fine-needle aspiration cytology in thyroid nodule. [Review]. *European annals of otorhinolaryngology, head & neck diseases*, 128: 159-164.
Population not in PICO
- Shammas, A., Degirmenci, B., Mountz, J. M., McCook, B. M., Branstetter, B., Bencherif, B., Joyce, J. M., Carty, S. E., Kuffner, H. A. & Avril, N. (2007) 18F-FDG PET/CT in patients with suspected recurrent or metastatic well-differentiated thyroid cancer.[Erratum appears in J Nucl Med. 2007 Mar;48(3):412 Note: Bencherif, Badreddine B [corrected to Bencherif, Badreddine]]. *Journal of Nuclear Medicine*, 48: 221-226.
Population not in PICO
- Shrestha, M., Crothers, B. A. & Burch, H. B. (2012) The impact of thyroid nodule size on the risk of malignancy and accuracy of fine-needle aspiration: a 10-year study from a single institution. *Thyroid*, 22: 1251-1256.
Population not in PICO
- Shulutko, A. M., Semikov, V. I., Ivanova, N. A., Seredin, V. P., Mironova, M. V., Patalova, A. R., Gorbacheva, A. V. & Kulikov, I. O. (2002) [Ultrasonic method of study and puncture biopsy in diagnosing thyroid nodules]. [Russian]. *Khirurgiia.(5):7-12, 2002., 7-12.*
Population not in PICO
- Song, J., Wang, D., Yuan, H. & Zong, S.-Y. (2008) Analysis of contrast-enhanced ultrasonography in detection of solitary thyroid nodules. [Chinese]. *Chinese Journal of Medical Imaging Technology*,

24: 44-47.

Population not in PICO

Southwick, H. W. (1981) Head and neck cancer: Early detection. *Cancer*, 47: 1188-1192.

Narrative review

Stavric, G. D., Karanfiski, B. T., Kalamaras, A. K., Serafimov, N. Z., Georgievska, B. S. & Korubin, V. H. (1980) Early diagnosis and detection of clinically non-suspected thyroid neoplasia by the cytologic method: a critical review of 1536 aspiration biopsies. *Cancer*, 45: 340-344.

Population not in PICO

Stevens, C., Lee, J. K., Sadatsafavi, M. & Blair, G. K. (2009) Pediatric thyroid fine-needle aspiration cytology: a meta-analysis (DARE structured abstract). *Journal of Pediatric Surgery*, 44: 2184-2191.

Population not in PICO

Suen, K. C. (2002) Fine-needle aspiration biopsy of the thyroid. *CMAJ*, 167: 491-495.

Narrative review

Szybinski, Z., Szot, W., Bobrowski, A., Huszno, B., Nowak, K., Popiela, T. & Chlap, Z. (1988) [Fine-needle biopsy in the early diagnosis of thyroid neoplasms]. [Polish]. *Endokrynologia Polska*, 39: 291-299.

Population not in PICO

Tagaya, N. & Kubota, K. (2012) Reevaluation of needlescopic surgery. *Surgical Endoscopy and Other Interventional Techniques*, 26: 137-143.

Population not in PICO

Takeyama, H., Tabei, I., Uchida, K. & Morikawa, T. (2009) Sentinel node biopsy for follicular tumours of the thyroid gland. *British Journal of Surgery*, 96: 490-495.

Population not in PICO

Todd, C. H. (2009) Management of thyroid disorders in primary care: Challenges and controversies. *Postgraduate Medical Journal*, 85: 655-659.

Narrative review

Tonjes, A. & Paschke, R. (573) [Diagnosis and therapy of thyroid nodules]. [Review] [22 refs] [German]. *Internist*, 46: 565-572.

Narrative review

Tranquart, F., Bleuzen, A., Pierre-Renoult, P., Chabrolle, C., Sam, G. M. & Lecomte, P. (2008) Elastasonography of thyroid lesions. [French]. *Journal de Radiologie*, 89: 35-39.

Population not in PICO

Treglia, G., Castaldi, P., Villani, M. F., Perotti, G., de, W. C., Filice, A., Ambrosini, V., Cremonini, N., Santimaria, M., Versari, A., Fanti, S., Giordano, A. & Rufini, V. (2012) Comparison of 18F-DOPA, 18F-FDG and 68Ga-somatostatin analogue PET/CT in patients with recurrent medullary thyroid carcinoma. *European Journal of Nuclear Medicine & Molecular Imaging*, 39: 569-580.

Population not in PICO

Varhaug, J. E., Segadal, E. & Heimann, P. (1981) The utility of fine needle aspiration biopsy cytology in the management of thyroid tumors. *World Journal of Surgery*, 5: 573-577.

Population not in PICO

Vassilatou, E., Proikas, K., Margari, N., Papadimitriou, N., Hadjidakis, D. & Dimitriadis, G. (2014) - An adolescent with a rare midline neck tumor: thyroid carcinoma in a thyroglossal duct cyst. - *Journal of Pediatric Hematology/Oncology*, 36: 407-409.

Not in PICO

Vera, M. I., Merono, T., Urrutia, M. A., Parisi, C., Morosan, Y., Rosmarin, M., Schnitman, M., Brites, F., Grisendi, S., Serrano, M. S., Luciani, W., Serrano, L., Zuk, C., De, B. G., Cejas, C., Faingold, M. C. & Brenta, G. (2014) - Differential profile of ultrasound findings associated with malignancy in mixed and solid thyroid nodules in an elderly female population. - *Journal of Thyroid Research*, 2014: 761653.

Not in PICO (secondary care)

- Verbeek Hans, H. G., de Groot Jan, W. B., Sluiter, W. J., Muller Kobold, A. C., Plukker John, T. M. & Links, T. P. (2012) Calcitonin testing for detection of medullary thyroid cancer in patients with thyroid nodules. *Cochrane Database of Systematic Reviews*.
Population not in PICO
- Verbeek, H. H., Plukker, J. T., Koopmans, K. P., de Groot, J. W., Hofstra, R. M., Muller Kobold, A. C., van der Horst-Schrivers AN, Brouwers, A. H. & Links, T. P. (2012) Clinical relevance of 18F-FDG PET and 18F-DOPA PET in recurrent medullary thyroid carcinoma. *Journal of Nuclear Medicine*, 53: 1863-1871.
Population not in PICO
- Vetshev, P. S., Chilingaridi, K. E., Loshchenov, V. B., Gabaidze, D. I., Vetshev, S. P., Baranova, O. V. & Ozerov, S. K. (2001) Comparative assessment of diagnostic methods in adenomas of the thyroid gland. [Russian]. *Khirurgiia*, 4-10.
Population not in PICO
- Vette, J. K. (1985) Computed tomography of the thyroid gland. *Acta Endocrinologica, Supplementum*.: 1-82.
Narrative review
- Vidal-Casariogo, A., Lopez-Gonzalez, L., Jimenez-Perez, A., Ballesteros-Pomar, M. D., Kyriakos, G., Urioste-Fondo, A., Alvarez-San, M. R., Cano-Rodriguez, I. & Jimenez-Garcia de la Marina JM (2012) Accuracy of ultrasound elastography in the diagnosis of thyroid cancer in a low-risk population. *Experimental & Clinical Endocrinology & Diabetes*, 120: 635-638.
Reference test not in PICO
- Voronetskii, I. B. & Varshavskii, I. (1989) [Standardization of diagnostic studies in thyroid diseases]. [Russian]. *Meditinskaiia Radiologiia*, 34: 16-20.
Narrative review
- Wale, A., Miles, K., Young, B., Zammit, C., Williams, A., Quin, J. & Dizdarevic, S. (2011) Accuracy and potential cost-effectiveness of 99mTc-Methoxyisobutylisonitrile (MIBI) scintigraphy for the assessment of thyroid nodules in the context of the British Thyroid Association (BTA) guidelines. *Nuclear Medicine Communications*, 32: 435-436.
Population not in PICO
- Wang, Q. C., Cheng, W., Wen, X., Li, J. B., Jing, H. & Nie, C. L. (2014) - Shorter distance between the nodule and capsule has greater risk of cervical lymph node metastasis in papillary thyroid carcinoma. - *Asian Pacific Journal of Cancer Prevention: Apjcp*, 15: 855-860.
Not in PICO
- Wang, Z., Zhang, H., Zhang, P., He, L. & Dong, W. (2014) - Diagnostic Value of Ultrasound-detected Calcification in Thyroid Nodules. - *Annals of the Academy of Medicine, Singapore*, 43: 102-106.
Not in PICO
- Wanis, K., Oucharek, J. & Groot, G. (2013) Quality of thyroid referrals in Saskatchewan. *Quality in Primary Care*, 21: 247-252.
Not in PICO
- Weiss, R. E. & Lado-Abeal, J. (2002) Thyroid nodules: diagnosis and therapy. *Current Opinion in Oncology*, 14: 46-52.
Narrative review
- Wojciechowski, B. & Kusmann, J. (2013) Thyroid nodules as secondary finding. *Langenbeck's Archives of Surgery*, 398: 1019.
Not in PICO
- Wolf, G., Aigner, R. M., Schaffler, G., Schwarz, T. & Krippel, P. (2003) Pathology results in [18F]fluorodeoxyglucose positron emission tomography of the thyroid gland. *Nuclear Medicine Communications*, 24: 1225-1230.
Population not in PICO
- Wolinski, K., Szkudlarek, M., Szczepanek-Parulska, E. & Ruchala, M. (2014) - Usefulness of different ultrasound features of malignancy in predicting the type of thyroid lesions: a meta-analysis of

prospective studies. - *Polskie Archiwum Medycyny Wewnętrznej*, 124: 97-104.

Not in PICO

Wu, S. Y. & Weiss, R. E. (2006) Radioiodine imaging in the primary care of thyroid disease.

Postgraduate Medicine, 119.

Narrative review

Yip, L., Farris, C., Kabaker, A. S., Hodak, S. P., Nikiforova, M. N., McCoy, K. L., Stang, M. T., Smith, K. J.,

Nikiforov, Y. E. & Carty, S. E. (2011) Cost impact of routine molecular testing for indeterminate thyroid nodule fine needle aspiration biopsies. *Thyroid*, 21: A42-A43.

Reference test not in PICO

Yokozawa, T., Fukata, S., Kuma, K., Matsuzuka, F., Kobayashi, A., Hirai, K., Miyauchi, A. & Sugawara,

M. (1996) Thyroid cancer detected by ultrasound-guided fine-needle aspiration biopsy. *World Journal of Surgery*, 20: 848-853.

Population not in PICO

BRAIN AND CENTRAL NERVOUS SYSTEM CANCERS

Review question:

What is the risk of brain and CNS cancer in patients presenting in primary care with symptom(s)?

Results

Literature search

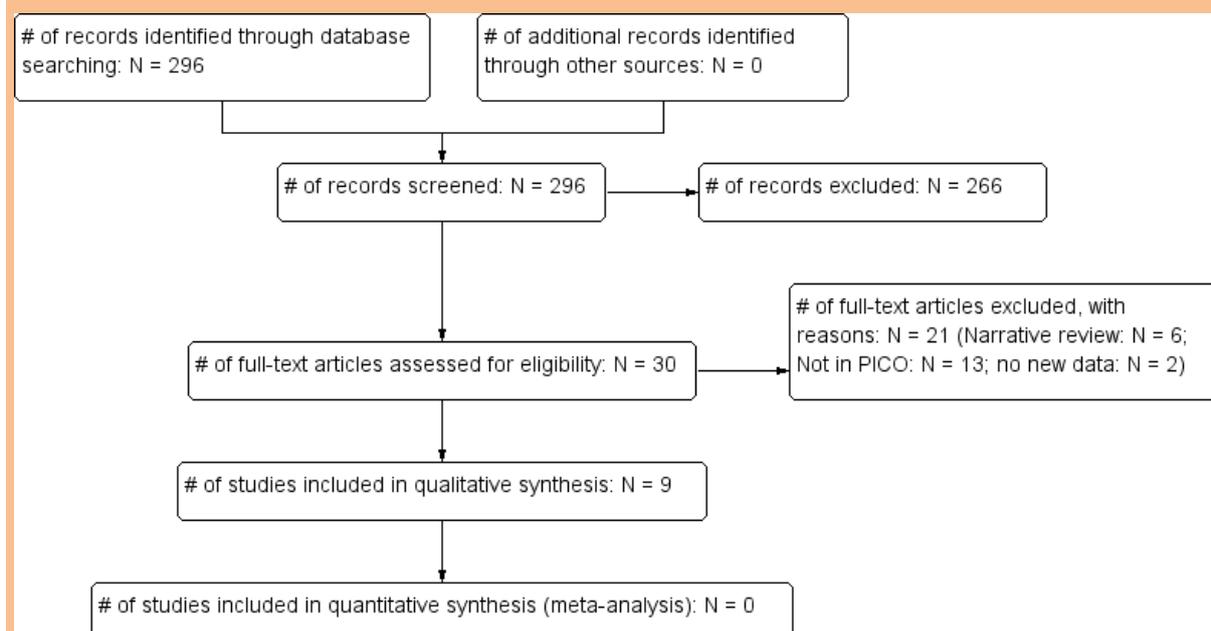
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2012	1668	138	20/02/2013
<i>Premedline</i>	1980-2012	24	1	20/02/2013
<i>Embase</i>	1980-2012	3631	174	25/02/2013
<i>Cochrane Library</i>	1980-2012	489	1	26/02/2013
<i>Psychinfo</i>	1980-2012	43	6	20/02/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2012	974	33	26/02/2013

Total References retrieved (after de-duplication): 277

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-12/08/2014	53	5	12/08/2014
<i>Premedline</i>	2013-12/08/2014	58	6	12/08/2014
<i>Embase</i>	2013-12/08/2014	304	6	12/08/2014
<i>Cochrane Library</i>	2013-12/08/2014	224	0	12/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-12/08/2014	87	2	12/08/2014

Total References retrieved (after de-duplication): 19



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included study in the figure below. The main issue to note is that a number of the studies employed case-control (or other non-consecutive, non-randomised) designs which have been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors may have gone some way in counteracting this influence. Other issues of concern include that some of the studies were conducted abroad and their direct relevance to UK-based primary care may therefore be limited, that the symptoms were underspecified in one study and therefore of limited use for the present purposes, and that some of the reference standards employed were of questionable quality and applicability.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Ansell (2009)	+	+	+	+	+	+	+
Dommett (2012, 2013)	+	+	+	+	+	+	+
Hamilton (2007)	+	+	+	+	?	+	+
Herr (1989)	+	+	?	+	+	+	?
Kernick (2008)	+	+	+	+	+	+	+
Kernick (2009)	+	+	+	+	+	+	+
Skiendziekowski (1980)	?	+	+	+	+	?	?

+	?	+
High	Unclear	Low

Study results

Table 1: Brain & CNS cancer: Study results for adult populations.

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI) Frequency
Hamilton (2007)	Headache	All patients	0.09 (0.08-0.1) Cases: 362/3505 Controls: 261/24021
Hamilton (2007)	Headache*	Patients 60-69 years	0.12 (NR)
Kernick (2008)	Undifferentiated headache	All patients	0.15 (0.12-0.19) 97/63921
Kernick (2008)	Undifferentiated headache	Patients < 50 years	0.08 (0.05-0.11) 32/40866
Kernick (2008)	Undifferentiated headache	Patients ≥ 50 years	0.28 (0.22-0.36) 65/23055
Kernick (2008)	Primary headache	All patients	0.045 (0.023-0.088)

			10/21758
Kernick (2008)	Primary headache	Patients < 50 years	0.03 (0.01-0.08) 5/16282
Kernick (2008)	Primary headache	Patients ≥ 50 years	0.09 (0.03-0.23) 5/5476
Hamilton (2007)	Motor loss	All patients	0.026 (0.024-0.03) Cases: 308/3505 Controls: 731/24021
Hamilton (2007)	New-onset seizure	All patients	1.2 (1-1.4) Cases: 154/3505 Controls: 8/24021
Hamilton (2007)	New-onset seizure*	Patients 60-69 years	2.3 (NR)
Hamilton (2007)	Confusion	All patients	0.2 (0.16-0.24) Cases: 109/3505 Controls: 47/24021
Hamilton (2007)	Memory loss	All patients	0.036 (0.026-0.052) Cases: 37/3505 Controls: 64/24021
Hamilton (2007)	Visual disorder	All patients	0.035 (0.025-0.051) Cases: 35/3505 Controls: 62/24021
Hamilton (2007)	Headache + any of the other symptoms reported by Hamilton (2007)	All patients	0.39 (0.31-0.48)
Herr (1989)	Dizziness	All patients	0 (0-3.7) 0/125
Skiendziekowski (1980)	Weakness and/or dizziness	All patients	0 (0-4.4) 0/106
Hamilton (2007)	Weakness	All patients	0.14 (0.11-0.18) Cases: 95/3505 Controls: 42/24021

* Peak PPVs for these symptoms are in this age group.

Table 2: Brain & CNS cancer: Positive predictive values for any childhood cancer: Patients aged 0-14 years

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI) Frequency
Dommett (2012)	Any NICE alert symptom 0-3 months before diagnosis	All patients	0.055 (0.047-0.065) Cases: 342/1267 Control: 211/15318
Dommett (2012)	Any NICE alert symptom 0-12 months before diagnosis	All patients	0.07 (0.064-0.078) Cases: 427/1267 Control: 829/15318
Dommett (2012)	Neurological symptoms 0-12 months before diagnosis	All patients	0.083 (0.067-0.105) Cases: 108/1267 Control: 207/15318
Dommett (2012)	Headache 0-12 months before diagnosis	All patients	0.064 (0.051-0.082) Cases: 90/1267 Control: 224/15318

Dommett (2013a)	Headache 0-3 months before diagnosis	All patients	0.06 (0.04-0.08) Cases: 73/1267 Control: 55/15318
Dommett (2013a)	Headache 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.13 (0.08-0.22)
Dommett (2012)	Lymphadenopathy 0-12 months before diagnosis	All patients	0.096 (0.074-0.126) Cases: 82/1267 Control: 136/15318
Dommett (2013a)	Lymphadenopathy 0-3 months before diagnosis	All patients	0.09 (0.06-0.13) Cases: 69/1267 Control: 33/15318
Dommett (2013a)	Lymphadenopathy 0-3 months before diagnosis and ≤ 3 consultations	All patients	0.2 (0.1-0.39)
Dommett (2012)	Lump/mass/swelling 0-12 months before diagnosis	All patients	0.172 (0.119-0.25) Cases: 56/1267 Control: 52/15318
Dommett (2013a)	Lump/mass/swelling below neck excluding abdomen 0-3 months before diagnosis	All patients	0.11 (0.06-0.2) Cases: 42/1267 Control: 16/15318
Dommett (2013a)	Lump/mass/swelling below neck excluding abdomen 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.3 (0.09-0.99)
Dommett (2012)	Fatigue 0-12 months before diagnosis	All patients	0.085 (0.06-0.121) Cases: 47/1267 Control: 88/15318
Dommett (2013a)	Fatigue 0-12 months before diagnosis	All patients	0.07 (0.04-0.12) Cases: 42/1267 Control: 24/15318
Dommett (2013a)	Fatigue 0-12 months before diagnosis and ≥ 3 consultations	All patients	0.12 (0.06-0.23)
Dommett (2012)	Back pain 0-12 months before diagnosis	All patients	0.088 (0.06-0.128) Cases: 40/1267 Control: 73/15318
Dommett (2012)	Bruising 0-12 months before diagnosis	All patients	0.08 (0.054-0.118) Cases: 38/1267 Control: 76/15318
Dommett (2013a)	Bruising 0-3 months before diagnosis	All patients	0.08 (0.05-0.13) Cases: 33/1267 Control: 18/15318
Dommett (2013a)	Bruising 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.38 (0.09-1.64)
Dommett (2013a)	Pallor 0-3 months before diagnosis	All patients	0.41 (0.12-1.34) Cases: 33/1267 Control: 18/15318

Dommett (2013a)	Pallor 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.76 (0.1-5.7)
Dommett (2013a)	Lump mass swelling head and neck 0-3 months before diagnosis	All patients	0.3 (0.1-0.84) Cases: 28/1267 Control: 4/15318
Dommett (2013a)	Lump mass swelling head and neck 0-3 months before diagnosis and ≤ 3 consultations	All patients	0.76 (0.1-5.7)
Dommett (2013a)	Abnormal movement 0-3 months before diagnosis	All patients	0.08 (0.04-0.14) Cases: 49/1267 Control: 26/15318
Dommett (2013a)	Abnormal movement 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.15 (0.07-0.32)
Dommett (2013a)	Bleeding 0-3 months before diagnosis	All patients	0.06 (0.03-0.1) Cases: 28/1267 Control: 21/15318
Dommett (2013a)	Bleeding 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.11 (0.04-0.31)
Dommett (2013a)	Visual symptoms 0-3 months before diagnosis	All patients	0.06 (0.03-0.1) Cases: 28/1267 Control: 21/15318
Dommett (2013a)	Visual symptoms 0-3 months before diagnosis and ≤ 3 consultations	All patients	0.23 (0.07-0.77)
Dommett (2013a)	Pain 0-3 months before diagnosis	All patients	0.04 (0.03-0.06) Cases: 42/1267 Control: 41/15318
Dommett (2013a)	Pain 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.14 (0.07-0.31)
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All patients	0.04 (0.03-0.07) Cases: 107/1267 Control: 102/15318
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.13 (0.08-0.19)
Dommett (2012)	Urinary symptoms 0-12 months before diagnosis	All patients	0.266 (0.117-0.609) Cases: 15/1267 Control: 9/15318
Dommett (2013a)	≥ 3 consultations	All patients	0.02
Dommett (2013a)	Childhood infection 0-3 months before diagnosis	All patients	Cases: 54/1267 Control: 236/15318
Dommett (2013a)	Upper respiratory tract infection 0-3 months before diagnosis	All patients	Cases: 143/1267 Control: 942/15318

Dommett (2013a)	Vomiting 0-3 months before diagnosis	All patients	Cases: 86/1267 Control: 105/15318
Dommett (2013a)	Cough 0-3 months before diagnosis	All patients	Cases: 77/1267 Control: 654/15318
Dommett (2013a)	Rash 0-3 months before diagnosis	All patients	Cases: 63/1267 Control: 555/15318
Dommett (2013a)	Abdominal pain 0-3 months before diagnosis	All patients	Cases: 60/1267 Control: 137/15318
Dommett (2013a)	Abdominal mass 0-3 months before diagnosis	All patients	Cases: 48/1267 Control: 0/15318
Dommett (2013a)	Fever 0-3 months before diagnosis	All patients	Cases: 49/1267 Control: 166/15318
Dommett (2013a)	Eye swelling 0-3 months before diagnosis	All patients	Cases: 39/1267 Control: 238/15318
Dommett (2013a)	Shortness of breath 0-3 months before diagnosis	All patients	Cases: 35/1267 Control: 221/15318
Dommett (2013a)	Constipation 0-3 months before diagnosis	All patients	Cases: 26/1267 Control: 61/15318
Dommett (2012)	Hepatosplenomegaly 0-12 months before diagnosis	All patients	2.19 (0.295-17.034) Cases: 14/1267 Control: 1/15318

The positive predictive values are calculated using Bayesian statistics.

Table 3: Brain & CNS cancer: Positive predictive values for central nervous system (CNS) child- or young adulthood cancer tumour

Study	Symptom(s)	Patient group	Positive predictive value % (95% CI) Frequency
Dommett (2013a)	Abnormal movement 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.11 (0.03-0.35)
Dommett (2013a)	Visual symptoms 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.07 (0.02-0.24)
Dommett (2013a)	Vomiting 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.04 (0.02-0.07)
Ansell (2009)	Vomiting and unsteadiness	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.15 (0.01-0.1) 1/654
Ansell (2009)	Vomiting and visual difficulties	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.088 (0.005-0.6) 1/1142
Ansell (2009)	Headache and unsteadiness	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.085 (0.005-0.6) 1/1172

		years	
Ansell (2009)	"All other symptom combinations (except vomiting or headache with anorexia) had a predictive probability [of a child having a brain tumour given a visit to a GP with both symptoms] of between 1 in 1500 and 1 in 8000 children". <i>The predictive probabilities of vomiting or headache with anorexia appeared to be even lower.</i>		
Dommett (2013a)	Headache 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.03 (0.02-0.06)
Kernick (2009)	Headache (any type)	All patients aged 5-17 years	0.03 (0.01-0.05) 13/48575
Kernick (2009)	Primary headache	All patients aged 5-17 years	0 (0-0.05) 0/9321
Kernick (2009)	Undifferentiated headache	All patients aged 5-17 years	0.03 (0.02-0.06) 13/38705
Dommett (2013a)	Pain 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.03 (0.01-0.08)
Dommett (2013a)	Seizure 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.02 (0.01-0.06)
Dommett (2013a)	≥ 3 consultations	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.01 (0-0.01)
Dommett (2013b)	Seizure	All CNS patients and controls aged 15-24 years	0.0238 (0.0082-0.0695) Cases: 18/154 Controls: 4/1906
Dommett (2013b)	Headache	All CNS patients and controls aged 15-24 years	0.0145 (0.0077-0.0276) Cases: 33/154 Controls: 12/1906
Dommett (2013b)	Vomiting	All CNS patients and controls aged 15-24 years	0.0116 (0.0041-0.031) Cases: 11/154 Controls: 5/1906
Dommett (2013b)	Pain	All CNS patients and controls aged 15-24 years	0.0029 (0.0014-0.006) Cases: 11/154 Controls: 20/1906
Dommett (2013b)	Visual symptoms	All CNS patients and controls aged 15-24 years	Cases: 8.4% Controls: 0%
Dommett (2013b)	≥ 3 consultations	All CNS patients and controls aged 15-24 years	0.0023 (0.0019-0.0029) Cases: 73/154 Controls: 165/1906

The positive predictive values are calculated using Bayesian statistics.

Evidence statement(s):

The positive predictive values of having a brain tumour in adulthood ranged from 0% (for dizziness and/or weakness) to 2.3% (for new-onset seizure in 60-69 year old patients) for symptomatic patients presenting to primary care (4 studies, N = 106588). The included studies were associated with 0-4 bias/applicability concerns each (see also Table 1).

The positive predictive values of having any childhood cancer ranged from 0.04% (for pain or musculoskeletal symptoms) to 2.19% (for hepatosplenomegaly) for symptomatic patients aged 0-14 years old presenting to primary care (1 study, N = 30855). The evidence quality is somewhat compromised by the case-control design of the study (see also Table 2).

The positive predictive values of having central nervous system childhood or young adulthood cancer tumours ranged from < 0.013% (for vomiting or headache with anorexia) to 0.15 (for vomiting in combination with unsteadiness) for patients aged 0-14 years old, from 0% (for primary headache) to 0.03% (for undifferentiated headache) for patients aged 5-17 years, and from 0.0029% (for pain) to 0.0238% (for seizure) for patients aged 15-24 years (3 studies, N = 79910). The evidence quality is somewhat compromised by the case-control design of two of the studies (see also Table 3).

Evidence tables

Ansell (2009)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	National population-based case-control study (United Kingdom Childhood Cancer Study; UKCCS)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> 195 children; mean (SE) age = 7.31 (0.27) years; 93 males/102 females; astrocytoma: N = 78; medulloblastoma: N = 46; other: N = 71.</p> <p><u>Controls:</u> 285 children; mean (SE) age = 7.25 (0.22) years; 142 males/143 females;</p> <p><u>Inclusion criteria:</u> Cases: Children aged 0–14 years newly diagnosed with cancer between 1992-1996 in Great Britain were eligible to take part. Children with brain tumours were recruited from 1992-1994. These data were systematically collected</p>

	<p>from primary care records by 4 of the 10 UKCCS regions: “GP records were abstracted for 195 of 221 (88%) children with brain tumours and for 286 controls.”</p> <p>Controls: (1-?)2 gender-, month and year of birth-, and region of residence-matched controls were randomly recruited from primary care population registers.</p> <p><u>Exclusion criteria</u>: None listed</p> <p><u>Clinical setting</u>: Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Relevant signs and symptoms were defined as those that might be suggestive of a brain tumour: Anorexia, abnormal movements, back problems, cognitive impairment, congenital anomalies, drowsiness, emotional problems, focal weakness, growth problems, head tilt, headache, hearing problems, hydrocephalus, incontinence, papilloedema, problem behaviour, seizures, unsteady on feet, visual problems, vomiting, other neurological signs and symptoms not already included.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Cancer diagnosis or not in their General Practice record.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes

Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Dommett (2012; 2013a,b)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based nested case-control study using data from the General Practice Research Database (GPRD)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> 1267 children; aged 0-4 years: N = 436; aged 5-14 years: N = 831; 703 males/564 females. Cancer type: Leukemia: N = 368; brain: N = 270; lymphoma: N = 142; bone: N = 107; soft tissue sarcoma: N = 91; renal: N = 82; neuroblastoma: N = 75; other ICD codes: N = 132. 1064 teenagers and young adults (TYA): 15-24 years: Gender not reported. Cancer type: Leukemia: N = 143; brain: N = 154; lymphoma: N = 270; bone: N = 96; soft tissue sarcoma: N = 100; other ICD codes: N = 301 (including testis: N = 60; skin: N = 49; ovary: N = 20 and thyroid: N = 17).</p> <p><u>Controls:</u> 15318 children; aged 0-4 years: N = 4802; aged 5-14 years: N = 10516; 8461 males/6857 females. 13206 TYA. Gender not reported</p> <p><u>Inclusion criteria:</u> The sample comprised all children and TYU aged 0–24 years, inclusive, drawn from all general practices contributing research-standard data to the GPRD between 1 January 1988 and 31 December 2010. To be included, the practices had to have been contributing research-standard data for a minimum of 1 year before each child’s date of cancer diagnosis or the index date (see below) for matched controls. Cases: Patients diagnosed with the following cancers: leukaemia, lymphoma, neuroblastoma, soft tissue sarcoma, hepatic, renal, bone and central nervous system tumours, using pre-defined medical codes used in the GPRD. The date of diagnosis for cases was defined as the date of pathological diagnosis, but if this was unavailable, the date of the first cancer code entered in the GPRD was used. Controls: Up to 13 controls (children with no diagnosis of cancer at any time)</p>

	were selected per case, using a computer-generated random sequence, matched on age (within 1 year), sex and practice, and had to be currently registered on the date of diagnosis of their matched case (the index date). <u>Exclusion criteria</u> : None listed <u>Clinical setting</u> : Primary care, UK.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	The GPRD uses just over 100 000 medical codes to encompass all primary care events, including both symptoms and diagnoses. From this list, libraries of codes were assembled representing individual alert symptoms derived from the NICE referral guidelines for suspected cancer in children. <i>No more information reported.</i>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Cancer diagnosis in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	This study is published in three papers. There is almost complete overlap between the patients used in Kernick (2009) with the patients aged 5-17 years in this study.

Hamilton (2007)

PATIENT SELECTION

A. risk of bias

Patient sampling	Population-based nested case-control study using data from the General Practice Research Database (GPRD)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability

Patient characteristics and setting	<p><u>Cases:</u> 3505 patients with 2397 <i>malignant tumours (incl 948 gliomas and 280 astrocytomas, and other rare tumours; the rest were benign)</i>; aged 18-29 years: N = 159 (malignant tumours N = 134); aged 30-39 years: N = 276 (malignant tumours N = 206); aged 40-49 years: N = 432 (malignant tumours N = 280); aged 50-59 years: N = 675 (malignant tumours N = 471); aged 60-69 years: N = 822 (malignant tumours N = 584); aged 70-79 years: N = 767 (malignant tumours N = 511); aged 80-89 years: N = 339 (malignant tumours N = 191); aged >90 years: N = 35 (malignant tumours N = 20); 1661 males/1844 females.</p> <p><u>Controls:</u> N = 17173 or 24824</p> <p><u>Inclusion criteria:</u> Cases: Patients aged 18 years or over with a brain tumour diagnosed between May 1988 and March 2006, and with at least 2 years of data before the first tumour code (the index date), who had consulted at least once within the 6 months before the index date Controls: 7 randomly selected, practice-, sex- and age (within 1 year)-matched controls were selected per case, who had consulted at least once within the 6 months before the index date.</p> <p><u>Exclusion criteria:</u> Controls: Prior brain tumour.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
-------------------------------------	--

Are there concerns that the included patients and setting do not match the review question?	Unclear concern
--	------------------------

INDEX TEST

A. Risk of bias

Index test	"Libraries of codes for clinical variables previously described with brain tumours were assembled... Occurrences of these variables in the 6 months before the index date in cases and controls were identified. Variables were retained only if they occurred in at least 1% of cases or controls..... Re-consultations with the same symptom were also retained if the subsequent
------------	---

	symptom was also present in 1% or more cases or controls. No restriction was placed on reporting of the variable before the 6 month period of study, except for seizures which were only used if the patient had no previous seizure or anticonvulsant therapy code in their records.”
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Brain tumour diagnosis in the UK’s General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	This study includes a significant minority with benign tumours (see “Patient characteristics and setting” above).
Herr (1989)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from a North American hospital emergency department
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability	
Patient characteristics and setting	137 patients “representing 46% of the logbook entries for dizziness over this period”; 12 patients were excluded due to missing data leaving 125 patients; 51 males/73 females; mean age (range) = 46.9 (18-82) years. <u>Inclusion criteria:</u> “From March 1, 1986, to August 1, 1987, we sought consecutive patients presenting to the Northwestern Memorial Hospital ED with a chief complaint of “dizzy,” “lightheaded,” “faint,” or synonymous phrase. Each was required to have one or more attributes of dizziness as described by Drachman and Hart [ref given] (Figure 1*). Syncope, medical problems, or previous dizziness were not exclusions provided dizziness was among the presenting chief complaints.” *A definite rotational sensation; a sensation of impending faint or loss of consciousness; disequilibrium or loss of balance without head sensation; ill-defined “lightheadedness” other than vertigo, syncope, or disequilibrium. <u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> Hospital emergency department, USA.
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	Chief complaint of “dizzy,” “lightheaded,” “faint,” or synonymous phrase, with one or more of the following attributes of dizziness: A definite rotational sensation; a sensation of impending faint or loss of consciousness; disequilibrium or loss of balance without head sensation; ill-defined “lightheadedness” other than vertigo, syncope, or disequilibrium.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Emergency physicians’ diagnosis and minimum 1-4 weeks follow up.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	

A. risk of bias		
Flow and timing	All patients appear to be accounted for.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES		
Kernick (2008)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Cases [patients with a code of headache in their records] from a case-control study using data from the General Practice Research Database (GPRD)	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>85679 patients with a primary or undifferentiated headache: Primary headache: N = 21758, with migraine (N = 15891), tension-type headache (N = 4987), and cluster headache (N = 880); 5795 males/15963 females; median (IQR) age = 38 (29-50) years. Undifferentiated headache: N = 63921; 23200 males/40721 females; median (IQR) age = 41 (30-58) years.</p> <p><u>Inclusion criteria:</u> Patients were aged 18 years or over, with a description of headache in their records and no other headache classification code in the previous year. Patients were accepted from the inception of the database in January 1987 to June 2005 who had at least 1 year of full data in their records after the index headache consultation.</p> <p><u>Exclusion criteria:</u> Patients with a secondary headache that had a further descriptor.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>	
Are there concerns that the included patients and setting do not match the review question?	Low concern	
INDEX TEST		
A. Risk of bias		
Index test	Index headache codes were categorised into primary headache (migraine, tension-type headache, or cluster headache). Secondary headaches that had a further descriptor were discarded. All other codes were classified as undifferentiated headache.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes	

Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Headache-related outcome/diagnosis in the UK's General Practice Research Database in the year after the index consultation.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Kernick (2009)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Cases [patients with a code of headache in their records] from a case-control study using data from the General Practice Research Database (GPRD)
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	48575 patients with a primary, secondary or undifferentiated headache (21180 males/27395 females; age bands: 5-8 years: N = 3623; 9-12 years: N = 13804; 13-17 years: N = 31148): Primary headache: N = 9321, with migraine (N = 7468), tension-type headache (N = 1565), and cluster headache (N = 288); Secondary headache: N = 549 Undifferentiated headache: N = 38705.

	<p><u>Inclusion criteria:</u> Patients were aged 5-17 years, with a description of headache in their records and no other headache classification code in the previous year. Patients were accepted from the inception of the database in January 1987 to June 2005 who had at least 1 year of full data in their records after the index headache consultation.</p> <p><u>Exclusion criteria:</u> None listed.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Index headache codes were categorised into primary headache (migraine, tension-type headache, or cluster headache) or secondary headaches if they had a further descriptor. All other codes were classified as undifferentiated headache.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Headache-related outcome/diagnosis in the UK's General Practice Research Database in the year after the index consultation.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

NOTES	There is almost complete overlap between the patients used in this study and the patients aged 5-17 years in Dommett (2012, 2013a,b).	
Skiendzielewski (1980)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective patient series from a North American hospital emergency department	
Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?	Unclear risk	
B. Concerns regarding applicability		
Patient characteristics and setting	106 patients; ca 35% were aged < 30 years; age range = 7-88 years; 38 males/68 females; N = 10 with weakness only, N = 85 with dizziness, and N = 15 with a combination of weakness and dizziness. <u>Inclusion criteria:</u> "We retrospectively studied the cases of 106 patients who presented to the Geisinger Medical Center Emergency Department with the chief complaints of weakness and/or dizziness during a six-month period. The patients were examined by a number of physicians whose experience varied from that of a first-year resident to a staff emergency physician". <u>Exclusion criteria:</u> Cases with specific muscle weakness, e.g., paralysis of a limb. <u>Clinical setting:</u> Hospital emergency department, USA.	
Are there concerns that the included patients and setting do not match the review question?	High concern	
INDEX TEST		
A. Risk of bias		
Index test	Weakness and/or dizziness. Special attention was given to the presence of true vertigo, current medications, physical findings, abnormal laboratory data, and diagnosis on discharge.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	"Follow-up was obtained either from records of subsequent outpatient visits or, more frequently, from personal telephone conversations." 1-7 months.	
Is the reference standard likely to correctly classify the target condition?	Unclear	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	

Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	

References

Included studies

- Ansell, P., Johnston, T., Simpson, J., Crouch, S., Roman, E., Picton, S., Ansell, P., Johnston, T., Simpson, J., Crouch, S., Roman, E. & Picton, S. (2010) Brain tumor signs and symptoms: analysis of primary health care records from the UKCCS. *Pediatrics*, 125: 112-119.
- Dommert, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of childhood cancer in primary care: A population-based nested case-control study. *British Journal of Cancer* 106[5], 982-987. 2012.
- Dommert, R. M., Redaniel, T., Stevens, M. C. G., Martin, R. M., and Hamilton, W. Risk of childhood cancer with symptoms in primary care: A population-based case-control study. *British Journal of General Practice*; DOI:10.3399/bjgp13X660742. 2013a.
- Dommert, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of cancer in teenagers and young adults in primary care: A population-based nested case-control study. *British Journal of Cancer* 2329-2333. 2013b.
- Hamilton, W., Kernick, D., Hamilton, W. & Kernick, D. (2007) Clinical features of primary brain tumours: a case-control study using electronic primary care records. *British Journal of General Practice*, 57: 695-699.
- Herr, R. D., Zun, L. & Mathews, J. J. (1989) A directed approach to the dizzy patient. *Ann Emerg Med*, 18: 664-672.
- Kernick, D., Stapley, S., Goadsby, P. J., Hamilton, W., Kernick, D., Stapley, S., Goadsby, P. J. & Hamilton, W. (2008) What happens to new-onset headache presented to primary care? A case-cohort study using electronic primary care records. *Cephalalgia*, 28: 1188-1195.
- Kernick, D., Stapley, S., Campbell, J., Hamilton, W., Kernick, D., Stapley, S., Campbell, J. & Hamilton, W. (2009) What happens to new-onset headache in children that present to primary care? A case-cohort study using electronic primary care records. *Cephalalgia*, 29: 1311-1316.
- Skiendzielewski, J. J. & Martyak, G. (1980) The weak and dizzy patient. *Ann Emerg Med*, 9: 353-356.

Excluded studies (with excl reason)

- (1999) Communication gaps in paediatric care. *International Journal for Quality in Health Care*, 11: 533-534.
Not in PICO
- Abbas, A. & Abbas, A. (1989) Headache. *Practitioner*, 233: 1081-1084.
Narrative review

- Abernethy Holland, A. J. L. (2008) Central Nervous System/Brain Tumour 2-week Referral Guidelines: Prospective 3-year Audit. *Clinical Oncology*, 20: 201-202.
Not in PICO
- Abramson, D. H., Beaverson, K., Sangani, P., Vora, R. A., Lee, T. C., Hochberg, H. M., Kirsztrot, J., Ranjithan, M., Abramson, D. H., Beaverson, K., Sangani, P., Vora, R. A., Lee, T. C., Hochberg, H. M., Kirsztrot, J. & Ranjithan, M. (2003) Screening for retinoblastoma: presenting signs as prognosticators of patient and ocular survival. *Pediatrics*, 112: 1248-1255.
Not in PICO
- Aggarwal, A. (2011) CNS neoplasm: A missed diagnosis. *Indian Journal of Pediatrics*, 78: 116-117.
Narrative review
- Ahrensberg, J. M., Schroder, H., Hansen, R. P., Olesen, F. & Vedsted, P. (2012) The initial cancer pathway for children - one-fourth wait more than 3 months. *Acta Paediatrica*, 101: 655-662.
Not in PICO
- Ahrensberg, J. M., Hansen, R. P., Olesen, F., Schröder, H. & Vedsted, P. (2012) Presenting symptoms of children with cancer: A primary-care population-based study. *British Journal of General Practice*, 62: e458-s465.
Not in PICO
- Ahrensberg, J. M., Olesen, F., Hansen, R. P., Schroder, H. & Vedsted, P. (2013) Childhood cancer and factors related to prolonged diagnostic intervals: a Danish population-based study. *British Journal of Cancer*, 108: 1280-1287.
Not in PICO
- Allcutt, D. A. M. (1992) Presentation and diagnosis of brain tumours. *British Journal of Hospital Medicine*, 47: 745-752.
Narrative review
- Almeida, C. & Machado, I. (2009) Early diagnosis in childhood cancer: The shortest way for the cure. *Pediatric Blood and Cancer*, Conference: 846.
Not in PICO
- Alvord, L. S. & Herr, R. D. (1994) ENG in the emergency room: Subtest results in acutely dizzy patients. *J AM Acad Audiol*, 5: 384-389.
Not in PICO: 21.5% (20/91) patients had unknown diagnosis, final 4-week diagnosis was based on 4-week follow up, and no consistent reference standard.
- Ang, S. H., Chan, Y. C., Mahadevan, M., Ang, S. H., Chan, Y. C. & Mahadevan, M. (2009) Emergency department headache admissions in an acute care hospital: why do they occur and what can we do about it? *Annals of the Academy of Medicine, Singapore*, 38: 1007-1010.
Not in PICO
- Antoneli, C. B. S. (2004) The Pediatrician's ability to recognize the presenting signs and symptoms of retinoblastoma. *Revista da Associação Médica Brasileira (1992)*, 50: 400-402.
Not in PICO
- Arce, D., Sass, P., Abul-Khoudoud, H., Arce, D., Sass, P. & Abul-Khoudoud, H. (2001) Recognizing spinal cord emergencies. [Review] [18 refs][Erratum appears in Am Fam Physician 2002 May 1;65(9):1751]. *American Family Physician*, 64: 631-638.
Narrative review
- Avery, J. K. (1996) Headache--an important symptom. *The Journal of the Arkansas Medical Society*, 92: 449-450.
Not in PICO
- Badr, H. (2009) Latency of pediatric brain tumors diagnosis in province of Delta, a team experience. *Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, 46: 323-328.
Not in PICO
- Baggesen, K. (1999) Leukocoria (white pupil) among children--mother is always right. *Tidsskrift for Den Norske Laegeforening*, 119: 794-795.
Not in PICO

- Bai S. (2011) Delay in the diagnosis of retinoblastoma in China. *Acta Ophthalmologica*, 89: e72-e74.
Not in PICO
- Balestrini, M. R., Micheli, R., Giordano, L., Lasio, G., Giombini, S., Balestrini, M. R., Micheli, R., Giordano, L., Lasio, G. & Giombini, S. (1994) Brain tumors with symptomatic onset in the first two years of life. *Childs Nervous System*, 10: 104-110.
Not in PICO
- Balmer, A. (2006) Diagnosis and current management of retinoblastoma. *Oncogene*, 25: 5341-5349.
Narrative review
- Balmer, A., Munier, F., Balmer, A. & Munier, F. (2007) Differential diagnosis of leukocoria and strabismus, first presenting signs of retinoblastoma. *Clinical Ophthalmology*, 1: 431-439.
Narrative review
- Bartleson, J. D. (2006) When and how to investigate the patient with headache. *Seminars in Neurology*, 26: 163-170.
Narrative review
- Bassi, A. (2010) A note-based study of how patients first present with primary brain tumors. *Neuro-Oncology*, Conference: September.
Not in PICO
- Becker, L. A., Green, L. A., Beaufait, D., Kirk, J., Froom, J., Freeman, W. L., Becker, L. A., Green, L. A., Beaufait, D., Kirk, J., Froom, J. & Freeman, W. L. (1993) Detection of intracranial tumors, subarachnoid hemorrhages, and subdural hematomas in primary care patients: a report from ASPN, Part 2. *Journal of Family Practice*, 37: 135-141.
Not in PICO
- Bird, S. (2010) Failure to diagnose: Brain tumour. *Australian Family Physician*, 39: 335-337.
Narrative review
- Blanco-Lago, R., M+ílaga-Di+®guez, I., Pardo-Vega, R., Escribano-Garc+ja, C., Bernardo-Fern+índez, B. & Fern+índez-Castro, A. (2012) Incidence and characteristics of tumours of the central nervous system among the paediatric population of asturias. new data about an incidence on the rise. *Revista de Neurologia*, 54: 530-536.
Not in PICO
- Boesert, P., Gruttner, C., van, E. R. & Haxel, B. (2014) - [Changes in taste ability in patients with vestibular schwannoma]. [German]. - *Laryngo- Rhino- Otologie*, 93: 450-454.
Not in PICO
- Boiardi, A., Salmaggi, A., Eoli, M., Lamperti, E., Silvani, A., Boiardi, A., Salmaggi, A., Eoli, M., Lamperti, E. & Silvani, A. (2004) Headache in brain tumours: a symptom to reappraise critically. [Review] [15 refs]. *Neurological Sciences*, 25 Suppl 3: S143-S147.
Narrative review
- Boranic, M. (2003) Solid malignant tumors in children. *Paediatrica Croatica, Supplement*, 47: 19-24.
Narrative review
- Borgheresi, A. (1985) Epilepsy as the first symptom of a cerebral tumour. Retrospective study of seventy cases. *Bollettino - Lega Italiana contro l'Epilessia*, 51-52: 119-121.
Not in PICO
- Bos, R. F., Ramaker, C., van Ouwkerk, W. J., Linszen, W. H. & Wolf, B. H. (2002) [Vomiting as a first neurological sign of brain tumors in children] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 146: 1393-1398.
Not in PICO
- Bracho, M. F. B. (2004) Clinical presentation and delay in the diagnosis of CNS tumours in children. *Revista Chilena de Pediatria*, 75: 327-332.
Not in PICO
- Brasme, J.-F. C. (2012) Interval between onset of symptoms and diagnosis of medulloblastoma in children: Distribution and determinants in a population-based study. *European Journal of*

- Pediatrics*, 171: 25-32.
Not in PICO
- Brasme, J. F., Morfouace, M., Grill, J., Martinot, A., Amalberti, R., Bons-Letouzey, C., Chalumeau, M., Brasme, J. F., Morfouace, M., Grill, J., Martinot, A., Amalberti, R., Bons-Letouzey, C. & Chalumeau, M. (2012) Delays in diagnosis of paediatric cancers: a systematic review and comparison with expert testimony in lawsuits. [Review]. *Lancet Oncology*, 13: e445-e459.
Not in PICO
- Brasme, J. F., Grill, J., Doz, F., Lacour, B., Valteau-Couanet, D., Gaillard, S., Delalande, O., Aghakhani, N., Puget, S. & Chalumeau, M. (2012) Long time to diagnosis of medulloblastoma in children is not associated with decreased survival or with worse neurological outcome. *PLoS ONE*, 7.
Not in PICO
- Brasme, J. F., Chalumeau, M., Doz, F., Lacour, B., Valteau-Couanet, D., Gaillard, S., Delalande, O., Aghakhani, N., Sainte-Rose, C., Puget, S., Grill, J., Brasme, J. F., Chalumeau, M., Doz, F., Lacour, B., Valteau-Couanet, D., Gaillard, S., Delalande, O., Aghakhani, N., Sainte-Rose, C., Puget, S. & Grill, J. (2012) Interval between onset of symptoms and diagnosis of medulloblastoma in children: distribution and determinants in a population-based study. *European Journal of Pediatrics*, 171: 25-32.
Not in PICO
- Brenner, M., Oakley, C., Lewis, D., Brenner, M., Oakley, C. & Lewis, D. (2008) The evaluation of children and adolescents with headache. [Review] [20 refs]. *Current Pain & Headache Reports*, 12: 361-366.
Narrative review
- Butros, L. J., Abramson, D. H., Dunkel, I. J., Butros, L. J., Abramson, D. H. & Dunkel, I. J. (2002) Delayed diagnosis of retinoblastoma: analysis of degree, cause, and potential consequences. *Pediatrics*, 109: E45.
Not in PICO
- Cabral, D. A. T. (1999) Malignancies in children who initially present with rheumatic complaints. *Journal of Pediatrics*, 134: 53-57.
Not in PICO
- Calderon-Garciduenas, A. L., Pacheco-Calleros, J., Castelan-Maldonado, E., Necedal-Rustrian, F. C., Calderon-Garciduenas, A. L., Pacheco-Calleros, J., Castelan-Maldonado, E. & Necedal-Rustrian, F. C. (2008) [Primary lymphoma of the central nervous system: 20 years' experience in a referral hospital]. [Spanish]. *Revista de Neurologia*, 46: 84-88.
Not in PICO
- Canty, C. A. & Canty, C. A. (2009) Retinoblastoma: an overview for advanced practice nurses. [Review] [23 refs]. *Journal of the American Academy of Nurse Practitioners*, 21: 149-155.
Narrative review
- Canzano, J. C. H. (1999) Utility of pupillary dilation for detecting leukocoria in patients with retinoblastoma. *Pediatrics*, 104: e44.
Not in PICO
- Cao, M.-H. (2003) Unusual cases of hearing loss in children. *Medecine et Hygiene*, 61: 1957-1961.
Not in PICO
- Carville, S. (2012) Diagnosis and management of headaches in young people and adults: Summary of NICE guidance. *BMJ (Online)*, 345.
Guideline
- Cea-Soriano, L., Wallander, M. A., Garcia Rodriguez, L. A., Cea-Soriano, L., Wallander, M. A. & Garcia Rodriguez, L. A. (2012) Epidemiology of meningioma in the United Kingdom. *Neuroepidemiology*, 39: 27-34.
Not in PICO

- Chacowry, P. K., Platon, A. & Delemont, C. (1724) [Imaging in the evaluation of headaches]. [French]. *Revue Medicale Suisse*, 9: 1720-1722.
Narrative review
- Chen, H. Y., Wu, D. L., Tsai, R. K., Chen, H. Y., Wu, D. L. & Tsai, R. K. (1998) Acute esotropia may be a presenting sign of intracranial neoplasm. *Kaohsiung Journal of Medical Sciences*, 14: 710-716.
Not in PICO
- Cheng, K.-S. (2009) Short Stature Without Neurological Manifestations in a Child with a Suprasellar Tumor. *Tzu Chi Medical Journal*, 21: 161-164.
Not in PICO
- Cho, J. C., Miller, A., Kettner, N. W., Cho, J. C. S., Miller, A. & Kettner, N. W. (2009) Cervical ependymoma in a male adolescent with neck and back pain. *Journal of Manipulative & Physiological Therapeutics*, 32: 695-700.
Not in PICO
- Ciobanu, A., Miron, I., Tansanu, I., Ciobanu, A., Miron, I. & Tansanu, I. (2012) [Features of brain stem tumors in children]. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 116: 56-61.
Not in PICO
- Comi, A. M., Backstrom, J. W., Burger, P. C., Duffner, P. K., Comi, A. M., Backstrom, J. W., Burger, P. C. & Duffner, P. K. (1998) Clinical and neuroradiologic findings in infants with intracranial ependymomas. Pediatric Oncology Group. *Pediatric Neurology*, 18: 23-29.
Not in PICO
- Crawford, J. R., Santi, M. R., Vezina, G., Myseros, J. S., Keating, R. F., LaFond, D. A., Rood, B. R., MacDonald, T. J. & Packer, R. J. (2007) CNS germ cell tumor (CNSGCT) of childhood: presentation and delayed diagnosis. *Neurology*, 68: 1668-1673.
Not in PICO
- Creutzig, U. G. (1995) Early diagnosis of neoplastic diseases in childhood. *Onkologie*, 18: 24-27.
Narrative review
- Crummer, R. W., Hassan, G. A., Crummer, R. W. & Hassan, G. A. (2004) Diagnostic approach to tinnitus. [Review] [21 refs]. *American Family Physician*, 69: 120-126.
Narrative review
- Dai, A. I., Backstrom, J. W., Burger, P. C., Duffner, P. K., Dai, A. I., Backstrom, J. W., Burger, P. C. & Duffner, P. K. (2003) Supratentorial primitive neuroectodermal tumors of infancy: clinical and radiologic findings. *Pediatric Neurology*, 29: 430-434.
Not in PICO
- Damek, D. M. (2009) Cerebral Edema, Altered Mental Status, Seizures, Acute Stroke, Leptomeningeal Metastases, and Paraneoplastic Syndrome. *Emergency Medicine Clinics of North America*, 27: 209-229.
Narrative review
- Dang-Tan, T., Trottier, H., Mery, L. S., Morrison, H. I., Barr, R. D., Greenberg, M. L. & Franco, E. L. (2008) Delays in diagnosis and treatment among children and adolescents with cancer in Canada. *Pediatric Blood & Cancer*, 51: 468-474.
Not in PICO
- Davies E. Clarke (2004) Early symptoms of brain tumours. *Journal of Neurology, Neurosurgery and Psychiatry*, 75: 1205-1206.
Not in PICO
- de Aguirre, J. C., Antoneli, C. B. G., Ribeiro, K. B., Simoes, M., Novaes, P. E. R. S., Chojniak, M. M. M. & Arias, V. (2007) Retinoblastoma in children older than 5 years of age. *Pediatric Blood & Cancer*, 48: 292-295.
Not in PICO
- De Donato, G. (1995) Incidence of normal hearing in acoustic neuroma. *Acta otorhinolaryngologica Italica : organo ufficiale della Societa italiana di otorinolaringologia e chirurgia cervico-facciale*,

15: 73-79.

Not in PICO

De Vile, C. J., Sufraz, R., Lask, B. D., Stanhope, R., De Vile, C. J., Sufraz, R., Lask, B. D. & Stanhope, R. (1995) Occult intracranial tumours masquerading as early onset anorexia nervosa. *BMJ*, 311: 1359-1360.

Not in PICO

De, R., Moffat, D. A., De, R. & Moffat, D. A. (506) The GP's role in acoustic neuroma. *Practitioner*, 248: 501-506.

Narrative review

Del Zoppo, P. (2009) Unforgettable cases in pediatric general practice: "Vomit of students and others". *Medico e Bambino*, 28: 187.

Not in PICO

DeVile, C. J. S. (1995) Occult intracranial tumours masquerading as early onset anorexia nervosa. *British Medical Journal*, 311: 1359-1360.

Not in PICO

Dixon-Woods, M., Findlay, M., Young, B., Cox, H., Heney, D., Dixon-Woods, M., Findlay, M., Young, B., Cox, H. & Heney, D. (2001) Parents' accounts of obtaining a diagnosis of childhood cancer. *Lancet*, 357: 670-674.

Not in PICO

Dobes, M., Shadbolt, B., Khurana, V. G., Jain, S., Smith, S. F., Smee, R., Dexter, M., Cook, R., Dobes, M., Shadbolt, B., Khurana, V. G., Jain, S., Smith, S. F., Smee, R., Dexter, M. & Cook, R. (2011) A multicenter study of primary brain tumor incidence in Australia (2000-2008). *Neuro-Oncology*, 13: 783-790.

Not in PICO

Dobrovoljac, M., Hengartner, H., Boltshauser, E. & Grotzer, M. A. (2002) Delay in the diagnosis of paediatric brain tumours. *European Journal of Pediatrics*, 161: 663-667.

Not in PICO

Dorner, L. (2007) Posterior fossa tumors in children: How long does it take to establish the diagnosis? *Child's Nervous System*, 23: 887-890.

Not in PICO

Dorransoro, M., I (2004) Malignant disease presenting as rheumatic manifestations. *Anales de Pediatria*, 61: 393-397.

Not in PICO

Dorsch, J. N. (2014) Neurologic syndromes of the head and neck. *Primary Care - Clinics in Office Practice*, 41: 133-149.

Narrative review

Dorsch, J. N. (2014) Neurologic syndromes of the head and neck. *Primary Care - Clinics in Office Practice*, 41: 133-149.

Narrative review

Drexler, E. D. & Drexler, E. D. (173) Severe headaches. When to worry, what to do. *Postgraduate Medicine*, 87: 164-173.

Narrative review

Edgeworth, J., Bullock, P., Bailey, A., Gallagher, A., Crouchman, M., Edgeworth, J., Bullock, P., Bailey, A., Gallagher, A. & Crouchman, M. (1996) Why are brain tumours still being missed? *Archives of Disease in Childhood*, 74: 148-151.

Not in PICO

Eitel, B. & Eitel, B. (1987) [Ambulatory diagnosis and outpatient management of patients with hypophyseal adenomas]. [German]. *Zeitschrift für Die Gesamte Innere Medizin und Ihre Grenzgebiete*, 42: 321-324.

Not in PICO

- El Shakankiry, H. (2012) Migraine in the paediatric age group: A diagnostic challenge. *Developmental Medicine and Child Neurology*, Conference: June.
Not in PICO
- Epelman, S. & Epelman, S. (2012) Preserving vision in retinoblastoma through early detection and intervention. *Current Oncology Reports*, 14: 213-219.
Narrative review
- Fattal-Valevski, A., Nissan, N., Kramer, U. & Constantini, S. (2013) Seizures as the clinical presenting symptom in children with brain tumors. *Journal of Child Neurology*, 28: 292-296.
Not in PICO
- Fazzini, F. (2006) Epilepsy secondary to early onset brain tumors (< 3 yrs). *Bollettino - Lega Italiana contro l'Epilessia*, 165-166.
Not in PICO
- Fern, L. A. C. (2011) How frequently do young people with potential cancer symptoms present in primary care? *British Journal of General Practice*, 61: e223-e230.
Not in PICO
- Fernandez, A. (2010) Prevalence of pituitary adenomas: A community-based, cross-sectional study in Banbury (Oxfordshire, UK). *Clinical Endocrinology*, 72: 377-382.
Not in PICO
- Fernandez, C. P. A. (2007) Clinical practice guideline for the diagnosis and treatment of craniopharyngioma and other parasellar lesions. *Endocrinologia y Nutricion*, 54: 13-22.
Narrative review
- Field, M., Shanley, S. & Kirk, J. (2007) Inherited cancer susceptibility syndromes in paediatric practice. *Journal of Paediatrics and Child Health*, 43: 219-229.
Narrative review
- Fleming, A. J., Chi, S. N., Fleming, A. J. & Chi, S. N. (2012) Brain tumors in children. [Review]. *Current Problems in Pediatric & Adolescent Health Care*, 42: 80-103.
Not in PICO
- Flores, L. E., Williams, D. L., Bell, B. A., O'Brien, M., Ragab, A. H., Flores, L. E., Williams, D. L., Bell, B. A., O'Brien, M. & Ragab, A. H. (1986) Delay in the diagnosis of pediatric brain tumors. *American Journal of Diseases of Children*, 140: 684-686.
Not in PICO
- Forgie, S. E. & Robinson, J. L. (2007) Pediatric malignancies presenting as a possible infectious disease. *BMC Infectious Diseases*, 7.
Not in PICO
- Forsyth, P. A., Posner, J. B., Forsyth, P. A. & Posner, J. B. (1993) Headaches in patients with brain tumors: a study of 111 patients. *Neurology*, 43: 1678-1683.
Not in PICO
- Fruhwald, M. C., Rutkowski, S., Fruhwald, M. C. & Rutkowski, S. (2011) Tumors of the central nervous system in children and adolescents. [Review]. *Deutsches Arzteblatt International*, 108: 390-397.
Narrative review
- Fu, X. (1996) Ocular symptoms of tumors at sella turcica region. *Yan ke xue bao = Eye science / "Yan ke xue bao" bian ji bu*, 12: 166-168.
Not in PICO
- Furuta, T., Tabuchi, A., Adachi, Y., Mizumatsu, S., Tamesa, N., Ichikawa, T., Tamiya, T., Matsumoto, K., Ohmoto, T., Furuta, T., Tabuchi, A., Adachi, Y., Mizumatsu, S., Tamesa, N., Ichikawa, T., Tamiya, T., Matsumoto, K. & Ohmoto, T. (1998) Primary brain tumors in children under age 3 years. *Brain Tumor Pathology*, 15: 7-12.
Not in PICO
- Galassi, E., Godano, U., Cavallo, M., Donati, R., Nasi, M. T., Galassi, E., Godano, U., Cavallo, M., Donati, R. & Nasi, M. T. (1989) Intracranial tumors during the 1st year of life.[Erratum appears in

- Childs Nerv Syst 1990 May;6(3):184]. *Childs Nervous System*, 5: 288-298.
Not in PICO
- Garcia, H. B. (2008) Suspicion of cancer in pediatrics. *Pediatrics Integral*, 12: 537-544.
Narrative review
- Gardner, M., Hess, C. & Josephson, S. (2013) Utilization and outcomes of cranial computed tomography in a pediatric population. *Neurology*, 80.
Not in PICO
- Garnett, M. R., Puget, S., Grill, J. & Sainte-Rose, C. (2007) Craniopharyngioma. *Orphanet Journal of Rare Diseases*, 2: 18.
Narrative review
- George, J. L., Marchal, J. C., George, J. L. & Marchal, J. C. (2010) [Orbital tumors in children: clinical examination, imaging, specific progression]. [French]. *Neuro-Chirurgie*, 56: 244-248.
Narrative review
- Gerber, N. U., Von Hoff, K., Von Bueren, A. O., Treulieb, W., Deinlein, F., Benesch, M., Zwiener, I., Soerensen, N., Warmuth-Metz, M., Pietsch, T., Mittler, U., Kuehl, J., Kortmann, R. D., Grotzer, M. A. & Rutkowski, S. (2012) A long duration of the prediagnostic symptomatic interval is not associated with an unfavourable prognosis in childhood medulloblastoma. *European Journal of Cancer*, 48: 2028-2036.
Not in PICO
- Giercke, K., Schutt, H., Giercke, K. & Schutt, H. (1983) [Early recognition of tumors of the CNS]. [German]. *Psychiatrie, Neurologie und Medizinische Psychologie*, 35: 541-546.
Not in PICO
- Goadsby, P. J. (2004) To scan or not to scan in headache. *British Medical Journal*, 329: 469-470.
Narrative review
- Goddard, A. G. K. (1999) Delay in diagnosis of retinoblastoma: Risk factors and treatment outcome. *British Journal of Ophthalmology*, 83: 1320-1323.
Not in PICO
- Goldman, A. (2006) Symptoms in children/young people with progressive malignant disease: United Kingdom Children's Cancer Study Group/Paediatric Oncology Nurses Forum Survey. *Pediatrics*, 117: e1179-e1186.
Not in PICO
- Gordon, G. S., Wallace, S. J., Neal, J. W., Gordon, G. S., Wallace, S. J. & Neal, J. W. (1995) Intracranial tumours during the first two years of life: presenting features. *Archives of Disease in Childhood*, 73: 345-347.
Not in PICO
- Grant, R. (2004) Overview: Brain tumour diagnosis and management/Royal College of Physicians guidelines. *Neurology in Practice*, 75: ii18-ii23.
Guideline
- Grattan-Smith, P. J., Ryan, M. M. & Procopis, P. G. (2000) Persistent or severe back pain and stiffness are ominous symptoms requiring prompt attention. *Journal of Paediatrics and Child Health*, 36: 208-212.
Not in PICO
- Grondin, R. T. S. (2009) Pediatric Brain Tumors. *Advances in Pediatrics*, 56: 249-269.
Narrative review
- Gurney, J. G., Mueller, B. A., Preston-Martin, S., McDaniel, A. M., Holly, E. A., Pogoda, J. M., Davis, R. L., Gurney, J. G., Mueller, B. A., Preston-Martin, S., McDaniel, A. M., Holly, E. A., Pogoda, J. M. & Davis, R. L. (1997) A study of pediatric brain tumors and their association with epilepsy and anticonvulsant use. *Neuroepidemiology*, 16: 248-255.
Not in PICO

- Haider S. (2008) Leukocoria in children. *Journal of Pediatric Ophthalmology and Strabismus*, 45: 179-180.
Not in PICO
- Haimi, M., Nahum, M. P. & Ben Arush, M. W. (2004) Delay in diagnosis of children with cancer: A retrospective study of 315 children. *Pediatric Hematology and Oncology*, 21: 37-48.
Not in PICO
- Haldorsen, I. S., Espeland, A., Larsen, J. L., Mella, O., Haldorsen, I. S., Espeland, A., Larsen, J. L. & Mella, O. (2005) Diagnostic delay in primary central nervous system lymphoma. *Acta Oncologica*, 44: 728-734.
Not in PICO
- Halperin, E. C., Watson, D. M. & George, S. L. (2001) Duration of symptoms prior to diagnosis is related inversely to presenting disease stage in children with medulloblastoma. *Cancer*, 91: 1444-1450.
Not in PICO
- Hamdan, A. & Mitchell, P. (2012) The Two-Week Wait Rule for Suspected Cns/Brain Tumours in the Uk: A Decade Analysis of Referral Patterns, Guideline Compliance and Diagnostic Efficacy. *Neuro-Oncology*, 14: 20.
Not in PICO
- Hamdan, A. & Mitchell, P. (2013) The two-week wait guideline for suspected CNS tumours: A decade analysis. *British Journal of Neurosurgery*, 27: 642-645.
Not in PICO
- Hamilton, W. (2008) The price of diagnosis. *British Journal of General Practice*, 58: 837-838.
Not in PICO
- Hamilton, W. (2009) The CAPER studies: Five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients. *British Journal of Cancer*, 101: S80-S86.
Narrative review
- Harcourt, J. P., Vijaya-Sekaran, S., Loney, E., Lennox, P., Harcourt, J. P., Vijaya-Sekaran, S., Loney, E. & Lennox, P. (1999) The incidence of symptoms consistent with cerebellopontine angle lesions in a general ENT out-patient clinic. *Journal of Laryngology & Otology*, 113: 518-522.
Not in PICO
- Hartley, P. (2001) Curing cancer in children - Early recognition and appropriate treatment are the key. *South African Medical Journal*, 91: 40-42.
Narrative review
- Hayashi, N., Kidokoro, H., Miyajima, Y., Fukazawa, T., Natsume, J., Kubota, T. & Kojima, S. (2010) How do the clinical features of brain tumours in childhood progress before diagnosis? *Brain and Development*, 32: 636-641.
Not in PICO
- Heathcote, A. C., Wormald, J. C. R. & Stocks, R. (2012) An unusual suspect causing behavioural problems and pituitary failure in a child. *BMJ Case Reports*.
Not in PICO
- Hered, R. W. (2011) Effective vision screening of young children in the pediatric office. *Pediatric Annals*, 40: 76-82.
Narrative review
- Higelin, F. G. (1997) Emergency medicine for the practitioner: headaches. *Revue Medicale de la Suisse Romande*, 117: 295-298.
Not in PICO
- Hoffman, R. M., Einstadter, D., Kroenke, K., Hoffman, R. M., Einstadter, D. & Kroenke, K. (1999) Evaluating dizziness. *American Journal of Medicine*, 107: 468-478.
Semi-systematic review, have checked included studies for relevance

- Holtedahl, K. (2012) Clinical competence and childhood cancer - A view from primary care. *Acta Paediatrica, International Journal of Paediatrics*, 101: 559-561.
Narrative review
- Huang, X., X (2012) Clinical features of intracranial vestibular schwannomas. *Oncology Letters*, 5: 57-62.
Not in PICO
- Idowu, O. (2007) Symptomatic primary intracranial neoplasms in Nigeria, West Africa. *Journal of Neurological Sciences*, 24: 212-218.
Not in PICO
- Inci, M. F. O. (2012) A rare presentation of craniopharyngioma: Delayed puberty. *BMJ Case Reports*, , 2012. Date of Publication: 2012.
Narrative review
- Ivey, J. B., Brown, R. D., Ivey, J. B. & Brown, R. D. (2007) She passed out again. Astrocytomas. *Pediatric Nursing*, 33: 430-431.
Not in PICO
- Jackson, C., Glasson, W., Jackson, C. & Glasson, W. (1998) Prevention of visual loss. Screening in general practice. *Australian Family Physician*, 27: 150-153.
Narrative review
- Jahn, K. & Jahn, K. (2009) [Vertigo in children. Clinical presentation, course and treatment]. [Review] [37 refs] [German]. *Nervenarzt*, 80: 900-908.
Narrative review
- Jaklewicz, H. & Dilling-Ostrowska, E. (1980) Psychiatric symptomatology in cerebral tumour in children. [Polish]. *Psychiatria Polska*, 4: 229-233.
Not in PICO
- Jellema, K., Overbeeke, J. J., Teepen, H. L., Visser, L. H., Jellema, K., Overbeeke, J. J., Teepen, H. L. J. M. & Visser, L. H. (2005) Time to diagnosis of intraspinal tumors. *European Journal of Neurology*, 12: 621-624.
Not in PICO
- Johnson, A. H., Jordan, C., Mazewski, C. M., Johnson, A. H., Jordan, C. & Mazewski, C. M. (2009) Off-therapy headaches in pediatric brain tumor patients: a retrospective review. *Journal of Pediatric Oncology Nursing*, 26: 354-361.
Not in PICO
- Jooma, R., Hayward, R. D., Grant, D. N., Jooma, R., Hayward, R. D. & Grant, D. N. (1984) Intracranial neoplasms during the first year of life: analysis of one hundred consecutive cases. *Neurosurgery*, 14: 31-41.
Not in PICO
- Joseph, E. & Joseph, E. (1983) Vertigo in children: two cases of 'scarlet face'. Authentic case histories from Australian general practice illustrating pitfalls in diagnosis and management. *Australian Family Physician*, 12: 516.
Not in PICO
- Kabbouche, M. A., Cleves, C., Kabbouche, M. A. & Cleves, C. (2010) Evaluation and management of children and adolescents presenting with an acute setting. *Seminars in Pediatric Neurology*, 17: 105-108.
Narrative review
- Kaimbo, W. K. M. (2002) Presenting signs of retinoblastoma in Congolese patients. *Bulletin de la Societe belge d'ophtalmologie*, 37-41.
Not in PICO
- Kaiserova, E. (2004) Early diagnostics of central nervous system tumours in children. *Lekarsky Obzor*, 53: 133-139.
Narrative review

- Kallio, M., Ilveskoski, I., Kallio, M. & Ilveskoski, I. (1995) [When should you suspect a brain tumor?]. [Review] [5 refs] [Finnish]. *Duodecim*, 111: 2009-2012.
Narrative review
- Kameda-Smith, M. M., White, M. A., George, E. J. & Brown, J. I. (2012) Time to diagnosis of paediatric posterior fossa tumours: an 11-year West of Scotland experience 2000-2011. *British Journal of Neurosurgery*.
Not in PICO
- Kameda-Smith, M. M., White, M. A., St George, E. J. & Brown, J. I. (2013) Time to diagnosis of paediatric posterior fossa tumours: an 11-year West of Scotland experience 2000-2011. *British Journal of Neurosurgery*, 27: 364-369.
Not in PICO
- Kantar, M., Ertan, Y., Turhan, T., Kitis, O., Anacak, Y., Akalin, T., Ersahin, Y., Cetingul, N., Kantar, M., Ertan, Y., Turhan, T., Kitis, O., Anacak, Y., Akalin, T., Ersahin, Y. & Cetingul, N. (2009) Anaplastic astroblastoma of childhood: aggressive behavior. *Childs Nervous System*, 25: 1125-1129.
Not in PICO
- Karatas, M. (2008) Central vertigo and dizziness: Epidemiology, differential diagnosis, and common causes. *Neurologist*, 14: 355-364.
Narrative review
- Kato, M., Nakamura, H., Terai, H., Konishi, S., Nagayama, R., Takaoka, K., Kato, M., Nakamura, H., Terai, H., Konishi, S., Nagayama, R. & Takaoka, K. (2008) Why does delay exist in the diagnosis of intradural spinal cord tumor despite the availability of MRI? *Journal of Clinical Neuroscience*, 15: 880-885.
Not in PICO
- Keeble, S., Abel, G. A., Saunders, C. L., McPhail, S., Walter, F. M., Neal, R. D., Rubin, G. P. & Lyratzopoulos, G. (2014) Variation in promptness of presentation among 10,297 patients subsequently diagnosed with one of 18 cancers: Evidence from a National Audit of Cancer Diagnosis in Primary Care. *International Journal of Cancer*, 135: 1220-1228.
Not in PICO
- Kerber, K. A., Meurer, W. J., West, B. T., Fendrick, A. M., Kerber, K. A., Meurer, W. J., West, B. T. & Fendrick, A. M. (2008) Dizziness presentations in U.S. emergency departments, 1995-2004. *Academic Emergency Medicine*, 15: 744-750.
Not in PICO (no reference standard)
- Kernick, D., Williams, S., Kernick, D. & Williams, S. (2011) Should GPs have direct access to neuroradiological investigation when adults present with headache? *British Journal of General Practice*, 61: 409-411.
Narrative review
- Kernick, D. P. A. (2008) Imaging patients with suspected brain tumour: Guidance for primary care. *British Journal of General Practice*, 58: 880-885.
Narrative review
- Kesser, B. W. & Kesser, B. W. (2010) Clinical thresholds for when to test for retrocochlear lesions: con. [Review] [15 refs]. *Archives of Otolaryngology -- Head & Neck Surgery*, 136: 727-729.
Narrative review
- Kieran, M. W., Walker, D., Frappaz, D., Prados, M., Kieran, M. W., Walker, D., Frappaz, D. & Prados, M. (2010) Brain tumors: from childhood through adolescence into adulthood. [Review]. *Journal of Clinical Oncology*, 28: 4783-4789.
Narrative review
- Klitbo, D. M., Nielsen, R., Illum, N. O., Wehner, P. S., Carlsen, N., Klitbo, D. M., Nielsen, R., Illum, N. O., Wehner, P. S. & Carlsen, N. (2011) Symptoms and time to diagnosis in children with brain tumours. *Danish Medical Bulletin*, 58: A4285.
Not in PICO

- Kochanova, I. S. (2004) Adenoma of the pituitary gland in the ophthalmologist's out-patient practice. *Ceska a Slovenska Oftalmologie*, 60: 348-355.
Not in PICO
- Kroenke, K., Hoffman, R. M., Einstadter, D., Kroenke, K., Hoffman, R. M. & Einstadter, D. (2000) How common are various causes of dizziness? A critical review. [Review] [40 refs]. *Southern Medical Journal*, 93: 160-167.
Semi-systematic review, have checked included studies for relevance
- Kroenke, K. L. (1992) Causes of persistent dizziness. A prospective study of 100 patients in ambulatory care. *Annals of Internal Medicine*, 117: 898-904.
Not in PICO (reference standard)
- Kukal, K., Dobrovoljac, M., Boltshauser, E., Ammann, R. A., Grotzer, M. A., Kukal, K., Dobrovoljac, M., Boltshauser, E., Ammann, R. A. & Grotzer, M. A. (2009) Does diagnostic delay result in decreased survival in paediatric brain tumours? *European Journal of Pediatrics*, 168: 303-310.
Not in PICO
- Kyprianou, I. & Nassab, R. (2005) A comparative study of referral patterns and management of patients with malignant brain tumours in Birmingham, UK, and Toronto, Canada. *British Journal of Neurosurgery*, 19: 229-234.
Not in PICO
- Larner, A. J. (2006) Referral guidelines for suspected central nervous system or brain tumours. *Journal of Neurology Neurosurgery and Psychiatry*, 77: 1305-1306.
Guideline
- Lateef, T. M., Grewal, M., McClintock, W., Chamberlain, J., Kaulas, H. & Nelson, K. B. (2009) Headache in Young Children in the Emergency Department: Use of Computed Tomography. *Pediatrics*, 124: E12-E17.
Not in PICO
- Lefavre, J. F., Cohen, S. R., Riski, J. E., Burstein, F. D., Lefavre, J. F., Cohen, S. R., Riski, J. E. & Burstein, F. D. (1997) Velopharyngeal incompetence as the presenting symptom of malignant brainstem tumor. *Cleft Palate-Craniofacial Journal*, 34: 154-158.
Not in PICO
- Leone, M. A., Ivashynka, A. V., Tonini, M. C., Bogliun, G., Montano, V., Ravetti, C., Gambaro, P., Paladin, F., Beghi, E., ARES (Alcohol Related Seizures) study group., Leone, M. A., Ivashynka, A. V., Tonini, M. C., Bogliun, G., Montano, V., Ravetti, C., Gambaro, P., Paladin, F., Beghi, E. & ARES (Alcohol Related Seizures) study group. (2011) Risk factors for a first epileptic seizure symptomatic of brain tumour or brain vascular malformation. A case control study. *Swiss Medical Weekly*, 141: w13155.
Not in PICO
- Lewis, D. W. (1996) Pediatric headaches: What do the children want? *Headache: The Journal of Head and Face Pain*, 36.
Not in PICO
- Listernick, R. (2003) A 9-year-old boy with bizarre behavior and growth delay. *Pediatric Annals*, 32: 292-295.
Not in PICO
- Lobo-Antunes, N. & Lobo-Antunes, N. (1999) [Urgent neurological consultation in children with systemic cancer]. [Review] [140 refs] [Spanish]. *Revista de Neurologia*, 29: 349-359.
Not in PICO
- Loh, A. H. P., Aung, L., Ha, C., Tan, A. M., Quah, T. C. & Chui, C. H. (2012) Diagnostic delay in pediatric solid tumors: A population based study on determinants and impact on outcomes. *Pediatric Blood and Cancer*, 58: 561-565.
Not in PICO
- Lovrencic-Huzjan, A., Jadrijevic-Tomas, A., Samovojska, D., Cindric, I., Bencina, B., Bedekovic, M. R. & Kes, V. B. (2013) One year study of vertigo in the neurological emergency room. *Acta Clinica*

- Croatica, Supplement*, 52: 73.
Not in PICO
- Lueder, G. T. (2005) The effect of initial recognition of abnormalities by physicians on outcome of retinoblastoma. *Journal of AAPOS*, 9: 383-385.
Not in PICO
- Lyratzopoulos, G., Abel, G. A., McPhail, S., Neal, R. D. & Rubin, P. (2013) Measures of promptness of cancer diagnosis in primary care: secondary analysis of national audit data on patients with 18 common and rarer cancers. *British Journal of Cancer*, 108: 686-690.
Not in PICO
- Madlon-Kay, D. J. (1985) Evaluation and outcome of the dizzy patient. *Journal of Family Practice*, 21: 109-113.
Not in PICO (some patients already had cancer, mean follow up (i.e., index test) = 6 months, 45/121 had unknown diagnosis)
- Mann, S. D. D. (1998) Intractable vomiting due to a brainstem lesion in the absence of neurological signs or raised intracranial pressure. *Gut*, 42: 875-877.
Not in PICO
- Matuja, W. B. & Matuja, W. B. (1991) Headache: pattern and features as experienced in a neurology clinic in Tanzania. *East African Medical Journal*, 68: 935-943.
Not in PICO
- McDonald, W. I. & McDonald, W. I. (1982) The symptomatology of tumours of the anterior visual pathways. *Canadian Journal of Neurological Sciences*, 9: 381-390.
Narrative review
- McGee, S., Burkett, K. W., McGee, S. & Burkett, K. W. (2000) Identifying common pediatric neurosurgical conditions in the primary care setting. [Review] [46 refs]. *Nursing Clinics of North America*, 35: 61-85.
Narrative review
- McIntosh, D. (2010) Delays in diagnosing cancer in children presenting via emergency departments in the West of Scotland: A retrospective case note review. *Pediatric Blood and Cancer*, Conference: 975-976.
Not in PICO
- McIntyre, F. L. & McIntyre, F. L. (1993) One in a million: when extraordinary cases occur in an ordinary practice. *Journal of Family Practice*, 36: 17-18.
Not in PICO
- Medina, L. S., Kuntz, K. M., Pomeroy, S., Medina, L. S., Kuntz, K. M. & Pomeroy, S. (2001) Children with headache suspected of having a brain tumor: a cost-effectiveness analysis of diagnostic strategies. *Pediatrics*, 108: 255-263.
Not in PICO
- Melamud, A. (2006) Retinoblastoma. *American Family Physician*, 73: 1039-1044.
Narrative review
- Melen, O. & Melen, O. (1987) Neuro-ophthalmologic features of pituitary tumors. [Review] [29 refs]. *Endocrinology & Metabolism Clinics of North America*, 16: 585-608.
Narrative review
- Mezue, W. C. O. (2012) Management of giant pituitary tumors affecting vision in Nigeria. *World Neurosurgery*, 77: 606-609.
Not in PICO
- Mi, S.-J. L. (2009) The first consultation in the eye of the 45 cases of sellar tumors. *International Journal of Ophthalmology*, 9: 798-799.
Not in PICO
- Moffat, D. A., Jones, S. E., Mahendran, S., Humphriss, R., Baguley, D. M., Moffat, D. A., Jones, S. E. M., Mahendran, S., Humphriss, R. & Baguley, D. M. (2004) Referral patterns in vestibular

- schwannomas --10 years on. *Clinical Otolaryngology & Allied Sciences*, 29: 515-517.
Not in PICO
- Molassiotis, A., Wilson, B., Brunton, L., Chandler, C., Molassiotis, A., Wilson, B., Brunton, L. & Chandler, C. (2010) Mapping patients' experiences from initial change in health to cancer diagnosis: a qualitative exploration of patient and system factors mediating this process. *European Journal of Cancer Care*, 19: 98-109.
Not in PICO
- Molassiotis, A., Wilson, B., Brunton, L., Chaudhary, H., Gattamaneni, R., McBain, C., Molassiotis, A., Wilson, B., Brunton, L., Chaudhary, H., Gattamaneni, R. & McBain, C. (2010) Symptom experience in patients with primary brain tumours: a longitudinal exploratory study. *European Journal of Oncology Nursing*, 14: 410-416.
Not in PICO
- Moll, G. W., Bock, H. G., Moll, G. W. & Bock, H. G. (2001) Two tumors detected by thyroid assessment in two children. *Endocrine Practice*, 7: 467-473.
Not in PICO
- Momota, H., Iwami, K., Fujii, M., Motomura, K., Natsume, A., Ogino, J., Hasegawa, T., Wakabayashi, T., Momota, H., Iwami, K., Fujii, M., Motomura, K., Natsume, A., Ogino, J., Hasegawa, T. & Wakabayashi, T. (2011) Rhabdoid glioblastoma in a child: case report and literature review. [Review]. *Brain Tumor Pathology*, 28: 65-70.
Not in PICO
- Morfouace, M., Chalumeau, M., Grill, J. & Brasme, J. F. (2011) Diagnostic delays of brain tumors in children: Determinants and consequences. *Archives de Pediatrie*, 18: H77-H78.
Not in PICO
- Morgan, M., Jenkins, L., Ridsdale, L., Morgan, M., Jenkins, L. & Ridsdale, L. (2007) Patient pressure for referral for headache: a qualitative study of GPs' referral behaviour. *British Journal of General Practice*, 57: 29-35.
Not in PICO
- Mrugala, M., Giglio, P., Keene, C. & Ferreira, M. (2014) Drop attacks secondary to an extra-axial tumor compressing the midbrain. *Neuro-Oncology*, 16: i135.
Not in PICO
- Mullaney, P. B. K. (1996) Retinoblastoma referral patterns in Saudi Arabia. *Ophthalmic Epidemiology*, 3: 35-46.
Not in PICO
- Munot, P. (2009) Paediatric brain tumours in a district general hospital in the UK: A 7-year experience. *Developmental Medicine and Child Neurology*, Conference: January.
Not in PICO
- Murtagh, J. (1488) Dizziness (vertigo). *Australian Family Physician*, 20: 1483-1485.
Narrative review
- Nagahiro, S., Matsukado, Y., Kaku, M., Wada, S., Urasaki, E., Nagahiro, S., Matsukado, Y., Kaku, M., Wada, S. & Urasaki, E. (1983) [Evaluation of blink reflexes in cerebellopontine angle tumors]. [Japanese]. *No to Shinkei - Brain & Nerve*, 35: 1117-1124.
Not in PICO
- Natalwala, A., Bharkhada, V., Noel, G., Cruickshank, G., Natalwala, A., Bharkhada, V., Noel, G. & Cruickshank, G. (2011) Comparison of time taken from initial presentation to histological diagnosis of Glioblastoma Multiforme (GBM) in Birmingham, United Kingdom and Strasbourg, France. *Clinical Neurology & Neurosurgery*, 113: 358-361.
Not in PICO
- Nucci, P. (2009) Abnormal head posture due to ocular problems: A review. *Current Pediatric Reviews*, 5: 105-111.
Narrative review

- O'Brien, A., Hugo, P., Stapleton, S., Lask, B. E.-M. A. & O'Brien, A. b. ac. u. (2001) "Anorexia saved my life": Coincidental anorexia nervosa and cerebral meningioma. [References]. *International Journal of Eating Disorders*, 30.
Not in PICO
- O'Brien, M., Curtis, C., D'Hemecourt, P., Proctor, M., O'Brien, M., Curtis, C., D'Hemecourt, P. & Proctor, M. (2009) Case report: a case of persistent back pain and constipation in a 5-year-old boy. *Physician & Sportsmedicine*, 37: 133-137.
Not in PICO
- O'Sullivan, E. (2002) Precocious puberty: A parent's perspective. *Archives of Disease in Childhood*, 86: 320-321.
Not in PICO
- Orlopp, K., Schmidt-Wolf, I. G., Urbach, H., Schlegel, U., Orlopp, K., Schmidt-Wolf, I. G. H., Urbach, H. & Schlegel, U. (2005) [Acute central nervous symptoms in oncologic patients]. [Review] [28 refs] [German]. *Internist*, 46: 19-29.
Narrative review
- Ozcan S.Evran (2008) Glioblastoma multiforme presenting with psychiatric symptoms in a primary care setting: review of isolated psychiatric symptoms with brain tumors. *Neurosurgery Quarterly*, 18: 148-150.
Not in PICO
- Pane, A. (2009) Diplopia - A symptom to take seriously. *Medicine Today*, 10: 74-76.
Narrative review
- Park, S. H., Chi, J. G., Cho, B. K., Wang, K. C., Park, S. H., Chi, J. G., Cho, B. K. & Wang, K. C. (1993) Spinal cord ganglioglioma in childhood. [Review] [22 refs]. *Pathology, Research & Practice*, 189: 189-196.
Not in PICO
- Parker, A. (1996) Difficulties in diagnosing intrinsic spinal cord tumours. *Archives of Disease in Childhood*, 75: 204-207.
Not in PICO
- Patel, H., Garg, B. P., Salanova, V., Boaz, J. C., Luerssen, T. G., Kalsbeck, J. E., Patel, H., Garg, B. P., Salanova, V., Boaz, J. C., Luerssen, T. G. & Kalsbeck, J. E. (2001) Tumor-related epilepsy in children. *Journal of Child Neurology*, 16: 141-145.
Not in PICO
- Paul, S. P., Debono, R. & Walker, D. (2013) Clinical update: Recognising brain tumours early in children. *Community Practitioner*, 86: 42-45.
Narrative review
- Pengiran Tengah, D. S., Byrne, P. O., Wills, A. J., Pengiran Tengah, D. S. N. A., Byrne, P. O. & Wills, A. J. (2003) Urgent 2-week referrals for CNS/brain tumours: a retrospective audit. *Clinical Oncology (Royal College of Radiologists)*, 15: 7-9.
Not in PICO
- Perek, D. & Perek-Polnik, M. (2003) [Brain tumors in children][Polish]. *Przegląd Lekarski*, 60: 27-34.
Narrative review
- Perek, D. (2005) Wrong interpretation of symptoms of posterior fossa tumors causing delay of diagnosis. *Pediatrics Polska*, 80: 80-84.
Not in PICO
- Perkins, P. D. & Perkins, P. D. (1986) Once in a lifetime: a case of a pineal tumour. *Journal of the Royal College of General Practitioners*, 36: 416-417.
Not in PICO
- Perry, J. J., Stiell, I. G., Wells, G. A., Mortensen, M., Lesiuk, H., Sivilotti, M., Kapur, A., Perry, J. J., Stiell, I. G., Wells, G. A., Mortensen, M., Lesiuk, H., Sivilotti, M. & Kapur, A. (2005) Attitudes and judgment of emergency physicians in the management of patients with acute headache.

Academic Emergency Medicine, 12: 33-37.

Not in PICO

Peters, K. S. (2004) Secondary headache and head pain emergencies. *Primary Care - Clinics in Office Practice*, 31: 381-393.

Narrative review

Phi, J. H., Kim, S. K., Kang, T. H., Wang, K. C., Phi, J. H., Kim, S. K., Kang, T. H. & Wang, K. C. (2012) Hydrocephalic fits: forgotten but not gone. *Childs Nervous System*, 28: 1863-1868.

Not in PICO

Pittner, M. (2010) Blindness due to unrecognized bilateral optic nerve sheath meningioma in a 14-year-old girl (case report). *Neuropediatrics*, Conference.

Not in PICO

Pollock, B. H., Krischer, J. P., Vietti, T. J., Pollock, B. H., Krischer, J. P. & Vietti, T. J. (1991) Interval between symptom onset and diagnosis of pediatric solid tumors. *Journal of Pediatrics*, 119: 725-732.

Not in PICO

Powell, H. R., Choa, D. I., Powell, H. R. F. & Choa, D. I. (2010) Should all patients referred for magnetic resonance imaging scans of their internal auditory meatus be followed up in ENT clinics? *European Archives of Oto-Rhino-Laryngology*, 267: 1361-1366.

Not in PICO

Prasad, J., Cousins, V. C., Prasad, J. & Cousins, V. C. (319) Asymmetrical hearing loss. *Australian Family Physician*, 37: 312-319.

Narrative review

Prashad, P. S., Marcus, C. L., Brown, L. W., Dlugos, D. J., Feygin, T., Harding, B. N., Heuer, G. G. & Mason, T. B. (2013) Brain tumor presenting as somnambulism in an adolescent. *Pediatric Neurology*, 49: 209-212.

Not in PICO

Provenzale, J. M. & Provenzale, J. M. (2010) Imaging findings of structural causes of epilepsy in children: a guide for the radiologist in the emergency room. *Emergency Radiology*, 17: 479-486.

Not in PICO

Puchner, M. J. F. (1998) Suprasellar meningioma. A disease still frequently diagnosed too late. *Deutsche medizinische Wochenschrift (1946)*, 123: 991-996.

Not in PICO

Purcell, C. (2011) Can we diagnose Brain Tumours in Children Earlier? An Irish Audit. *British Journal of Neurosurgery*, Conference: 565-566.

Not in PICO

Qaddoumi, I. (2010) Characterization of intracranial neoplasms in the first 120 days of life. *Neuro-Oncology*, Conference: ii84.

Not in PICO

Raab, C. P., Gartner, J. C., Jr., Raab, C. P. & Gartner, J. C. J. (2009) Diagnosis of childhood cancer. [Review] [33 refs]. *Primary Care; Clinics in Office Practice*, 36: 671-684.

Narrative review

Rajan, B., Ashley, S., Thomas, D. G., Marsh, H., Britton, J., Brada, M., Rajan, B., Ashley, S., Thomas, D. G., Marsh, H., Britton, J. & Brada, M. (1997) Craniopharyngioma: improving outcome by early recognition and treatment of acute complications. *International Journal of Radiation Oncology, Biology, Physics*, 37: 517-521.

Not in PICO

Ramcharan, R., Midha, R., Ramcharan, R. & Midha, R. (2004) Clinical presentation and physical examination. [Review] [16 refs]. *Neurosurgery Clinics of North America*, 15: 125-132.

Narrative review

Ramelli, G. P., von der, W. N., Stanga, Z., Mullis, P. E., Buergi, U., Ramelli, G. P., von der Weid, N., Stanga, Z., Mullis, P. E. & Buergi, U. (1998) Suprasellar germinomas in childhood and adolescence:

- diagnostic pitfalls. *Journal of Pediatric Endocrinology*, 11: 693-697.
Not in PICO
- Reulecke, B. C., Erker, C. G., Fiedler, B. J., Niederstadt, T. U., Kurlemann, G., Reulecke, B. C., Erker, C. G., Fiedler, B. J., Niederstadt, T. U. & Kurlemann, G. (2008) Brain tumors in children: initial symptoms and their influence on the time span between symptom onset and diagnosis. *Journal of Child Neurology*, 23: 178-183.
Not in PICO
- Rho, Y. I., Chung, H. J., Suh, E. S., Lee, K. H., Eun, B. L., Nam, S. O., Kim, W. S., Eun, S. H., Kim, Y. O., Rho, Y. I., Chung, H. J., Suh, E. S., Lee, K. H., Eun, B. L., Nam, S. O., Kim, W. S., Eun, S. H. & Kim, Y. O. (2011) The role of neuroimaging in children and adolescents with recurrent headaches--multicenter study. *Headache*, 51: 403-408.
Not in PICO
- Rittman, T., Corns, R., Kumar, A., Bhangoo, R., Ashkan, K., Rittman, T., Corns, R., Kumar, A., Bhangoo, R. & Ashkan, K. (2012) Is referral to the neuro-oncology MDT safe? *British Journal of Neurosurgery*, 26: 321-324.
Not in PICO
- Ruggieri, M., Iannetti, P., Polizzi, A., La, M., I, Spalice, A., Giliberto, O., Platania, N., Gabriele, A. L., Albanese, V., Pavone, L., Ruggieri, M., Iannetti, P., Polizzi, A., La Mantia, I., Spalice, A., Giliberto, O., Platania, N., Gabriele, A. L., Albanese, V. & Pavone, L. (2005) Earliest clinical manifestations and natural history of neurofibromatosis type 2 (NF2) in childhood: a study of 24 patients. *Neuropediatrics*, 36: 21-34.
Not in PICO
- Ruis, C., van den Berg, E., van Stralen, H. E., Huenges Wajer, I. M., Biessels, G. J., Kappelle, L. J., Postma, A. & van Zandvoort, M. J. (2014) - Symptom Checklist 90-Revised in neurological outpatients. - *Journal of Clinical & Experimental Neuropsychology: Official Journal of the International Neuropsychological Society*, 36: 170-177.
Not in PICO
- Rutkowski S. (2005) Brain tumors in children. Diagnostics and interdisciplinary therapeutic strategies. *Onkologe*, 11: 1090-1100.
Narrative review
- Rutkowski, S. & Rutkowski, S. (2007) Timely identification of suspected paediatric CNS tumours. *Lancet Oncology*, 8: 664.
Narrative review
- Rutkowski, S. (2008) Childhood brain tumors. Clinical symptoms and diagnostic standards. *Monatsschrift fur Kinderheilkunde*, 156: 1165-1172.
Narrative review
- Saffra, N. K. (2011) Isolated sixth cranial nerve palsy as the presenting symptom of a rapidly expanding ACTH positive pituitary adenoma: a case report. *BMC ophthalmology*, 11: 2011.
Not in PICO
- Saito, N. (1996) Pineal tumor and alternating skew deviation. *Neuro-Ophthalmology Japan*, 13: 304-308.
Not in PICO
- Sakata, H. (2012) Vertigo and disequilibrium during early childhood. *Equilibrium Research*, 71: 253-263.
Narrative review
- Sakuma, T. (2002) A case of acoustic neurinoma occurring in a 5-year-old child. *Practica Oto-Rhino-Laryngologica*, 95: 585-590.
Not in PICO
- Salander, P., Bergenheim, A. T., Hamberg, K., Henriksson, R., Salander, P., Bergenheim, A. T., Hamberg, K. & Henriksson, R. (1999) Pathways from symptoms to medical care: a descriptive study of symptom development and obstacles to early diagnosis in brain tumour patients. *Family*

Practice, 16: 143-148.
Not in PICO

Sam, M. C., So, E. L., Sam, M. C. & So, E. L. (2001) Significance of epileptiform discharges in patients without epilepsy in the community. *Epilepsia*, 42: 1273-1278.
Not in PICO

Samuelsson, K. (1997) Clinical assessment without direct contact with the patient. Very delayed diagnosis of brain tumor. *Lakartidningen*, 94: 3075-3076.
Not in PICO

Sanchez Echaniz, J. (1991) Migraine in a pediatric emergency service. *Anales Espanoles de Pediatria*, 34: 267-271.
Setting not in PICO

Saxena, A. (2009) Growing pains - Diagnose with care! *European Journal of Paediatric Neurology*, Conference: September.
Not in PICO

Scalzone, M. (2009) Diencephalic syndrome and brain tumours: A rare cause of growth failure. *European Journal of Oncology*, 14: 53-56.
Narrative review

Segal, D. L. (2012) Delay in diagnosis of primary intradural spinal cord tumors. *Surgical Neurology International*, 3.
Not in PICO

Seregard, S. (1996) A study of children with retinoblastoma. Diagnosis is often delayed. *Lakartidningen*, 93: 1133-1135.
Not in PICO

Sethi, R. V., Marino, R., Niemierko, A., Tarbell, N. J., Yock, T. I. & MacDonald, S. M. (2013) Delayed diagnosis in children with intracranial germ cell tumors. *Journal of Pediatrics*, 163: 1448-1453.
Not in PICO

Shay, V., Fattal-Valevski, A., Beni-Adani, L., Constantini, S., Shay, V., Fattal-Valevski, A., Beni-Adani, L. & Constantini, S. (2012) Diagnostic delay of pediatric brain tumors in Israel: a retrospective risk factor analysis. *Childs Nervous System*, 28: 93-100.
Not in PICO

Shedid, D. B. (2004) Clinical presentation of spinal tumors. *Neurosurgery Quarterly*, 14: 224-228.
Narrative review

Silvani, A., Gaviani, P., Lamperti, E., Botturi, A., Ferrari, D., Simonetti, G., Salmaggi, A., Silvani, A., Gaviani, P., Lamperti, E., Botturi, A., Ferrari, D., Simonetti, G. & Salmaggi, A. (2011) Malignant gliomas: early diagnosis and clinical aspects. *Neurological Sciences*, 32 Suppl 2: S207-S208.
Narrative review

Simon, J. W., Kaw, P., Simon, J. W. & Kaw, P. (2001) Commonly missed diagnoses in the childhood eye examination. [Review] [16 refs]. *American Family Physician*, 64: 623-628.
Narrative review

Skinner, S. A. (1988) Early diagnosis of brain tumor. *Postgraduate Medicine*, 83: 117-124.
Narrative review

Sloane, P. D., Dallara, J., Roach, C., Bailey, K. E., Mitchell, M., McNutt, R., Sloane, P. D., Dallara, J., Roach, C., Bailey, K. E., Mitchell, M. & McNutt, R. (1994) Management of dizziness in primary care. *Journal of the American Board of Family Practice*, 7: 1-8.
Not in PICO

Snyder, H., Robinson, K., Shah, D., Brennan, R. & Handrigan, M. (1993) Signs and symptoms of patients with brain tumors presenting to the emergency department. *Journal of Emergency Medicine*, 11: 253-258.
Not in PICO

Snyder, M. C. T. (2011) A bitter pill to swallow. *Journal of Investigative Medicine*, Conference: 380.
Not in PICO

- Soucy, E. A., Gao, F., Gutmann, D. H., Dunn, C. M., Soucy, E. A., Gao, F., Gutmann, D. H. & Dunn, C. (2012) Developmental delays in children with neurofibromatosis type 1. *Journal of Child Neurology*, 27: 641-644.
Not in PICO
- Spira, P. J. & Spira, P. J. (1984) Headaches. A specialist's view. *Australian Family Physician*, 13: 8-12.
Narrative review
- Strain, J. D. (2007) ACR Appropriateness Criteria on Headache-Child. *JACR Journal of the American College of Radiology*, 4: 18-23.
Narrative review
- Stricker, S. J. (2006) Evaluation and treatment of the child with tiptoe gait. *International Pediatrics*, 21: 91-96.
Narrative review
- Subaciute, J. & Subaciute, J. (2002) [Early diagnosis of spinal cord schwannoma: the significance of the pain syndrome]. [Lithuanian]. *Medicina (Kaunas)*, 38: 1086-1088.
Not in PICO
- Taieb, C. R. (2011) Prevalence and procedure for vertigo follow-up in France. *Value in Health, Conference: A318*.
Not in PICO
- Tan, A. (1991) Non-neurological manifestations of intracranial tumours: a report of four cases. *The Journal of the Singapore Paediatric Society*, 33: 173-177.
Not in PICO
- Tarnag, D.-C. (1995) Diabetes insipidus as an early sign of pineal tumor. *American Journal of Nephrology*, 15: 161-164.
Not in PICO
- Taylor, M., Couto-Silva, A. C., Adan, L., Trivin, C., Sainte-Rose, C., Zerah, M., Valteau-Couanet, D., Doz, F., Chalumeau, M. & Brauner, R. (2012) Hypothalamic-pituitary lesions in pediatric patients: Endocrine symptoms often precede neuro-ophthalmic presenting symptoms. *Journal of Pediatrics*, 161: 855-863.
Not in PICO
- Tengah, D. S. N. A., Byrne, P. O. & Wills, A. J. (2003) Urgent 2-week referrals for CNS/brain tumours: A retrospective audit. *Clinical Oncology*, 15: 7-9.
Not in PICO
- Teo, W. Y. & Myseros, J. S. (2014) - The gut or the brain?-gastrointestinal misdiagnoses of infantile brain tumors. - *Childs Nervous System*, 30: 1449-1453.
Not in PICO
- Teppo, H., Heikkinen, J., Laitakari, K., Alho, O. P., Teppo, H., Heikkinen, J., Laitakari, K. & Alho, O. P. (2009) Diagnostic delays in vestibular schwannoma. *Journal of Laryngology & Otology*, 123: 289-293.
Not in PICO
- Thimm, A. (2010) Optic pathway gliomas in children with neurofibromatosis type 1: A long term study in 38 patients. *Neuropediatrics, Conference*.
Not in PICO
- Thomas, V. (2011) Review of presenting symptoms and time to diagnosis of children with primary brain tumours. *Archives of Disease in Childhood, Conference: April*.
Not in PICO
- Thulesius, H., Pola, J., Hakansson, A., Thulesius, H., Pola, J. & Hakansson, A. (2000) Diagnostic delay in pediatric malignancies--a population-based study. *Acta Oncologica*, 39: 873-876.
Not in PICO
- Traccis S.Zoroddu (2004) Evaluating patients with vertigo: Bedside examination. *Neurological Sciences*, 25: S16-S19.
Narrative review

- Trojanowski, T., Kaminski, S., Golabek, W., Pawlik, Z., Siwiec, H., Trojanowski, T., Kaminski, S., Golabek, W., Pawlik, Z. & Siwiec, H. (1990) [Diagnosis of cerebello-pontine angle tumors]. [Polish]. *Polski Tygodnik Lekarski*, 45: 561-563.
Not in PICO
- Vazquez Roman, S., Martinez, A. A., Llorente, O. L., Rojo, C. P., Hinojosa, B. J., Vazquez Roman, S., Martinez Anton, A., Llorente Otones, L., Rojo Conejo, P. & Hinojosa Bernal, J. (2008) [Initial signs and symptoms of brain tumors in children]. [Spanish]. *Neurologia*, 23: 215-219.
Not in PICO
- Visudhiphan, P. (1982) Torticollis as the presenting sign in cervical spine infection and tumor. *Clinical Pediatrics*, 21: 71-76.
Not in PICO
- Wadud, S. A., Ahmed, S., Choudhury, N. & Chowdhury, D. (2014) - Evaluation of ophthalmic manifestations in patients with intracranial tumours. - *Mymensingh Medical Journal: MMJ*, 23: 268-271.
Not in PICO
- Wagner, U., Granditsch, G., Wagner, U. & Granditsch, G. (1986) [Failure to thrive as a main symptom of intracranial tumors in early childhood]. [German]. *Padiatrie und Padologie*, 21: 147-153.
Not in PICO
- Walker, D., Chu, T., Shah, A., Wilne, S. & Coleman, M. (2014) A new clinical guideline (2007) and national awareness campaign (2011) accelerated brain tumour diagnosis in uk children (headsmart-be brain tumour aware). *Neuro-Oncology*, 16: i26.
Not in PICO
- Wallach, M. (2006) Shorter time to diagnosis and improved stage at presentation in Swiss patients with retinoblastoma treated from 1963 to 2004. *Pediatrics*, 118: e1493-e1498.
Not in PICO
- White, J. (2012) Delay in the diagnosis of retinoblastoma: An update. *Clinical and Experimental Ophthalmology*, Conference: December.
Not in PICO
- White, J. R., Carlson, M. L., Van Gompel, J. J., Neff, B. A., Driscoll, C. L., Lane, J. I. & Link, M. J. (2013) Lipomas of the cerebellopontine angle and internal auditory canal: Primum Non Nocere. *Laryngoscope*, 123: 1531-1536.
Not in PICO
- White, M. A. J. (2009) Posterior fossa tumours in children: Time to diagnosis. *British Journal of Neurosurgery*, Conference: 472-473.
Not in PICO
- Wiet, R. J., Monsell, E. M., Hotaling, A. J., Wiet, R. J., Monsell, E. M. & Hotaling, A. J. (130) Hearing and balance disorders. How to recognize, when to refer. *Postgraduate Medicine*, 77: 119-130.
Narrative review
- Williams, L. (2012) A web-based electronic neurology referral system: A solution for an overburdened healthcare system? *Irish Medical Journal*, 105.
Not in PICO
- Wilne, S., Collier, J., Kennedy, C., Koller, K., Grundy, R., Walker, D., Wilne, S., Collier, J., Kennedy, C., Koller, K., Grundy, R. & Walker, D. (2007) Presentation of childhood CNS tumours: a systematic review and meta-analysis. *Lancet Oncology*, 8: 685-695.
Not in PICO
- Wilne, S., Koller, K., Collier, J., Kennedy, C., Grundy, R., Walker, D., Wilne, S., Koller, K., Collier, J., Kennedy, C., Grundy, R. & Walker, D. (2010) The diagnosis of brain tumours in children: a guideline to assist healthcare professionals in the assessment of children who may have a brain tumour. [Review] [32 refs]. *Archives of Disease in Childhood*, 95: 534-539.
Guideline

- Wilne, S., Walker, D., Wilne, S. & Walker, D. (2010) Spine and spinal cord tumours in children: a diagnostic and therapeutic challenge to healthcare systems. [Review] [32 refs]. *Archives of Disease in Childhood Education & Practice*, 95: 47-54.
Narrative review
- Wilne, S., Collier, J., Kennedy, C., Jenkins, A., Grout, J., Mackie, S., Koller, K., Grundy, R., Walker, D., Wilne, S., Collier, J., Kennedy, C., Jenkins, A., Grout, J., Mackie, S., Koller, K., Grundy, R. & Walker, D. (2012) Progression from first symptom to diagnosis in childhood brain tumours. *European Journal of Pediatrics*, 171: 87-93.
Not in PICO
- Wilne, S. H., Ferris, R. C., Nathwani, A., Kennedy, C. R., Wilne, S. H., Ferris, R. C., Nathwani, A. & Kennedy, C. R. (2006) The presenting features of brain tumours: a review of 200 cases. *Archives of Disease in Childhood*, 91: 502-506.
Not in PICO
- Wilson, M., Cummins, C. L., Macpherson, L., Sun, Y., Natarajan, K., Grundy, R. G., Arvanitis, T. N., Kauppinen, R. A. & Peet, A. C. (2013) Magnetic resonance spectroscopy metabolite profiles predict survival in paediatric brain tumours. *European Journal of Cancer*, 49: 457-464.
Not in PICO
- Wilson, P. E., Oleszek, J. L. & Clayton, G. H. (2007) Pediatric spinal cord tumors and masses. *Journal of Spinal Cord Medicine*, 30: S15-S20.
Not in PICO
- Wirix, M. (2000) Delayed diagnosis of retinoblastoma. *Bulletin de la Societe belge d'ophtalmologie*, 37-41.
Not in PICO
- Wolf, G. (1980) Early symptoms of brain tumors. *Fortschritte der Medizin*, 98: 1215-1218.
Not in PICO
- Wong, B. Y., Capper, R., Wong, B. Y. W. & Capper, R. (2012) Incidence of vestibular schwannoma and incidental findings on the magnetic resonance imaging and computed tomography scans of patients from a direct referral audiology clinic. *Journal of Laryngology & Otology*, 126: 658-662.
Not in PICO
- Xie, C., Ahmed, A. & Banerjee, A. (2013) A comparison of primary care access to non-trauma computed tomography (CT) and magnetic resonance imaging (MRI) of the brain with hospital clinician referrals. *Clinical Radiology*, 68: S8-S9.
Not in PICO
- Young, G., Toretsky, J. A., Campbell, A. B., Eskenazi, A. E., Young, G., Toretsky, J. A., Campbell, A. B. & Eskenazi, A. E. (2000) Recognition of common childhood malignancies. [Review] [18 refs]. *American Family Physician*, 61: 2144-2154.
Narrative review
- Yule, S. M., Hide, T. A., Cranney, M., Simpson, E., Barrett, A., Yule, S. M., Hide, T. A., Cranney, M., Simpson, E. & Barrett, A. (2001) Low grade astrocytomas in the West of Scotland 1987-96: treatment, outcome, and cognitive functioning. *Archives of Disease in Childhood*, 84: 61-64.
Not in PICO
- Zajac, A., Gergont, A., Krocza, S., Wesolowska, E., Zajac, A., Gergont, A., Krocza, S. & Wesolowska, E. (2008) [Clinical manifestation of neoplasm cerebri in children hospitalized in pediatric neurology department]. [Polish]. *Przegląd Lekarski*, 65: 813-818.
Not in PICO
- Zalewska-Szewczyk, B., Zielinska, E., Zakrzewski, K., Bulas, M., Andrzejewski, W., Bodalski, J., Zalewska-Szewczyk, B., Zielinska, E., Zakrzewski, K., Bulas, M., Andrzejewski, W. & Bodalski, J. (2005) [Prognosis of clinical course of primary brain tumours in children in relationship to the duration and characteristic features of initial clinical symptoms]. [Polish]. *Medycyna Wieku Rozwojowego*, 9: 567-578.
Not in PICO

Zapala, D. A. & Zapala, D. A. (2008) The importance of sudiologic red flags in patient management decisions. [References]. *Journal of the American Academy of Audiology*, .19.

Not in PICO

Zelwianska, B., Gucwa-Piotrowska, G., Lis-Hille, A., Krocza, S., Zelwianska, B., Gucwa-Piotrowska, G., Lis-Hille, A. & Krocza, S. (2008) [Types of diagnosis in the outpatient practice during the years 2006-2007]. [Polish]. *Przegląd Lekarski*, 65: 769-772.

Not in PICO

Zhang, C. H., Zhang, T. C., Zhong, J. S., Li, Y. W., Zhang, C. M., Zhang, C. h., Zhang, T. c., Zhong, J. s., Li, Y. w. & Zhang, C. m. (2004) [Early diagnosis of the tumors in orbital apex and optic nerve]. [Chinese]. *Chung-Hua Yen Ko Tsa Chih [Chinese Journal of Ophthalmology]*, 40: 34-36.

Not in PICO

Zhang, R. (2007) [Misdiagnosis of facial never tumor]. *Zhonghua er bi yan hou tou jing wai ke za zhi = Chinese journal of otorhinolaryngology head and neck surgery*, 42: 817-820.

Not in PICO

Review question:

Which investigations of symptoms of suspected brain and CNS cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

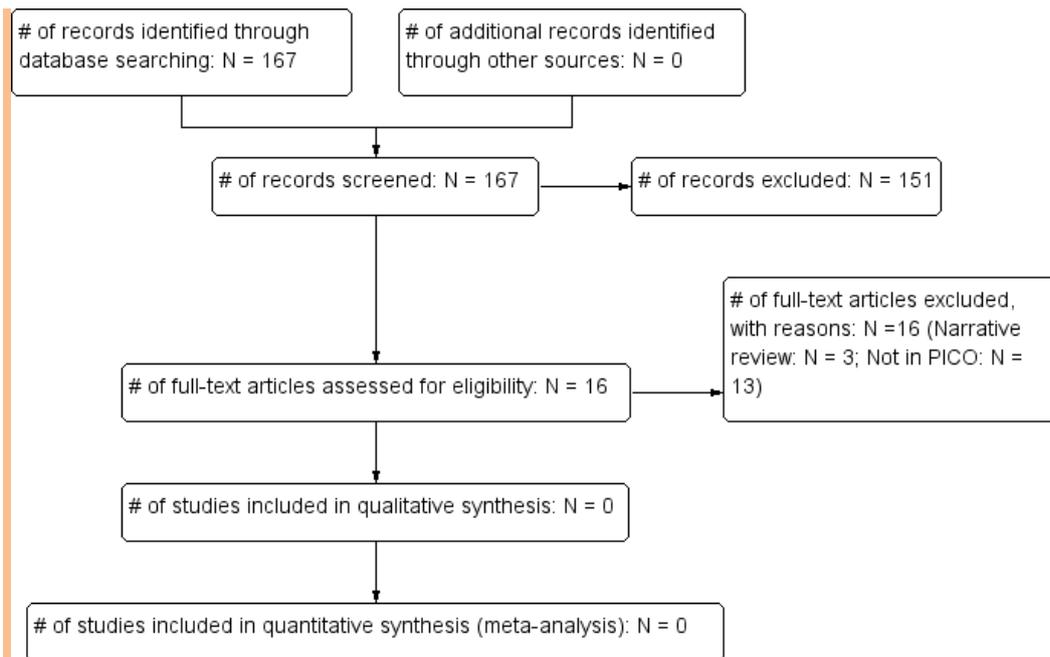
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-6/2013	1173	101	17/06/2013
<i>Premedline</i>	1980-6/2013	112	6	19/06/2013
<i>Embase</i>	1980-6/2013	2171	90	19/06/2013
<i>Cochrane Library</i>	1980-6/2013	209	2	19/06/2013
<i>Psychinfo</i>	1980-6/2013	62	2	17/02/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-6/2013	57	1	19/06/2013

Total References retrieved (after de-duplication): 162

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	6/2013-12/08/2014	40	2	12/08/2014
<i>Premedline</i>	6/2013-12/08/2014	22	1	12/08/2014
<i>Embase</i>	6/2013-12/08/2014	62	6	12/08/2014
<i>Cochrane Library</i>	6/2013-12/08/2014	96	0	12/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	6/2013-12/08/2014	22	0	12/08/2014

Total References retrieved (after de-duplication): 5



Study results

No evidence was identified pertaining to the diagnostic accuracy of CT or MRI scans in patients with suspected brain or CNS cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

(2001) Promoting self-referral for advanced imaging. *Effective Clinical Practice*, 4: 93-94.

Not in PICO

Abramovich, S. J. (1987) Auditory brain stem response and computed tomography in acoustic tumour investigations. *Journal of Laryngology and Otology*, 101: 334-345.

Narrative review

Abul-Kasem, K., Thurnher, M., Puchner, S., Overgaard, A. & Sundgren, P. (2009) Multimodal magnetic resonance imaging increases the overall diagnostic accuracy in brain tumors. *Neuroradiology*, 51: S146.

Abstract only. Not in PICO.

Ahrensberg, J. M., Olesen, F., Hansen, R. P., Schroder, H. & Vedsted, P. (2013) Childhood cancer and factors related to prolonged diagnostic intervals: a Danish population-based study. *British Journal of Cancer*, 108: 1280-1287.

Not in PICO

Allcutt, D. A. & Mendelow, A. D. (1992) Presentation and diagnosis of brain tumours. [Review] [11 refs]. *British Journal of Hospital Medicine*, 47: 745-752.

Narrative review

Aprile, I., Bencivenga, S., Loreti, F. & Torni, C. (2011) Intracranial tumour characterization: Whole brain evaluation with MR perfusion images and SPECT-CT. *Neuroradiology Journal*, 24: 838-845.

Not in PICO

- Baba, K., Akhter, S., Jan, G. M. & Shah, A. (2002) Cerebrospinal fluid cytology in "brain tumours" - A study over a period of 10 years (1991-2000). *JK Practitioner*, 9: 101-102.
Not in PICO
- Badiane, M., Afidja, A., Ba-Diop, S., Badiane, S. B., Niang, E. H. & Ba-Ly, A. (1998) [Diagnostic x-ray computed tomography of craniocerebral tumors. Apropos of 108 cases collected at the Soweto Center of Dakar]. [Review] [8 refs] [French]. *Dakar Medical*, 43: 34-36.
Not in PICO
- Baehring, J. M., Bi, W. L., Bannykh, S., Piepmeier, J. M. & Fulbright, R. K. (2007) Diffusion MRI in the early diagnosis of malignant glioma. *Journal of Neuro-Oncology*, 82: 221-225.
Not in PICO
- Barrett, J. A. Development of an evidence based referral protocol for early diagnosis of vestibular schwannomas. Dissertation Abstracts International: Section B: The Sciences and Engineering 69[8-B], 4639. 2009.
Not in PICO
- Batista, D. L., Riar, J., Keil, M. & Stratakis, C. A. (2007) Diagnostic tests for children who are referred for the investigation of Cushing syndrome. *Pediatrics*, 120: e575-e586.
Not in PICO
- Bauherz, G. (1996) [Usefulness of headache classification in the planning of radiological studies]. [Review] [15 refs] [French]. *Revue Medicale de Bruxelles*, 17: 293-299.
Narrative review
- Becker, L. A., Green, L. A., Beaufait, D., Kirk, J., From, J. & Freeman, W. L. (1993) Detection of intracranial tumors, subarachnoid hemorrhages, and subdural hematomas in primary care patients: a report from ASPN, Part 2. *Journal of Family Practice*, 37: 135-141.
Not in PICO
- Becker, L. A., Green, L. A., Beaufait, D., Kirk, J., From, J. & Freeman, W. L. (1993) Use of CT scans for the investigation of headache: a report from ASPN, Part 1. *Journal of Family Practice*, 37: 129-134.
Not in PICO (no reference standard for the CT-negative patients)
- Benamore, R. E., Wright, D. & Britton, I. (2005) Is primary care access to CT brain examinations effective? *Clinical Radiology*, 60: 1083-1089.
Not in PICO
- Berns, S. & Pearl, G. (2006) Middle ear adenoma. [Review] [11 refs]. *Archives of Pathology & Laboratory Medicine*, 130: 1067-1069.
Narrative review
- Beuthien-Baumann, B., Bredow, J., Burchert, W., Fuchtner, F., Bergmann, R., Alheit, H. D., Reiss, G., Hliscs, R., Steinmeier, R., Franke, W. G., Johannsen, B. & Kotzerke, J. (2003) 3-O-methyl-6-[18F]fluoro-L-DOPA and its evaluation in brain tumour imaging. *European Journal of Nuclear Medicine & Molecular Imaging*, 30: 1004-1008.
Not in PICO
- Bhat, S., Yadav, S. P., Suri, V., Patir, R., Kurkure, P., Kellie, S. & Sachdeva, A. (2011) Management of childhood brain tumors: Consensus report by the pediatric hematology oncology (PHO) chapter of Indian Academy of Pediatrics (IAP). *Indian Journal of Pediatrics*, 78: 1510-1519.
Guideline
- Blagoveshchenskaia, N. S., Egorova, V. K. & Tumanova, A. A. (1989) The early diagnosis of acoustic neurinomas. [Russian]. *Zhurnal voprosy neirokhirurgii imeni N. N.*: 52-54.
Not in PICO
- Blews, D. E., Wang, H., Kumar, A. J., Robb, P. A., Phillips, P. C. & Bryan, R. N. (1990) Intradural spinal metastases in pediatric patients with primary intracranial neoplasms: Gd-DTPA enhanced MR vs CT myelography. *Journal of Computer Assisted Tomography*, 14: 730-735.
Not in PICO

- Bonneville, J. F., Cattin, F., Racle, A., Bouchareb, M., Boulard, D., Potelon, P. & Tang, Y. S. (1989) Dynamic CT of the laterosellar extradural venous spaces. *Ajnr: American Journal of Neuroradiology*, 10: 535-542.
Not in PICO
- Bonneville, J. F. (2000) Pituitary adenomas: value of MR imaging. [French]. *Journal de Radiologie*, 81: 939-942.
Narrative review
- Brasme, J. F., Morfouace, M., Grill, J., Martinot, A., Amalberti, R., Bons-Letouzey, C. & Chalumeau, M. (2012) Delays in diagnosis of paediatric cancers: a systematic review and comparison with expert testimony in lawsuits. [Review]. *Lancet Oncology*, 13: e445-e459.
Not in PICO
- Brasme, J. F., Chalumeau, M., Doz, F., Lacour, B., Valteau-Couanet, D., Gaillard, S., Delalande, O., Aghakhani, N., Sainte-Rose, C., Puget, S. & Grill, J. (2012) Interval between onset of symptoms and diagnosis of medulloblastoma in children: distribution and determinants in a population-based study. *European Journal of Pediatrics*, 171: 25-32.
Not in PICO
- Chacowry, P. K., Platon, A. & Delemont, C. (1724) [Imaging in the evaluation of headaches]. [French]. *Revue Medicale Suisse*, 9: 1720-1722.
Narrative review
- Chandana, S. R., Movva, S., Arora, M. & Singh, T. (2008) Primary brain tumors in adults. *American Family Physician*, 77: 1423-1430.
Narrative review
- Cheng, G., Smith, R. & Tan, A. K. (2003) Cost comparison of auditory brainstem response versus magnetic resonance imaging screening of acoustic neuroma. *Journal of Otolaryngology*, 32: 394-399.
Not in PICO
- Chu, C. M., Rasalkar, D. D., Hu, Y. J., Cheng, F. W. T., Li, C. K. & Chu, W. C. W. (2011) Clinical presentations and imaging findings of neuroblastoma beyond abdominal mass and a review of imaging algorithm. *British Journal of Radiology*, 84: 81-91.
Not in PICO
- Chuang, S. & Harwood-Nash, D. (1986) Tumors and cysts. *Neuroradiology*, 28: 463-475.
Narrative review
- Clarke, C. E., Edwards, J., Nicholl, D. J. & Sivaguru, A. (2010) Imaging results in a consecutive series of 530 new patients in the Birmingham Headache Service. *Journal of Neurology*, 257: 1274-1278.
Not in PICO
- Cordeiro, J. G., Pinsker, M., Trippel, M., Nikkhah, G. & Reithmeier, T. (2011) Value of F-FET PET in comparison to stereotactic serial biopsy in the diagnosis of brain lesions. *Acta Neurochirurgica*, 153: 735.
Not in PICO
- Costantini, D. L., Vali, R., Chan, J., McQuattie, S. & Charron, M. (2013) Dual-time-point FDG PET/CT for the evaluation of pediatric tumors. *American Journal of Roentgenology*, 200: 408-413.
Not in PICO
- Damgaard-Pedersen, K. (1980) CT and IVU in the diagnosis of Wilms' tumour. A comparative study. *Pediatric Radiology*, 9: 207-211.
Not in PICO
- Davatzikos, C., Zacharaki, E. I., Gooya, A. & Clark, V. (2011) Multi-parametric analysis and registration of brain tumors: constructing statistical atlases and diagnostic tools of predictive value. *Conference Proceedings: ...Annual International Conference of the IEEE Engineering in Medicine & Biology Society*, 2011: 6979-6981.
Not in PICO

- Dawes, P. J. D. & Basiouny, H. E. (1999) Outcome of using magnetic resonance imaging as an initial screen to exclude vestibular schwannoma in patients presenting with unilateral tinnitus. *Journal of Laryngology and Otology*, 113: 818-822.
Not in PICO
- De, R. & Moffat, D. A. (506) The GP's role in acoustic neuroma. *Practitioner*, 248: 501-504.
Narrative review
- Djupesland, P., Sauer, T. & Freng, A. (1993) Puncture cytology in tumors of the head and neck region. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 113: 1985-1987.
Not in PICO
- Dorsch, J. N. (2014) Neurologic syndromes of the head and neck. *Primary Care - Clinics in Office Practice*, 41: 133-149.
Narrative review
- Dort, J. C., Cook, E. F., Watson, C., Shaw, G., Brown, D. K. & Eggermont, J. J. (2009) Power spectrum auditory brainstem response: novel approach to the evaluation of patients with unilateral auditory symptoms. *Journal of Otolaryngology: Head and Neck Surgery*, 38: 59-66.
Not in PICO
- Dubrulle, F., Delomez, J., Kiaei, A., Berger, P., Vincent, C., Vaneecloo, F. M. & Lemaitre, L. (2002) Mass screening for retrocochlear disorders: low-field-strength (0.2-T) versus high-field-strength (1.5-T) MR imaging. *Ajnr: American Journal of Neuroradiology*, 23: 918-923.
Not in PICO
- Duncan, G. & Caird, F. I. (1991) Review of 18 years' experience of a diagnostic geriatric neurology referral service. *Scottish Medical Journal*, 36: 139-142.
Not in PICO
- Fayed, N. & Modrego, P. J. (2005) The contribution of magnetic resonance spectroscopy and echoplanar perfusion-weighted MRI in the initial assessment of brain tumours. *Journal of Neuro-Oncology*, 72: 261-265.
Not in PICO
- Ferda, J., Ferdova, E., Marik, K., Mracek, J. & Hes, O. (2013) Pre-bioptical imaging of gliomas using PET/CT with application of 18F-fluorothymidine. [Czech]. *Ceska Radiologie*, 67: 19-24.
Not in PICO
- Fink, K. & Fink, J. (2013) Imaging of brain metastases. *Surgical neurology international*, 4: S209-S219.
Narrative review
- Floeth, F. W., Pauleit, D., Wittsack, H. J., Langen, K. J., Reifenberger, G., Hamacher, K., Messing-Junger, M., Zilles, K., Weber, F., Stummer, W., Steiger, H. J., Woebker, G., Muller, H. W., Coenen, H. & Sabel, M. (2005) Multimodal metabolic imaging of cerebral gliomas: positron emission tomography with [18F]fluoroethyl-L-tyrosine and magnetic resonance spectroscopy. *Journal of Neurosurgery*, 102: 318-327.
Not in PICO
- Forsyth, P. A. & Posner, J. B. (1993) Headaches in patients with brain tumors: a study of 111 patients. *Neurology*, 43: 1678-1683.
Not in PICO
- Franko, A., Holjar-Erlic, I., Miletic, D., Eskinja, N., Krstulja, M., Petranovic, D., Mendrila, I. & Kucic-Brusic, S. (2006) Importance of computed tomography and magnetic resonance in the diagnosis of brain tumors. [Croatian]. *Medicina*, 42: 98-102.
Not in PICO
- Galasko, D., Kwo-On-Yuen PF & Thal, L. (1988) Intracranial mass lesions associated with late-onset psychosis and depression. [Review] [95 refs]. *Psychiatric Clinics of North America*, 11: 151-166.
Narrative review
- Gardner, M., Hess, C. & Josephson, S. (2013) Utilization and outcomes of cranial computed tomography in a pediatric population. *Neurology*, 80.
Not in PICO

- Garon, B. R., Sierzant, T. & Ormiston, C. (186) Silent aspiration: results of 2,000 video fluoroscopic evaluations. *Journal of Neuroscience Nursing*, 41: 178-185.
Not in PICO
- George, J. L. & Marchal, J. C. (2010) [Orbital tumors in children: clinical examination, imaging, specific progression]. [French]. *Neuro-Chirurgie*, 56: 244-248.
Narrative review
- Giussani, C., Poliakov, A., Ferri, R. T., Plawner, L. L., Browd, S. R., Shaw, D. W. W., Filardi, T. Z., Hoepfner, C., Geyer, J. R., Olson, J. M., Douglas, J. G., Villavicencio, E. H., Ellenbogen, R. G. & Ojemann, J. G. (2010) DTI fiber tracking to differentiate demyelinating diseases from diffuse brain stem glioma. *Neuroimage*, 52: 217-223.
Not in PICO
- Goodman, J. (1988) Neck pain. *Primary Care - Clinics in Office Practice*, 15: 689-708.
Narrative review
- Grant, R. (2004) Overview: Brain tumour diagnosis and management/Royal College of Physicians guidelines. *Neurology in Practice*, 75: ii18-ii23.
Guideline
- Hadjivassiliou, M., Alder, S. J., Van Beek, E. J., Hanney, M. B., Lorenz, E., Rao, D. G., Sharrack, B. & Tindale, W. B. (2009) PET scan in clinically suspected paraneoplastic neurological syndromes: a 6-year prospective study in a regional neuroscience unit. *Acta Neurologica Scandinavica*, 119: 186-193.
Not in PICO
- Hamdan, A. & Mitchell, P. (2013) The two-week wait guideline for suspected CNS tumours: A decade analysis. *British Journal of Neurosurgery*, 27: 642-645.
Not in PICO
- Hamlin, J. A. & Hasso, A. N. (1994) Magnetic resonance imaging of the skull base. *Topics in Magnetic Resonance Imaging*, 6: 183-201.
Narrative review
- Hankey, G. J. & Stewart-Wynne, E. G. (1987) An analysis of cranial computerized tomography scanning in private neurological practice. *Clinical & Experimental Neurology*, 23: 187-190.
Not in PICO
- Harcourt, J. P., Vijaya-Sekaran, S., Loney, E. & Lennox, P. (1999) The incidence of symptoms consistent with cerebellopontine angle lesions in a general ENT out-patient clinic. *Journal of Laryngology & Otology*, 113: 518-522.
Not in PICO
- Harder, H. (1988) Audiovestibular tests in the diagnosis of cerebellopontine angle tumours. *Acta Oto-Laryngologica Supplement*, 452: 5-11.
Not in PICO
- Havlik, R., Kollar, A. & Lejska, M. (2000) Recommendation of a diagnostic algorithm in suspected tumours of the VIIIth cranial nerve. [Czech]. *Otorinolaryngologie a Foniatrie*, 49: 101-104.
Narrative review
- Heller, M., Wohrle, M., Jend, H. H., Hormann, K. & Helmke, K. (1983) [The value of CT in the diagnosis of tumours of the cerebello-pontine angle. Comparison of various radiological, clinical and otological examination]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 139: 48-55.
Not in PICO (very specific brain tumours)
- Hill, T. W., Nielsen, M. K. & Nepper-Rasmussen, J. (2013) Admission criteria to the Danish Brain Cancer Program are moderately associated with magnetic resonance imaging findings. *Danish Medical Journal*, 60: A4580.
Not in PICO
- Holveck, A., Grand, S., Boini, S., Kirchin, M., Le Bas, J. F., Dietemann, J. L., Bracard, S. & Kremer, S. (2010) Dynamic susceptibility contrast-enhanced MRI evaluation of cerebral intraventricular

- tumors: preliminary results. *Journal of Neuroradiology. Journal de Neuroradiologie*, 37: 269-275.
Not in PICO
- Hutter, A., Schwetye, K. E., Bierhals, A. J. & McKinstry, R. C. (2003) Brain neoplasms: epidemiology, diagnosis, and prospects for cost-effective imaging. [Review] [87 refs]. *Neuroimaging Clinics of North America*, 13: 237-250.
Narrative review
- Jadvar, H., Connolly, L. P., Fahey, F. H. & Shulkin, B. L. (2007) PET and PET/CT in pediatric oncology. [Review] [190 refs]. *Seminars in Nuclear Medicine*, 37: 316-331.
Not in PICO
- Jellema, K., Overbeeke, J. J., Teepen, H. L. & Visser, L. H. (2005) Time to diagnosis of intraspinal tumors. *European Journal of Neurology*, 12: 621-624.
Not in PICO
- Jeong, H. J., Chung, J. K., Kim, Y. K., Kim, C. Y., Kim, D. G., Jeong, J. M., Lee, D. S., Jung, H. W. & Lee, M. C. (2002) Usefulness of whole-body (18)F-FDG PET in patients with suspected metastatic brain tumors. *Journal of Nuclear Medicine*, 43: 1432-1437.
Not in PICO
- Kameda-Smith, M. M., White, M. A., St George, E. J. & Brown, J. I. (2013) Time to diagnosis of paediatric posterior fossa tumours: an 11-year West of Scotland experience 2000-2011. *British Journal of Neurosurgery*, 27: 364-369.
Not in PICO
- Kan, S. (2014) - [Imaging diagnosis of central nervous system malignant lymphoma]. [Japanese]. - *Brain & Nerve / Shinkei Kenkyu no Shinpo*, 66: 917-926.
Narrative review
- Kanou, Y., Arita, K., Kurisu, K., Tomohide, A. & Iida, K. (2002) Clinical implications of dynamic MRI for pituitary adenomas: Clinical and histologic analysis. *Journal of Clinical Neuroscience*, 9: 659-663.
Not in PICO
- Kellie, S. J. (1995) Brain tumours in children: Clinical features and management. *Modern Medicine of Australia*, 38: 42-53.
Narrative review
- Kernick, D. & Williams, S. (2011) Should GPs have direct access to neuroradiological investigation when adults present with headache? *British Journal of General Practice*, 61: 409-411.
Narrative review
- Kernick, D. P., Ahmed, F., Bahra, A., Dowson, A., Elrington, G., Fontebasso, M., Giffin, N. J., Lipscombe, S., MacGregor, A., Peatfield, R., Weatherby, S., Whitmarsh, T. & Goadsby, P. J. (2008) Imaging patients with suspected brain tumour: guidance for primary care. *British Journal of General Practice*, 58: 880-885.
Narrative review
- Kesser, B. W. (2010) Clinical thresholds for when to test for retrocochlear lesions: con. [Review] [15 refs]. *Archives of Otolaryngology -- Head & Neck Surgery*, 136: 727-729.
Narrative review
- Kim, D. W., Jung, S. A., Kim, C. G. & Park, S. A. (2010) The efficacy of dual time point F-18 FDG PET imaging for grading of brain tumors. *Clinical Nuclear Medicine*, 35: 400-403.
Not in PICO
- Kim, S. H., Chang, W. S., Kim, J. P., Minn, Y. K., Choi, J., Chang, J. W., Kim, T. S., Park, Y. G. & Chang, J. H. (2011) Peripheral compressing artifacts in brain tissue from stereotactic biopsy with sidecutting biopsy needle: A pitfall for adequate glioma grading. *Clinical Neuropathology*, 30: 328-332.
Not in PICO
- Knox, J., Chuni, C., Naqvi, Z., Crawford, P. & Waring, W. S. (2012) Presentations to an acute medical unit due to headache: A review of 306 consecutive cases. *Acute Medicine*, 11: 144-149.
Not in PICO

- Ko, M. W., Turkeltaub, P. E., Lee, E. B., Gonatas, N. K., Volpe, N. J., Moster, M. L. & Galetta, S. L. (2009) Primary diffuse leptomeningeal gliomatosis mimicking a chronic inflammatory meningitis. *Journal of the Neurological Sciences*, 278: 127-131.
Narrative review
- Kovanlikaya, A., Karabay, N., Cakmakci, H., Uysal, K., Olgun, N. & Ergor, G. (2003) Surveillance imaging and cost effectivity in pediatric brain tumors. *European Journal of Radiology*, 47: 188-192.
Not in PICO
- Kwan, T. L., Tang, K. W., Pak, K. K. & Cheung, J. Y. (2004) Screening for vestibular schwannoma by magnetic resonance imaging: analysis of 1821 patients. *Hong Kong Medical Journal*, 10: 38-43.
Not in PICO
- Lafosse, P. (1983) [Use of computer tomography in the diagnosis of syndromes of the cerebellopontine angle]. [French]. *Annales d'Oto-Laryngologie et de Chirurgie Cervico-Faciale*, 100: 217-221.
Not in PICO
- Lafosse, P. (1983) Diagnostic value of computed tomography imaging in cerebellopontine angle syndrome. [French]. *Annales d'Oto-Laryngologie et de Chirurgie Cervico-Faciale*, 100: 217-221.
Not in PICO
- Lambrinides, K. & Reichert, M. (111) MR imaging of pineoblastomas. *Radiologic Technology*, 66: 106-110.
Narrative review
- Lee, J.-S., Park, Y.-S., Kwon, J.-T., Nam, T.-K., Lee, T.-J. & Kim, J.-K. (2011) Radiological apoplexy and its correlation with acute clinical presentation, angiogenesis and tumor microvascular density in pituitary adenomas. *Journal of Korean Neurosurgical Society*, 50: 281-287.
Not in PICO
- Li, H.-H., Sun, W.-G., Liu, H. & Fan, G.-G. (2012) Value of half-dose contrast-enhanced three dimensional fluid-attenuated inversion recovery sequence in diagnosis of brain metastasis tumors. [Chinese]. *Chinese Journal of Interventional Imaging and Therapy*, 9: 593-596.
Not in PICO
- Lis, E., Bilsky, M. H., Pisinski, L., Boland, P., Healey, J. H., O'malley, B. & Krol, G. (2004) Percutaneous CT-guided biopsy of osseous lesion of the spine in patients with known or suspected malignancy. *AJNR*, American: 1583-1588.
Not in PICO
- Lovrencic-Huzjan, A., Jadrijevic-Tomas, A., Samovojska, D., Cindric, I., Bencina, B., Bedekovic, M. R. & Kes, V. B. (2013) One year study of vertigo in the neurological emergency room. *Acta Clinica Croatica, Supplement*, 52: 73.
Not in PICO
- Maki, J. L., Marr, B. P. & Abramson, D. H. (2009) Diagnosis of retinoblastoma: how good are referring physicians? *Ophthalmic Genetics*, 30: 199-205.
Not in PICO
- Manaka, S. (1988) [Diagnosis of early stage of brain tumors]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1285-1294.
Narrative review
- Martin-Berra, J. C., Alvaro, L. C., Aranzabal, I., Freijo, M. M., Huete, B. & Cortina, C. (2002) [Non tumoural cerebral biopsies: an analysis of 50 cases]. [Spanish]. *Revista de Neurologia*, 34: 306-309.
Not in PICO
- Matsuhisa, A., Toriihara, A., Kubota, K., Makino, T., Mizusawa, H. & Shibuya, H. (2012) Utility of F-18 FDG PET/CT in screening for paraneoplastic neurological syndromes. *Clinical Nuclear Medicine*, 37: 39-43.
Not in PICO

- Mayr, N. A., Yuh, W. T., Muhonen, M. G., Fisher, D. J., Nguyen, H. D., Ehrhardt, J. C., Wen, B. C., Doornbos, J. F. & Hussey, D. H. (1994) Cost-effectiveness of high-dose MR contrast studies in the evaluation of brain metastases (Structured abstract). *American Journal of Neuroradiology*, 15: 1053-1061.
Not in PICO
- McFadyen, M. B. (2004) First seizures, the epilepsies and other paroxysmal disorders prospective audit of a first seizure clinic. *Scottish Medical Journal*, 49: 126-130.
Not in PICO
- McGann, G. M. & Platts, A. (1991) Computed tomography of cranial metastatic malignant melanoma: features, early detection and unusual cases. *British Journal of Radiology*, 64: 310-313.
Not in PICO
- Medina, L. S., Kuntz, K. M. & Pomeroy, S. (2001) Children with headache suspected of having a brain tumor: a cost-effectiveness analysis of diagnostic strategies. *Pediatrics*, 108: 255-263.
Not in PICO
- Melzer, H. I., Coppenrath, E., Schmid, I., Albert, M. H., von, S. D., Tudball, C., Bartenstein, P. & Pfluger, T. (2011) 123I-MIBG scintigraphy/SPECT versus 18F-FDG PET in paediatric neuroblastoma. *European Journal of Nuclear Medicine & Molecular Imaging*, 38: 1648-1658.
Not in PICO
- Mentzel, H. J., Kentouche, K., Sauner, D., Fleischmann, C., Vogt, S., Gottschild, D., Zintl, F. & Kaiser, W. A. (2004) Comparison of whole-body STIR-MRI and 99mTc-methylene-diphosphonate scintigraphy in children with suspected multifocal bone lesions. *European Radiology*, 14: 2297-2302.
Not in PICO
- Mertens, K., Bolcaen, J., Ham, H., Deblaere, K., Van den Broecke, C., Boterberg, T., De, V. F. & Goethals, I. (2012) The optimal timing for imaging brain tumours and other brain lesions with 18F-labelled fluoromethylcholine: a dynamic positron emission tomography study. *Nuclear Medicine Communications*, 33: 954-959.
Not in PICO
- Meyer, J. S., Harty, M. P. & Khademian, Z. (2002) Imaging of neuroblastoma and Wilms' tumor. *Magnetic Resonance Imaging Clinics of North America*, 10: 275-302.
Narrative review
- Miabi, Z. (2011) Metastatic brain tumors: a retrospective review in East Azarbyjan (Tabriz). *Acta Medica Iranica*, 49: 115-117.
Not in PICO
- Milstein, J. M., Cohen, M. E. & Sinks, L. F. (1985) The influence and reliability of neurologic assessment and Karnofsky performance score on prognosis. *Cancer*, 56: Suppl-6.
Narrative review
- Mizuno, M., Yoshioka, K., Ito, K., Takegoshi, H. & Sasaki, T. (1995) The changing profile of acoustic neuromas in recent years. [Japanese]. *Equilibrium Research*, 54: 450-457.
Not in PICO
- Moffat, D. A., Jones, S. E., Mahendran, S., Humphriss, R. & Baguley, D. M. (2004) Referral patterns in vestibular schwannomas --10 years on. *Clinical Otolaryngology & Allied Sciences*, 29: 515-517.
Not in PICO
- Molassiotis, A., Wilson, B., Brunton, L. & Chandler, C. Mapping patients' experiences from initial change in health to cancer diagnosis: A qualitative exploration of patient and system factors mediating this process. [References]. *European Journal of Cancer Care* 19[1], 98-109. 2010.
Not in PICO
- Muroff, L. R. & Runge, V. M. (1995) The use of MR contrast in neoplastic disease of the brain. [Review] [70 refs]. *Topics in Magnetic Resonance Imaging*, 7: 137-157.
Narrative review

- Natalwala, A., Bharkhada, V., Noel, G. & Cruickshank, G. (2011) Comparison of time taken from initial presentation to histological diagnosis of Glioblastoma Multiforme (GBM) in Birmingham, United Kingdom and Strasbourg, France. *Clinical Neurology & Neurosurgery*, 113: 358-361.
Not in PICO
- Nilsson, J. & Bjorkengren, U. (1996) [A study of referrals: what is the outcome of cranial computer tomography? Medical and economic benefits!]. [Swedish]. *Lakartidningen*, 93: 3365-3368.
Not in PICO
- Nishimoto, A. & Furuta, T. (1988) [Early diagnosis of metastatic brain tumor]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1484-1490.
Narrative review
- Nishiyama, Y., Yamamoto, Y., Fukunaga, K., Satoh, K., Kunishio, K. & Ohkawa, M. (2001) Comparison of 99Tcm-MIBI with 201Tl chloride SPET in patients with malignant brain tumours. *Nuclear Medicine Communications*, 22: 631-639.
Not in PICO
- Papanikolaou, V., Khan, M. H. & Keogh, I. J. (2010) Incidental findings on MRI scans of patients presenting with audiovestibular symptoms. *BMC Ear, Nose and Throat Disorders*, 10.
Not in PICO
- Parker, A., Robinson, R. O. & Bullock, P. (1996) Difficulties in diagnosing intrinsic spinal cord tumours. *Archives of Disease in Childhood*, 75: 204-207.
Not in PICO
- Pascual-Castroviejo, I., Villarejo, F., Perez-Higueras, A., Morales, C. & Pascual-Pascual, S. I. (1983) Childhood choroid plexus neoplasms. A study of 14 cases less than 2 years old. *European Journal of Pediatrics*, 140: 51-56.
Not in PICO
- Patel, R. R., Subramaniam, R. M., Mandrekar, J. N., Hammack, J. E., Lowe, V. J. & Jett, J. R. (2008) Occult malignancy in patients with suspected paraneoplastic neurologic syndromes: value of positron emission tomography in diagnosis. *Mayo Clinic Proceedings*, 83: 917-922.
Not in PICO
- Paul, S. P., Debono, R. & Walker, D. (2013) Clinical update: Recognising brain tumours early in children. *Community Practitioner*, 86: 42-45.
Narrative review
- Pauleit, D., Floeth, F., Tellmann, L., Hamacher, K., Hautzel, H., Muller, H. W., Coenen, H. H. & Langen, K. J. (2004) Comparison of O-(2-18F-fluoroethyl)-L-tyrosine PET and 3-123I-iodo-alpha-methyl-L-tyrosine SPECT in brain tumors. *Journal of Nuclear Medicine*, 45: 374-381.
Not in PICO
- Pech, A., Cannoni, M., Sarrat, P., Bernard, P., Thomassin, J. M., Zanaret, M., Triglia, J. M. & Giovanni, A. (1988) Contribution of nuclear magnetic resonance in the neuro-otologic diagnosis of acoustic neuroma. Screening and evaluation of its extension. [French]. *Annales d'oto-laryngologie et de chirurgie cervico faciale : bulletin de la Societe d'oto-laryngologie des hopitaux de Paris*, 105: 39-45.
Not in PICO
- Peponis, N. T. (1986) Diagnosis of acoustic neuroma. *Journal of the American Osteopathic Association*, 86: 369-378.
Narrative review
- Petiot, P., Herbin, P., Vighetto, A. & Aimard, G. (1995) False negative results by X scanners in intracranial tumors in adults. [French]. *Revue Neurologique*, 151: 734-738.
Not in PICO
- Pettet, G., Renowden, S. & Mortimer, A. (2012) Use of MRI in the investigation of suspected acoustic neuroma. A retrospective review of 1000 scans. *Clinical Radiology*, 67: S25.
Not in PICO

- Plotkin, M., Blechschmidt, C., Auf, G., Nyuyki, F., Geworski, L., Denecke, T., Brenner, W. & Stockhammer, F. (2010) Comparison of F-18 FET-PET with F-18 FDG-PET for biopsy planning of non-contrast-enhancing gliomas. *European Radiology*, 20: 2496-2502.
Not in PICO
- Porto, L., Kieslich, M., Bartels, M., Schwabe, D., Zanella, F. E. & Du, M. R. (2010) Leptomeningeal metastases in pediatrics: magnetic resonance image manifestations and correlation with cerebral spinal fluid cytology. *Pediatrics International*, 52: 541-546.
Not in PICO
- Powell, H. R. & Choa, D. I. (2010) Should all patients referred for magnetic resonance imaging scans of their internal auditory meatus be followed up in ENT clinics? *European Archives of Oto-Rhino-Laryngology*, 267: 1361-1366.
Not in PICO
- Prashad, P. S., Marcus, C. L., Brown, L. W., Dlugos, D. J., Feygin, T., Harding, B. N., Heuer, G. G. & Mason, T. B. (2013) Brain tumor presenting as somnambulism in an adolescent. *Pediatric Neurology*, 49: 209-212.
Not in PICO
- Purcell, C., Qassim, A., Alcutt, D., Sattar, T., Crimmins, D., Nicholson, A. J. & Caird, J. (2011) Can we diagnose Brain Tumours in Children Earlier? An Irish Audit. *British Journal of Neurosurgery*, 25: 565-566.
Not in PICO
- Raber, E., Dort, J. C., Seveck, R. & Winkelaar, R. (1997) Asymmetric hearing loss: toward cost-effective diagnosis. *Journal of Otolaryngology*, 26: 88-91.
Not in PICO
- Ramelli, G. P., von der, W. N., Stanga, Z., Mullis, P. E. & Buergi, U. (1998) Suprasellar germinomas in childhood and adolescence: diagnostic pitfalls. *Journal of Pediatric Endocrinology*, 11: 693-697.
Not in PICO
- Rao, P. (2008) Role of MRI in paediatric neurooncology. [Review] [30 refs]. *European Journal of Radiology*, 68: 259-270.
Narrative review
- Reulecke, B. C., Erker, C. G., Fiedler, B. J., Niederstadt, T. U. & Kurlemann, G. (2008) Brain tumors in children: initial symptoms and their influence on the time span between symptom onset and diagnosis. *Journal of Child Neurology*, 23: 178-183.
Not in PICO
- Rizzo, D., Freneaux, P., Brisse, H., Louvrier, C., Lequin, D., Nicolas, A., Ranchere, D., Verkarre, V., Jouvret, A., Dufour, C., Edan, C., Stephan, J. L., Orbach, D., Sarnacki, S., Pierron, G., Parfait, B., Peuchmaur, M., Delattre, O. & Bourdeaut, F. (2012) SMARCB1 deficiency in tumors from the peripheral nervous system: a link between schwannomas and rhabdoid tumors? *American Journal of Surgical Pathology*, 36: 964-972.
Not in PICO
- Ruckenstein, M. J. (1995) A practical approach to dizziness questions to bring vertigo and other causes into focus. *Postgraduate Medicine*, 97: 70-78+81.
Narrative review
- Saga, T., Kawashima, H., Araki, N., Takahashi, J. A., Nakashima, Y., Higashi, T., Oya, N., Mukai, T., Hojo, M., Hashimoto, N., Manabe, T., Hiraoka, M. & Togashi, K. (2006) Evaluation of primary brain tumors with FLT-PET: usefulness and limitations. *Clinical Nuclear Medicine*, 31: 774-780.
Not in PICO
- Sato, Y. (1992) Pediatric primary brain tumors. [Review] [37 refs]. *Topics in Magnetic Resonance Imaging*, 4: 64-77.
Narrative review

- Savitz, M. H. (1992) Free-hand CT-guided needle for biopsy and drainage of intracerebral lesions. Ten years experience. *International Surgery*, 77: 211-215.
Not in PICO
- Scarabino, T., Giannatempo, G. M., Nemore, F., Popolizio, T. & Stranieri, A. (2005) Supratentorial low-grade gliomas. *Neuroradiology*. [Review] [14 refs]. *Journal of Neurosurgical Sciences*, 49: 73-76.
Narrative review
- Schuknecht, B., Huber, P., Buller, B. & Nadjmi, M. (1992) Spinal leptomeningeal neoplastic disease. Evaluation by MR, myelography and CT myelography. *European Neurology*, 32: 11-16.
Not in PICO
- Seidl, Z., Vymazal, J., Mechl, M., Goyal, M., Herman, M., Colosimo, C., Pasowicz, M., Yeung, R., Paraniak-Gieszczyk, B., Yemen, B., Anzalone, N., Citterio, A., Schneider, G., Bastianello, S. & Ruscalleda, J. (2012) Does higher gadolinium concentration play a role in the morphologic assessment of brain tumors? Results of a multicenter intraindividual crossover comparison of gadobutrol versus gadobenate dimeglumine (the MERIT Study). *Ajnr: American Journal of Neuroradiology*, 33: 1050-1058.
Not in PICO
- Sethi, R. V., Marino, R., Niemierko, A., Tarbell, N. J., Yock, T. I. & MacDonald, S. M. (2013) Delayed diagnosis in children with intracranial germ cell tumors. *Journal of Pediatrics*, 163: 1448-1453.
Not in PICO
- Shaffer, K. A., Houghton, V. M. & Wilson, C. R. (1980) High resolution computed tomography of the temporal bone. *Radiology*, 134: 409-414.
Not in PICO
- Shay, V., Fattal-Valevski, A., Beni-Adani, L. & Constantini, S. (2012) Diagnostic delay of pediatric brain tumors in Israel: A retrospective risk factor analysis. *Child's Nervous System*, 28: 93-100.
Not in PICO
- Sheen, V., Tucker, M. A., Abramson, D. H., Seddon, J. M. & Kleinerman, R. A. (2008) Cancer screening practices of adult survivors of retinoblastoma at risk of second cancers. *Cancer*, 113: 434-441.
Not in PICO
- Sighvatsson, V., Ericson, K. & Tomasson, H. (1998) Optimising contrast-enhanced cranial CT for detection of brain metastases. *Acta Radiologica*, 39: 718-722.
Not in PICO
- Skinner, S. A. (1988) Early diagnosis of brain tumor. *Postgraduate Medicine*, 83: 117-124.
Narrative review
- Snelling, J. D., Krywawych, M., Majithia, A. & Harcourt, J. P. (2008) The compliance, true positive and false negative rates of the Charing Cross protocol for magnetic resonance imaging screening for cerebellopontine angle lesions. *Journal of Laryngology & Otology*, 122: 255-258.
Not in PICO
- Sotaniemi, K. A., Rantala, M., Pyhtinen, J. & Myllyla, V. V. (1991) Clinical and CT correlates in the diagnosis of intracranial tumours. *Journal of Neurology Neurosurgery and Psychiatry*, 54: 645-647.
Not in PICO
- Steiger, J. R. (2005) Audiologic referral criteria: Sample clinic guidelines. *Hearing Journal*, 58: 38-42.
Not in PICO
- Straathof, C. S., de Bruin, H. G., Dippel, D. W. & Vecht, C. J. (1999) The diagnostic accuracy of magnetic resonance imaging and cerebrospinal fluid cytology in leptomeningeal metastasis. *Journal of Neurology*, 246: 810-814.
Not in PICO
- Struffert, T., Grunwald, I., Roth, C. & Reith, W. (1988) [Spinal intradural tumors]. [Review] [6 refs] [German]. *Radiologe*, 44: 1211-1227.
Narrative review

- Tadmor, R., Harwood-Nash, D. C. F. & Savoiaro, M. (1980) Brain tumors in the first two years of life: CT diagnosis. *American Journal of Neuroradiology*, 1: 411-417.
Not in PICO
- Thakkar, S. D., Feigen, U. & Mautner, V. F. (1999) Spinal tumours in neurofibromatosis type 1: an MRI study of frequency, multiplicity and variety. *Neuroradiology*, 41: 625-629.
Not in PICO
- Thomas, L. & Honnorat, J. (2014) [Brain metastases: epidemiology, diagnosis and imaging]. [French]. *La Revue du praticien*, 64: 668-673.
Narrative review
- Thorsteinsson, R., Sorensen, M., Jensen, T. L., Bernhardtson, T. M., Gjerris, F., Carstensen, H., Schmiegelow, K. & Raaschou-Nielsen, O. (2005) [Central nervous system tumours in children. An evaluation of the completeness and validity of the Cancer Registry]. [Danish]. *Ugeskrift for Laeger*, 167: 3782-3785.
Not in PICO
- Thorsteinsson, R., Sorensen, M., Jensen, T. L., Bernhardtson, T. M., Gjerris, F., Carstensen, H., Schmiegelow, K. & Raaschou-Nielsen, O. (2005) Completeness and validity of registration of childhood CNS tumours in the Danish Cancer Registry. [Danish]. *Ugeskrift for Laeger*, 167: 3782-3785.
Not in PICO
- Tyutin, L. A., Zeidlits, V. N., Pozdnyakova, O. F. & Rokhlin, G. D. (1993) Brain tumors in MR imaging. [Russian]. *Vestnik Rentgenologii i Radiologii*, 68: 10-13.
Not in PICO
- van der Sande, J. J., Kroger, R. & Boogerd, W. (1990) Multiple spinal epidural metastases; an unexpectedly frequent finding. *Journal of Neurology, Neurosurgery & Psychiatry*, 53: 1001-1003.
Not in PICO
- Vander, B. T., Asenbaum, S., Bartenstein, P., Halldin, C., Kapucu, O., Van, L. K., Varrone, A., Tatsch, K. & European Association of Nuclear Medicine (EANM) (2006) EANM procedure guidelines for brain tumour imaging using labelled amino acid analogues. *European Journal of Nuclear Medicine & Molecular Imaging*, 33: 1374-1380.
Not in PICO; guideline
- Vandervelde, C. & Connor, S. E. (2009) Diagnostic yield of MRI for audiovestibular dysfunction using contemporary referral criteria: correlation with presenting symptoms and impact on clinical management. *Clinical Radiology*, 64: 156-163.
Not in PICO
- Warbey, V. S., Ferner, R. E., Dunn, J. T., Calonje, E. & O'Doherty, M. J. (2009) [18F]FDG PET/CT in the diagnosis of malignant peripheral nerve sheath tumours in neurofibromatosis type-1. *European journal of nuclear medicine and molecular imaging*, 36: 751-757.
Not in PICO
- Weckesser, M., Langen, K. J., Rickert, C. H., Kloska, S., Straeter, R., Hamacher, K., Kurlemann, G., Wassmann, H., Coenen, H. H. & Schober, O. (2005) O-(2-[18F]fluoroethyl)-L-tyrosine PET in the clinical evaluation of primary brain tumours. *European Journal of Nuclear Medicine & Molecular Imaging*, 32: 422-429.
Not in PICO
- Weissman, D. E., Gilbert, M., Wang, H. & Grossman, S. A. (1985) The use of computed tomography of the spine to identify patients at high risk for epidural metastases. *Journal of Clinical Oncology*, 3: 1541-1544.
Not in PICO
- White, J. R., Carlson, M. L., Van Gompel, J. J., Neff, B. A., Driscoll, C. L., Lane, J. I. & Link, M. J. (2013) Lipomas of the cerebellopontine angle and internal auditory canal: Primum Non Nocere. *Laryngoscope*, 123: 1531-1536.
Not in PICO

- Wills, A. (2011) Direct access to brain mr imaging for headache in primary care; Better than an aspirin? *Journal of Neurology, Neurosurgery and Psychiatry*, 82: 1-2.
Not in PICO
- Wilne, S., Koller, K., Collier, J., Kennedy, C., Grundy, R. & Walker, D. (2010) The diagnosis of brain tumours in children: a guideline to assist healthcare professionals in the assessment of children who may have a brain tumour. [Review] [32 refs]. *Archives of Disease in Childhood*, 95: 534-539.
Guideline
- Wilson, M., Cummins, C. L., Macpherson, L., Sun, Y., Natarajan, K., Grundy, R. G., Arvanitis, T. N., Kauppinen, R. A. & Peet, A. C. (2013) Magnetic resonance spectroscopy metabolite profiles predict survival in paediatric brain tumours. *European Journal of Cancer*, 49: 457-464.
Not in PICO
- Wirix, M., Parys-Vanginderdeuren, R., Casteels, I. & Uyttebroeck, A. (2000) Delayed diagnosis of retinoblastoma. *Bulletin de la Societe Belge d Ophtalmologie*.(278):37-41, 2000., 37-41.
Not in PICO
- Wong, B. Y. & Capper, R. (2012) Incidence of vestibular schwannoma and incidental findings on the magnetic resonance imaging and computed tomography scans of patients from a direct referral audiology clinic. *Journal of Laryngology & Otology*, 126: 658-662.
Not in PICO
- Wong, J. J., Huda, S. & Wieshmann, U. C. (2012) An unusual presentation of an epidermoid brain tumour: a tale of two specialties. *BMJ Case Reports*, 2012, 2012.
Not in PICO
- Wong, M. L. & Brackmann, D. E. (1981) Computed cranial tomography in acoustic tumor diagnosis. *JAMA*, 245: 2497-2500.
Not in PICO
- Xiangsong, Z., Xinjian, W., Yong, Z. & Weian, C. (2008) ¹³N-NH₃: a selective contrast-enhancing tracer for brain tumor. *Nuclear Medicine Communications*, 29: 1052-1058.
Not in PICO
- Xie, C., Ahmed, A. & Banerjee, A. (2013) A comparison of primary care access to non-trauma computed tomography (CT) and magnetic resonance imaging (MRI) of the brain with hospital clinician referrals. *Clinical Radiology*, 68: S8-S9.
Not in PICO
- Yagishita, A., Kanzaki, J. & Shiga, H. (1983) Diagnosis of small acoustic tumors by air CT cisternography. [Japanese]. *Neurologia Medico-Chirurgica*, 23: 441-446.
Not in PICO
- Yamamoto, Y., Nishiyama, Y., Kimura, N., Kameyama, R., Kawai, N., Hatakeyama, T., Kaji, M. & Ohkawa, M. (2008) ¹¹C-Acetate PET in the evaluation of brain glioma: Comparison with ¹¹C-Methionine and ¹⁸F-FDG-PET. *Molecular Imaging and Biology*, 10: 281-287.
Not in PICO
- You, J. J., Gladstone, J., Symons, S., Rotstein, D., Laupacis, A. & Bell, C. M. (2011) Patterns of care and outcomes after computed tomography scans for headache. *American Journal of Medicine*, 124: 58-63.
Not in PICO
- Zhou, C. W., Zhang, H. M. & Ouyang, H. (2004) [Intracranial metastasis of malignant tumors: clinical characteristics and MR imaging features]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]*, 26: 554-557.
Not in PICO
- Zhou, H., Chen, M. & Zhao, D. (2013) Longitudinal MRI evaluation of intracranial development and vascular characteristics of breast cancer brain metastases in a mouse model. *PLoS ONE [Electronic Resource]*, 8: e62238.
Not in PICO

Zielinska-Bliniewska, H., Michalska, J., Pietkiewicz, P., Milonski, J., Kusmierczyk, K. & Olszewski, J. (2011) Posterior cranial fossa tumours as a cause of sudden hearing deterioration and/or vertigo. [Polish]. *Otolaryngologia Polska*, 65: 98-101.

Not in PICO

Zyss, T. & Goscinski, I. (1996) [Can psychiatric examination be useful in early diagnosis of intracranial expansion processes?]. [Polish]. *Psychiatria Polska*, 30: 151-158.

Not in PICO

HAEMATOLOGICAL CANCERS

LEUKEMIA

Review question:

What is the risk of leukaemia in adults and children presenting in primary care with symptom(s)?

Results

Literature search

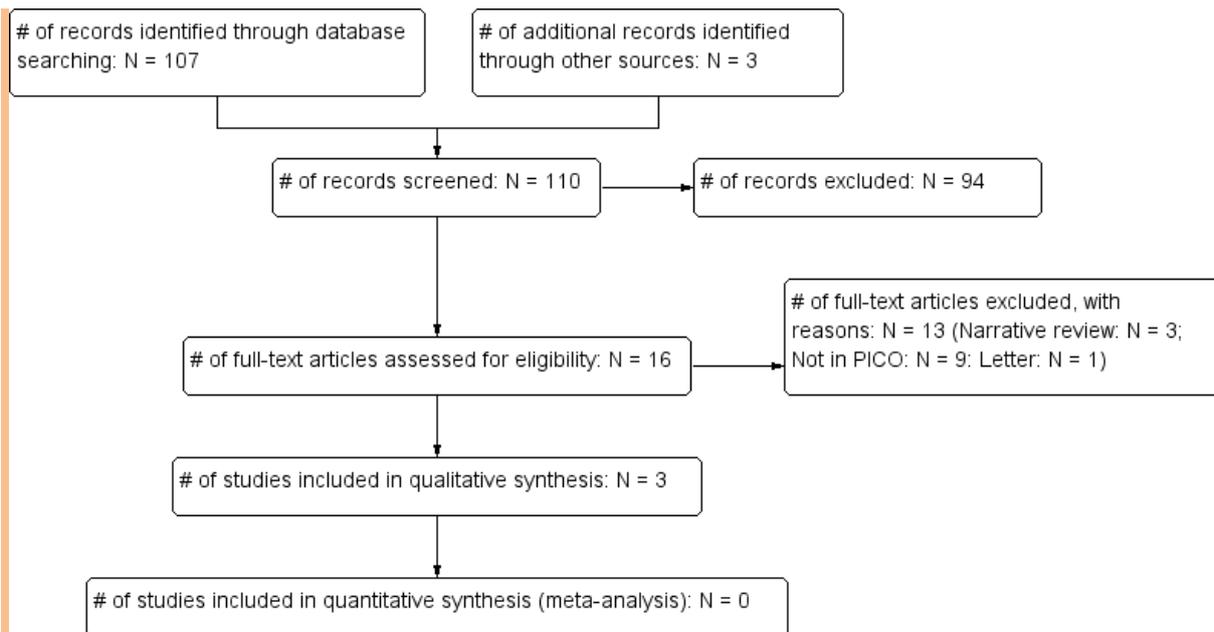
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	1689	42	11/03/2013
<i>Premedline</i>	All-2012	33	1	11/03/2013
<i>Embase</i>	All-2012	3598	57	13/03/2013
<i>Cochrane Library</i>	All-2012	427	0	13/03/2013
<i>Psychinfo</i>	All-2012	12	0	11/03/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	648	10	18/03/2013
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search

Total References retrieved (after de-duplication): 98

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	3/2013-18/08/2014	30	3	18/08/2014
<i>Premedline</i>	3/2013-18/08/2014	85	7	18/08/2014
<i>Embase</i>	3/2013-18/08/2014	195	4	18/08/2014
<i>Cochrane Library</i>	3/2013-18/08/2014	88	0	18/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	3/2013-18/08/2014	135	3	18/08/2014

Total References retrieved (after de-duplication): 9



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included studies in the figure below. One main issue to note is that one study employed a case-control design which has been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors may have gone some way in counteracting this influence. Another potential threat to the applicability of the findings concerns the fact that the second study employed a patient sample which may not be directly applicable to the current question.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Dommett (2013a,b)	⊖	+	+	+	+	+	+
Hallsisey (1990)	+	+	+	+	?	+	+

⊖ High ? Unclear + Low

Study results

Table 1: Leukaemia: Positive predictive values for leukaemia/lymphoma childhood cancer

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)
Dommett (2013a)	Bruising 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.53 (0.07-3.91)
Dommett (2013a)	Pallor 0-3 months before	All included leukemia/	0.43 (0.06-3.15)

	diagnosis	lymphoma patients and controls aged 0-14 years	
Dommett (2013a)	Lump mass swelling head and neck 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.35 (0.05-2.65)
Dommett (2013a)	Fatigue 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.07 (0.03-0.15)
Dommett (2013a)	Lymphadenopathy 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.06 (0.04-0.11)
Dommett (2013a)	Lump mass swelling below neck excluding abdomen 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.05 (0.02-0.13)
Dommett (2013a)	Bleeding 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.03 (0.01-0.08)
Dommett (2013a)	Pain 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.03 (0.01-0.06)
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.02 (0.01-0.03)
Dommett (2013a)	Fever 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01 (0.01-0.01)
Dommett (2013a)	Abdominal pain 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01 (0-0.01)
Dommett (2013a)	≥ 3 consultations	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01 (0.01-0.01)

The positive predictive values are calculated using Bayesian statistics.

Table 2: Leukaemia: Positive predictive values for teenage and young adult, and adult leukaemia

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)
Dommett (2013b)	Bruising	All leukaemia patients and controls aged 15-24 years	0.0117 (0.004-0.0343) Cases: 9/143

			Controls: 5/1799
Dommett (2013b)	Fatigue	All leukaemia patients and controls aged 15-24 years	0.0121 (0.0052-0.0282) Cases: 15/143 Controls: 8/1799
Dommett (2013b)	Lymphadenopathy	All leukaemia patients and controls aged 15-24 years	0.0151 (0.004-0.0578) Cases: 7/143 Controls: 3/1799
Dommett (2013b)	≥ 3 consultations	All leukaemia patients and controls aged 15-24 years	0.0038 (0.003-0.0048) Cases: 74/143 Controls: 125/1799
Hallissey (1990)	Dyspepsia	All patients	0.04 (0.002-0.3) 1/2585

The positive predictive values are calculated using Bayesian statistics for Dommett (2013b).

Evidence statement(s):

The positive predictive values of having leukaemia/lymphoma childhood cancer ranged from 0.01% (for fever and abdominal pain) to 0.53% (for bruising) for patients aged 0-14 years old, the positive predictive values of having young adulthood leukaemia ranged from 0.0117% (for bruising) to 0.0151% (for lymphadenopathy) for patients aged 15-24 years (1 study, N = 30855), and the positive predictive value of having adulthood leukaemia was 0.04% (for dyspepsia) for patients aged > 40 years (1 study, N = 2585) . Both studies were associated with 1 bias/applicability concern (see also Tables 1-2).

Evidence tables

Dommett (2013a,b)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based nested case-control study using data from the General Practice Research Database (GPRD)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	Cases: 1267 children; aged 0-4 years: N = 436; aged 5-14 years: N = 831; 703 males/564 females. Cancer type: Leukemia: N = 368; brain: N = 270; lymphoma: N = 142; bone: N = 107; soft tissue sarcoma: N = 91; renal: N = 82; neuroblastoma: N = 75;

	<p>other ICD codes: N = 132.</p> <p>1064 teenagers and young adults (TYA): 15-24 years: Gender not reported. Cancer type: Leukemia: N = 143; brain: N = 154; lymphoma: N = 270; bone: N = 96; soft tissue sarcoma: N = 100; other ICD codes: N = 301 (including testis: N = 60; skin: N = 49; ovary: N = 20 and thyroid: N = 17).</p> <p><u>Controls:</u></p> <p>15318 children; aged 0-4 years: N = 4802; aged 5-14 years: N = 10516; 8461 males/6857 females.</p> <p>13206 TYA. Gender not reported</p> <p><u>Inclusion criteria:</u></p> <p>The sample comprised all children and TYU aged 0–24 years, inclusive, drawn from all general practices contributing research-standard data to the GPRD between 1 January 1988 and 31 December 2010. To be included, the practices had to have been contributing research-standard data for a minimum of 1 year before each child’s date of cancer diagnosis or the index date (see below) for matched controls.</p> <p>Cases: Patients diagnosed with the following cancers: leukaemia, lymphoma, neuroblastoma, soft tissue sarcoma, hepatic, renal, bone and central nervous system tumours, using pre-defined medical codes used in the GPRD. The date of diagnosis for cases was defined as the date of pathological diagnosis, but if this was unavailable, the date of the first cancer code entered in the GPRD was used.</p> <p>Controls: Up to 13 controls (children with no diagnosis of cancer at any time) were selected per case, using a computer-generated random sequence, matched on age (within 1 year), sex and practice, and had to be currently registered on the date of diagnosis of their matched case (the index date).</p> <p><u>Exclusion criteria:</u> None listed</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
<u>A. Risk of bias</u>	
Index test	The GPRD uses just over 100 000 medical codes to encompass all primary care events, including both symptoms and diagnoses. From this list, libraries of codes were assembled representing individual alert symptoms derived from the NICE referral guidelines for suspected cancer in children. <i>No more information reported.</i>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
<u>A. risk of bias</u>	

Reference standard(s)	Cancer diagnosis in the UK's General Practice Research Database.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
<u>B. Concerns regarding applicability</u>		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
<u>A. risk of bias</u>		
Flow and timing	All patients appear to be accounted for.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	This study is published in three papers.	
Hallissey (1990)		
PATIENT SELECTION		
<u>A. risk of bias</u>		
Patient sampling	Propective consecutive patient series from a group of 10 general practices in England.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
<u>B. Concerns regarding applicability</u>		
Patient characteristics and setting	<p>N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia.</p> <p><u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia</p> <p><u>Exclusion criteria:</u> None listed.</p> <p><u>Clinical setting:</u> Primary care, England.</p>	
Are there concerns that the included patients and setting do not match the review question?	Unclear concern	
INDEX TEST		
<u>A. Risk of bias</u>		
Index test	Dyspepsia of any degree	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	

Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	2659 patients were seen and 2585 attended for investigation
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), cirrinomatosis of unknown primary (7).

References

Included studies

Dommett, R. M., Redaniel, T., Stevens, M. C. G., Martin, R. M., and Hamilton, W. Risk of childhood cancer with symptoms in primary care: A population-based case-control study. *British Journal of General Practice*; DOI:10.3399/bjgp13X660742. 2013a.

Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of cancer in teenagers and young adults in primary care: A population-based nested case-control study. *British Journal of Cancer* 2329-2333. 2013b.

Hallissey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.

Excluded studies (with excl reason)

- (1967) Role of the dentist in detection and prevention of systemic diseases. *Journal of the American Dental Association (1939)*, 75: 1291-1292.
Not in PICO
- Abel, G. A., Friese, C. R., Magazu, L. S., Richardson, L. C., Fernandez, M. E., De Zengotita, J. J. & Earle, C. C. (2008) Delays in referral and diagnosis for chronic hematologic malignancies: A literature review. *Leukemia & Lymphoma*, 49: 1352-1359.
Not in PICO
- Abel, G. A., Friese, C. R., Neville, B. A., Wilson, K. M., Hastings, B. T., Earle, C. C., Keating, N. L., Richardson, L. C., Abel, G. A., Friese, C. R., Neville, B. A., Wilson, K. M., Hastings, B. T., Earle, C. C., Keating, N. L. & Richardson, L. C. (2012) Referrals for suspected hematologic malignancy: a survey of primary care physicians. *American Journal of Hematology*, 87: 634-636.
Not in PICO
- Adekha, S. & Chadha, T. (2013) Bernard Soulier Syndrome associated with acute myeloid leukemia. *Indian Journal of Medical Sciences*, 67: 145-147.
Not in PICO
- Ahrensberg, J. M., Olesen, F., Hansen, R. P., Schroder, H. & Vedsted, P. (2013) Childhood cancer and factors related to prolonged diagnostic intervals: a Danish population-based study. *British Journal of Cancer*, epub ahead of print.
Not in PICO
- AUDO-GIANOTTI, G. B. (1963) EARLY DIAGNOSIS OF MALIGNANT BLOOD DISEASES. *Il Cancro*, 16: 1963.
Not in PICO
- Ayremlou, P. (2012) Demographic and prognostic factors of 455 patients with acute leukemia admitted to two referral hospitals in Tehran-Iran during ten years (2001-2011). *Iranian Journal of Cancer Prevention*, 5: 157-163.
Not in PICO
- Bansal, D. & Totadri, S. (2014) - Common hematological disorders in children.[Erratum appears in Indian J Pediatr. 2014 Jun;81(6):635]. - *Indian Journal of Pediatrics*, 81: 42-50.
Narrative review
- Bansal, D. & Totadri, S. (2014) Common hematological disorders in children. *Indian Journal of Pediatrics*, 81: 42-50.
Narrative review
- Baughan, P., Keatings, J. & O'Neill, B. (2011) Urgent suspected cancer referrals from general practice: audit of compliance with guidelines and referral outcomes. *British Journal of General Practice*, 61: e700-e706.
Not in PICO
- Bedu-Addo, G., Ampem, A. Y. & Bates, I. (2013) The role of bone marrow aspirate and trephine samples in haematological diagnoses in patients referred to a teaching hospital in Ghana. *Ghana Medical Journal*, 47: 74-78.
Not in PICO
- Bernbeck, B., Wuller, D., Janssen, G., Wessalowski, R., Gobel, U. & Schneider, D. T. (2009) Symptoms of childhood acute lymphoblastic leukemia: red flags to recognize leukemia in daily practice. *Klinische Padiatrie*, 221: 369-373.
Not in PICO
- Bhaskar, M. E. (2011) Nail changes in a patient with leukaemia. *BMJ*, 342: 177.
Not in PICO
- Bleyer, A. (2009) CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology*, 36: 207-212.
Narrative review

- Cabral, D. A. T. (1999) Malignancies in children who initially present with rheumatic complaints. *Journal of Pediatrics*, 134: 53-57.
Not in PICO
- Campbell, E. W., Jr., Smith, M. R., Campbell, E. W. J. & Smith, M. R. (1996) Hematology for primary care physicians. *Disease-a-Month*, 42: 131-194.
Narrative review
- Canfield, K. N., Spector, L. G., Robison, L. L., Lazovich, D., Roesler, M., Olshan, A. F., Smith, F. O., Heerema, N. A., Barnard, D. R., Blair, C. K., Ross, J. A., Canfield, K. N., Spector, L. G., Robison, L. L., Lazovich, D., Roesler, M., Olshan, A. F., Smith, F. O., Heerema, N. A., Barnard, D. R., Blair, C. K. & Ross, J. A. (2004) Childhood and maternal infections and risk of acute leukaemia in children with Down syndrome: a report from the Children's Oncology Group. *British Journal of Cancer*, 91: 1866-1872.
Not in PICO
- Cardwell, C. R., McKinney, P. A., Patterson, C. C., Murray, L. J., Cardwell, C. R., McKinney, P. A., Patterson, C. C. & Murray, L. J. (2008) Infections in early life and childhood leukaemia risk: a UK case-control study of general practitioner records. *British Journal of Cancer*, 99: 1529-1533.
Not in PICO
- Carriere, B. (2001) Vertebral fractures as initial signs for acute lymphoblastic leukemia. *Pediatric Emergency Care*, 17: 258-261.
Not in PICO
- Casado, P. R., Barrios, L. M., de Inocencio, A. J., Baro, F. M., Vivanco Martinez, J. L., Casado Picon, R., Barrios Lopez, M., de Inocencio Arocena, J., Baro Fernandez, M. & Vivanco Martinez, J. L. (2010) [Musculoskeletal pain: a common initial sign of acute lymphoblastic leukaemia]. [Spanish]. *Anales de Pediatría*, 72: 428-431.
Not in PICO
- Cavkaytar, O. (2010) Limping as an initial symptom of acute leukemia. *Cocuk Sagligi ve Hastaliklari Dergisi*, 53: 295-297.
Narrative review
- Clarke, R. T., Jones, C. H. D., Mitchell, C. D. & Thompson, M. J. (2014) 'Shouting from the roof tops': A qualitative study of how children with leukaemia are diagnosed in primary care. *BMJ Open*, 4.
Not in PICO
- Clarke, R. T., Jones, C. H., Mitchell, C. D. & Thompson, M. J. (2014) - 'Shouting from the roof tops': a qualitative study of how children with leukaemia are diagnosed in primary care. - *BMJ Open*, 4: e004640.
Duplicate
- Clarke, R. T., Jones, C. H. D., Mitchell, C. D. & Thompson, M. J. (2014) 'Shouting from the roof tops': a qualitative study of how children with leukaemia are diagnosed in primary care. *BMJ Open*, 4.
Duplicate
- Creutzig, U., van den Heuvel-Eibrink MM, Gibson, B., Dworzak, M. N., Adachi, S., de, B. E., Harbott, J., Hasle, H., Johnston, D., Kinoshita, A., Lehrnbecher, T., Leverger, G., Mejstrikova, E., Meshinchi, S., Pession, A., Raimondi, S. C., Sung, L., Stary, J., Zwaan, C. M., Kaspers, G. J. & Reinhardt, D. (2012) Diagnosis and management of acute myeloid leukemia in children and adolescents: recommendations from an international expert panel. *Blood*, 120: 3187-3205.
Narrative review/guideline
- Cwiklinska, M., Balwierz, W., Cwiklinska, M. & Balwierz, W. (2009) [Osteoarticular pains as early manifestation of malignancies in children]. [Polish]. *Przegląd Lekarski*, 66: 39-44.
Not in PICO
- da Fonseca, M. A. & da Fonseca, M. A. (2007) Head and neck extramedullary disease as the initial presentation of acute myelogenous leukemia in a child. *Journal of Dentistry for Children (Chicago, Ill,)*. 74: 241-244.
Not in PICO

- Davis, A. S., Viera, A. J. & Mead, M. D. (2014) Leukemia: An overview for primary care. *American Family Physician*, 89: 731-738.
Narrative review
- Davis, A. S., Viera, A. J. & Mead, M. D. (2014) - Leukemia: an overview for primary care. [Review]. - *American Family Physician*, 89: 731-738.
Duplicate
- Davis, A. S., Viera, A. J. & Mead, M. D. (2014) Leukemia: An Overview for Primary Care. *American Family Physician*, 89: 731-738.
Duplicate
- Delaney, M., Schellhase, K. G., Young, S., Geiger, S., Fink, A., Mast, A. E., Delaney, M., Schellhase, K. G., Young, S., Geiger, S., Fink, A. & Mast, A. E. (2011) Blood center practice and education for blood donors with anemia. *Transfusion*, 51: 929-936.
Not in PICO
- Dorransoro Martin, I., Merino Munoz, R., Sastre-Urguelles, A., Garcia-Miguel Garcia-Rosado, P. & Garcia-Consuegra, M. J. (2004) [Malignant disease presenting as rheumatic manifestations]. [Spanish]. *Anales de Pediatría*, 61: 393-397.
Not in PICO
- Dutschke, K., Siebenburger, H. & Schrader, W. (1998) [Acute lymphatic leukemia of the T-cell line. Visual impairment as the initial symptom] [German]. *Ophthalmologe*, 95: 831-834.
Not in PICO
- Edgren, G., Bagnardi, V., Bellocco, R., Hjalgrim, H., Rostgaard, K., Melbye, M., Reilly, M., Adami, H. O., Hall, P., Nyren, O., Edgren, G., Bagnardi, V., Bellocco, R., Hjalgrim, H., Rostgaard, K., Melbye, M., Reilly, M., Adami, H. O., Hall, P. & Nyren, O. (2010) Pattern of declining hemoglobin concentration before cancer diagnosis. *International Journal of Cancer*, 127: 1429-1436.
Not in PICO
- Entin, E. & Entin, E. (1993) Family medicine: a small vignette. *Rhode Island Medicine*, 76: 275.
Not in PICO
- Ferguson, R. H. (1978) Connective tissue disease: when to suspect malignancies. *Geriatrics*, 33: 26-31.
Not in PICO
- Fodor, A. (1978) Early symptoms and signs of malignant hemopathies. *Viata Medicală; Revista de Informare Profesională Științifică a Cadrelor Medii Sanitare*, 26: 97-99.
Not in PICO
- Follows, G. A. C. (2001) Fast-track referral system for patients with haematological malignancy. *Clinical and Laboratory Haematology*, 23: 333-334.
Not in PICO
- Foran, J. M., Shammo, J. M., Foran, J. M. & Shammo, J. M. (2012) Clinical presentation, diagnosis, and prognosis of myelodysplastic syndromes. [Review]. *American Journal of Medicine*, 125: S6-13.
Narrative review
- Forlenza, C. J. & Levy, A. S. (2013) Pathology turnaround time in pediatric oncology: a tool to prepare patients and families for the diagnostic waiting period. *Journal of Pediatric Hematology/Oncology*, 35: 534-536.
Not in PICO
- Gans, R. O. B. (1999) Clinical thinking and decision-making in practice. A man with deep venous thrombosis. *Nederlands Tijdschrift Voor Geneeskunde*, 143: 2307-2312.
Not in PICO
- Garcia Hernandez, B. (2008) Suspicion of cancer in pediatrics. *Pediatrica Integral*, 12: 537-544.
Narrative review
- Goss, J. F. (2003) Blood disorders: sickle cell disease & leukemia--more similar than you may think. *JEMS : a journal of emergency medical services*, 28: 72-84.
Not in PICO

Green, A. E. (1978) Haematology in general practice - some moral tales. *Update*, 17: 973-981.
Not in PICO

Gunawan, S., Sepang, F. & Mantik, M. (2013) Health Knowledge and Belief of Primary Health Care Provider About Childhood Leukemia in Manado. *Pediatric Blood & Cancer*, 60: 181.
Not in PICO

Hamilton, W. (2012) Emergency admissions of cancer as a marker of diagnostic delay. *British Journal of Cancer*, 107: 1205-1206.
Not in PICO

Heckner, F. (1969) Early diagnosis of malignant blood diseases. *Zeitschrift fur Allgemeinmedizin*, 45: 1423-1426.
Not in PICO

Hippisley-Cox, J. (2013) Symptoms and risk factors to identify men with suspected cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice*, 63: e1-e10.
Not in PICO (reports cancer risk overall, not limited to blood cancers)

Hippisley-Cox, J. & Coupland, C. (2013) Symptoms and risk factors to identify women with suspected cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice*, 63: e11-e21.
Not in PICO (reports cancer risk overall, not limited to blood cancers)

Hooker, W. P. (2003) Lessons for us all. One doctor's experience with a fatal illness [4]. *Canadian Family Physician*, 49: 147-148.
Not in PICO

Howell, D. A., Smith, A. G., Jack, A., Patmore, R., Macleod, U., Mironska, E. & Roman, E. (2013) Time-to-diagnosis and symptoms of myeloma, lymphomas and leukaemias: a report from the Haematological Malignancy Research Network. *BMC Hematology*, 13: 9.
Not in PICO

HUTCHISON, J. H. & HUTCHISON, J. H. (1965) CHILD CARE IN GENERAL PRACTICE. ANAEMIA IN INFANCY AND CHILDHOOD. *British Medical Journal*, 1: 701-703.
Not in PICO

Huttenlocher, A. (1997) Evaluation of the erythrocyte sedimentation rate in children presenting with limp, fever, or abdominal pain. *Clinical Pediatrics*, 36: 339-344.
Not in PICO (secondary care)

Hutter, J. J. (2010) Childhood leukemia. *Pediatrics in Review*, 31: 234-241.
Narrative review

Jaffe, D., Fleisher, G., Grosflam, J., Jaffe, D., Fleisher, G. & Grosflam, J. (1985) Detection of cancer in the pediatric emergency department. *Pediatric Emergency Care*, 1: 11-15.
Not in PICO

Jandial S. (2008) Examination of the musculoskeletal system in children - a simple approach. *Paediatrics and Child Health*, 18: 47-55.
Narrative review

Jayachandran, N. V. T. (2009) Cutaneous vasculitis as a presenting manifestation of acute myeloid leukemia. *International Journal of Rheumatic Diseases*, 12: 70-73.
Not in PICO

Jonsson, O. G., Sartain, P., Ducore, J. M. & Buchanan, G. R. (1990) Bone pain as an initial symptom of childhood acute lymphoblastic leukemia: association with nearly normal hematologic indexes. *Journal of Pediatrics*, 117: 233-237.
Not in PICO

Kecmanovic, Z., V (1961) Ophthalmologic symptoms as first signs in leukaemia (serbian). *Medicinski Pregled*, 14: 355-357.
Not in PICO

- Khan, A. M. K. (2010) Myelodysplastic syndromes: What a primary care physician needs to know. *Disease-a-Month*, 56: 468-478.
Narrative review
- Khan, A. M. K. (2012) Why are myelosplastic syndromes unrecognized and underdiagnosed?: a primary care perspective. *American Journal of Medicine*, 125: S15-S17.
Not in PICO
- Kubba, H. (2006) Childhood epistaxis. *Clinical Otolaryngology*, 31: 212-213.
Narrative review
- Kuroda, H., Ishikawa, K., Jomen, W., Yoshida, M., Yamada, M., Abe, T., Sakurai, T., Fujii, S., Maeda, M., Matsuno, T., Sato, M., Fujita, M., Nagashima, K., Ieko, M. & Kato, J. (2013) Primary myelofibrosis complicated by acquired hemophilia A and subsequent development of acute myeloid leukemia. *Rinsho Ketsueki - Japanese Journal of Clinical Hematology*, 54: 2192-2198.
Not in PICO
- Kvezereli-Kopadze, A., Mtvarelidze, Z., Kvezereli-Kopadze, M., Kvezereli-Kopadze, A., Mtvarelidze, Z. & Kvezereli-Kopadze, M. (2008) [Autoimmune haemolytic anaemia - as a mask of acute erythroleukaemia]. [Russian]. *Georgian Medical News, News.:* 43-47.
Not in PICO
- Lee, S. M., Kim, D. G., Bang, D., Lee, S. M., Kim, D. G. & Bang, D. (1994) Persistent erythema infectiosum-like rash as a prodrome of acute lymphocytic leukemia. *Pediatric Dermatology*, 11: 156-159.
Not in PICO
- Lefevre, Y., Ceroni, D., Laedermann, A., de, R., V, de, C. G., Ayse, H. O., Kaelin, A., Lefevre, Y., Ceroni, D., Laedermann, A., de Rosa, V., de Coulon, G., Ayse, H. O. & Kaelin, A. (2009) Pediatric leukemia revealed by a limping episode: a report of four cases. *Orthopaedics & traumatology, surgery & research*, 95: 77-81.
Not in PICO
- Lins, M. M., Amorim, M., Vilela, P., Viana, M., Ribeiro, R. C., Pedrosa, A., Lucena-Silva, N., Howard, S. C. & Pedrosa, F. (2012) Delayed diagnosis of leukemia and association with morbid-mortality in children in Pernambuco, Brazil. *Journal of Pediatric Hematology/Oncology*, 34: e271-e276.
Not in PICO
- Listernick, R. (2011) A 16-year-old girl with leg pain and swelling. *Pediatric Annals*, 40: 536-537.
Not in PICO
- Lewis, S. (2000) Malignant disease and the adolescent. *Journal of the Royal College of Physicians of London*, 34: 27-31.
Narrative review
- Ma, S. K., Chan, G. C., Ha, S. Y., Chiu, D. C., Lau, Y. L. & Chan, L. C. (1997) Clinical presentation, hematologic features and treatment outcome of childhood acute lymphoblastic leukemia: a review of 73 cases in Hong Kong. *Hematological Oncology*, 15: 141-149.
Not in PICO
- Mahmoudi, S., Mehrazmay, A., Salesi, M. & Mamishi, S. (2014) Fever of unknown origin: A retrospective study of 95 children in an Iranian referral hospital. *British Journal of Biomedical Science*, 71: 40-42.
Not in PICO
- Mansour, K. M., Kuypers, F. A., Wang, T. N., Miller, A. M., Larkin, S. K., Morris, C. R., Mansour, K. M., Kuypers, F. A., Wang, T. N., Miller, A. M., Larkin, S. K. & Morris, C. R. (2011) Secretory phospholipase A2: a marker of infection in febrile children presenting to a pediatric ED. *American Journal of Emergency Medicine*, 29: 1163-1168.
Not in PICO (secondary care)
- Maurer, C. & Hallek, M. (2013) [Chronic lymphocytic leukemia]. [Review] [German]. *Deutsche Medizinische Wochenschrift*, 138: 2153-2166.
Narrative review

- Murray, M. J. N. (2008) Unresponsive asthma: Don't forget mediastinal masses. *BMJ (Clinical research ed)*, 336: 521-522.
Letter
- Musiej-Nowakowska, E., Rostropowicz-Denisiewicz, K., Musiej-Nowakowska, E. & Rostropowicz-Denisiewicz, K. (1986) Differential diagnosis of neoplastic and rheumatic diseases in children. *Scandinavian Journal of Rheumatology*, 15: 124-128.
Not in PICO
- Nagarajarao, H. S. A. (2009) Unusual presentation of chronic myelogenous leukemia as multiple skin chloromas. *Acta Cytologica*, 53: 235-238.
Not in PICO
- Nguyen, H. S., Haider, K. M. & Ackerman, L. L. (2013) Unusual causes of papilledema: Two illustrative cases. *Surgical neurology international*, 4: 60.
Not in PICO
- Nortje, C. J. (2003) General practitioner's radiology case 16. Acute leukemia. *SADJ : journal of the South African Dental Association = tydskrif van die Suid-Afrikaanse Tandheelkundige Vereniging*, 58: 393.
Not in PICO
- Oscier, D. (2004) Guidelines on the diagnosis and management of chronic lymphocytic leukaemia. *British Journal of Haematology*, 125: 294-317.
Guideline
- Peter, S. A., Cervantes, J. F., Peter, S. A. & Cervantes, J. F. (1995) Hypercalcemia associated with adult T-cell leukemia/lymphoma (ATL). [Review] [15 refs]. *Journal of the National Medical Association*, 87: 746-748.
Not in PICO
- Picon, R. C. L. (2010) Musculoskeletal pain: A common initial sign of acute lymphoblastic leukaemia. *Anales de Pediatria*, 72: 428-431.
Not in PICO
- Pieczyrak, R. (2010) Fever as a symptom in the internal disease daily practice. *Internal Medicine Journal*, Conference: March.
Not in PICO
- Plezbart, J. A., Bose, M., Carlisle, G., Plezbart, J. A., Bose, M. & Carlisle, G. (1994) Chronic myelogenous leukemia in a 16-yr-old. *Journal of Manipulative & Physiological Therapeutics*, 17: 610-613.
Not in PICO
- Raab, C. P. & Gartner, J. C. (2009) Diagnosis of Childhood Cancer. *Primary Care*, 36: 671-+.
Narrative review
- Racil, Z., Buresova, L., Brejcha, M., Prochazkova, J., Zounar, R., Timilsina, S., Razga, F., Toskova, M., Cetkovsky, P., Mayer, J., Racil, Z., Buresova, L., Brejcha, M., Prochazkova, J., Zounar, R., Timilsina, S., Razga, F., Toskova, M., Cetkovsky, P. & Mayer, J. (2011) Clinical and laboratory features of leukemias at the time of diagnosis: an analysis of 1,004 consecutive patients. *American Journal of Hematology*, 86: 800-803.
Not in PICO
- Ramesh, P. M., Marwaha, R. K., Anish, T. S., Ramesh, P. M., Marwaha, R. K. & Anish, T. S. (2011) Childhood cancer in developing society: A roadmap of health care. *Indian journal of medical and paediatric oncology : official journal of Indian Society of Medical & Paediatric Oncology*, 32: 30-33.
Not in PICO
- Reddy, S. C. J. (1998) Retinal changes in chronic leukemia. *Biomedical Research*, 9: 125-129.
Not in PICO

- Reuss-Borst, M. A. (2005) The association of rheumatic diseases with hemato-/oncological disorders. *Zeitschrift fur Rheumatologie*, 64: 3-11.
Narrative review
- Robazzi, T. C. M. V. (2007) Osteoarticular manifestations as initial presentation of acute leukemias in children and adolescents in Bahia, Brazil. *Journal of Pediatric Hematology/Oncology*, 29: 622-626.
Not in PICO
- Roman, E., Simpson, J., Ansell, P., Kinsey, S., Mitchell, C. D., McKinney, P. A., Birch, J. M., Greaves, M. & Eden, T. (2007) Childhood acute lymphoblastic leukemia and infections in the first year of life: a report from the United Kingdom Childhood Cancer Study. *American Journal of Epidemiology*, 165: 496-504.
Not in PICO
- Roushan, N. (2007) Acute leukemia presenting with ascites and confusion [7]. *Leukemia and Lymphoma*, 48: 1234-1236.
Not in PICO
- Saraswatula, A., McShane, D., Tideswell, D., Burke, G. A. A., Williams, D. M., Nicholson, J. C. & Murray, M. J. (2009) Mediastinal masses masquerading as common respiratory conditions of childhood: a case series. *European Journal of Pediatrics*, 168: 1395-1399.
Narrative review
- Sauter, D., Spiekermann, K., Feuring-Buske, M., Braess, J., Sauter, D., Spiekermann, K., Feuring-Buske, M. & Braess, J. (2007) [Nonsymptomatic leukocytosis]. [German]. *MMW Fortschritte der Medizin*, 149: 29-32.
Narrative review
- Savage, D. G., Szydlo, R. M. & Goldman, J. M. (1997) Clinical features at diagnosis in 430 patients with chronic myeloid leukaemia seen at a referral centre over a 16-year period. *British Journal of Haematology*, 96: 111-116.
Not in PICO
- Schaller, J. (1972) Arthritis as a presenting manifestation of malignancy in children. *Journal of Pediatrics*, 81: 793-797.
Not in PICO
- Scott, R. B. (1993) Common blood disorders: A primary care approach. *Geriatrics*, 48: 72-80.
Narrative review
- Serwint, J. R., Dias, M. M., Chang, H., Sharkey, M., Walker, A. R., Serwint, J. R., Dias, M. M., Chang, H., Sharkey, M. & Walker, A. R. (2005) Outcomes of febrile children presumed to be immunocompetent who present with leukopenia or neutropenia to an ambulatory setting. *Clinical Pediatrics*, 44: 593-600.
Not in PICO
- Silverstein, M. N. K. (1963) Leukemia with osteoarticular symptoms and signs. *Annals of Internal Medicine*, 59: 637-645.
Not in PICO
- Singer, J. & Henry, S. (2008) Upper airway obstruction as the presenting manifestation of leukemia. *Pediatric Emergency Care*, 24: 310-312.
Not in PICO
- Smith, L. B., Valdes, Y., Check, W. E., Britt, P. M., Frankel, L. S., Smith, L. B., Valdes, Y., Check, W. E., Britt, P. M. & Frankel, L. S. (2007) Juvenile myelomonocytic leukemia presenting with facial nerve paresis: a unique presentation. [Review] [7 refs]. *Journal of Pediatric Hematology/Oncology*, 29: 770-773.
Not in PICO
- Stobbe, H. & Stobbe, H. (1979) [Contents and methodological aspects in the early diagnosis of leukemia and malignant lymphomas]. [German]. *Zeitschrift fur Arztliche Fortbildung (Jena)*, 73: 667-668.
Input as "Not in PICO (1979)", but is actually also "Narrative review"

- Sweet, J. M. & Sweet, J. M. (2004) The numb chin syndrome: a critical sign for primary care physicians. *Archives of Internal Medicine*, 164: 1347-1348.
Not in PICO
- Tazi, L. (2009) Priapism as the first manifestation of chronic myeloid leukemia. *Annals of Saudi Medicine*, 29: 412-October.
Not in PICO
- Teo, W. Y., Chan, M. Y., Ng, K. C. & Tan, A. M. (2012) Bony presentations of childhood haematological malignancy to the emergency room. *Journal of Paediatrics and Child Health*, 48: 311-316.
Not in PICO
- Thomas, W. (2013) Co-incidental finding of pancytopenia. *British Journal of Medical Practitioners*, 5.
Not in PICO
- Thulesius, H., Pola, J. & Hakansson, A. (2000) Diagnostic delay in pediatric malignancies - A population-based study. *Acta Oncologica*, 39: 873-876.
Not in PICO
- Torgerson, S. R., Haddad, R. Y., Atallah, E., Torgerson, S. R., Haddad, R. Y. & Atallah, E. (2012) Chronic myelogenous leukemia for primary care physicians. [Review]. *Disease-a-Month*, 58: 168-176.
Narrative review
- Tsai, M. J., Yan, D. C., Chiang, B. L., Chou, C. C., Hsieh, K. H., Lin, K. H., Tsai, M. J., Yan, D. C., Chiang, B. L., Chou, C. C., Hsieh, K. H. & Lin, K. H. (1995) Childhood leukemia mimicking juvenile rheumatoid arthritis. *Chung-Hua Min Kuo Hsiao Erh Ko i Hsueh Hui Tsa Chih*, 36: 274-278.
Not in PICO
- Usul, A. C., Paydas, S., Gunaldi, M., Bozkurt, D. B., Ercolak, V., Zorludemir, S. & Acikalin, A. (2013) Sweet syndrome in a patient with chronic lymphocytic leukemia/small lymphocytic lymphoma: curious lymphocyte/neutrophil fluctuations. *Turkish Journal of Haematology*, 30: 413-415.
Not in PICO
- van der Haring, I. S., Witjes, M. J., van der Haring, I. S. & Witjes, M. J. H. (2006) [Diagnostic considerations concerning a case of an unusual gingivitis]. [Dutch]. *Nederlands Tijdschrift Voor Tandheelkunde*, 113: 284-287.
Not in PICO
- Welles, S. L., Levine, P. H., Joseph, E. M., Goberdhan, L. J., Lee, S., Miotti, A., Cervantes, J., Bertoni, M., Jaffe, E., Dosik, H., Welles, S. L., Levine, P. H., Joseph, E. M., Goberdhan, L. J., Lee, S., Miotti, A., Cervantes, J., Bertoni, M., Jaffe, E. & Dosik, H. (1994) An enhanced surveillance program for adult T-cell leukemia in central Brooklyn. *Leukemia*, 8 Suppl 1: S111-S115.
Not in PICO
- Werner, A. H., Scarfone, R., Mostoufi-Moab, S., Werner, A. H., Scarfone, R. & Mostoufi-Moab, S. (2010) A febrile young infant with splenomegaly and ecchymoses. *Pediatric Emergency Care*, 26: 442-444.
Not in PICO
- Williams, P. D., Williams, A. R., Kelly, K. P., Dobos, C., Gieseking, A., Connor, R., Ridder, L., Potter, N. & Del, F. D. (2012) A symptom checklist for children with cancer: the Therapy-Related Symptom Checklist-Children. *Cancer Nursing*, 35: 89-98.
Not in PICO
- Young, G., Toretsky, J. A., Campbell, A. B., Eskenazi, A. E., Young, G., Toretsky, J. A., Campbell, A. B. & Eskenazi, A. E. (2000) Recognition of common childhood malignancies. [Review] [18 refs]. *American Family Physician*, 61: 2144-2154.
Narrative review
- Zombori, L., Kovacs, G., Csoka, M. & Derfalvi, B. (2013) Rheumatic symptoms in childhood leukaemia and lymphoma-a ten-year retrospective study. *Pediatric Rheumatology*, 11.
Not in PICO

Zwimpfer, J. & Zwimpfer, J. (2000) [Case from general practice. Splenomegaly. Hairy-cell leukemia]. [German]. *Praxis*, 89: 1160-1161.
Not in PICO

Review question:

Which investigations of symptoms of suspected leukemia should be done with clinical responsibility retained by primary care?

Results

Literature search

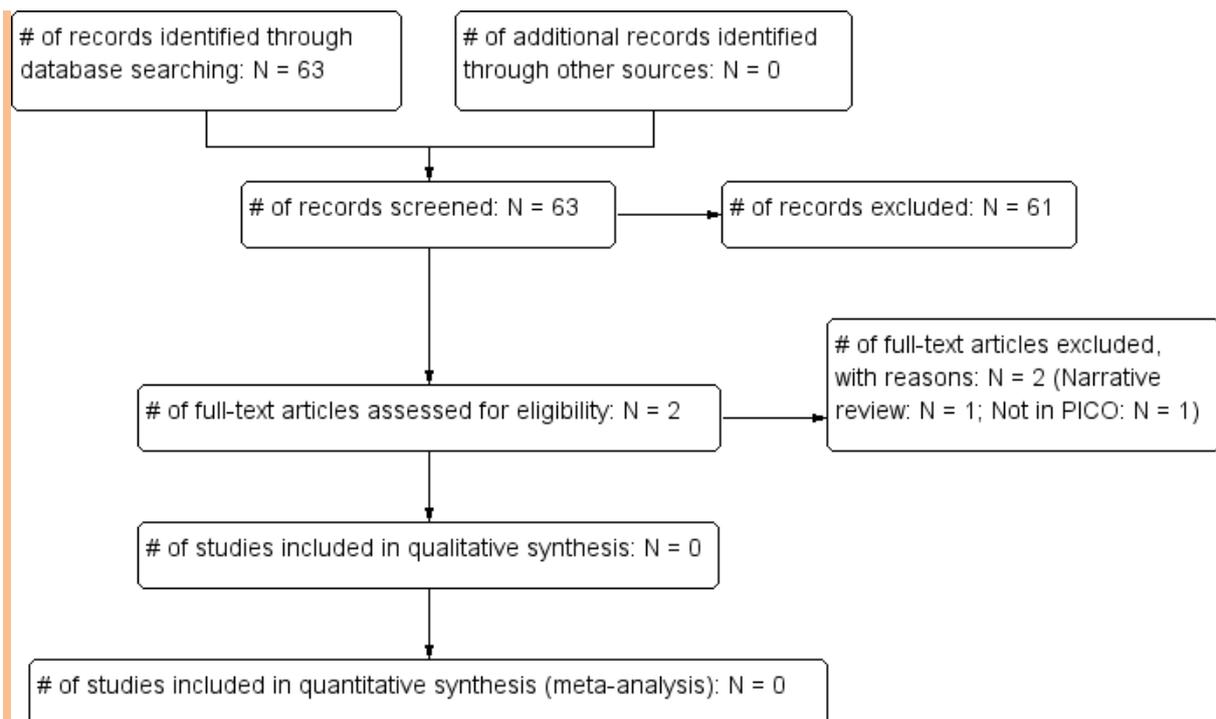
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	239	34	18/04/2013
<i>Premedline</i>	1980-2013	28	8	18/04/2013
<i>Embase</i>	1980-2013	261	21	18/04/2013
<i>Cochrane Library</i>	1980-2013	7	0	18/04/2013
<i>Psychinfo</i>	1980-2013	2	0	18/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	57	5	18/04/2013

Total References retrieved (after de-duplication): 57

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-18/08/2014	10	2	18/08/2014
<i>Premedline</i>	4/2013-18/08/2014	30	2	18/08/2014
<i>Embase</i>	4/2013-18/08/2014	51	3	18/08/2014
<i>Cochrane Library</i>	4/2013-18/08/2014	11	0	18/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	4/2013-18/08/2014	11	1	18/08/2014

Total References retrieved (after de-duplication): 6



Study results

No evidence was identified pertaining to the diagnostic accuracy of white blood cell count in patients with suspected leukaemia where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Alekha, S. & Chadha, T. (2013) Bernard Soulier Syndrome associated with acute myeloid leukemia. *Indian Journal of Medical Sciences*, 67: 145-147.

Not in PICO

Avery, P. R. & Avery, A. C. (2004) Molecular methods to distinguish reactive and neoplastic lymphocyte expansions and their importance in transitional neoplastic states. [Review] [83 refs]. *Veterinary Clinical Pathology*, 33: 196-207.

Narrative review

Bansal, D. & Totadri, S. (2014) Common hematological disorders in children. *Indian Journal of Pediatrics*, 81: 42-50.

Narrative review

Bansal, D. & Totadri, S. (2014) Common hematological disorders in children. *Indian Journal of Pediatrics*, 81: 42-50.

Narrative review

Bedu-Addo, G., Ampem, A. Y. & Bates, I. (2013) The role of bone marrow aspirate and trephine samples in haematological diagnoses in patients referred to a teaching hospital in Ghana. *Ghana Medical Journal*, 47: 74-78.

Not in PICO

- Bennett, M., Higgins, E., Curran, S. & Marren, P. (2010) Leukaemia cutis mimicking florid rhinophymatous rosacea. *British Journal of Dermatology*, 163: 443.
Not in PICO
- Bernbeck, B., Wuller, D., Janssen, G., Wessalowski, R., Gobel, U. & Schneider, D. T. (2009) Symptoms of Childhood Acute Lymphoblastic Leukemia: Red Flags to Recognize Leukemia in Daily Practice. *Klinische Padiatrie*, 221: 369-373.
Not in PICO
- Bindels, L. B., Porporato, P., Dewulf, E. M., Verrax, J., Neyrinck, A. M., Martin, J. C., Scott, K. P., Buc, C. P., Feron, O., Muccioli, G. G., Sonveaux, P., Cani, P. D. & Delzenne, N. M. (2012) Gut microbiota-derived propionate reduces cancer cell proliferation in the liver. *British Journal of Cancer*, 107: 1337-1344.
Not in PICO
- Bode, B. & Tinguely, M. (2012) [Role of cytology in hematopathological diagnostics]. [Review] [German]. *Pathologe*, 33: 316-323.
Narrative review
- Brasme, J. F., Morfouace, M., Grill, J., Martinot, A., Amalberti, R., Bons-Letouzey, C. & Chalumeau, M. (2012) Delays in diagnosis of paediatric cancers: a systematic review and comparison with expert testimony in lawsuits. [Review]. *Lancet Oncology*, 13: e445-e459.
Not in PICO
- Buddula, A. & Assad, D. (2011) Peripheral T-Cell lymphoma manifested as gingival enlargement in a patient with chronic lymphocytic leukemia. *Journal of Indian Society of Periodontology*, 15: 67-69.
Not in PICO
- Calpin, C., Dick, P., Poon, A. & Feldman, W. (1998) Is bone marrow aspiration needed in acute childhood idiopathic thrombocytopenic purpura to rule out leukemia? *Archives of Pediatrics & Adolescent Medicine*, 152: 345-347.
Not in PICO
- Campbell, E. W., Jr. & Smith, M. R. (1996) Hematology for primary care physicians. *Disease-a-Month*, 42: 131-194.
Narrative review
- Cronin, C. G., Cashell, T., Mhuircheartaigh, J. N., Swords, R., Murray, M., O'Sullivan, G. J. & O'Keefe, D. (2009) Bone biopsy of new suspicious bone lesions in patients with primary carcinoma: prevalence and probability of an alternative diagnosis. *AJR.American Journal of Roentgenology*, 193: W407-W410.
Not in PICO
- Davis, A. S., Viera, A. J. & Mead, M. D. (2014) - Leukemia: an overview for primary care. [Review]. - *American Family Physician*, 89: 731-738.
Narrative review
- Davis, A. S., Viera, A. J. & Mead, M. D. (2014) Leukemia: An Overview for Primary Care. *American Family Physician*, 89: 731-738.
Duplicate
- Derman, O., Okstuz-Kanbur, N., Yenicesu, I. & Klink, E. (2005) Iron deficiency anemia in a group of Turkish adolescents: frequency and contributing factors. *International Journal of Adolescent Medicine & Health*, 17: 179-186.
Not in PICO
- Dommett, R. M., Redaniel, M. T., Stevens, M. C., Hamilton, W. & Martin, R. M. (2013) Features of cancer in teenagers and young adults in primary care: a population-based nested case-control study. *British Journal of Cancer*, 108: 2329-2333.
Already included
- Dorransoro, M., I, Merino, M. R., Sastre-Urguelles, A., Garcia-Miguel Garcia-Rosado, P. & Garcia-Consuegra, M. J. (2004) [Malignant disease presenting as rheumatic manifestations]. [Spanish].

- Anales de Pediatria*, 61: 393-397.
Not in PICO
- Forgie, S. E. & Robinson, J. L. (2007) Pediatric malignancies presenting as a possible infectious disease. *BMC Infectious Diseases*, 7.
Not in PICO
- Forlenza, C. J. & Levy, A. S. (2013) Pathology turnaround time in pediatric oncology: a tool to prepare patients and families for the diagnostic waiting period. *Journal of Pediatric Hematology/Oncology*, 35: 534-536.
Not in PICO
- Franco, A., Lewis, K. N., Blackmon, J. M. & Manaloor, E. J. (2010) Hyperostosis - an unusual radiographic presentation of Myelodysplastic Syndrome transformed to Acute Myeloid Leukemia. *Journal of Radiology Case Reports*, 4: 18-25.
Not in PICO
- Gandhi, J. (2009) Natural killer cell leukaemia. *BMJ Case Reports*, 2009, 2009.
Not in PICO
- Garrett Kevin, M. K. M., Hoffer, F. A., Behm, F. G., Gow, K. W., Hudson, M. M. & Sandlund, J. T. (2002) Interventional radiology techniques for the diagnosis of lymphoma or leukemia. *Pediatric Radiology*, 32: 653-662.
Not in PICO
- Goldschmidt, N., Libson, E., Bloom, A., Amir, G. & Paltiel, O. (2003) Clinical utility of computed tomography-guided core needle biopsy in the diagnostic re-evaluation of patients with lymphoproliferative disorders and suspected disease progression. *Annals of Oncology*, 14: 1438-1441.
Not in PICO
- Haase, R., Merkel, N., Diwan, O., Elsner, K. & Kramm, C. M. (2009) Leukapheresis and exchange transfusion in children with acute leukemia and hyperleukocytosis. A single center experience. *Klinische Padiatrie*, 221: 374-378.
Not in PICO
- Hager, H. B. (2012) Basophilia-is microscopic examination worth the effort? *International Journal of Laboratory Hematology*, 34: 115-116.
Not in PICO
- Hajda, M., Koranyi, K., Salomvary, B. & Bajcsay, A. (2005) [Clinical presentation, differential diagnosis and treatment of lacrimal gland tumours]. [Hungarian]. *Magyar Onkologia*, 49: 65-70.
Not in PICO
- Howell, D. A., Smith, A. G., Jack, A., Patmore, R., Macleod, U., Mironska, E. & Roman, E. (2013) Time-to-diagnosis and symptoms of myeloma, lymphomas and leukaemias: a report from the Haematological Malignancy Research Network. *BMC Hematology*, 13: 9.
Not in PICO
- Itoh, M., Oki, M., Yanagi, H., Oka, A., Tajiri, S., Fukuda, R., Ozawa, H. & Takagi, A. (2012) Disseminated mucormycosis infection after the first course of dose-modified R-EPOCH for advanced-stage lymphoma. *Journal of Infection & Chemotherapy*, 18: 395-398.
Not in PICO
- Khan, A. M., Komrokji, R. S. & Haddad, R. Y. (2010) Myelodysplastic syndromes: What a primary care physician needs to know. *Disease-a-Month*, 56: 468-478.
Narrative review
- Kuroda, H., Ishikawa, K., Jomen, W., Yoshida, M., Yamada, M., Abe, T., Sakurai, T., Fujii, S., Maeda, M., Matsuno, T., Sato, M., Fujita, M., Nagashima, K., Ieko, M. & Kato, J. (2013) Primary myelofibrosis complicated by acquired hemophilia A and subsequent development of acute myeloid leukemia. *Rinsho Ketsueki - Japanese Journal of Clinical Hematology*, 54: 2192-2198.
Not in PICO

- Lamki, Z. A., Wali, Y. A., Shah, W. M. & Zachariah, M. (2004) Relapsed acute leukemia in children: Oman Experience. *Pediatric Hematology and Oncology*, 21: 167-173.
Not in PICO
- Lehmitz, R. & Pahnke, J. (2009) Involvement of CNS in leukaemia and lymphomas--CSF meningeosis and immunocytochemical phenotyping. [German]. *Fortschritte der Neurologie-Psychiatrie*, 77: S37-S38.
Narrative review
- Linden, A., Zankovich, R., Theissen, P., Diehl, V. & Schicha, H. (1989) Malignant lymphoma: bone marrow imaging versus biopsy. *Radiology*, 173: 335-339.
Not in PICO
- Mackie, K. E., Zhou, Z., Robbins, P., Bulsara, M. & Zheng, M. H. (2011) Histopathology of femoral head donations: a retrospective review of 6161 cases. *Journal of Bone & Joint Surgery - American Volume*, 93: 1500-1509.
Not in PICO
- Mahmoudi, S., Mehrazmay, A., Salesi, M. & Mamishi, S. (2014) Fever of unknown origin: A retrospective study of 95 children in an Iranian referral hospital. *British Journal of Biomedical Science*, 71: 40-42.
Not in PICO
- Mates, M., Heyd, J., Souroujon, M., Ben, S. A., Manny, N. & Hershko, C. (1995) The haematologist as watchdog of community health by full blood count. *QJM*, 88: 333-339.
Not in PICO
- Matos, D. M. & Falcao, R. P. (2011) Monoclonal B-cell lymphocytosis: a brief review for general clinicians. *Sao Paulo Medical Journal*, 129: 171-175.
Narrative review
- Maurer, C. & Hallek, M. (2013) [Chronic lymphocytic leukemia]. [Review] [German]. *Deutsche Medizinische Wochenschrift*, 138: 2153-2166.
Narrative review
- McDermott, M. K. & Bell, E. M. (1999) A review of Waldenstrom's macroglobulinemia. [Review] [17 refs]. *Clinical Journal of Oncology Nursing*, 3: 107-111.
Narrative review
- Menezes, L. & Rao, J. R. (2012) Acute myelomonocytic leukemia presenting with gingival enlargement as the only clinical manifestation. *Journal of Indian Society of Periodontology*, 16: 597-601.
Not in PICO
- Mohsenin, A., Sinard, J. & Huang, J. J. (2012) Necrobiotic xanthogranuloma and chronic lymphocytic leukemia of the conjunctiva masquerading as scleritis and uveitis. *Clinical Ophthalmology*, 6: 2045-2047.
Not in PICO
- Morse, E. E., Yamase, H. T., Greenberg, B. R., Sporn, J., Harshaw, S. A., Kiraly, T. R., Ziemba, R. A. & Fallon, M. A. (1994) The role of flow cytometry in the diagnosis of lymphoma: a critical analysis. *Annals of Clinical & Laboratory Science*, 24: 6-11.
Not in PICO
- Nagarajarao, H. S., Akhtar, I., Heard, K. & Baliga, M. (2009) Unusual Presentation of Chronic Myelogenous Leukemia as Multiple Skin Chloromas Report of a Case with Clinical and Cytologic Correlation. *Acta Cytologica*, 53: 235-238.
Not in PICO
- Nguyen, H. S., Haider, K. M. & Ackerman, L. L. (2013) Unusual causes of papilledema: Two illustrative cases. *Surgical neurology international*, 4: 60.
Not in PICO
- Oscier, D., Fegan, C., Hillmen, P., Illidge, T., Johnson, S., Maguire, P., Matutes, E. & Milligan, D. (2004) Guidelines on the diagnosis and management of chronic lymphocytic leukaemia. *British Journal of*

Haematology, 125: 294-317.

Guideline

Petrasch, S. (1998) [Management of hematologic systemic diseases and rare tumor entities with manifestations in the oromaxillofacial area]. [Review] [74 refs] [German]. *Mund-, Kiefer- und Gesichtschirurgie*, 2: 172-180.

Narrative review

Price, E. A., Mehra, R. & Schrier, S. L. (2009) Iron deficiency is a common cause of anemia in elderly outpatients, however iron repletion frequently does not fully correct the anemia. *Blood*, 114.

Not in PICO

Raab, C. P. & Gartner, J. C., Jr. (2009) Diagnosis of childhood cancer. [Review] [33 refs]. *Primary Care; Clinics in Office Practice*, 36: 671-684.

Narrative review

Ravoet, C., Demartin, S., Gerard, R., Dehon, M., Peny, M. O., Petit, B., Delannoy, A. & Husson, B. (2004) Contribution of flow cytometry to the diagnosis of malignant and non malignant conditions in lymph node biopsies. *Leukemia & Lymphoma*, 45: 1587-1593.

Not in PICO

Rawstron, A. C., Green, M. J., Kuzmicki, A., Kennedy, B., Fenton, J. A., Evans, P. A., O'Connor, S. J., Richards, S. J., Morgan, G. J., Jack, A. S. & Hillmen, P. (2002) Monoclonal B lymphocytes with the characteristics of "indolent" chronic lymphocytic leukemia are present in 3.5% of adults with normal blood counts. *Blood*, 100: 635-639.

Not in PICO

Rosati, P., Jenkner, A., De, V. R., Boldrini, R., Chiodi, P., Celesti, L. & Giampaolo, R. (2011) 'Tell me about your pain': abdominal pain and a history of bullying. *BMJ Case Reports*, 2011, 2011.

Not in PICO

Rosbach, H.-C. (2009) Diagnostic pitfalls in acute leukemia. *Fetal and Pediatric Pathology*, 28: 69-77.

Narrative review

Sauter, D., Spiekermann, K., Feuring-Buske, M. & Braess, J. (1933) [Nonsymptomatic leukocytosis]. [German]. *MMW Fortschritte der Medizin*, 149: 29-32.

Narrative review

Schindhelm, R. K., van Marwijk Kooy, M. R., Coenen, J. L., Huijgens, P. C. & Kuiper-Kramer, P. A. (2010) [Monoclonal B-cell lymphocytosis: physiological entity or preliminary stage of chronic lymphocytic leukaemia?]. [Review] [17 refs] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 154: A1520.

Narrative review

Schleiffenbaum, B. E., Ruegg, R., Zimmermann, D. & Fehr, J. (1996) Early diagnosis of low grade malignant lymphoma and chronic lymphocytic leukaemia. Verification of morphologically suspected malignancy in blood lymphocytes by flow cytometry. *European Journal of Haematology*, 57: 341-348.

Not in PICO

Schroeder, M. A. & Blum, W. (2010) Evidence-based mini-review: Should patients over the age of 60 with INT-2 or high-risk myelodysplastic syndrome undergo allogeneic stem cell transplantation prior to progression to acute myelogenous leukemia?. [Review]. *Hematology*, 2010: 322-324.

Not in PICO

Serwint, J. R., Dias, M. M., Chang, H., Sharkey, M. & Walker, A. R. (2005) Outcomes of febrile children presumed to be immunocompetent who present with leukopenia or neutropenia to an ambulatory setting. *Clinical Pediatrics*, 44: 593-600.

Not in PICO

Shakoor, K. A. (1989) Fine needle aspiration cytology in advanced pediatric tumors. *Pediatric Pathology*, 9: 713-718.

Not in PICO

- Shields, J. A., Shields, C. L., Ehya, H., Eagle, R. C., Jr. & De, P. P. (1993) Fine-needle aspiration biopsy of suspected intraocular tumors. The 1992 Urwick Lecture. *Ophthalmology*, 100: 1677-1684.
Not in PICO
- Smellie, W. S. A., Forth, J., Smart, S. R. S., Galloway, M. J., Irving, W., Bareford, D., Collinson, P. O., Kerr, K. G., Summerfield, G., Carey, P. J. & Minhas, R. (2007) Best practice in primary care pathology: review 7. *Journal of Clinical Pathology*, 60: 458-465.
Narrative review
- Sykakis, E. & Patwary, S. N. (2011) Acute myeloid leukaemia presenting as gaze palsy. *Case Reports in Ophthalmology*, 2: 343-346.
Not in PICO
- Taamallah-Malek, I., Chebbi, A., Bouladi, M., Nacef, L., Bouguila, H. & Ayed, S. (2013) [Massive bilateral subconjunctival hemorrhage revealing acute lymphoblastic leukemia]. [French]. *Journal Francais d Ophthalmologie*, 36: e45-e48.
Not in PICO
- Tani, E., Costa, I., Svedmyr, E. & Skoog, L. (1995) Diagnosis of lymphoma, leukemia, and metastatic tumor involvement of the cerebrospinal fluid by cytology and immunocytochemistry. *Diagnostic Cytopathology*, 12: 14-22.
Not in PICO
- Teo, W.-Y., Chan, M.-Y., Ng, K.-C. & Tan, A.-M. (2012) Bony presentations of childhood haematological malignancy to the emergency room. *Journal of Paediatrics and Child Health*, 48: 311-316.
Not in PICO
- Torgerson, S. R., Haddad, R. Y. & Atallah, E. (2012) Chronic Myelogenous Leukemia for Primary Care Physicians. *Disease-a-Month*, 58: 168-176.
Narrative review
- Urabe, A. (1988) [Diagnosis of leukemia and lymphoma]. [Japanese]. *Gan No Rinsho - Japanese Journal of Cancer Clinics*, 34: 1445-1448.
Narrative review
- Usul, A. C., Paydas, S., Gunaldi, M., Bozkurt, D. B., Ercolak, V., Zorludemir, S. & Acikalin, A. (2013) Sweet syndrome in a patient with chronic lymphocytic leukemia/small lymphocytic lymphoma: curious lymphocyte/neutrophil fluctuations. *Turkish Journal of Haematology*, 30: 413-415.
Not in PICO
- Varshney, R., Deka, M., Bhattacharya, J. & Gogoi, P. K. (2012) Clinico-haematological analysis of haematological malignancy, a hospital based study. *Indian Journal of Hematology and Blood Transfusion*, 28: 245.
Not in PICO
- Wakely, P. E., Jr. & Kornstein, M. J. (1996) Aspiration cytopathology of lymphoblastic lymphoma and leukemia: the MCV experience. *Pediatric Pathology & Laboratory Medicine*, 16: 243-252.
Not in PICO
- Zombori, L., Kovacs, G., Csoka, M. & Derfalvi, B. (2013) Rheumatic symptoms in childhood leukaemia and lymphoma-a ten-year retrospective study. *Pediatric Rheumatology*, 11.
Not in PICO

MYELOMA

Review question:

What is the risk of myeloma in patients presenting in primary care with symptom(s)?

Results

Literature search results

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	565	16	09/04/2013
<i>Premedline</i>	1980--2013	74	9	10/04/2013
<i>Embase</i>	1980--2013	773	35	11/04/2013
<i>Cochrane Library</i>	1980--2013	684	0	10/04/2013
<i>Psychinfo</i>	1980--2013	21	3	11/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980--2013	545	7	12/04/2013

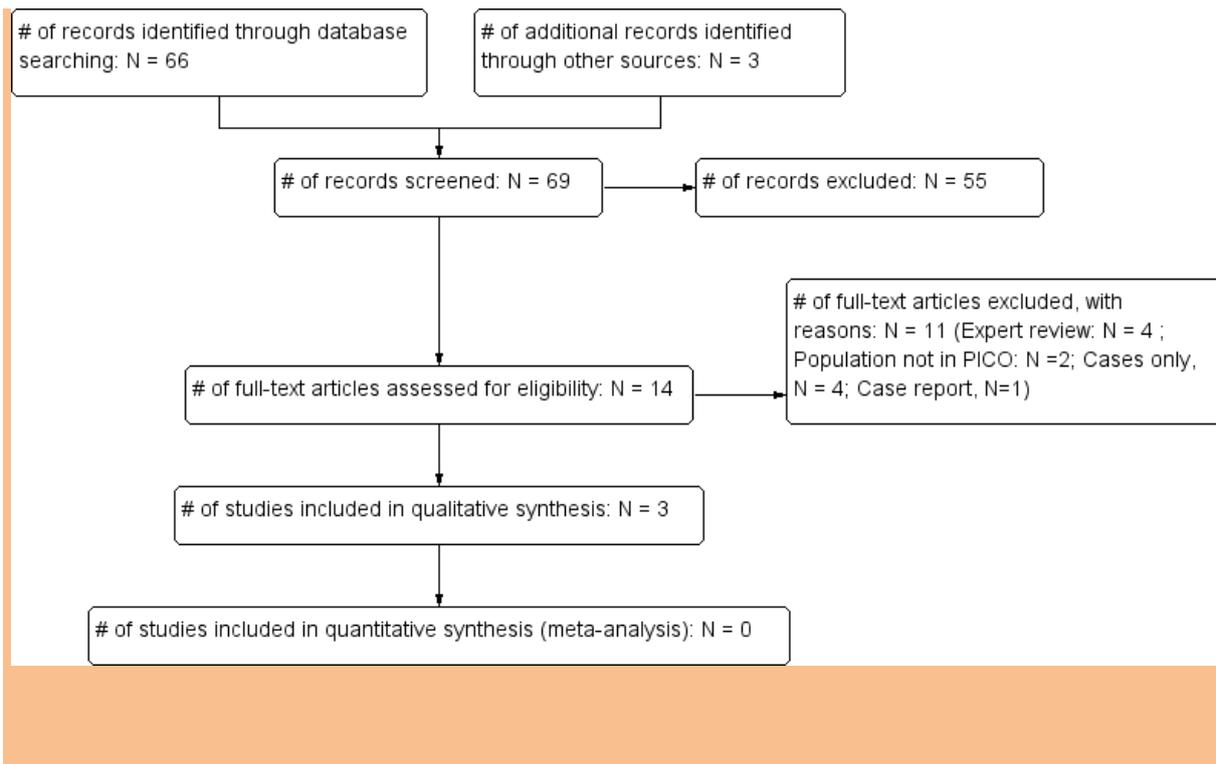
Total references retrieved (after de-duplication): 60

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-19/08/2014	20	0	19/08/2014
<i>Premedline</i>	4/2013-19/08/2014	40	3	19/08/2014
<i>Embase</i>	4/2013-19/08/2014	38	3	19/08/2014
<i>Cochrane Library</i>	4/2013-19/08/2014	349	0	19/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	4/2013-19/08/2014	44	2	19/08/2014

Total References retrieved (after de-duplication): 6

Study flow diagram



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issues to note are (1) that two of the studies employed samples of patients that are not directly representative of an unselected symptomatic population of patients presenting to the UK-based GP, and (2) that two of the studies employed patient selection methods that were not clearly consecutive or random in nature, which, in turn, may result in inflated estimates of the positive predictive values. However, the statistics employed by Shephard (2014) may have gone some way in counteracting this influence.

Risk of bias summary

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Deyo (1988)	?	+	?	+	-	+	+
Shephard (2014)	-	+	+	+	+	+	+
Suarez-Almazor (1997)	+	+	?	+	?	+	+

 High	 Unclear	 Low
--	---	---

Study results

Table 1: Myeloma: Positive predictive values of individual symptoms for myeloma in patients aged > 14-15 years

Study	Symptom(s)	Patient group	PPV % (95% CI) for myeloma; prevalence of myeloma
Deyo (1988)	Back pain	All patients	0.05 (0.003-0.3); 1/1975
Suarez-Almazor (1997)	Acute low back pain	All patients	0 (0-0.5) or 0.21 (0.04-0.83) 0-2/963 Unclear if diagnosis was prior to symptom
Shephard (2014)	Joint pain	Patients ≥ 60 years	0.05 (0.04-0.06)
Shephard (2014)	Shortness of breath	Patients ≥ 60 years	0.06 (0.05-0.06)
Shephard (2014)	Chest infection	Patients ≥ 60 years	0.06 (0.05-0.06)
Shephard (2014)	Chest pain	Patients ≥ 60 years	0.1 (0.09-0.11)
Shephard (2014)	Fracture	Patients ≥ 60 years	0.1 (0.08-0.12)
Shephard (2014)	Nausea	Patients ≥ 60 years	0.1 (0.08-0.12)

Shephard (2014)	Combined bone pain	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Nosebleeds	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Back pain	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Weight loss	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2014)	Rib pain	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2014)	Low haemoglobin	Patients ≥ 60 years	0.17 (0.16-0.19)
Shephard (2014)	Leucopenia	Patients ≥ 60 years	0.3 (0.2-0.3)
Shephard (2014)	Low platelets	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2014)	Raised inflammatory markers	Patients ≥ 60 years	0.2 (0.18-0.22)
Shephard (2014)	Raised creatinine	Patients ≥ 60 years	0.08 (0.08-0.09)
Shephard (2014)	Raised MVC	Patients ≥ 60 years	0.18 (0.16-0.22)
Shephard (2014)	Hypercalcaemia	Patients ≥ 60 years	0.7 (0.5-1)

Abbreviations: CI, confidence interval; FP, False positives; PPV, positive predictive value; TP, True positives; NR, Not reported.

Table 2: Myeloma: Positive predictive value of symptom combinations for myeloma in patients aged > 14-15 years

Study	Symptom(s)	Patient group	PPV % (95% CI) for myeloma; prevalence of myeloma
Shephard (2014)	Joint pain and shortness of breath	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Joint pain and chest infection	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Joint pain and chest pain	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Joint pain and fracture	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Joint pain and nausea	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Joint pain and combined bone pain	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Joint pain and nosebleeds	Patients ≥ 60 years	Non-calculable
Shephard (2014)	Joint pain and back pain	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Joint pain and	Patients ≥ 60	Non-calculable

	weight loss	years	
Shephard (2014)	Joint pain and rib pain	Patients ≥ 60 years	0.7 (NR)
Shephard (2014)	Shortness of breath and chest infection	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Shortness of breath and chest pain	Patients ≥ 60 years	0.1 (0.05-0.1)
Shephard (2014)	Shortness of breath and fracture	Patients ≥ 60 years	0.1 (0.1-0.3)
Shephard (2014)	Shortness of breath and nausea	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Shortness of breath and combined bone pain	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2014)	Shortness of breath and nosebleeds	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Shortness of breath and back pain	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Shortness of breath and weight loss	Patients ≥ 60 years	0.1 (0.1-0.3)
Shephard (2014)	Shortness of breath and rib pain	Patients ≥ 60 years	0.2 (NR)
Shephard (2014)	Chest infection and chest pain	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2014)	Chest infection and fracture	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2014)	Chest infection and nausea	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Chest infection and combined bone pain	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Chest infection and nosebleeds	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Chest infection and back pain	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2014)	Chest infection and weight loss	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Chest infection and rib pain	Patients ≥ 60 years	0.2 (NR)
Shephard (2014)	Chest pain and fracture	Patients ≥ 60 years	0.3 (0.2-0.6)

Shephard (2014)	Chest pain and nausea	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2014)	Chest pain and combined bone pain	Patients ≥ 60 years	0.2 (0.1-0.4)
Shephard (2014)	Chest pain and nosebleeds	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Chest pain and back pain	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2014)	Chest pain and weight loss	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Chest pain and rib pain	Patients ≥ 60 years	0.9 (NR)
Shephard (2014)	Fracture and nausea	Patients ≥ 60 years	0.2 (0.1-0.4)
Shephard (2014)	Fracture and combined bone pain	Patients ≥ 60 years	0.8 (NR)
Shephard (2014)	Fracture and nosebleeds	Patients ≥ 60 years	Non-calculable
Shephard (2014)	Fracture and back pain	Patients ≥ 60 years	0.5 (0.3-0.9)
Shephard (2014)	Fracture and weight loss	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Fracture and rib pain	Patients ≥ 60 years	0.7 (NR)
Shephard (2014)	Nausea and combined bone pain	Patients ≥ 60 years	0.6 (NR)
Shephard (2014)	Nausea and nosebleeds	Patients ≥ 60 years	Non-calculable
Shephard (2014)	Nausea and back pain	Patients ≥ 60 years	0.4 (0.2-0.6)
Shephard (2014)	Nausea and weight loss	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Nausea and rib pain	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Combined bone pain and nosebleeds	Patients ≥ 60 years	Non-calculable
Shephard (2014)	Combined bone pain and back pain	Patients ≥ 60 years	0.5 (0.3-0.8)
Shephard (2014)	Combined bone pain and weight loss	Patients ≥ 60 years	Non-calculable
Shephard (2014)	Combined bone pain and rib pain	Patients ≥ 60 years	0.5 (NR)
Shephard (2014)	Nosebleeds and back pain	Patients ≥ 60 years	1.5 (NR)

Shephard (2014)	Nosebleeds and weight loss	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Nosebleeds and rib pain	Patients ≥ 60 years	Non-calculable
Shephard (2014)	Back pain and weight loss	Patients ≥ 60 years	0.5 (NR)
Shephard (2014)	Back pain and rib pain	Patients ≥ 60 years	1.1 (NR)
Shephard (2014)	Weight loss and rib pain	Patients ≥ 60 years	Non-calculable
Shephard (2014)	Back pain first episode and low haemoglobin	Patients ≥ 60 years	0.5 (0.4-0.7)
Shephard (2014)	Back pain first episode and leucopenia	Patients ≥ 60 years	0.6 (0.4-1.2)
Shephard (2014)	Back pain first episode and low platelets	Patients ≥ 60 years	0.7 (0.4-1.3)
Shephard (2014)	Back pain first episode and raised inflammatory markers	Patients ≥ 60 years	0.6 (0.4-0.7)
Shephard (2014)	Back pain first episode and raised creatinine	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2014)	Back pain first episode and raised MCV	Patients ≥ 60 years	0.4 (0.3-0.6)
Shephard (2014)	Back pain first episode and hypercalcaemia	Patients ≥ 60 years	4 (NR)
Shephard (2014)	Back pain second episode and low haemoglobin	Patients ≥ 60 years	0.9 (0.6-1.3)
Shephard (2014)	Back pain second episode and leucopenia	Patients ≥ 60 years	2 (NR)
Shephard (2014)	Back pain second episode and low platelets	Patients ≥ 60 years	0.7 (NR)
Shephard (2014)	Back pain second episode and raised inflammatory markers	Patients ≥ 60 years	1.1 (0.7-1.6)
Shephard (2014)	Back pain	Patients ≥ 60	0.5 (0.3-0.7)

	second episode and raised creatinine	years	
Shephard (2014)	Back pain second episode and raised MCV	Patients ≥ 60 years	0.8 (0.4-1.6)
Shephard (2014)	Back pain second episode and hypercalcaemia	Patients ≥ 60 years	>10 (NR)
Shephard (2014)	Shortness of breath and low haemoglobin	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2014)	Shortness of breath and leucopenia	Patients ≥ 60 years	0.3 (0.2-0.6)
Shephard (2014)	Shortness of breath and low platelets	Patients ≥ 60 years	0.3 (0.1-0.5)
Shephard (2014)	Shortness of breath and raised inflammatory markers	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2014)	Shortness of breath and raised creatinine	Patients ≥ 60 years	0.1 (0.07-0.11)
Shephard (2014)	Shortness of breath and raised MCV	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2014)	Shortness of breath and hypercalcaemia	Patients ≥ 60 years	1.5 (NR)
Shephard (2014)	Chest pain and low haemoglobin	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2014)	Chest pain and leucopenia	Patients ≥ 60 years	0.3 (0.1-0.6)
Shephard (2014)	Chest pain and low platelets	Patients ≥ 60 years	0.3 (0.2-0.6)
Shephard (2014)	Chest pain and raised inflammatory markers	Patients ≥ 60 years	0.5 (0.3-0.6)
Shephard (2014)	Chest pain and raised creatinine	Patients ≥ 60 years	0.2 (0.1-0.2)
Shephard (2014)	Chest pain and raised MCV	Patients ≥ 60 years	0.3 (0.2-0.6)
Shephard (2014)	Chest pain and	Patients ≥ 60	1.9 (NR)

	hypercalcaemia	years	
Shephard (2014)	Chest infection and low haemoglobin	Patients ≥ 60 years	0.2 (0.2-0.3)
Shephard (2014)	Chest infection and leucopenia	Patients ≥ 60 years	0.3 (0.1-0.5)
Shephard (2014)	Chest infection and low platelets	Patients ≥ 60 years	0.2 (0.1-0.4)
Shephard (2014)	Chest infection and raised inflammatory markers	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2014)	Chest infection and raised creatinine	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Chest infection and raised MCV	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2014)	Chest infection and hypercalcaemia	Patients ≥ 60 years	2 (NR)
Shephard (2014)	Nosebleeds and low haemoglobin	Patients ≥ 60 years	0.4 (0.2-0.8)
Shephard (2014)	Nosebleeds and leucopenia	Patients ≥ 60 years	> 10 (NR)
Shephard (2014)	Nosebleeds and low platelets	Patients ≥ 60 years	1.2 (NR)
Shephard (2014)	Nosebleeds and raised inflammatory markers	Patients ≥ 60 years	0.9 (NR)
Shephard (2014)	Nosebleeds and raised creatinine	Patients ≥ 60 years	0.2 (0.1-0.4)
Shephard (2014)	Nosebleeds and raised MCV	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Nosebleeds and hypercalcaemia	Patients ≥ 60 years	NR
Shephard (2014)	Fracture and low haemoglobin	Patients ≥ 60 years	0.3 (0.2-0.4)
Shephard (2014)	Fracture and leucopenia	Patients ≥ 60 years	> 10 (NR)
Shephard (2014)	Fracture and low platelets	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Fracture and raised inflammatory markers	Patients ≥ 60 years	0.4 (0.2-0.6)
Shephard (2014)	Fracture and	Patients ≥ 60	0.2 (0.1-0.4)

	raised creatinine	years	
Shephard (2014)	Fracture and raised MCV	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Fracture and hypercalcaemia	Patients ≥ 60 years	> 10 (NR)
Shephard (2014)	Nausea and low haemoglobin	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2014)	Nausea and leucopenia	Patients ≥ 60 years	0.4 (NR)
Shephard (2014)	Nausea and low platelets	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Nausea and raised inflammatory markers	Patients ≥ 60 years	0.3 (0.2-0.5)
Shephard (2014)	Nausea and raised creatinine	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2014)	Nausea and raised MCV	Patients ≥ 60 years	0.3 (0.2-0.7)
Shephard (2014)	Nausea and hypercalcaemia	Patients ≥ 60 years	1 (NR)
Shephard (2014)	Combined bone pain and low haemoglobin	Patients ≥ 60 years	0.5 (0.3-1)
Shephard (2014)	Combined bone pain and leucopenia	Patients ≥ 60 years	> 5 (NR)
Shephard (2014)	Combined bone pain and low platelets	Patients ≥ 60 years	0.1 (NR)
Shephard (2014)	Combined bone pain and raised inflammatory markers	Patients ≥ 60 years	0.5 (0.3-0.9)
Shephard (2014)	Combined bone pain and raised creatinine	Patients ≥ 60 years	0.2 (0.1-0.4)
Shephard (2014)	Combined bone pain and raised MCV	Patients ≥ 60 years	0.5 (NR)
Shephard (2014)	Combined bone pain and hypercalcaemia	Patients ≥ 60 years	1.4 (NR)
Shephard (2014)	Joint pain and low haemoglobin	Patients ≥ 60 years	0.2 (0.1-0.3)
Shephard (2014)	Joint pain and leucopenia	Patients ≥ 60 years	0.3 (NR)
Shephard (2014)	Joint pain and	Patients ≥ 60	0.2 (NR)

	low platelets	years	
Shephard (2014)	Joint pain and raised inflammatory markers	Patients ≥ 60 years	0.1 (0.1-0.2)
Shephard (2014)	Joint pain and raised creatinine	Patients ≥ 60 years	0.1 (0.05-0.13)
Shephard (2014)	Joint pain and raised MCV	Patients ≥ 60 years	0.2 (NR)
Shephard (2014)	Joint pain and hypercalcaemia	Patients ≥ 60 years	> 10 (NR)
Shephard (2014)	Rib pain and low haemoglobin	Patients ≥ 60 years	0.9 (NR)
Shephard (2014)	Rib pain and leucopenia	Patients ≥ 60 years	0.5 (NR)
Shephard (2014)	Rib pain and low platelets	Patients ≥ 60 years	NR
Shephard (2014)	Rib pain and raised inflammatory markers	Patients ≥ 60 years	0.4 (0.2-0.8)
Shephard (2014)	Rib pain and raised creatinine	Patients ≥ 60 years	0.8 (NR)
Shephard (2014)	Rib pain and raised MCV	Patients ≥ 60 years	1.1 (NR)
Shephard (2014)	Rib pain and hypercalcaemia	Patients ≥ 60 years	> 10 (NR)
Shephard (2014)	Weight loss and low haemoglobin	Patients ≥ 60 years	0.4 (0.?-0.7)
Shephard (2014)	Weight loss and leucopenia	Patients ≥ 60 years	0.5 (NR)
Shephard (2014)	Weight loss and low platelets	Patients ≥ 60 years	0.5 (NR)
Shephard (2014)	Weight loss and raised inflammatory markers	Patients ≥ 60 years	0.6 (0.3-1.1)
Shephard (2014)	Weight loss and raised creatinine	Patients ≥ 60 years	0.5 (NR)
Shephard (2014)	Weight loss and raised MCV	Patients ≥ 60 years	0.6 (NR)
Shephard (2014)	Weight loss and hypercalcaemia	Patients ≥ 60 years	0.5 (NR)

Abbreviations: CI, confidence interval; FP, False positives; PPV, positive predictive value; TP, True positives, NR, Not reported. Shepard (2014) reports that PPVs were not calculated if < 5 cases had the feature(s) and CIs were omitted where < 10 cases or controls had the combined features.

Evidence statements:

The positive predictive values for myeloma of single symptoms presenting in a primary care setting ranged from 0% (for 'acute low back pain') to 0.7% (for hypercalcaemia in patients aged ≥ 60 years; 3 studies, N = 17798). The studies were subject to 1-3 bias or applicability concerns (See also Table 1).

The positive predictive values for myeloma of symptom pairs presenting in a primary care setting ranged from 0.1% (for raised creatinine with 'shortness of breath'/ chest infection / joint pain, and for joint pain with 'raised inflammatory markers'/back pain/ 'combined bone pain'/ nausea/fracture/chest pain/ 'shortness of breath', and for 'shortness of breath' with chest infection / chest pain/ fracture/ nausea/ nosebleeds/ back pain/ weight loss, and for chest infection with nosebleeds/nausea, and for chest pain with weight loss; all in patients aged ≥ 60 years) to $> 10\%$ (for hypercalcaemia with 'back pain second episode'/ fracture / joint pain/rib pain, and for leucopenia with nosebleeds/fracture; all in patients aged ≥ 60 years; 1 study, N = 14860). The study was subject to 1 bias concern (see also Table 2).

Evidence tables

Deyo (1988)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive? patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 1975, mean (SD; range) age = 39.5 (15.4; 15-86) years, 62% females. 54% of the patients were seeking medical care for back pain for the first time and 76% of the patients had had back pain for < 3 months. 3% had a history of back pain surgery. Maximal back pain in the low back (84%) or in the upper back (16%).</p> <p><u>Inclusion criteria:</u> Patients who sought treatment between March 1982 and September 1984 in the walk-in clinic of a public hospital where virtually all patients are self-referred. In each case back pain was part of the chief complaint.</p> <p><u>Exclusion criteria:</u> Neck pain.</p> <p><u>Clinical setting:</u> Walk-in clinic of a public hospital; this clinic is a source of primary care for indigent persons in a county in the USA with a population of approximately 1 million.</p>
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	Back pain; not further specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	The reference standard consisted of a search on each patient name in the institutional tumour registry ≥ 6 months after the index visit. The registry included every patient with a histological diagnosis of cancer made in the authors' hospital system regardless of site of care. The authors point out that "while this method might fail to identify cancer patients who sought care elsewhere, it is likely that most patients sought follow-up for a particular illness at the same facility.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	It is a concern that some patients with cancer might have been missed due to the choice of reference standard because this would result in an underestimation of the positive predictive value. 38/1975 patients were found in the tumour registry. Of those 38, 13 patients had tumours that were probable causes of back pain, and 4 of these 13 patients already had a diagnosis of cancer at presentation. The 9/1975 patients who had undiagnosed cancer that the back pain could be attributed to had: Lymphoma (NOS; 2), cancer of unknown primary (1), prostate cancer (1), retroperitoneal liposarcoma (1), lung cancer (1), renal cell (1), multiple myeloma (1), mucinous adenocarcinoma (of gallbladder?; 1)
Shephard (2014)	
PATIENT SELECTION	
A. risk of bias	

Patient sampling	Matched case-control study using patients in the UK's Clinical Practice Research Database (CPRD).	
Was a consecutive or random sample of patients enrolled?	No	
Was a case-control design avoided?	No	
Did the study avoid inappropriate exclusions?	Yes	
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes	
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes	
Could the selection of patients have introduced bias?	High risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p><u>Cases:</u> N = 2703, 1449 males/ 1254 females, median age at diagnosis = 73 (IQR = 64-80) years; median number of consultations in the year before diagnosis = 16 (IQR = 10-25); UK.</p> <p><u>Controls:</u> N = 12157; 6359 males/ 5798 females; median age at matched-case diagnosis = 73 (IQR = 65-80) years median number of consultations in the year before diagnosis = 8 (IQR = 4-14); UK.</p> <p><u>Inclusion criteria:</u> Cases: Patients aged ≥ 40 years with one of 23 myeloma diagnostic codes in the CPRD between January 2000 and December 2009, with min. 1 year of data before diagnosis. The first instance of a myeloma cancer code was assigned the data of diagnosis/index date. Controls: Up to 5 controls per case, matched on sex, general practice, and to 1 year of age of the case. The index date was the index date of the matched case.</p> <p><u>Exclusion criteria:</u> Any case or control with less than 1 year of data before the index date; cases without controls; controls with myeloma; controls with only one line consisting of incomplete data (suggestion they had not sought medical care after registration).</p> <p><u>Clinical setting:</u> UK primary care</p>	
Are there concerns that the included patients and setting do not match the review question?	Low concern	
INDEX TEST		
A. Risk of bias		
Index test	<p>“Symptoms, diseases and abnormal investigations reported in the myeloma literature and from patient online support groups were studied”. “The GPRD contains over 100,000 medical codes; several codes can potentially be associated with each feature. A symptom library of codes was compiled for each feature. Occurrences of features were identified in the year before the index date. Only those features present in $\geq 2\%$ of cases or controls were retained (this was invariably cases).” “Abnormal investigation results were defined as the patient having a test value falling outside their local laboratory’s normal range. Patients with a normal laboratory result were grouped with those who had not been tested.” “Some tests were grouped together. The raised inflammatory markers variable was a composite of any</p>	

	of abnormal erythrocyte sedimentation rate, plasma viscosity, or C-reactive protein, as different local laboratories had local preferences for the inflammatory marker of choice; similarly abnormal liver function tests reflected a raised value of any of the hepatic enzymes reported by each laboratory. In clinical practice, haemoglobin, white cell count and platelets are normally requested together ('the full blood count'). We used these slightly differently in our analyses; for the multivariable analyses, a composite variable 'cytopenia' was deemed to be positive if any of the haemoglobin, white cell count or platelets was abnormally low; for positive predictive values (see below) the three different cell types were analysed separately. Bone pain codes often had an anatomical descriptor as well as the words 'bone pain'. We retained 'rib pain', 'back pain' and 'joint pain' as separate entities; remaining bone pain codes, such as 'tibial pain' were merged with the generic 'bone pain' code, making a group we called 'combined bone pain'.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
<u>A. risk of bias</u>	
Reference standard(s)	One of 23 myeloma diagnostic codes in the CPRD.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
<u>A. risk of bias</u>	
Flow and timing	A total of 16233 patients were identified, 13503 controls and 2730 cases. After the exclusion criteria were applied there were 12157 controls and 2703 cases.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

NOTES	62 symptoms and 22 abnormal test results were considered initially.	
Suarez-Almazor (1997)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective consecutive patient series	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 1550, of whom N = 331 had chronic (> 3 months?) back pain, N = 963 had acute (< 3 months) low back pain, and N = 256 had back pain of unspecified duration. Of the patients with acute low back pain, 442 were males, and it appears that the mean (SD) age = 42.2 (15.6) years for the patients with acute low back pain, 14/963 had a history of cancer</p> <p><u>Inclusion criteria:</u> All patients aged ≥ 18 years presenting to four family clinics in Edmonton (Alberta, Canada) between January 1 1992 and December 31 1993 with low back pain or leg pain compatible with sciatic pain for which no visit had been made within the past 12 months.</p> <p><u>Exclusion criteria:</u> Low back pain attributable to visceral pain (e.g., urinary infection, inflammatory pelvic disease), previous diagnosis of ankylosing spondylitis, pregnancy.</p> <p><u>Clinical setting:</u> Four family clinics in Edmonton (Alberta, Canada), two of which are university-affiliated and hospital-based, with the other two based in the community.</p>	
Are there concerns that the included patients and setting do not match the review question?	Unclear concern	
INDEX TEST		
A. Risk of bias		
Index test	Acute (< 3 months) low back pain; not further specified.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Follow up consisting of chart review after a minimum of 2 years. Patients were considered to have cancer if recorded in the physician notes or in reports from laboratory or diagnostic tests.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)	

Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	The results are only presented for the patients with acute low back pain.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	13/963 patients with acute low back pain had active cancer. 3 of those 13 patients had the cancer diagnosis prior to the index visit; 3/13 patients had tumours that were probable causes of the acute low back pain (spinal infiltrates from multiple myeloma [2] and metastatic bone disease with compression fractures [1]), and 10/13 patients had cancer that was not considered to have caused the acute low back pain (bladder cancer [3], colon [1], breast [1], thyroid [1], lung [1], prostate [1], endometrium [1], oesophagus [1]). However, as it is not reported which of these patients already had a diagnosis of cancer pre-index visit, it is not possible to present the data accurately for the individual cancers.

References

Included studies

Deyo, R. A. and Diehl, A. K. Cancer as a cause of back pain: Frequency, clinical presentation, and diagnostic strategies. *Journal of General Internal Medicine* 3, 230-238. 1-11-1988.

Shephard, E.A., Neal, R.D., Rose, P., Walter, F.M., Litt, E.J., Hamilton, W.T. Quantifying the risk of myeloma from symptoms reported in primary care patients: A large case-control study using electronic records. In press. *British Journal of General Practice*.

Suarez-Almazor, M. E., Belseck, E., Russell, A. S., and Mackel, J. V. Use of lumbar radiographs for the early diagnosis of low back pain. Proposed guidelines would increase utilization. *JAMA* 277[22], 1782-1786. 11-6-1997.

Excluded studies (with exclusion reason)

Abel, G. A., Friese, C. R., Magazu, L. S., Richardson, L. C., Fernandez, M. E., De Zengotita, J. J. & Earle, C. C. (2008) Delays in referral and diagnosis for chronic hematologic malignancies: A literature review. *Leukemia & Lymphoma*, 49: 1352-1359.

Exclusion reason : expert review

Abel, G. A., Friese, C. R., Neville, B. A., Wilson, K. M., Hastings, B. T., Earle, C. C., Keating, N. L. & Richardson, L. C. (2012) Referrals for suspected hematologic malignancy: A survey of primary care physicians. *American Journal of Hematology*, 87: 634-636.

Exclusion reason : expert review

Adam, Z., Bednarik, J., Neunauer, J., Chaloupka, R., Vorlicek, J., Vanicek, J., Pour, L., Cermakova, Z., Weinreb, M., Scudla, V., Maisnar, V., Straub, J., Schutzova, M. & Gregora, E. (1999) Recommended diagnostic steps for general practitioners attending patients with difficulties that could indicate multiple myeloma. [Czech]. *Prakticky Lekar*, 86: 25.

Exclusion reason : expert review

Adam, Z., Bednarik, J., Neubauer, J., Chaloupka, R., Fojtik, Z., Vanicek, J., Pour, L., Cermakova, Z., Scudla, V., Maisnar, V., Straub, J., Schutzova, M., Gregora, E., Weinreb, M., Stuchlikova, K., Stanicek, J., Hajek, R., Krejci, M., Vorlicek, J. & Czech Myeloma Society (2006) [Recommendations for early identification of damage to the skeleton by malignant processes, and for early diagnosis of multiple myeloma]. [Czech]. *Vnitřní Lekarství*, 52: Suppl-31.

Exclusion reason : expert review

Alvarez-Cordoves, M. M., Mirpuri-Mirpuri, P. G. & Perez-Monje, A. (2013) [Diagnosis of multiple myeloma in primary care. Suspicion with an appropriate clinical history]. [Spanish]. *Semergen Sociedad Espanola de Medicina Rural y Generalista*, 39: e21-e24.

Exclusion reason : Narrative review

American Academy of Family Physicians (2008) Information from your family doctor. Multiple myeloma: what you should know. *American Family Physician*, 78: 860.

Exclusion reason : expert review

Antunes, N. L. (2001) The spectrum of neurologic disease in children with systemic cancer. *Pediatric Neurology*, 25: 227-235.

Exclusion reason : population not in PICO

Artz, A. S. & Thirman, M. J. (2011) Unexplained anemia predominates despite an intensive evaluation in a racially diverse cohort of older adults from a referral anemia clinic. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences*, 66: 925-932.

Exclusion reason : population not in PICO

Behdad, A., Ross, C. W., Jacques, J., Kota, U., Brown, N. A., Keren, D. & Stoolman, L. (2013) Utility of 9-color, 11-parameter flow cytometry for detection of plasma cell neoplasms: A comparison with bone marrow morphologic findings and concurrent M-protein studies in serum and urine. *Blood*, 122.

Exclusion reason : Not in PICO

Berrady, R., Baybay, H., Khammar, Z., Lahlou, M., Lamchacht, L., Gallouj, S., El, H. A., Mernissi, F.-Z. & Bono, W. (2012) Acquired ichthyosis and haematological malignancies: Five cases. [French]. *Annales de Dermatologie et de Venereologie*, 139: January.

Exclusion reason : population not in PICO

Bianchi, G., Richardson, P. G. & Anderson, K. C. (2014) Best Treatment Strategies in High-Risk Multiple Myeloma: Navigating a Gray Area. *Journal of Clinical Oncology*, 32: 2125-2132.

Exclusion reason : Not in PICO

Buchner-Daley, L., Brady-West, D. & McGrowder, D. (2012) Clinical and Biochemical Profile of Monoclonal Gammopathies in Caribbean Patients in a Resource-limited Setting. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 13: 6501-6504.

Exclusion reason : population not in PICO

Burnand, J., Waeber, G. & Duchosal, M. A. (2010) [Hematological malignancy: management of anemia and leukopenia by primary care physicians]. [French]. *Revue Medicale Suisse*, 5: 2147-2148.

Exclusion reason : expert review

Chan, D. T., Craig, K., Donovan, K. & Phillips, A. (2006) Myeloma renal disease: presentation and outcome. *Nephron*, 104: c126-c131.

Exclusion reason : population not in PICO

Charakidis, M. & Russell, D. J. (2010) Spontaneous splenic rupture in Waldenström's macroglobulinemia: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 4: 300.

Exclusion reason : case report

Chua, T. & Hyder, A. (2010) Gastrointestinal histoplasmosis and the role of narrow band imaging. *American Journal of Gastroenterology*. Conference: 75th Annual Scientific Meeting of the American College of Gastroenterology San Antonio, TX United States. Conference Start: 20101015 Conference End: 20101020. Conference Publication: (var.pagings), 105: October.

Exclusion reason : case report

Clark, P. & Wroblewski, T. (2011) Unexpected MRI findings in a 24 year-old male with newly diagnosed acute lymphoblastic leukemia with hip pain. *Journal of General Internal Medicine*. Conference: 34th Annual Meeting of the Society of General Internal Medicine Phoenix, AZ United States. Conference Start: 20110504 Conference End: 20110507. Conference Publication: (var.pagings), 26: May.

Exclusion reason : case report

Cohen, Y., Gutwein, O., Garach-Jehoshua, O., Bar-Haim, A. & Kornberg, A. (2013) GPRC5D is a promising marker for monitoring the tumor load and to target multiple myeloma cells. *Hematology*, 18: 348-351.

Exclusion reason : Not in PICO

Dharmarajan, T. S. & Thadisina, S. (2011) Anemia in the old: Possible indicator of serious underlying disease, warrants evaluation. S. Thadisina MD, RO Russell MD, TS Dharmarajan MD, AGSF Montefiore Medical Center (North), Bronx, NY. *Journal of the American Geriatrics Society*. Conference: 2011 Annual Scientific Meeting of the American Geriatrics Society National Harbor, MD United States. Conference Start: 20110511 Conference End: 20110514. Conference Publication: (var.pagings), 59: April.

Exclusion reason : case report

dos Santos, V. M., Brito, E. F. O., Paz, B. C. S. & Leal, C. T. (2012) Rib Plasmacytoma and IgA Multiple Myeloma with Hyperviscosity Syndrome. *Archives of Iranian Medicine*, 15: 517-519.

Exclusion reason : case report

Dvorak, C. (2006) Common complaints, difficult diagnosis: Multiple myeloma. [References]. *Journal of the American Academy of Nurse Practitioners*, 18: 190-194.

Exclusion reason : case report

Edgren, G., Bagnardi, V., Bellocco, R., Hjalgrim, H., Rostgaard, K., Melbye, M., Reilly, M., Adami, H. O., Hall, P. & Nyren, O. (2010) Pattern of declining hemoglobin concentration before cancer diagnosis. *International Journal of Cancer*, 127: 1429-1436.

Exclusion reason : population not in PICO

El, S. U., Hassan, T., Besheer, M., El, B. R., El, G. K. & Morad, M. H. (2009) Skeletal manifestations in children with different hematological diseases and hematological malignancies at Zagazig university hospital [retrospective study from 1998 to 2008]. *Haematologica*. Conference: 14th Congress of the European Hematology Association Berlin Germany. Conference Start: 20090604 Conference End: 20090607. Conference Publication: (var.pagings), 94: June.

Exclusion reason : population not in PICO

Engelhardt, M., Terpos, E., Kleber, M., Gay, F., Wasch, R., Morgan, G., Cavo, M., van de Donk, N., Beilhack, A., Bruno, B., Johnsen, H. E., Hajek, R., Driessen, C., Ludwig, H., Beksac, M., Boccadoro, M., Straka, C., Brighen, S., Gramatzki, M., Larocca, A., Lokhorst, H., Magarotto, V., Morabito, F., Dimopoulos, M. A., Einsele, H., Sonneveld, P. & Palumbo, A. (2014) European Myeloma Network recommendations on the evaluation and treatment of newly diagnosed patients with multiple myeloma. *Haematologica*, 99: 232-242.

Exclusion reason : Not in PICO

Eslick, R. & Talaulikar, D. (2013) Multiple myeloma: from diagnosis to treatment. *Australian Family Physician*, 42: 684-688.

Exclusion reason : Narrative review

Fadul, N. A., El Osta, B., Dalal, S., Poulter, V. A. & Bruera, E. (2008) Comparison of symptom burden among patients referred to palliative care with hematologic malignancies versus those with solid tumors. [References]. *Journal of Palliative Medicine*, 11: 422-427.

Exclusion reason : population not in PICO

Faiman, B. (2007) Clinical updates and nursing considerations for patients with multiple myeloma. [Review] [52 refs]. *Clinical Journal of Oncology Nursing*, 11: 831-840.

Exclusion reason : expert review

- Foran, J. M. & Shammo, J. M. (2012) Clinical presentation, diagnosis, and prognosis of myelodysplastic syndromes. [Review]. *American Journal of Medicine*, 125: Suppl-13.
Exclusion reason : expert review
- Friese, C. R., Abel, G. A., Magazu, L. S., Neville, B. A., Richardson, L. C. & Earle, C. C. (2009) Diagnostic delay and complications for older adults with multiple myeloma. *Leukemia & Lymphoma*, 50: 392-400.
Exclusion reason : cases only
- Fujimi, A., Hashimoto, A., Kanisawa, Y., Okuda, T., Minami, S., Doi, T., Matsuno, T., Ishikawa, K. & Uemura, N. (2013) Loss of CD23 expression after bortezomib plus dexamethasone therapy in CCND1/IGH-positive multiple myeloma. *Rinsho Ketsueki - Japanese Journal of Clinical Hematology*, 54: 224-228.
Exclusion reason : case report
- Galhotra, R., Saggar, K., Gupta, K. & Singh, P. (2012) Primary isolated extramedullary plasmacytoma of mesentery: A rare case report. *The gulf journal of oncology*, 1: 81-84.
Exclusion reason : case report
- George, E. D. & Sadovsky, R. (1999) Multiple myeloma: recognition and management. [Review] [31 refs]. *American Family Physician*, 59: 1885-1894.
Exclusion reason : expert review
- Guyen, G. S., Uzun, O., Cakir, B., Akova, M. & Unal, S. (2006) Infectious complications in patients with hematological malignancies consulted by the Infectious Diseases team: a retrospective cohort study (1997-2001). *Supportive Care in Cancer*, 14: 52-55.
Exclusion reason : population not in PICO
- Hepguler, S. (2011) Differential diagnosis of low back pain. *Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi*.Conference: 23rd National Physical Medicine and Rehabilitation Congress Antalya Turkey.Conference Start: 20110511 Conference End: 20110515.Conference Publication: (var.pagings), 57: 2011.
Exclusion reason : expert review
- Heringer, L. & Crevensten, H. (2010) Recurrent paralysis due to hyperthyroidism causing hypokalemia. *Journal of General Internal Medicine*.Conference: 33rd Annual Meeting of the Society of General Internal Medicine Minneapolis, MN United States.Conference Start: 20100428 Conference End: 20100501.Conference Publication: (var.pagings), 25: June.
Exclusion reason : case report
- Howell, D. A., Smith, A. G., Jack, A., Patmore, R., Macleod, U., Mironska, E. & Roman, E. (2013) Time-to-diagnosis and symptoms of myeloma, lymphomas and leukaemias: a report from the Haematological Malignancy Research Network. *BMC Hematology*, 13: 9.
Exclusion reason : Not in PICO
- Jahanmir, J. (2012) First report of hemialgia as a presenting symptom in multiple myeloma. *Journal of Hospital Medicine*.Conference: 2012 Annual Meeting of the Society of Hospital Medicine, SHM 2012 San Diego, CA United States.Conference Start: 20120401 Conference End: 20120404.Conference Publication: (var.pagings), 7: March.
Exclusion reason : case report
- Kapoor, J., Trinidad, A., Mochloulis, G. & Mohamid, W. (2012) Plasmacytoma of the atlas presenting as hoarseness: a rare cause of unilateral vocal fold palsy. *Journal of Laryngology & Otology*, 126: 870-872.
Exclusion reason : case report
- Kariyawasan, C. C., Hughes, D. A., Jayatilake, M. M. & Mehta, A. B. (2007) Multiple myeloma: causes and consequences of delay in diagnosis. *QJM*, 100: 635-640.
Exclusion reason : cases only
- Karwicki, L., Kmiecik, M. & Kopka, M. (2003) Surgical treatment of metastatic tumors to long bones in the material of the Unit. *Ortopedia Traumatologia Rehabilitacja*, 5: 358-363.
Exclusion reason : population not in PICO

- Kelly, M. B., Meenaghan, T. & Dowling, M. (2010) Myeloma: making sense of a complex blood cancer. *British Journal of Nursing*, 19: 1415-1421.
Exclusion reason : expert review
- Krych, M. (2005) [Acute renal failure]. [Review] [33 refs] [German]. *Internist*, 46: 30-38.
Exclusion reason : expert review
- Li, N., Lv, Y., Zeng, H., He, F., Yao, Y. & He, X. (2012) Renal impairment in multiple myeloma: presenting features in different departments. *Journal of Huazhong University of Science and Technology. Medical Sciences*, 32: 65-68.
Exclusion reason : population not in PICO
- Magee, C., Vella, J. P., Tormey, W. P. & Walshe, J. J. (1998) Multiple myeloma and renal failure: one center's experience. *Renal Failure*, 20: 597-606.
Exclusion reason : population not in PICO
- Mistry, P. K., Sadan, S., Yang, R., Yee, J. & Yang, M. (2007) Consequences of diagnostic delays in type 1 Gaucher disease: the need for greater awareness among hematologists-oncologists and an opportunity for early diagnosis and intervention. *American Journal of Hematology*, 82: 697-701.
Exclusion reason : population not in PICO
- Mutevelizade, G., Reyhan, M. & Yapar, A. F. (2012) Evaluation skin metastasis with 18FFDG PET/CT. *European Journal of Nuclear Medicine and Molecular Imaging. Conference: 25th Annual Congress of the European Association of Nuclear Medicine, EANM 2012 Milan Italy. Conference Start: 20121027 Conference End: 20121031. Conference Publication: (var.pagings)*, 39: October.
Exclusion reason : population not in PICO
- Nathrath, M. & Teichert, V. L., I (2009) Oncologic causes of bone pain. [German]. *Monatsschrift fur Kinderheilkunde*, 157: July.
Exclusion reason : expert review
- Nau, K. C. & Lewis, W. D. (2008) Multiple myeloma: diagnosis and treatment. [Review] [29 refs]. *American Family Physician*, 78: 853-859.
Exclusion reason : expert review
- Ozer, A. O., Unalacak, M. & Unluoglu, I. (2014) A case of multiple myeloma at a family medicine outpatient clinic. [Turkish]. *Konuralp Tip Dergisi*, 6: 64-66.
Exclusion reason : Not in PICO
- Patriarca, F., Fanin, R., Silvestri, F., Russo, D. & Baccarani, M. (1998) Multiple myeloma: presenting features and survival according to hospital referral. *Eastern Cooperative Study Group on Monoclonal Gammopathies. Leukemia & Lymphoma*, 30: 551-562.
Exclusion reason : population not in PICO
- Phongtankuel, V. & Ward, L. (2011) Oh my aching back! A classic diagnosis of multiple myeloma. *Journal of General Internal Medicine. Conference: 34th Annual Meeting of the Society of General Internal Medicine Phoenix, AZ United States. Conference Start: 20110504 Conference End: 20110507. Conference Publication: (var.pagings)*, 26: May.
Exclusion reason : case report
- Prideaux, S. M., Conway, O. E. & Chevassut, T. J. (2014) - The genetic architecture of multiple myeloma. [Review]. - *Advances in Hematology*, 2014: 864058.
Exclusion reason : Narrative review
- Rajer, M. & Kovac, V. (2008) Malignant spinal cord compression. *Radiology and Oncology*, 42: 01.
Exclusion reason : expert review
- Ramon Rodriguez, L. G., Rivera-Keeling, C., Arencibia-Nunez, A., Avila-Cabrera, O. M., Izquierdo-Cano, L., Espinosa-Estrada, E., Gonzalez-Pinedo, L., Quintero-Sierra, Y., Gutierrez-Diaz, A. & Hernandez-Padron, C. (2013) Clinical and laboratory characterization of multiple myeloma at the Institute of Hematology and Immunology. *Revista Cubana de Hematologia, Inmunologia y Hemoterapia*, 29: 382-397.
Exclusion reason : Not in PICO

- Reisfield, G. M., Paulian, G. D. & Wilson, G. R. (2005) "Johnny can't read": Another cause of failed analgesia. [References]. *American Journal of Hospice & Palliative Medicine*, 22: 433-436.
Exclusion reason : case report
- Rentschler, J., Herrmann, R., Fischer, N., Potthast, S. & Vetter, M. (2011) Lenalidomide in heavily pretreated angioimmunoblastic T-cell lymphoma (AITL). *Journal of Clinical Oncology*.Conference: ASCO Annual Meeting 2011 Chicago, IL United States.Conference Start: 20110603 Conference End: 20110607.Conference Publication: (var.pagings), 29: 20.
Exclusion reason : case report
- Roberts, C. C., Daffner, R. H., Weissman, B. N., Bancroft, L., Bennett, D. L., Blebea, J. S., Bruno, M. A., Fries, I. B., Germano, I. M., Holly, L., Jacobson, J. A., Luchs, J. S., Morrison, W. B., Olson, J. J., Payne, W. K., Resnik, C. S., Schweitzer, M. E., Seeger, L. L., Taljanovic, M., Wise, J. N. & Lutz, S. T. (2010) ACR Appropriateness Criteria on Metastatic Bone Disease. *JACR Journal of the American College of Radiology*, 7: June.
Exclusion reason : expert review
- Romera, M., Heras, I., Castilla, C., Nieto, J. B., Manchado, J. J., Perez-Ceballos, E., Amigo, M. L., Lozano, M. & Vicente, V. (2011) Clinical features and outcome of respiratory syncytial virus infection in 26 haematologic disorders patients. *Bone Marrow Transplantation*.Conference: European Group for Blood and Marrow Transplantation, EBMT 2011 Paris France.Conference Start: 20110403 Conference End: 20110406.Conference Publication: (var.pagings), 46: April.
Exclusion reason : population not in PICO
- Samson, D. (2001) Diagnosis and management of multiple myeloma. *British Journal of Haematology*, 115.
Exclusion reason : expert review
- Scherber, R., Dueck, A. C., Johansson, P., Barbui, T., Barosi, G., Vannucchi, A. M., Passamonti, F., Andreasson, B., Ferarri, M. L., Rambaldi, A., Samuelsson, J., Birgegard, G., Tefferi, A., Harrison, C. N., Radia, D. & Mesa, R. A. (2011) The Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF): international prospective validation and reliability trial in 402 patients. *Blood*, 118: 401-408.
Exclusion reason : population not in PICO
- Sethi, B., Butola, K. S. & Kumar, Y. (2012) A Diagnostic Dilemma: Waldenstrom's Macroglobulinemia/Plasma Cell Leukemia. *Case Reports in Pathology Print*, 2012: 271407.
Exclusion reason : case report
- Shebl, F. M., Warren, J. L., Eggers, P. W. & Engels, E. A. (2012) Cancer risk among elderly persons with end-stage renal disease: A population-based case-control study. *BMC Nephrology*, 13: 65.
Exclusion reason : population not in PICO
- Siddiqui, I., Bhally, H. S., Niaz, Q. & Burney, I. A. (2002) Tumor-induced hypercalcemia: predictors of early mortality. *JPMMA.The Journal of the Pakistan Medical Association*, 52: Aug.
Exclusion reason : population not in PICO
- Silvestris, F., Cafforio, P., Tucci, M. & Dammacco, F. (2002) Negative regulation of erythroblast maturation by Fas-L+/TRAIL+ highly malignant plasma cells: A major pathogenetic mechanism of anemia in multiple myeloma. *Blood*, 99: 15.
Exclusion reason : population not in PICO
- Tandon, N. & Gupta, S. (2014) - Cryptosporidiosis causing severe persistent diarrhea in a patient with multiple myeloma: A Case report and brief review of literature. - *Indian journal of medical and paediatric oncology : official journal of Indian Society of Medical & Paediatric Oncology*, 35: 93-95.
Exclusion reason : Not in PICO
- Teo, W. Y., Chan, M. Y., Ng, K. C. & Tan, A. M. (2012) Bony presentations of childhood haematological malignancy to the emergency room. *Journal of Paediatrics & Child Health*, 48: 311-316.
Exclusion reason : cases only

Tucci, M., Grinello, D., Cafforio, P., Silvestris, F. & Dammacco, F. (2002) Anemia in multiple myeloma: role of deregulated plasma cell apoptosis. [Review] [44 refs]. *Leukemia & Lymphoma*, 43: 1527-1533.

Exclusion reason : population not in PICO

Udiawar, M., Bejnariu, C. & Davies, S. (2012) Metastatic haematological malignancy presenting as a sellar mass. *BMJ Case Reports*, 2012, 2012.

Exclusion reason : case report

Varma, S., Varma, N., Reddy, V., Naseem, S., Bose, P. & Malhotra, P. (2012) Detection of paroxysmal nocturnal hemoglobinuria-phenotype in patients with chronic lymphocytic leukemia and multiple myeloma. *Indian Journal of Pathology and Microbiology*, 55: April-June.

Exclusion reason : population not in PICO

Waldmann, A., Barragan, B., Cursaru, V., Heberlein, C., Hrianka, M., Richter, F. & Sadzuga, R. (2010) Detecting myeloma-ways to shortening an often painful and tedious patient odyssey: Results from an international survey conducted by myeloma euronet, The European network of myeloma patient groups. *Haematologica*.Conference: 15th Congress of the European Hematology Association, EHA 2010 Barcelona Spain.Conference Start: 20100610 Conference End: 20100613.Conference Publication: (var.pagings), 95: June.

Exclusion reason : cases only

Weckmann, M. (2012) Delirium incidence and cause in younger hospitalized patients with advanced cancer. *Journal of Pain and Symptom Management*.Conference: Annual Assembly of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association 2012 Denver, CO United States.Conference Start: 20120307 Conference End: 2012, 43: February.

Exclusion reason : population not in PICO

Zagroda, M., Prystupa, A. & Mosiewicz, J. (2013) Diverse clinical presentation in the course of multiple myeloma. *Family Medicine and Primary Care Review*, 15: 423-425.

Exclusion reason : Not in PICO

Review question:

Which investigations of symptoms of suspected myeloma should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	618	49	08/04/2013
<i>Premedline</i>	1980-2013	39	11	08/04/2013
<i>Embase</i>	1980-2013	636	54	08/04/2013
<i>Cochrane Library</i>	1980-2013	646	3	09/04/2013
<i>Psychinfo</i>	1980-2013	2	0	08/04/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	66	11	09/04/2013

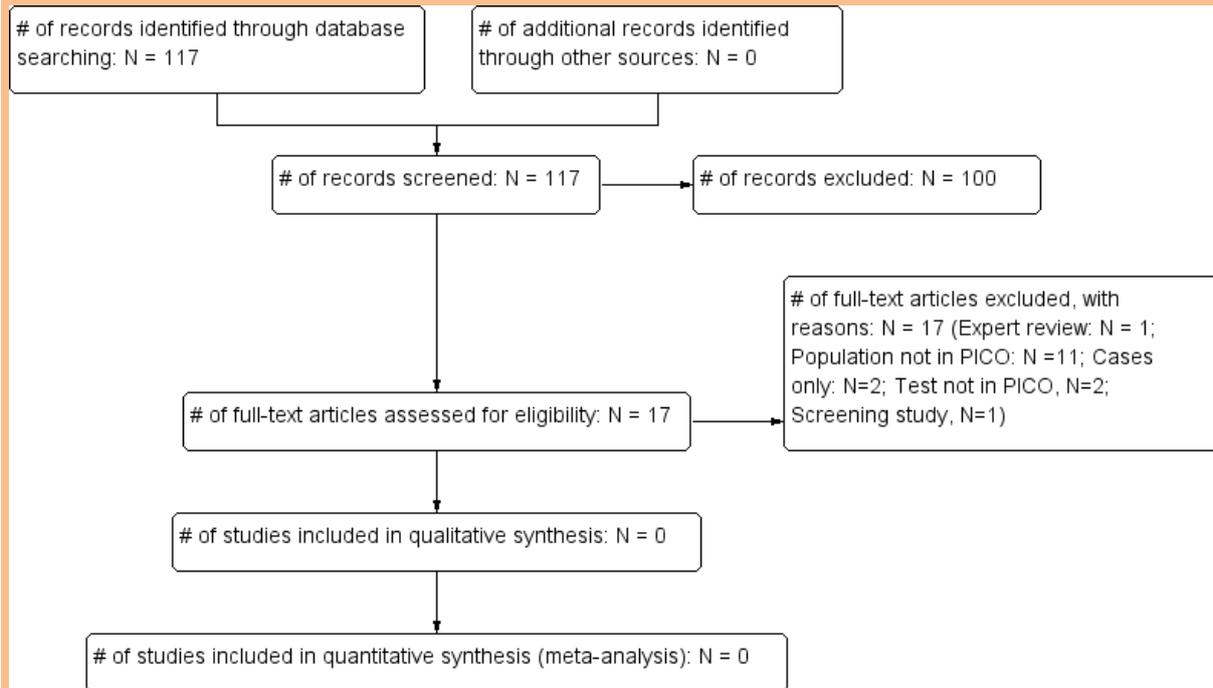
Total References retrieved (after de-duplication): 109

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	4/2013-19/08/2014	15	0	19/08/2014

Premedline	4/2013-19/08/2014	49	5	19/08/2014
Embase	4/2013-19/08/2014	52	4	19/08/2014
Cochrane Library	4/2013-19/08/2014	345	0	19/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	4/2013-19/08/2014	5	1	19/08/2014

Total References retrieved (after de-duplication): 8



Study results

No evidence was identified pertaining to the diagnostic accuracy of paraprotein/serum electrophoresis/Bence-Jones protein tests, ESR, X-ray, viscosity or calcium tests in patients with suspected myeloma cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

(2002) Can blood tests detect cancer early? Health News, 8: 4.

Exclusion reason : expert review

Abadie, J. M. & Bankson, D. D. (2006) Assessment of serum free light chain assays for plasma cell disorder screening in a Veterans Affairs population. Annals of Clinical & Laboratory Science, 36: 157-162.

Exclusion reason : screening study

Abi-Fadel, F., Desai, N. R., Vatandoust, G., Said, R., Gottesman, A. & Terjanian, T. (2010) Monoclonal gammopathy of undetermined significance with amyloid deposition in the lung and non-amyloid eosinophilic deposition in the brain: a case report. *Case Reports in Medicine*, 2010: 406102.

Exclusion reason : case report

Adam, Z., Bednarik, J., Neubauer, J., Chaloupka, R., Fojtik, Z., Vanicek, J., Pour, L., Cermakova, Z., Scudla, V., Maisnar, V., Straub, J., Schutzova, M., Gregora, E., Weinreb, M., Stuchlikova, K., Stanicek, J., Hajek, R., Krejci, M., Vorlicek, J. & Czech Myeloma Society (2006) [Recommendations for early identification of damage to the skeleton by malignant processes, and for early diagnosis of multiple myeloma]. [Czech]. *Vnitřní Lekarství*, 52: Suppl-31.

Exclusion reason : expert review

Adam, Z., Bednarik, J., Neunauer, J., Chaloupka, R., Vorlicek, J., Vanicek, J., Pour, L., Cermakova, Z., Weinreb, M., Scudla, V., Maisnar, V., Straub, J., Schutzova, M. & Gregora, E. (2006) Recommended diagnostic steps for general practitioners attending patients with difficulties that could indicate multiple myeloma. [Czech]. *Praktický Lekar*, 86: 396-410.

Exclusion reason : repeat publication

Adam, Z., Bolcak, K., Stanicek, J., Buchler, T., Pour, L., Krejci, M., Prasek, J., Neubauer, J., Vorlicek, J. & Hajek, R. (2007) Fluorodeoxyglucose positron emission tomography in multiple myeloma, solitary plasmocytoma and monoclonal gammopathy of unknown significance. *Neoplasma*, 54: 536-540.

Exclusion reason : population not in PICO

Ahmad, M. (2007) Continuous ambulatory peritoneal dialysis in patients with renal failure due to multiple myeloma. *International Urology & Nephrology*, 39: 629-633.

Exclusion reason : population not in PICO

Albain, K. S., Unger, J. M., Crowley, J. J., Coltman, C. A., Jr. & Hershman, D. L. (2009) Racial disparities in cancer survival among randomized clinical trials patients of the Southwest Oncology Group. *Journal of the National Cancer Institute*, 101: 984-992.

Exclusion reason : population not in PICO

Almeshhedani, M., Salamat, A. & Al-Ismael, S. (2009) Evaluating the potential use of risk categorisation in the management of MGUS. *Haematologica*, 94: 389-390.

Exclusion reason : population not in PICO

Alvarez-Cordoves, M. M., Mirpuri-Mirpuri, P. G. & Perez-Monje, A. (2013) [Diagnosis of multiple myeloma in primary care. Suspicion with an appropriate clinical history]. [Spanish]. *Semergen Sociedad Espanola de Medicina Rural y Generalista*, 39: e21-e24.

Exclusion reason : Narrative review

Artz, A. S. & Thirman, M. J. (2011) Unexplained anemia predominates despite an intensive evaluation in a racially diverse cohort of older adults from a referral anemia clinic. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences*, 66: 925-932.

Exclusion reason : population not in PICO

Barlogie, B., Epstein, J., Selvanayagam, P. & Alexanian, R. (1989) Plasma cell myeloma--new biological insights and advances in therapy. [Review] [172 refs]. *Blood*, 73: 865-879.

Exclusion reason : expert review

Bassani-Sternberg, M., Barnea, E., Beer, I., Avivi, I., Katz, T. & Admon, A. (2009) Cancer diagnostics based analysis of the serum soluble hla class I peptidome. *European Journal of Immunology*, 39: S609-S610.

Exclusion reason : population not in PICO

Behdad, A., Ross, C. W., Jacques, J., Kota, U., Brown, N. A., Keren, D. & Stoolman, L. (2013) Utility of 9-color, 11-parameter flow cytometry for detection of plasma cell neoplasms: A comparison with bone marrow morphologic findings and concurrent M-protein studies in serum and urine. *Blood*, 122.

Exclusion reason : Not in PICO

Bergesio, F., Ciciani, A. M., Santostefano, M., Brugnano, R., Manganaro, M., Palladini, G., Palma, A. M. D., Gallo, M., Tosi, P. L. & Salvadori, M. (2007) Renal involvement in systemic amyloidosis - An Italian retrospective study on epidemiological and clinical data at diagnosis. *Nephrology Dialysis Transplantation*, 22: 1608-1618.

Exclusion reason : population not in PICO

Bhatnagar, N., Rabin, N., West, P. & Luckit, J. (2010) Detection and referral of serum paraproteins identified by discretionary testing. *British Journal of Haematology*, 149: 79-80.

Exclusion reason : cases only

Bianchi, G., Richardson, P. G. & Anderson, K. C. (2014) Best Treatment Strategies in High-Risk Multiple Myeloma: Navigating a Gray Area. *Journal of Clinical Oncology*, 32: 2125-2132.

Exclusion reason : Not in PICO

Bowden, M., Crawford, J., Cohen, H. J. & Noyama, O. (1993) A comparative study of monoclonal gammopathies and immunoglobulin levels in Japanese and United States elderly.[Erratum appears in *J Am Geriatr Soc* 1993 Jun;41(6):622]. *Journal of the American Geriatrics Society*, 41: 11-14.

Exclusion reason : screening study

Buchner-Daley, L., Brady-West, D. & McGrowder, D. (2012) n, cases only Clinical and Biochemical Profile of Monoclonal Gammopathies in Caribbean Patients in a Resource-limited Setting. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 13: 6501-6504.

Exclusion reason : cases only

Burkhardt, R., Frisch, B. & Kettner, G. (1980) The clinical study of micro-metastatic cancer by bone biopsy. *Bulletin du Cancer*, 67: 291-305.

Exclusion reason : population not in PICO

Chan, D. T., Craig, K., Donovan, K. & Phillips, A. (2006) Myeloma renal disease: presentation and outcome. *Nephron*, 104: c126-c131.

Exclusion reason : population not in PICO

Chang, H., Stewart, A. K., Qi, X. Y., Li, Z. H., Yi, Q. L. & Trudel, S. (2005) Immunohistochemistry accurately predicts FGFR3 aberrant expression and t(4;14) in multiple myeloma. *Blood*, 106: 353-355.

Exclusion reason : test not in PICO

Chennuru, S., Koduri, J. & Baumann, M. A. (2008) Risk factors for symptomatic hypocalcaemia complicating treatment with zoledronic acid. *Internal Medicine Journal*, 38: 635-637.

Exclusion reason : population not in PICO

Chew, S. T., Fitzwilliam, J., Indridason, O. S. & Kovalik, E. C. (1999) Role of urine and serum protein electrophoresis in evaluation of nephrotic-range proteinuria. *American Journal of Kidney Diseases*, 34: 135-139.

Exclusion reason : population not in PICO

He, Y., Wheatley, K., Glasmacher, A., Ross, H., Djulbegovic, B. (2003). Early versus deferred treatment for early stage multiple myeloma. *Cochrane Database of Systematic Reviews*, issue 1.

Exclusion reason : test not in PICO

Cohen, H. J., Crawford, J., Rao, M. K., Pieper, C. F. & Currie, M. S. (1998) Racial differences in the prevalence of monoclonal gammopathy in a community-based sample of the elderly.[Erratum appears in *Am J Med* 1998 Oct;105(4):362]. *American Journal of Medicine*, 104: 439-444.

Exclusion reason : screening study

Cohen, Y., Gutwein, O., Garach-Jehoshua, O., Bar-Haim, A. & Kornberg, A. (2013) GPRC5D is a promising marker for monitoring the tumor load and to target multiple myeloma cells. *Hematology*, 18: 348-351.

Exclusion reason : Not in PICO

Colon-Emeric, C., Yballe, L., Sloane, R., Pieper, C. F. & Lyles, K. W. (2000) Expert physician recommendations and current practice patterns for evaluating and treating men with osteoporotic hip fracture. *Journal of the American Geriatrics Society*, 48: 1261-1263.

Exclusion reason : population not in PICO
Comenzo, R. L. (2009) How I treat amyloidosis. *Blood*, 114: 3147-3157.

Exclusion reason : expert review
Coyne, M. R. E., Wellik, L., Braggio, E., O'Dwyer, M. E., Santocanale, C., Valdez, R., Bergsagel, P. L. & Chesi, M. (2011) Examining measures of proliferation for use in risk stratification of myeloma. *Blood*, 118.

Exclusion reason : expert review
Cronin, C. G., Cashell, T., Mhuirheartaigh, J. N., Swords, R., Murray, M., O'Sullivan, G. J. & O'Keeffe, D. (2009) Bone biopsy of new suspicious bone lesions in patients with primary carcinoma: prevalence and probability of an alternative diagnosis. *AJR.American Journal of Roentgenology*, 193: W407-W410.

Exclusion reason : population not in PICO
Decaux, O., Cuggia, M., Ruelland, A., Cazalets, C., Cador, B., Jago, P. & Grosbois, B. (2006) [Monoclonal gammopathies of undetermined significance and their progression over time. Retrospective study of 190 patients]. [French]. *Presse Medicale*, 35: 1143-1150.

Exclusion reason : population not in PICO
Desport, E., Bridoux, F., Sirac, C., Delbes, S., Bender, S., Fernandez, B., Quellard, N., Lacombe, C., Goujon, J. M., Lavergne, D., Abraham, J., Touchard, G., Femand, J. P. & Jaccard, A. (2012) AL Amyloidosis. *Orphanet Journal of Rare Diseases*, 7.

Exclusion reason : expert review
Dharmarajan, T. S. & Thadisina, S. (2011) Anemia in the old: Possible indicator of serious underlying disease,warrants evaluation. S. Thadisina MD, RO Russell MD, TS Dharmarajan MD, AGSF Montefiore Medical Center (North), Bronx, NY. *Journal of the American Geriatrics Society*, 59: S120.

Exclusion reason : case report
Djunic, I. S., Elezovic, I., Milosevic-Jovcic, N., Ilic, V., Antic, D., Vidovic, A. & Tomin, D. (2009) Acquired von Willebrand syndrome in patients with multiple myeloma. *Journal of Thrombosis and Haemostasis*, 7: 841.

Exclusion reason : population not in PICO
Doyle, A., Soutar, R. & Geddes, C. C. (2009) Multiple myeloma in chronic kidney disease. Utility of discretionary screening using serum electrophoresis. *Nephron*, 111: c7-11.

Exclusion reason : screening study
Doyle, L. M., Gundrum, J. D., Farnen, J. P., Wright, L. J., Kranig, J. A. I. & Go, R. S. (2009) Determining why and which clinicians order serum protein electrophoresis (SPEP), subsequent diagnoses based on indications, and clinical significance of routine follow-up: A study of patients with monoclonal gammopathy of undetermined significance (MGUS). *Blood*, 114.

Exclusion reason : population not in PICO
Dunfack, G., V, Bertaud, G., V, Duvauferrier, R., Bourde, A., Morelli, J. & Lasbleiz, J. (2012) Ontology driven decision support systems for medical diagnosis - an interactive form for consultation in patients with plasma cell disease. *Studies in Health Technology & Informatics*, 180: 108-112.

Exclusion reason : test not in PICO
Durham, B. H., Afify, A., Jess, H., Song, J. Y., Dwyre, D. M. & Chen, M. (2013) Pragmatic algorithm for improving the diagnostic quality of fine needle aspiration cytopathology in the classification of hematolymphoid proliferations. *Laboratory Investigation*, 93: 474A.

Exclusion reason : population not in PICO
Elis, A., Radnay, J., Shapiro, H., Itzhaky, D., Manor, Y. & Lishner, M. (2006) Should bone marrow examination be routinely performed for the diagnosis of monoclonal gammopathy of undetermined significance? *Israel Medical Association Journal: Imaj*, 8: 840-842.

Exclusion reason : population not in PICO
Ferrero, S., Capello, D., Svaldi, M., Boi, M., Gatti, D., Drandi, D., Rossi, D., Barbiero, S., Mantoan, B., Mantella, E., Zanni, M., Ghione, P., Larocca, A., Passera, R., Bertoni, F., Gattei, V., Forconi, F.,

- Laurenti, L., Del, P. G., Marasca, R., Cortelazzo, S., Gaidano, G., Palumbo, A., Boccadoro, M. & Ladetto, M. (2012) Multiple myeloma shows no intra-disease clustering of immunoglobulin heavy chain genes. *Haematologica*, 97: 849-853.
Exclusion reason : test not in PICO
- Eslick, R. & Talaulikar, D. (2013) Multiple myeloma: from diagnosis to treatment. *Australian Family Physician*, 42: 684-688.
Exclusion reason : Narrative review
- Fonseca, R. & Stewart, A. K. (2007) Targeted therapeutics for multiple myeloma: the arrival of a risk-stratified approach. [Review] [98 refs]. *Molecular Cancer Therapeutics*, 6: 802-810.
Exclusion reason : expert review
- Fuchida, S., Okano, A., Hatsuse, M., Murakami, S., Haruyama, H. & Shimazaki, C. (2012) [Successful treatment with lenalidomide plus dexamethasone for multiple myeloma complicated with systemic amyloidosis]. [Japanese]. *Rinsho Ketsueki - Japanese Journal of Clinical Hematology*, 53: 1937-1939.
Exclusion reason : case report
- Fujimi, A., Hashimoto, A., Kanisawa, Y., Okuda, T., Minami, S., Doi, T., Matsuno, T., Ishikawa, K. & Uemura, N. (2013) Loss of CD23 expression after bortezomib plus dexamethasone therapy in CCND1/IGH-positive multiple myeloma. *Rinsho Ketsueki - Japanese Journal of Clinical Hematology*, 54: 224-228.
Exclusion reason : case report
- Gala, J. L., McLachlan, J. M., Bell, D. R., Michaux, J. L. & Ma, D. D. (1994) Specificity and sensitivity of immunocytochemistry for detecting P-glycoprotein in haematological malignancies. *Journal of Clinical Pathology*, 47: 619-624.
Exclusion reason : population not in PICO
- Galhotra, R., Saggarr, K., Gupta, K. & Singh, P. (2012) Primary isolated extramedullary plasmacytoma of mesentery: A rare case report. *The gulf journal of oncology*, 1: 81-84.
Exclusion reason : case report
- Garrett, K. M., Hoffer, F. A., Behm, F. G., Gow, K. W., Hudson, M. M. & Sandlund, J. T. (2002) Interventional radiology techniques for the diagnosis of lymphoma or leukemia. *Pediatric Radiology*, 32: 653-662.
Exclusion reason : population not in PICO
- Gkatzamanidou, M., Terpos, E., Papatheodorou, A., Eleutherakis-Papaiakovou, E., Dimopoulos, M. A. & Kastiris, E. (2011) Circulating angiogenic cytokines are elevated in patients with smoldering myeloma; Implications into disease biology. *Blood*, 118.
Exclusion reason : population not in PICO
- Gleeson, T. G., Moriarty, J., Shortt, C. P., Gleeson, J. P., Fitzpatrick, P., Byrne, B., McHugh, J., O'Connell, M., O'Gorman, P. & Eustace, S. J. (2009) Accuracy of whole-body low-dose multidetector CT (WBLDCT) versus skeletal survey in the detection of myelomatous lesions, and correlation of disease distribution with whole-body MRI (WBMRI). *Skeletal Radiology*, 38: 225-236.
Exclusion reason : test not in PICO
- Grey, M. R. & Kelsey, P. (1998) Delayed diagnosis and unnecessary percutaneous biopsies in cases of myeloma presenting as chest wall tumours. *Clinical and Laboratory Haematology*, 20: 259-262.
Exclusion reason : not primary care
- Grosbois, B., Decaux, O., Guenet, L., Goasguen, J. & Jego, P. (1085) [Nosology and management of monoclonal gammopathy]. [French]. *Bulletin de l'Academie Nationale de Medecine*, 193: 1069-1085.
Exclusion reason : expert review
- Hallek, M., Neumann, C., Schaffer, M., Danhauser-Riedl, S., von, B. N., de, V. G., Druker, B. J., Yasukawa, K., Griffin, J. D. & Emmerich, B. (1997) Signal transduction of interleukin-6 involves

- tyrosine phosphorylation of multiple cytosolic proteins and activation of Src-family kinases Fyn, Hck, and Lyn in multiple myeloma cell lines. *Experimental Hematology*, 25: 1367-1377.
Exclusion reason : population not in PICO
- Heringer, L. & Crevensten, H. (2010) Recurrent paralysis due to hyperthyroidism causing hypokalemia. *Journal of General Internal Medicine*, 25: S544-S545.
Exclusion reason : case report
- Hofmeister, C. C., Yang, X., Pichiorri, F., Chen, P., Rozewski, D. M., Johnson, A. J., Lee, S., Liu, Z., Garr, C. L., Hade, E. M., Ji, J., Schaaf, L. J., Benson, D. M., Jr., Kraut, E. H., Hicks, W. J., Chan, K. K., Chen, C. S., Farag, S. S., Grever, M. R., Byrd, J. C. & Phelps, M. A. (2011) Phase I trial of lenalidomide and CCI-779 in patients with relapsed multiple myeloma: evidence for lenalidomide-CCI-779 interaction via P-glycoprotein. *Journal of Clinical Oncology*, 29: 3427-3434.
Exclusion reason : population not in PICO
- Howell, D. A., Smith, A. G., Jack, A., Patmore, R., Macleod, U., Mironska, E. & Roman, E. (2013) Time-to-diagnosis and symptoms of myeloma, lymphomas and leukaemias: a report from the Haematological Malignancy Research Network. *BMC Hematology*, 13: 9.
Exclusion reason : Not in PICO
- Hu, H., Wang, L., Xu, H., Peng, J. & Jia, Y. (2014) - Clinical analysis of six cases of multiple myeloma first presenting with coagulopathy. - *Blood Coagulation & Fibrinolysis*, 25: 553-556.
Exclusion reason : Not in PICO
- Ichikawa, T. & Kumazaki, T. (2000) Clinical usefulness of computed tomography arteriography and computed tomography during arterial portography for the diagnosis of early and early advanced hepatocellular carcinoma. *Journal of Nippon Medical School = Nihon Ika Daigaku Zasshi*, 67: 105-109.
Exclusion reason : population not in PICO
- Jakubowska-Pietkiewicz, E., Szczepaniak-Kubat, A., Zalewska-Szewczyk, B. & Chlebna-Sokol, D. (2010) Skeletal status at diagnosis in children with hematologic malignancy - Pilot study. *Advances in Clinical and Experimental Medicine*, 19: 531-535.
Exclusion reason : population not in PICO
- Jauch, A., Neben, K., Hielscher, T., Hillengass, J., Lehnert, N., Raab, S. R., Hose, D., Granzow, M., Ho, A. D., Goldschmidt, H. & Bartram, C. R. (2013) The chromosomal abnormalities deletion 17p13, t(4;14), and gain 1q21 predict progression from smoldering to symptomatic multiple myeloma. *Medizinische Genetik*, 25: 105-106.
Exclusion reason : population not in PICO
- Jin, X., Chen, Y., Yu, N., Zuo, X., Song, S., Yin, X., Huang, Y., Zhang, W. & Chen, J. (2013) Detection of galactomannan and (1-3)-beta-D-glucan for early diagnosis of invasive Aspergillosis in hematological cancer patients. *International Journal of Pharmacology*, 9: 86-91.
Exclusion reason : population not in PICO
- Kitamura, M., Yamaguchi, H., Murakawa, K., Murao, T. & Iizuka, Y. (1982) Screening for multiple myeloma using routine laboratory test results. *Clinical Biochemistry*, 15: 17-21.
Exclusion reason : population not in PICO
- Kleber, M., Hieke, S., Koch, B., Ihorst, G., Wasch, R., Schumacher, M. & Engelhardt, M. (2012) Conditional survival analysis in a large cohort of multiple myeloma patients provides detailed information about long-term survival and constitutes a different way to identify patients with extended life expectancy. *Blood*, 120.
Exclusion reason : not primary care
- Klincova, M., Mikulasova, A., Kovarova, L., Sandecka, V., Radocha, J., Maisnar, V., Adam, Z., Krejci, M., Pour, L., Zahradova, L., Krivanova, A., Szturz, P. & Hajek, R. (2011) Prognosis of high-risk group of monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM). [Czech]. *Onkologie*, 5: 146-150.
Exclusion reason : expert review

- Krishnarmannam, V., Gilbert, W., Green, T., Santos, M., Goodin, J., Lewis, R. E. & Cruse, J. M. (2012) HLA-A*7401 and HLA-c*0401 allelic disease association with plasma cell neoplasia. *FASEB Journal*, 26.
Exclusion reason : test not in PICO
- Kyle, R. A. & Rajkumar, S. V. (2007) Monoclonal Gammopathy of Undetermined Significance and Smoldering Multiple Myeloma. *Hematology/Oncology Clinics of North America*, 21: 1093-1113.
Exclusion reason : expert review
- Kyrtsonis, M.-C., Dedoussis, G., Zervas, C., Perifanis, V., Baxevanis, C., Stamatelou, M. & Maniatis, A. (1996) Soluble interleukin-6 receptor (sIL-6R), a new prognostic factor in multiple myeloma. *British Journal of Haematology*, 93: 398-400.
Exclusion reason : test not in PICO
- Lammeren-Venema, D., Regelink, J. C., Riphagen, I. I., Zweegman, S., Hoekstra, O. S. & Zijlstra, J. M. (2012) 18F-fluoro-deoxyglucose positron emission tomography in assessment of myeloma-related bone disease: a systematic review (DARE structured abstract). *Cancer*, 118: 1971-1981.
Exclusion reason : test not in PICO
- Li, N., Lv, Y., Zeng, H., He, F., Yao, Y. & He, X. (2012) Renal impairment in multiple myeloma: presenting features in different departments. *Journal of Huazhong University of Science and Technology. Medical Sciences*, 32: 65-68.
Exclusion reason : population not in PICO
- Magee, C., Vella, J. P., Tormey, W. P. & Walshe, J. J. (1998) Multiple myeloma and renal failure: one center's experience. *Renal Failure*, 20: 597-606.
Exclusion reason : not primary care
- Magony, S., Valkusz, Z., Csajbok, E., Sepp, K., Gardi, J., Szecsi, M., Julesz, J. & Wittmann, T. (2013) [In the labyrinth of calcium metabolism]. [Hungarian]. *Orvosi Hetilap*, 154: 351-355.
Exclusion reason : case report
- Malik, D. B. & Aggarwal, S. (2014) Normolipemic xanthomas; A rare cutaneous finding leading to diagnosis of multiple myeloma. *Journal of General Internal Medicine*, 29: S396-S397.
Exclusion reason : Not in PICO
- Martinez, A., Aymerich, M., Castillo, M., Colomer, D., Bellosillo, B., Campo, E. & Villamor, N. (2003) Routine use of immunophenotype by flow cytometry in tissues with suspected hematological malignancies. *Cytometry Part B, Clinical Cytometry*, 56: 8-15.
Exclusion reason : test not in PICO
- Mbagaya, W. & Barth, J. H. (2011) Hyperlipidaemia as initial presentation of myeloma. *Atherosclerosis*, 218: e6-e7.
Exclusion reason : case report
- Mohr, R. & Gross, R. (1980) Plasmocytoma. [German]. *Deutsches Arzteblatt*, 77: 2721-2727.
Exclusion reason : expert review
- Mylin, A. K., Rasmussen, T., Johansen, J. S., Knudsen, L. M., Norgaard, P. H., Lenhoff, S., Dahl, I. M., Johnsen, H. E. & Nordic Myeloma Study Group (2006) Serum YKL-40 concentrations in newly diagnosed multiple myeloma patients and YKL-40 expression in malignant plasma cells. *European Journal of Haematology*, 77: 416-424.
Exclusion reason : test not in PICO
- Nageshwaran, S., Majumdar, K. & Russell, S. (2012) Hypergammaglobulinemia, normal serum albumin and hypercalcaemia: a case of systemic sarcoidosis with initial diagnostic confusion. *BMJ Case Reports*, 2012, 2012.
Exclusion reason : case report
- Nau, K. C. & Lewis, W. D. (2008) Multiple myeloma: Diagnosis and treatment. *American Family Physician*, 78: 853-859.
Exclusion reason : expert review
- Ninomiya, S., Fukuno, K., Kanemura, N., Goto, N., Kasahara, S., Yamada, T., Tsurumi, H. & Moriwaki, H. (2010) IgG type multiple myeloma and concurrent IgA type monoclonal gammopathy of

- undetermined significance complicated by necrotizing skin ulcers due to type I cryoglobulinemia. *Journal of Clinical & Experimental Hematopathology*, 50: 71-74.
Exclusion reason : case report
- O'Connell, T. X., Horita, T. J. & Kasravi, B. (2005) Understanding and interpreting serum protein electrophoresis. *American Family Physician*, 71: 105-112.
Exclusion reason : not primary care
- Ong, F., Hermans, J., Noordijk, E. M., Wijermans, P. W., Seelen, P. J., de Kieviet, W., Gerrits, W. B. J., Kluin, P. M. & Kluin-Nelemans, J. C. (1997) A population-based registry on paraproteinaemia in the Netherlands. *British Journal of Haematology*, 99: 914-920.
Exclusion reason : population not in PICO
- Palladini, G., Russo, P., Bosoni, T., Verga, L., Sarais, G., Lavatelli, F., Nuvolone, M., Obici, L., Casarini, S., Donadei, S., Albertini, R., Righetti, G., Marini, M., Graziani, M. S., D'Eril, G. V. M., Moratti, R. & Merlini, G. (2009) Identification of Amyloidogenic Light Chains Requires the Combination of Serum-Free Light Chain Assay with Immunofixation of Serum and Urine. *Clinical Chemistry*, 55: 499-504.
Exclusion reason : test not in PICO
- Papageorgiou, A., Ziakas, P. D., Tzioufas, A. G. & Voulgarelis, M. (2013) Indications for bone marrow examination in autoimmune disorders with concurrent haematologic alterations. *Clinical & Experimental Rheumatology*, 31: 76-83.
Exclusion reason : population not in PICO
- Peruzzi, B., Carretti, F., Rondelli, T., Caporale, R., Fanelli, A. & Grazia Gelli, A. M. (2012) Seven-color flow cytometry for evaluation of bone marrow plasma cells disorders: Different aberrant phenotype with different aggressiveness. *Cytometry Part B - Clinical Cytometry*, 82B: 401-402.
Exclusion reason : test not in PICO
- Pettersson, D., Mellstedt, H. & Holm, G. (1980) Immunoglobulin isotypes on monoclonal blood lymphocytes in human plasma cell myeloma. *Journal of Clinical & Laboratory Immunology*, 3: 93-98.
Exclusion reason : test not in PICO
- Portier, M., Lees, D., Caron, E., Jourdan, M., Boiron, J. M., Bataille, R. & Klein, B. (1992) Up-regulation of interleukin (IL)-6 receptor gene expression in vitro and in vivo in IL-6 deprived myeloma cells. *FEBS Letters*, 302: 35-38.
Exclusion reason : population not in PICO
- Rajeswaran, C., Spencer, J., Barth, J. H. & Orme, S. M. (2007) Utility of biochemical screening in the context of evaluating patients with a presumptive diagnosis of osteoporosis. *Clinical Rheumatology*, 26: 362-365.
Exclusion reason : population not in PICO
- Ramon Rodriguez, L. G., Rivera-Keeling, C., Arencibia-Nunez, A., Avila-Cabrera, O. M., Izquierdo-Cano, L., Espinosa-Estrada, E., Gonzalez-Pinedo, L., Quintero-Sierra, Y., Gutierrez-Diaz, A. & Hernandez-Padron, C. (2013) Clinical and laboratory characterization of multiple myeloma at the Institute of Hematology and Immunology. *Revista Cubana de Hematologia, Inmunologia y Hemoterapia*, 29: 382-397.
Exclusion reason : Not in PICO
- Raza, S., TaherNazerHussain, F., Patnaik, M., Knudson, R., Van, D. D. & Tefferi, A. (2011) Autosomal monosomies among 24,262 consecutive cytogenetic studies: prevalence, chromosomal distribution and clinicopathologic correlates of sole abnormalities. *American Journal of Hematology*, 86: 353-356.
Exclusion reason : test not in PICO
- Renuga, G., Babu, A. & Arumugam, K. R. (2008) Molecular characterization of plasma proteins to confirm the risk factor for regression to multiple myeloma. *Asian Journal of Microbiology, Biotechnology and Environmental Sciences*, 10: 229-234.
Exclusion reason : test not in PICO

- Rimsza, L. M., Campbell, K., Dalton, W. S., Salmon, S., Willcox, G. & Grogan, T. M. (1999) The major vault protein (MVP), a new multidrug resistance associated protein, is frequently expressed in multiple myeloma. *Leukemia & Lymphoma*, 34: 315-324.
Exclusion reason : test not in PICO
- Ross, J. R., Saunders, Y., Edmonds, P. M., Patel, S., Wonderling, D., Normand, C. & Broadley, K. (2004) A systematic review of the role of bisphosphonates in metastatic disease. [Review] [335 refs]. *Health Technology Assessment (Winchester, England)*, 8: 1-176.
Exclusion reason : treatment study
- Savini, P., Lanzi, A., Castagnari, B., Gollini, C., Re, G., Musardo, G. & Stefanini, G. F. (2009) Proposal for the management of the MGUS. *Haematologica*, 94: 244-245.
Exclusion reason : expert review
- Schmidt, G. P., Schoenberg, S. O., Reiser, M. F. & Baur-Melnyk, A. (2005) Whole-body MR imaging of bone marrow. [Review] [40 refs]. *European Journal of Radiology*, 55: 33-40.
Exclusion reason : test not in PICO
- Schmidt, G. P., Baur, A., Stäbler, A., Schoenberg, S. O., Steinborn, M., Baltin, V. & Reiser, M. F. (2005) [Estimation of diffuse bone marrow infiltration of the spine in multiple myeloma: correlation of MRT with histological results]. *RöFo : Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin*, 177: 745-750.
Exclusion reason : test not in PICO
- Sethi, B., Butola, K. S. & Kumar, Y. (2012) A Diagnostic Dilemma: Waldenstrom's Macroglobulinemia/Plasma Cell Leukemia. *Case Reports in Pathology Print*, 2012: 271407.
Exclusion reason : case report
- Shaheen, S. P. & Levinson, S. S. (2009) Serum free light chain analysis may miss monoclonal light chains that urine immunofixation electrophoreses would detect. *Clinica Chimica Acta*, 406: 162-166.
Exclusion reason : population not in PICO
- Sharma, A., Tripathi, M., Satyam, A. & Kumar, L. (2009) Study of antioxidant levels in patients with multiple myeloma. *Leukemia & Lymphoma*, 50: 809-815.
Exclusion reason : test not in PICO
- Smellie, W. S. A. & Spickett, G. P. (2006) Cases in primary care laboratory medicine - Paraprotein management. *British Medical Journal*, 333: 185-187.
Exclusion reason : editorial
- Smith, D. B., Harris, M., Gowland, E., Chang, J. & Scarffe, J. H. (1986) Non-secretory multiple myeloma: a report of 13 cases with a review of the literature. *Hematological Oncology*, 4: 307-313.
Exclusion reason : cases only
- Suzuki, S., Ikusaka, M., Miyahara, M. & Shikino, K. (2014) - Positron emission tomography findings in a patient with multiple myeloma of polymyalgia rheumatica-like symptoms caused by paraneoplastic syndrome. - *BMJ Case Reports*, 2014, 2014..
Exclusion reason : Not in PICO
- Takemura, Y., Hayashi, K., Miyoshi, K., Mori, S., Kugai, N. & Sekiguchi, S. (1992) [Laboratory tests in primary care medicine: "essential laboratory tests" (2). Usefulness of hematological, biochemical and serological tests in diagnosis of new outpatients]. [Japanese]. *Rinsho Byori - Japanese Journal of Clinical Pathology*, 40: 403-409.
Exclusion reason : population not in PICO
- Talbot, R. W., Bannister, J. J. & Hills, N. H. (1984) A haematuria diagnostic service in a district general hospital. *Annals of the Royal College of Surgeons of England*, 66: 348-350.
Exclusion reason : population not in PICO
- Tate, J., Caldwell, G., Daly, J., Gillis, D., Jenkins, M., Jovanovich, S., Martin, H., Steele, R., Wienholt, L. & Mollee, P. (2012) Recommendations for standardized reporting of protein electrophoresis in Australia and New Zealand. *Annals of Clinical Biochemistry*, 49: 242-256.

Exclusion reason : expert review

Thakkinstian, A., Tran, H., Reeves, G., Murch, S. & Attia, J. (2008) A clinical decision rule to aid ordering of serum and urine protein electrophoresis for case-finding of paraproteins in hospitalized inpatients. *Journal of General Internal Medicine*, 23: 1688-1692.

Exclusion reason : not primary care

Van Zaanen, H. C., Lokhorst, H. M., Aarden, L. A., Rensink, H. J., Warnaar, S. O. & Van Oers, M. H. (1998) Blocking interleukin-6 activity with chimeric anti-IL6 monoclonal antibodies in multiple myeloma: effects on soluble IL6 receptor and soluble gp130. *Leukemia & Lymphoma*, 31: 551-558.

Exclusion reason : test not in PICO

Vardiman, J. (2011) Classification of hematologic neoplasms: Current and future approaches for the myeloid neoplasms. *International Journal of Laboratory Hematology*, 33: 1-2.

Exclusion reason : expert review

Varshney, R., Deka, M., Bhattacharya, J. & Gogoi, P. K. (2012) Clinico-haematological analysis of haematological malignancy, a hospital based study. *Indian Journal of Hematology and Blood Transfusion*, 28: 245.

Exclusion reason : not primary care

Vieillard, M. H., Boutry, N., Chastanet, P., Duquesnoy, B., Cotten, A. & Cortet, B. (2005) Contribution of percutaneous biopsy to the definite diagnosis in patients with suspected bone tumor. *Joint, Bone, Spine: Revue du Rhumatisme*, 72: 53-60.

Exclusion reason : test not in PICO

Vladutiu, A. O. (1987) Prevalence of M-proteins in serum of hospitalized patients. Physicians' response to finding M-proteins in serum protein electrophoresis. *Annals of Clinical & Laboratory Science*, 17: 157-161.

Exclusion reason : test not in PICO

Wahane, R. N., Lele, V. R. & Bobhate, S. K. (2007) Fine needle aspiration cytology of bone tumors. *Acta Cytologica*, 51: 711-720.

Exclusion reason : test not in PICO

Waldmann, A., Barragan, B., Cursaru, V., Heberlein, C., Hrianka, M., Richter, F. & Sadzuga, R. (2010) Detecting myeloma-ways to shortening an often painful and tedious patient odyssey: Results from an international survey conducted by myeloma euronet, The European network of myeloma patient groups. *Haematologica*, 95: 389.

Exclusion reason : cases only

Watanaboonyongcharoen, P., Nakorn, T. N., Rojnuckarin, P., Lawasut, P. & Intragumtornchai, T. (2012) Prevalence of monoclonal gammopathy of undetermined significance in Thailand. *International Journal of Hematology*, 95: 176-181.

Exclusion reason : screening study

Wei, A. & Juneja, S. (2003) Bone marrow immunohistology of plasma cell neoplasms. *Journal of Clinical Pathology*, 56: 406-411.

Exclusion reason : test not in PICO

Wilson, A. B., Prout, M. N., Neogi, T. & Jick, S. (2012) The role of surveillance bias in the incidence of the myelodysplastic syndromes and chronic myeloproliferative disorders. *Pharmacoepidemiology and Drug Safety*, 21: 336.

Exclusion reason : test not in PICO

Zagroda, M., Prystupa, A. & Mosiewicz, J. (2013) Diverse clinical presentation in the course of multiple myeloma. *Family Medicine and Primary Care Review*, 15: 423-425.

Exclusion reason : Not in PICO

Zhang, H., Zhang, L., Wang, J., Ma, Y., Zhang, J., Mo, F., Zhang, W., Yan, S., Yang, G. & Lin, B. (2009) Proteomic analysis of bone tissues of patients with osteonecrosis of the femoral head. *Omics a Journal of Integrative Biology*, 13: 453-466.

Exclusion reason : test not in PICO

Zhang, L., Li, J., Yang, H., Luo, Z. & Zou, J. (2012) Histological evaluation of bone biopsy results during PVP or PKP of vertebral compression fractures. *Oncology Letters*, 5: 135-138.

Exclusion reason : test not in PICO

Zhang, S., Suvannasankha, A., Crean, C. D., White, V. L., Chen, C. S. & Farag, S. S. (2011) The novel histone deacetylase inhibitor, AR-42, inhibits gp130/Stat3 pathway and induces apoptosis and cell cycle arrest in multiple myeloma cells. *International Journal of Cancer*, 129: 204-213.

Exclusion reason : test not in PICO

Zima, T., Spicka, I., Stipek, S., Crkovska, J., Platenik, J., Merta, M. & Tesar, V. (1996) Antioxidant enzymes and lipid peroxidation in patients with multiple myeloma. *Neoplasma*, 43: 69-73.

Exclusion reason : population not in PICO

NON-HODGKIN'S LYMPHOMA

Review question:

What is the risk of Non-Hodgkin's lymphoma in patients presenting in primary care with symptom(s)?

Results

Literature search

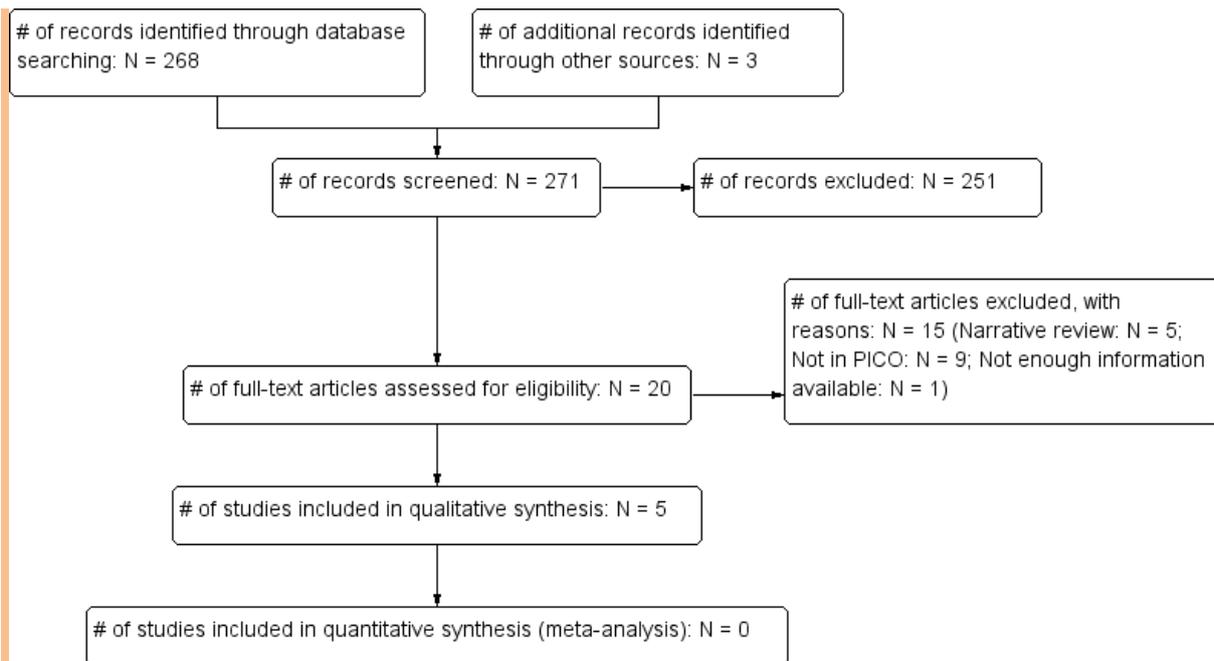
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	1184	141	16/10/12
<i>Premedline</i>	All-2012	18	5	16/10/12
<i>Embase</i>	All-2012	856	102	18/10/12
<i>Cochrane Library</i>	All-2012	89	0	18/10/12
<i>Psychinfo</i>	All-2012	4	1	16/10/12
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	71	26	18/10/12
<i>Biomed Central</i>	All-2012	244	9	18/10/12

Total References retrieved (after de-duplication): 256

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	10/2012-20/08/2014	48	2	20/08/2014
<i>Premedline</i>	10/2012-20/08/2014	44	7	20/08/2014
<i>Embase</i>	10/2012-20/08/2014	93	3	20/08/2014
<i>Cochrane Library</i>	10/2012-20/08/2014	78	0	20/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	10/2012-20/08/2014	12	0	20/08/2014

Total References retrieved (after de-duplication): 12



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issue to note is that 2/3 studies employed samples of patients that are not directly representative of an unselected symptomatic population of patients presenting to the UK-based GP, and that there was some uncertainty about the verification of the outcome for some of the patients. Dommett (2012; 2013a,b) employed a case-control design which has been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors may have gone some way in counteracting this influence.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Deyo (1988)	?	+	?	+	-	+	+
Dommett (2012, 2013)	-	+	+	+	+	+	+
Williamson (1985)	+	+	+	?	+	+	+

- High	? Unclear	+ Low
---	---	--

Study results

Table 1: Non-Hodgkin's lymphoma: Adult and mixed age populations

Study	Symptom(s)	Patient group	Result
Deyo (1988)	Back pain	All patients	0.1 (0.02-0.41) 2/1975 7 had other types of cancer: lymphoma (NOS): N = 2, unknown primary: N = 1, Prostate: N = 1, retroperitoneal liposarcoma: N = 1, lung cancer: N = 1, renal cell: N = 1, multiple myeloma: N = 1, mucinous adenocarcinoma (of gallbladder?): N = 1
Williamson (1985)	Lymphadenopathy	All patients	0.8 (0.1-3.2) TP = 2, FP = 247 Cancer: Hodgkin's: N = 1 Adenocarcinoma: N = 1

TP = True positives, FP = False positives.

Table 2: Non-Hodgkin's lymphoma: Positive predictive values for leukaemia/lymphoma childhood cancer

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)
Domett (2013a)	Bruising 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.53 (0.07-3.91)
Domett (2013a)	Pallor 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.43 (0.06-3.15)
Domett (2013a)	Lump mass swelling head and neck 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.35 (0.05-2.65)
Domett (2013a)	Fatigue 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.07 (0.03-0.15)
Domett (2013a)	Lymphadenopathy 0-3 months before diagnosis	All leukemia/lymphoma patients and	0.06 (0.04-0.11)

		controls aged 0-14 years	
Dommett (2013a)	Lump mass swelling below neck excluding abdomen 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.05 (0.02-0.13)
Dommett (2013a)	Bleeding 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.03 (0.01-0.08)
Dommett (2013a)	Pain 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.03 (0.01-0.06)
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.02 (0.01-0.03)
Dommett (2013a)	Fever 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01 (0.01-0.01)
Dommett (2013a)	Abdominal pain 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01(0-0.01)
Dommett (2013a)	≥ 3 consultations	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01(0.01-0.01)

The positive predictive values are calculated using Bayesian statistics.

Table 3: Non-Hodgkin's lymphoma: Positive predictive values for teenage and young adult lymphoma

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2013b)	Lump mass swelling head and neck	All lymphoma patients and controls aged 15-24 years	0.5034 (0.0696-3.68) Cases: 35/270 Controls: 1/3350
Dommett (2013b)	Lump mass swelling below neck excluding abdomen	All lymphoma patients and controls aged 15-24 years	0.0279 (0.0152-0.0515) Cases: 29/270 Controls: 15/3350
Dommett (2013b)	Lymphadenopathy	All lymphoma patients and controls aged 15-24 years	0.278 (0.1-0.75) Cases: 77/270 Controls: 4/3350
Dommett (2013b)	'Lump mass swelling head and neck', 'lymphadenopathy' and 'lump mass swelling	All lymphoma patients and controls aged 15-24 years	0.0903 (0.057-0.1425)

	below neck excluding abdomen' combined as a single symptom		
Dommett (2013b)	≥ 3 consultations	All lymphoma patients and controls aged 15-24 years	0.0086 (0.0075-0.0099) Cases: 175/270 Controls: 294/3350

The positive predictive values are calculated using Bayesian statistics.

Evidence statement(s):

Adult and mixed age populations

Back pain (1 study, N = 1975) and lymphadenopathy (1 study, N = 249) presenting in a primary care setting do not appear to confer a markedly increased risk of Hodgkin's/Non-Hodgkin's lymphoma, although the study populations are probably not directly representative of the typical unselected symptomatic UK GP population (see also Table 1).

Children and teenagers and young adults

The positive predictive values of having leukaemia/lymphoma childhood cancer ranged from 0.01% (for fever and abdominal pain) to 0.53% (for bruising) for patients aged 0-14 years old, and the positive predictive values of having young adulthood lymphoma ranged from 0.0279% (for 'lump mass swelling below the neck excluding the abdomen') to 0.5034% (for 'lump mass swelling head and neck') for patients aged 15-24 years (1 study, N = 30855). The evidence quality is somewhat compromised by the case-control design of the study (see also Tables 2-3).

Evidence tables

Deyo (1988)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive? patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 1975, mean (SD; range) age = 39.5 (15.4; 15-86) years, 62% females. 54% of the patients were seeking medical care for back pain for the first time and 76% of the patients had had back pain for < 3 months. 3% had a history of back pain surgery. Maximal back pain in the low back (84%) or in the upper back (16%).</p> <p><u>Inclusion criteria:</u> Patients who sought treatment between March 1982 and September 1984 in the walk-in clinic of a public hospital where virtually all patients are self-referred. In each case back pain was part of the chief complaint.</p> <p><u>Exclusion criteria:</u> Neck pain.</p> <p><u>Clinical setting:</u> Walk-in clinic of a public hospital; this clinic is a source of primary care for indigent persons in a county in the USA with a population of</p>

	approximately 1 million.	
Are there concerns that the included patients and setting do not match the review question?		High concern
INDEX TEST		
A. Risk of bias		
Index test	Back pain; not further specified.	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	The reference standard consisted of a search on each patient name in the institutional tumour registry ≥ 6 months after the index visit. The registry included every patient with a histological diagnosis of cancer made in the authors' hospital system regardless of site of care. The authors point out that "while this method might fail to identify cancer patients who sought care elsewhere, it is likely that most patients sought follow-up for a particular illness at the same facility.	
Is the reference standard likely to correctly classify the target condition?		Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?		No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All the patients are accounted for in the results.	
Was there an appropriate interval between index test and reference standard?		Yes (probably)
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		Yes
Could the patient flow have introduced bias?		Low risk
NOTES	It is a concern that some patients with cancer might have been missed due to the choice of reference standard because this would result in an underestimation of the positive predictive value. 38/1975 patients were found in the tumour registry. Of those 38, 13 patients had tumours that were probable causes of back pain, and 4 of these 13	

	patients already had a diagnosis of cancer at presentation. The 9/1975 patients who had undiagnosed cancer that the back pain could be attributed to had: Lymphoma (NOS; 2), cancer of unknown primary (1), prostate cancer (1), retroperitoneal liposarcoma (1), lung cancer (1), renal cell (1), multiple myeloma (1), mucinous adenocarcinoma (of gallbladder?; 1)
--	---

Dommett (2012; 2013a,b)

PATIENT SELECTION

A. risk of bias

Patient sampling	Population-based nested case-control study using data from the General Practice Research Database (GPRD)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability

Patient characteristics and setting	<p><u>Cases:</u> 1267 children; aged 0-4 years: N = 436; aged 5-14 years: N = 831; 703 males/564 females. Cancer type: Leukemia: N = 368; brain: N = 270; lymphoma: N = 142; bone: N = 107; soft tissue sarcoma: N = 91; renal: N = 82; neuroblastoma: N = 75; other ICD codes: N = 132. 1064 teenagers and young adults (TYA): 15-24 years: Gender not reported. Cancer type: Leukemia: N = 143; brain: N = 154; lymphoma: N = 270; bone: N = 96; soft tissue sarcoma: N = 100; other ICD codes: N = 301 (including testis: N = 60; skin: N = 49; ovary: N = 20 and thyroid: N = 17).</p> <p><u>Controls:</u> 15318 children; aged 0-4 years: N = 4802; aged 5-14 years: N = 10516; 8461 males/6857 females. 13206 TYA. Gender not reported</p> <p><u>Inclusion criteria:</u> The sample comprised all children and TYU aged 0–24 years, inclusive, drawn from all general practices contributing research-standard data to the GPRD between 1 January 1988 and 31 December 2010. To be included, the practices had to have been contributing research-standard data for a minimum of 1 year before each child’s date of cancer diagnosis or the index date (see below) for matched controls. Cases: Patients diagnosed with the following cancers: leukaemia, lymphoma, neuroblastoma, soft tissue sarcoma, hepatic, renal, bone and central nervous system tumours, using pre-defined medical codes used in the GPRD. The date of diagnosis for cases was defined as the date of pathological diagnosis, but if this was unavailable, the date of the first cancer code entered in the GPRD was used.</p>
-------------------------------------	--

	Controls: Up to 13 controls (children with no diagnosis of cancer at any time) were selected per case, using a computer-generated random sequence, matched on age (within 1 year), sex and practice, and had to be currently registered on the date of diagnosis of their matched case (the index date). Exclusion criteria: None listed Clinical setting: Primary care, UK.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	The GPRD uses just over 100 000 medical codes to encompass all primary care events, including both symptoms and diagnoses. From this list, libraries of codes were assembled representing individual alert symptoms derived from the NICE referral guidelines for suspected cancer in children. <i>No more information reported.</i>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Cancer diagnosis in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	This study is published in three papers.

Williamson (1985)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective consecutive patient series
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 249, mean age = 24 years, 26% were < 15 years; 58% females. <u>Inclusion criteria:</u> Patients seen at the Family Medical Care Centre of the University of Missouri-Columbia, between July 1 19978 and June 30 1983 whose diagnoses were coded as “enlarged lymph nodes, not infected” (ICHPPC 266) and “lymphadenitis, acute” (ICHPPC 209). <u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> Family Medical Care Centre of the University of Missouri-Columbia.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Diagnoses coded as “enlarged lymph nodes, not infected” (ICHPPC 266) and “lymphadenitis, acute” (ICHPPC 209).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Diagnoses were accepted if verified by history, physical examination or laboratory tests. Outcomes were determined, where possible, from the medical record. Follow up was considered adequate to determine an adverse outcome if one of four criteria were met: 1) A definite diagnosis was made, 2) The nodes were documented to be resolving, 3) There was at least one chart entry for any condition at least 6 months after the index visit for lymphadenopathy, or 4) The patient was reached by telephone and determined to have a favourable outcome.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	11/249 patients did not fit the criteria for adequate follow up: 3/11 had return visits showing no increase in the size of the nodes, 6/11 had nodes < 1 cm in size and were told to come back if the nodes did not resolve, 2/11 presented with cervical lymph nodes described as 1 cm in size and follow up examination was not recommended. None of these 11 patients could be reached by phone.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk
NOTES	The author note that the study would not have included all the patients presenting with enlarged lymph nodes during the study period because not all such patients would have the diagnosis noted as required for study entry, e.g., a diagnosis of infectious mononucleosis made on the first visit would probably have been coded as such and not as enlarged lymph nodes.

References

Included studies

- Deyo, R. A. and Diehl, A. K. Cancer as a cause of back pain: Frequency, clinical presentation, and diagnostic strategies. *Journal of General Internal Medicine* 3, 230-238. 1-11-1988.
- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of childhood cancer in primary care: A population-based nested case-control study. *British Journal of Cancer* 106[5], 982-987. 2012.
- Dommett, R. M., Redaniel, T., Stevens, M. C. G., Martin, R. M., and Hamilton, W. Risk of childhood cancer with symptoms in primary care: A population-based case-control study. *British Journal of General Practice*; DOI:10.3399/bjgp13X660742. 2013a.
- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of cancer in teenagers and young adults in primary care: A population-based nested case-control study. *British Journal of Cancer* 2329-2333. 2013b.
- Williamson, H. A., Jr. Lymphadenopathy in a family practice: a descriptive study of 249 cases. *Journal of Family Practice* 20[5], 449-452. 1985.

Excluded studies (with excl reason)

- Abrams, D. I., Lewis, B. J., and Volberding, P. A. Lymphadenopathy: endpoint or prodrome? Update of a 24-month prospective study. *Annals of the New York Academy of Sciences* 437, 207-215. 1984.
Excl reason: Discussion paper/not in PICO
- Adegboye, V. O., Ogunseyinde, A. O., Obajimi, M. O., Ogunbiyi, O., Brimmo, A. I., and Adebo, O. A. Presentation of primary mediastinal masses in Ibadan. *East African Medical Journal* 80[9], 484-487. 2003.
Excl reason: Not in PICO

Ahmed, S., Kussick, S. J., Siddiqui, A. K., Bhuiya, T. A., Khan, A., Sarewitz, S., Steinberg, H., Sison, C. P., and Rai, K. R. Bronchial-associated lymphoid tissue lymphoma: a clinical study of a rare disease. *European Journal of Cancer* 40[9], 1320-1326. 2004.
Excl reason: Not in PICO

Ahmed, S., Shahid, R. K., Sison, C. P., Fuchs, A., and Mehrotra, B. Orbital lymphomas: A clinicopathologic study of a rare disease. *American Journal of the Medical Sciences* 331[2], 79-83. 2006.
Excl reason: Not in PICO

Aizenberg, D. and Berlin, C. An unusual cause of the piriformis syndrome. *Journal of General Internal Medicine* 25, S491. 2010. Springer New York.
Excl reason: Not in PICO

Akpata, O. Orofacial surgical emergencies. *West African Journal of Medicine* 30[5], 313-318. 2011.
Excl reason: Narrative review/Not in PICO

Al Diab, A. R., Aleem, A., Qayum, A., Al Askar, A. S., and Ajarim, D. S. Clinico-Pathological Pattern of Extranodal Non-Hodgkin's Lymphoma in Saudi Arabia. *Asian Pacific Journal of Cancer Prevention* 12[12], 3277-3282. 2011.
Excl reason: Not in PICO

Allam, Wafa, Ismaili, Nabil, Elmajjaoui, Sanaa, Elgueddari, Bel, Ismaili, Mohammed, and Errihani, Hassan. Primary Nasopharyngeal non-Hodgkin lymphomas: a retrospective review of 26 Moroccan patients. *BMC Ear, Nose and Throat Disorders* 9[1], 11. 2009.
Excl reason: Not in PICO

Allgar, V. L. and Neal, R. D. General practitioners' management of cancer in England: secondary analysis of data from the National Survey of NHS Patients - Cancer. *European Journal of Cancer Care* 14[5], 409-416. 2005.
Excl reason: Not in PICO

Allgar, V. L. and Neal, R. D. Delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS Patients: Cancer. *British Journal of Cancer* 92[11], 1959-1970. 2005.
Excl reason: Not in PICO

Allhiser, J. N., McKnight, T. A., and Shank, J. C. Lymphadenopathy in a family practice. *Journal of Family Practice* 12[1], 27-32. 1981.
Excl reason: Retrospective case series of 80 patients based on case notes. Authors looked for cases of lymphadenopathy or acute lymphadenitis in the records. 19% of the cases were discovered by the physician (i.e., not patients consulting for this symptom). No aetiology recorded for 29% (N = 23) of the cases, and no cancers recorded as aetiology for the other 71%, but no clear verification of cause and final diagnoses not reported.

Arce-Salinas, C. A., Morales-Velazquez, J. L., Villasenor-Ovies, P., and Muro-Cruz, D. Classical fever of unknown origin (FUO): current causes in Mexico. *Revista de Investigacion Clinica* 57[6], 762-769. 2005.
Excl reason: Not in PICO

Ashraf, F. Primary pancreatic lymphoma mimicking adenocarcinoma of pancreas. *American Journal of Gastroenterology* 105, S214. 2010. Nature Publishing Group.
Excl reason: Not in PICO

Back, H., Gustavsson, B., Ridell, B., Rodjer, S., and Westin, J. Primary gastrointestinal lymphoma incidence, clinical presentation, and surgical approach. *Journal of Surgical Oncology* 33[4], 234-238. 1986.
Excl reason: Not in PICO

Bailey, A. A., Debinski, H. S., Appleyard, M. N., Remedios, M. L., Hooper, J. E., Walsh, A. J., and Selby, W. S. Diagnosis and outcome of small bowel tumors found by capsule endoscopy: A three-center Australian experience. *American Journal of Gastroenterology* 101[10], 2237-2243. 2006.
Excl reason: Not in PICO

- Bakshi, N. and Maghfoor, I. The current lymphoma classification: New concepts and practical applications-triumphs and woes. *Annals of Saudi Medicine* 32[3], 296-305. 2012.
Excl reason: Narrative review
- Baldini, Chiara, Giusti, Laura, Ciregia, Federica, Da Valle, Ylenia, Giacomelli, Camillo, Donadio, Elena, Ferro, Francesco, Galimberti, Sara, Donati, Valentina, Bazzichi, Laura, Bombardieri, Stefano, and Lucacchini, Antonio. Correspondence between salivary proteomic pattern and clinical course in primary Sjogren syndrome and non-Hodgkin's lymphoma: a case report. *Journal of Translational Medicine* 9[1], 188. 2011.
Excl reason: Not in PICO
- Barr, L. C., Glees, J. P., and Gazet, J. C. Diagnostic laparotomy in suspected malignant lymphoma. *Annals of the Royal College of Surgeons of England* 66[6], 402-404. 1984.
Excl reason: Not in PICO
- Barroca, H. & Bom-Successo, M. (2014) Fine needle biopsy with cytology in paediatrics: The importance of a multidisciplinary approach and the role of ancillary techniques. *Cytopathology*, 25: 6-20.
Excl reason: Narrative review
- Basavaraj, K. F., Ramalingam, K., Sarkar, A. & Muddaiah, S. (2012) Primary non-Hodgkin's lymphoma of gingiva in a 28-year-old HIV-positive patient. *Journal of Natural Science Biology & Medicine*, 3: 189-191.
Excl reason: Not in PICO
- Baumgartner, J. E., Rachlin, J. R., Beckstead, J. H., Meeker, T. C., Levy, R. M., Wara, W. M., and Rosenblum, M. L. Primary central nervous system lymphomas: natural history and response to radiation therapy in 55 patients with acquired immunodeficiency syndrome. *Journal of Neurosurgery* 73[2], 206-211. 1990.
Excl reason: Not in PICO
- Bazemore, A. W. and Smucker, D. R. Lymphadenopathy and malignancy. [Review] [32 refs]. *American Family Physician* 66[11], 2103-2110. 1-12-2002.
Excl reason: Narrative review
- Beck, P. L., Gill, M. J., and Sutherland, L. R. HIV-associated non-Hodgkin's lymphoma of the gastrointestinal tract. *American Journal of Gastroenterology* 91[11], 2377-2381. 1996.
Excl reason: Not in PICO
- Beelte, S., Haas, R., Germing, U., and Jansing, P. J. [Paradigm change in the assessment of myeloid and lymphoid neoplasms associated with occupational benzene exposure]. [Review] [45 refs] [German]. *Medizinische Klinik* 104[3], 197-203. 15-3-2009.
Excl reason: Narrative review
- Ben, Rejeb A., Kchir, N., Bouali, M. R., Ebdelli, N., Fsili, R., Khediri, F., Ben, Ayedo F., Zitouna, M. M., Ben, Mami N., Kacem, M., Filali, A., and Ben, Ammar A. Gastric MALT lymphoma. A clinico-pathological study of 65 cases. Relationship to *Helicobacter pylori*. *Tunisie Medicale* 78[8-9], 484-493. 2000.
Excl reason: Not in PICO
- Benson, M. K. and Hasley, P. A rash decision: Not simply another atopic dermatitis! *Journal of General Internal Medicine* 26, S436-S437. 2011. Springer New York.
Excl reason: Not in PICO
- Bosch, X., Foix, A., Jordan, A., Coca, A., and Lopez-Soto, A. Outpatient Quick Diagnosis Units for the evaluation of suspected severe diseases: an observational, descriptive study. *Clinics (Sao Paulo, Brazil)* 66[5], 737-741. 2011.
Excl reason: Not in PICO
- Brant, J. M., Beck, S., Dudley, W. N., Cobb, P., Pepper, G., and Miaskowski, C. Symptom trajectories in posttreatment cancer survivors. *Cancer Nursing* 34[1], 67-77. 2011.
Excl reason: Not in PICO

Brockmeyer, N. and Barthel, B. Clinical manifestations and therapies of AIDS associated tumors. [Review] [244 refs]. *European Journal of Medical Research* 3[3], 127-147. 23-3-1998.
Excl reason: Narrative review

Buis, J. and de Jongh, T. O. [Examining the lymph nodes]. [Review] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde* 155, A2652. 2011.
Excl reason: Narrative review

Burg, G., Kempf, W., Cozzio, A., Dobbeling, U., Feit, J., Golling, P., Michaelis, S., Scharer, L., Nestle, F., and Dummer, R. Cutaneous malignant lymphomas: update 2006. [Review] [97 refs]. *Journal der Deutschen Dermatologischen Gesellschaft* 4[11], 914-933. 2006.
Excl reason: Narrative review

Calderon-Garciduenas, A. L., Pacheco-Calleros, J., Castelan-Maldonado, E., and Necedal-Rustrian, F. C. [Primary lymphoma of the central nervous system: 20 years' experience in a referral hospital]. [Spanish]. *Revista de Neurologia* 46[2], 84-88. 16-1-2008.
Excl reason: Not in PICO

Campbell, E. W., Jr. and Smith, M. R. Hematology for primary care physicians. *Disease-a-Month* 42[3], 131-194. 1996.
Excl reason: Narrative review

Carroccio, A., Iannitto, E., Di, Prima L., Cirrincione, S., Troncone, R., Paparo, F., Trapani, L. G., Gucciardi, A., Aversa, M. R., Montalto, G., and Notarbartolo, A. Screening for celiac disease in non-Hodgkin's lymphoma patients: A serum anti-transglutaminase-based approach. *Digestive Diseases and Sciences* 48[8], 1530-1536. 1-8-2003.
Excl reason: Not in PICO

Caruso, M. L. and Rizzi, E. Gastric Malt lymphoma: a clinicopathological study. *Anticancer Research* 18[5B], 3781-3783. 1998.
Excl reason: Not in PICO

Caturelli, E., Bartolucci, F., Biasini, E., Vigliotti, M. L., Andriulli, A., Siena, D. A., Attino, V., and Bisceglia, M. Diagnosis of liver nodules observed in chronic liver disease patients during ultrasound screening for early detection of hepatocellular carcinoma. *American Journal of Gastroenterology* 97[2], 397-405. 2002.
Excl reason: Not in PICO

Cekic, S., Risimic, D., Stankovic-Babic, G., Babic, R., Jaksic, V., Jovanovic, I., and Dordevic-Jocic, J. Papilledema as a diagnostic challenge - Report of three cases. *Central European Journal of Medicine* 7[1], 100-107. 2012.
Excl reason: Not in PICO

Chau, I., Kelleher, M. T., Cunningham, D., Norman, A. R., Wotherspoon, A., Trott, P., Rhys-Evans, P., Querci Della, Rovere G., Brown, G., Allen, M., Waters, J. S., Haque, S., Murray, T., and Bishop, L. Rapid access multidisciplinary lymph node diagnostic clinic: analysis of 550 patients. *British Journal of Cancer* 88[3], 354-361. 10-2-2003.
Excl reason: Not in PICO

Cheng, A. L., Su, I. J., Chen, Y. C., Uen, W. C., and Wang, C. H. Characteristic clinicopathologic features of Epstein-Barr virus-associated peripheral T-cell lymphoma. *Cancer* 72[3], 909-916. 1-8-1993.
Excl reason: Not in PICO

Cherian, S., Das, S., Mauzo, S., Koya, H. H., Varghese, D. & Hussain, R. (2013) Primary pulmonary lymphoma: An extremely rare disease. *Chest*, 144.
Excl reason: Not in PICO

Chiang, I. P., Wang, H. H., Cheng, A. L., Lin, J. T., and Su, I. J. Low-grade gastric B-cell lymphoma of mucosa-associated lymphoid tissue: clinicopathologic analysis of 19 cases. *Journal of the Formosan Medical Association* 95[11], 857-865. 1996.
Excl reason: Not in PICO

Choi, Y. R., An, J. Y., Kim, M. K., Han, H.-S., Lee, K. H., Kim, S.-W., Lee, K. M. & Choe, K. H. (2013) The diagnostic efficacy and safety of endobronchial ultrasound-guided transbronchial needle

aspiration as an initial diagnostic tool. *Korean Journal of Internal Medicine*, 28: 660-667.

Excl reason: Not in PICO

Cholongitas, Evangelos, Papadakis, Emanouil, Kaklamanis, Loukas, and Dasenaki, Maria. Peripheral facial palsy in elderly: Not always a benign condition. [References]. *Geriatrics & Gerontology International* 9[1], 100-101. 2009.

Excl reason: Not in PICO

Cisleanu, D., Vladareanu, A. M., Bumbea, H., Radesi, S., Voican, I., Ciufu, C., Marinescu, C., Onisai, M., Nicolescu, A., Dervesteanu, M., Dobrea, C., Popov, V., Colita, D., and Mut-Popescu, D. Outcome of aggressive ATL-HTLV1 patients after CHOP21 as first line treatment - Bucharest experience. *Haematologica* 94, 404-405. 2009. Haematologica Journal Office.

Excl reason: Not in PICO

Coe, A., Conway, J., Evans, J., Goebel, M. & Mishra, G. (2013) The yield of EUS-FNA in undiagnosed upper abdominal adenopathy is very high. *Journal of Clinical Ultrasound*, 41: 210-213.

Excl reason: Not in PICO

Connolly, A. A. and MacKenzie, K. Paediatric neck masses--a diagnostic dilemma. *Journal of Laryngology & Otology* 111[6], 541-545. 1997.

Excl reason: Not in PICO

Cornalba, G. P., Dore, R., and Colombo, E. [Abdominal manifestations in immunocompromised patients]. [Review] [30 refs] [Italian]. *Radiologia Medica* 87[5:Suppl 2], Suppl-61. 1994.

Excl reason: Not in PICO

Cuschieri, A. Malignant tumours of the stomach. [Review] [53 refs]. *Recenti Progressi in Medicina* 81[6], 374-386. 1990.

Excl reason: Narrative review

Das, S. K., Saha, S. K., Das, A., Halder, A. K., Banerjee, S. N., and Chakraborty, M. A study of comparison of efficacy and safety of talc and povidone iodine for pleurodesis of malignant pleural effusions. *Journal of the Indian Medical Association* 106[9], 589-590. 20-11-0592.

Excl reason: Not in PICO

Davis, R. D., Jr., Oldham, H. N., Jr., and Sabiston, D. C., Jr. Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management, and results. *Annals of Thoracic Surgery* 44[3], 229-237. 1987.

Excl reason: Not in PICO

de-The, G. Epstein-Barr virus and Burkitt's lymphoma worldwide: the causal relationship revisited. *IARC Scientific Publications* [60], 165-176. 1985.

Excl reason: Not in PICO

Doberneck, R. C. The diagnostic yield of lymph node biopsy. *Archives of Surgery* 118[10], 1203-1205. 1983.

Excl reason: Not in PICO

Dodd III, G. D., Greenler, D. P., and Confer, S. R. Thoracic and abdominal manifestations of lymphoma occurring in the immunocompromised patient. *Radiologic Clinics of North America* 30[3], 597-610. 1992.

Excl reason: Not in PICO

Doolabh, N., Anthony, T., Simmang, C., Bieligg, S., Lee, E., Huber, P., Hughes, R., and Turnage, R. Primary colonic lymphoma. *Journal of Surgical Oncology* 74[4], 257-262. 2000.

Excl reason: Not in PICO

Dowd, T. R. Primary care approach to lymphadenopathy. *Nurse Practitioner* 19[12], 36-4. 1994.

Excl reason: Narrative summary

Du, M. Q. and Isaccson, P. G. Gastric MALT lymphoma: from aetiology to treatment. [Review] [74 refs]. *Lancet Oncology* 3[2], 97-104. 2002.

Excl reason: Narrative review

Dughayli, Mohamad, Baidoun, Fadi, and Lupovitch, Aaron. Synchronous perforation of non-Hodgkin's lymphoma of the small intestine and colon: a case report. *Journal of Medical Case*

Reports 5[1], 57. 2011.

Excl reason: Not in PICO

Duncavage, J. A., Campbell, B. H., Hanson, G. A., Kun, L. E., Hansen, R. M., Toohill, R. J., and Malin, T. C. Diagnosis of malignant lymphomas of the nasal cavity, paranasal sinuses and nasopharynx. *Laryngoscope* 93[10], 1276-1280. 1983.

Excl reason: Not in PICO

Edgren, G., Bagnardi, V., Bellocco, R., Hjalgrim, H., Rostgaard, K., Melbye, M., Reilly, M., Adami, H. O., Hall, P., and Nyren, O. Pattern of declining hemoglobin concentration before cancer diagnosis. *International Journal of Cancer* 127[6], 1429-1436. 1-9-2010.

Excl reason: Not in PICO

Elgendy, I. Y. & Lo, M. C. (2014) - Unilateral lower extremity swelling as a rare presentation of non-Hodgkin's lymphoma. - *BMJ Case Reports*, 2014, 2014..

Excl reason: Not in PICO

Ellis, D., Jaffe, R., Green, M., Janosky, J. J., Lombardo-Lane, S., Shapiro, R., Scantlebury, V., Vivas, C., and Jordan, M. L. Epstein-Barr virus-related disorders in children undergoing renal transplantation with tacrolimus-based immunosuppression. *Transplantation* 68[7], 997-1003. 15-10-1999.

Excl reason: Not in PICO

Evron, E., Goland, S., Klepfish, A., Malnick, S. D. H., Sokolowski, N., and Sthoeger, Z. M. Primary multifocal lymphoma of bone presenting as hypercalcemic crisis: Report of a rare manifestation of extranodal lymphoma. *Leukemia & Lymphoma* 34[1-2], 197-200. 1999.

Excl reason: Not in PICO

Ezzie, M. E., Janssen, W. J., O'Brien, J. M., Fox, C. C., and Schwarz, M. I. Clinical problem-solving. Failure to respond--a 52-year-old man presented to his primary care physician with dyspnea and cough. *New England Journal of Medicine* 358[1], 70-74. 3-1-2008.

Excl reason: Not in PICO

Farrer, F. Cancer screening in primary care. *SA Pharmaceutical Journal* 77[9], 41-45. 2010.

Excl reason: Narrative review/Not in PICO

Ferrario, A., Aghemo, A., Goldaniga, M. C., Merli, M., Vincenti, D., Rossi, F. G., De, Gasperi E., Olivero, B., Cro, L., Rattotti, S., Arcaini, L., Onida, F., and Baldini, L. Indolent B-Cell lymphomas treated upfront with antiviral therapy: A series of 13 patients. *Blood* 116[21]. 19-11-2010. American Society of Hematology.

Excl reason: Not in PICO

Ferrer, R. Lymphadenopathy: differential diagnosis and evaluation. [Review] [12 refs]. *American Family Physician* 58[6], 1313-1320. 15-10-1998.

Excl reason: Narrative review

Fijten, G. H. and Blijham, G. H. Unexplained lymphadenopathy in family practice. An evaluation of the probability of malignant causes and the effectiveness of physicians' workup. *Journal of Family Practice* 27[4], 373-376. 1988.

Excl reason: Not in PICO

Foster, T., Miller, J. D., Boye, M. E., and Russell, M. W. Economic Burden of Follicular Non-Hodgkin's Lymphoma. *Pharmacoeconomics* 27[8], 657-679. 2009.

Excl reason: Narrative review

Frederiksen, B. L., Brown, P. D., Dalton, S. O., Steding-Jessen, M., and Osler, M. Socioeconomic inequalities in prognostic markers of non-Hodgkin lymphoma: Analysis of a national clinical database. *European Journal of Cancer* 47[6], 910-917. 2011.

Excl reason: Not in PICO

Friedman, D. R., Coan, A. D., Smith, S. K., Herndon II, J. E., and Abernethy, A. P. Informational needs assessment of non-Hodgkin lymphoma survivors and their physicians. *American Journal of Hematology* 85[7], 528-532. 2010.

Excl reason: Not in PICO

- Friedmann, A. M. Evaluation and management of lymphadenopathy in children. [Review] [7 refs]. *Pediatrics in Review* 29[2], 53-60. 2008.
Excl reason: Narrative review
- Frikha, Zied, Abid, Leila, Abid, Dorra, Mallek, Souad, Frikha, Imed, Abdennadher, Mohamed, Rekik, Noomen, and Kammoun, Samir. Cardiac tamponade and paroxysmal third-degree atrioventricular block revealing a primary cardiac non-Hodgkin large B-cell lymphoma of the right ventricle: a case report. *Journal of Medical Case Reports* 5[1], 433. 2011.
Excl reason: Not in PICO
- Front, D., Bar-Shalom, R., Epelbaum, R., Haim, N., Ben-Arush, M. W., Ben-Shahar, M., Gorenberg, M., Kleinhaus, U., Parmett, S., Kolodny, G. M., and Israel, O. Early detection of lymphoma recurrence with gallium-67 scintigraphy. *Journal of Nuclear Medicine* 34[12], 2101-2104. 1993.
Excl reason: Not in PICO
- Gallego, C., Gonzalez-Diaz, S., Del Carmen, Zarate M., Arias-Cruz, A., Garcia-Calderin, D., Salas, K. Y. M., Calva, M., and Sansores, L. A. D. CVID: A common but still underdiagnosed disease. *World Allergy Organization Journal* 5, S207-S208. 2012. Lippincott Williams and Wilkins.
Excl reason: Not in PICO
- Galvao, Neto A., Shaft, N., Protiva, P., Oroszi, G., and Sahakian, A. Colonic mantle cell lymphoma in situ: A report of a unique case. *Virchows Archiv* 457[2], 255-256. 2010. Springer Verlag.
Excl reason: Not in PICO
- Garment, A., Demopoulos, B., and Caesar, E. P. Neck swelling and night sweating. *Journal of General Internal Medicine* 25, S533-S534. 2010. Springer New York.
Excl reason: Not in PICO
- Geh, J. I. and Spittle, M. F. Oncological problems in AIDS--a review of the clinical features and management. [Review] [74 refs]. *Annals of the Academy of Medicine, Singapore* 25[3], 380-391. 1996.
Excl reason: Narrative review
- Genta, R. M. The gastritis connection: prevention and early detection of gastric neoplasms. [Review] [55 refs]. *Journal of Clinical Gastroenterology* 36[5:Suppl], Suppl-9. 2003.
Excl reason: Narrative review
- Genvresse, I., Luftner, D., Spath-Schwalbe, E., and Buttgereit, F. Prevalence and clinical significance of anticardiolipin and anti-beta2-glycoprotein-I antibodies in patients with non-Hodgkin's lymphoma. *European Journal of Haematology* 68[2], 84-90. 2002.
Excl reason: Not in PICO
- Ghai, S., Pattison, J., Ghai, S., O'Malley, M. E., Khalili, K., and Stephens, M. Primary gastrointestinal lymphoma: spectrum of imaging findings with pathologic correlation. [Review] [39 refs]. *Radiographics* 27[5], 1371-1388. 2007.
Excl reason: Narrative review
- Gonzalez, Q. H., Heslin, M. J., Davila-Cervantes, A., Alvarez-Tostado, J., De Los Monteros, A. E., Shore, G., and Vickers, S. M. Primary colonic lymphoma. *American Surgeon* 74[3], 214-216. 2008.
Excl reason: Not in PICO
- Gosche, J. R. and Vick, L. Acute, subacute, and chronic cervical lymphadenitis in children. [Review] [21 refs]. *Seminars in Pediatric Surgery* 15[2], 99-106. 2006.
Excl reason: Narrative review
- Graili, P., Bakhshayeshkaram, M., and Zahirifard, S. Lymphoma diagnosis on computed tomography guided needle biopsy. *Journal of Thoracic Imaging* 24[3], w1-w2. 2009. Lippincott Williams and Wilkins.
Excl reason: Not in PICO
- Gregory, R. K., Cunningham, D., Fisher, T. A., Rhys-Evans, P., Middleton, G. W., Bishop, L., Wotherspoon, A., Trott, P. A., and Nash, A. G. Investigating lymphadenopathy--report on the first 12 months of the lymph node diagnostic clinic at the Royal Marsden Hospital. *Postgraduate*

Medical Journal 76[899], 566-568. 2000.
 Excl reason: Not in PICO (referred patients)

Groothoff, J. W. Long-term outcomes of children with end-stage renal disease. [Review] [30 refs].
 Pediatric Nephrology 20[7], 849-853. 2005.
 Excl reason: Not in PICO

Grosfeld, J. L., Skinner, M. A., Rescorla, F. J., West, K. W., and Scherer, L. R., III. Mediastinal tumors in children: experience with 196 cases. *Annals of Surgical Oncology* 1[2], 121-127. 1994.
 Excl reason: Not in PICO

Guccion, J. G., Gibert, C. L., Ortega, L. G., and Hadfield, T. L. Cat scratch disease and acquired immunodeficiency disease: diagnosis by transmission electron microscopy. *Ultrastructural Pathology* 20[3], 195-202. 1996.
 Excl reason: Not in PICO

Guiliani, P., Gicquel, N., Lepain, C., and Peziere, N. AIDS and lymphoma. Some problems for the patient care team. [French]. *Soins; la revue de reference infirmiere* [538-539], 10-13. 1990.
 Excl reason: Not in PICO

Guindi, M. Role of Helicobacter pylori in the pathogenesis of gastric carcinoma and progression of lymphoid nodules to lymphoma. [Review] [39 refs]. *Canadian Journal of Gastroenterology* 13[3], 224-227. 1999.
 Excl reason: Narrative review

Gumustas, O. G., Gumustas, A., Yalcin, R., Savci, G., and Soylu, R. A. Unusual causes of small bowel obstruction and contemporary diagnostic algorithm. [Review] [30 refs]. *Journal of Medical Imaging & Radiation Oncology* 52[3], 208-215. 2008.
 Excl reason: Not in PICO

Gunatilake, S. S. & Wimalaratna, H. (2014) - Angioedema as the first presentation of B-cell non-Hodgkin lymphoma - an unusual case with normal C1 esterase inhibitor level: a case report. - *BMC Research Notes*, 7: 495.
 Excl reason: Not in PICO

Gupta, R. and Bhardwaj, S. Bilateral primary non Hodgkin's lymphoma of the breast: A rare case report. *JK Science* 14[1], 43-44. 2011.
 Excl reason: Not in PICO

Guyen, G. S., Uzun, O., Cakir, B., Akova, M., and Unal, S. Infectious complications in patients with hematological malignancies consulted by the Infectious Diseases team: a retrospective cohort study (1997-2001). *Supportive Care in Cancer* 14[1], 52-55. 2006.
 Excl reason: Not in PICO

Hakkou, J., Rostom, S., Bahiri, R., and Hajjaj-Hassouni, N. Paraneoplastic rheumatic syndromes: Report of eight cases and review of literature. *Rheumatology International* 32[6], 1485-1489. 2012.
 Excl reason: Not in PICO

Haldorsen, I. S., Espeland, A., Larsen, J. L., and Mella, O. Diagnostic delay in primary central nervous system lymphoma. *Acta Oncologica* 44[7], 728-734. 2005.
 Excl reason: Not in PICO

Hamburger, J. Sjogren's syndrome - Managing oral and systemic symptoms via a multi-disciplinary approach. *Oral Diseases* 10[5], 306-309. 2004.
 Excl reason: Not in PICO

Han, S. H., Maeng, Y. H., Kim, Y. S., Jo, J. M., Kwon, J. M., Kim, W. K. & Kim, M. O. (2014) Primary anaplastic large cell lymphoma of the lung presenting with acute atelectasis. *Thoracic Cancer*, 5: 78-81.
 Excl reason: Not in PICO

Hanaoka, M., Tsukimori, K., Hojo, S., Abe, Y., Mutou, T., Muta, K., Iwasa, A., Yao, T., and Nakano, H. B-cell lymphoma during pregnancy associated with hemophagocytic syndrome and placental

involvement. *Clinical Lymphoma & Myeloma* 7[7], 486-490. 2007.

Excl reason: Not in PICO

Harrington, K. J., Michalaki, V. J., Vini, L., Nutting, C. M., Syrigos, K. N., A'Hern, R., and Harmer, C. L. Management of non-Hodgkin's lymphoma of the thyroid: the Royal Marsden Hospital experience. *British Journal of Radiology* 78[929], 405-410. 2005.

Excl reason: Not in PICO

Hart, S., Horsman, J. M., Radstone, C. R., Hancock, H., Goepel, J. R., and Hancock, B. W. Localised extranodal lymphoma of the head and neck: The Sheffield Lymphoma Group experience (1971-2000). *Clinical Oncology* 16[3], 186-192. 2004.

Excl reason: Not in PICO

Hartmann, M. and Sartor, K. [Primary malignant lymphoma of the brain]. [Review] [26 refs] [German]. *Radiologe* 37[1], 42-50. 1997.

Excl reason: Narrative review

Hashimoto, S., Kitahara, T., Arimoto, T., Kamada, T., Shirato, H., Nishioka, T., and Nojima, T. [A clinical and pathological study of non-Hodgkin's lymphoma of the nasal cavity and paranasal sinuses]. [Japanese]. *Nippon Igaku Hoshasen Gakkai Zasshi - Nippon Acta Radiologica* 53[6], 679-687. 25-6-1993.

Excl reason: Not in PICO

Heitman, B. and Irizarry, A. Infectious disease causes of lymphadenopathy: localized versus diffuse. [Review] [50 refs]. *Lippincott's Primary Care Practice* 3[1], 19-38. 1999.

Excl reason: Narrative review

Hiller, E. [Malignant Hodgkin's and non-Hodgkin's lymphomas]. [German]. *MMW Fortschritte der Medizin* 147[9], 31-34. 3-3-2005.

Excl reason: Narrative review

Hojo, A., Nakayama, H., Aramaki, O., Higaki, T., Moriguchi, M., Sugitani, M., Miura, K., Takeuchi, J., Nishiyama, R., Moriyama, M. & Takayama, T. (2013) Diagnostic value of open biopsy for malignant T-cell lymphoma of the liver. *International Surgery*, 98: 13-18.

Excl reason: Not in PICO

Hojsak, I., Misak, Z., and Kolacek, S. Coeliac disease today: The search for complications and associated disorders. [Croatian]. *Paediatrica Croatica* 49[2], 79-84. 2005.

Excl reason: Narrative review

Holstein, K., Janning, M., Marx, G., Lentz, B., Bokemeyer, C., and Langer, F. Another case of acquired haemophilia (AH) associated with a myeloproliferative neoplasm (MPN): Implications for the differential diagnosis of underlying malignancies. *Hamostaseologie* 32[1], A86. 2012. Schattauer GmbH.

Excl reason: Not in PICO

Hong, J., Kim, J. H., Park, J. & Lee, J. H. (2013) Clinical symptom or sign-directed surveillance can be more useful in detecting relapse compared to routine imaging in patients with diffuse large b-cell lymphoma in remission. *Blood*, 122.

Excl reason: Not in PICO

Horton, K. M. and Fishman, E. K. Multidetector-row computed tomography and 3-dimensional computed tomography imaging of small bowel neoplasms: current concept in diagnosis. [Review] [29 refs]. *Journal of Computer Assisted Tomography* 28[1], 106-116. 2004.

Excl reason: Narrative review

Huang, JiaJia, Jiang, WenQi, Xu, RuiHua, Huang, HuiQiang, Lv, Yue, Xia, ZhongJun, Sun, XiaoFei, Guan, ZhongZhen, Lin, TongYu, and Li, ZhiMing. Primary gastric non-Hodgkin's lymphoma in Chinese patients: clinical characteristics and prognostic factors. *BMC Cancer* 10[1], 358. 2010.

Excl reason: Not in PICO

Huda, S., Tyne, H., and Iniesta, I. B-cell non-hodgkin lymphoma presenting with diplopia, ataxia, and subacute polyneuropathy: Neoplastic vs paraneoplastic? *Journal of Neurology, Neurosurgery*

and Psychiatry 81[11], e41. 2010. BMJ Publishing Group.

Excl reason: Not in PICO

Huhn, D. Clinical aspects and therapy of malignant lymphomas in AIDS--symptomatology of AIDS encephalopathy. [German]. *Verhandlungen der Deutschen Gesellschaft für Innere Medizin* 92, 330-336. 1986.

Excl reason: Not in PICO

Ichimaru, M., Kamiyama, S., Moriuchi, Y., Kuraishi, Y., Usui, N., Toki, H., Okabe, K., Niho, Y., Shibuya, T., and Umei, T. [Clinical study on the effect of natural alpha-interferon (HLBI) in the treatment of adult T-cell leukemia]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]* 15[10], 2975-2981. 1988.

Excl reason: Not in PICO

Imteyaz, H. & Stern, M. (2013) N-type calcium channel binding antibodies in a patient with paraneoplastic cerebellar degeneration in association with non-hodgkins lymphoma: A case report. *PM and R*, 5: S183.

Excl reason: Not in PICO

Jakubowska-Pietkiewicz, E., Szczepaniak-Kubat, A., Zalewska-Szewczyk, B., and Chlebna-Sokol, D. Skeletal status at diagnosis in children with hematologic malignancy - Pilot study. *Advances in Clinical and Experimental Medicine* 19[4], 531-535. 2010.

Excl reason: Not in PICO

Jett, J. R. Mediastinal tumors. *Respirology* 15, 18. 2010. Blackwell Publishing.

Excl reason: Narrative review

Johnson, P. T., Nazarian, L. N., Feld, R. I., Needleman, L., Lev-Toaff, A. S., Segal, S. R., and Halpern, E. J. Sonographically guided renal mass biopsy: indications and efficacy. *Journal of Ultrasound in Medicine* 20[7], 749-753. 20-11-0755.

Excl reason: Not in PICO

Jordan, R., Diss, T. C., Lench, N. J., Isaacson, P. G., and Speight, P. M. Immunoglobulin gene rearrangements in lymphoplasmacytic infiltrates of labial salivary glands in Sjogren's syndrome. A possible predictor of lymphoma development. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics* 79[6], 723-729. 1995.

Excl reason: Not in PICO

Joshi, P. V., Lele, V. R. & Shaikh, I. (2013) Mortui vivos docent--the dead teach the living: 18-fluorodeoxyglucose positron emission tomography-computed tomography findings in a case of intravascular B cell lymphoma. *Journal of Cancer Research & Therapeutics*, 9: 141-144.

Excl reason: Not in PICO

Jovanovic, J., Brkic, S., Klasnja, B., and Fabri, M. [Epstein-Barr, hepatitis B and hepatitis C virus infections and their oncogenic potentials]. [Croatian]. *Medicinski Pregled* 50[11-12], 499-504. 1997.

Excl reason: Narrative review

Jovic, R., Vlaski, L., Komazec, Z., and Canji, K. [Results of treatment of deep neck abscesses and phlegmons]. [Croatian]. *Medicinski Pregled* 52[9-10], 402-408. 1999.

Excl reason: Not in PICO

Kalauch, A., Benter, T., Kroschinsky, F., Stroszczyński, C., Kellermann, S., Ehninger, G., and Schuler, M. Sezary Syndrome: Infiltration of the gastric wall - Does it matter? *Onkologie* 34, 135. 2011. S. Karger AG.

Excl reason: Not in PICO

Kapoor, A. Pulmonary lymphomatoid granulomatosis : An uncommon cause of multiple pulmonary nodules. *Chest* 140[4 MEETING ABSTRACT]. 2011. American College of Chest Physicians.

Excl reason: Not in PICO

Karakayli, G., Beckham, G., Orengo, I., and Rosen, T. Exfoliative dermatitis. *American Family Physician* 59[3], 625-630. 1-2-1999.

Excl reason: Narrative review

- Karolina, O.-H., Osmola-Mankowska, A., Silny, W., Danczak-Pazdrowska, A. & Polanska, A. (2013) The possibility of monitoring using the highfrequency ultrasound in patients with the primary cutaneous t-cell lymphoma. *Skin Research and Technology*, 19: e586.
Excl reason: Not in PICO
- Kassis, J., Maeda, A., Teramoto, N., Takada, K., Wu, C., Klein, G., and Wells, A. EBV-expressing AGS gastric carcinoma cell sublines present increased motility and invasiveness. *International Journal of Cancer* 99[5], 644-651. 10-6-2002.
Excl reason: Not in PICO
- Kawaguchi, S., Nakazawa, S., Yoshino, J., and Ichikawa, T. Clinical diagnosis of benign lymphoma of the stomach. [Japanese]. *Stomach and Intestine* 16[2], 137-144. 1981.
Excl reason: Not in PICO
- Khadzhiev, E., Popova, L., and Raikov, Kh. [Autoimmune hemolytic anemia in malignant lymphomas]. [Bulgarian]. *Vutreshni Bolesti* 28[6], 56-60. 1989.
Excl reason: Not in PICO
- Khojasteh, A., Reynolds, R. D., and Khojasteh, C. A. Malignant lymphoreticular lesions in patients with immune disorders resembling acquired immunodeficiency syndrome (AIDS): review of 80 cases. [Review] [39 refs]. *Southern Medical Journal* 79[9], 1070-1075. 1986.
Excl reason: Narrative review
- Khorana, A., Bunn, P., McLaughlin, P., Vose, J., Stewart, C., and Czuczman, M. S. A phase II multicenter study of CAMPATH-1H antibody in previously treated patients with nonbulky non-Hodgkin's lymphoma. *Leukemia & Lymphoma* 41[1-2], 77-87. 2001.
Excl reason: Not in PICO
- Kinlen, L. J. Childhood leukaemia and non-Hodgkins lymphoma in young people living close to nuclear reprocessing sites. *Biomedicine & Pharmacotherapy* 47[10], 429-434. 1993.
Excl reason: Narrative review
- Kojima, M., Motoori, T., and Nakamura, S. Benign, atypical and malignant lymphoproliferative disorders in rheumatoid arthritis patients. [Review] [44 refs]. *Biomedicine & Pharmacotherapy* 60[10], 663-672. 2006.
Excl reason: Narrative review
- Kortsik, C. S., Heine, M., Staedt, U., Kirschstein, W., and Gladisch, R. [Malignant tumor-like abdominal lymphoma in Whipple's disease]. [German]. *Deutsche Medizinische Wochenschrift* 114[28-29], 1107-1109. 14-7-1989.
Excl reason: Not in PICO
- Kose, D., Paksoy, Y., Koksal, Y. & Unal, E. (2014) - Neurological complication of non Hodgkin lymphoma in childhood: experience from a single center in Turkey. - *Childs Nervous System*, 30: 639-645.
Excl reason: Not in PICO
- Krejsgaard, T., Odum, N., Geisler, C., Wasik, M. A., and Woetmann, A. Regulatory T cells and immunodeficiency in mycosis fungoides and Sezary syndrome. [Review]. *Leukemia* 26[3], 424-432. 2012.
Excl reason: Narrative review
- Krishnan, A., Shirkhoda, A., Tehranzadeh, J., Armin, A. R., Irwin, R., and Les, K. Primary bone lymphoma: radiographic-MR imaging correlation. [Review] [27 refs]. *Radiographics* 23[6], 1371-1383. 1384.
Excl reason: Narrative review
- Kutikova, L., Bowman, L., Chang, S., Long, S. R., Arning, M., and Crown, W. H. Medical costs associated with non-Hodgkin's lymphoma in the United States during the first two years of treatment. *Leukemia & Lymphoma* 47[8], 1535-1544. 2006.
Excl reason: Not in PICO
- Labenz, J. and Malfertheiner, P. European guidelines on the diagnosis and therapy of Helicobacter pylori infections (Maastricht consensus report). [German]. *Munchener Medizinische*

Wochenschrift 139[24], 30-32. 1997.

Excl reason: Guideline

Lai, Y., Zhang, M., Wang, L., Yang, A., Li, J., Zhang, X., Zhou, X., Hong, T., Qian, J. & Zhong, D. (2014) Uveitis and T cell lymphoma: A rare but notable relationship. *Medical Oncology*, 31.

Excl reason: Not in PICO

Lee, S. C., Hong, S. W., Lee, Y. S., Jeong, J. J., Nam, K. H., Chung, W. Y., Chang, H. S., and Park, C. S. Primary thyroid mucosa-associated lymphoid tissue lymphoma; a clinicopathological study of seven cases. *Journal of The Korean Surgical Society* 81[6], 374-379. 2011.

Excl reason: Not in PICO

Leslie, L. A., Lebowitz, B., Neugut, A. I., Gregory, Mears J., Bhagat, G., and Green, P. H. Incidence of lymphoproliferative disorders in patients with celiac disease. *American Journal of Hematology* 87[8], 754-759. 2012.

Excl reason: Not in PICO

Lukic, S., Marjanovic, G., and Zivanovic, J. Palpable lymphadenopathy in primary care. *Acta Facultatis Medicae Naissensis* 28[1], 17-23. 2011.

Excl reason: Narrative review

Madan, A., Sethi, P. & Tripathi, K. (2013) Upper extremity venous thrombosis-calm before the storm. *Journal of General Internal Medicine*, 28: S415.

Excl reason: Not in PICO

Mady, S. M. Managing lumps in the neck. [Review] [4 refs]. *Practitioner* 242[1587], 472-475. 1998.

Excl reason: Narrative review

Maher, N., O'Brien, Y., Milner, M., and Gleeson, N. Lymphoma-the great masquerader. *Irish Journal of Medical Science* 180, S134-S135. 2011. Springer.

Excl reason: Not in PICO

Maksimovic, Z., Cvetkovic, S., Markovic, M., Perisic, M., Colic, M., and Putnik, S. [Differential diagnosis of deep vein thrombosis]. [Serbian]. *Srpski Arhiv Za Celokupno Lekarstvo* 129[1-2], 13-17. 2001.

Excl reason: Not in PICO

Malfertheiner, P. Current European concepts in the management of *Helicobacter pylori* infection. The Maastricht consensus report. *Gut* 41[1], 8-13. 1997.

Excl reason: Narrative review/guideline

Mann, G., Attarbaschi, A., Steiner, M., Simonitsch, I., Strobl, H., Urban, C., Meister, B., Haas, O., Dworzak, M., and Gadner, H. Early and reliable diagnosis of non-Hodgkin lymphoma in childhood and adolescence: Contribution of cytomorphology and flow cytometric immunophenotyping. *Pediatric Hematology and Oncology* 23[3], 167-176. 2006.

Excl reason: Not in PICO

Marshall, N. A., Culligan, D. J., Johnston, P. W., Millar, C., Barker, R. N., and Vickers, M. A. CD4+ T-cell responses to Epstein-Barr virus (EBV) latent membrane protein 1 in infectious mononucleosis and EBV-associated non-Hodgkin lymphoma: Th1 in active disease but Tr1 in remission. *British Journal of Haematology* 139[1], 81-89. 2007.

Excl reason: Not in PICO

Matsukura, N. [*Helicobacter pylori* infection and gastric diseases--pathogenesis and effects of eradication]. [Review] [59 refs] [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]* 29[8], 1341-1349. 2002.

Excl reason: Narrative review

Matsuo, T., Fujiwara, N., and Nakata, Y. First presenting signs or symptoms of sarcoidosis in a Japanese population. *Japanese Journal of Ophthalmology* 49[2], 149-152. 2005.

Excl reason: Not in PICO

McQueen, A., Martin, S. A., and Lio, P. A. Derm emergencies: detecting early signs of trouble. *Journal of Family Practice* 61[2], 71-78. 2012.

Excl reason: Narrative/educational review

Megraud, F. Helicobacter pylori infection: Review and practice. [French]. Presse Medicale 39[7-8], 815-822. 2010.
Excl reason: Narrative review

Meier, J. D. & Grimmer, J. F. (2014) - Evaluation and management of neck masses in children. [Review]. - *American Family Physician*, 89: 353-358.
Excl reason: Narrative review

Melbye, M., Smedby, K. E., Lehtinen, T., Rostgaard, K., Glimelius, B., Munksgaard, L., Schollkopf, C., Sundstrom, C., Chang, E. T., Koskela, P., Adami, H. O., and Hjalgrim, H. Atopy and risk of non-Hodgkin lymphoma. *Journal of the National Cancer Institute* 99[2], 158-166. 17-1-2007.
Excl reason: Not in PICO

Miller, K. C., Musial, L., Whitworth, A., and Chanan-Khan, A. Management of patients with chronic lymphocytic leukemia treated with lenalidomide. [Review]. *Clinical Journal of Oncology Nursing* 14[4], 491-499. 2010.
Excl reason: Narrative review

Misawa, S., Tsuda, S., Taniwaki, M., Horiike, S., Ariyama, Y., Hirakawa, K., Ueda, Y., Kaneko, H., Nakao, M., and Kashima, K. [A combined consecutive therapy with fosfomycin and sulbactam/cefoperazone for bacterial infections associated with hematological diseases]. [Japanese]. *Japanese Journal of Antibiotics* 48[4], 514-521. 1995.
Excl reason: Not in PICO

Montes Teves, P. A., Soria Medina, J. I., Gamarra Espinoza, Z. I., and Monge, Salgado E. [The physician's attitude towards infection by Helicobacter pylori in clinical practice]. [Spanish]. *Revista de Gastroenterologia del Peru* 22[3], 221-227. 2002.
Excl reason: Not in PICO

Morita, R., Yoshii, M., Nakajima, K., Kohsaka, T., Miki, M., and Torizuka, K. Clinical evaluation of serum ferritin to iron ratio in malignant diseases. *European Journal of Nuclear Medicine* 6[7], 331-336. 1981.
Excl reason: Not in PICO

Morrow, T. J., Volpe, S., Gupta, S., Tannous, R. E., and Fridman, M. Anemia of cancer in intermediate-grade non-Hodgkin's lymphoma. *Southern Medical Journal* 95[8], 889-896. 2002.
Excl reason: Not in PICO

Morse, E. E., Yamase, H. T., Greenberg, B. R., Sporn, J., Harshaw, S. A., Kiraly, T. R., Ziemba, R. A., and Fallon, M. A. The role of flow cytometry in the diagnosis of lymphoma: a critical analysis. *Annals of Clinical & Laboratory Science* 24[1], 6-11. 1994.
Excl reason: Not in PICO

Mueller, N. Overview: viral agents and cancer. [Review] [18 refs]. *Environmental Health Perspectives* 103, Suppl-61. 1995.
Excl reason: Narrative review

Munir, N. and Bradley, P. J. Diagnosis and management of neoplastic lesions of the submandibular triangle. *Oral Oncology* 44[3], 251-260. 2008.
Excl reason: Not in PICO

Musiej-Nowakowska, E. and Rostropowicz-Denisiewicz, K. Differential diagnosis of neoplastic and rheumatic diseases in children. *Scandinavian Journal of Rheumatology* 15[2], 124-128. 1986.
Excl reason: Not in PICO

Naito, Y., Okabe, Y., Kawahara, A., Taira, T., Yamagushi, T., Abe, H., Arikawa, S., Nakayama, M., Yasumoto, M., Eriguchi, N., Naito, H., Kage, M., and Yano, H. Guide to diagnosing primary pancreatic lymphoma, B-cell type: immunocytochemistry improves the diagnostic accuracy of endoscopic ultrasonography-guided fine needle aspiration cytology. *Diagnostic Cytopathology* 40[8], 732-736. 2012.
Excl reason: Not in PICO

Nakamura, S., Aoyagi, K., Iwanaga, S., Yao, T., Tsuneyoshi, M., and Fujishima, M. Synchronous and metachronous primary gastric lymphoma and adenocarcinoma: a clinicopathological study of 12

patients. *Cancer* 79[6], 1077-1085. 15-3-1997.

Excl reason: Not in PICO

Naranji, I., Zakri, R. H. & Liston, T. (2013) Mantle cell lymphoma presenting as a pelvi-ureteric junction obstruction: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 7: 105.

Excl reason: Not in PICO

Narsana, N., Xie, J., Singhvi, G., and Aron, J. A case of non-hodgkins lymphoma mimicking metastatic colorectal cancer. *American Journal of Gastroenterology* 105, S320. 2010. Nature Publishing Group.

Excl reason: Not in PICO

Naserallah, Z. and Al, Maher M. Clinical picture and outcome of poor risk non-Hodgkin's lymphoma in Saudi children. *International Pediatrics* 9[4], 247-250. 1994.

Excl reason: Not in PICO

Nau, K. C. and Lewis, W. D. Multiple myeloma: diagnosis and treatment. [Review] [29 refs]. *American Family Physician* 78[7], 853-859. 1-10-2008.

Excl reason: Narrative review

Navani, N., Nankivell, M., Woolhouse, I., Harrison, R. N., Munavvar, M., Oltmanns, U., Falzon, M., Kocjan, G., Rintoul, R. C., and Janes, S. M. Endobronchial ultrasound-guided transbronchial needle aspiration for the diagnosis of intrathoracic lymphadenopathy in patients with extrathoracic malignancy: a multicenter study. *Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer* 6[9], 1505-1509. 2011.

Excl reason: Not in PICO

Neal, R. D. and Allgar, V. L. Sociodemographic factors and delays in the diagnosis of six cancers: analysis of data from the 'National Survey of NHS Patients: Cancer'. *British Journal of Cancer* 92[11], 1971-1975. 2005.

Excl reason: Not in PICO

Nicola, P., Cartoni, C., Romani, C., Brunetti, G. A., D'Elia, G. M., Cupelli, L., Tendas, A., de, Fabritiis P., Mandelli, F., and Foa, R. Epidemiology, features and outcome of pain in patients with advanced hematological malignancies followed in a home care program: an Italian survey. *Annals of Hematology* 86[9], 671-676. 2007.

Excl reason: Not in PICO

Nishimura, H. [Diagnosis of soft tissue tumors: 10 checkpoints]. [Review] [32 refs] [Japanese]. *Nippon Igaku Hoshasen Gakkai Zasshi - Nippon Acta Radiologica* 61[6], 275-291. 2001.

Excl reason: Narrative review

Nishimura, H. Diagnosis of soft tissue tumors: 10 checkpoints. [Japanese]. *Nihon Igaku Hoshasen Gakkai zasshi Nippon*[6], 275-291. 2001.

Excl reason: Narrative review

Niv, Y. and Abuksis, G. Survey of the opinions, knowledge and practices of surgeons and internists regarding *Helicobacter pylori* test-and-treat policy. *Journal of Clinical Gastroenterology* 36[2], 139-143. 2003.

Excl reason: Not in PICO

Nuernberg, D., Ignee, A., and Dietrich, C. F. [Ultrasound in gastroenterology--liver and spleen]. [Review] [92 refs] [German]. *Zeitschrift fur Gastroenterologie* 44[9], 991-1000. 2006.

Excl reason: Narrative review

Nurnberg, D. [Ultrasound of adrenal gland tumours and indications for fine needle biopsy (uFNB)]. [Review] [116 refs] [German]. *Ultraschall in der Medizin* 26[6], 458-469. 2005.

Excl reason: Narrative summary

Ogwang, M. D., Zhao, W., Ayers, L. W., and Mbulaiteye, S. M. Accuracy of Burkitt lymphoma diagnosis in constrained pathology settings: importance to epidemiology. *Archives of Pathology & Laboratory Medicine* 135[4], 445-450. 2011.

Excl reason: Not in PICO

- Ol'khova, E. B., Shumeiko, N. K., and Fomichev, M. I. [Mesadenitis in children with acute abdominal pain syndrome: clinical and echographic parallels]. [Review] [Russian]. *Vestnik Rentgenologii i Radiologii*.(3):45-8, 2011 Jul-Aug. [3], 45-48. 2011.
Excl reason: Narrative review
- Otrock, Z. K., Hatoum, H. A., Uthman, I. W., Taher, A. T., Saab, S., and Shamseddine, A. I. Non-Hodgkin's lymphoma in a woman with adult-onset Still's disease: a case report. *Journal of Medical Case Reports [Electronic Resource]* 2, 73. 2008.
Excl reason: Not in PICO
- Paauw, D. S., Wenrich, M. D., Curtis, J. R., Carline, J. D., and Ramsey, P. G. Ability of primary care physicians to recognize physical findings associated with HIV infection. *JAMA* 274[17], 1380-1382. 1-11-1995.
Excl reason: Not in PICO
- Pagano, J. S. Epstein-Barr virus: the first human tumor virus and its role in cancer. [Review] [24 refs]. *Proceedings of the Association of American Physicians* 111[6], 573-580. 1999.
Excl reason: Narrative review
- Pasic, S., Minic, A., Djuric, P., Micic, D., Kuzmanovic, M., Sarjanovic, L., and Markovic, M. Fever of unknown origin in 185 paediatric patients: a single-centre experience. *Acta Paediatrica* 95[4], 463-466. 2006.
Excl reason: Not in PICO
- Patel, H. and Sisson, S. Wegeners granulomatosis in a patient with fever of unknown origin. *Journal of General Internal Medicine* 25, S564. 2010. Springer New York.
Excl reason: Not in PICO
- Paulaviciene, R., Asoklis, R., Malysko, K., Petroska, D., Kryzauskaite, L., and Rutkauskaite, D. Diagnostic aspects and immunologic identification potentials of ocular adnexal lymphoma: Report of selected cases. *Acta Ophthalmologica* 90, 80. 2012. Blackwell Publishing Ltd.
Excl reason: Not in PICO
- Perkins, S. L., Segal, G. H., and Kjeldsberg, C. R. Work-up of lymphadenopathy in children. [Review] [18 refs]. *Seminars in Diagnostic Pathology* 12[4], 284-287. 1995.
Excl reason: Narrative review
- Pietinalho, A., Ohmichi, M., Hiraga, Y., Lofroos, A. B., and Selroos, O. The mode of presentation of sarcoidosis in Finland and Hokkaido, Japan. A comparative analysis of 571 Finnish and 686 Japanese patients. *Sarcoidosis Vasculitis & Diffuse Lung Diseases* 13[2], 159-166. 1996.
Excl reason: Not in PICO
- Pittman, M. E., Chen, L., Frater, J. L., Hassan, A., Nguyen, T. T., and Kreisel, F. Utility of cerebrospinal fluid in the diagnosis of non-hodgkin lymphoma. *Laboratory Investigation* 92, 103A. 2012. Nature Publishing Group.
Excl reason: Not in PICO
- Pongas, G., Hamilos, G., Rolston, K. V., and Kontoyiannis, D. P. Formal adult infectious disease specialist consultations in the outpatient setting at a comprehensive cancer center (1998-2008): diverse and impactful. *Supportive Care in Cancer* 20[2], 261-265. 2012.
Excl reason: Not in PICO
- Puryrsko, A. S., Coppa, C. P., Kalady, M. F., Pai, R. K., Leao Filho, H. M., Thupili, C. R. & Remer, E. M. (2014) - Benign and malignant tumors of the rectum and perirectal region. - *Abdominal Imaging*, 39: 824-852.
Excl reason: Narrative review
- Pylypchuk, R. D., Schouten, L. J., Goldbohm, R. A., Schouten, H. C., and van den Brandt, P. A. Body mass index, height, and risk of lymphatic malignancies: a prospective cohort study. *American Journal of Epidemiology* 170[3], 297-307. 1-8-2009.
Excl reason: Not in PICO
- Raderer, M., Puspok, A., Stummvoll, G., Langle, F., and Chott, A. Early cancer of the stomach arising after successful treatment of gastric MALT lymphoma in patients with autoimmune disease.

Scandinavian Journal of Gastroenterology 38[3], 294-297. 2003.
 Excl reason: Not in PICO

Ragupathy, K. & Bappa, L. (2013) Primary vaginal Non-Hodgkin lymphoma: Gynecologic diagnosis of a hematologic malignancy. *Journal of Lower Genital Tract Disease*, 17: 326-329.
 Excl reason: Not in PICO

Raza, K. and Dunitz, J. 19 Year old patient with "Recurrent asthma". *American Journal of Respiratory and Critical Care Medicine* 181[1 Meeting Abstracts]. 1-5-2010. American Thoracic Society.
 Excl reason: Not in PICO

Reamy, B. V., Bunt, C. W., and Fletcher, S. A diagnostic approach to pruritus. *American Family Physician* 84[2], 195-202. 15-7-2011.
 Excl reason: Narrative review

Reddy, U., Bewick, J., Good, C., Chevassut, T., and Das-Purkayastha, P. K. Diffuse large B-cell lymphoma: An unusual cause of severe otalgia and facial palsy. *BMJ Case Reports* . 2012.
 Excl reason: Not in PICO

Ridolfo, A. L., Santambrogio, S., Mainini, F., Vago, L., Gervasoni, C., Gori, A., Parravicini, C., Monforte, A. A., and Galli, M. High frequency of non-Hodgkin's lymphoma in patients with HIV-associated Kaposi's sarcoma. *AIDS* 10[2], 181-185. 1996.
 Excl reason: Not in PICO

Riederer, A., Zietz, C., Ihrler, S., and Vogl, T. [Cystic lymphoepithelial lesions in the head and neck area in HIV-infected patients]. [German]. *Laryngo- Rhino- Otologie* 73[4], 209-214. 1994.
 Excl reason: Not in PICO

Robotin, M. C., Law, M. G., Milliken, S., Goldstein, D., Garsia, R. J., Dolan, G. M., Kaldor, J. M., and Grulich, A. E. Clinical features and predictors of survival of AIDS-related non-Hodgkin's lymphoma in a population-based case series in Sydney, Australia. *Hiv Medicine* 5[5], 377-384. 2004.
 Excl reason: Not in PICO

Romera, M., Heras, I., Castilla, C., Nieto, J. B., Manchado, J. J., Perez-Ceballos, E., Amigo, M. L., Lozano, M., and Vicente, V. Clinical features and outcome of respiratory syncytial virus infection in 26 haematologic disorders patients. *Bone Marrow Transplantation* 46, S224. 2011. Nature Publishing Group.
 Excl reason: Not in PICO

Rubio-Rivas, M., Vidaller, A., Pujol, I. Farriols, and Mast, R. [Rapid diagnosis unit in a third level hospital. Descriptive study of the first year and a half]. [Spanish]. *Revista Clinica Espanola* 208[11], 561-563. 2008.
 Excl reason: Not in PICO

Ruffer, J. U., Flechtner, H., Heim, M., Schwarz, R., and Weis, J. [Cancer fatigue syndrome]. [German]. *Versicherungsmedizin* 55[1], 3-7. 1-3-2003.
 Excl reason: Not in PICO

Rustagi, T., DeVries, K., and Diez, L. Screening colonoscopy in chronic hepatitis C patients. *American Journal of Gastroenterology* 105, S562-S563. 2010. Nature Publishing Group.
 Excl reason: Not in PICO

Saber, M. M., Zeeneldin, A. A., Samra, M. A. & Farag, S. A. (2013) Primary gastrointestinal lymphoma in an Egyptian district: a study using a population-based cancer registry. *Journal of Egyptian National Cancer Institute*, 25: 95-101.
 Excl reason: Not in PICO

Saito, R., Ishizuka, E., Iwasaki, A., Chiba, K., Ambo, T., and Kobayashi, K. Malignant lymphoma of the testis: A case report. [Japanese]. *Nishinohon Journal of Urology* 57[9], 1016-1018. 1995.
 Excl reason: Not in PICO

Sakakihara, Y. [Primary care in pediatrics: Immediate diagnosis in first visit]. [Review] [0 refs] [Japanese]. *Nippon Rinsho - Japanese Journal of Clinical Medicine* 64[11], 2164. 2006.
 Excl reason: Narrative review? (Japanese one page article)

Sauter, E. R., Arensman, R. M., and Falterman, K. W. Thymic enlargement in children. *American Surgeon* 57[1], 21-23. 1991.
Excl reason: Not in PICO

Savage, S. A., Wotherspoon, H. A., Fitzsimons, E. J., and MacKenzie, K. Cervical lymphadenopathy resulting in a diagnosis of lymphoma. *Scottish Medical Journal* 53[3], 13-16. 2008.
Excl reason: Not in PICO

Schechter, M. T., Boyko, W. J., Jeffries, E., Willoughby, B., Nitz, R., and Constance, P. The Vancouver Lymphadenopathy-AIDS Study: 1. Persistent generalized lymphadenopathy. *Canadian Medical Association Journal* 132[11], 1273-1279. 1-6-1985.
Excl reason: Not in PICO

Schleiffenbaum, B. and Fehr, J. Value of the blood picture and flow cytometry immunotyping in the early diagnosis of low-grade lymphoma. [German]. *Therapeutische Umschau Revue*[2], 117-122. 1996.
Excl reason: Narrative review

Schleiffenbaum, B. and Fehr, J. [Value of the blood picture and flow cytometry immunotyping in the early diagnosis of low-grade lymphoma]. [Review] [15 refs] [German]. *Therapeutische Umschau* 53[2], 117-122. 1996.
Excl reason: Narrative review

Schmidt, N., Kostev, K., Ziller, V., Kowall, B. & Rathmann, W. (2014) Association of diabetes and cancer-diagnoses in primary care practices in Germany. *Journal of Clinical Oncology*, 32.
Excl reason: Published as abstract only. Not enough information available to ascertain relevance.

Schroder, J. [Enlarged lymph nodes as an incidental finding. How can carcinoma be excluded?]. [German]. *MMW Fortschritte der Medizin* 143[7], 30-32. 15-2-2001.
Excl reason: Narrative review

Schusterbauer, C., Cairoli, A., and Ketterer, N. [Management of lymphoma and pregnancy]. [French]. *Revue Medicale Suisse* 5[204], 1104-1106. 1108.
Excl reason: Narrative review

Scully, C. and Felix, D. H. Oral medicine--update for the dental practitioner lumps and swellings. *British Dental Journal* 199[12], 763-770. 24-12-2005.
Excl reason: Narrative review

Sengupta, S. and Pal, R. Clinicopathological correlates of pediatric head and neck cancer. *Journal of Cancer Research and Therapeutics* 5[3], 181-185. 2009.
Excl reason: Not in PICO

Sharma, A., Bajpai, J., Raina, V., and Mohanti, B. K. HIV-associated non-Hodgkins lymphoma: Experience from a regional cancer center. *Indian Journal of Cancer* 47[1], 35-39. 2010.
Excl reason: Not in PICO

Sheth, S., Ali, S., and Fishman, E. Imaging of renal lymphoma: patterns of disease with pathologic correlation. [Review] [49 refs]. *Radiographics* 26[4], 1151-1168. 2006.
Excl reason: Narrative review

Shibuya, T., Osada, T., Mori, H., Matsumoto, K., Beppu, K., Sakamoto, N., Nagahara, A., Otaka, M., Ogihara, T., and Watanabe, S. Use of double balloon endoscopy for the early diagnosis of small intestinal malignant neoplasms. *Gastrointestinal Endoscopy* 69[5], AB200. 2009. Mosby Inc.
Excl reason: Not in PICO

Small, M., Vidyarthi, G., Boyd, W., and Haley, J. A. Amyloidosis in a patient with maltoma of stomach. *American Journal of Gastroenterology* 105, S41. 2010. Nature Publishing Group.
Excl reason: Not in PICO

Snarski, E., Drozd, J., Ejno, T., Brzezinski, R., Szarewicz, H., and Wiktor-Jedrzejczak, W. [Time to diagnosis as an index of efficiency of the health care system--lymphoma study]. [Polish]. *Wiadomosci Lekarskie* 59[1-2], 58-60. 2006.
Excl reason: Not in PICO

- Soderholm, A. L., Lindqvist, C., Heikinheimo, K., Forssell, K., and Happonen, R. P. Non-Hodgkin's lymphomas presenting through oral symptoms. *International Journal of Oral & Maxillofacial Surgery* 19[3], 131-134. 1990.
Excl reason: Not in PICO
- Spillane, J. A., Kendall, B. E., and Moseley, I. F. Cerebral lymphoma: Clinical radiological correlation. *Journal of Neurology Neurosurgery and Psychiatry* 45[3], 199-208. 1982.
Excl reason: Not in PICO
- Sposto, R., Meadows, A. T., Chilcote, R. R., Steinherz, P. G., Kjeldsberg, C., Kadin, M. E., Krailo, M. D., Termuhlen, A. M., Morse, M., and Siegel, S. E. Comparison of long-term outcome of children and adolescents with disseminated non-lymphoblastic non-hodgkin lymphoma treated with COMP or daunomycin-comp: A report from the children's cancer group. *Medical and Pediatric Oncology* 37[5], 432-441. 2001.
Excl reason: Not in PICO
- Srinivasan, R. E., Turner, A. G., and Panda, M. Lymphomas can "cry wolf" too. *Journal of General Internal Medicine* 26, S408. 2011. Springer New York.
Excl reason: Not in PICO
- Srinivasan, S., Takeshita, K., Holkova, B., Czuczman, M. S., Miller, K., Bernstein, Z. P., Driscoll, D., and Chanan-Khan, A. Clinical characteristics of gastrointestinal lymphomas associated with AIDS (GI-ARL) and the impact of HAART. *Hiv Clinical Trials* 5[3], 140-145. 2004.
Excl reason: Not in PICO
- Stenstad, T. [Adult-onset Still's disease. An underdiagnosed condition?]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening* 115[29], 3616-3618. 30-11-1995.
Excl reason: Not in PICO
- Stiefelhagen, P. [Enlarged lymph nodes. Routine general practice finding]. [German]. *MMW Fortschritte der Medizin* 143, Suppl-42. 2001.
Excl reason: Narrative review
- Stohlner, V., Chatzizacharias, N. A., Parthasarathy, M. & Groot-Wassink, T. (2013) Jejunojejunal Intussusception as the Initial Presentation of Non-Hodgkin's B-Cell Lymphoma in an Adult Patient: A Case Report and Review of the Literature. *Case Reports in Surgery*, 2013: 619031.
Excl reason: Not in PICO
- Subortseva, I., Lepkov, S., Poddybnaya, I., Storogakov, G., Kovrigina, A., Kolomyicev, O., Kosura, S., and Malihova, O. Simultaneous development of hepatocellular carcinoma and non-hodgkin lymphoma in a patient with chronic hepatitis C. *Hepatology International* 5[1], 382-383. 2011. Springer New York.
Excl reason: Not in PICO
- Subortseva, I. N., Poddubnaya, I., Kovrigina, A. M., Kokosadze, N. V., and Osmanov, D. S. Difficulties in differential diagnosis of primary pulmonary lymphoma. *Journal of Thoracic Oncology* 5[5 SUPPL. 1], S115. 2010. International Association for the Study of Lung Cancer.
Excl reason: Not in PICO
- Suresh, S., Saifuddin, A., and O'Donnell, P. Lymphoma presenting as a musculoskeletal soft tissue mass: MRI findings in 24 cases. *European Radiology* 18[11], 2628-2634. 2008.
Excl reason: Not in PICO
- Tao, J., Shelat, S. G., Jaffe, E. S., and Bagg, A. Aggressive Epstein-Barr virus-associated, CD8+, CD30+, CD56+, surface CD3-, natural killer (NK)-like cytotoxic T-cell lymphoma. *American Journal of Surgical Pathology* 26[1], 111-118. 2002.
Excl reason: Not in PICO
- te Raa, G. D., van Oers, M. H., and Kater, A. P. Monoclonal B-cell lymphocytosis: Recommendations from the Dutch Working Group on CLL for daily practice. *Netherlands Journal of Medicine* 70[5], 236-241. 2012.
Excl reason: Narrative review

- Teo, W.-Y., Chan, M.-Y., Ng, K.-C., and Tan, A.-M. Bony presentations of childhood haematological malignancy to the emergency room. *Journal of Paediatrics and Child Health* 48[4], 311-316. 2012.
Excl reason: Not in PICO
- Thalhammer-Scherrer, R., Veitl, M., Exner, M., Schneider, B., Geissler, K., Simonitsch, I., and Schwarzingler, I. Role of immunological lymphocyte subset typing as a screening method for lymphoid malignancies in daily routine practice. *Cytometry* 42[1], 5-10. 15-2-2000.
Excl reason: Not in PICO
- Tobinai, K. Current management of adult T-cell leukemia/lymphoma. *Oncology (Williston Park)* 23[14], 1250-1256. 2009.
Excl reason: Narrative review
- Tomiak, C. Prognosis of Primary Sjogren's Syndrome with Special Regard to the Risk of Lymphoma. *Aktuelle Rheumatologie* 33[6], 325-336. 2008.
Excl reason: Narrative review
- Tsachouridou, O., Christoforidou, A., Metallidis, S., Papaioannou, M., Kollaras, P., Kolokotronis, A., Chrysanthidis, T., Pilalas, D., and Markou, K. Plasmablastic lymphoma of the oral cavity, a B cell-derived lymphoma associated with HIV infection: A case series. *European Archives of Oto-Rhino-Laryngology* 269[6], 1713-1719. 2012.
Excl reason: Not in PICO
- Tsai, M. S., Kuo, C. Y., Wang, M. C., Wu, H. C., Chien, C. C., and Liu, J. W. Clinical features and risk factors for mortality in Aeromonas bacteremic adults with hematologic malignancies. *Journal of Microbiology, Immunology & Infection* 39[2], 150-154. 2006.
Excl reason: Not in PICO
- Urushizaki, I. [Palliative therapy in cancer. 4. Palliation of the symptoms from a malignant tumor. (2)]. [Review] [32 refs] [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]* 17[8:Pt 1], t-35. 1990.
Excl reason: Narrative review
- Vanis, N., Mesihovic, R., Ibricevic, L. & Dobrila-Dintinjana, R. (2013) Predictive value of endoscopic ultrasound in diagnosis and staging of primary gastric lymphoma. *Collegium Antropologicum*, 37: Suppl-7.
Excl reason: Not in PICO
- Varoczy, L., Danko, A., Simon, Z., Gergely, L., Rész, Z., and Illes, A. Malignant lymphomas in the elderly: A single institute experience highlights future directions. *Archives of Gerontology and Geriatrics* 45[1], 43-53. 2007.
Excl reason: Not in PICO
- Vasil'ev, V. I., Probatova, N. A., Tupitsin, N. N., Varlamova, E. I., Logvinenko, O. A., Rodionova, E. B., Kovrigina, A. M., Kokosadze, N. V., Panin, M. G., Gaiduk, I. V., Gorbunova, T. V., Kondrat'eva, T. T., Sholokhova, E. N., Simonova, M. V., Safonova, T. N., and Radenska-Lopovok, S. G. [MALT-lymphomas in Sjogren's disease]. [Russian]. *Terapevticheskii Arkhiv* 78[1], 45-52. 2006.
Excl reason: Not in PICO
- Vaughn, C. P., Crockett, D. K., Lin, Z., Lim, M. S., and Elenitoba-Johnson, K. S. Identification of proteins released by follicular lymphoma-derived cells using a mass spectrometry-based approach. *Proteomics* 6[10], 3223-3230. 2006.
Excl reason: Not in PICO
- Verghese, G., Refaat, S. & Karar, A. (2013) Unusual presentation of diffuse large B-cell lymphoma (DLBCL) as acute osteomyelitis of the femur. *Journal of the Bahrain Medical Society*, 24: 140-144.
Excl reason: Not in PICO
- Voulgarelis, M., Dafni, U. G., Isenberg, K. A., and Moutsopoulos, H. M. Malignant lymphoma in primary Sjogren's syndrome - A multicenter, retrospective, clinical study by the European concerted action on Sjogren's syndrome. *Arthritis and Rheumatism* 42[8], 1765-1772. 1999.
Excl reason: Not in PICO

Vowles, R. H., Ghiacy, S., and Jefferis, A. F. A clinic for the rapid processing of patients with neck masses. *Journal of Laryngology & Otology* 112[11], 1061-1064. 1998.
Excl reason: Not in PICO

Wagner, H. J. and Knyrim, K. Relief of malignant obstructive jaundice by endoscopic or percutaneous insertion of metal stents. *Bildgebung/Imaging* 60[2], 76-82. 1993.
Excl reason: Not in PICO

Wakely, P. E., Jr. and Kornstein, M. J. Aspiration cytopathology of lymphoblastic lymphoma and leukemia: the MCV experience. *Pediatric Pathology & Laboratory Medicine* 16[2], 243-252. 1996.
Excl reason: Not in PICO

Walker, T. L. and Lopez, G. E. A case of an abdominal mass: follicular lymphoma. *Permanente Journal* 15[4], 61-64. 2011.
Excl reason: Not in PICO

Watanabe, H. Malignant lymphoma of the stomach. Collected eighty-seven cases. [Japanese]. *Stomach and Intestine* 15[9], 909-910. 1980.
Excl reason: Not in PICO

Webb, T. H., Lillemoe, K. D., Pitt, H. A., Jones, R. J., and Cameron, J. L. Pancreatic lymphoma. Is surgery mandatory for diagnosis or treatment? *Annals of Surgery* 209[1], 25-30. 1989.
Excl reason: Not in PICO

Welles, S. L., Levine, P. H., Joseph, E. M., Goberdhan, L. J., Lee, S., Miotti, A., Cervantes, J., Bertoni, M., Jaffe, E., and Dosik, H. An enhanced surveillance program for adult T-cell leukemia in central Brooklyn. *Leukemia* 8, Suppl-5. 1994.
Excl reason: Not in PICO

Wennekes, L., Ottevanger, P. B., Raemaekers, J. M., Schouten, H. C., De Kok, M. W. E., Punt, C. J. A., Grol, R. P., Wollersheim, H. C., and Hermens, R. P. Development and Measurement of Guideline-Based Indicators for Patients With Non-Hodgkin's Lymphoma. *Journal of Clinical Oncology* 29[11], 1436-1444. 2011.
Excl reason: Not in PICO

Wesnes, K. A., Brooker, H., and Edgar, C. The disruptions to cognition, everyday function, and quality of life in oncology patients: A therapeutic opportunity? *Neurotherapeutics* 7[3], 331-332. 2010. Elsevier Inc.
Excl reason: Not in PICO

Wierecky, J. and Bokemeyer, C. [Compression syndromes]. [Review] [28 refs] [German]. *Internist* 46[1], 9-18. 2005.
Excl reason: Narrative review

Williams, N. P., Shirley, S. E., Williams, E., Wharfe, G., and Hanchard, B. Malignant lymphoma of gastric mucosa-associated lymphoid tissue in Jamaica. *West Indian Medical Journal* 48[3], 150-154. 1999.
Excl reason: Narrative review

Wood, L. A., Coupland, R. W., North, S. A., and Palmer, M. C. Outcome of advanced stage low grade follicular lymphomas in a population-based retrospective cohort. *Cancer* 85[6], 1361-1368. 15-3-1999.
Excl reason: Not in PICO

Woods, W. G. The use and significance of biologic markers in the evaluation and staging of a child with cancer. *Cancer* 58[2:Suppl], Suppl-8. 15-7-1986.
Excl reason: Narrative review

Wutzler, P., Farber, I., and Sauerbrei, A. Demonstration of Epstein-Barr virus in malignant non-Hodgkin's lymphomas. *Oncology* 43[4], 224-229. 1986.
Excl reason: Not in PICO

Yamada, Y., Kamihira, S., Murata, K., Yamamura, M., Maeda, T., Tsukasaki, K., Jubash, T., Atogami, S., Sohda, H., Taguchi, T., and Tomonaga, M. Frequent hepatic involvement in adult T cell leukemia:

comparison with non-Hodgkin's lymphoma. *Leukemia & Lymphoma* 26[3-4], 327-335. 1997.
 Excl reason: Not in PICO

Yamashita, H., Takahashi, Y., Kano, T., Kaneko, H., and Mimori, A. [Malignant lymphoma presenting as inflammation of unknown origin]. [Japanese]. *Nihon Rinsho Meneki Gakkai Kaishi* 35[2], 136-143. 2012.
 Excl reason: Not in PICO

Yang, J. and Yuan, G. [Primary intracranial malignant lymphoma: report of 40 cases]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]* 34[2], 102-103. 1996.
 Excl reason: Not in PICO

Yano, M., Yamakawa, Y., Niwa, H., Fukai, I., Kiriya, M., Saito, Y., Kani, H., Sasaki, H., and Masaoka, A. [Clinical considerations from sixteen cases with mediastinal malignant lymphoma]. [Japanese]. *Nippon Kyobu Geka Gakkai Zasshi - Journal of the Japanese Association for Thoracic Surgery* 44[8], 1114-1118. 1996.
 Excl reason: Not in PICO

Yao, M., Cheng, A. L., Su, I. J., Lin, M. T., Uen, W. C., Tien, H. F., Wang, C. H., and Chen, Y. C. Clinicopathological spectrum of haemophagocytic syndrome in Epstein-Barr virus-associated peripheral T-cell lymphoma. *British Journal of Haematology* 87[3], 535-543. 1994.
 Excl reason: Not in PICO

Yokota, T., Meguro, K., Yamada, Y., Kikuchi, S., Yamauchi, H., and Hatori, M. Diffuse peritonitis caused by perforation of ileal lymphoma: Two case reports and clinicopathological features of 81 cases in Japan. *Leukemia and Lymphoma* 47[6], 1157-1159. 2006.
 Excl reason: Not in PICO

Yoshihara, T. Bilateral enlargement of the submandibular glands - Clinical and pathological appearance. [Japanese]. *Practica Oto-Rhino-Laryngologica* 95[6], 555-561. 2002.
 Excl reason: Not in PICO/narrative review

Young, G., Toretsky, J. A., Campbell, A. B., and Eskenazi, A. E. Recognition of common childhood malignancies. [Review] [18 refs]. *American Family Physician* 61[7], 2144-2154. 1-4-2000.
 Excl reason: Narrative review

Yu, Xue, Chen, Wendy, and O'Connell, Dianne. Improved survival for non-Hodgkin lymphoma patients in New South Wales, Australia. *BMC Cancer* 10[1], 231. 2010.
 Excl reason: Not in PICO

Zafrani, E. S., Leclercq, B., Vernant, J. P., Pinaudeau, Y., Chomette, G., and Dhumeaux, D. Massive blastic infiltration of the liver: a cause of fulminant hepatic failure. *Hepatology* 3[3], 428-432. 1983.
 Excl reason: Not in PICO

Zajkowska, J. M., Garkowski, A., Zajkowska, A., Pancewicz, S. A., and Letmanowski, M. Cases of cancer diagnosed at the Department of Infectious Diseases and Neuroinfections at the Medical University of Bialystok. [Polish]. *Nowotwory* 62[3], 163-167. 2012.
 Excl reason: Not in PICO

Zawitkowska-Klaczynska, J., Katski, K., Nurzynska-Flak, J., and Kowalczyk, J. Primary chest tumours in children. *Annales Universitatis Mariae Curie-Sklodowska - Sectio d - Medicina* 58[2], 106-110. 2003.
 Excl reason: Not in PICO

Zenone, T. Parotid gland non-Hodgkin lymphoma in primary Sjogren syndrome. *Rheumatology International* 32[5], 1387-1390. 2012.
 Excl reason: Not in PICO

Zhang, J., Grubor, V., Love, C. L., Banerjee, A., Richards, K. L., Mieczowski, P., Dunphy, C. H., Choi, W. W. L., Auv, W.-Y., Srivastava, G., Lugar, P. L., Rizzieri, D. A., Lagoo, A. S., Bernal-Mizrachi, L., Mann, K. P., Flowers, C. R., Naresh, K. N., Evens, A. M., Gordon, L. I., Czader, M. B., Gill, J. I., Hsi, E. D., Liu, Q., Fan, A., Walsh, K., Jima, D. D., Luftig, M., Ni, T., Zhu, J., Chadburn, A., Levy, S., Dunson, D. B., and Dave, S. S. The genetic landscape of immune-competent and HIV lymphoma.

Infectious Agents and Cancer 7. 19-4-2012. BioMed Central Ltd.

Excl reason: Not in PICO

Zhou, Q. T., Zhu, H., and He, B. [Clinical analysis of lymphoma with chest involvement: report of 25 cases]. [Chinese]. *Chung-Hua Nei Ko Tsa Chih Chinese Journal of Internal Medicine* 48[10], 846-849. 2009.

Excl reason: Not in PICO

Ziaei, M., Elgohary, M. A. & Bremner, F. D. (2013) Palinopsia as the initial manifestation of non-hodgkin's lymphoma. *International Ophthalmology*, 33: 553-556.

Excl reason: Not in PICO

Zlotnick, D. M., Merrens, E. J., Fingar, E. L., and Levy, N. B. A 69-year-old male presenting with hypotension and anasarca. *American Journal of Hematology* 83[4], 311-314. 2008.

Excl reason: Not in PICO

Zullo, A., Hassan, C., Cristofari, F., Iegri, C., Villiva, N., Andriani, A., and Morini, S. Can we eradicate gastric MALT-lymphoma?. [Italian]. *Italian Journal of Medicine* 4[3], 154-158. 2010.

Excl reason: Narrative review

Review question:

Which investigations of symptoms of suspected Non-Hodgkin's lymphoma cancer should be done with clinical responsibility retained by primary care?

Results

Literature search

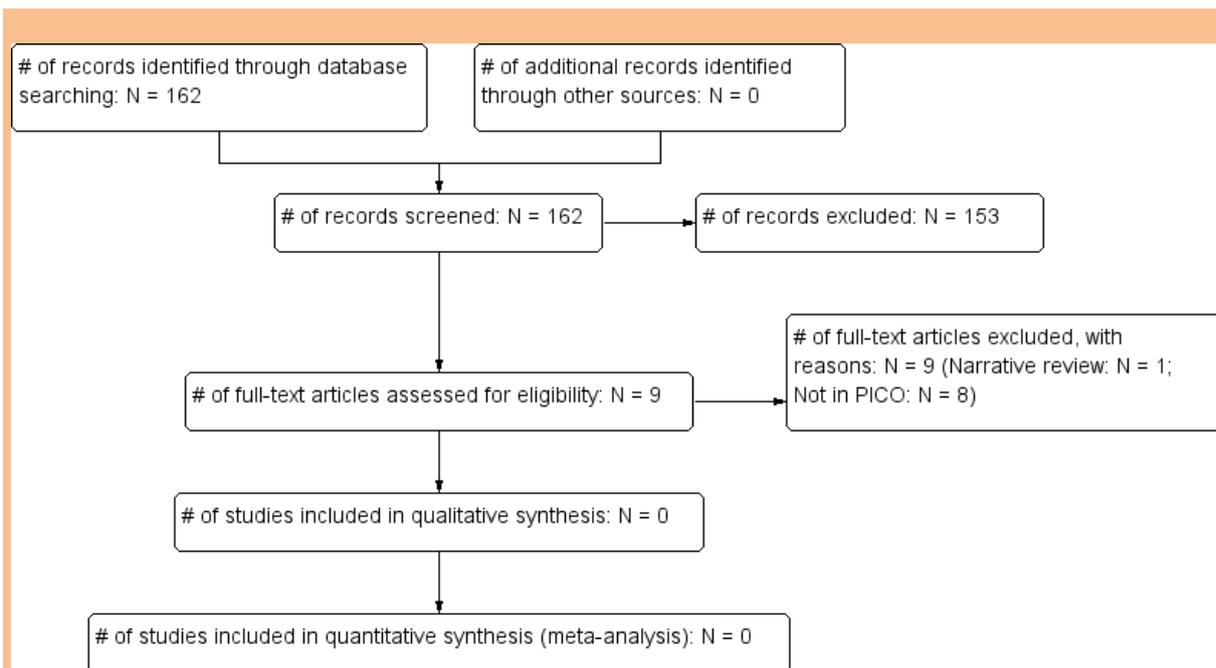
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2012	320	102	20/12/2012
<i>Premedline</i>	1980-2012	3	1	07/01/2013
<i>Embase</i>	1980-2012	331	64	20/12/2012
<i>Cochrane Library</i>	1980-2012	31	0	07/01/2013
<i>Psychinfo</i>	1980-2012	0	0	07/01/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2012	31	2	07/01/2013
<i>Biomed Central</i>	1980-2012	312	1	07/01/2013

Total References retrieved (after de-duplication): 140

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	2013-20/08/2014	19	5	20/08/2014
<i>Premedline</i>	2013-20/08/2014	5	4	20/08/2014
<i>Embase</i>	2013-20/08/2014	87	16	20/08/2014
<i>Cochrane Library</i>	2013-20/08/2014	19	0	20/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	2013-20/08/2014	3	0	20/08/2014

Total References retrieved (after de-duplication): 22



Study results

No evidence was identified pertaining to the diagnostic accuracy of CT scan, ultrasound, chest X-ray or LDH in patients with suspected non-hodgkin's lymphoma cell cancer where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies

Abel, G. A., Vanderplas, A., Rodriguez, M. A., Crosby, A. L., Czuczman, M. S., Niland, J. C., Gordon, L. I., Millenson, M., Zelenetz, A. D., Friedberg, J. W., and LaCasce, A. S. High rates of surveillance imaging for treated diffuse large B-cell lymphoma: findings from a large national database. *Leukemia & Lymphoma* 53[6], 1113-1116. 2012.

Excl reason: Not relevant to PICO

Alzubi, A., Zollei, I., Krenacs, L., Intzedy, K., and Hudak, J. [Primary T-cell lymphoma of the small bowel]. [Hungarian]. *Magyar Sebeszet* 61[2], 79-83. 2008.

Excl reason: Single Case/Foreign Language

Ambrosini, V., Rubello, D., Castellucci, P., Nanni, C., Farsad, M., Zinzani, P., Alavi, A., Tehranipour, N., Al-Nahhas, A., and Fanti, S. Diagnostic role of 18F-FDG-PET in gastric MALT lymphoma. *Nuclear Medicine Review* 9[1], 37-40. 2006.

Excl reason: Population not relevant to PICO

Amezyane, T., Lecoules, S., Bordier, L., Blade, J. S., Desrame, J., Bechade, D., Coutant, G., and Algayres, J. P. [Humoral hypercalcemia revealing a malignant non hodgkin lymphoma]. [French]. *Annales d Endocrinologie* 69[1], 58-62. 2008.

Excl reason: Single Case/Foreign Language

Antunes, A. A., Nesrallah, L. J., and Srougi, M. Non-Hodgkin lymphoma of the bladder. *International Braz J Urol* 30[6], 499-501. 2004.

Excl reason: Single Case

Aroor, A. R., Rama, P. S., Seshadri, S., Teerthanath, S. & Raghuraj, U. (2014) A study of clinical characteristics of mediastinal mass. *Journal of Clinical and Diagnostic Research*, 8: 77-80.
Excl reason: Not in PICO

Asai, S., Miyachi, H., Oshima, S., Kawakami, C., Kubota, M., and Ando, Y. A scoring system for ultrasonographic differentiation between cervical malignant lymphoma and benign lymphadenitis. *Rinsho Byori - Japanese Journal of Clinical Pathology* 49[6], 613-619. 2001.
Excl reason: Not relevant to PICO

Ashraf, F. Primary pancreatic lymphoma mimicking adenocarcinoma of pancreas. *American Journal of Gastroenterology* 105, S214. 2010. Nature Publishing Group.
Excl reason: Single Case

Baba, H. A., Tietze, L., Merkelbach, S., and Fuzesi, L. Diagnosis of non-Hodgkin lymphoma of the maxilla with support of polymerase chain reaction. *General & Diagnostic Pathology* 142[1], 53-57. 1996.
Excl reason: Single Case

Banno, S., Nitta, M., Takada, K., Hasegawa, R., Niimi, T., and Yamamoto, T. [Non-Hodgkin's lymphoma with pulmonary involvement and various immunological abnormalities in an elderly patient]. [Japanese]. *Nippon Ronen Igakkai Zasshi - Japanese Journal of Geriatrics* 30[6], 506-510. 1993.
Excl reason: Single Case/Foreign Language

Barroca, H. & Bom-Successo, M. (2014) Fine needle biopsy with cytology in paediatrics: The importance of a multidisciplinary approach and the role of ancillary techniques. *Cytopathology*, 25: 6-20.
Excl reason: Narrative review

Basavaraj, K. F., Ramalingam, K., Sarkar, A. & Muddaiah, S. (2012) Primary non-Hodgkin's lymphoma of gingiva in a 28-year-old HIV-positive patient. *Journal of Natural Science Biology & Medicine*, 3: 189-191.
Excl reason: Not in PICO

Beissert, M., Jenett, M., Wetzler, T., Hinterseher, I., Kessler, C., and Hahn, D. Enlarged lymph nodes of the neck: evaluation with parallel extended field-of-view sonographic sequences. *Journal of Ultrasound in Medicine* 19[3], 195-200. 2000.
Excl reason: Not relevant to PICO

Benchekrout, A., Qarro, A., Kasmaoui, H., Iken, A., Marzouk, M., and Faik, M. [Primary and bilateral non-Hodgkin's lymphoma of the adrenal gland (a case report and literature review)]. [French]. *Annales de Chirurgie* 128[8], 557-560. 2003.
Excl reason: Single Case/Foreign Language

Benson, M. K. and Hasley, P. A rash decision: Not simply another atopic dermatitis! *Journal of General Internal Medicine* 26, S436-S437. 2011. Springer New York.
Excl reason: Single Case/Expert Review

Berberoglu, K., Unal, S. N., Kebudi, R., Turkmen, C., and Cantez, S. Role of ^{99m}Tc-hexakis-2-methoxyisobutylisonitrile for detecting marrow metastases in childhood solid tumours. *Nuclear Medicine Communications* 26[12], 1075-1080. 2005.
Excl reason: Not relevant to PICO

Bianchi, C., Scamuzzi, C., and Mattioli, F. P. [Non-Hodgkin's lymphoma with perianal localization in patients with acquired immunodeficiency syndrome: a case report]. [Italian]. *Annali Italiani di Chirurgia* 67[2], 277-280. 1996.
Excl reason: Expert Review/Foreign Language

Bisdas, S., Fetscher, S., Feller, A. C., Baghi, M., Knecht, R., Gstoettner, W., Vogl, T. J., and Balzer, J. O. Primary B cell lymphoma of the sphenoid sinus: CT and MRI characteristics with correlation to perfusion and spectroscopic imaging features. *European Archives of Oto-Rhino-Laryngology* 264[10], 1207-1213. 2007.
Excl reason: Outcomes not relevant to PICO

- Braun, B. and Dormeyer, H. H. Ultrasonically guided fine needle aspiration biopsy of hepatic and pancreatic space-occupying lesions and percutaneous abscess drainage. *Klinische Wochenschrift* 59[12], 707-712. 15-6-1981.
Excl reason: Not relevant to PICO
- Brocker, K. A., Alt, C. D., Eichbaum, M., Sohn, C., Kauczor, H. U., and Hallscheidt, P. Imaging of female pelvic malignancies regarding MRI, CT, and PET/CT : part 1. [Review]. *Strahlentherapie und Onkologie* 187[10], 611-618. 2011.
Excl reason: Expert Review
- Browder, D. A. and Erhard, R. E. Decision making for a painful hip: A case requiring referral. *Journal of Orthopaedic & Sports Physical Therapy* 35[11], 738-744. 2005.
Excl reason: Single Case/Not relevant to PICO
- Buess, M., Steuerwald, M., Wegmann, W., and Rothen, M. Obstructive jaundice caused by enteropathy-associated T-cell lymphoma in a patient with celiac sprue. *Journal of Gastroenterology* 39[11], 1110-1113. 2004.
Excl reason: Single Case
- Cavanna, L., Vallisa, D., Lazzaro, A., Civardi, G., Berte, R., Moroni, C. F., Bernuzzi, P., Arcari, A., and Anselmi, E. On the Need of Biopsy Confirmation at Suspected First Recurrence of Cancer [4]. *American Journal of Clinical Oncology: Cancer Clinical Trials* 27[2], 212-213. 2004.
Excl reason: Expert Review
- Chan-Kai, B. T. and Yen, M. T. Combined positron emission tomography/computed tomography imaging of orbital lymphoma. *American Journal of Ophthalmology* 140[3], 531-533. 2005.
Excl reason: Single Case
- Cherian, S., Das, S., Mauzo, S., Koya, H. H., Varghese, D. & Hussain, R. (2013) Primary pulmonary lymphoma: An extremely rare disease. *Chest*, 144.
Excl reason: Not in PICO
- Choi, Y. R., An, J. Y., Kim, M. K., Han, H.-S., Lee, K. H., Kim, S.-W., Lee, K. M. & Choe, K. H. (2013) The diagnostic efficacy and safety of endobronchial ultrasound-guided transbronchial needle aspiration as an initial diagnostic tool. *Korean Journal of Internal Medicine*, 28: 660-667.
Excl reason: Not in PICO
- Coe, A., Conway, J., Evans, J., Goebel, M. & Mishra, G. (2013) The yield of EUS-FNA in undiagnosed upper abdominal adenopathy is very high. *Journal of Clinical Ultrasound*, 41: 210-213.
Excl reason: Not in PICO
- Cwiklinska, M., Czogała, M., Balwierz, W., Hnatko-Kolacz, M., Moryl-Bujakowska, A., Malinowska, I., Sladek, M., Wiczorek, M., Fyderek, K., Matysiak, M., Rygielska, M., and Sierhej, I. [Hemophagocytic syndrome in children with different underlying conditions]. [Polish]. *Przegląd Lekarski* 67[6], 430-435. 2010.
Excl reason: Not relevant to PICO
- Davidson, P., De, W. K. & Kulasegaram, R. (2014) A retrospective analysis of chest and abdomen CT scanning in an unselected HIV-positive population. *HIV Medicine*, 15: 130.
Excl reason: Not in PICO
- Davis, R. D., Jr., Oldham, H. N., Jr., and Sabiston, D. C., Jr. Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management, and results. *Annals of Thoracic Surgery* 44[3], 229-237. 1987.
Excl reason: Expert Review
- dos Santos, Lucas. Is there a role for consolidative radiotherapy in the treatment of aggressive and localized Non-Hodgkin Lymphoma? A systematic review with meta-analysis. *BMC Cancer* 12[288]. 2012.
Excl reason: Not relevant to PICO
- Duncavage, J. A., Campbell, B. H., Hanson, G. A., Kun, L. E., Hansen, R. M., Toohill, R. J., and Malin, T. C. Diagnosis of malignant lymphomas of the nasal cavity, paranasal sinuses and nasopharynx.

Laryngoscope 93[10], 1276-1280. 1983.
 Excl reason: Not relevant to PICO

Ellenrieder, V., Beckh, K., Muller, D., Klatt, S., and Adler, G. Intrahepatic high-grade malignant non-Hodgkin lymphoma in a patient with chronic hepatitis C infection. *Zeitschrift fur Gastroenterologie* 34[5], 283-285. 1996.
 Excl reason: Single Case

Fass, L. Imaging and cancer: A review. *Molecular Oncology* 2[2], 115-152. 2008.
 Excl reason: Expert Review

Ferone, D., Semino, C., Boschetti, M., Cascini, G. L., Minuto, F., and Lastoria, S. Initial staging of lymphoma with octreotide and other receptor imaging agents. [Review] [92 refs]. *Seminars in Nuclear Medicine* 35[3], 176-185. 2005.
 Excl reason: Expert Review

Fey, M. F. [Salient clinical features of lymphoma and related lymphoproliferative disorders]. [German]. *Therapeutische Umschau* 67[10], 491-495. 2010.
 Excl reason: Expert Review/Foreign Language

Flox, Camacho A., Hernandez, Hernandez F., Salguero, Bodes R., Sanchez, Perez, I, Carbonell, Porras A., and Tascon, Perez J. [Primary cardiac lymphoma: diagnosis by transjugular biopsy]. [Spanish]. *Revista Espanola de Cardiologia* 56[11], 1141-1144. 2003.
 Excl reason: Single Case/Foreign Language

Ford, C., Patel, P., Burney, K., Fernandez, C., Fisher, R. & Youd, P. (2014) Should we investigate mesenteric panniculitis?: UK experience of 58 patients. *Gut*, 63: A101.
 Excl reason: Not in PICO

Fornari, F., Civardi, G., Cavanna, L., Rossi, S., Buscarini, E., Di, Stasi M., Sbolli, G., and Buscarini, L. Ultrasonically guided fine-needle aspiration biopsy: A highly diagnostic procedure for hepatic tumors. *American Journal of Gastroenterology* 85[8], 1009-1013. 1990.
 Excl reason: Not relevant to PICO

Front, D., Bar-Shalom, R., Epelbaum, R., Haim, N., Ben-Arush, M. W., Ben-Shahar, M., Gorenberg, M., Kleinhaus, U., Parmett, S., and Kolodny, G. M. Early detection of lymphoma recurrence with gallium-67 scintigraphy. *Journal of Nuclear Medicine* 34[12], 2101-2104. 1993.
 Excl reason: Intervention not relevant to PICO

Funauchi, M., Ikoma, S., Kishimoto, K., Shimazu, H., Nozaki, Y., Sugiyama, M., and Kinoshita, K. A case of adult onset Still's disease showing marked accumulation in the liver and spleen, on positron emission tomography-CT images. *Rheumatology International* 28[10], 1061-1064. 2008.
 Excl reason: Single case

Garrett, K. M., Hoffer, F. A., Behm, F. G., Gow, K. W., Hudson, M. M., and Sandlund, J. T. Interventional radiology techniques for the diagnosis of lymphoma or leukemia. *Pediatric Radiology* 32[9], 653-662. 2002.
 Excl reason: Interventions not relevant to PICO

Gentile, M., Cutrona, G., Fabris, S., Pesce, E., Di, Raimondo F., Di, Renzo N., Mauro, F. R., Cantaffa, R., Brugiattelli, M., Merli, F., Baldini, L., Quintana, G., Iannitto, E., Di, Tonno P., Fragasso, A., Molica, S., Callea, V., Sacchi, S., Federico, M., Neri, A., Ferrarini, M., and Morabito, F. Inclusion of total body CT scan in the initial work-up of CLL patients with early-stage on clinical grounds: preliminary Results of a prospective, multicenter o-cll1-GISL study. *Haematologica* 94, 375. 2009. *Haematologica Journal Office*.
 Excl reason: Not in PICO

Ghai, S., Pattison, J., Ghai, S., O'Malley, M. E., Khalili, K., and Stephens, M. Primary gastrointestinal lymphoma: spectrum of imaging findings with pathologic correlation. [Review] [39 refs]. *Radiographics* 27[5], 1371-1388. 2007.
 Excl reason: Expert Review

Goldschmidt, N., Libson, E., Bloom, A., Amir, G., and Paltiel, O. Clinical utility of computed tomography-guided core needle biopsy in the diagnostic re-evaluation of patients with

lymphoproliferative disorders and suspected disease progression. *Annals of Oncology* 14[9], 1438-1441. 2003.
 Excl reason: Not relevant to PICO

Gomez-Leon, N., Pinilla, I., Rodriguez-Vigil, B., Hernandez, D., Reza, M., and Madero, R. Integrated PET/CT scanner in oncology applications: A radiologic perspective. [Spanish]. *Radiologia* 49[1], 29-36. 2007.
 Excl reason: Not relevant to PICO

Gould, P. V. and Saikali, S. A comparison of digitized frozen section and smear preparations for intraoperative neurotelepathology. *Analytical Cellular Pathology* 35[2], 85-91. 2012.
 Excl reason: Comparisons not relevant to PICO

Graziosi, L., Bugiantella, W., Cavazzoni, E., Cantarella, F., Porcari, M., Baffa, N., and Donini, A. Role of FDG-PET/CT in follow-up of patients treated with resective gastric surgery for tumour. *Annali Italiani di Chirurgia* 82[2], 125-129. 2011.
 Excl reason: Not relevant to PICO

Grubstein, A., Shitrit, D., Sapir, E. E., Cohen, M., and Kramer, M. R. Pulmonary amyloidosis: Detection with PET-CT. *Clinical Nuclear Medicine* 30[6], 420-421. 2005.
 Excl reason: Not relevant to PICO

Gutte, H., Hojgaard, L., and Kjaer, A. Early clinical experience and impact of 18F-FDG PET. *Nuclear Medicine Communications* 26[11], 989-994. 2005.
 Excl reason: Not relevant to PICO

Hachisuka, Y. and Uomoto, M. A case of pulmonary mucosa-associated lymphoid tissue type lymphoma with low-grade accumulation of 18-fluorodeoxyglucose on positron emission tomography. [Japanese]. *Japanese Journal of Lung Cancer* 48[1], 56-61. 2008.
 Excl reason: Single Case

Hahm, M. H., Kim, H. J., Shin, K. M., Cho, S. H., Park, J. Y., Jung, J. H., Jeong, J. Y. & Bae, J. H. (2014) - Concurrent invasive ductal carcinoma of the breast and malignant follicular lymphoma, initially suspected to be metastatic breast cancer: a case report. - *Journal of Breast Cancer*, 17: 91-97.
 Excl reason: Not in PICO

Haldorsen, I. S., Espeland, A., Larsen, J. L., and Mella, O. Diagnostic delay in primary central nervous system lymphoma. *Acta Oncologica* 44[7], 728-734. 2005.
 Excl reason: Not relevant to PICO

Han, S. H., Maeng, Y. H., Kim, Y. S., Jo, J. M., Kwon, J. M., Kim, W. K. & Kim, M. O. (2014) Primary anaplastic large cell lymphoma of the lung presenting with acute atelectasis. *Thoracic Cancer*, 5: 78-81.
 Excl reason: Not in PICO

Hartmann, M. and Sartor, K. [Primary malignant lymphoma of the brain]. [Review] [26 refs] [German]. *Radiologe* 37[1], 42-50. 1997.
 Excl reason: Expert Review/Foreign Language

Hausdorf, G., Erttmann, R., Hubner, C., and Winkler, K. [Sonographic findings in malignant lymphoblastic T-cell lymphomas in childhood]. [German]. *Onkologie* 5[6], 284-288. 1982.
 Excl reason: Not relevant to PICO/Foreign Language

Heisner, K., Jordan, K., Paul, S., Rosenwald, A., and Voigt, W. Granulocytic sarcoma with primary compression of spinal court as precursor of a acute myeloid leukemia: A case report. *Onkologie* 33[6], 142. 2010. S. Karger AG.
 Excl reason: Single Case

Hesselmann, V., Zahringer, M., Krug, B., Wesselmann, C., Haferkamp, K., Wickenhauser, C., and Lackner, K. Computed-tomography-guided percutaneous core needle biopsies of suspected malignant lymphomas: impact of biopsy, lesion, and patient parameters on diagnostic yield. *Acta Radiologica* 45[6], 641-645. 2004.
 Excl reason: Not relevant to PICO

- Ho, C. L. Clinical PET imaging--an Asian perspective. [Review] [53 refs]. *Annals of the Academy of Medicine, Singapore* 33[2], 155-165. 2004.
Excl reason: Expert Review
- Hojo, A., Nakayama, H., Aramaki, O., Higaki, T., Moriguchi, M., Sugitani, M., Miura, K., Takeuchi, J., Nishiyama, R., Moriyama, M. & Takayama, T. (2013) Diagnostic value of open biopsy for malignant T-cell lymphoma of the liver. *International Surgery*, 98: 13-18.
Excl reason: Not in PICO
- Hong, J., Kim, J. H., Park, J. & Lee, J. H. (2013) Clinical symptom or sign-directed surveillance can be more useful in detecting relapse compared to routine imaging in patients with diffuse large b-cell lymphoma in remission. *Blood*, 122.
Excl reason: Not in PICO
- Horton, K. M. and Fishman, E. K. Multidetector-row computed tomography and 3-dimensional computed tomography imaging of small bowel neoplasms: current concept in diagnosis. [Review] [29 refs]. *Journal of Computer Assisted Tomography* 28[1], 106-116. 2004.
Excl reason: Expert Review
- Huang, W. C., Tsai, C. C., Chan, C. C., Lai, H. Y., and Huang, S. H. Imprint cytology in diagnosing primary non-Hodgkin's lymphoma of the breast during intraoperative frozen consultation: a case report. *Acta Cytologica* 54[5:Suppl], Suppl-70. 2010.
Excl reason: Single Case
- Hubner, K. F., Buonocore, E., Singh, S. K., Gould, H. R., and Cotten, D. W. Characterization of chest masses by FDG positron emission tomography. *Clinical Nuclear Medicine* 20[4], 293-298. 1995.
Excl reason: Comparison not relevant to PICO
- Imai, A., Kawabata, I., and Tamaya, T. Primary brain malignant lymphoma newly diagnosed during pregnancy. *Journal of Medicine* 26[5-6], 333-336. 1995.
Excl reason: Not relevant to PICO
- Imteyaz, H. & Stern, M. (2013) N-type calcium channel binding antibodies in a patient with paraneoplastic cerebellar degeneration in association with non-hodgkins lymphoma: A case report. *PM and R*, 5: S183.
Excl reason: Not in PICO
- Iwanami, T., Kuwata, T., Iwata, T., and Kawaguchi, M. Pulmonary malignant lymphoma presenting as a cavity containing nodule. [Japanese]. *Japanese Journal of Lung Cancer* 52[3], 296-299. 2012.
Excl reason: Single Case
- Jawa, A., Mehta, S., Grupp, S., Kramer, S. S., Carpentieri, D. F., and Dormans, J. P. Face and thigh swelling in a 6-year-old girl. *Clinical Orthopaedics & Related Research*.(415):309-18, 2003 Oct. [415], 309-318. 2003.
Excl reason: Not relevant to PICO
- Johnson, C. D., Kent, D. M., Varjabedian, G. C., and Lepoudre, C. Malignant lymphoma of the maxillary sinus. [Review] [15 refs]. *Journal of the American Osteopathic Association* 93[2], 252-258. 1993.
Excl reason: Expert Review
- Joshi, P. V., Lele, V. R. & Shaikh, I. (2013) Mortui vivos docent--the dead teach the living: 18-fluorodeoxyglucose positron emission tomography-computed tomography findings in a case of intravascular B cell lymphoma. *Journal of Cancer Research & Therapeutics*, 9: 141-144.
Excl reason: Not in PICO
- Kalkner, M., Rehn, S., Andersson, T., Elvin, A., Hagberg, H., Lindgren, P. G., Sundstrom, C., and Glimelius, B. Diagnostics of malignant lymphomas with ultrasound guided 1.2 mm biopsy-gun. *Acta Oncologica* 33[1], 33-37. 1994.
Excl reason: Intervention not relevant to PICO
- Karolina, O.-H., Osmola-Mankowska, A., Silny, W., Danczak-Pazdrowska, A. & Polanska, A. (2013) The possibility of monitoring using the highfrequency ultrasound in patients with the primary

cutaneous t-cell lymphoma. *Skin Research and Technology*, 19: e586.
 Excl reason: Not in PICO

Kashiwagi, S., Onoda, N., Asano, Y., Morisaki, T., Aomatsu, N., Yoshii, M., Nakamura, M., Kawajiri, H., Takashima, T., Osawa, M., Ishikawa, T., Wakasa, K., and Hirakawa, K. [Ultrasound guided vacuum-assisted biopsy for diagnosis of malignant lymphoma]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]* 38[12], 2526-2528. 2011.
 Excl reason: Intervention not relevant to PICO/Foreign Language

Kato, H., Naganuma, T., Iizawa, Y., Kitagawa, M., Tanaka, M., and Isaji, S. Primary non-Hodgkin's lymphoma of the gallbladder diagnosed by laparoscopic cholecystectomy. *Journal of Hepato-Biliary-Pancreatic Surgery* 15[6], 659-663. 2008.
 Excl reason: Single Case

Kato, K. (2014) - [Malignant lymphoma and adult T-cell leukemia-lymphoma]. [Review] [Japanese]. - *Rinsho Ketsueki - Japanese Journal of Clinical Hematology*, 55: 191-200.
 Excl reason: Not in PICO

Kawakami, K., Nomura, H., Watanabe, Y., and Momma, F. [Primary pancreatic lymphoma with elevated serum CA19-9 level]. [Japanese]. *Rinsho Ketsueki - Japanese Journal of Clinical Hematology* 43[4], 292-297. 2002.
 Excl reason: Single Case/Foreign Language

Kawashima, S., Okita, K., Yamawaki, T., Matsukawa, N., and Ojika, K. [Case of paraneoplastic limbic encephalitis associated with malignant B cell lymphoma]. [Review] [10 refs] [Japanese]. *Brain & Nerve / Shinkei Kenkyu no Shinpo* 61[2], 208-212. 2009.
 Excl reason: Single Case/Foreign Language

Kirby, A. M. and Mikhaeel, N. G. The role of FDG PET in the management of lymphoma: what is the evidence base?. [Review] [123 refs]. *Nuclear Medicine Communications* 28[5], 335-354. 2007.
 Excl reason: Expert Review

Komatsuda, T., Ishida, H., Konno, K., Sato, M., Hosino, T., Naganuma, H., Hirata, M., Watanabe, S., and Miyashita, M. Primary malignant lymphoma of the liver not associated with AIDS: US and Doppler findings. *Ultrasound International* 9[1], 1-7. 2003.
 Excl reason: Not relevant to PICO

Krishnan, A., Shirkhoda, A., Tehranzadeh, J., Armin, A. R., Irwin, R., and Les, K. Primary bone lymphoma: radiographic-MR imaging correlation. [Review] [27 refs]. *Radiographics* 23[6], 1371-1383. 1384.
 Excl reason: Expert Review

Lane, K. A. and Bilyk, J. R. Preliminary study of positron emission tomography in the detection and management of orbital malignancy. *Ophthalmic Plastic & Reconstructive Surgery* 22[5], 361-365. 2006.
 Excl reason: Not relevant to PICO

Leitha, T., Glaser, C., Pruckmayer, M., Rasse, M., Millesi, W., Lang, S., Nasel, C., Backfrieder, W., and Kainberger, F. Technetium-99m-MIBI in primary and recurrent head and neck tumors: contribution of bone SPECT image fusion. *Journal of Nuclear Medicine* 39[7], 1166-1171. 1998.
 Excl reason: Intervention/Population not relevant to PICO

Li, L., Wu, Q. L., Liu, L. Z., Mo, Y. X., Xie, C. M., Zheng, L., Chen, L., and Wu, P. H. Value of CT-guided core-needle biopsy in diagnosis and classification of malignant lymphomas using automated biopsy gun. *World Journal of Gastroenterology* 11[31], 4843-4847. 21-8-2005.
 Excl reason: Intervention not relevant to PICO

Linden, A., Zankovich, R., Theissen, P., Diehl, V., and Schicha, H. Malignant lymphoma: bone marrow imaging versus biopsy. *Radiology* 173[2], 335-339. 1989.
 Excl reason: Check relevance

Madan, A., Sethi, P. & Tripathi, K. (2013) Upper extremity venous thrombosis-calm before the storm. *Journal of General Internal Medicine*, 28: S415.
 Excl reason: Not in PICO

- Maher, N., O'Brien, Y., Milner, M., and Gleeson, N. Lymphoma-the great masquerader. *Irish Journal of Medical Science* 180, S134-S135. 2011. Springer.
Excl reason: Single Case
- Marquez Moreno, A. J., Manas, Uxo J., Amores, Ramirez F., Aguilar, Cuevas R., Ortega Jimenez, M. V., Leiva, Vera C., and Perez, Rodriguez D. [Synchronous chromophobe renal carcinoma and centrocytic lymphoma]. [Spanish]. *Archivos Espanoles de Urologia* 56[4], 415-417. 2003.
Excl reason: Single Case/Foreign Language
- Mathews, M. S., Bota, D. A., Kim, R. C., Hasso, A. N., and Linskey, M. E. Primary leptomenigeal plasmablastic lymphoma. *Journal of Neuro-Oncology* 104[3], 835-838. 2011.
Excl reason: Single Case
- McCormick, Z. and Casey, E. B cell lymphoma initially presenting as cervical radiculitis: A case report. *PM and R* 4[10 SUPPL. 1], S277. 2012. Elsevier Inc.
Excl reason: Single Case
- Meier, J. D. & Grimmer, J. F. (2014) - Evaluation and management of neck masses in children. [Review]. - *American Family Physician*, 89: 353-358.
Excl reason: Narrative review
- Michallet, A. S., Trotman, J., and Tychyj-Pinel, C. Role of early PET in the management of diffuse large B-cell lymphoma. [Review]. *Current Opinion in Oncology* 22[5], 414-418. 2010.
Excl reason: Expert Review
- Minamimoto, R., Senda, M., Terauchi, T., Jinnouchi, S., Inoue, T., Iinuma, T., Inoue, T., Ito, K., Iwata, H., Uno, K., Oku, S., Oguchi, K., Tsukamoto, E., Nakashima, R., Nishizawa, S., Fukuda, H., Murano, T., and Yoshida, T. Analysis of various malignant neoplasms detected by FDG-PET cancer screening program: based on a Japanese Nationwide Survey. *Annals of Nuclear Medicine* 25[1], 45-54. 2011.
Excl reason: Not relevant to PICO
- Mitsufuji, T., Fujimitsu, R., Ida, M., Urakawa, H., Kora, S., Takeshita, M., Miyajima, S., and Yoshimitsu, K. Papillary renal cell carcinoma with extensive paraaortic nodal metastasis mimicking malignant lymphoma. *Magnetic Resonance in Medical Sciences* 10[3], 201-204. 2011.
Excl reason: Single Case
- Mizusawa, H., Okaneya, T., Yoneyama, T., and Taguchi, I. [Primary malignant lymphoma of the adrenal gland: a case report]. [Japanese]. *Hinyokika Kiyo - Acta Urologica Japonica* 41[12], 991-994. 1995.
Excl reason: Single Case/Foreign Language
- Mohler, M., Gutzler, F., Kallinowski, B., Goeser, T., and Stremmel, W. Primary hepatic high-grade non-Hodgkin's lymphoma and chronic hepatitis C infection. *Digestive Diseases and Sciences* 42[11], 2241-2245. 1997.
Excl reason: Not relevant to PICO
- Morimoto, Y., Kuriyama, S., Yoshiji, H., Matsumoto, M., Masui, K., Sakamoto, T., Kojima, H., Yoshikawa, M., Fukui, H., and Nakae, D. A case of early gastric malignant lymphoma diagnosed and completely resected by strip biopsy. *Journal of Gastroenterology* 30[2], 248-253. 1995.
Excl reason: Single Case
- Mukasa, K., Noh, J. Y., Kunii, Y., Matsumoto, M., Sato, S., Yasuda, S., Suzuki, M., Ito, K., and Ito, K. Prevalence of malignant tumors and adenomatous lesions detected by ultrasonographic screening in patients with autoimmune thyroid diseases. *Thyroid* 21[1], 37-41. 2011.
Excl reason: Not relevant to PICO
- Naito, Y., Okabe, Y., Kawahara, A., Taira, T., Yamagushi, T., Abe, H., Arikawa, S., Nakayama, M., Yasumoto, M., Eriguchi, N., Naito, H., Kage, M., and Yano, H. Guide to diagnosing primary pancreatic lymphoma, B-cell type: immunocytochemistry improves the diagnostic accuracy of endoscopic ultrasonography-guided fine needle aspiration cytology. *Diagnostic Cytopathology* 40[8], 732-736. 2012.
Excl reason: Single Case

Nakamura, K., Sasaki, M., Kunitake, N., Kimura, M., Watanabe, T., Sasaki, T., Terashima, H., Kuwabara, Y., Sakai, S., and Masuda, K. Relapse patterns of localized non-Hodgkin's lymphoma of the head and neck after clinical remission: results of a strict follow-up procedure. *International Journal of Clinical Oncology* 6[6], 302-305. 2001.
Excl reason: Not relevant to PICO

Nakao, K., Waga, S., Sakaida, H., Sakakura, M., Tocho, H., Ohno, H., and Miyazaki, M. [Primary spinal intramedullary malignant lymphoma: case report]. [Review] [19 refs] [Japanese]. *No Shinkei Geka - Neurological Surgery* 22[6], 583-587. 1994.
Excl reason: Single Case/Foreign Language

Nakazato, T., Suzuki, K., Mihara, A., Sanada, Y., Yoshida, S., and Kakimoto, T. [Intravascular large B-cell lymphoma with pontine involvement successfully treated with R-hyper-CVAD/R-MTX-Ara-C regimen]. [Japanese]. *Rinsho Ketsueki - Japanese Journal of Clinical Hematology* 51[2], 148-152. 2010.
Excl reason: Single Case/Foreign Language

Naranji, I., Zakri, R. H. & Liston, T. (2013) Mantle cell lymphoma presenting as a pelvi-ureteric junction obstruction: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 7: 105.
Excl reason: Not in PICO

Narsana, N., Xie, J., Singhvi, G., and Aron, J. A case of non-hodgkins lymphoma mimicking metastatic colorectal cancer. *American Journal of Gastroenterology* 105, S320. 2010. Nature Publishing Group.
Excl reason: Single Case

Nattermann, C. and Dancygier, H. [Endosonography of stomach tumors]. [Review] [51 refs] [German]. *Leber, Magen, Darm* 22[6], 211-219. 1992.
Excl reason: Expert Review/Foreign Language

Neef, B., Kunzig, B., Sinn, I., Kieninger, G., and von, Gaisberg U. [Primary pancreatic lymphoma. A rare cause of pain-free icterus]. [German]. *Deutsche Medizinische Wochenschrift* 122[1-2], 12-17. 3-1-1997.
Excl reason: Single Case/Foreign Language

Neef, B., Kunzig, B., Sinn, I., Kieninger, C., and Gaisberg, U. V. Primary malignant non-Hodgkin pancreatic lymphoma, a rare cause of of pain-free jaundice. [German]. *Deutsche Medizinische Wochenschrift* 122[1-2], 12-17. 1997.
Excl reason: Expert Review

Ng, E. and Ilsen, P. F. Orbital metastases. *Optometry (St.Louis, Mo.)* 81[12], 647-657. 2010.
Excl reason: Not relevant to PICO

Nortje, C. J. General practitioner's radiology case 63. Burkitt's lymphoma. *SADJ* 63[4], 248. 2008.
vNot relevant to PICO

Nozawa, A., Mizuno, S., Hoshi, H., Kuroda, E., Isaji, M., and Yasuda, K. A case of bilateral adrenal malignant lymphoma with high accumulation of 67Ga-citrate. [Japanese]. *Japanese Journal of Clinical Radiology* 44[6], 729-732. 1999.
Excl reason: Single Case

O'Donnell, K. R. and Kane, P. D. You're the flight surgeon. Non-Hodgkins lymphoma. [Review] [5 refs]. *Aviation Space & Environmental Medicine* 74[7], 785-787. 2003.
Excl reason: Expert Review

Odemis, B., Parlak, E., Basar, O., Yuksel, O., and Sahin, B. Biliary tract obstruction secondary to malignant lymphoma: experience at a referral center. *Digestive Diseases & Sciences* 52[9], 2323-2332. 2007.
Excl reason: Not relevant to PICO

Ohtaki, Y., Ishii, G., Hasegawa, T., and Nagai, K. Adult neuroblastoma arising in the superior mediastinum. *Interactive Cardiovascular & Thoracic Surgery* 13[2], 220-222. 2011.
Excl reason: Single Case

- Okazaki, A., Katoh, S., Noda, M., Katsumata, Y., Shirouzu, I., and Maehara, T. [Clinical usefulness of ⁶⁷Ga-citrate scintigraphy combined early image in malignant lymphoma--detection of abdominal lesions]. [Japanese]. *Nippon Igaku Hoshasen Gakkai Zasshi - Nippon Acta Radiologica* 50[8], 1007-1015. 25-8-1990.
Excl reason: Foreign Language/Not relevant to PICO
- Omori, K., Tetsuhara, K., Hiramoto, H., Shoda, H., Sanefuji, H., and Okamoto, N. [A case of primary small intestinal malignant lymphoma found based on multiple pulmonary nodules with cavitation]. [Japanese]. *Nihon Kokyuki Gakkai Zasshi* 48[7], 497-501. 2010.
Excl reason: Single Case/Foreign Language
- Orita, Y., Sato, Y., Kondo, E., Ishihara, H., Hirai, H., Hanakawa, H., Onoda, T., Igawa, T., Saito, R., Nishizaki, K., and Yoshino, T. Minimally invasive procedure for accurate diagnosis of mucosa-associated lymphoid tissue lymphoma of the head and neck. *Japanese Journal of Clinical Oncology* 42[4], 325-330. 2012.
Excl reason: Single Case
- Ota, H., Ito, Y., Matsuzuka, F., Kuma, S., Fukata, S., Morita, S., Kobayashi, K., Nakamura, Y., Kakudo, K., Amino, N., and Miyauchi, A. Usefulness of ultrasonography for diagnosis of malignant lymphoma of the thyroid. *Thyroid* 16[10], 983-987. 2006.
Excl reason: Not relevant to PICO
- Pedote, P., Gaudio, F., Moschetta, M., Cimmino, A., Specchia, G., and Angelelli, G. CT-guided needle biopsy performed with modified coaxial technique in the diagnosis of malignant lymphomas. *Radiologia Medica* 115[8], 1292-1303. 2010.
Excl reason: Intervention not relevant to PICO
- Picardi, M., Gennarelli, N., Ciancia, R., De, Renzo A., Gargiulo, G., Ciancia, G., Sparano, L., Zeppa, P., Martinelli, V., Pettinato, G., Lobello, R., Pane, F., and Rotoli, B. Randomized comparison of power Doppler ultrasound-directed excisional biopsy with standard excisional biopsy for the characterization of lymphadenopathies in patients with suspected lymphoma. *Journal of Clinical Oncology* 22[18], 3733-3740. 15-9-2004.
Excl reason: Comparison not relevant to PICO
- Pickhardt, P. J., Kim, D. H., Meiners, R. J., Wyatt, K. S., Hanson, M. E., Barlow, D. S., Cullen, P. A., Remtulla, R. A., and Cash, B. D. Colorectal and extracolonic cancers detected at screening CT colonography in 10,286 asymptomatic adults. *Radiology* 255[1], 83-88. 2010.
Excl reason: Not relevant to PICO
- Qiao, W. L., Zhao, J. H., Wang, C., He, Z. Y., Wang, T. S., and Xing, Y. [Comparison of ¹⁸F-FDG coincidence SPECT imaging and computed tomography in the initial staging and therapeutic evaluation of lymphomas]. [Chinese]. *Chung-Hua Chung Liu Tsa Chih [Chinese Journal of Oncology]* 29[7], 536-539. 2007.
Excl reason: Foreign Language/Population not relevant
- Ragupathy, K. & Bappa, L. (2013) Primary vaginal Non-Hodgkin lymphoma: Gynecologic diagnosis of a hematologic malignancy. *Journal of Lower Genital Tract Disease*, 17: 326-329.
Excl reason: Not in PICO
- Rahman, S., Rahman, W., and Rahman, F. A case of facial swelling and proptosis. *Dental Update* 31[9], 553-554. 2004.
Excl reason: Single Case
- Reamy, B. V., Bunt, C. W., and Fletcher, S. A diagnostic approach to pruritus.[Summary for patients in *Am Fam Physician*. 2011 Jul 15;84(2):203; PMID: 21766770]. *American Family Physician* 84[2], 195-202. 15-7-2011.
Excl reason: Not relevant to PICO
- Romer, W., Hanauske, A. R., Ziegler, S., Thodtmann, R., Weber, W., Fuchs, C., Enne, W., Herz, M., Nerl, C., Garbrecht, M., and Schwaiger, M. Positron emission tomography in non-Hodgkin's lymphoma: assessment of chemotherapy with fluorodeoxyglucose. *Blood* 91[12], 4464-4471. 15-

6-1998.

Excl reason: Not relevant to PICO

Saber, M. M., Zeeneldin, A. A., Samra, M. A. & Farag, S. A. (2013) Primary gastrointestinal lymphoma in an Egyptian district: a study using a population-based cancer registry. *Journal of Egyptian National Cancer Institute*, 25: 95-101.

Excl reason: Not in PICO

Sakata, R., Makiyama, K., Noguchi, G., Sano, F., Nakaigawa, N., Yao, M., Nakayama, T., Yamanaka, S., and Kubota, Y. [A case of retroperitoneal angioleiomyoma resected by laparoscopy]. [Japanese]. *Hinyokika Kyo - Acta Urologica Japonica* 58[2], 75-78. 2012.

Excl reason: Single Case/Foreign Language

Saraswatula, A., McShane, D., Tideswell, D., Burke, G. A. A., Williams, D. M., Nicholson, J. C., and Murray, M. J. Mediastinal masses masquerading as common respiratory conditions of childhood: A case series. *European Journal of Pediatrics* 168[11], 1395-1399. 2009.

Excl reason: Not relevant to PICO

Sasaki, Y., Yamagishi, F., Suzuki, K., Miyazawa, H., Sugimoto, N., and Abe, Y. [Primary pulmonary malignant lymphoma of the T-cell type]. [Japanese]. *Nihon Kyobu Shikkan Gakkai Zasshi. Japanese Journal of Thoracic Diseases* 33[12], 1454-1458. 1995.

Excl reason: Single Case/Foreign Language

Sato, K., Ozaki, K., Fujiwara, S., Oh, I., Matsuyama, T., Ohmine, K., Suzuki, T., Mori, M., Nagai, T., Muroi, K., and Ozawa, K. Incidental carcinomas detected by PET/CT scans in patients with malignant lymphoma. *International Journal of Hematology* 92[4], 647-650. 2010.

Excl reason: Outcomes not relevant to PICO

Scholmerich, J., Volk, B. A., and Gerok, W. Value and limitations of abdominal ultrasound in tumour staging--liver metastasis and lymphoma. *European Journal of Radiology* 7[4], 243-245. 1987.

Excl reason: Not relevant to PICO

Schwartz, A., Gospodarowicz, M. K., Khalili, K., Pintilie, M., Goddard, S., Keller, A., and Tsang, R. W. An audit of imaging test utilization for the management of lymphoma in an oncology hospital: implications for resource planning? *British Journal of Radiology* 79[938], 116-122. 2006.

Excl reason: Not relevant to PICO

Shinoda, M., Nagura, E., Uchida, K., Kimura, M., Mukoyama, M., and Yamada, H. A case of malignant lymphoma, highly suspected to be of pancreatic origin, with multiple nodular hepatic invasions. [Japanese]. *Japanese Journal of Cancer and Chemotherapy* 21[14], 2517-2520. 1994.

Excl reason: Single Case

Sklair-Levy, M., Polliack, A., Shaham, D., Applbaum, Y. H., Gillis, S., Ben-Yehuda, D., Sherman, Y., and Libson, E. CT-guided core-needle biopsy in the diagnosis of mediastinal lymphoma. *European Radiology* 10[5], 714-718. 2000.

Excl reason: Intervention not relevant to PICO

Soldani, S., Roni, P., Filidei, M., Castiglioni, M., and Riccioni, N. Diagnostic value of ultrasound-guided FNAB in the evaluation of osteolytic bone lesions suspected for metastases. [Italian]. *Giornale Italiano di Ultrasonologia* 8[1], 31-35. 1997.

Excl reason: Not relevant to PICO

Stohlner, V., Chatzizacharias, N. A., Parthasarathy, M. & Groot-Wassink, T. (2013) Jejunojejunal Intussusception as the Initial Presentation of Non-Hodgkin's B-Cell Lymphoma in an Adult Patient: A Case Report and Review of the Literature. *Case Reports in Surgery*, 2013: 619031.

Excl reason: Not in PICO

Subortseva, I. N., Poddubnaya, I., Kovrigina, A. M., Kokosadze, N. V., and Osmanov, D. S. Difficulties in differential diagnosis of primary pulmonary lymphoma. *Journal of Thoracic Oncology* 5[5 SUPPL. 1], S115. 2010. International Association for the Study of Lung Cancer.

Excl reason: Not relevant to PICO

Sudhoff, T., Hollerbach, S., Wilhelms, I., Willert, J., Reiser, M., Topalidis, T., Schmiegel, W., and Graeven, U. [Clinical utility of EUS-FNA in upper gastrointestinal and mediastinal disease].

[German]. *Deutsche Medizinische Wochenschrift* 129[42], 2227-2232. 15-10-2004.
 Excl reason: Not relevant to PICO

Suresh, S., Saifuddin, A., and O'Donnell, P. Lymphoma presenting as a musculoskeletal soft tissue mass: MRI findings in 24 cases. *European Radiology* 18[11], 2628-2634. 2008.
 Excl reason: Not relevant to PICO

Takahashi, M., Matsumoto, H., Fujita, Y., Sato, K., Takeda, A., Yamazaki, Y., and Tobise, K. [A case of malignant lymphoma showing a stratum of lymphoma cells]. [Japanese]. *Nihon Kokyuki Gakkai Zasshi* 38[10], 792-796. 2000.
 Excl reason: Single Case/Foreign Language

Takahashi, R., Nishikawa, M., Nomi, F., Kusano, N., Kakemizu, N., and Ishigatsubo, Y. [Case of intravascular lymphoma diagnosed by transbronchial lung biopsy, with transient spontaneous remission]. [Japanese]. *Nihon Kokyuki Gakkai Zasshi* 48[11], 825-830. 2010.
 Excl reason: Single Case/Foreign Language

Takahashi, Y., Yamashita, S., Kiyosawa, M., Mochizuki, M., Kumagai, J., and Tokumaru, A. Malignant lymphoma presenting as orbital apex syndrome. [Japanese]. *Folia Ophthalmologica Japonica* 52[6], 523-527. 2001.
 Excl reason: Single Case

Tamai, Y., Murakami, E., Nakamori, Y., Mizutani, M., and Sekine, T. [A case of gastric stenosis due to primary gastric malignant lymphoma during administration of R-CHOP]. [Japanese]. *Gan to Kagaku Ryoho [Japanese Journal of Cancer & Chemotherapy]* 38[8], 1371-1373. 2011.
 Excl reason: Single Case/Foreign Language

Tambo, M., Fujimoto, K., Miyake, M., Hoshiyama, F., Matsushita, C., and Hirao, Y. Clinicopathological review of 46 primary retroperitoneal tumors. *International Journal of Urology* 14[9], 785-788. 2007.
 Excl reason: Not relevant to PICO

Tao, H., Nakata, M., Saeki, H., Kurita, A., and Takashima, S. Unsuspected Primary Pulmonary Malignant Lymphoma. *Japanese Journal of Thoracic and Cardiovascular Surgery* 50[12], 533-536. 2002.
 Excl reason: Single Case

Terada, T. Primary signet-ring cell carcinoma of the lung: a case report with an immunohistochemical study. *International Journal of Clinical & Experimental Pathology* 5[2], 171-174. 2012.
 Excl reason: Single Case

Terauchi, T., Murano, T., Daisaki, H., Kanou, D., Shoda, H., Kakinuma, R., Hamashima, C., Moriyama, N., and Kakizoe, T. Evaluation of whole-body cancer screening using 18F-2-deoxy-2-fluoro-D-glucose positron emission tomography: a preliminary report. *Annals of Nuclear Medicine* 22[5], 379-385. 2008.
 Excl reason: Population not relevant to PICO

Thompson, D. R., Faust, T. W., Stone, M. J., and Polter, D. E. Hepatic failure as the presenting manifestation of malignant lymphoma. *Clinical Lymphoma* 2[2], 123-128. 2001.
 Excl reason: Not relevant to PICO

Toma, P., Granata, C., Rossi, A., and Garaventa, A. Multimodality imaging of Hodgkin disease and non-Hodgkin lymphomas in children. [Review] [55 refs]. *Radiographics* 27[5], 1335-1354. 2007.
 Excl reason: Expert Review

Utsunomiya, D., Awai, K., Urata, J., Hirayama, T., and Yamashita, Y. Primary cardiac lymphoma: Computed tomography and magnetic resonance imaging features. *Japanese Journal of Radiology* 27[6], 243-246. 2009.
 Excl reason: Single case

Vanis, N., Mesihovic, R., Ibricevic, L. & Dobrila-Dintinjana, R. (2013) Predictive value of endoscopic ultrasound in diagnosis and staging of primary gastric lymphoma. *Collegium Antropologicum*, 37: Suppl-7.
 Excl reason: Not in PICO

Verghese, G., Refaat, S. & Karar, A. (2013) Unusual presentation of diffuse large B-cell lymphoma (DLBCL) as acute osteomyelitis of the femur. *Journal of the Bahrain Medical Society*, 24: 140-144.
Excl reason: Not in PICO

Wachter, D., Tschischka, S., Huegens-Penzel, M., Kuchelmeister, K., Bohle, R. M., Boker, D. K., and Nestler, U. T-cell lymphoma mimicking schwannoma of a cervical nerve root. *Neurosurgical Review* 32[1], 117-121. 20-1-0021.
Excl reason: Not relevant to PICO

Wahab, M. F., El-Gindy, I. M., and Fathy, G. M. Screening tests for diagnosis of cervical lymphadenopathy presenting as prolonged fever. *Journal of the Egyptian Public Health Association* 73[5-6], 538-562. 1998.
Excl reason: Not relevant to PICO

Wang, J., Sun, N. C., Renslo, R., Chuang, C. C., Tabbarah, H. J., Barajas, L., and French, S. W. Clinically silent primary adrenal lymphoma: a case report and review of the literature. [Review] [49 refs]. *American Journal of Hematology* 58[2], 130-136. 1998.
Excl reason: Expert review

Webb, T. H., Lillemoe, K. D., Pitt, H. A., Jones, R. J., and Cameron, J. L. Pancreatic lymphoma. Is surgery mandatory for diagnosis or treatment? *Annals of Surgery* 209[1], 25-30. 1989.
Excl reason: Not relevant to PICO

Weber, W. A., Avril, N., and Schwaiger, M. Relevance of positron emission tomography (PET) in oncology. [Review] [168 refs]. *Strahlentherapie und Onkologie* 175[8], 356-373. 1999.
Excl reason: Expert Review

Weber, W. A. 18F-FDG PET in non-Hodgkin's lymphoma: qualitative or quantitative? *Journal of Nuclear Medicine* 48[10], 1580-1582. 2007.
Excl reason: No data

Wennekes, L., Ottevanger, P. B., Raemaekers, J. M., Schouten, H. C., De Kok, M. W. E., Punt, C. J. A., Grol, R. P., Wollersheim, H. C., and Hermens, R. P. Development and Measurement of Guideline-Based Indicators for Patients With Non-Hodgkin's Lymphoma. *Journal of Clinical Oncology* 29[11], 1436-1444. 2011.
Excl reason: Not relevant to PICO

Willson, T., Sambo, T., Fontaine, J.-P., Connolly, M. & Podbielski, F. (2014) Primary pulmonary T-cell lymphoma presenting as bilateral interstitial infiltrates. *Chest*, 145.
Excl reason: Not in PICO

Winde, G., Hecker, A., Schmid, U., and Keller, R. The prognosis of primary malignancies of the small intestine. [German]. *Chirurgische Praxis* 62[3], 399-413. 2004.
Excl reason: Expert Review/Foreign Language

Yang, J. and Yuan, G. [Primary intracranial malignant lymphoma: report of 40 cases]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]* 34[2], 102-103. 1996.
Excl reason: Excl reason: Not relevant to PICO/Foreign Language

Yucel, C., Ozdemir, H., and Isik, S. Role of endosonography in the evaluation of gastric malignancies. *Journal of Ultrasound in Medicine* 18[4], 283-288. 1999.
Excl reason: Expert Review

Zepeda-Gomez, S., Camacho, J., Oviedo-Cardenas, E., and Lome-Maldonado, C. Gastric infiltration of diffuse large B-cell lymphoma: Endoscopic diagnosis and improvement of lesions after chemotherapy. *World Journal of Gastroenterology* 14[27], 4407-4409. 21-7-2008.
Excl reason: Single Case

Zhou, Q. T., Zhu, H., and He, B. [Clinical analysis of lymphoma with chest involvement: report of 25 cases]. [Chinese]. *Chung-Hua Nei Ko Tsa Chih Chinese Journal of Internal Medicine* 48[10], 846-849. 2009.
Excl reason: Foreign Language

Ziaei, M., Elgohary, M. A. & Bremner, F. D. (2013) Palinopsia as the initial manifestation of non-hodgkin's lymphoma. *International Ophthalmology*, 33: 553-556.

Excl reason: Not in PICO

Ztot, S., Cherradi, R., Haddour, L., Belhaj, S., Kettani, F., Benmimoun, E. G., and Arharbi, M. [Primary cardiac lymphoma. Report of a case]. [French]. *Archives des Maladies du Coeur et des Vaisseaux* 95[1], 61-64. 2002.

Excl reason: Expert Review/Foreign Language

HODGKIN'S LYMPHOMA

Review question:

What is the risk of Hodgkin's lymphoma in patients presenting in primary care with symptom(s)?

Results

Literature search

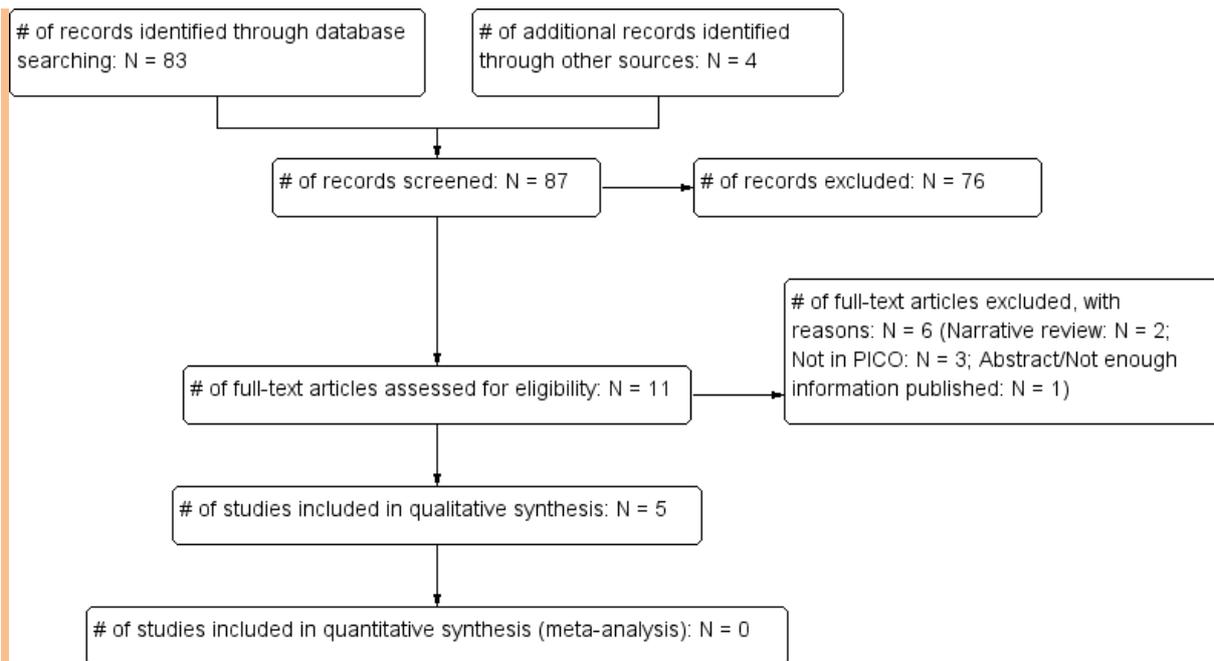
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	356	35	25/10/2012
<i>Premedline</i>	All-2012	8	0	25/10/2012
<i>Embase</i>	All-2012	587	49	25/10/2012
<i>Cochrane Library</i>	All-2012	124	0	25/10/2012
<i>Psychinfo</i>	All-2012	8	0	25/10/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	184	6	25/10/2012
<i>Biomed Central</i>	All-2012	279	2	25/10/2012

Total References retrieved (after de-duplication): 83

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	10/2012-26/08/2014	12	0	26/08/2014
<i>Premedline</i>	10/2012-26/08/2014	27	0	26/08/2014
<i>Embase</i>	10/2012-26/08/2014	224	0	26/08/2014
<i>Cochrane Library</i>	10/2012-26/08/2014	37	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	10/2012-26/08/2014	42	0	26/08/2014

Total References retrieved (after de-duplication): 0



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issue to note is that 2/3 studies employed samples of patients that are not directly representative of an unselected symptomatic population of patients presenting to the UK-based GP, and that there was some uncertainty about the verification of the outcome for some of the patients. Dommett (2012; 2013a,b) employed a case-control design which has been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors may have gone some way in counteracting this influence.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Deyo (1988)	?	+	?	+	-	+	+
Dommett (2012, 2013)	-	+	+	+	+	+	+
Williamson (1985)	+	+	+	?	+	+	+

- High	? Unclear	+ Low
---	---	--

Study results

Table 1: Hodgkin's lymphoma: Adult and mixed age populations

Study	Symptom(s)	Patient group	PPVs (95% CI)
Deyo (1988)	Back pain	All patients	0.1 (0.02-0.41) 2/1975 7 had other types of cancer: lymphoma (NOS): N = 2, unknown primary: N = 1, Prostate: N = 1, retroperitoneal liposarcoma: N = 1, lung cancer: N = 1, renal cell: N = 1, multiple myeloma: N = 1, mucinous adenocarcinoma (of gallbladder?): N = 1
Williamson (1985)	Lymphadenopathy	All patients	0.8 (0.1-3.2) TP = 2, FP = 247 Cancer: Hodgkin's: N = 1 Adenocarcinoma: N = 1

TP = True positives, FP = False positives.

Table 2: Hodgkin's lymphoma: Positive predictive values for leukaemia/lymphoma childhood cancer

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)
Dommett (2013a)	Bruising 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.53 (0.07-3.91)
Dommett (2013a)	Pallor 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.43 (0.06-3.15)
Dommett (2013a)	Lump mass swelling head and neck 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.35 (0.05-2.65)
Dommett (2013a)	Fatigue 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.07 (0.03-0.15)
Dommett (2013a)	Lymphadenopathy 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.06 (0.04-0.11)

Dommett (2013a)	Lump mass swelling below neck excluding abdomen 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.05 (0.02-0.13)
Dommett (2013a)	Bleeding 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.03 (0.01-0.08)
Dommett (2013a)	Pain 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.03 (0.01-0.06)
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.02 (0.01-0.03)
Dommett (2013a)	Fever 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01 (0.01-0.01)
Dommett (2013a)	Abdominal pain 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01(0-0.01)
Dommett (2013a)	≥ 3 consultations	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01(0.01-0.01)

The positive predictive values are calculated using Bayesian statistics.

Table 3: Hodgkin's lymphoma: Positive predictive values for teenage and young adult lymphoma

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2013b)	Lump mass swelling head and neck	All lymphoma patients and controls aged 15-24 years	0.5034 (0.0696-3.68) Cases: 35/270 Controls: 1/3350
Dommett (2013b)	Lump mass swelling below neck excluding abdomen	All lymphoma patients and controls aged 15-24 years	0.0279 (0.0152-0.0515) Cases: 29/270 Controls: 15/3350
Dommett (2013b)	Lymphadenopathy	All lymphoma patients and controls aged 15-24 years	0.278 (0.1-0.75) Cases: 77/270 Controls: 4/3350
Dommett (2013b)	'Lump mass swelling head and neck', 'lymphadenopathy' and 'lump mass swelling below neck excluding abdomen' combined as a single symptom	All lymphoma patients and controls aged 15-24 years	0.0903 (0.057-0.1425)

Dommett (2013b)	≥ 3 consultations	All lymphoma patients and controls aged 15-24 years	0.0086 (0.0075-0.0099) Cases: 175/270 Controls: 294/3350
-----------------	-------------------	---	--

The positive predictive values are calculated using Bayesian statistics.

Evidence statement(s):

Adult and mixed age populations

Back pain (1 study, N = 1975) and lymphadenopathy (1 study, N = 249) presenting in a primary care setting do not appear to confer a markedly increased risk of Hodgkin's/Non-Hodgkin's lymphoma, although the study populations are probably not directly representative of the typical unselected symptomatic UK GP population (see also Table 1).

Children and teenagers and young adults

The positive predictive values of having leukaemia/lymphoma childhood cancer ranged from 0.01% (for fever and abdominal pain) to 0.53% (for bruising) for patients aged 0-14 years old, and the positive predictive values of having young adulthood lymphoma ranged from 0.0279% (for 'lump mass swelling below the neck excluding the abdomen') to 0.5034% (for 'lump mass swelling head and neck') for patients aged 15-24 years (1 study, N = 30855). The evidence quality is somewhat compromised by the case-control design of the study (see also Tables 2-3).

Evidence tables

Deyo (1988)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive? patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1975, mean (SD; range) age = 39.5 (15.4; 15-86) years, 62% females. 54% of the patients were seeking medical care for back pain for the first time and 76% of the patients had had back pain for < 3 months. 3% had a history of back pain surgery. Maximal back pain in the low back (84%) or in the upper back (16%). <u>Inclusion criteria:</u> Patients who sought treatment between March 1982 and September 1984 in the walk-in clinic of a public hospital where virtually all patients are self-referred. In each case back pain was part of the chief complaint. <u>Exclusion criteria:</u> Neck pain. <u>Clinical setting:</u> Walk-in clinic of a public hospital; this clinic is a source of primary care for indigent persons in a county in the USA with a population of approximately 1 million.
Are there concerns that the included patients and setting do not match the review question?	High concern

INDEX TEST	
A. Risk of bias	
Index test	Back pain; not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	The reference standard consisted of a search on each patient name in the institutional tumour registry ≥ 6 months after the index visit. The registry included every patient with a histological diagnosis of cancer made in the authors' hospital system regardless of site of care. The authors point out that "while this method might fail to identify cancer patients who sought care elsewhere, it is likely that most patients sought follow-up for a particular illness at the same facility.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	It is a concern that some patients with cancer might have been missed due to the choice of reference standard because this would result in an underestimation of the positive predictive value. 38/1975 patients were found in the tumour registry. Of those 38, 13 patients had tumours that were probable causes of back pain, and 4 of these 13 patients already had a diagnosis of cancer at presentation. The 9/1975 patients who had undiagnosed cancer that the back pain could be attributed to had: Lymphoma (NOS; 2), cancer of unknown primary (1), prostate cancer

	(1), retroperitoneal liposarcoma (1), lung cancer (1), renal cell (1), multiple myeloma (1), mucinous adenocarcinoma (of gallbladder?; 1)
Dommett (2012; 2013a,b)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based nested case-control study using data from the General Practice Research Database (GPRD)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> 1267 children; aged 0-4 years: N = 436; aged 5-14 years: N = 831; 703 males/564 females. Cancer type: Leukemia: N = 368; brain: N = 270; lymphoma: N = 142; bone: N = 107; soft tissue sarcoma: N = 91; renal: N = 82; neuroblastoma: N = 75; other ICD codes: N = 132. 1064 teenagers and young adults (TYA): 15-24 years: Gender not reported. Cancer type: Leukemia: N = 143; brain: N = 154; lymphoma: N = 270; bone: N = 96; soft tissue sarcoma: N = 100; other ICD codes: N = 301 (including testis: N = 60; skin: N = 49; ovary: N = 20 and thyroid: N = 17).</p> <p><u>Controls:</u> 15318 children; aged 0-4 years: N = 4802; aged 5-14 years: N = 10516; 8461 males/6857 females. 13206 TYA. Gender not reported</p> <p><u>Inclusion criteria:</u> The sample comprised all children and TYU aged 0–24 years, inclusive, drawn from all general practices contributing research-standard data to the GPRD between 1 January 1988 and 31 December 2010. To be included, the practices had to have been contributing research-standard data for a minimum of 1 year before each child’s date of cancer diagnosis or the index date (see below) for matched controls. Cases: Patients diagnosed with the following cancers: leukaemia, lymphoma, neuroblastoma, soft tissue sarcoma, hepatic, renal, bone and central nervous system tumours, using pre-defined medical codes used in the GPRD. The date of diagnosis for cases was defined as the date of pathological diagnosis, but if this was unavailable, the date of the first cancer code entered in the GPRD was used. Controls: Up to 13 controls (children with no diagnosis of cancer at any time) were selected per case, using a computer-generated random sequence, matched on age (within 1 year), sex and practice, and had to be currently</p>

	registered on the date of diagnosis of their matched case (the index date). Exclusion criteria: None listed Clinical setting: Primary care, UK.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	The GPRD uses just over 100 000 medical codes to encompass all primary care events, including both symptoms and diagnoses. From this list, libraries of codes were assembled representing individual alert symptoms derived from the NICE referral guidelines for suspected cancer in children. <i>No more information reported.</i>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Cancer diagnosis in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	This study is published in three papers.
Williamson (1985)	
PATIENT SELECTION	

A. risk of bias	
Patient sampling	Retrospective consecutive patient series
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 249, mean age = 24 years, 26% were < 15 years; 58% females. Inclusion criteria: Patients seen at the Family Medical Care Centre of the University of Missouri-Columbia, between July 1 19978 and June 30 1983 whose diagnoses were coded as “enlarged lymph nodes, not infected” (ICHPPC 266) and “lymphadenitis, acute” (ICHPPC 209). Exclusion criteria: None listed Clinical setting: Family Medical Care Centre of the University of Missouri-Columbia.
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Diagnoses coded as “enlarged lymph nodes, not infected” (ICHPPC 266) and “lymphadenitis, acute” (ICHPPC 209).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Diagnoses were accepted if verified by history, physical examination or laboratory tests. Outcomes were determined, where possible, from the medical record. Follow up was considered adequate to determine an adverse outcome if one of four criteria were met: 1) A definite diagnosis was made, 2) The nodes were documented to be resolving, 3) There was at least one chart entry for any condition at least 6 months after the index visit for lymphadenopathy, or 4) The patient was reached by telephone and determined to have a favourable outcome.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined	Low concern

by the reference standard does not match the question?	
FLOW AND TIMING	
A. risk of bias	
Flow and timing	11/249 patients did not fit the criteria for adequate follow up: 3/11 had return visits showing no increase in the size of the nodes, 6/11 had nodes < 1 cm in size and were told to come back if the nodes did not resolve, 2/11 presented with cervical lymph nodes described as 1 cm in size and follow up examination was not recommended. None of these 11 patients could be reached by phone.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk
NOTES	The author note that the study would not have included all the patients presenting with enlarged lymph nodes during the study period because not all such patients would have the diagnosis noted as required for study entry, e.g., a diagnosis of infectious mononucleosis made on the first visit would probably have been coded as such and not as enlarged lymph nodes.

References

Included studies

- Deyo, R. A. and Diehl, A. K. Cancer as a cause of back pain: Frequency, clinical presentation, and diagnostic strategies. *Journal of General Internal Medicine* 3, 230-238. 1-11-1988.
- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of childhood cancer in primary care: A population-based nested case-control study. *British Journal of Cancer* 106[5], 982-987. 2012.
- Dommett, R. M., Redaniel, T., Stevens, M. C. G., Martin, R. M., and Hamilton, W. Risk of childhood cancer with symptoms in primary care: A population-based case-control study. *British Journal of General Practice*; DOI:10.3399/bjgp13X660742. 2013a.
- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of cancer in teenagers and young adults in primary care: A population-based nested case-control study. *British Journal of Cancer* 2329-2333. 2013b.
- Williamson, H. A., Jr. Lymphadenopathy in a family practice: a descriptive study of 249 cases. *Journal of Family Practice* 20[5], 449-452. 1985.

Excluded studies (with excl reason)

- Certificated training: Enlarged lymph nodes - Finding in general practice. [German]. *MMW-Fortschritte der Medizin* 142[17], I-XII. 27-4-2000.
Excl reason: Narrative review
- Acikel, C. H., Kir, T., Komurcu, S., Kilic, S., Ozett, A., Rzayev, M., Arpaci, F., Ozturk, B., Ogur, R., Ataergin, S., Kuzhan, O., and Hasde, M. Some sociodemographic and diagnostic characteristics of military patients treated in the Department of Medical Oncology, Gulhane Military Medical Academy. *Military Medicine* 171[5], 420-424. 2006.
Excl reason: Not in PICO
- Ahmed, S., Shahid, R. K., Sison, C. P., Fuchs, A., and Mehrotra, B. Orbital lymphomas: A clinicopathologic study of a rare disease. *American Journal of the Medical Sciences* 331[2], 79-83. 2006.
Excl reason: Not in PICO

Au, W. Y., Gascoyne, R. D., Gallagher, R. E., Le, N., Klasa, R. D., Liang, R. H. S., Choy, C., Foo, W., and Connors, J. M. Hodgkin's lymphoma in Chinese migrants to British Columbia: A 25-year survey. *Annals of Oncology* 15[4], 626-630. 2004.
Excl reason: Not in PICO

Bennett, M., Higgins, E., Curran, S., and Marren, P. Leukaemia cutis mimicking florid rhinophymatous rosacea. *British Journal of Dermatology* 163[2], 443. 2010. Blackwell Publishing Ltd.
Excl reason: Not in PICO

Bien, E., Stachowicz-Stencel, T., Zawitkowska-Klaczynska, J., Adamkiewicz-Drozynska, E., Odoj, T., Polczynska, K., Mitura-Lesiuk, M., Stefanowicz, J., Sierota, D., Szolkiewicz, A., Birkholz, D., Hennig, M., Kowalczyk, J. R., and Balcerska, A. [Clinical characteristics and therapy outcome in children with stage IV Hodgkin's lymphoma--the experience of two oncological centres]. [Polish]. *Medycyna Wieku Rozwojowego* 10[3:Pt 1], t-8. 2006.
Excl reason: Not in PICO

Bleyer, A. CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology* 36[3], 207-212. 2009.
Excl reason: Narrative review

Brabant, G., Toogood, A. A., Shalet, S. M., Frobisher, C., Lancashire, E. R., Reulen, R. C., Winter, D. L., and Hawkins, M. M. Hypothyroidism following childhood cancer therapy-an under diagnosed complication. *International Journal of Cancer* 130[5], 1145-1150. 1-3-2012.
Excl reason: Not in PICO

Broccia, G., Gabbas, A., and Longinotti, M. Newly diagnosed cases of hematologic malignancies in Sardinia in the early 2000s: An estimation of their number, age and geographic distribution on the basis of a previous epidemiologic survey. *Haematologica* 90[3], 429-430. 2005.
Excl reason: Not in PICO

Cainelli, F., Tanko, M. N., and Vento, S. The challenge of lymphomas in sub-Saharan Africa. *The Lancet Oncology* 11[7], 610-611. 2010.
Excl reason: Not in PICO

Calza, L., Manfredi, R., Colangeli, V., Dentale, N., and Chiodo, F. Hodgkin's disease in the setting of human immunodeficiency virus infection. *Scandinavian Journal of Infectious Diseases* 35[2], 136-141. 2003.
Excl reason: Not in PICO

Carbone, A. and Gloghini, A. "Intrafollicular neoplasia" of nodular lymphocyte predominant Hodgkin lymphoma: description of a hypothetic early step of the disease. [Review]. *Human Pathology* 43[5], 619-628. 2012.
Excl reason: Narrative review

Carvalho, P. C., Carvalho, Mda G., Degraive, W., Lilla, S., De, Nucci G., Fonseca, R., Spector, N., Musacchio, J., and Domont, G. B. Differential protein expression patterns obtained by mass spectrometry can aid in the diagnosis of Hodgkin's disease. *Journal of Experimental Therapeutics & Oncology* 6[2], 137-145. 2007.
Excl reason: Narrative review

Cohen, A. J., Thompson, L., Edwards, F. H., and Bellamy, R. F. Primary cysts and tumors of the mediastinum. *Annals of Thoracic Surgery* 51[3], 378-386. 1991.
Excl reason: Not in PICO

Crouch, S., Simpson, J., Ansell, P., Kane, E., Howell, D., Smith, A., Newton, R., Jack, A., and Roman, E. Illness patterns prior to diagnosis of lymphoma: Analysis of UK medical records. *Cancer Epidemiology* 35[2], 145-150. 2011.
Excl reason: Case-control comparison of number of visits to GP for infectious & non-infectious diagnoses in 15 years prior to diagnosis, but omitted data in the year prior to diagnosis in order not to swamp earlier effects. Same data as Newton 2007

Damion, J. and Hybels, R. L. The neck mass. 2. Inflammatory and neoplastic causes. *Postgraduate Medicine* 81[6], 97-103. 106.
 Excl reason: Narrative review

Danilenko, A. A. and Shakhtarina, S. V. [Hodgkin's disease and second malignancies]. [Review] [70 refs] [Russian]. *Voprosy Onkologii* 55[6], 692-702. 2009.
 Excl reason: Not in PICO

Edgren, G., Bagnardi, V., Bellocco, R., Hjalgrim, H., Rostgaard, K., Melbye, M., Reilly, M., Adami, H.-O., Hall, P., and Nyren, O. Pattern of declining hemoglobin concentration before cancer diagnosis. *International Journal of Cancer* 127[6], 1429-1436. 1-9-2010.
 Excl reason: Not in PICO

El, Safy U., Rifky, E. H., Badr, M., Hassan, T., Beshier, M., El, Garbey K., and Hussein, O. Retrospective analytical study of musculoskeletal manifestations of pediatric oncology in the last two decade at east delta of Egypt. *Pediatric Blood and Cancer* 53[5], 853-854. 2009. Wiley-Liss Inc.
 Excl reason: Not in PICO

Forsyth, C. and Joshua, D. Hodgkin's disease: A GP's guide to diagnosis and management. *Modern Medicine of Australia* 39[6], 127-135. 1996.
 Excl reason: Narrative review

Friedmann, A. M. Evaluation and management of lymphadenopathy in children. *Pediatrics in Review* 29[2], 53-60. 2008.
 Excl reason: Narrative review

Ganesan, P., Kumar, L., Raina, V., Sharma, A., Bakhshi, S., Sreenivas, V., Vijayaraghavan, M., and Thulkar, S. Hodgkin's lymphoma--long-term outcome: an experience from a tertiary care cancer center in North India. *Annals of Hematology* 90[10], 1153-1160. 2011.
 Excl reason: Not in PICO

Ganz, P. A., Moinpour, C. M., Pauler, D. K., Kornblith, A. B., Gaynor, E. R., Balcerzak, S. P., Gatti, G. S., Erba, H. P., McCoy, S., Press, O. W., and Fisher, R. I. Health status and quality of life in patients with early-stage Hodgkin's disease treated on Southwest Oncology Group Study 9133. *Journal of Clinical Oncology* 21[18], 3512-3519. 15-9-2003.
 Excl reason: Not in PICO

Garcia, Hernandez B. Suspicion of cancer in pediatrics. [Spanish]. *Pediatrica Integral* 12[6], 537-544. 2008.
 Excl reason: Narrative review

Gelfand, J. M., Shin, D. B., Neimann, A. L., Wang, X., Margolis, D. J., and Troxel, A. B. The risk of lymphoma in patients with psoriasis. *Journal of Investigative Dermatology* 126[10], 2194-2201. 30-10-2006.
 Excl reason: Not in PICO

Glass, C. Role of the primary care physician in Hodgkin lymphoma. *American Family Physician* 78[5], 615-622. 1-9-2008.
 Excl reason: Narrative review

Glass, C. Information from your family doctor. Hodgkin lymphoma: a cancer of the lymph nodes. *American Family Physician* 78[5], 625-626. 1-9-2008.
 Excl reason: Patient education material

Glass, C. Information from your family doctor. Hodgkin lymphoma: a cancer of the lymph nodes. *American Family Physician* 78[5], 625-626. 1-9-2008.
 Excl reason: Patient education material

Gobbi, P. G., Parrinello, G. A., and Di, Prisco U. New clinical criteria for the assessment of liver involvement in Hodgkin's disease. *European Journal of Cancer and Clinical Oncology* 18[12], 1243-1249. 1982.
 Excl reason: Not in PICO

Gordon, L. M., Johnson, R. H., Au, M. A., and Albritton, K. H. Primary care referral patterns for adolescent and young adult (AYA) cancer patients: A multistate study. *Journal of Clinical*

Oncology 29[15 SUPPL. 1]. 20-5-2011. American Society of Clinical Oncology.
 Excl reason: Not in PICO

Guccion, J. G., Gibert, C. L., Ortega, L. G., and Hadfield, T. L. Cat scratch disease and acquired immunodeficiency disease: diagnosis by transmission electron microscopy. *Ultrastructural Pathology* 20[3], 195-202. 1996.
 Excl reason: Not in PICO

Guven, M., Ozturk, B., Sayal, A., and Ozet, A. Lipid peroxidation and antioxidant system in the blood of patients with Hodgkin's disease. *Clinical Biochemistry* 33[3], 209-212. 2000.
 Excl reason: Not in PICO

Hajda, M., Koranyi, K., Salomvary, B., and Bajcsay, A. [Clinical presentation, differential diagnosis and treatment of lacrimal gland tumours]. [Hungarian]. *Magyar Onkologia* 49[1], 65-70. 2005.
 Excl reason: Not in PICO

Hiller, E. [Malignant Hodgkin's and non-Hodgkin's lymphomas]. [German]. *MMW Fortschritte der Medizin* 147[9], 31-34. 3-3-2005.
 Excl reason: Narrative review

Howell, D. A., Shellens, R., Roman, E., Garry, A. C., Patmore, R., and Howard, M. R. Haematological malignancy: Are patients appropriately referred for specialist palliative and hospice care? A systematic review and meta-analysis of published data. *Palliative Medicine* 25[6], 630-641. 2011.
 Excl reason: Not in PICO

Huhn, D. [Clinical aspects and therapy of malignant lymphomas in AIDS--symptomatology of AIDS encephalopathy]. [German]. *Verhandlungen der Deutschen Gesellschaft fur Innere Medizin* 92, 330-336. 1986.
 Excl reason: Not in PICO

Isaacson, P. G. Haematopathology practice: the commonest problems encountered in a consultation practice. [Review] [18 refs]. *Histopathology* 50[7], 821-834. 2007.
 Excl reason: Narrative review

James, B. O., Ajayi, S. O., Ogun, O. A., and Oladokun, R. E. Factors influencing time to diagnosis of childhood cancer in Ibadan, Nigeria. *African Health Sciences* 9[4], 247-253. 2009.
 Excl reason: Not in PICO

Kasper, Ekkehard, Lam, Fred, Luedi, Markus, Zinn, Pascal, and Pihan, German. Primary epidural lymphocyte-depleted Hodgkin's lymphoma of the thoracic spine - presentation of a rare disease variant. *BMC Neurology* 12[1], 64. 2012.
 Excl reason: Not in PICO

Khojasteh, A., Reynolds, R. D., and Khojasteh, C. A. Malignant lymphoreticular lesions in patients with immune disorders resembling acquired immunodeficiency syndrome (AIDS): review of 80 cases. [Review] [39 refs]. *Southern Medical Journal* 79[9], 1070-1075. 1986.
 Excl reason: Narrative review

Killeen, M. R. Approaches to the measurement of depressive symptomatology in children with cancer: attempting to circumvent the effects of defensiveness. *Journal of Child & Family Nursing* 3[2], 139-141. 2000.
 Excl reason: Not in PICO

Kouroukis, C. T., Chia, S., Verma, S., Robson, D., Desbiens, C., Cripps, C., and Mikhael, J. Canadian supportive care recommendations for the management of neutropenia in patients with cancer. *Current Oncology* 15[1], 9-23. 2008.
 Excl reason: Not in PICO

Kristensen, P., Hilt, B., Svendsen, K., and Grimsrud, T. K. Incidence of lymphohaematopoietic cancer at a university laboratory: a cluster investigation. *European Journal of Epidemiology* 23[1], 11-15. 2008.
 Excl reason: Not in PICO

Laskar, S., Gupta, T., Vimal, S., Muckaden, M. A., Saikia, T. K., Pai, S. K., Naresh, K. N., and Dinshaw, K. A. Consolidation radiation after complete remission in Hodgkin's disease following six cycles of

doxorubicin, bleomycin, vinblastine, and dacarbazine chemotherapy: Is there a need? *Journal of Clinical Oncology* 22[1], 62-68. 2004.

Excl reason: Not in PICO

Lukic, S., Marjanovic, G., and Zivanovic, J. Palpable lymphadenopathy in primary care. *Acta Facultatis Medicae Naissensis* 28[1], 17-23. 2011.

Excl reason: Narrative review

Meekes, I., Van Der Staak, F., and Van, Oostrom C. Results of splenectomy performed on a group of 91 children. *European Journal of Pediatric Surgery* 5[1], 19-22. 1995.

Excl reason: Not in PICO

Miettinen, M., Franssila, K. O., and Saxen, E. Hodgkin's disease, lymphocytic predominance nodular. Increased risk for subsequent non-Hodgkin's lymphomas. *Cancer* 51[12], 2293-2300. 1983.

Excl reason: Not in PICO

Milliken, S. T., Clezy, K. R., Cooper, S. G., and Romeril, K. HIV-related lymphoma and other malignancies. *Medical Journal of Australia* 164[8], 489-491. 15-4-1996.

Excl reason: Not in PICO

Milliken, S. T., Clezy, K. R., Cooper, S. G., and Romeril, K. R. Managing HIV. Part 5: Treating secondary outcomes. 5.13 HIV-related lymphoma and other malignancies. *The Medical journal of Australia* 164[8], 489-491. 15-4-1996.

Excl reason: Not in PICO

Morrison, C., Gordon, S., and Yeo, T. P. Hodgkin's disease in primary care. [Review] [21 refs]. *Nurse Practitioner* 25[7], 44-50. 1956.

Excl reason: Narrative review

Morse, E. E., Yamase, H. T., Greenberg, B. R., Sporn, J., Harshaw, S. A., Kiraly, T. R., Ziemba, R. A., and Fallon, M. A. The role of flow cytometry in the diagnosis of lymphoma: A critical analysis. *Annals of Clinical and Laboratory Science* 24[1], 6-11. 1994.

Excl reason: Not in PICO

Moses, S. Pruritus. *American Family Physician* 68[6], 1135-1146. 15-9-2003.

Excl reason: Narrative review

Nakamura, S. [Overview of 2008 WHO Classification of Malignant Lymphoma]. [Japanese]. *Rinsho byori The*[11], 1105-1111. 2010.

Excl reason: Narrative review

Nay, C., Luthi, F., Ketterer, N., Bauer, J., and Leyvraz, S. Overview on cancer in young adults. [French]. *Revue Medicale Suisse* 3[112], 1305-1310. 23-5-2007.

Excl reason: Narrative review

Newton, R., Crouch, S., Ansell, P., Simpson, J., Willett, E. V., Smith, A., Burton, C., Jack, A., and Roman, E. Hodgkin's lymphoma and infection: findings from a UK case-control study. *British Journal of Cancer* 97[9], 1310-1314. 5-11-2007.

Excl reason: Case-control comparison of number of visits to GP for infectious & non-infectious diagnoses in 15 years prior to diagnosis, but omitted data in the year prior to diagnosis in order not to swamp earlier effects. Same data as Crouch 2011. Only data included for the year prior to diagnosis was no of cases & controls visiting their GP at least once split by infectious/non-infectious diagnosis (including tiredness & malaise). No further split into individual symptoms.

Ng, A. K., Li, S., Neuberg, D., Silver, B., Weeks, J., and Mauch, P. Factors influencing treatment recommendations in early-stage Hodgkin's disease: a survey of physicians. *Annals of Oncology* 15[2], 261-269. 2004.

Excl reason: Not in PICO

Odemis, B., Parlak, E., Basar, O., Yuksel, O., and Sahin, B. Biliary tract obstruction secondary to malignant lymphoma: experience at a referral center. *Digestive Diseases & Sciences* 52[9], 2323-2332. 2007.

Excl reason: Not in PICO

- Pagano, J. S. Epstein-Barr virus: The first human tumor virus and its role in cancer. *Proceedings of the Association of American Physicians* 111[6], 573-580. 1999.
Excl reason: Narrative review
- Pollock, B. H., Krischer, J. P., and Vietti, T. J. Interval between symptom onset and diagnosis of pediatric solid tumors. *Journal of Pediatrics* 119[5], 725-732. 1991.
Excl reason: Not in PICO
- Pongas, G., Hamilos, G., Rolston, K. V., and Kontoyiannis, D. P. Formal adult infectious disease specialist consultations in the outpatient setting at a comprehensive cancer center (1998-2008): diverse and impactful. *Supportive Care in Cancer* 20[2], 261-265. 2012.
Excl reason: Not in PICO
- Proctor, S. J. and Wilkinson, J. A web-based study concept designed to progress clinical research for 'orphan' disease areas in haematological oncology in the elderly: the SHIELD programme. *Critical Reviews in Oncology-Hematology* 61[1], 79-83. 2007.
Excl reason: Not in PICO
- Razavi, D., Delvaux, N., Bredart, A., Paesmans, M., Debusscher, L., Bron, D., and Stryckmans, P. Screening for psychiatric disorders in a lymphoma out-patient population. *European Journal of Cancer* 28A[11], 1869-1872. 1992.
Excl reason: Not in PICO
- Reamy, B. V., Bunt, C. W., and Fletcher, S. A diagnostic approach to pruritus. *American Family Physician* 84[2], 195-202. 15-7-2011.
Excl reason: Narrative review
- Rose, C., Stovall, E., Ganz, P. A., Desch, C., and Hewitt, M. Cancer Quality Alliance: Blueprint for a better cancer care system. *CA: A Cancer Journal for Clinicians* 58[5], 266-292. 2008.
Excl reason: Not in PICO
- Ruffer, J. U., Flechtner, H., Heim, M., Schwarz, R., and Weis, J. [Cancer fatigue syndrome]. [German]. *Versicherungsmedizin* 55[1], 3-7. 1-3-2003.
Excl reason: Not in PICO
- Schleiffenbaum, B. and Fehr, J. Value of the blood picture and flow cytometry immunotyping in the early diagnosis of low-grade lymphoma. [German]. *Therapeutische Umschau Revue*[2], 117-122. 1996.
Excl reason: Narrative review
- Schott, A. F. Leukemia and lymphoma. *Primary Care Update for Ob/Gyns* 4[1], 6-14. 1997.
Excl reason: Narrative review
- Siddiqi, T. and Joyce, R. M. A case of HIV-negative primary effusion lymphoma treated with bortezomib, pegylated liposomal doxorubicin, and rituximab. *Clinical Lymphoma & Myeloma* 8[5], 300-304. 2008.
Excl reason: Not in PICO
- Smith, S. Unravelling diagnostic delay of hodgkin lymphoma in the teenage and young adult population - A substantive investigation. *European Journal of Cancer* 47, S310. 2011. Elsevier Ltd.
Excl reason: Published as abstract only, so not possible to check in more detail. May be published in full when update search done
- Spencer, A., Reed, K., and Arthur, C. Pilot study of an outpatient-based approach for advanced lymphoma using vinorelbine, gemcitabine and filgrastim. *Internal Medicine Journal* 37[11], 760-766. 2007.
Excl reason: Not in PICO
- Thompson, C. A., Mauck, K., Havyer, R., Bhagra, A., Kalsi, H., and Hayes, S. N. Care of the adult Hodgkin lymphoma survivor. [Review]. *American Journal of Medicine* 124[12], 1106-1112. 2011.
Excl reason: Not in PICO
- Timms, J. M., Bell, A., Flavell, J. R., Murray, P. G., Rickinson, A. B., Traverse-Glehen, A., Berger, F., and Delecluse, H.-J. Target cells of Epstein-Barr-virus (EBV)-positive post-transplant

lymphoproliferative disease: Similarities to EBV-positive Hodgkin's lymphoma. *Lancet* 361[9353], 217-223. 18-1-2003.

Excl reason: Not in PICO

van den Akker, Machiel, Zudekov, Vadiem, Moser, Asher, and Kapelushnik, Joseph. An osseous lesion in a 10-year-old boy with Hodgkin's lymphoma: a case report. *Journal of Medical Case Reports* 5[1], 511. 2011.

Excl reason: Not in PICO

Varnum, S. M., Webb-Robertson, B. J., Hessol, N. A., Smith, R. D., and Zangar, R. C. Plasma biomarkers for detecting Hodgkin's lymphoma in HIV patients. *PLoS ONE [Electronic Resource]* 6[12], e29263. 2011.

Excl reason: Not in PICO

Waller, H. D. [Hodgkin's disease--current problems in etiology and clinical picture]. [Review] [23 refs] [German]. *Strahlentherapie* 161[4], 191-196. 1985.

Excl reason: Narrative review

Wesnes, K. A., Brooker, H., and Edgar, C. The disruptions to cognition, everyday function, and quality of life in oncology patients: A therapeutic opportunity? *Neurotherapeutics* 7[3], 331-332. 2010. Elsevier Inc.

Excl reason: Not in PICO

White, L. N. Cancer prevention and detection: from twenty to sixty-five years of age. *Oncology Nursing Forum* 13[2], 59-64. 1986.

Excl reason: Narrative review

Wilkinson, A. R., Mahore, S. D., and Maimoon, S. A. FNAC in the diagnosis of lymph node malignancies: A simple and sensitive tool. *Indian Journal of Medical and Paediatric Oncology* 33[1], 21-24. 2012.

Excl reason: Not in PICO

Yamashita, H., Takahashi, Y., Kano, T., Kaneko, H., and Mimori, A. Malignant lymphoma presenting as inflammation of unknown origin. *Japanese Journal of Clinical Immunology* 35[2], 136-143. 2012.

Excl reason: Not in PICO

Yano, M., Yamakawa, Y., Niwa, H., Fukai, I., Kiriya, M., Saito, Y., Kani, H., Sasaki, H., and Masaoka, A. [Clinical considerations from sixteen cases with mediastinal malignant lymphoma]. [Japanese]. *Nippon Kyobu Geka Gakkai Zasshi - Journal of the Japanese Association for Thoracic Surgery* 44[8], 1114-1118. 1996.

Excl reason: Not in PICO

Yeole, B. B. and Jussawalla, D. J. Descriptive epidemiology of lymphatic malignancies in Greater Bombay. *Oncology Reports* 5[3], 771-777. 1998.

Excl reason: Not in PICO

Ying, J., Li, H., Murray, P., Gao, Z., Chen, Y.-W., Wang, Y., Lee, K. Y., Chan, A. T. C., Ambinder, R. F., Srivastava, G., and Tao, Q. Tumor-specific methylation of the 8p22 tumor suppressor gene *DLC1* is an epigenetic biomarker for Hodgkin, nasal NK/T-cell and other types of lymphomas. *Epigenetics* 2[1], 15-21. 2007.

Excl reason: Not in PICO

Review question:

Which investigations of symptoms of suspected Hodgkin's lymphoma should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	89	20	14/05/2013

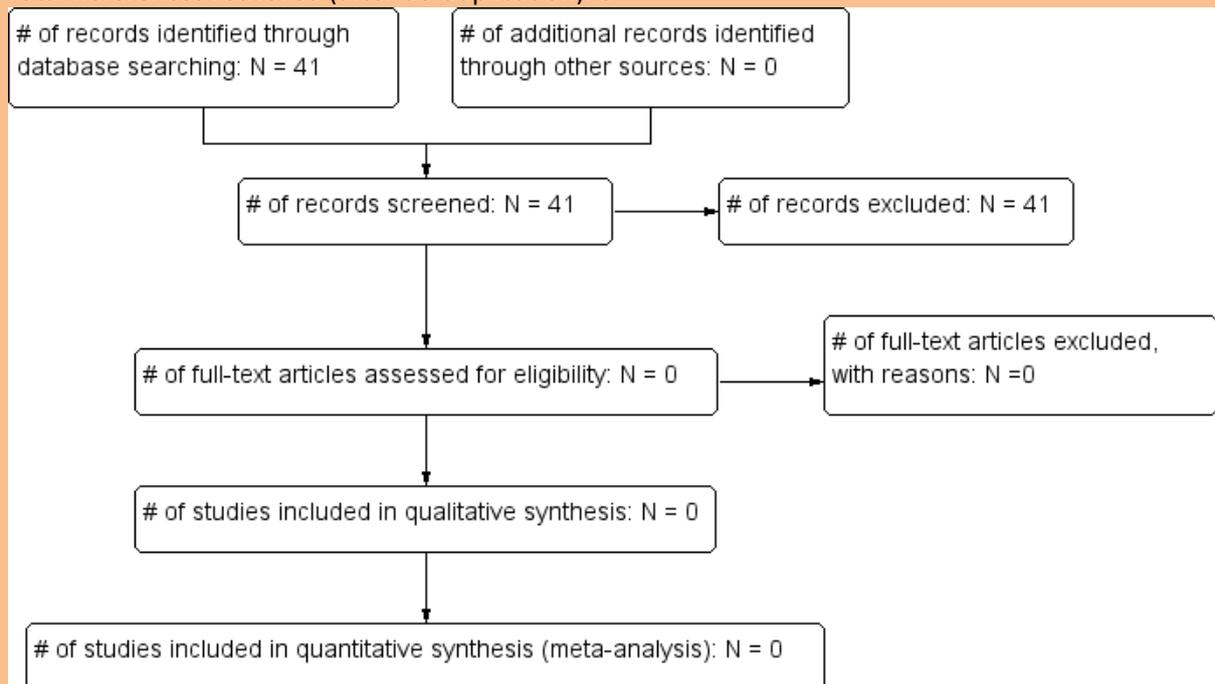
Premedline	1980-2013	5	2	14/05/2013
Embase	1980-2013	71	19	14/05/2013
Cochrane Library	1980-2013	31	1	14/05/2013
Psychinfo	1980-2013	2	0	14/05/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	8	3	14/05/2013

Total References retrieved (after de-duplication): 38

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	5/2013-26/08/2014	6	0	26/08/2014
Premedline	5/2013-26/08/2014	7	2	26/08/2014
Embase	5/2013-26/08/2014	17	1	26/08/2014
Cochrane Library	5/2013-26/08/2014	4	0	26/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	5/2013-26/08/2014	2	0	26/08/2014

Total References retrieved (after de-duplication): 3



Study results

No evidence was identified pertaining to the diagnostic accuracy of chest x-ray, CT scan, ultrasound or LDH in patients with suspected Hodgkin's lymphoma where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Bares, R., Galonska, P., Dempke, W., Handt, S., Bull, U. & Osieka, R. (1993) Somatostatin receptor scintigraphy in malignant lymphoma: first results and comparison with glucose metabolism measured by positron-emission tomography. *Hormone & Metabolic Research - Supplement*, 27: 56-58.

Not in PICO

Coleman, M. & Kostakoglu, L. (2006) Early 18F-labeled fluoro-2-deoxy-D-glucose positron emission tomography scanning in the lymphomas: changing the paradigms of treatments? *Cancer*, 107: 1425-1428.

Narrative review

Eich, H. T., Staar, S., Gossmann, A., Hansemann, K., Skripnitchenko, R., Kocher, M., Semrau, R., Engert, A., Josting, A., Franklin, J., Krug, B., Diehl, V. & Muller, R.-P. (2004) Centralized radiation oncologic review of cross-sectional imaging of Hodgkin's disease leads to significant changes in required involved field - Results of a quality assurance program of the German Hodgkin Study Group. *International Journal of Radiation Oncology Biology Physics*, 58: 1121-1127.

Not in PICO

El-Galaly, T. C., Mylam, K. J., Brown, P., Specht, L., Christiansen, I., Munksgaard, L., Johnsen, H. E., Loft, A., Bukh, A., Iyer, V., Nielsen, A. L. & Hutchings, M. (2012) Positron emission tomography/computed tomography surveillance in patients with Hodgkin lymphoma in first remission has a low positive predictive value and high costs. *Haematologica-the Hematology Journal*, 97: 931-936.

Not in PICO

Friedmann, A. M. (2008) Evaluation and management of lymphadenopathy in children. *Pediatrics in Review*, 29: 53-60.

Narrative review

Gallamini, A.; Borra, A. (2014). Role of PET in lymphoma. *Current Treatment Options in Oncology*, 15, 248-61.

Not in PICO

Garrett Kevin, M. K. M., Hoffer, F. A., Behm, F. G., Gow, K. W., Hudson, M. M. & Sandlund, J. T. (2002) Interventional radiology techniques for the diagnosis of lymphoma or leukemia. *Pediatric Radiology*, 32: 653-662.

Not in PICO

Gerrits, C. J., Overhagen, H., Lom, K., Adriaansen, H. J. & Löwenberg, B. (1994) Ultrasound examination of pathological cervical lymph nodes in patients with non-Hodgkin's lymphoma and Hodgkin's disease. *British journal of haematology.*, 88: 626-628.

Not in PICO

Glass, C. (2008) Role of the primary care physician in Hodgkin lymphoma. *American Family Physician*, 78: 615-626.

Narrative review

Goldschmidt, N., Libson, E., Bloom, A., Amir, G. & Paltiel, O. (2003) Clinical utility of computed tomography-guided core needle biopsy in the diagnostic re-evaluation of patients with lymphoproliferative disorders and suspected disease progression. *Annals of Oncology*, 14: 1438-1441.

Not in PICO

Hesselmann, V., Zahringer, M., Krug, B., Wesselmann, C., Haferkamp, K., Wickenhauser, C. & Lackner, K. (2004) Computed-tomography-guided percutaneous core needle biopsies of suspected malignant lymphomas: impact of biopsy, lesion, and patient parameters on diagnostic yield. *Acta Radiologica*, 45: 641-645.

Not in PICO

- Hodgson, D. C., Grunfeld, E., Gunraj, N. & Del, G. L. (2010) A population-based study of follow-up care for Hodgkin lymphoma survivors: Opportunities to improve surveillance for relapse and late effects. *Cancer*, 116: 3417-3425.
Not in PICO
- Hutchings, M., Loft, A., Hansen, M., Pedersen, L. M., Berthelsen, A. K., Keiding, S., D'Amore, F., Boesen, A. M., Roemer, L. & Specht, L. (2006) Position emission tomography with or without computed tomography in the primary staging of Hodgkin's lymphoma. *Haematologica-the Hematology Journal*, 91: 482-489.
Not in PICO
- Jabshetty, S., Malakkla, N., Khatri, V. & Friedman, H. (2011) Primary Hodgkin's lymphoma: A rare cause of solitary pulmonary nodule. *Journal of General Internal Medicine*, 26: S524.
Not in PICO
- Kalkner, M., Rehn, S., Andersson, T., Elvin, A., Hagberg, H., Lindgren, P. G., Sundstrom, C. & Glimelius, B. (1994) Diagnostics of malignant lymphomas with ultrasound guided 1.2 MM biopsy- gun. *Acta Oncologica*, 33: 33-37.
Not in PICO
- Kirby, A. M. & Mikhaeel, N. G. (2007) The role of FDG PET in the management of lymphoma: what is the evidence base?. [Review] [123 refs]. *Nuclear Medicine Communications*, 28: 335-354.
Narrative review
- Li, L., Wu, Q.-L., Liu, L.-Z., Mo, Y.-X., Xie, C.-M., Zheng, L., Chen, L. & Wu, P.-H. (2005) Value of CT-guided core-needle biopsy in diagnosis and classification of malignant lymphomas using automated biopsy gun. *World Journal of Gastroenterology*, 11: 4843-4847.
Not in PICO
- Linden, A., Zankovich, R., Theissen, P., Diehl, V. & Schicha, H. (1989) Malignant lymphoma: bone marrow imaging versus biopsy. *Radiology*, 173: 335-339.
Not in PICO
- Liu, Y. (2012) Concurrent FDG Avid Nasopharyngeal Lesion and Generalized Lymphadenopathy on PET-CT Imaging Is Indicative of Lymphoma in Patients with HIV Infection. *AIDS Research & Treatment*, 2012: 764291.
Not in PICO
- Morrison, C., Gordon, S. & Yeo, T. P. (1956) Hodgkin's disease in primary care. *The Nurse practitioner*, 25: 44, 47-50, 56.
Narrative review
- Moses, S. (2003) Pruritus. *American Family Physician*, 68: 1135-1146.
Narrative review
- Munker, R., Glass, J., Griffeth, L. K., Sattar, T., Zamani, R., Heldmann, M., Shi, R. & Lilien, D. L. (2004) Contribution of PET imaging to the initial staging and prognosis of patients with Hodgkin's disease. *Annals of Oncology*, 15: 1699-1704.
Not in PICO
- Neufang, K. F. & Beyer, D. (1983) [Conventional diagnosis of lymphadenopathies--value of conventional roentgen examination and supplementation of other imaging technics]. [German]. *Rontgen-Blatter*, 36: 30-44.
Narrative review
- Odemis, B., Parlak, E., Basar, O., Yuksel, O. & Sahin, B. (2007) Biliary tract obstruction secondary to malignant lymphoma: experience at a referral center. *Digestive Diseases & Sciences*, 52: 2323-2332.
Not in PICO
- Omur, O.; Baran, Y.; Oral, A.; Ceylan, Y. (2014). Fluorine-18 fluorodeoxyglucose PET-CT for extranodal staging of non-Hodgkin and Hodgkin lymphoma. *Diagnostic & Interventional Radiology*, 20, 185-92.
Not in PICO

- Pan, Z. G., Hunter, W. J. & Deng, C. S. (2010) Postmortem diagnosis of Hodgkin lymphoma: An issue regarding to fine needle aspiration biopsy. *Laboratory Investigation*, 90: 11A.
Not in PICO
- Raab, C. P. & Gartner, J. C., Jr. (2009) Diagnosis of childhood cancer. [Review] [33 refs]. *Primary Care; Clinics in Office Practice*, 36: 671-684.
Narrative review
- Reamy, B. V., Bunt, C. W. & Fletcher, S. (2011) A diagnostic approach to pruritus.[Summary for patients in Am Fam Physician. 2011 Jul 15;84(2):203; PMID: 21766770]. *American Family Physician*, 84: 195-202.
Narrative review
- Richardson, S. E., Sudak, J., Warbey, V., Ramsay, A. & McNamara, C. J. (2012) Routine bone marrow biopsy is not necessary in the staging of patients with classical Hodgkin lymphoma in the 18F-fluoro-2-deoxyglucose positron emission tomography era. *Leukemia & Lymphoma*, 53: 381-385.
Not in PICO
- Sato, K., Ozaki, K., Fujiwara, S.-I., Oh, I., Matsuyama, T., Ohmine, K., Suzuki, T., Mori, M., Nagai, T., Muroi, K. & Ozawa, K. (2010) Incidental carcinomas detected by PET/CT scans in patients with malignant lymphoma. *International Journal of Hematology*, 92: 647-650.
Not in PICO
- Savage, S. A. H., Wotherspoon, H. A., Fitzsimons, E. J. & MacKenzie, K. (2008) Cervical lymphadenopathy resulting in a diagnosis of lymphoma. *Scottish Medical Journal*, 53: 13-16.
Not in PICO
- Sklair-Levy, M., Polliack, A., Shaham, D., Applbaum, Y. H., Gillis, S., Ben-Yehuda, D., Sherman, Y. & Libson, E. (2000) CT-guided core-needle biopsy in the diagnosis of mediastinal lymphoma. *European Radiology*, 10: 714-718.
Not in PICO
- Tappauf, M., Lackner, H., Sovinz, P., Schwinger, W., Benesch, M., Strenger, V., Schmidt, S. & Urban, C. (2011) Multifocal osseous involvement in a patient with Hodgkin lymphoma. *Monatsschrift fur Kinderheilkunde*, 159: 326.
Not in PICO
- Toma, P., Granata, C., Rossi, A. & Garaventa, A. (2007) Multimodality imaging of Hodgkin disease and non-Hodgkin lymphomas in children. [Review] [55 refs]. *Radiographics*, 27: 1335-1354.
Narrative review
- Treglia, G., Lococo, F., Petrone, G., Stefanelli, A., Carnassale, G., Calcagni, M. L., Granone, P. & Giordano, A. (2013) A Rare Case of Primary Thymic Hodgkin Lymphoma in an Elderly Patient Detected by 18F-FDG PET/CT. *Clinical Nuclear Medicine*, 38: e236-e238.
Not in PICO
- Vanis,N.; Mesihovic,R.; Ibricevic,L.; Dobrila-Dintinjana,R. (2013). Predictive value of endoscopic ultrasound in diagnosis and staging of primary gastric lymphoma. *Collegium Antropologicum*, 37, 291-7.
Not in PICO
- Wickmann, L., Luders, H. & Dorffel, W. (2003) 18-FDG-PET-findings in children and adolescents with Hodgkin's disease: Retrospective evaluation of the correlation to other imaging procedures in initial staging and to the predictive value of follow up examinations. [German]. *Klinische Padiatrie*, 215: 146-150.
Not in PICO
- Williams, E. & Ledingham, J. (2010) Biopsy proven Hodgkin'S Lymphoma (HL) and sarcoid in a patient with Rheumatoid Arthritis (RA). *Rheumatology*, 49: i40-i41.
Not in PICO
- Yasuda, I., Tsurumi, H., Omar, S., Iwashita, T., Kojima, Y., Yamada, T., Sawada, M., Takami, T., Moriwaki, H. & Soehendra, N. (2006) Endoscopic ultrasound-guided fine-needle aspiration

biopsy for lymphadenopathy of unknown origin. *Endoscopy*, 38: 919-924.

Not in PICO

You, J. J., Inculet, R. I., Sukhbinder, K. D. T., Chan, A. M., Freeman, M., Cline, K. J., Pritchard, K. I., Dayes, I. S., Gu, C.-S., Julian, J. A., Gulenchyn, K. Y., Evans, W. K. & Levine, M. N. (2012) Positron emission tomography/computed tomography (PET/CT) for the diagnosis of recurrent cancer (PETREC): A multicenter, prospective cohort study. *Journal of Clinical Oncology*, 30.

Not in PICO

Zhou, Q. T., Zhu, H. & He, B. (2009) [Clinical analysis of lymphoma with chest involvement: report of 25 cases]. [Chinese]. *Chung-Hua Nei Ko Tsa Chih Chinese Journal of Internal Medicine*, 48: 846-849.

Not in PICO

SARCOMAS

BONE SARCOMA

Review question:

What is the risk of bone sarcoma in patients presenting in primary care with symptom(s)?

Results

Literature search

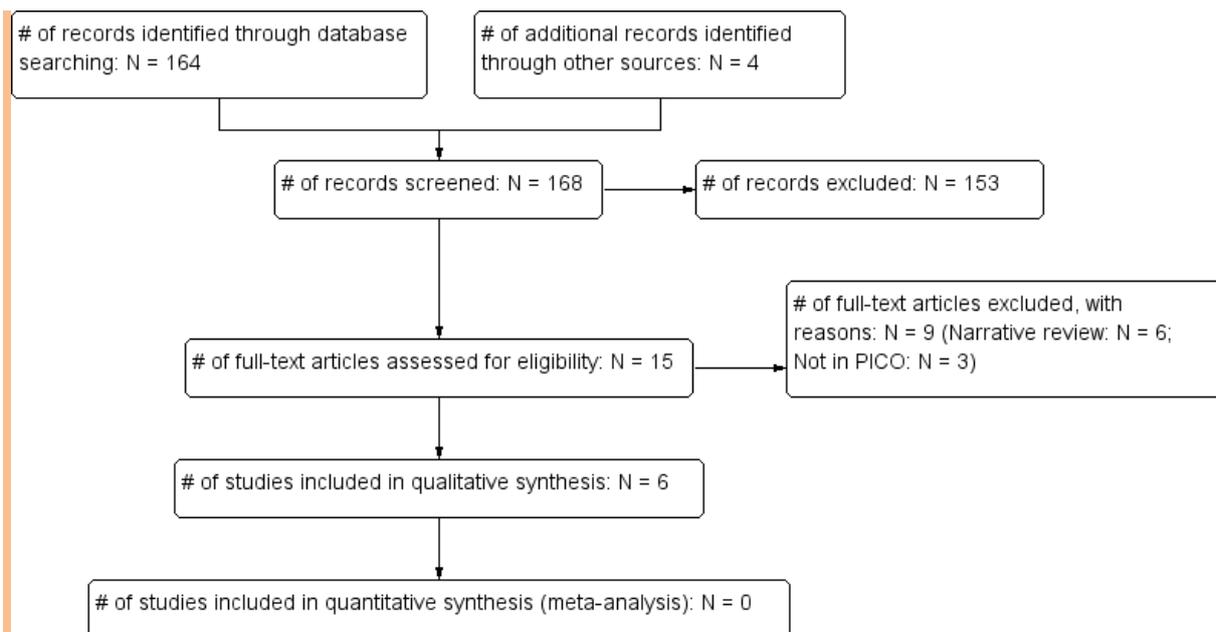
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	2069	78	11/10/12
<i>Premedline</i>	All-2012	57	8	11/10/12
<i>Embase</i>	All-2012	2009	76	11/10/12
<i>Cochrane Library</i>	All-2012	407	2	15/10/12
<i>Psychinfo</i>	All-2012	10	1	11/10/12
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	706	14	15/10/12
<i>Biomed Central</i>	All-2012	138	5	15/10/12

Total References retrieved (after de-duplication): 155

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	10/2012-26/08/2014	85	1	26/08/2014
<i>Premedline</i>	10/2012-26/08/2014	60	4	26/08/2014
<i>Embase</i>	10/2012-26/08/2014	258	6	26/08/2014
<i>Cochrane Library</i>	10/2012-26/08/2014	262	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	10/2012-26/08/2014	134	0	26/08/2014

Total References retrieved (after de-duplication): 9



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main issue to note is that 4/5 studies employed samples of patients that are not directly representative of an unselected symptomatic population of patients presenting to the UK-based GP. In the case of Pharisa (2009) whose sample consisted of patients presenting as emergencies, the symptom spectrum is likely to be of the more severe kind than those typically seen by a GP in the UK, but in the other cases (e.g., presentations to physiotherapists, chiropractors and hospital-based walk-in and family clinics) it is unclear how the patients differ from those of primary current interest. Dommett (2012, 2013a,b) only presented results for bone and soft tissue sarcoma in combination and also employed a case-control design which has been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors may have gone some way in counteracting this influence. Finally, two studies employed reference standards that are at some (unknown level of) risk of failing to identify all patients with cancer, which means that the relevant PPVs may be underestimated (to the extent that the reference standards have failed to identify patients with cancer).

	<u>Risk of Bias</u>				<u>Applicability Concerns</u>		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Deyo (1988)	?	+	?	+	-	+	+
Dommett (2012, 2013)	-	+	+	+	+	+	+
Henschke (2009)	+	+	+	+	-	+	+
Pharisa (2009)	+	+	+	+	-	+	+
Suarez-Almazor (1997)	+	+	?	+	?	+	+

 High	 Unclear	 Low
---	--	--

Study results

Table 1: Bone sarcoma: Patients aged > 14-15 years

Study	Symptom(s)	Patient group	PPVs (95% CI); prevalence
Deyo (1988)	Back pain	All patients	0 (0-0.2) 0/1975 None had bone sarcoma, but N = 9 had other types of cancer
Suarez-Almazor (1997)	Acute low back pain	All patients	TP = 0-1, FP = 962-963 Unclear if diagnosis prior to symptom
Henschke (2009)	Acute low back pain	All patients	0 (0-0.4) 0/1172 None had cancer
Henschke (2009)	Acute low back pain + age at onset < 20 years or > 55 years	Subgroup with both symptoms	0 (0-1.7) 0/281 None had cancer
Henschke (2009)	Acute low back pain + previous history of cancer	Subgroup with both symptoms	0 (0-9.6) 0/46 None had cancer
Henschke (2009)	Acute low back pain + tried bed rest, but no relief	Subgroup with both symptoms	0 (0-2.4) 0/192 None had cancer
Henschke (2009)	Acute low back pain + unexplained weight loss	Subgroup with both symptoms	0 (0-69) 0/3

			None had cancer
Henschke (2009)	Acute low back pain + insidious onset	Subgroup with both symptoms	0 (0-2.3) 0/202 None had cancer
Henschke (2009)	Acute low back pain + systemically unwell	Subgroup with both symptoms	0 (0-15.5) 0/27 None had cancer
Henschke (2009)	Acute low back pain + constant progressive non-mechanical pain	Subgroup with both symptoms	0 (0-13) 0/33 None had cancer
Henschke (2009)	Acute low back pain + sensory level altered from trunk down	Subgroup with both symptoms	0 (0-20.9) 0/19 None had cancer

TP = True positives, FP = False positives.

Table 2: Bone sarcoma: Positive predictive values for child- or young adulthood bone tumour/soft tissue sarcoma

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2013a)	Lump mass swelling below neck excluding abdomen 0-3 months before diagnosis	All bone tumour/soft tissue sarcoma patients and controls aged 0-14 years	0.03 (0.01-0.14)
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All bone tumour/soft tissue sarcoma patients and controls aged 0-14 years	0.01 (0-0.01)
Dommett (2013a)	Trauma 0-3 months before diagnosis	All bone tumour/soft tissue sarcoma patients and controls aged 0-14 years	0 (0-0)
Dommett (2013a)	≥ 3 consultations	All bone tumour/soft tissue sarcoma patients and controls aged 0-14 years	0 (0-0)
Dommett (2013b)	Lump mass swelling	All bone tumour/soft tissue sarcoma patients and controls aged 15-24 years	0.0415 (0.0124-0.1392) Cases: 19/196 Controls: 3/2438
Dommett (2013b)	Musculoskeletal symptoms	All bone tumour/soft tissue sarcoma patients and controls aged 15	0.0093 (0.0058-0.0151) Cases: 37/196 Controls: 26/2438
Dommett (2013b)	Chest pain	All bone tumour/soft tissue sarcoma patients and controls aged 15	0.0027 (0.001-0.0077) Cases: 5/196 Controls: 12/2438
Dommett (2013b)	≥ 3 consultations	All bone tumour/soft tissue sarcoma patients and controls aged 15	0.003 (0.0024-0.0037) Cases: 86/196

			Controls: 189/2438
Pharisa (2009)	Neck pain	Children ≤ 16 years	0 (0-2.75) 0/ 170

The positive predictive values are calculated using Bayesian statistics. TP = true positives, FP = false positives

Evidence statement(s):

Adult patients

Acute low back pain alone (2 studies, N = 2135) or in combination with other single risk factors/symptoms (1 study, N = 19-281), and back pain (1 study, N = 1975) presenting in a primary care setting do not appear to confer an increased risk of bone sarcoma, although the study populations are probably not directly representative of the typical unselected symptomatic UK GP population (see also Table 1).

Children, teenage and young adult patients

The positive predictive values of having childhood or young adulthood bone sarcoma tumour/soft tissue sarcoma ranged from 0% (for trauma) to 0.03% (for 'lump mass swelling below neck excluding abdomen') for patients aged 0-14 years old, and from 0.0027% (for chest pain) to 0.0415% (for 'lump mass swelling') for patients aged 15-24 years (1 study, N = 30855). The evidence quality is somewhat compromised by the case-control design of the study (see also Table 2).

Neck pain (1 study, N = 170) presenting in a primary care setting does not appear to confer an increased risk of bone sarcoma, although the study population is not directly representative of the typical unselected symptomatic UK GP population (see also Table 2).

Evidence tables

Deyo (1988)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive? patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1975, mean (SD; range) age = 39.5 (15.4; 15-86) years, 62% females. 54% of the patients were seeking medical care for back pain for the first time and 76% of the patients had had back pain for < 3 months. 3% had a history of back pain surgery. Maximal back pain in the low back (84%) or in the upper back (16%). <u>Inclusion criteria:</u> Patients who sought treatment between March 1982 and

	September 1984 in the walk-in clinic of a public hospital where virtually all patients are self-referred. In each case back pain was part of the chief complaint. <u>Exclusion criteria:</u> Neck pain. <u>Clinical setting:</u> Walk-in clinic of a public hospital; this clinic is a source of primary care for indigent persons in a county in the USA with a population of approximately 1 million.
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	Back pain; not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	The reference standard consisted of a search on each patient name in the institutional tumour registry \geq 6 months after the index visit. The registry included every patient with a histological diagnosis of cancer made in the authors' hospital system regardless of site of care. The authors point out that "while this method might fail to identify cancer patients who sought care elsewhere, it is likely that most patients sought follow-up for a particular illness at the same facility.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and reference standard?	Yes (probably)
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes

Could the patient flow have introduced bias?		Low risk
NOTES	<p>It is a concern that some patients with cancer might have been missed due to the choice of reference standard because this would result in an underestimation of the positive predictive value.</p> <p>38/1975 patients were found in the tumour registry. Of those 38, 13 patients had tumours that were probable causes of back pain, and 4 of these 13 patients already had a diagnosis of cancer at presentation. The 9/1975 patients who had undiagnosed cancer that the back pain could be attributed to had: Lymphoma (NOS; 2), cancer of unknown primary (1), prostate cancer (1), retroperitoneal liposarcoma (1), lung cancer (1), renal cell (1), multiple myeloma (1), mucinous adenocarcinoma (of gallbladder?; 1)</p>	
Dommett (2012; 2013a,b)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Population-based nested case-control study using data from the General Practice Research Database (GPRD)	
Was a consecutive or random sample of patients enrolled?	No	
Was a case-control design avoided?	No	
Did the study avoid inappropriate exclusions?	Yes	
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes	
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes	
Could the selection of patients have introduced bias?		High risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p><u>Cases:</u> 1267 children; aged 0-4 years: N = 436; aged 5-14 years: N = 831; 703 males/564 females. Cancer type: Leukemia: N = 368; brain: N = 270; lymphoma: N = 142; bone: N = 107; soft tissue sarcoma: N = 91; renal: N = 82; neuroblastoma: N = 75; other ICD codes: N = 132. 1064 teenagers and young adults (TYA): 15-24 years: Gender not reported. Cancer type: Leukemia: N = 143; brain: N = 154; lymphoma: N = 270; bone: N = 96; soft tissue sarcoma: N = 100; other ICD codes: N = 301 (including testis: N = 60; skin: N = 49; ovary: N = 20 and thyroid: N = 17).</p> <p><u>Controls:</u> 15318 children; aged 0-4 years: N = 4802; aged 5-14 years: N = 10516; 8461 males/6857 females. 13206 TYA. Gender not reported</p> <p><u>Inclusion criteria:</u> The sample comprised all children and TYU aged 0–24 years, inclusive, drawn from all general practices contributing research-standard data to the GPRD between 1 January 1988 and 31 December 2010. To be included, the practices had to have been contributing research-standard data for a minimum of 1 year before each child’s date of cancer diagnosis or the index</p>	

	<p>date (see below) for matched controls.</p> <p>Cases: Patients diagnosed with the following cancers: leukaemia, lymphoma, neuroblastoma, soft tissue sarcoma, hepatic, renal, bone and central nervous system tumours, using pre-defined medical codes used in the GPRD. The date of diagnosis for cases was defined as the date of pathological diagnosis, but if this was unavailable, the date of the first cancer code entered in the GPRD was used.</p> <p>Controls: Up to 13 controls (children with no diagnosis of cancer at any time) were selected per case, using a computer-generated random sequence, matched on age (within 1 year), sex and practice, and had to be currently registered on the date of diagnosis of their matched case (the index date).</p> <p><u>Exclusion criteria</u>: None listed</p> <p><u>Clinical setting</u>: Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	The GPRD uses just over 100 000 medical codes to encompass all primary care events, including both symptoms and diagnoses. From this list, libraries of codes were assembled representing individual alert symptoms derived from the NICE referral guidelines for suspected cancer in children. <i>No more information reported.</i>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Cancer diagnosis in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for.

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	This study is published in three papers.
Henschke (2009)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective consecutive patient series
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 1172, mean (SD) age = 43.97 (15.1) years, 626 males/546 females; Primary care physician consulted: Medical practitioner (N = 267), physiotherapist (N = 851), chiropractor (N = 54); Previous episode of low back pain (N = 888); Duration of low back pain: < 1 week (N = 696), 1-2 weeks (N = 145), 2-3 weeks (N = 174), 3-4 weeks (N = 73), 4-5 weeks (N = 30), 5-6 weeks (N = 54).</p> <p><u>Inclusion criteria</u>: Consecutive English-speaking (and writing) patients aged ≥ 14 years with acute low back pain who presented for a first consultation to participating primary care providers in the Sydney region of Australia. <i>Please note that in Australia, the majority of primary care management for low back pain is provided by general medical practitioners, physiotherapists and chiropractors.</i></p> <p><u>Exclusion criteria</u>: Diagnosis of serious pathology prior to the consultation, which was considered to be the cause of the current episode of low back pain.</p> <p><u>Clinical setting</u>: Primary care (including physiotherapy and chiropractice)</p>
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	An episode of acute low back pain was defined as pain in the area bounded superiorly by T12 and inferiorly by the buttock crease, lasting for more than 24 hours but less than 6 weeks, and preceded by a period of at least 1 month without back pain. Patients remained eligible if they also had pain that referred beyond this region.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or	Low concern

interpretation differ from the review question?		
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	<p>The reference standard consisted of close follow up for 12 months. Participants were contacted by telephone 6 weeks, 3 months, and 12 months after the initial consultation. At each follow up contact, participants were asked the following question: “Low back pain is occasionally the result of a fracture, infection, arthritis, or cancer. Has a health care provider said that your back pain is caused by one of these rare diseases?” Participants were also prompted to provide any further details of a diagnosis or explanation for their low back pain that had been provided to them. All patients with potentially serious pathology were subsequently examined by a study rheumatologist. At each follow up contact, participants were also questioned to establish whether they had recovered from the episode of low back pain. Recovery was defined as 1 month with no pain, no interference with function due to pain, and return to previous work status for 1 month.</p> <p>Patients suspected by their primary care clinician of having a serious spinal pathology and those who reported having a serious spinal pathology during the follow up period were referred immediately to 1 of 2 study rheumatologists for a clinical assessment. Within 2 weeks from the time of referral, the rheumatologists examined each patient in their clinics and were additionally provided with the complete medical histories and all test results.</p>	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for in the results	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	Please note that the primary care physician consulted were: Medical practitioner: N = 267, physiotherapist: N = 851, chiropractor: N = 54	
Pharisa (2009)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective consecutive patient series	

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 170 (61 females/109 males), mean age = 9.05 years, median age = 9 years (range = 7 weeks to 16 years). A history of trauma was clearly reported in 106 of the children and clinical examination revealed restricted neck movements in 48 of these patients and painful movements without restriction in 28 of these patients. None of the patients had a neurological deficit on initial physical examination.</p> <p><u>Inclusion criteria:</u> All children aged ≤ 16 years presenting with neck pain and/or restricted neck movements from October 2004 to September 2005. Although any child with a complaint of neck pain was considered for inclusion in the study, only those whose neck pain was confirmed during medical examination were included.</p> <p><u>Exclusion criteria:</u> Toxic-appearing children with obvious signs of meningitis</p> <p><u>Clinical setting:</u> Emergency department of the Children's Hospital of Lausanne, Switzerland</p>
Are there concerns that the included patients and setting do not match the review question?	High concern
INDEX TEST	
A. Risk of bias	
Index test	"Neck pain confirmed during medical examination"
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Chart review and follow-up, including telephone calls to paediatricians to confirm final diagnosis
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	

Flow and timing	Follow up data were obtained by telephone in 134/170 patients, but final diagnoses are presented for all 170 patients.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Suarez-Almazor (1997)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective consecutive patient series
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 1550, of whom N = 331 had chronic (> 3 months?) back pain, N = 963 had acute (< 3 months) low back pain, and N = 256 had back pain of unspecified duration. Of the patients with acute low back pain, 442 were males, and it appears that the mean (SD) age = 42.2 (15.6) years for the patients with acute low back pain, 14/963 had a history of cancer</p> <p><u>Inclusion criteria:</u> All patients aged ≥ 18 years presenting to four family clinics in Edmonton (Alberta, Canada) between January 1 1992 and December 31 1993 with low back pain or leg pain compatible with sciatic pain for which no visit had been made within the past 12 months.</p> <p><u>Exclusion criteria:</u> Low back pain attributable to visceral pain (e.g., urinary infection, inflammatory pelvic disease), previous diagnosis of ankylosing spondylitis, pregnancy.</p> <p><u>Clinical setting:</u> Four family clinics in Edmonton (Alberta, Canada), two of which are university-affiliated and hospital-based, with the other two based in the community.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Acute (< 3 months) low back pain; not further specified.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	

A. risk of bias	
Reference standard(s)	Follow up consisting of chart review after a minimum of 2 years. Patients were considered to have cancer if recorded in the physician notes or in reports from laboratory or diagnostic tests.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	The results are only presented for the patients with acute low back pain.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	13/963 patients with acute low back pain had active cancer. 3 of those 13 patients had the cancer diagnosis prior to the index visit; 3/13 patients had tumours that were probable causes of the acute low back pain (spinal infiltrates from multiple myeloma [2] and metastatic bone disease with compression fractures [1]), and 10/13 patients had cancer that was not considered to have caused the acute low back pain (bladder cancer [3], colon [1], breast [1], thyroid [1], lung [1], prostate [1], endometrium [1], oesophagus [1]). However, as it is not reported which of these patients already had a diagnosis of cancer pre-index visit, it is not possible to present the data accurately for the individual cancers.

References

Included studies

- Deyo, R. A. and Diehl, A. K. Cancer as a cause of back pain: Frequency, clinical presentation, and diagnostic strategies. *Journal of General Internal Medicine* 3, 230-238. 1-11-1988.
- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of childhood cancer in primary care: A population-based nested case-control study. *British Journal of Cancer* 106[5], 982-987. 2012.
- Dommett, R. M., Redaniel, T., Stevens, M. C. G., Martin, R. M., and Hamilton, W. Risk of childhood cancer with symptoms in primary care: A population-based case-control study. *British Journal of General Practice*; DOI:10.3399/bjgp13X660742. 2013a.
- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of cancer in teenagers and young adults in primary care: A population-based nested case-control study. *British Journal of Cancer* 2329-2333. 2013b.
- Henschke, N., Maher, C. G., Refshauge, K. M., Herbert, R. D., Cumming, R. G., Bleasel, J., York, J., Das, A., and McAuley, J. H. Prevalence of and screening for serious spinal pathology in

patients presenting to primary care settings with acute low back pain. *Arthritis & Rheumatism* 60[10], 3072-3080. 2009.

Pharisa, C., Lutz, N., Roback, M. G., and Gehri, M. Neck complaints in the pediatric emergency department: A consecutive case series of 170 children. *Pediatric Emergency Care* 25[12], 823-826. 2009.

Suarez-Almazor, M. E., Belseck, E., Russell, A. S., and Mackel, J. V. Use of lumbar radiographs for the early diagnosis of low back pain. Proposed guidelines would increase utilization. *JAMA* 277[22], 1782-1786. 11-6-1997.

Excluded studies (with excl reason)

(1998) Practice guidelines: uterine corpus--sarcomas. Society of Gynecologic Oncologists Clinical Practice Guidelines. *Oncology (Williston Park)*, 12: 284-286.
Guideline

(2002) Information from your family doctor. Osteosarcoma. *American Family Physician*, 65: 1135-1136.

Patient information material

Abughazaleh, K. & Kawar, N. (2011) Osteonecrosis of the jaws: What the physician needs to know: Practical considerations. *Disease-a-Month*, 57: 231-241.

Narrative review

Ahrensberg, J. M., Schroder, H., Hansen, R. P., Olesen, F. & Vedsted, P. (2012) The initial cancer pathway for children - one-fourth wait more than 3 months. *Acta Paediatrica*, 101: 655-662.

Not in PICO

Albregts, A. E. & Rapini, R. P. (1995) Malignancy in Maffucci's syndrome. [Review] [31 refs]. *Dermatologic Clinics*, 13: 73-78.

Narrative review

Araujo, F. I., Monteiro, A. & Kalil, R. K. (2010) Giant cell-rich osteosarcoma - Two cases report and literature review. *Histopathology*, 57: 14-15.

Not in PICO

Arndt, C. A. S., Rose, P. S., Folpe, A. L. & Laack, N. N. (2012) Common Musculoskeletal Tumors of Childhood and Adolescence. *Mayo Clinic Proceedings*, 87: 475-487.

Not in PICO

Ashwood, N., Witt, J. D., Hallam, P. J. & Cobb, J. P. (2003) Analysis of the referral pattern to a supraregional bone and soft tissue tumour service. *Annals of the Royal College of Surgeons of England*, 85: 272-276.

Not in PICO

Babic, M., Milenkovic, Z. & Basic, H. (2002) Manual percutaneous method for diagnosis of spinal tumors. *Zentralblatt fur Neurochirurgie*, 63: 120-123.

Not in PICO

Baker, A. D. L. & Burke, J. G. (2008) Back Pain: background, aetiology, diagnosis and treatment. *Foundation Years*, 4: 302-308.

Narrative review

Barbera, C. & Lewis, M. M. (1988) Office evaluation of bone tumors. [Review] [33 refs]. *Orthopedic Clinics of North America*, 19: 821-838.

Narrative review

Barsa, P. & Hackel, M. (2003) Red Flags in the diagnosis and treatment of the low back pain. [Czech]. *Bolest*, 6: 171-175.

Narrative review

Bates, D. W. & Reuler, J. B. (1988) Back pain and epidural spinal cord compression. [Review] [52 refs]. *Journal of General Internal Medicine*, 3: 191-197.

Narrative review

- Baumgartner, E. & Vischer, T. L. (1997) Back pain: Current approaches. [French]. *Schweizerische Medizinische Wochenschrift*, 127: 1901-1910.
Narrative review
- Bell, W. C., Klein, M. J., Pitt, M. J. & Siegal, G. P. (2006) Molecular pathology of chondroid neoplasms: part 1, benign lesions. [Review] [41 refs]. *Skeletal Radiology*, 35: 805-813.
Narrative review
- Bethapudi, S., Ritchie, D. A., MacDuff, E. & Straiton, J. (2014) Imaging in osteofibrous dysplasia, osteofibrous dysplasia-like adamantinoma, and classic adamantinoma. *Clinical Radiology*, 69: 200-208.
Not in PICO
- Biau, D. J., Weiss, K. R., Bhumbra, R. S., Davidson, D., Brown, C., Wunder, J. S. & Ferguson, P. C. (2013) Using the CUSUM test to control the proportion of inadequate open biopsies of musculoskeletal tumors. *Clinical Orthopaedics & Related Research*, 471: 905-914.
Not in PICO
- Biedermann, H. & Koch, L. (1996) Differential diagnosis of KISS syndrome. [German]. *Manuelle Medizin*, 34: 73-81.
Narrative review
- Bielack, S. S., Carrle, D., Harges, J., Schuck, A. & Paulussen, M. (2008) Bone Tumors in Adolescents and Young Adults. *Current Treatment Options in Oncology*, 9: 67-80.
Narrative review
- Biswas, D., Saha, S. & Bera, S. P. (2007) Relative distribution of the tumours of ear, nose and throat in the paediatric patients. *International Journal of Pediatric Otorhinolaryngology*, 71: 801-805.
Not in PICO
- Bleyer, A., Morgan, S. & Barr, R. (2006) Proceedings of a workshop: bridging the gap in care and addressing participation in clinical trials. *Cancer*, 107: Suppl-8.
Not in PICO
- Bovee, J. V. (2008) Multiple osteochondromas. *Orphanet journal of rare diseases*, 3: 3.
Narrative review
- Cabral, D. A. & Tucker, L. B. (1999) Malignancies in children who initially present with rheumatic complaints. *Journal of Pediatrics*, 134: 53-57.
Not in PICO
- Chadha, N. K. & Forte, V. (2009) Pediatric head and neck malignancies. [Review] [41 refs]. *Current Opinion in Otolaryngology & Head & Neck Surgery*, 17: 471-476.
Narrative review
- Costelloe, C. M., Chuang, H. H., Chasen, B. A., Pan, T., Fox, P. S., Bassett, R. L. & Madewell, J. E. (2013) Bone Windows for Distinguishing Malignant from Benign Primary Bone Tumors on FDG PET/CT. *Journal of Cancer*, 4: 524-530.
Not in PICO
- Craft, A. (1988) What can we do for the child with malignant disease? *Practitioner*, 232: 584-589.
Narrative review
- Cuffy, M., Abir, F. & Longo, W. E. (2006) Management of less common tumors of the colon, rectum, and anus. [Review] [164 refs]. *Clinical Colorectal Cancer*, 5: 327-337.
Narrative review
- Desandes, E., Lacour, B., Sommelet, D., White-Koning, M., Velten, M., Tretarre, B., Marr, A., Maarouf, N., Guizard, A. V., Delafosse, P., Danzon, A., Cotte, C. & Brugieres, L. (2007) Cancer adolescent pathway in France between 1988 and 1997. *European Journal of Oncology Nursing*, 11: 74-81.
Not in PICO
- Dhillon, M. S., Singh, B., Singh, D. P., Prabhu, V. & Nagi, O. N. (1994) Primary bone tumors of the talus. *Journal of the American Podiatric Medical Association*, 84: 379-384.
Not in PICO

- Didolkar, M. M., Anderson, M. E., Hochman, M. G., Rissmiller, J. G., Goldsmith, J. D., Gebhardt, M. G. & Wu, J. S. (2013) Image guided core needle biopsy of musculoskeletal lesions: Are nondiagnostic results clinically useful? *Clinical Orthopaedics and Related Research*, 471: 3601-3609.
Not in PICO
- Donthineni, R. & Ofluoglu, O. (2010) Solitary enchondromas of long bones: pattern of referral and outcome. *Acta Orthopaedica et Traumatologica Turcica*, 44: 397-402.
Not in PICO
- Downie, A., Williams, C. M., Henschke, N., Hancock, M. J., Ostelo, R. W. J. G., De Vet, H. C. W., Macaskill, P., Irwig, L., Van Tulder, M. W., Koes, B. W. & Maher, C. G. (2013) Red flags to screen for malignancy and fracture in patients with low back pain: Systematic review. *BMJ (Online)*, 347. Systematic review, checked for relevant studies.
- Drudge-Coates, L. & Rajbabu, K. (2008) Diagnosis and management of malignant spinal cord compression: part 1. [Review] [30 refs]. *International Journal of Palliative Nursing*, 14: 110-116.
Narrative review
- Dyrop, H. B., Safwat, A., Vedsted, P., Maretty-Nielsen, K., Hansen, B. H., Jorgensen, P. H., Baad-Hansen, T., Bungler, C. & Keller, J. (2013) Cancer patient pathways shortens waiting times and accelerates the diagnostic process of suspected sarcoma patients in Denmark. *Health Policy*, 113: 110-117.
Not in PICO
- Earl, H. & Souhami, R. L. (1990) Adolescent bone tumours. [Review] [3 refs]. *Practitioner*, 234: 816-818.
Narrative review
- Eaton, K. D. & Frieze, D. A. (2008) Cancer pain: Perspectives of a medical oncologist. *Current Pain and Headache Reports*, 12: 270-276.
Not in PICO
- Eggesbo, H. B. (2012) Imaging of sinonasal tumours. [Review]. *Cancer Imaging*, 12: 136-152.
Narrative review
- El, S. U., Hassan, T., Besheer, M., El, B. R., El, G. K. & Morad, M. H. (2009) Skeletal manifestations in children with different hematological diseases and hematological malignancies at Zagazig university hospital [retrospective study from 1998 to 2008]. *Haematologica*, 94: 690.
Not in PICO
- Erol, B., Bezer, M. & Guven, O. (2004) Evaluation of pediatric musculoskeletal tumors. *Marmara Medical Journal*, 17: 140-145.
Narrative review
- Eyre, R., Feltbower, R., James, P., Blakey, K., Mubwandarikwa, E., Forman, D., McKinney, P., Pearce, M. & McNally, R. (2010) The epidemiology of bone cancer in 0 - 39 year olds in northern England, 1981 - 2002. *BMC Cancer*, 10: 357.
Not in PICO
- Ferreira, N. & Marais, L. C. (2012) Osteosarcoma presentation stages at a tumour unit in South Africa. *South African Medical Journal.Suid-Afrikaanse Tydskrif Vir Geneeskunde*, 102: 673-676.
Not in PICO
- Fletcher, C. D. (2008) Undifferentiated sarcomas: what to do? And does it matter? A surgical pathology perspective. *Ultrastructural Pathology*, 32: 31-36.
Not in PICO
- Frincu, D. L., Francu, L. L., Chirana, A., Calin, D., Nitescu, A. & Crisan-Dabija, R. (2002) Quantitative histopathological criteria in predicting the giant bone cell tumors's grading. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 106: 147-153.
Not in PICO
- Frink, S. J., Snearly, W. & Parsons, T. W., III (1998) Malignant tumors about the knee. [Review] [33 refs]. *American Journal of Knee Surgery*, 11: 257-266.
Narrative review

- George, A. & Grimer, R. (2012) Early symptoms of bone and soft tissue sarcomas: could they be diagnosed earlier? *Annals of the Royal College of Surgeons of England*, 94: 261-266.
Not in PICO
- Gereige, R. & Kumar, M. (2010) Bone lesions: Benign and malignant. *Pediatrics in Review*, 31: 355-363.
Narrative review
- Ghandhi, D., Ayoub, A. F., Pogrel, M. A., MacDonald, G., Brocklebank, L. M. & Moos, K. F. (2006) Ameloblastoma: a surgeon's dilemma. *Journal of Oral & Maxillofacial Surgery*, 64: 1010-1014.
Not in PICO
- Gordon, L. M., Johnson, R. H., Au, M. A. & Albritton, K. H. (2011) Primary care referral patterns for adolescent and young adult (AYA) cancer patients: A multistate study. *Journal of Clinical Oncology*, 29.
Not in PICO
- Gosling, T., Probst, C., Langer, F., Rosenthal, H., Brunnemer, U. & Krettek, C. (679) [Diagnostics and treatment of primary bone tumors]. [Review] [German]. *Chirurg*, 81: 657-678.
Narrative review
- Goyal, S., Roscoe, J., Ryder, W. D., Gattamaneni, H. R. & Eden, T. O. (2004) Symptom interval in young people with bone cancer. *European Journal of Cancer*, 40: 2280-2286.
Not in PICO
- Gray, A. J. (2005) Back pain in children and adolescents. *Medicine Today*, 6: 27-33.
Narrative review
- Grobler, L. J. (1998) Back and leg pain in older adults: Presentation, diagnosis, and treatment. *Clinics in Geriatric Medicine*, 14: 543-576.
Narrative review
- Grossi, M. (1998) Management and longterm complications of pediatric cancer. *Pediatric Clinics of North America*, 45: 1637-+.
Narrative review
- Gundlach, K. K. (1981) [Indications for suspected tumor in syndromes involving the mouth, jaw and face]. [German]. *Deutsche Zahnärztliche Zeitschrift*, 36: 712-716.
Narrative review
- Harms, D. (1995) New entities, concepts, and questions in childhood tumor pathology. *General & diagnostic pathology*, 141: 1-14.
Narrative review
- Hashimoto, N., Rabo, C. S., Okita, Y., Kinoshita, M., Kagawa, N., Fujimoto, Y., Morii, E. I., Kishima, H., Maruno, M., Kato, A. & Yoshimine, T. (2012) Slower growth of skull base meningiomas compared with non-skull base meningiomas based on volumetric and biological studies: Clinical article. *Journal of Neurosurgery*, 116: 574-580.
Not in PICO
- Heare, T., Hensley, M. A. & Dell'Orfano, S. (2009) Bone tumors: osteosarcoma and Ewing's sarcoma. *Current Opinion in Pediatrics*, 21: 365-372.
Narrative review
- Heick, J. D., Bustillo, K. L. & Farris, J. W. (2014) Recognition of signs and symptoms of a Type 1 chondrosarcoma: a case report. *Physiotherapy Theory & Practice*, 30: 49-55.
Not in PICO
- Helwig, H. (1980) Early diagnosis of malignant bone tumors in childhood. [German]. *Padiatrische Praxis*, 23: 79-85.
Narrative review
- Henschke, N., Maher, C. G., Ostelo, R. W., de Vet, H. C., Macaskill, P. & Irwig, L. (2013) Red flags to screen for malignancy in patients with low-back pain. [Review]. *Cochrane Database of Systematic Reviews*, 2: CD008686.
Systematic review, included studies checked for relevance.

- Hill, C. E., Boyce, L. & van der Ploeg, I. D. (2014) Spontaneous resolution of a solitary osteochondroma of the distal femur: a case report and review of the literature. *Journal of Pediatric Orthopaedics, Part B*, 23: 73-75.
Not in PICO
- Hobusch, G. & Holzer, G. (2011) Osteoporosis and fractures in primary malign bone tumours. [German]. *Journal fur Mineralstoffwechsel*, 18: 64-68.
Narrative review
- Jackson, C. G., Cueva, R. A., Thedinger, B. A. & Glasscock III, M. E. (1990) Conservation surgery for glomus jugulare tumors: The value of early diagnosis. *Laryngoscope*, 100: 1031-1036.
Not in PICO
- Jellema, K., Overbeeke, J. J., Teepen, H. L. & Visser, L. H. (2005) Time to diagnosis of intraspinal tumors. *European Journal of Neurology*, 12: 621-624.
Not in PICO
- Joines, J. D., McNutt, R. A., Carey, T. S., Deyo, R. A. & Rouhani, R. (2001) Finding cancer in primary care outpatients with low back pain: a comparison of diagnostic strategies. *Journal of General Internal Medicine*, 16: 14-23.
Not in PICO
- Joshi, A., Magar, S. R., Chand, P., Panth, R. & Khatri Chhetri, B. R. (2013) Tru-cut biopsy as the initial method of tissue diagnosis in bone tumors with soft tissue extension. *Indian Journal of Orthopaedics*, 47: 195-199.
Not in PICO
- Jurgens, H. (1990) Ewing's sarcoma in children and adolescents: Update of the German GPO-CESS studies. *British Journal of Cancer*, 62: 327-328.
Not in PICO
- Kato, M., Nakamura, H., Terai, H., Konishi, S., Nagayama, R. & Takaoka, K. (2008) Why does delay exist in the diagnosis of intradural spinal cord tumor despite the availability of MRI? *Journal of Clinical Neuroscience*, 15: 880-885.
Not in PICO
- Khoo, M. M. Y. & Saifuddin, A. (2013) The role of MRI in image-guided needle biopsy of focal bone and soft tissue neoplasms. *Skeletal Radiology*, 42: 905-915.
Narrative review
- Khysh, I. T. & Tolstopiatov, B. A. (1980) Errors in the early diagnosis of primary tumors of the pelvic bones. [Russian]. *Khirurgiia*, 74-78.
Russian. Narrative review?
- Kidane, B., Gandhi, R., Sarro, A., Valiante, T. A., Harvey, B. J. & Rampersaud, Y. R. (2011) Is referral to a spine surgeon a double-edged sword? Patient concerns before consultation. *Canadian Family Physician*, 57: 803-810.
Not in PICO
- Kim, H. J. & Green, D. W. (2008) Adolescent back pain. *Current Opinion in Pediatrics*, 20: 37-45.
Narrative review
- Kirchner, J., Schmidt, H., Esther, A. H. & Schilling, M. (1999) Rothmund Thomson syndrome and osteosarcoma. [German]. *Rontgenpraxis*, 52: 71-73.
Narrative review
- Kotru, M. & Singh, N. (2007) The value of recognizing suspect diagnoses in the triple diagnosis of giant cell tumor of bone. *Indian Journal of Orthopaedics*, 41: 97-100.
Narrative review
- Kozlowski, K., Azouz, E. M., Campbell, J., Marton, D., Morris, L., Padovani, J., Sprague, P., Beluffi, G., Berzero, G. F. & Cherubino, P. (1988) Primary bone tumours of the hand. Report of 21 cases. *Pediatric Radiology*, 18: 140-148.
Not in PICO

- Kuchuk, M., Addison, C. L., Clemons, M., Kuchuk, I. & Wheatley-Price, P. (2013) Incidence and consequences of bone metastases in lung cancer patients. *Journal of Bone Oncology*, 2: 22-29.
Not in PICO
- Kwong, D. L. W., Ha, S. Y., Chau, K. Y., Choi, P. H. K., Chan, G. C. F., Kwong, P. W. K. & Lau, Y. L. (1998) Multidisciplinary management of osteosarcoma: Experience in Hong Kong. *Pediatric Hematology and Oncology*, 15: 229-236.
Not in PICO
- Lahl, M., Fisher, V. L. & Laschinger, K. (2008) Ewing's sarcoma family of tumors: An overview from diagnosis to survivorship. *Clinical Journal of Oncology Nursing*, 12: 89-97.
Narrative review
- Leithner, A. & Windhager, R. (2007) [Bone and soft tissue tumors: diagnostic principles]. [German]. *Wiener Medizinische Wochenschrift*, 157: 21-26.
Narrative review
- Li, X. & Hemminki, K. (2002) Parental cancer as a risk factor for bone cancer: a nation-wide study from Sweden. *Journal of Clinical Epidemiology*, 55: 111-114.
Not in PICO
- Li, Y., Dang, T. A. & Man, T. K. (2012) Plasma proteomic profiling of pediatric osteosarcoma. *Methods in Molecular Biology*, 818: 81-96.
Narrative review
- Mackey, J. R., Wood, L., Nabholz, J.-M., Jensen, J. & Venner, P. (2000) A Phase II trial of triamcinolone hexacetonide for symptomatic recurrent malignant ascites. *Journal of Pain and Symptom Management*, 19: 193-199.
Not in PICO
- Marec-Berard, P., Delafosse, C. & Foussat, C. (2005) [Cancer-related bone pain in children]. [Review] [40 refs] [French]. *Archives de Pediatrie*, 12: 191-198.
Narrative review
- Mastrangelo, G., Fadda, E., Cegolon, L., Montesco, M. C., Ray-Coquard, I., Buja, A., Fedeli, U., Frasson, A., Spolaore, P. & Rossi, C. R. (2010) A European project on incidence, treatment, and outcome of sarcoma. *BMC Public Health*, 10: 188.
Not in PICO
- Mattiassich, G., Ensaf, F., Hager, M. & Wechselberger, G. (2012) A suspected malignancy in osteolytic bone tumour of the thumb. *BMJ Case Reports*, 2012, 2012.
Not in PICO
- Mazur, J. M. & Stauffer, E. S. (1981) Evaluation and treatment of bone tumors. *The Journal of family practice*, 12: 333-341.
Narrative review
- Merchant, S., Cheifetz, R., Knowling, M., Khurshed, F. & McGahan, C. (2012) Practice referral patterns and outcomes in patients with primary retroperitoneal sarcoma in British Columbia. *American Journal of Surgery*, 203: 632-638.
Not in PICO
- Muscolo, D. L., Ayerza, M. A., Makino, A., Costa-Paz, M. & Aponte-Tinao, L. A. (2003) Tumors about the knee misdiagnosed as athletic injuries. *Journal of Bone & Joint Surgery - American Volume*, 85-A: 1209-1214.
Not in PICO
- Myriokefalitaki, E., D'Costa, D., Smith, M. & Ahmed, A. S. (2013) Primary bone metastasis as initial presentation of endometrial cancer (stage IVb). *Archives of Gynecology & Obstetrics*, 288: 739-746.
Not in PICO
- Ngwenya, S. (2006) General practitioner's pathology case 8. *SADJ*, 61: 360.
Not in PICO

- Ngwenya, S. (2006) General practitioner's pathology. Case 2. Diagnosis: Oral Kaposi's sarcoma with secondary ulceration. *SADJ*, 61: 079.
Not in PICO
- Niemeyer, P., Delling, G., Werner, M., Simank, H. G. & Bernd, L. (2003) [Telecommunication and telepathology in orthopedic oncology. Possibilities in diagnosis and therapy of primary malignant bone tumors]. [German]. *Orthopade*, 32: 949-954.
Not in PICO
- Ochsner, P. E. (1986) [Tumors of the child's foot]. [German]. *Orthopade*, 15: 227-232.
Narrative review
- Ottaviani, D., Ferracini, R., Ferrero, G., Ciuffreda, L. & Bertetto, O. (2004) 'Osteo-Oncology Multidisciplinary Care Group': A Novel Approach to the Metastatic and Primary Bone Tumor Patient. the Molinette Experience. *Annals of Oncology*, 15: 52.
Not in PICO
- Pallini, R., Maira, G., Pierconti, F., Falchetti, M. L., Alvino, E., Cimino-Reale, G., Fernandez, E., D'Ambrosio, E. & Larocca, L. M. (2003) Chordoma of the skull base: Predictors of tumor recurrence. *Journal of Neurosurgery*, 98: 812-822.
Not in PICO
- Pan, K. L., Zolqarnain, A. & Chia, Y. Y. (2006) Delay in treatment of primary malignant and aggressive musculoskeletal tumours. *Medical Journal of Malaysia*, 61: Suppl-6.
Not in PICO
- Patel, D. R., Moore, M. D. & Greydanus, D. E. (2007) Musculoskeletal diagnosis in adolescents. [Review] [12 refs]. *Adolescent Medicine*, 18: 1-10.
Narrative review
- Pecherstorfer, M., Brenner, K. & Zojer, N. (2003) Current management strategies for hypercalcemia. *Treatments in Endocrinology*, 2: 273-292.
Narrative review
- Perrier, L., Buja, A., Mastrangelo, G., Vecchiato, A., Sandona, P., Ducimetiere, F., Blay, J. Y., Gilly, F. N., Siani, C., Biron, P., Ranchere-Vince, D., Decouvelaere, A. V., Thiesse, P., Bergeron, C., Dei Tos, A. P., Coindre, J. M., Rossi, C. R. & Ray-Coquard, I. (2012) Clinicians' adherence versus non adherence to practice guidelines in the management of patients with sarcoma: a cost-effectiveness assessment in two European regions. *BMC Health Services Research*, 12: 82.
Not in PICO
- Philip, T., Blay, J. Y., Brunat-Mentigny, M., Carrie, C., Chauvot, P., Farsi, F., Fervers, B., Gentet, J. C., Giammarile, F., Kohler, R., Mathoulin, S., Patricot, L. M. & Thiesse, P. (1999) Standards, Options and Recommendations (SOR) for diagnosis, treatment and follow-up of osteosarcoma. *Bulletin du Cancer*, 86: 159-176.
Guideline
- Piccirillo, E., Agarwal, M., Rohit, Khrais, T. & Sanna, M. (2004) Management of temporal bone hemangiomas. *Annals of Otolaryngology, Rhinology & Laryngology*, 113: 431-437.
Not in PICO
- Pohlig, F., Lenze, U., Lenze, F. W., Muhlhofer, H., Schauwecker, J., Rechl, H. & von Eisenhart-Rothe, R. (2013) [Biopsies from bone and soft tissue sarcoma : a nationwide survey in Germany]. [German]. *Orthopade*, 42: 934-940.
Not in PICO
- Pollack, E. S. (1993) Emergency department presentation of childhood malignancies. *Emergency Medicine Clinics of North America*, 11: 517-529.
Narrative review
- Porta, S. J., Garzon, R. C., Fernandez, O. A. & Gomez-Batiste, X. (2008) Cancer pain epidemiology: A review. [Spanish]. *Medicina Paliativa*, 15: 307-314.
Not in PICO

- Potratz, J., Dirksen, U., Jurgens, H. & Craft, A. (2012) Ewing Sarcoma: Clinical State-of-the-Art. *Pediatric Hematology and Oncology*, 29: 1-11.
Narrative review
- Prado, F. O., Nishimoto, I. N., Perez, D. E., Kowalski, L. P. & Lopes, M. A. (2009) Head and neck chondrosarcoma: Analysis of 16 cases. *British Journal of Oral and Maxillofacial Surgery*, 47: 555-557.
Not in PICO
- Przewozny, T., Stodulski, D. & Stankiewicz, C. (2011) [Major salivary gland disorders in children and adolescents]. [Polish]. *Otolaryngologia Polska*, 65: 350-356.
Not in PICO
- Quinn, R. H., Randall, R. L., Benevenia, J., Berven, S. H. & Raskin, K. A. (2013) Contemporary management of metastatic bone disease: tips and tools of the trade for general practitioners. *The Journal of bone and joint surgery, American*: 1887-1895.
Narrative review
- Raab, C. P. & Gartner, J. C., Jr. (2009) Diagnosis of childhood cancer. [Review] [33 refs]. *Primary Care; Clinics in Office Practice*, 36: 671-684.
Narrative review
- Ralston, S. H., Boyce, B. F., Cowan, R. A., Gardner, M. D., Fraser, W. D. & Boyle, I. T. (1989) Contrasting mechanisms of hypercalcemia in patients with early and advanced humoral hypercalcemia of malignancy. *Journal of Bone and Mineral Research*, 4: 103-111.
Not in PICO
- Rawal, Y. B., Angiero, F., Allen, C. M., Kalmar, J. R., Sedghizadeh, P. P. & Steinhilber, A. M. (2006) Gnathic osteoblastoma: clinicopathologic review of seven cases with long-term follow-up. *Oral Oncology*, 42: 123-130.
Not in PICO
- Reichelt, A. (1982) Clinical manifestations of primary malignant bone tumors. [German]. *Therapiewoche*, 32: 321-324.
Narrative review
- Reid, R. (2007) Update on sarcomas of bone and soft tissue. [Review] [9 refs]. *Scottish Medical Journal*, 52: 31-35.
Narrative review
- Riedel, R. F., Larrier, N., Dodd, L., Kirsch, D., Martinez, S. & Brigman, B. E. (2009) The Clinical Management of Chondrosarcoma. *Current Treatment Options in Oncology*, 10: 94-106.
Narrative review
- Riley, R. D., Burchill, S. A., Abrams, K. R., Heney, D., Sutton, A. J., Jones, D. R., Lambert, P. C., Young, B., Wailoo, A. J. & Lewis, I. J. (2003) A systematic review of molecular and biological markers in tumours of the Ewing's sarcoma family. [Review] [84 refs]. *European Journal of Cancer*, 39: 19-30.
Not in PICO
- Ritter, J. & Bielack, S. S. (2010) Osteosarcoma. *Annals of Oncology*, 21: 320-325.
Narrative review
- Robben, B. J. & Jutte, P. C. (2012) [A boy with a painful knee: bone tumour or stress fracture?]. [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 156: A4465.
Not in PICO
- Rodrigues, K. E. & de, C. B. (2003) [Early diagnosis of childhood cancer: a team responsibility]. [Review] [33 refs] [Portuguese]. *Revista da Associacao Medica Brasileira*, 49: 29-34.
Narrative review
- Ruff, R. L. & Lanska, D. J. (1989) Epidural metastases in prospectively evaluated veterans with cancer and back pain. *Cancer*, 63: 2234-2241.
Not in PICO; found in the van Hoogen review
- Russell, E. C., Dunn, N. L. & Massey, G. V. (1999) Lymphomas and bone tumors: clinical presentation, management, and potential late effects of current treatment strategies. [Review] [37 refs].

- Adolescent Medicine State of the Art Reviews*, 10: 419-435.
Narrative review
- Saber, B., Nawal, A., Mohamed, F. & Hassan, E. (2008) Primary osteosarcoma of the breast: case report. *Cases Journal*, 1: 80.
Not in PICO
- Sampson, V. B., Gorlick, R., Kamara, D. & Anders, K. E. (2013) A review of targeted therapies evaluated by the pediatric preclinical testing program for osteosarcoma. *Frontiers in Oncology*, 3: 132.
Narrative review
- Schaser, K. D., Bail, H. J., Haas, N. P. & Melcher, I. (2002) [Treatment concepts of benign bone tumors and tumor-like bone lesions]. [Review] [61 refs] [German]. *Chirurg*, 73: 1181-1190.
Narrative review
- Schatz, J., Soper, J., McCormack, S., Healy, M., Deady, L. & Brown, W. (2010) Imaging of tumors in the ankle and foot. *Topics in Magnetic Resonance Imaging*, 21: 37-50.
Narrative review
- Schnurr, C., Pippas, M., Stuetzer, H., Delank, K. S., Michael, J. W. & Eysel, P. (2008) Treatment delay of bone tumours, compilation of a sociodemographic risk profile: a retrospective study. *BMC Cancer*, 8: 22.
Not in PICO
- Schubiner, J. M. & Simon, M. A. (1987) Primary bone tumors in children. *Orthopedic Clinics of North America*, 18: 577-595.
Narrative review
- Senac, M. O., Jr., Isaacs, H. & Gwinn, J. L. (1986) Primary lesions of bone in the 1st decade of life: retrospective survey of biopsy results. *Radiology*, 160: 491-495.
Not in PICO
- Shanahan, E. M. & Buchbinder, R. (2010) The painful shoulder. *Medicine Today*, 11: 73-79.
Narrative review
- Shaw, P. H. S., Adams, R., Jordan, C. & Crosby, T. D. L. (2007) A clinical review of the investigation and management of carcinoma of unknown primary in a single cancer network. *Clinical Oncology*, 19: 87-95.
Not in PICO
- Shedid, D. & Benzel, E. C. (2004) Clinical presentation of spinal tumors. *Neurosurgery Quarterly*, 14: 224-228.
Narrative review
- Shimose, S., Sugita, T., Kubo, T., Matsuo, T., Nobuto, H. & Ochi, M. (2008) Differential diagnosis between osteomyelitis and bone tumors. *Acta Radiologica*, 49: 928-933.
Not in PICO
- Singer, F. R. & Fernandez, M. (1987) Therapy of hypercalcemia of malignancy. *American Journal of Medicine*, 82: 34-41.
Narrative review
- Skotakova, J., Mach, V., Bajciová, V., Mudry, P. & Ondrus, S. (2006) [Malignant tumors of long bones in children: differential diagnosis and the role of imaging methods]. [Czech]. *Acta Chirurgiae Orthopaedicae et Traumatologiae Cechoslovaca*, 73: 183-189.
Not in PICO
- Soldatos, T., McCarthy, E. F., Attar, S., Carrino, J. A. & Fayad, L. M. (2011) Imaging features of chondrosarcoma. [Review]. *Journal of Computer Assisted Tomography*, 35: 504-511.
Narrative review
- Sroczyk, L., Cader, J. & Wieckiewicz, W. (2009) Gardner's syndrome - Literature review. [Polish]. *Gastroenterologia Polska*, 16: 248-250.
Narrative review

- Stella, G., De, S. N., Boero, S. & Rondinella, F. (1998) Benign tumors of the pediatric spine: statistical notes. *La Chirurgia degli organi di movimento*, 83: 15-21.
Not in PICO
- Stephen, J. P. (1983) Back pain in childhood and adolescence. *Australian Family Physician*, 12: 335-340.
Narrative review
- Strangio, L. & Brudner, C. (1995) When pain cuts to the bone. *RN*, 58: 28-29.
Not in PICO
- Streitbuegger, A., Harges, J., Gebert, C., Ahrens, H., Winkelmann, W. & Gosheger, G. (882) [Cartilage tumours of the bone. Diagnosis and therapy]. [Review] [26 refs] [German]. *Orthopade*, 35: 871-881.
Narrative review
- Subbiah, V., Anderson, P., Lazar, A. J., Burdett, E., Raymond, K. & Ludwig, J. A. (2009) Ewing's Sarcoma: Standard and Experimental Treatment Options. *Current Treatment Options in Oncology*, 10: 126-140.
Narrative review
- Sulko, J., Olipra, W. & Oberc, A. (2011) [Ischial tuberosity fractures in children]. [Polish]. *Chirurgia Narzadow Ruchu i Ortopedia Polska*, 76: 134-137.
Not in PICO
- Sundaresan, N. (1986) Chordomas. *Clinical Orthopaedics and Related Research*, NO.: 135-142.
Narrative review
- Teo, H. E. & Peh, W. C. (2004) Primary bone tumors of adulthood. *Cancer Imaging*, 4: 74-83.
Narrative review
- Thun, M. J. & Sinks, T. (2004) Understanding cancer clusters. *Ca-A Cancer Journal for Clinicians*, 54: 273-280.
Narrative review
- Toepfer, A., Lenze, U., Holzapfel, B. M., Rechl, H., von Eisenhart-Rothe, R. & Gollwitzer, H. (581) [Tumors of the foot: diagnostics and therapy]. [German]. *Orthopade*, 41: 563-580.
Narrative review
- Tucker, W. S. & Nasser-Sharif, F. J. (1997) Benign skull lesions. *Canadian Journal of Surgery*, 40: 449-455.
Not in PICO
- Ulaner, G., Hwang, S., Lefkowitz, R. A., Landa, J. & Panicek, D. M. (2013) Musculoskeletal tumors and tumor-like conditions: Common and avoidable pitfalls at imaging in patients with known or suspected cancer: Part A: Benign conditions that may mimic malignancy. *International Orthopaedics*, 37: 871-876.
Narrative review
- Ulaner, G., Hwang, S., Landa, J., Lefkowitz, R. A. & Panicek, D. M. (2013) Musculoskeletal tumours and tumour-like conditions: Common and avoidable pitfalls at imaging in patients with known or suspected cancer: Part B: Malignant mimics of benign tumours. *International Orthopaedics*, 37: 877-882.
Narrative review
- van den Hoogen, H. M., Koes, B. W., van Eijk, J. T. & Bouter, L. M. (1995) On the accuracy of history, physical examination, and erythrocyte sedimentation rate in diagnosing low back pain in general practice. A criteria-based review of the literature. *Spine*, 20: 318-327.
Review, not systematic, but checked references and ordered an additional 2.
- van Staa, T. P., Selby, P., Leufkens, H. G., Lyles, K., Sprafka, J. M. & Cooper, C. (2002) Incidence and natural history of Paget's disease of bone in England and Wales. *Journal of Bone & Mineral Research*, 17: 465-471.
Not in PICO

- van, D. B. & Freyschmidt, J. (2002) [Standardized procedure for suspected bone tumor]. [German]. *Chirurg*, 73: 1153-1161.
Narrative review
- Vera, L., Dolcino, M., Mora, M., Oddo, S., Gualco, M., Minuto, F. & Giusti, M. (2011) Primary hyperparathyroidism diagnosed after surgical ablation of a costal mass mistaken for giant-cell bone tumor: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 5: 596.
Not in PICO
- Verdegaal, S. H., Bovee, J. V., Pansuriya, T. C., Grimer, R. J., Ozger, H., Jutte, P. C., San, J. M., Biau, D. J., van der Geest, I. C., Leithner, A., Streitburger, A., Klenke, F. M., Gouin, F. G., Campanacci, D. A., Marec-Berard, P., Hogendoorn, P. C., Brand, R. & Taminiau, A. H. (2011) Incidence, predictive factors, and prognosis of chondrosarcoma in patients with Ollier disease and Maffucci syndrome: an international multicenter study of 161 patients. *The Oncologist*, 16: 1771-1779.
Not in PICO
- Vijay, H., Navil, V., Vaibhav, J., Chopra, A., Goel, A. & Sood, R. (2009) Body aches, tender bones and rapid loss of weight: a case report. *Cases Journal*, 2: 37.
Not in PICO
- Vitzthum, E. H., Krumbholz, S. & Willenberg, E. (1982) Problems of an early recognition of spinal tumours. [German]. *Zentralblatt fur Neurochirurgie*, 43: 151-158.
Not in PICO
- Von Hochstetter, A. R. (1987) Suspected neoplastic lesion of bone: Biopsy planning by the pathologist. [German]. *Schweizerische Medizinische Wochenschrift*, 117: 1302-1306.
Narrative review
- von Salis-Soglio, G. & Prietzel, T. (606) [Diagnostic methods in suspected malignant bone and soft tissue tumors]. [German]. *Orthopade*, 31: 595-605.
Not in PICO
- von Salis-Soglio, G. & Prietzel, T. (2002) Diagnostic procedures for suspected malignant tumors of bone and soft tissues. [German]. *Orthopade*, 31: 595-607.
Not in PICO
- Wakiaga, J. M., Onyango, J. F. & Awange, D. O. (1997) Clinico-pathological analysis of jaw tumours and tumour-like conditions at the Kenyatta national hospital. *East African Medical Journal*, 74: 65-68.
Not in PICO
- Waller, D. A. & Newman, R. J. (1990) Primary bone tumours of the thoracic skeleton: an audit of the Leeds regional bone tumour registry. *Thorax*, 45: 850-855.
Not in PICO
- Ward, S. (1999) Orthopaedic oncology for the nononcologist orthopaedist: introduction and common errors to avoid. *Instructional Course Lectures*, 48: 577-586.
Narrative review
- Wayte, N., Da, S. L., Chenevix-Trench, G. & Lakhani, S. R. (2008) What's in a cancer syndrome? Genes, phenotype and pathology. *Pathology*, 40: 247-259.
Narrative review
- Weber, K., Damron, T. A., Frassica, F. J. & Sim, F. H. (2008) Malignant bone tumors. *Instructional Course Lectures*, 57: 673-688.
Narrative review
- Widhe, B. & Widhe, T. (2000) Initial symptoms and clinical features in osteosarcoma and Ewing sarcoma. *Journal of Bone and Joint Surgery - Series A*, 82: 667-674.
Not in PICO
- Widhe, B., Widhe, T. & Bauer, H. C. (2007) Ewing sarcoma of the rib--initial symptoms and clinical features: tumor missed at the first visit in 21 of 26 patients. *Acta Orthopaedica*, 78: 840-844.
Not in PICO

Widhe, B. & Bauer, H. C. (2011) Diagnostic difficulties and delays with chest wall chondrosarcoma: a Swedish population based Scandinavian Sarcoma Group study of 106 patients. *Acta Oncologica*, 50: 435-440.

Not in PICO

Winters, M. E., Kluetz, P. & Zilberstein, J. (2006) Back pain emergencies. [Review] [82 refs]. *Medical Clinics of North America*, 90: 505-523.

Narrative review

Yanagisawa, Y., Furue, H., Kawamata, T., Uta, D., Yamamoto, J., Furuse, S., Katafuchi, T., Imoto, K., Iwamoto, Y. & Yoshimura, M. (2010) Bone cancer induces a unique central sensitization through synaptic changes in a wide area of the spinal cord. *Molecular Pain*, 6: 38.

Not in PICO

Yang, R.-S. (2001) The application of expandable endoprosthetic reconstruction for limb salvage surgery in the skeletally immature patients. *Biomedical Engineering - Applications, Basis and Communications*, 13: 141-147.

Narrative review

Yesilova, E., Akgunlu, F., Dolanmaz, D., Yasar, F. & Sener, S. (2007) Osteosarcoma: a case report. *European journal of dentistry*, 1: 60-63.

Not in PICO

Yiannakopoulos, C. K., Foufa, K., Theocharakis, S., Stamoulis, E. & Maniatis, V. (2012) Osteoid osteoma of the radial styloid mimicking wrist arthritis: a case study. *Hand Surgery*, 17: 225-228.

Not in PICO

Young, P. S., Bell, S. W., MacDuff, E. M. & Mahendra, A. (2013) Primary osseous tumors of the hindfoot: why the delay in diagnosis and should we be concerned? *Clinical Orthopaedics & Related Research*, 471: 871-877.

Not in PICO

Zawitkowska-Klaczynska, J., Katski, K., Nurzynska-Flak, J. & Kowalczyk, J. (2003) Primary chest tumours in children. *Annales Universitatis Mariae Curie-Sklodowska - Sectio d - Medicina*, 58: 106-110.

Not in PICO

Zhang, D., Chen, L., Ni, C.-F., Liu, Y.-Z., Jin, Y.-H., Zhu, X.-L. & Zou, J.-W. (2013) Percutaneous coaxial biopsy in diagnosis of musculoskeletal tumors. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 29: 1493-1496.

Not in PICO

Review question:

Which investigations of symptoms of suspected bone sarcoma should be done with clinical responsibility retained by primary care?

Results

Literature search

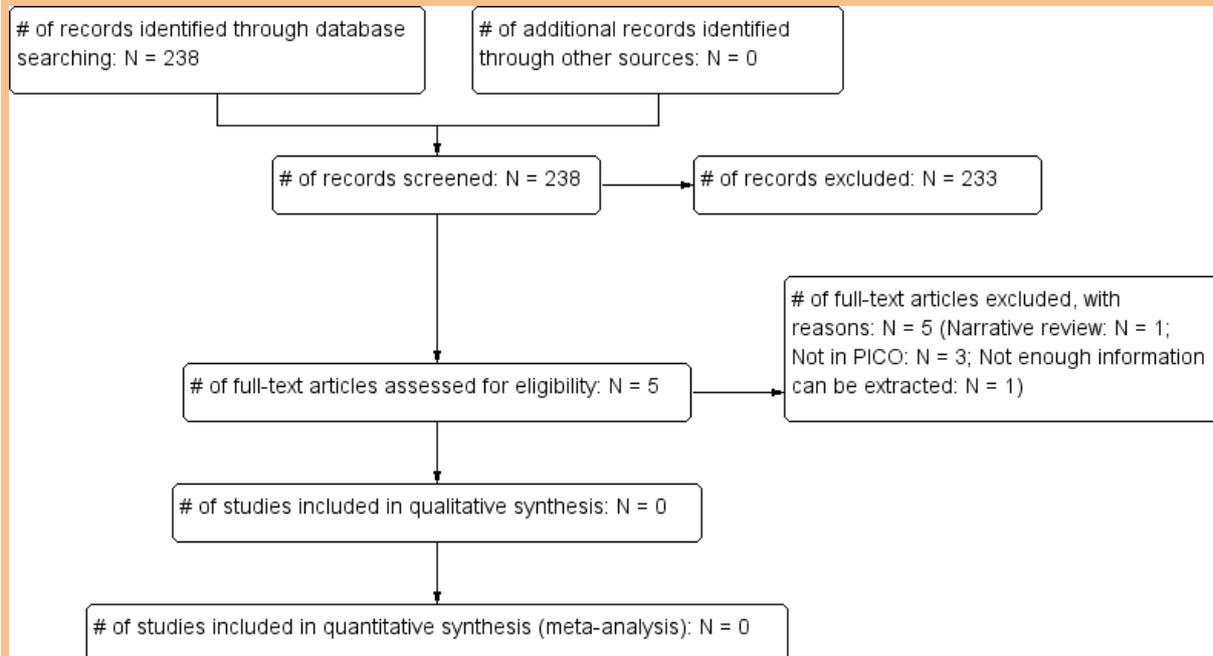
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	1289	104	25/03/2013
Premedline	1980-2013	100	16	25/03/2013
Embase	1980-2013	1277	125	27/03/2013
Cochrane Library	1980-2013	158	6	27/03/2013
Psychinfo	1980-2013	10	0	27/03/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	166	9	27/03/2013

Total References retrieved (after de-duplication): 219

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	3/2013-26/08/2014	60	7	26/08/2014
<i>Premedline</i>	3/2013-26/08/2014	98	11	26/08/2014
<i>Embase</i>	3/2013-26/08/2014	104	9	26/08/2014
<i>Cochrane Library</i>	3/2013-26/08/2014	116	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	3/2013-26/08/2014	26	0	26/08/2014

Total References retrieved (after de-duplication): 19



Study results

No evidence was identified pertaining to the diagnostic accuracy of x-ray, calcium or alkaline phosphatase in patients with suspected bone sarcoma where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Aboulafia, A. J., Levin, A. M. & Blum, J. (2002) Prereferral evaluation of patients with suspected bone and soft tissue tumors. *Clinical Orthopaedics and Related Research*, 83-88.

Not in PICO

- Adams, S. C., Potter, B. K., Pitcher, D. J. & Temple, H. T. (2010) Office-based core needle biopsy of bone and soft tissue malignancies: an accurate alternative to open biopsy with infrequent complications. *Clinical Orthopaedics and Related Research*, 468: 2774-2780.
Not in PICO
- Ahrensberg, J. M., Schroder, H., Hansen, R. P., Olesen, F. & Vedsted, P. (2012) The initial cancer pathway for children - one-fourth wait more than 3 months. *Acta Paediatrica*, 101: 655-662.
Not in PICO
- Aitchison, F. A., Poon, F. W., Hadley, M. D., Gray, H. W. & Forrester, A. W. (1992) Vertebral metastases and an equivocal bone scan: value of magnetic resonance imaging. *Nuclear Medicine Communications*, 13: 429-431.
Not in PICO
- Ak, I., Sivrikoz, M. C., Entok, E. & Vardareli, E. (2010) Discordant findings in patients with non-small-cell lung cancer: absolutely normal bone scans versus disseminated bone metastases on positron-emission tomography/computed tomography. *European Journal of Cardio-Thoracic Surgery*, 37: 792-796.
Not in PICO
- Altay, M., Bayrakci, K., Yildiz, Y., Erekul, S. & Saglik, Y. (2007) Secondary chondrosarcoma in cartilage bone tumors: Report of 32 patients. *Journal of Orthopaedic Science*, 12: 415-423.
Not in PICO
- Alyas, F. & Saifuddin, A. (2008) Fluid-fluid levels in bone neoplasms: variation of T1-weighted signal intensity of the superior to inferior layers--diagnostic significance on magnetic resonance imaging. *European Radiology*, 18: 2642-2651.
Not in PICO
- Araujo, F. I., Monteiro, A. & Kalil, R. K. (2010) Giant cell-rich osteosarcoma - Two cases report and literature review. *Histopathology*, 57: 14-15.
Not in PICO
- Ashwood, N., Witt, J. D., Hallam, P. J. & Cobb, J. P. (2003) Analysis of the referral pattern to a supraregional bone and soft tissue tumour service. *Annals of the Royal College of Surgeons of England*, 85: 272-276.
Not in PICO
- Badiane, M., Afidja, A., Ba-Diop, S., Badiane, S. B., Niang, E. H. & Ba-Ly, A. (1998) Diagnostic x-ray computed tomography of craniocerebral tumors. Apropos of 108 cases collected at the Soweto Center of Dakar. [French]. *Dakar Medical*, 43: 34-36.
Not in PICO
- Bahgat, M., Bahgat, Y., Bahgat, A. & Elwany, Y. (2012) Chondrosarcoma of the nasal septum. *BMJ Case Reports*, 2012, 2012.
Not in PICO
- Balogh, L., Postenyi, Z., Haasz, V., Polyak, A., Marian, T., Garai, I., Galuska, L., Balkay, L., Trencsenyi, G., Nagy, T., Trencsenyi, J., Janoki, G., Janoki, G., Torok, R. & Thuroczy, J. (2011) PET/CT imaging in dogs and cats - Tumor target scale and unusual uptake. *Nuclear Medicine Review*, 14: A10.
Not in PICO
- Bastiaannet, E., Groen, H., Jager, P. L., Cobben, D. C., Graaf, W. T., Vaalburg, W. & Hoekstra, H. J. (2004) The value of FDG-PET in the detection, grading and response to therapy of soft tissue and bone sarcomas: a systematic review and meta-analysis (DARE structured abstract). *Cancer Treatment Reviews*, 30: 83-101.
Not in PICO
- Begic, A., Kucukalic-Selimovic, E., Obralic, N., Duric, O., Lacevic, N. & Skopljak, A. (2006) Correlation between bone scintigraphy and tumor markers in patients with breast carcinoma. *Bosnian Journal of Basic Medical Sciences*, 6: 75-77.
Not in PICO

- Beheshti, M., Vali, R., Waldenberger, P., Fitz, F., Nader, M., Loidl, W., Broinger, G., Stoiber, F., Foglman, I. & Langsteger, W. (2008) Detection of bone metastases in patients with prostate cancer by 18F fluorocholine and 18F fluoride PET-CT: a comparative study. *European Journal of Nuclear Medicine and Molecular Imaging*, 35: 1766-1774.
Not in PICO
- Bell, S. W., Young, P. S. & Mahendra, A. (2012) Primary bone tumours of the talus: the Scottish Bone Tumour Registry experience. *Journal of Foot & Ankle Surgery*, 18: 277-282.
Not in PICO
- Benchakroun, M., El, B. A., Kharmaz, M., Zaddoug, O., Chiboub, H., El, Y. M., Hermas, M., Wahbi, S., Ouazzani, N. & El, M. M. (2004) Osteoid osteoma in the foot (10 cases report). [French]. *Medecine et Chirurgie du Pied*, 20: 23-38.
Not in PICO
- Berrey, B. H., Jr. (1989) The treacherous biopsy. *Military Medicine*, 154: 171-174.
Not in PICO
- Bethapudi, S., Ritchie, D. A., MacDuff, E. & Straiton, J. (2014) Imaging in osteofibrous dysplasia, osteofibrous dysplasia-like adamantinoma, and classic adamantinoma. *Clinical Radiology*, 69: 200-208.
Not in PICO
- Bethapudi, S., Ritchie, D. A., MacDuff, E. & Straiton, J. (2014) - Imaging in osteofibrous dysplasia, osteofibrous dysplasia-like adamantinoma, and classic adamantinoma. [Review]. - *Clinical Radiology*, 69: 200-208.
Narrative review
- Biau, D. J., Weiss, K. R., Bhumbra, R. S., Davidson, D., Brown, C., Wunder, J. S. & Ferguson, P. C. (2013) Using the CUSUM test to control the proportion of inadequate open biopsies of musculoskeletal tumors. *Clinical Orthopaedics & Related Research*, 471: 905-914.
Not in PICO
- Bikle, D. D. (1997) Biochemical markers in the assessment of bone disease. *American Journal of Medicine*, 103: 427-436.
Narrative review
- Blay, J. Y., Sleijfer, S., Schoffski, P., Kawai, A., Brodowicz, T., Demetri, G. D. & Maki, R. G. (2014) - International expert opinion on patient-tailored management of soft tissue sarcomas. [Review]. - *European Journal of Cancer*, 50: 679-689.
Not in PICO
- Bombardieri, E., Martinetti, A., Miceli, R., Mariani, L., Castellani, M. R. & Seregini, E. (1997) Can bone metabolism markers be adopted as an alternative to scintigraphic imaging in monitoring bone metastases from breast cancer? *European Journal of Nuclear Medicine*, 24: 1349-1355.
Not in PICO
- Bombardieri, E., Aktolun, C., Baum, R. P., Bishof-Delaloye, A., Buscombe, J., Chatal, J. F., Maffioli, L., Moncayo, R., Morteimans, L. & Reske, S. N. (2003) Bone scintigraphy: procedure guidelines for tumour imaging. *European Journal of Nuclear Medicine & Molecular Imaging*, 30: BP99-106.
Not in PICO
- Bommer, K. K., Ramzy, I. & Mody, D. (1997) Fine-needle aspiration biopsy in the diagnosis and management of bone lesions - A study of 450 cases. *Cancer Cytopathology*, 81: 148-156.
Not in PICO
- Bovee, J. V. (2008) Multiple osteochondromas. [Review] [86 refs]. *Orphanet Journal Of Rare Diseases*, 3: 3.
Narrative review
- Brechot, J. M., Roche, N., Marichy, C., Lebeau, B., Debieuvre, D., Darneau, G., Coste, E., Grivau, M., Falchero, L., Vlastos, F., Souquet, P. J. & Groupe d'Oncologie de la Societe de Pneumologie de Langue Francaise (2005) [Treatment of anemia and bone metastasis in metastatic non-small-cell

- lung cancer. A French survey]. [French]. *Revue de Pneumologie Clinique*, 61: t-9.
Not in PICO
- Bruns, J., Yazigee, O., Werner, M., Delling, G. & Hossfeld, D. K. (2006) Use of biopsy for confirming musculoskeletal tumors. [German]. *Onkologe*, 12: 119-127.
Narrative review
- Bruns, J., Delling, G., Henne-Bruns, D. & Hossfeld, D. K. (2008) Biopsy of tumors of the musculoskeletal system. *Deutsches Arzteblatt International*, 105: 492-497.
Narrative review
- Burkhardt, R., Frisch, B. & Kettner, G. (1980) The clinical study of micro-metastatic cancer by bone biopsy. *Bulletin du Cancer*, 67: 291-305.
Not in PICO
- Bussieres, A. E., Taylor, J. A. M. & Peterson, C. (2008) Diagnostic Imaging Practice Guidelines for Musculoskeletal Complaints in Adults-An Evidence-Based Approach-Part 3: Spinal Disorders. *Journal of Manipulative and Physiological Therapeutics*, 31: 33-88.
Guideline
- Caglar, M., Velipasaoglu, Z. & Tuncel, M. (2010) SPECT-CT offers high diagnostic accuracy when findings on planar bone scintigraphy are inconclusive. *European Journal of Nuclear Medicine and Molecular Imaging*, 37: S211-S212.
Not in PICO
- Casadei, R., Ferraro, A., Ferruzzi, A., Biagini, R. & Ruggieri, P. (1991) Bone tumors of the foot: epidemiology and diagnosis. *Chirurgia Degli Organi di Movimento*, 76: 47-62.
Not in PICO
- Casazza, B. A. (2012) Diagnosis and treatment of acute low back pain. [Review]. *American Family Physician*, 85: 343-350.
Not in PICO
- Chao, T. Y., Ho, C. L., Lee, S. H., Chen, M. M., Janckila, A. & Yam, L. T. (2004) Tartrate-resistant acid phosphatase 5b as a serum marker of bone metastasis in breast cancer patients. *Journal of Biomedical Science*, 11: 511-516.
Not in PICO
- Chen, G., Zhang, M., Hu, J., Jiang, X., Wang, C. & Li, B. (2010) Clinical application of 18F-FDG PET/CT in detection of primary tumors of multiple bone metastatic tumors. [Chinese]. *Journal of Shanghai Jiaotong University (Medical Science)*, 30: 1039-1042.
Not in PICO
- Costelloe, C. M., Chuang, H. H., Chasen, B. A., Pan, T., Fox, P. S., Bassett, R. L. & Madewell, J. E. (2013) Bone Windows for Distinguishing Malignant from Benign Primary Bone Tumors on FDG PET/CT. *Journal of Cancer*, 4: 524-530.
Not in PICO
- Cronin, C. G., Cashell, T., Mhuircheartaigh, J. N., Swords, R., Murray, M., O'Sullivan, G. J. & O'Keefe, D. (2009) Bone biopsy of new suspicious bone lesions in patients with primary carcinoma: prevalence and probability of an alternative diagnosis. *AJR.American Journal of Roentgenology*, 193: W407-W410.
Not in PICO
- Daffner, R. H., Lupetin, A. R., Dash, N., Deeb, Z. L., Sefczek, R. J. & Schapiro, R. L. (1986) MRI in the detection of malignant infiltration of bone marrow. *AJR.American Journal of Roentgenology*, 146: 353-358.
Not in PICO
- Dane, F., Turk, H. M., Sevinc, A., Buyukberber, S., Camci, C. & Tarakcioglu, M. (2008) Markers of bone turnover in patients with lung cancer. *Journal of the National Medical Association*, 100: 425-428.
Not in PICO

- Daniel, J., Ullah, E., Wahab, S. & Kumar, J. (2009) Relevance of MRI in prediction of malignancy of musculoskeletal system--a prospective evaluation. *BMC musculoskeletal disorders*, 10: 125.
Not in PICO
- De Ioris, M. A., Prete, A., Cozza, R., Podda, M., Manzitti, C., Pession, A., Schiavello, E., Contoli, B., Balter, R., Fagioli, F., Bisogno, G., Amoroso, L., Locatelli, F. & Luksch, R. (2013) Ewing Sarcoma of the Bone in Children under 6 Years of Age. *PLoS ONE*, 8.
Not in PICO
- Delling, G., Jobke, B., Burisch, S. & Werner, M. (1281) [Cartilage tumors. Classification, conditions for biopsy and histologic characteristics]. [Review] [30 refs] [German]. *Orthopade*, 34: 1267-1281.
Narrative review
- Dhanoa, A., Singh, V. A., Mansor, A., Yusof, M. Y., Lim, K. T. & Thong, K. L. (2012) Acute haematogenous community-acquired methicillin-resistant *Staphylococcus aureus* osteomyelitis in an adult: case report and review of literature. *BMC Infectious Diseases*, 12: 270.
Not in PICO
- Didolkar, M. M., Anderson, M. E., Hochman, M. G., Rissmiller, J. G., Goldsmith, J. D., Gebhardt, M. G. & Wu, J. S. (2013) Image guided core needle biopsy of musculoskeletal lesions: Are nondiagnostic results clinically useful? *Clinical Orthopaedics and Related Research*, 471: 3601-3609.
Not in PICO
- Dollahite, H. A., Tatum, L., Moinuddin, S. M. & Carnesale, P. G. (1989) Aspiration biopsy of primary neoplasms of bone. *Journal of Bone & Joint Surgery - American Volume*, 71: 1166-1169.
Not in PICO
- Domett, R., Stevens, M., Redaniel, T., Hamilton, W. & Martin, R. (2013) Features of cancer in teenagers and young adults (TYA) presenting to primary care in the uk: A population-based nested case-control study. *Pediatric Blood and Cancer*, 60: 3.
Already included
- Donthineni, R. & Ofluoglu, O. (2010) Solitary enchondromas of long bones: Pattern of referral and outcome. *Acta Orthopaedica et Traumatologica Turcica*, 44: 397-402.
Not in PICO
- Dotan, Z. A. (2008) Bone imaging in prostate cancer. [Review] [73 refs]. *Nature Clinical Practice Urology*, 5: 434-444.
Not in PICO
- Downie, A., Williams, C. M., Henschke, N., Hancock, M. J., Ostelo, R. W. J. G., De Vet, H. C. W., Macaskill, P., Irwig, L., Van Tulder, M. W., Koes, B. W. & Maher, C. G. (2013) Red flags to screen for malignancy and fracture in patients with low back pain: Systematic review. *BMJ (Online)*, 347.
Systematic review, checked for relevant studies.
- Duda, S. H., Johst, U., Krahmer, K., Pereira, P., Konig, C., Schafer, J., Huppert, P., Schott, U., Bohm, P. & Claussen, C. D. (2001) [Technique and results of CT-guided percutaneous bone biopsy]. [German]. *Orthopade*, 30: 545-550.
Not in PICO
- Dyrop, H. B., Safwat, A., Vedsted, P., Maretty-Nielsen, K., Hansen, B. H., Jorgensen, P. H., Baad-Hansen, T., Bunger, C. & Keller, J. (2013) Cancer patient pathways shortens waiting times and accelerates the diagnostic process of suspected sarcoma patients in Denmark. *Health Policy*, 113: 110-117.
Not in PICO
- Edeiken, B. & deSantos, L. A. (1983) Percutaneous needle biopsy of the irradiated skeleton. *Radiology*, 146: 653-655.
Not in PICO
- Etchebehere, M., De Camargo, O. P., Croci, A. T., De Oliveira, C. R. C. M. & Baptista, A. M. (1999) The role of percutaneous biopsy in the definitive histological diagnosis of suspected cartilaginous bone lesions prior to surgery. [Portuguese]. *Revista Brasileira de Ortopedia*, 34: 77-80.
Not in PICO

- Fayad, L. M., Bluemke, D. A., Weber, K. L. & Fishman, E. K. (2006) Characterization of pediatric skeletal tumors and tumor-like conditions: specific cross-sectional imaging signs. [Review] [9 refs]. *Skeletal Radiology*, 35: 259-268.
Not in PICO
- Fogelman, I., Cook, G., Israel, O. & Van der Wall, H. (2005) Positron emission tomography and bone metastases. [Review] [36 refs]. *Seminars in Nuclear Medicine*, 35: 135-142.
Not in PICO
- Fottner, A., Baur-Melnyk, A., Birkenmaier, C., Jansson, V. & Durr, H.-R. (2009) Stress fractures presenting as tumours: A retrospective analysis of 22 cases. *International Orthopaedics*, 33: 489-492.
Not in PICO
- Frank, J. A., Ling, A., Patronas, N. J., Carrasquillo, J. A., Horvath, K., Hickey, A. M. & Dwyer, A. J. (1990) Detection of malignant bone tumors: MR imaging vs scintigraphy. *American Journal of Roentgenology*, 155: 1043-1048.
Not in PICO
- Freeman, S. J., Sonoda, L. I., Seshadri, N., Howard, W., Set, P. A. & Balan, K. K. (2010) What is the significance of solitary bony abnormalities on bone scintigrams of children with malignancy? *Pediatric Hematology & Oncology*, 27: 380-386.
Not in PICO
- Friedrich, P., Ortiz, R., Strait, K., Fuentes, S., Gamboa, Y., Arambu, I., Ah-Chu-Sanchez, M., London, W., Rodriguez-Galindo, C., Antillon-Klussmann, F., Baez, F. & Central American Association of Pediatric Hematologists Oncologists AHOPCA (2013) Pediatric sarcoma in Central America: outcomes, challenges, and plans for improvement. *Cancer*, 119: 871-879.
Not in PICO
- Fukutomi, M., Yokota, M., Chuman, H., Harada, H., Zaitzu, Y., Funakoshi, A., Wakasugi, H. & Iguchi, H. (2001) Increased incidence of bone metastases in hepatocellular carcinoma. *European Journal of Gastroenterology & Hepatology*, 13: 1083-1088.
Not in PICO
- George, A. & Grimer, R. (2012) Early symptoms of bone and soft tissue sarcomas: Could they be diagnosed earlier? *Annals of the Royal College of Surgeons of England*, 94: e261-e266.
Not in PICO
- George, J. L. & Marchal, J. C. (2010) [Orbital tumors in children: clinical examination, imaging, specific progression]. [French]. *Neuro-Chirurgie*, 56: 244-248.
Narrative review
- Gnanasegaran, G., Cook, G., Adamson, K. & Fogelman, I. (2009) Patterns, variants, artifacts, and pitfalls in conventional radionuclide bone imaging and SPECT/CT. [Review] [106 refs]. *Seminars in Nuclear Medicine*, 39: 380-395.
Narrative review
- Griffiths, H. J., Galloway, H. R., Thompson, J., Suh, J.-S., Nelson, T. E., Everson, L., Edlin, J. P., Lynn, B. J. & Lang, D. (1993) The use of MRI in the diagnosis of benign and malignant bone and soft tissue tumours. *Australasian Radiology*, 37: 35-39.
Not in PICO
- Gussetis, E. S., Schwabe, D., Gerein, V. & Kornhuber, B. (1997) Differential diagnosis based on immunological-phenotyping in suspected malignant bone marrow involvement in childhood. *Pediatric Hematology & Oncology*, 14: 29-41.
Not in PICO
- Hajdarbegovic, E. & Nijsten, T. (2014) - [A man with a painful and swollen ankle]. [Dutch]. - *Nederlands Tijdschrift voor Geneeskunde*, 158: A6894.
Not in PICO
- Heck, R. K., O'Malley, A. M., Kellum, E. L., Donovan, T. B., Ellzey, A. & Witte, D. A. (2007) Errors in the MRI evaluation of musculoskeletal tumors and tumorlike lesions. *Clinical Orthopaedics and*

- Related Research*, 28-33.
Not in PICO
- Hefti, F. (1993) [Malignant bone tumors--is amputation still necessary today?]. [Review] [55 refs] [German]. *Schweizerische Rundschau fur Medizin Praxis*, 82: 307-315.
Narrative review
- Heick, J. D., Bustillo, K. L. & Farris, J. W. (2014) Recognition of signs and symptoms of a Type 1 chondrosarcoma: a case report. *Physiotherapy Theory & Practice*, 30: 49-55.
Not in PICO
- Helwig, H. (1980) Early diagnosis of malignant bone tumors in childhood. [German]. *Padiatrische Praxis*, 23: 79-85.
Narrative review
- Henschke, N., Maher, C. G., Ostelo, R. W., de Vet, H. C., Macaskill, P. & Irwig, L. (2013) Red flags to screen for malignancy in patients with low-back pain. [Review]. *Cochrane Database of Systematic Reviews*, 2: CD008686.
Systematic review, included studies checked for relevance.
- Hill, C. E., Boyce, L. & van der Ploeg, I. D. (2014) Spontaneous resolution of a solitary osteochondroma of the distal femur: a case report and review of the literature. *Journal of Pediatric Orthopaedics, Part B*, 23: 73-75.
Not in PICO
- Hoffer, F. A. (2002) Primary skeletal neoplasms: osteosarcoma and ewing sarcoma. [Review] [20 refs]. *Topics in Magnetic Resonance Imaging*, 13: 231-239.
Narrative review
- Holzapfel, B. M., Ludemann, M., Holzapfel, D. E., Rechl, H. & Rudert, M. (2012) Open biopsy of bone and soft tissue tumors. Guidelines for precise surgical procedures. [German]. *Operative Orthopadie und Traumatologie*, 24: 403-417.
Not in PICO
- Horikoshi, H., Kikuchi, A., Onoguchi, M., Sjostrand, K. & Edenbrandt, L. (2012) Computer-aided diagnosis system for bone scintigrams from Japanese patients: Importance of training database. *Annals of Nuclear Medicine*, 26: 622-626.
Not in PICO
- Hsu, P.-K., Hsu, H.-S., Lee, H.-C., Hsieh, C.-C., Wu, Y.-C., Wang, L.-S., Huang, B.-S., Hsu, W.-H. & Huang, M.-H. (2006) Management of primary chest wall tumors: 14 years' clinical experience. *Journal of the Chinese Medical Association*, 69: 377-382.
Not in PICO
- Hu, Y. G. (251) Arteriographic findings in bone tumors: experience with 170 cases. [Chinese]. *Zhonghua wai ke za zhi [Chinese journal of surgery]*, 28: 195-197, 251.
Not in PICO
- Huang, H., Chen, Y. P., Cao, G. H. & Lin, Z. C. (2005) [Magnetic resonance imaging and radiography for diagnosis of lower limb osteosarcoma: a comparative study]. [Chinese]. *Di Yi Junyi Daxue Xuebao*, 25: 1552-1554.
Not in PICO
- Jia, Z. Y. & Deng, H. F. (2007) [Preliminary application of 99Tc(m)-MIBI scintigraphy for judgment of bone malignant and benign lesions]. [Chinese]. *Sichuan da Xue Xue Bao.Yi Xue Ban/Journal of Sichuan University.Medical Science Edition*, 38: 689-692.
Not in PICO
- Joerger, M. & Huober, J. (2012) Diagnostic and prognostic use of bone turnover markers. [Review]. *Recent Results in Cancer Research*, 192: 197-223.
Narrative review
- Joines, J. D., McNutt, R. A., Carey, T. S., Deyo, R. A. & Rouhani, R. (2001) Finding cancer in primary care outpatients with low back pain: a comparison of diagnostic strategies. *Journal of General*

- Internal Medicine*, 16: 14-23.
Not in PICO
- Joshi, A., Magar, S. R., Chand, P., Panth, R. & Khatri Chhetri, B. R. (2013) Tru-cut biopsy as the initial method of tissue diagnosis in bone tumors with soft tissue extension. *Indian Journal of Orthopaedics*, 47: 195-199.
Not in PICO
- Jung, K., Lein, M., Stephan, C., Von, H. K., Semjonow, A., Sinha, P., Loening, S. A. & Schnorr, D. (2004) Comparison of 10 serum bone turnover markers in prostate carcinoma patients with bone metastatic spread: diagnostic and prognostic implications. *International Journal of Cancer*, 111: 783-791.
Not in PICO
- Kabukcuoglu, F., Kabukcuoglu, Y., Kuzgun, U. & Evren, I. (1998) Fine needle aspiration of malignant bone lesions. *Acta Cytologica*, 42: 875-882.
Not in PICO
- Kafchitsas, K., Habermann, B., Tonak, M. & Kurth, A. A. (2010) Bone tumours of the vertebral column. [German]. *Osteologie*, 19: 332-339.
Narrative review
- Kao, C. H., Hsieh, J. F., Tsai, S. C., Ho, Y. J. & Yen, R. F. (2000) Comparison and discrepancy of 18F-2-deoxyglucose positron emission tomography and Tc-99m MDP bone scan to detect bone metastases. *Anticancer Research*, 20: 2189-2192.
Not in PICO
- Katabi, M., Anract, P., Forest, M. & Tomeno, B. (1996) Low grade intramedullary osteosarcoma. A study of eight cases. [French]. *Revue de Chirurgie Orthopedique et Reparatrice de l'Appareil Moteur*, 82: 208-215.
Not in PICO
- Khoo, M. M. Y. & Saifuddin, A. (2013) The role of MRI in image-guided needle biopsy of focal bone and soft tissue neoplasms. *Skeletal Radiology*, 42: 905-915.
Narrative review
- Kobayashi, M., Okabayashi, T., Sano, T. & Araki, K. (2005) Metastatic bone cancer as a recurrence of early gastric cancer -- characteristics and possible mechanisms. [Review] [27 refs]. *World Journal of Gastroenterology*, 11: 5587-5591.
Not in PICO
- Konig, R., van, K. G. & Braun, A. (1983) [Contribution of computer tomography to the evaluation of space-occupying processes and abnormalities of the skeletal system]. [German]. *Computertomographie*, 3: 25-31.
Not in PICO
- Korholz, D., Verheyen, J., Kemperdick, H. F. & Gobel, U. (1998) Evaluation of follow-up investigations in osteosarcoma patients: suggestions for an effective follow-up program. *Medical & Pediatric Oncology*, 30: 52-58.
Not in PICO
- Korholz, D., Verheyen, J., Engelbrecht, V., Guillaume, T., Vosberg, H. & Gobel, U. (2000) [Follow-up of patients with osteosarcoma and Ewing's sarcoma: a retrospective cost-benefit analysis]. [German]. *Klinische Padiatrie*, 212: 220-223.
Not in PICO
- Kornaat, P. R., Camerlinck, M., Vanhoenacker, F. M., De, P. G. & Kroon, H. M. (2010) Brodie's abscess revisited. [Review] [12 refs]. *Jbr-Btr: Organe de la Societe Royale Belge de Radiologie*, 93: 81-86.
Narrative review
- Kotru, M. & Singh, N. (2007) The value of recognizing suspect diagnoses in the triple diagnosis of giant cell tumor of bone. *Indian Journal of Orthopaedics*, 41: 97-100.
Narrative review

- Kozlowski, K., Azouz, E. M., Campbell, J., Marton, D., Morris, L., Padovani, J., Sprague, P., Beluffi, G., Berzero, G. F. & Cherubino, P. (1988) Primary bone tumours of the hand. Report of 21 cases. *Pediatric Radiology*, 18: 140-148.
Not in PICO
- Kraková, D. A. (2012) Aspects of ortopedical oncology. [Czech]. *Onkologie*, 6: 190-194.
Narrative review
- Krasnow, A. Z., Hellman, R. S., Timins, M. E., Collier, B. D., Anderson, T. & Isitman, A. T. (1997) Diagnostic bone scanning in oncology. *Seminars in Nuclear Medicine*, 27: 107-141.
Narrative review
- Krishnan, A., Shirkhoda, A., Tehranzadeh, J., Armin, A. R., Irwin, R. & Les, K. (2003) Primary Bone Lymphoma: Radiographic-MR Imaging Correlation. *Radiographics*, 23: 1371-1383.
Narrative review
- Kuchuk, M., Addison, C. L., Clemons, M., Kuchuk, I. & Wheatley-Price, P. (2013) Incidence and consequences of bone metastases in lung cancer patients. *Journal of Bone Oncology*, 2: 22-29.
Not in PICO
- Kuleta-Bosak, E., Kluczevska, E., Machnik-Broncel, J., Madziara, W., Ciupinska-Kajor, M., Sojka, D., Rogala, W., Juszczyk, J. & Wilk, R. (2010) Suitability of imaging methods (X-ray, CT, MRI) in the diagnostics of Ewing's sarcoma in children - analysis of own material. *Polish Journal of Radiology*, 75: 18-28.
Not in PICO
- Lammeren-Venema, D., Regelink, J. C., Riphagen, I. I., Zweegman, S., Hoekstra, O. S. & Zijlstra, J. M. (2012) 18F-fluoro-deoxyglucose positron emission tomography in assessment of myeloma-related bone disease: a systematic review (DARE structured abstract). *Cancer*, 118: 1971-1981.
Not in PICO
- Langer, S. W., Kamby, C., Thomsen, H. S., Sorensen, T., Hvid-Jacobsen, K., Dombernowsky, P. & Nielsen, S. L. (1993) [The value of bone marrow scintigraphy in patients with recurrent breast cancer]. [Danish]. *Ugeskrift for Laeger*, 155: 778-782.
Not in PICO
- Leithner, A. & Windhager, R. (2007) Guidelines for the biopsy of bone and soft tissue tumours. [German]. *Orthopade*, 36: 167-175.
Not in PICO
- Leithner, A., Maurer-Ertl, W. & Windhager, R. (2009) Biopsy of bone and soft tissue tumours: hints and hazards. *Recent Results in Cancer Research*, Fortschritte: 3-10.
Not in PICO
- Levecq, L., De, P. P. & Guagnini, A. P. (2005) [Epidemiology of ocular and orbital lesions referred to an ocular oncology center]. [French]. *Journal Francais d Ophthalmologie*, 28: 840-844.
Not in PICO
- Lewis, V. O., Morris, C. D. & Parsons, T. W. (2013) Malignant and benign bone tumors that you are likely to see. *Instructional Course Lectures*, 62: 535-549.
Narrative review
- Li, S., Xue, H. D., Sun, F. & Jin, Z. Y. (2009) [Feasibility and clinical value of whole body diffusion weighted magnetic resonance imaging in detection of bone metastases]. [Chinese]. *Chung-Kuo i Hsueh Ko Hsueh Yuan Hsueh Pao Acta Academiae Medicinae Sinicae*, 31: 192-199.
Not in PICO
- Li, X. & Hemminki, K. (2002) Parental cancer as a risk factor for bone cancer: a nation-wide study from Sweden. *Journal of Clinical Epidemiology*, 55: 111-114.
Not in PICO
- Lis, E., Bilsky, M. H., Pisinski, L., Boland, P., Healey, J. H., O'malley, B. & Krol, G. (2004) Percutaneous CT-guided biopsy of osseous lesion of the spine in patients with known or suspected malignancy. *Ajnr: American Journal of Neuroradiology*, 25: 1583-1588.
Not in PICO

- Malhas, A. M., Grimer, R. J., Abudu, A., Carter, S. R., Tillman, R. M. & Jeys, L. (2011) The final diagnosis in patients with a suspected primary malignancy of bone. *Journal of Bone & Joint Surgery - British Volume*, 93: 980-983.
Not in PICO
- Malhas, A. M., Sumathi, V. P., James, S. L., Menna, C., Carter, S. R., Tillman, R. M., Jeys, L. & Grimer, R. J. (2012) Low-grade central osteosarcoma: a difficult condition to diagnose. *Sarcoma*, 2012: 764796.
Not in PICO
- Malik, A., Wigney, L., Murray, S. & Gerrand, C. H. (2007) The effectiveness of "two-week" referrals for suspected bone and soft tissue sarcoma. *Sarcoma*, 2007.
Not in PICO
- Mankin, H. J., Mankin, C. J. & Simon, M. A. (1996) The hazards of the biopsy, revisited - For the members of the Musculoskeletal Tumor Society. *Journal of Bone and Joint Surgery-American Volume*, 78A: 656-663.
Not in PICO
- Martin, C. T., Morcuende, J., Buckwalter, J. A. & Miller, B. J. (2012) Prereferral MRI Use in Patients with Musculoskeletal Tumors Is Not Excessive. *Clinical Orthopaedics and Related Research*, 470: 3240-3245.
Not in PICO
- Matsui, R. (1999) Quantitative assessment of 201Tl-SPECT in tumors of bone and soft tissue. [Japanese]. *Kakuigaku*, 36: 219-228.
Not in PICO
- Mattiassich, G., Ensaf, F., Hager, M. & Wechselberger, G. (2012) A suspected malignancy in osteolytic bone tumour of the thumb. *BMJ Case Reports*, 2012, 2012.
Not in PICO
- Mattiassich, G., Ensaf, F., Hager, M. & Wechselberger, G. (2012) A suspected malignancy in osteolytic bone tumour of the thumb. *BMJ Case Reports*, 2012, 2012.
Not in PICO
- Mazur, J. M. & Stauffer, E. S. (1981) Evaluation and treatment of bone tumors. *The Journal of family practice*, 12: 333-341.
Narrative review
- Meijer, W. G., van, d., V, Jager, P. L., van der Jagt, E. J., Piers, B. A., Kema, I. P., de Vries, E. G. & Willemsse, P. H. (2003) Bone metastases in carcinoid tumors: clinical features, imaging characteristics, and markers of bone metabolism. *Journal of Nuclear Medicine*, 44: 184-191.
Not in PICO
- Mende, U., Ewerbeck, V., Krempien, B., Ludwig, R., Peichardt, P., Troger, J., Zoller, J. & Braun, A. (1992) Sonography in the therapy-related diagnosis and follow-up of primary bone and soft tissue tumors. [German]. *Bildgebung/Imaging*, 59: 4-14.
Not in PICO
- Mentzel, H.-J., Kentouche, K., Sauner, D., Fleischmann, C., Vogt, S., Gottschild, D., Zintl, F. & Kaiser, W. A. (2004) Comparison of whole-body STIR-MRI and 99mTc-methylene-diphosphonate scintigraphy in children with suspected multifocal bone lesions. *European Radiology*, 14: 2297-2302.
Not in PICO
- Merrill, R. M., Baker, R. K., Lyon, J. L. & Gren, L. H. (2009) Healthcare claims for identifying the level of diagnostic investigation and treatment of cancer. *Medical Science Monitor*, 15: H25-H31.
Not in PICO
- Mespreuve, M., De, B. F. & Van, D. R. (1989) [Osteoid osteoma of the spine]. [Dutch]. *Journal Belge de Radiologie*, 72: 73-78.
Narrative review

- Milo, Y., Robenpor, M., Tamir, G., Ekstein, J. & Hauben, D. J. (1994) Reliability of plain X-ray and computed tomography in diagnosis of invasive tumors of the scalp. *European Journal of Plastic Surgery*, 17: 184-188.
Not in PICO
- Min, R., Zun, Z., Lizheng, W., Minjun, D., Shengwen, L., Wenjun, Y. & Chenping, Z. (2011) Oral and maxillofacial desmoid-type fibromatoses in an eastern Chinese population: a report of 20 cases. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics*, 111: 340-345.
Not in PICO
- Moore, D. W. O., Line, B., Dziuban, J. & McKneally, M. F. (1990) Nuclear scan-guided rib biopsy. *Journal of Thoracic and Cardiovascular Surgery*, 99: 620-621.
Not in PICO
- Myriokefalitaki, E., D'Costa, D., Smith, M. & Ahmed, A. S. (2013) Primary bone metastasis as initial presentation of endometrial cancer (stage IVb). *Archives of Gynecology & Obstetrics*, 288: 739-746.
Not in PICO
- Nagata, Y., Shiraishi, K. & Matsuyama, H. (2012) [A case of primary chondrosarcoma difficult to differentiate from retroperitoneal tumor]. [Japanese]. *Hinyokika Kyo - Acta Urologica Japonica*, 58: 605-608.
Not in PICO
- Neubauer, H., Evangelista, L., Hassold, N., Winkler, B., Schlegel, P. G., Kostler, H., Hahn, D. & Beer, M. (2012) Diffusion-weighted MRI for detection and differentiation of musculoskeletal tumorous and tumor-like lesions in pediatric patients. *World Journal of Pediatrics*, 8: 342-349.
Not in PICO
- Ng, E. S., Saw, A., Sengupta, S., Nazarina, A. R. & Path, M. (2002) Giant cell tumour of bone with late presentation: Review of treatment and outcome. *Journal of Orthopaedic Surgery*, 10: 120-128.
Not in PICO
- Ngwenya, S. (2006) General practitioner's pathology. Case 2. Diagnosis: Oral Kaposi's sarcoma with secondary ulceration. *SADJ*, 61: 079.
Not in PICO
- Niemeyer, P., Delling, G., Werner, M., Simank, H. G. & Bernd, L. (2003) [Telecommunication and telepathology in orthopedic oncology. Possibilities in diagnosis and therapy of primary malignant bone tumors]. [German]. *Orthopade*, 32: 949-954.
Not in PICO
- Nishiyama, Y., Yamamoto, Y., Toyama, Y., Satoh, K., Ohkawa, M. & Tanabe, M. (2000) Diagnostic value of Tl-201 and three-phase bone scintigraphy for bone and soft-tissue tumors. *Clinical Nuclear Medicine*, 25: 200-205.
Not in PICO
- Nthumba, P. M. (2012) Osteosarcoma of the jaws: a review of literature and a case report on synchronous multicentric osteosarcomas. *World Journal of Surgical Oncology*, 10.
Not in PICO
- O'Connor, M. I. (2007) Musculoskeletal imaging: What information is important to the orthopedic oncologist? *Seminars in Musculoskeletal Radiology*, 11: 273-278.
Narrative review
- Ochsner, P. E. (1986) [Tumors of the child's foot]. [German]. *Orthopade*, 15: 227-232.
Narrative review
- Otsuka, N., Fukunaga, M., Furukawa, Y. & Tanaka, H. (1994) The usefulness of early whole body bone scintigraphy in the detection of bone metastasis from prostatic cancer. [Japanese]. *Kakuigaku*, 31: 541-550.
Not in PICO

- Palma, O., Canali, N., Scaroni, P. & Torri, A. M. (1989) Fine needle aspiration biopsy: its use in the management of orbital and intraocular tumors. *Tumori*, 75: 589-593.
Not in PICO
- Palmerini, E., Staals, E. L., Ferrari, S. & Bacci, G. (2009) Diagnosis and prognosis for the Ewing family of tumors. *Expert Opinion on Medical Diagnostics*, 3: 445-452.
Narrative review
- Panzica, M., Luke, U., Mommsen, P. & Krettek, C. (2014) - [Biopsy and approach routes for bone tumors. Where and how much is sufficient?]. [German]. - *Unfallchirurg*, 117: 501-509.
Narrative review
- Parkkola, R. K., Mattila, K. T., Heikkila, J. T., Ekfors, T. O., Kallajoki, M. A., Komu, M. E., Vaara, T. J. & Aro, H. T. (2001) Dynamic contrast-enhanced MR imaging and MR-guided bone biopsy on a 0.23 T open imager. *Skeletal Radiology*, 30: 620-624.
Not in PICO
- Patel, D. R., Moore, M. D. & Greydanus, D. E. (2007) Musculoskeletal diagnosis in adolescents. [Review] [12 refs]. *Adolescent Medicine*, 18: 1-10.
Narrative review
- Pecherstorfer, M., Brenner, K. & Zojer, N. (2003) Current management strategies for hypercalcemia. *Treatments in Endocrinology*, 2: 273-292.
Not in PICO
- Pectasides, D., Farmakis, D., Nikolaou, M., Kanakis, I., Kostopoulou, V., Papaconstantinou, I., Karamanos, N. K., Economopoulos, T. & Raptis, S. A. (2005) Diagnostic value of bone remodeling markers in the diagnosis of bone metastases in patients with breast cancer. *Journal of Pharmaceutical & Biomedical Analysis*, 37: 171-176.
Not in PICO
- Peterson, J. J., Bancroft, L. W. & Kransdorf, M. J. (2005) Principles of tumor imaging. [Review] [28 refs]. *European Journal of Radiology*, 56: 319-330.
Narrative review
- Philip, T., Blay, J. Y., Brunat-Mentigny, M., Carrie, C., Chauvot, P., Farsi, F., Fervers, B., Gentet, J. C., Giammarile, F., Kohler, R., Mathoulin, S., Patricot, L. M. & Thiesse, P. (1999) Standards, Options and Recommendations (SOR) for diagnosis, treatment and follow-up of osteosarcoma. *Bulletin du Cancer*, 86: 159-176.
Guideline
- Piccirillo, E., Agarwal, M., Rohit, Khrais, T. & Sanna, M. (2004) Management of temporal bone hemangiomas. *Annals of Otolaryngology, Rhinology & Laryngology*, 113: 431-437.
Not in PICO
- Pilkington, G. R. & Pallesen, G. (1989) Phenotypic characterization of non-haemopoietic small cell tumours of childhood with monoclonal antibodies to leucocytes, epithelial cells and cytoskeletal proteins. *Histopathology*, 14: 347-357.
Not in PICO
- Plate, A. M., Steiner, G. & Posner, M. A. (2006) Malignant tumors of the hand and wrist. *The Journal of the American Academy of Orthopaedic Surgeons*, 14: 680-692.
Narrative review
- Pohlig, F., Kirchhoff, C., Lenze, U., Schauwecker, J., Burgkart, R., Rechl, H. & von Eisenhart-Rothe, R. (2012) Percutaneous core needle biopsy versus open biopsy in diagnostics of bone and soft tissue sarcoma: a retrospective study. *European Journal of Medical Research*, 17: 29.
Not in PICO
- Pohlig, F., Lenze, U., Lenze, F. W., Muhlhofer, H., Schauwecker, J., Rechl, H. & von Eisenhart-Rothe, R. (2013) [Biopsies from bone and soft tissue sarcoma : a nationwide survey in Germany]. [German]. *Orthopade*, 42: 934-940.
Not in PICO

- Pollahne, W., Pfeifer, M. & Minne, H. W. (2007) [Use of imaging procedures in the diagnostics of osteoporosis interpretation of x-rays and bone density measurements]. [German]. *Wiener Medizinische Wochenschrift*, 157: 593-605.
Not in PICO
- Porter, A. D., Simpson, A. H., Davis, A. M., Griffin, A. M. & Bell, R. S. (1994) Diagnosis and Management of Sacral Bone-Tumors. *Canadian Journal of Surgery*, 37: 473-478.
Not in PICO
- Pozmogov, A. I. (1991) [The potentials for the x-ray diagnosis of early forms of malignant neoplasms in basic locations]. [Russian]. *Vrachebnoe Delo*.(3):6-11, 1991 Mar., 6-11.
In Russian. Not enough information can be extracted to ascertain relevance
- Preteseille, O., Barral, F. G., Court, L., Russias, B., Manet, L., Tanji, P., Mosnier, J. F., Fessy, M. H. & Thomas, T. (2003) [Value of percutaneous core needle biopsy in the investigation of a suspected bone tumor]. [French]. *Journal de Radiologie*, 84: 693-697.
Not in PICO
- Puls, F., Niblett, A. J. & Mangham, D. C. (2014) Molecular pathology of bone tumours: Diagnostic implications. *Histopathology*, 64: 461-476.
Narrative review
- Puls, F., Niblett, A. J. & Mangham, D. C. (2014) - Molecular pathology of bone tumours: diagnostic implications. - *Histopathology*, 64: 461-476.
Duplicate
- Qu, X., Huang, X., Yan, W., Wu, L. & Dai, K. (2012) A meta-analysis of 18fdg-pet-ct, 18fdg-pet, mri and bone scintigraphy for diagnosis of bone metastases in patients with lung cancer. [Review]. *European Journal of Radiology*, 81: 1007-1015.
Not in PICO
- Quinn, R. H., Randall, R. L., Benevenia, J., Berven, S. H. & Raskin, K. A. (2013) Contemporary management of metastatic bone disease: tips and tools of the trade for general practitioners. *The Journal of bone and joint surgery, American*: 1887-1895.
Narrative review
- Raab, C. P. & Gartner, J. C., Jr. (2009) Diagnosis of childhood cancer. [Review] [33 refs]. *Primary Care; Clinics in Office Practice*, 36: 671-684.
Narrative review
- Ralston, S. H., Boyce, B. F., Cowan, R. A., Gardner, M. D., Fraser, W. D. & Boyle, I. T. (1989) Contrasting mechanisms of hypercalcemia in patients with early and advanced humoral hypercalcemia of malignancy. *Journal of Bone and Mineral Research*, 4: 103-111.
Not in PICO
- Rapidis, A. D., Archondakis, G., Anteriotis, D. & Skouteris, C. A. (1997) Chondrosarcomas of the skull base: review of the literature and report of two cases. [Review] [29 refs]. *Journal of Cranio-Maxillo-Facial Surgery*, 25: 322-327.
Not in PICO
- Rattier, C., Rossi, D., Rossi, I., Siles, S., Coulange, C., Rampal, M. & Serment, G. (1995) Bone scintigraphy and classical prognostic factors in prostatic carcinoma at stage M1b. [French]. *Medecine Nucleaire*, 19: 159-168.
Not in PICO
- Rawal, Y. B., Angiero, F., Allen, C. M., Kalmar, J. R., Sedghizadeh, P. P. & Steinhilber, A. M. (2006) Gnathic osteoblastoma: clinicopathologic review of seven cases with long-term follow-up. *Oral Oncology*, 42: 123-130.
Not in PICO
- Ray-Coquard, I., Montesco, M. C., Coindre, J. M., Dei Tos, A. P., Lurkin, A., Ranchere-Vince, D., Vecchiato, A., Decouvelaere, A. V., Mathoulin-Pelissier, S., Albert, S., Cousin, P., Cellier, D., Toffolatti, L., Rossi, C. R., Blay, J. Y. & Conticanet group (2012) Sarcoma: concordance between initial diagnosis and centralized expert review in a population-based study within three European

- regions. *Annals of Oncology*, 23: 2442-2449.
Not in PICO
- Reichelt, A. (1982) Clinical manifestations of primary malignant bone tumors. [German]. *Therapiewoche*, 32: 321-324.
Narrative review
- Riley, R. D., Burchill, S. A., Abrams, K. R., Heney, D., Sutton, A. J., Jones, D. R., Lambert, P. C., Young, B., Wailoo, A. J. & Lewis, I. J. (2003) A systematic review of molecular and biological markers in tumours of the Ewing's sarcoma family. [Review] [84 refs]. *European Journal of Cancer*, 39: 19-30.
Not in PICO
- Robinson, L. A. (1997) Radioisotope-guided surgical biopsy of suspected osseous metastases. *Cancer Control*, 4: 517-522.
Not in PICO
- Romero, J., Exner, G. U., Hodler, J. & Von Hochstetter, A. R. (1991) Use of MRI in the differential diagnosis of fatigue fractures and bone tumors. [German]. *Zeitschrift fur Orthopadie und Ihre Grenzgebiete*, 129: 305-312.
Not in PICO
- Ropper, A. E., Cahill, K. S., Hanna, J. W., McCarthy, E. F., Gokaslan, Z. L. & Chi, J. H. (2011) Primary Vertebral Tumors: A Review of Epidemiologic, Histological, and Imaging Findings, Part I: Benign Tumors. *Neurosurgery*, 69: 1171-1180.
Narrative review
- Rowe, R. G., Thomas, D. G., Schuetze, S. M., Hafez, K. S., Lawlor, E. R. & Chugh, R. (2013) Ewing sarcoma of the kidney: case series and literature review of an often overlooked entity in the diagnosis of primary renal tumors. *Urology*, 81: 347-353.
Not in PICO
- Ruhs, S. A., el-Khoury, G. Y. & Chrischilles, E. A. (1996) A cost minimization approach to the diagnosis of skeletal neoplasms. *Skeletal Radiology*, 25: 449-454.
Not in PICO
- Saifuddin, A., Mitchell, R., Burnett, S. J., Sandison, A. & Pringle, J. A. (2000) Ultrasound-guided needle biopsy of primary bone tumours. *Journal of Bone & Joint Surgery - British Volume*, 82: 50-54.
Not in PICO
- Sampson, V. B., Gorlick, R., Kamara, D. & Anders, K. E. (2013) A review of targeted therapies evaluated by the pediatric preclinical testing program for osteosarcoma. *Frontiers in Oncology*, 3: 132.
Narrative review
- Sato, N., Hino, M. & Sano, M. (2003) Detection of bone metastases in routine follow-up after treatment for primary breast cancer. *Breast Cancer*, 10: 335-340.
Not in PICO
- Scharf, S. & Zhao, Q. H. (1999) Radionuclide bone scanning in routine clinical practice. [Review] [10 refs]. *Lippincott's Primary Care Practice*, 3: 521-528.
Narrative review
- Schatz, J., Soper, J., McCormack, S., Healy, M., Deady, L. & Brown, W. (2008) Imaging of tumors in the ankle and foot. *Techniques in Foot and Ankle Surgery*, 7: 208-223.
Narrative review
- Schmidt, G. P., Schoenberg, S. O., Reiser, M. F. & Baur-Melnyk, A. (2005) Whole-body MR imaging of bone marrow. [Review] [40 refs]. *European Journal of Radiology*, 55: 33-40.
Narrative review
- Schnurr, C., Pippas, M., Stuetzer, H., Delank, K. S., Michael, J. W. & Eysel, P. (2008) Treatment delay of bone tumours, compilation of a sociodemographic risk profile: a retrospective study. *BMC cancer*, 8: 22.
Not in PICO

- Schweiberer, L., Baumgart, R. & Zeiler, C. (1997) Instrumental diagnosis for therapy decision making-what is possible and desirable, what is essential and what is superfluous?. [German]. *Langenbecks Archiv fur Chirurgie, Supplement.:* 410-414.
Narrative review
- Scutellari, P. N., Addonisio, G., Righi, R. & Giganti, M. (2000) [Diagnostic imaging of bone metastases]. [Italian]. *Radiologia Medica*, 100: 429-435.
Not in PICO
- Scutellari, P. N., Antinolfi, G., Galeotti, R. & Giganti, M. (2003) [Metastatic bone disease. Strategies for imaging]. [Review] [46 refs] [Italian]. *Minerva Medica*, 94: 77-90.
Not in PICO
- Senac, M. O., Jr., Isaacs, H. & Gwinn, J. L. (1986) Primary lesions of bone in the 1st decade of life: retrospective survey of biopsy results. *Radiology*, 160: 491-495.
Not in PICO
- Sergieva, S. B., Alexandrova, E., Baichev, G., Nikolcheva, L., Milev, A. & Dimitrov, B. (2010) Clinical application of SPECT-CT in cancer patients with suspected bone metastases. *European Journal of Nuclear Medicine and Molecular Imaging*, 37: S440-S441.
Not in PICO
- Shaffer, K. A., Houghton, V. M. & Wilson, C. R. (1980) High resolution computed tomography of the temporal bone. *Radiology*, 134: 409-414.
Not in PICO
- Shie, P., Cardarelli, R., Brandon, D., Erdman, W. & Rahim, N. A. (2008) Meta-analysis: comparison of F-18 fluorodeoxyglucose-positron emission tomography and bone scintigraphy in the detection of bone metastases in patients with breast cancer (DARE structured abstract). *Clinical Nuclear Medicine*, 33: 97-101.
Not in PICO
- Siller, C. S. & Lewis, I. J. (2010) Update and review of the management of bone tumours. *Paediatrics and Child Health*, 20: 103-108.
Narrative review
- Skoldenberg, E., Soderberg, M., Wangberg, J. & Ljungman, G. (2011) Cutting needle biopsies in the management of childhood tumors. *Pediatric Blood and Cancer*, 57: 747.
Not in PICO
- Skotakova, J., Mach, V., Bajciová, V., Mudry, P. & Ondrus, S. (2006) Malignant tumors of long bones in children: Differential diagnosis and the role of imaging methods. [Czech]. *Acta Chirurgiae Orthopaedicae et Traumatologiae Cechoslovaca*, 73: 183-189.
Not in PICO
- Skrzynski, M. C., Biermann, S., Montag, A. & Simon, M. A. (1996) Diagnostic accuracy and charge-savings of outpatient core needle biopsy compared with open biopsy of musculoskeletal tumors (Structured abstract). *Journal of Bone and Joint Surgery.American volume.*, 78A: 644-649.
Not in PICO
- Smolarz, K., Jungehulsing, M., Krug, B., Linden, A., Gohring, U. J. & Schicha, H. (1990) [Magnetic resonance tomography of the bone marrow in cancer patients with a solitary area of increased uptake in the bone scintigram]. [German]. *Nuclear-Medizin*, 29: 269-273.
Not in PICO
- Soldani, S., Roni, P., Filidei, M., Castiglioni, M. & Riccioni, N. (1997) Diagnostic value of ultrasound-guided FNAB in the evaluation of osteolytic bone lesions suspected for metastases. [Italian]. *Giornale Italiano di Ultrasonologia*, 8: 31-35.
Not in PICO
- Song, W. S., Jeon, D. G., Cho, W. H., Kong, C. B., Cho, S. H., Lee, J. W. & Lee, S. Y. (2014) - Plain radiologic findings and chronological changes of incipient phase osteosarcoma overlooked by primary physicians. - *Clinics in Orthopedic Surgery*, 6: 230-235.
Not in PICO

- Souza, F. F., de, A. M., O'Regan, K., Jagganathan, J., Krajewski, K. & Ramaiya, N. (2013) Malignant primary chest wall neoplasms: A pictorial review of imaging findings. *Clinical Imaging*, 37: 8-17.
Not in PICO
- Steinborn, M. M., Heuck, A. F., Tiling, R., Bruegel, M., Gauger, L. & Reiser, M. F. (1999) Whole-body bone marrow MRI in patients with metastatic disease to the skeletal system. *Journal of Computer Assisted Tomography*, 23: 123-129.
Not in PICO
- Steve, M., Ernenwein, D., Chaine, A., Bertolus, C., Goudot, P. & Ruhin-Poncet, B. (2011) [Jaw osteosarcomas]. [French]. *Revue de Stomatologie et de Chirurgie Maxillo-Faciale*, 112: 286-292.
Not in PICO
- Streitbuerger, A., Harges, J., Gebert, C., Ahrens, H., Winkelmann, W. & Gosheger, G. (1982) [Cartilage tumours of the bone. Diagnosis and therapy]. [Review] [26 refs] [German]. *Orthopade*, 35: 871-881.
Narrative review
- Strobel, K., Exner, U. E., Stumpe, K. D., Hany, T. F., Bode, B., Mende, K., Veit-Haibach, P., von Schulthess, G. K. & Hodler, J. (2008) The additional value of CT images interpretation in the differential diagnosis of benign vs. malignant primary bone lesions with 18F-FDG-PET/CT. *European Journal of Nuclear Medicine & Molecular Imaging*, 35: 2000-2008.
Not in PICO
- Talbot, J.-N., Paycha, F. & Balogova, S. (2011) Diagnosis of bone metastasis: Recent comparative studies of imaging modalities. *Quarterly Journal of Nuclear Medicine and Molecular Imaging*, 55: 374-410.
Not in PICO
- Tamiolakis, D., Tsamis, I., Thomaidis, V., Lambropoulou, M., Alexiadis, G., Venizelos, I., Jivanakis, T. & Papadopoulos, N. (2007) Oral complaints caused from metastases to the mandible and maxilla. *Chirurgia (Bucuresti)*, 102: 439-442.
Not in PICO
- Tan, J. Z., Schlicht, S. M., Powell, G. J., Thomas, D., Slavin, J. L., Smith, P. J. & Choong, P. F. (2006) Multidisciplinary approach to diagnosis and management of osteosarcoma - a review of the St Vincent's Hospital experience. *International Seminars in Surgical Oncology*, 3: 38.
Not in PICO
- Tanveer, N. & Mishra, K. (2014) - Chordoma Cutis - A Diagnosis not to be Missed. - *Journal of Clinical and Diagnostic Research JCDR*, 8: FD17-FD18.
Not in PICO
- Tappauf, M., Lackner, H., Sovinz, P., Schwinger, W., Benesch, M., Strenger, V., Schmidt, S. & Urban, C. (2011) Multifocal osseous involvement in a patient with Hodgkin lymphoma. *Monatsschrift fur Kinderheilkunde*, 159: 326.
Not in PICO
- Tateishi, U., Gladish, G. W., Kusumoto, M., Hasegawa, T., Yokoyama, R., Tsuchiya, R. & Moriyama, N. (2003) Chest Wall Tumors: Radiologic Findings and Pathologic Correlation - Part 2. Malignant Tumors. *Radiographics*, 23: 1491-1508.
Not in PICO
- Taylor, J. A. M. & Bussieres, A. (2012) Diagnostic imaging for spinal disorders in the elderly: a narrative review. *Chiropractic and Manual Therapies*, 20.
Narrative review
- Teo, H. E. & Peh, W. C. (2004) Primary bone tumors of adulthood. *Cancer Imaging*, 4: 74-83.
Narrative review
- Thorban, S., Roder, J. D. & Siewert, J. R. (1999) Detection of micrometastasis in bone marrow of pancreatic cancer patients. *Annals of Oncology*, 10: Suppl-3.
Not in PICO

- Thrall, J. H. & Ellis, B. I. (1987) Skeletal metastases. *Radiologic Clinics of North America*, 25: 1155-1170.
Narrative review
- Trigg, S. D. (2004) Biopsy of hand, wrist, and forearm tumors. *Hand Clinics*, 20: 131-135.
Narrative review
- Tucker, W. S. & Nasser-Sharif, F. J. (1997) Benign skull lesions. *Canadian Journal of Surgery*, 40: 449-455.
Not in PICO
- Ulaner, G., Hwang, S., Lefkowitz, R. A., Landa, J. & Panicek, D. M. (2013) Musculoskeletal tumors and tumor-like conditions: Common and avoidable pitfalls at imaging in patients with known or suspected cancer: Part A: Benign conditions that may mimic malignancy. *International Orthopaedics*, 37: 871-876.
Narrative review
- Ulaner, G., Hwang, S., Landa, J., Lefkowitz, R. A. & Panicek, D. M. (2013) Musculoskeletal tumours and tumour-like conditions: Common and avoidable pitfalls at imaging in patients with known or suspected cancer: Part B: Malignant mimics of benign tumours. *International Orthopaedics*, 37: 877-882.
Narrative review
- Ulaner, G. A., Magnan, H., Healey, J. H., Weber, W. A. & Meyers, P. A. (2014) - Is methylene diphosphonate bone scan necessary for initial staging of Ewing sarcoma if 18F-FDG PET/CT is performed? - *AJR*, American Journal of Roentgenology. 202: 859-867.
Not in PICO
- van de Sande, M. A., Bramer, J. A., Jutte, P. C., Schreuder, H. W. & Dijkstra, P. D. (2010) [Diagnosis and treatment of bone metastasis]. [Review] [Dutch]. *Nederlands Tijdschrift Voor Geneeskunde*, 154: A2125.
Narrative review
- Van Der Woude, H.-J., Verstraete, K. L., Hogendoorn, P. C. W., Taminiau, A. H. M., Hermans, J. & Bloem, J. L. (1998) Musculoskeletal tumors: Does fast dynamic contrast-enhanced subtraction MR imaging contribute to the characterization? *Radiology*, 208: 821-828.
Not in PICO
- Van Hoof, V. O., Van Oosterom, A. T., Lepoutre, L. G. & De Broe, M. E. (1992) Alkaline phosphatase isoenzyme patterns in malignant disease. *Clinical Chemistry*, 38: 2546-2551.
Not in PICO
- van, D. B. & Freyschmidt, J. (2002) [Standardized procedure for suspected bone tumor]. [German]. *Chirurg*, 73: 1153-1161.
Narrative review
- Venkateswaran, L., Rodriguez-Galindo, C., Merchant, T. E., Poquette, C. A., Rao, B. N. & Pappo, A. S. (2001) Primary Ewing tumor of the vertebrae: Clinical characteristics, prognostic factors, and outcome. *Medical and Pediatric Oncology*, 37: 30-35.
Not in PICO
- Vieillard, M.-H., Boutry, N., Chastanet, P., Duquesnoy, B., Cotten, A. & Cortet, B. (2005) Contribution of percutaneous biopsy to the definite diagnosis in patients with suspected bone tumor. *Joint Bone Spine*, 72: 53-60.
Not in PICO
- Von Hochstetter, A. R. (1987) Suspected neoplastic lesion of bone: Biopsy planning by the pathologist. [German]. *Schweizerische Medizinische Wochenschrift*, 117: 1302-1306.
Narrative review
- Von Salis-Soglio, G. & Prietzel, T. (2002) Diagnostic procedures for suspected malignant tumors of bone and soft tissues. [German]. *Orthopade*, 31: 595-607.
Narrative review

- Wahane, R. N., Lele, V. R. & Bobhate, S. K. (2007) Fine needle aspiration cytology of bone tumors. *Acta Cytologica*, 51: 711-720.
Not in PICO
- Waimann, C. A., Lu, H. & Suarez Almazor, M. E. (2011) Rheumatic manifestations of primary and metastatic bone tumors and paraneoplastic bone disease. [Review]. *Rheumatic Diseases Clinics of North America*, 37: 527-549.
Narrative review
- Walther, C., Domanski, H. A., von Steyern, F. V., Mandahl, N. & Mertens, F. (2011) Chromosome banding analysis of cells from fine-needle aspiration biopsy samples from soft tissue and bone tumors: is it clinically meaningful? *Cancer genetics*, 204: 203-206.
Not in PICO
- Wang, K., Allen, L., Fung, E., Chan, C. C., Chan, J. C. & Griffith, J. F. (2005) Bone scintigraphy in common tumors with osteolytic components. [Review] [0 refs]. *Clinical Nuclear Medicine*, 30: 655-671.
Narrative review
- Weissbach, L. (2006) [Diagnostic work-up of bone metastases of genitourinary tumors and their treatment with bisphosphonates. Interdisciplinary consensus conference, Frankfurt, 2006]. [Review] [18 refs] [German]. *Urologe (Ausg.A)*, 45: 1527-1531.
Not in PICO
- Widhe, B., Widhe, T. & Bauer, H. C. (2007) Ewing sarcoma of the rib--initial symptoms and clinical features: tumor missed at the first visit in 21 of 26 patients. *Acta Orthopaedica*, 78: 840-844.
Not in PICO
- Widhe, B. & Bauer, H. C. (2011) Diagnostic difficulties and delays with chest wall chondrosarcoma: a Swedish population based Scandinavian Sarcoma Group study of 106 patients. *Acta Oncologica*, 50: 435-440.
Not in PICO
- Winderen, M., Stenwig, A. E., Solheim, O. P., Saeter, G. & Aas, M. (1999) Dynamic bone scintigraphy for evaluation of tumor response after preoperative chemotherapy. A retrospective study of osteosarcoma and Ewing's sarcoma patients. *Acta Orthopaedica Scandinavica, Supplement*, 70: 11-17.
Not in PICO
- Wisanuyotin, T., Mitchai, J., Sirichativapee, W., Kosuwon, W., Sumnanoont, C. & Jeeravipoolvarn, P. (2009) Tissue imprint for intra-operative evaluation of musculoskeletal tumors. *Journal of the Medical Association of Thailand*, 92: 654-659.
Not in PICO
- Wong, K. F., Chan, J. K. & Ma, S. K. (1993) Solid tumour with initial presentation in the bone marrow--a clinicopathologic study of 25 adult cases. [Review] [15 refs]. *Hematological Oncology*, 11: 35-42.
Not in PICO
- Xie, J.-B., Chen, J.-T. & Song, X.-H. (2011) Diagnosis value of 18FDG-PET/CT and 99Tcm-MDP bone scan in bone metastases of tumors: A meta-analysis. *Chinese Journal of Evidence-Based Medicine*, 11.
Not in PICO
- Xu, D. Y. (1988) [An X-ray analysis of 22 cases of malignant giant cell tumor of bone (with emphasis on reliable signs of early malignant changes)]. [Chinese]. *Chung-Hua Fang She Hsueh Tsa Chih Chinese Journal of Radiology*, 22: 208-211.
Not in PICO
- Yamamoto, Y., Kawaguchi, Y., Kawase, Y., Maeda, Y. & Nishiyama, Y. (2011) A comparative study of F-18 FDG PET and 201Tl scintigraphy for detection of primary malignant bone and soft-tissue tumors. *Clinical Nuclear Medicine*, 36: 290-294.
Not in PICO

- Yang, H. L., Liu, T., Wang, X. M., Xu, Y. & Deng, S. M. (2011) Diagnosis of bone metastases: a meta-analysis comparing 18FDG PET, CT, MRI and bone scintigraphy (DARE structured abstract). *European Radiology*, 21: 2604-2617.
Not in PICO
- Yang, Z. M., Shen, C. C., Li, H., Shi, Z. L. & Tao, H. M. (2012) Current treatment of sacral giant cell tumour of bone: A review. *Journal of International Medical Research*, 40: 415-425.
Narrative review
- Yao, L., Nelson, S. D., Seeger, L. L., Eckardt, J. J. & Eilber, F. R. (1999) Primary musculoskeletal neoplasms: Effectiveness of core-needle biopsy. *Radiology*, 212: 682-686.
Not in PICO
- Yasui, K., Kanazawa, S., Tanaka, A. & Hiraki, Y. (1996) [Percutaneous CT guided bone biopsy in patients with suspected bone neoplasm]. [Japanese]. *Nippon Igaku Hoshasen Gakkai Zasshi - Nippon Acta Radiologica*, 56: 178-182.
Not in PICO
- Young, P. S., Bell, S. W., MacDuff, E. M. & Mahendra, A. (2013) Primary osseous tumors of the hindfoot: why the delay in diagnosis and should we be concerned? *Clinical Orthopaedics & Related Research*, 471: 871-877.
Not in PICO
- Zeng, H., Kang, B., Liu, G. & Tang, X. (2013) Ultrasonographic diagnosis of bone tumor of the knee and its clinical implication. *Journal of Tongji Medical University = Tong ji yi ke da xue xue bao*, 21: 236-237, 245.
Not in PICO
- Zhang, D., Chen, L., Ni, C.-F., Liu, Y.-Z., Jin, Y.-H., Zhu, X.-L. & Zou, J.-W. (2013) Percutaneous coaxial biopsy in diagnosis of musculoskeletal tumors. [Chinese]. *Chinese Journal of Medical Imaging Technology*, 29: 1493-1496.
Not in PICO
- Zhang, L., Li, J., Yang, H., Luo, Z. & Zou, J. (2012) Histological evaluation of bone biopsy results during PVP or PKP of vertebral compression fractures. *Oncology Letters*, 5: 135-138.
Not in PICO
- Zhang, X.-B., Zhang, X.-Z., Huang, Z.-G. & Wang, W. (2009) CT-guided percutaneous biopsy of malignant musculoskeletal tumors: An analysis of its diagnostic accuracy. [Chinese]. *Journal of Interventional Radiology*, 18: 834-837.
Not in PICO
- Zhao, H. & Wang, L. (2011) Whole body diffusion weighted imaging with background suppression for diagnosing bone metastases. [Chinese]. *Chinese Journal of Clinical Oncology*, 38: 677-679.
Not in PICO
- Zharkov, P. L. (2000) [Problems in the radiologic diagnosis of osteogenic sarcoma]. [Russian]. *Voprosy Onkologii*, 46: 699-703.
Narrative review
- Zieger, M. (1982) [Diagnosis of occult skeletal metastasis: alkaline phosphatase versus skeletal scintigraphy]. [German]. *Medizinische Klinik - Praxis-Ausg*, 77: 44-50.
Not in PICO
- Zieger, M. (1982) Detection of occult bony metastasis: Alkaline phosphatase versus bony scintigraphy. [German]. *Medizinische Klinik*, 77: 360-363.
Not in PICO
- Zissimopoulos, A., Bantis, A., Stellos, K., Petrakis, G. & Matthaios, D. (2008) Association between bone scintigraphy and serum levels of procollagen (I) and PSA in the detection of bone disease in prostate cancer patients. *Journal of B.U.On.*, 13: 69-74.
Not in PICO

SOFT TISSUE SARCOMA

Review question:

What is the risk of soft tissue sarcoma in patients presenting in primary care with symptom(s)?

Results

Literature search

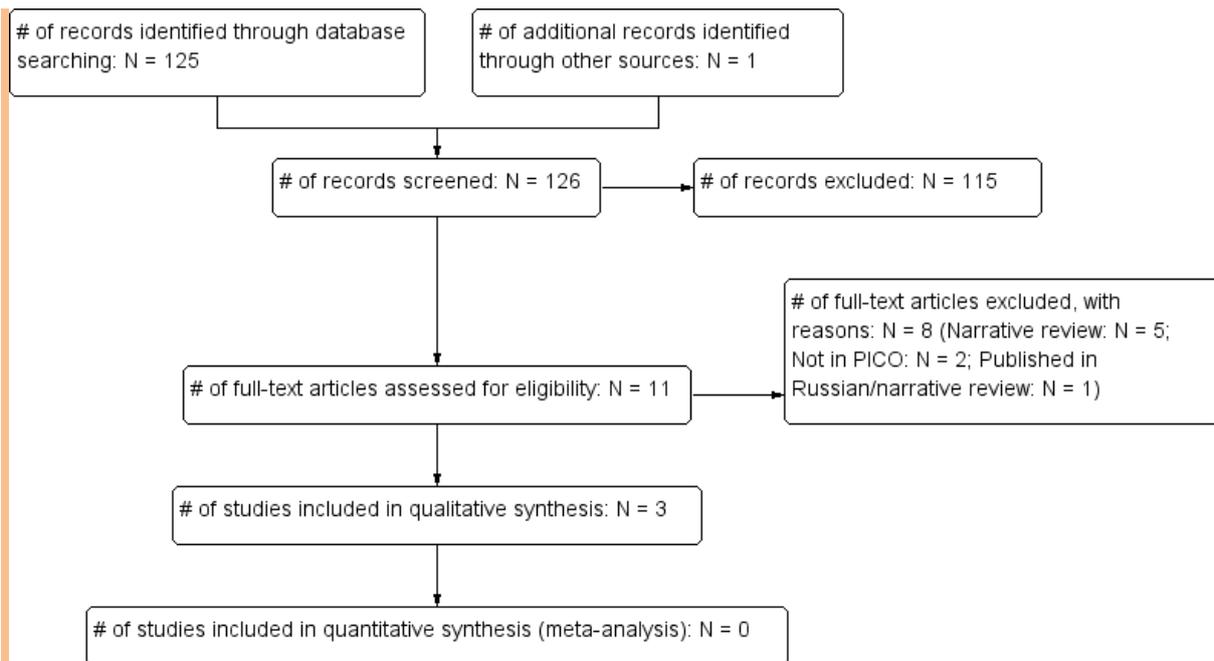
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	389	66	08/11/2012
<i>Premedline</i>	All-2012	26	6	08/11/2012
<i>Embase</i>	All-2012	287	63	08/11/2012
<i>Cochrane Library</i>	All-2012	82	0	08/11/2012
<i>Psychinfo</i>	All-2012	20	2	08/11/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	192	6	08/11/2012
<i>Biomed Central</i>	All-2012	128	4	08/11/2012

Total References retrieved (after de-duplication): 118

Update Search

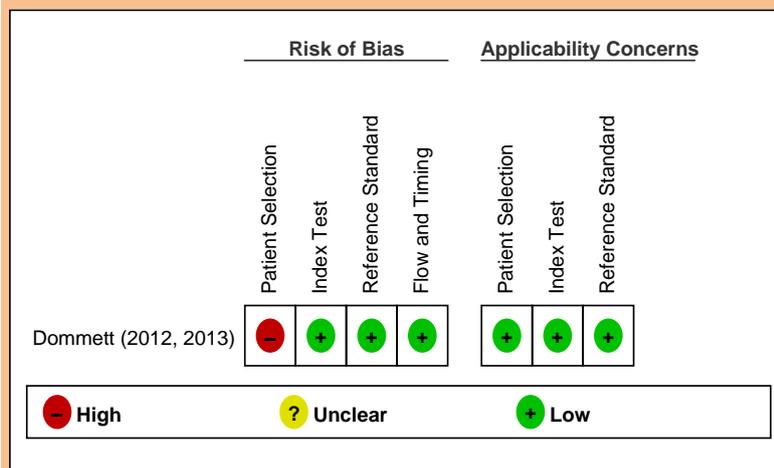
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	11/2012-26/08/2014	61	2	26/08/2014
<i>Premedline</i>	11/2012-26/08/2014	56	4	26/08/2014
<i>Embase</i>	11/2012-26/08/2014	23	2	26/08/2014
<i>Cochrane Library</i>	11/2012-26/08/2014	27	0	26/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	11/2012-26/08/2014	25	0	26/08/2014

Total References retrieved (after de-duplication): 7



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included study in the figure below. The main issue to note is that the study only presented results for bone and soft tissue sarcoma in combination and also employed a case-control design which has been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors may have gone some way in counteracting the influence of the latter.



Study results

Table 1: Soft tissue sarcoma: Positive predictive values for child- or young adulthood bone cancer tumour/soft tissue sarcoma

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2013a)	Lump mass swelling below neck excluding	All bone cancer tumour/soft tissue	0.03 (0.01-0.14)

	abdomen 0-3 months before diagnosis	sarcoma patients and controls aged 0-14 years	
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All bone cancer tumour/soft tissue sarcoma patients and controls aged 0-14 years	0.01 (0-0.01)
Dommett (2013a)	Trauma 0-3 months before diagnosis	All bone cancer tumour/soft tissue sarcoma patients and controls aged 0-14 years	0 (0-0)
Dommett (2013a)	≥ 3 consultations	All bone cancer tumour/soft tissue sarcoma patients and controls aged 0-14 years	0 (0-0)
Dommett (2013b)	Lump mass swelling	All bone cancer tumour/soft tissue sarcoma patients and controls aged 15-24 years	0.0415 (0.0124-0.1392) Cases: 19/196 Controls: 3/2438
Dommett (2013b)	Musculoskeletal symptoms	All bone cancer tumour/soft tissue sarcoma patients and controls aged 15-24 years	0.0093 (0.0058-0.0151) Cases: 37/196 Controls: 26/2438
Dommett (2013b)	Chest pain	All bone cancer tumour/soft tissue sarcoma patients and controls aged 15-24 years	0.0027 (0.001-0.0077) Cases: 5/196 Controls: 12/2438
Dommett (2013b)	≥ 3 consultations	All bone cancer tumour/soft tissue sarcoma patients and controls aged 15-24 years	0.003 (0.0024-0.0037) Cases: 86/196 Controls: 189/2438

The positive predictive values are calculated using Bayesian statistics.

Evidence statement(s):

The positive predictive values of having childhood or young adulthood bone cancer tumour/soft tissue sarcoma ranged from 0% (for trauma) to 0.03% (for 'lump mass swelling below neck excluding abdomen') for patients aged 0-14 years old, and from 0.0027% (for chest pain) to 0.0415% (for 'lump mass swelling') for patients aged 15-24 years (1 study, N = 30855). The evidence quality is somewhat compromised by the case-control design of the study (see also Table 1).

Evidence tables

Dommett (2012; 2013a,b)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based nested case-control study using data from the General Practice Research Database (GPRD)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> 1267 children; aged 0-4 years: N = 436; aged 5-14 years: N = 831; 703 males/564 females. Cancer type: Leukemia: N = 368; brain: N = 270; lymphoma: N = 142; bone: N = 107; soft tissue sarcoma: N = 91; renal: N = 82; neuroblastoma: N = 75; other ICD codes: N = 132. 1064 teenagers and young adults (TYA): 15-24 years: Gender not reported. Cancer type: Leukemia: N = 143; brain: N = 154; lymphoma: N = 270; bone: N = 96; soft tissue sarcoma: N = 100; other ICD codes: N = 301 (including testis: N = 60; skin: N = 49; ovary: N = 20 and thyroid: N = 17).</p> <p><u>Controls:</u> 15318 children; aged 0-4 years: N = 4802; aged 5-14 years: N = 10516; 8461 males/6857 females. 13206 TYA. Gender not reported</p> <p><u>Inclusion criteria:</u> The sample comprised all children and TYU aged 0–24 years, inclusive, drawn from all general practices contributing research-standard data to the GPRD between 1 January 1988 and 31 December 2010. To be included, the practices had to have been contributing research-standard data for a minimum of 1 year before each child’s date of cancer diagnosis or the index date (see below) for matched controls. Cases: Patients diagnosed with the following cancers: leukaemia, lymphoma, neuroblastoma, soft tissue sarcoma, hepatic, renal, bone and central nervous system tumours, using pre-defined medical codes used in the GPRD. The date of diagnosis for cases was defined as the date of pathological diagnosis, but if this was unavailable, the date of the first cancer code entered in the GPRD was used. Controls: Up to 13 controls (children with no diagnosis of cancer at any time) were selected per case, using a computer-generated random sequence, matched on age (within 1 year), sex and practice, and had to be currently registered on the date of diagnosis of their matched case (the index date).</p> <p><u>Exclusion criteria:</u> None listed <u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting	Low concern

do not match the review question?		
INDEX TEST		
A. Risk of bias		
Index test	The GPRD uses just over 100 000 medical codes to encompass all primary care events, including both symptoms and diagnoses. From this list, libraries of codes were assembled representing individual alert symptoms derived from the NICE referral guidelines for suspected cancer in children. <i>No more information reported.</i>	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Cancer diagnosis in the UK's General Practice Research Database.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	This study is published in three papers.	

References

Included studies

Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of childhood cancer in primary care: A population-based nested case-control study. *British Journal of Cancer* 106[5], 982-987. 2012.

Dommett, R. M., Redaniel, T., Stevens, M. C. G., Martin, R. M., and Hamilton, W. Risk of childhood cancer with symptoms in primary care: A population-based case-control study. *British Journal of General Practice*; DOI:10.3399/bjgp13X660742. 2013a.

Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of cancer in teenagers and young adults in primary care: A population-based nested case-control study. *British Journal of Cancer* 2329-2333. 2013b.

Excluded studies (with excl reason)

(1998) Practice guidelines: uterine corpus--sarcomas. Society of Gynecologic Oncologists Clinical Practice Guidelines. *Oncology (Williston Park)*, 12: 284-286.
Guideline

(2006) New report on childhood cancer shows early detection can save thousands of children's lives. *European Journal of Oncology*, 11: 65-67.
Narrative review

Abbas, M., Dammrich, M. E., Braubach, P., Meinardus, A., Kramer, M. W., Merseburger, A. S., Herrmann, T. R., Grunwald, V. & Kreipe, H. H. (2014) - Synovial sarcoma of the kidney in a young patient with a review of the literature. - *Rare Tumors*, 6: 5393.
Not in PICO

Abellan, J. F., Lamo De Espinosa, J. M., Duart, J., Patino-Garcia, A., Martin-Algarra, S., Martinez-Monge, R. & San-Julian, M. (2009) Nonreferral of possible soft tissue sarcomas in adults: A dangerous omission in policy. *Sarcoma*, 2009.
Not in PICO

Aboulafia, A. J., Levin, A. M. & Blum, J. (2002) Prereferral evaluation of patients with suspected bone and soft tissue tumors. *Clinical Orthopaedics and Related Research*, 83-88.
Not in PICO

Ajekigbe, L. & Stothard, J. (2006) The effectiveness of sodium tetradecyl sulfate in the treatment of wrist ganglia. *Canadian Journal of Plastic Surgery*, 14: 28-30.
Not in PICO

Alvegard, T., Sundby, H. K., Bauer, H. & Rydholm, A. (2009) The Scandinavian Sarcoma Group: 30 years' experience. *Acta Orthopaedica, Supplement*, 80: 1-104.
Not in PICO

Amstalden, E. M. I., Alvarenga, M., Goncalves, J. C. B. & Cassone, A. E. (2010) Perivascular epithelioid cell tumor (PEComa) of bone and soft tissue - Relate of two cases. *Histopathology*, 57: 21.
Not in PICO

Anderson, B. D. & Schoenfeldt, M. (1330) Clinical trials referral resource. Current clinical trials in rhabdomyosarcoma. *Oncology (Williston Park)*, 19: 1319-1320.
Not in PICO

Arbiser, Z. K., Folpe, A. L. & Weiss, S. W. (2001) Consultative (expert) second opinions in soft tissue pathology. Analysis of problem-prone diagnostic situations. *American Journal of Clinical Pathology*, 116: 473-476.
Not in PICO

Barzi, D. M., Sami, S. H. & Fallah, E. (2014) - Pseudo-aneurysm of anterior tibia artery simulating a soft tissue sarcoma: a case report. - *Acta Medica Iranica*, 52: 234-237.
Not in PICO

Bennis, M., Dalsing, M., Sawchuck, A. & Wurtz, L. D. (2006) Soft tissue sarcomas may present with deep vein thrombosis. *Journal of Vascular Surgery*, 43: 788-793.
Not in PICO

Bleyer, A. (2009) CAUTION! Consider Cancer: Common Symptoms and Signs for Early Detection of Cancer in Young Adults. *Seminars in Oncology*, 36: 207-212.
Narrative review

- Browder, D. A. & Erhard, R. E. (2005) Decision making for a painful hip: A case requiring referral. *Journal of Orthopaedic & Sports Physical Therapy*, 35: 738-744.
Not in PICO
- Bruns, J., Delling, G., Henne-Bruns, D. & Hossfeld, D. K. (2008) Biopsy of tumors of the musculoskeletal system. *Deutsches Arzteblatt International*, 105: 492-497.
Narrative review
- Bui, B. N., Blay, J. Y., Bonichon, F., Bonvalot, S., Chevalier-Place, A., Coindre, J. M., Delannes, M., Le Cesne, A., Morice, P., Ray-Coquard, I., Pautier, P., Le Pechoux, C., Stoeckle, E., Taieb, S. & Bosquet, L. (2007) Clinical practice guidelines: 2006. Update of recommendations for the management of patients with soft tissue sarcoma (sarcoma of the extremity, uterine sarcoma and retroperitoneal sarcoma). *Oncologie*, 9: 173-177.
Guideline
- Cerdan Carbonero, M. T., Sanz, L. R. & Martinez, R. C. (2005) Improving communication between levels of health care: Direct referral of patients to a "one-stop" service for major outpatient surgery. [Spanish]. *Atencion Primaria*, 35: 283-287.
Not in PICO
- Chadha, N. K. & Forte, V. (2009) Pediatric head and neck malignancies. [Review] [41 refs]. *Current Opinion in Otolaryngology & Head & Neck Surgery*, 17: 471-476.
Narrative review
- Chao, C., McMasters, K. M. & Edwards, M. J. (2002) Advances in the treatment of soft-tissue sarcomas. [Review] [21 refs]. *Journal of the Kentucky Medical Association*, 100: 10-16.
Narrative review
- Chaudrey, K., Naseer, T., Khan, S., Alexis, R., Grosman, I. & Zachary, K. (2010) Glomus tumor a diagnostic challenge-a report of 2 cases. *American Journal of Gastroenterology*, 105: S170-S171.
Not in PICO
- Chotel, F., Unnithan, A., Chandrasekar, C. R., Parot, R., Jeys, L. & Grimer, R. J. (2008) Variability in the presentation of synovial sarcoma in children: A plea for greater awareness. *Journal of Bone and Joint Surgery - Series B*, 90: 1090-1096.
Not in PICO
- Chou, L. B., Ho, Y. Y. & Malawer, M. M. (2009) Tumors of the foot and ankle: Experience with 153 cases. *Foot and Ankle International*, 30: 836-841.
Not in PICO
- Clark, M. A. & Thomas, J. M. (2005) Delay in referral to a specialist soft-tissue sarcoma unit. *European Journal of Surgical Oncology*, 31: 443-448.
Not in PICO
- Coffin, C. M. & Dehner, L. P. (1998) Pathologic evaluation of pediatric soft tissue tumors. *American Journal of Clinical Pathology*, 109: S38-S52.
Narrative review
- Comba, P., Fazzo, L. & Berrino, F. (2004) [Soft tissue sarcomas in Mantua: epidemiological evidence and perspectives for environmental remediation]. [Italian]. *Epidemiologia e Prevenzione*, 28: 266-271.
Not in PICO
- Cooper, T. M., Sheehan, M., Collins, D. & O'Connor, T. P. (1996) Soft tissue sarcoma of the extremity. *Annals of the Royal College of Surgeons of England*, 78: 453-456.
Not in PICO
- Costani, G., Rabitti, P., Mambrini, A., Bai, E. & Berrino, F. (2000) Soft tissue sarcomas in the general population living near a chemical plant in Northern Italy. *Tumori*, 86: 381-383.
Not in PICO
- Cutts, S., Andrea, F., Piana, R. & Haywood, R. (2012) The management of soft tissue sarcomas. [Review]. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland*, 10: 25-32.
Narrative review

- Daigeler, A., Vogt, P. M., Busch, K., Pennekamp, W., Weyhe, D., Lehnhardt, M., Steinstraesser, L., Steinau, H. U. & Kuhnen, C. (2007) Elastofibroma dorsi--differential diagnosis in chest wall tumours. *World Journal of Surgical Oncology*, 5: 15.
Not in PICO
- Daigeler, A., Kuhnen, C., Hauser, J., Goertz, O., Tilkorn, D., Steinstraesser, L., Steinau, H. U. & Lehnhardt, M. (2008) Alveolar soft part sarcoma: clinicopathological findings in a series of 11 cases. *World Journal of Surgical Oncology*, 6: 71.
Not in PICO
- Damron, T. A. & Heiner, J. (2000) Distant soft tissue metastases: a series of 30 new patients and 91 cases from the literature. [Review] [55 refs]. *Annals of Surgical Oncology*, 7: 526-534.
Not in PICO
- Damron, T. A., Beauchamp, C. P., Rougraff, B. T. & Ward, W. G. (2003) Soft-tissue lumps and bumps. *Journal of Bone and Joint Surgery - Series A*, 85: 1142-1155.
Narrative review
- Desandes, E., Lacour, B., Sommelet, D., White-Koning, M., Velten, M., Tretarre, B., Marr, A., Maarouf, N., Guizard, A. V., Delafosse, P., Danzon, A., Cotte, C. & Brugieres, L. (2007) Cancer adolescent pathway in France between 1988 and 1997. *European Journal of Oncology Nursing*, 11: 74-81.
Not in PICO
- Desandes, E., Bonnay, S., Berger, C., Brugieres, L., Clavel, J., Isfan, F., Lacour, B., Laurence, V., Sommelet, D. & Tron, I. (2010) Quality of management of adolescents with cancer in France. *Pediatric Blood and Cancer*, 55: 789.
Not in PICO
- Didolkar, M. M., Anderson, M. E., Hochman, M. G., Rissmiller, J. G., Goldsmith, J. D., Gebhardt, M. G. & Wu, J. S. (2013) Image guided core needle biopsy of musculoskeletal lesions: Are nondiagnostic results clinically useful? *Clinical Orthopaedics and Related Research*, 471: 3601-3609.
Not in PICO
- Elliott, R. S., Flint, M. & French, G. (2012) Refer prior to biopsy of suspected appendicular soft tissue sarcoma. *New Zealand Medical Journal*, 125: 12-19.
Not in PICO
- Femiano, F., Cozzolino, S. & Malzone, A. (1990) [Gardner's syndrome]. [Italian]. *Archivio Stomatologico*, 31: 437-439.
Narrative review
- Fleegler, E. J. (1994) An approach to soft tissue sarcomas of the hand and upper limb. *Journal of Hand Surgery*, 19: 411-419.
Narrative review
- Fletcher, C. D. (2008) Undifferentiated sarcomas: what to do? And does it matter? A surgical pathology perspective. *Ultrastructural Pathology*, 32: 31-36.
Not in PICO
- Fletcher, C. D. (2014) - The evolving classification of soft tissue tumours - an update based on the new 2013 WHO classification. [Review]. - *Histopathology*, 64: 2-11.
Narrative review
- Fletcher, C. D. M. (2014) The evolving classification of soft tissue tumours - an update based on the new 2013 WHO classification. *Histopathology*, 64: 2-11.
Narrative review
- Forgie, S. & Robinson, J. (2007) Pediatric malignancies presenting as a possible infectious disease. *BMC Infectious Diseases*, 7: 44.
Not in PICO
- Frink, S. J., Snearly, W. & Parsons 3rd.T.W. (1998) Malignant tumors about the knee. *The American journal of knee surgery*, 11: 257-266.
Narrative review

- Gartner, L., Pearce, C. J. & Saifuddin, A. (2009) The role of the plain radiograph in the characterisation of soft tissue tumours. [Review] [43 refs]. *Skeletal Radiology*, 38: 549-558.
Not in PICO
- George, A. & Grimer, R. (2012) Early symptoms of bone and soft tissue sarcomas: Could they be diagnosed earlier? *Annals of the Royal College of Surgeons of England*, 94: e261-e266.
Not in PICO
- Giudice, G., Cardone, F., Giancaspero, G. & Vollono, E. (1996) Sarcomas of tissues: Risk and prognostic factors. [Italian]. *Rivista Italiana di Chirurgia Plastica*, 28: 95-100.
Narrative review
- Glencross, J., Balasubramanian, S. P., Bacon, J., Robinson, M. H. & Reed, M. W. (2003) An audit of the management of soft tissue sarcoma within a health region in the UK. *European Journal of Surgical Oncology*, 29: 670-675.
Not in PICO
- Gragera, M. B. G., Blanco, F. A. & Garcia, B. F. (1999) Nasopharyngeal cancer presented with cervical nodes. [Spanish]. *MEDIFAM - Revista de Medicina Familiar y Comunitaria*, 9: 50-54.
Narrative review
- Granowetter, L. Pediatric oncology: A medical overview. 9-34. 1994.
Ref Type: Generic
Ref ID: 114
Reprint: Not in File
Abstract: (from the chapter) present basic medical information about childhood cancer / [present] an overview of the characteristics, manifestations, and current thought regarding etiology / [present] information about establishing and explaining the diagnosis and treatment plans to the family / [discuss] the course and general principles of cancer treatment / [discuss] the most common pediatric malignancies [e.g., acute lymphoblastic and nonlymphoblastic leukemia, brain tumors, lymphomas, Wilms' tumor, neuroblastoma, bone tumors and soft tissue sarcomas, and retinoblastoma] / [summarize the] late effects of treatment (PsycINFO Database Record (c) 2012 APA, all rights reserved)
Notes: DB - PsycINFO
AN - Book: 1994-98308-001
SO - Bearison, David J [Ed]; Mulhern, Raymond K [Ed]. (1994). Pediatric psychooncology: Psychological perspectives on children with cancer. (pp. 9-34). xvi, 247 pp. New York, NY, US: Oxford University Press; US
- n
- Grimer, R. J., Taylor, W. S. J., Carter, S. R., Tillman, R. M., Abudu, A. & Jeys, L. (2010) "Two-week waits" - Are they leading to earlier diagnosis of soft-tissue sarcomas? *Sarcoma*, 2010.
Not in PICO
- Grovas, A., Fremgen, A., Rauck, A., Ruymann, F. B., Hutchinson, C. L., Winchester, D. P. & Menck, H. R. (1997) The National Cancer Data Base report on patterns of childhood cancers in the United States. *Cancer*, 80: 2321-2332.
Not in PICO
- Gustafson, P., Dreinhofer, K. E. & Rydholm, A. (1994) Soft tissue sarcoma should be treated at a tumor center. A comparison of quality of surgery in 375 patients. *Acta Orthopaedica Scandinavica*, 65: 47-50.
Not in PICO
- Habrand, J. L. & Le, P. C. (2003) Local control of childhood and adult soft tissue sarcomas. *European Journal of Cancer, Supplement*, 1: 221-236.
Not in PICO

Harms, D. (1995) New entities, concepts, and questions in childhood tumor pathology. *General & diagnostic pathology*, 141: 1-14.
 Narrative review

Hasegawa, T., Matsuno, Y., Shimoda, T., Umeda, T., Yokoyama, R. & Hirohashi, S. (2001) Proximal-type epithelioid sarcoma: a clinicopathologic study of 20 cases. *Modern Pathology*, 14: 655-663.
 Not in PICO

Heim-Hall, J. & Yohe, S. L. (2008) Application of immunohistochemistry to soft tissue neoplasms. [Review] [182 refs]. *Archives of Pathology & Laboratory Medicine*, 132: 476-489.
 Narrative review

Hogh, J., Sneppen, O., Nordentoft, A. M., Jensen, O. M. & Wethelund, J. O. (1988) [Extravisceral soft tissue sarcoma. Basis for referral and prognoses in 145 cases]. [Danish]. *Ugeskrift for Laeger*, 150: 1408-1411.
 Not in PICO

Hooper, G. (2011) Sarcoma services in New Zealand. *New Zealand Medical Journal*, 124: 5-6.
 Not in PICO

Hussein, R. & Smith, M. A. (2005) Soft tissue sarcomas: are current referral guidelines sufficient? *Annals of the Royal College of Surgeons of England*, 87: 171-173.
 Not in PICO

Iqbal, C. W., St, P. S. & Ishitani, M. B. (2011) Pediatric dermatofibrosarcoma protuberans: multi-institutional outcomes. *Journal of Surgical Research*, 170: 69-72.
 Not in PICO

Johnson, G. D., Smith, G., Dramis, A. & Grimer, R. J. (2008) Delays in referral of soft tissue sarcomas. *Sarcoma*, 2008.
 Not in PICO

Joshi, A., Magar, S. R., Chand, P., Panth, R. & Khatri Chhetri, B. R. (2013) Tru-cut biopsy as the initial method of tissue diagnosis in bone tumors with soft tissue extension. *Indian Journal of Orthopaedics*, 47: 195-199.
 Not in PICO

Kim, S., Chun, M., Wang, H., Cho, S., Oh, Y. T., Kang, S. H. & Yang, J. (2007) Bone metastasis from primary hepatocellular carcinoma: characteristics of soft tissue formation. *Cancer Research & Treatment*, 39: 104-108.
 Not in PICO

Kleinerman, R., Schonfeld, S. & Tucker, M. (2012) Sarcomas in Hereditary Retinoblastoma. *Clinical Sarcoma Research*, 2: 15.
 Narrative review

Klosky, J. L. & Spunt, S. L. Sarcoma. [References]. 187-190. 2010.
 Ref Type: Generic
 Ref ID: 113
 Reprint: Not in File
 Abstract: (from the chapter) Bone and soft tissue sarcomas are a heterogeneous group of cancers that arise from primitive mesenchymal cells throughout the body. Population-based data suggest that these cancers account for approximately 0.9% of cancer cases overall, but 13% of cancers in pediatric patients. Aggressive multimodality therapy, including various combinations of surgery, chemotherapy, and radiotherapy, is generally necessary for cure. Currently, the overall 5-year survival rate of patients with bone and soft tissue sarcomas is about two-thirds of that of the general population. Thus, sarcomas produce considerable morbidity as well as mortality. This chapter reviews the major clinical features, treatment, and outcomes of bone and soft tissue sarcomas, and addresses the major psychological issues facing individuals affected by these rare tumors. (PsycINFO Database Record (c) 2012 APA, all rights reserved)
 Notes: DB - PsycINFO
 AN - Book: 2010-06876-025

SO - Holland, Jimmie C [Ed]; Breitbart, William S [Ed]; Jacobsen, Paul B [Ed]; Lederberg, Marguerite S [Ed]; Loscalzo, Matthew J [Ed]; McCorkle, Ruth [Ed]. (2010). *Psycho-oncology* (2nd ed.). (pp. 187-190). xxv, 685 pp. New York, NY, US: Oxford University Press; US

n

Kransdorf, M. J. (1995) Benign soft-tissue tumors in a large referral population: distribution of specific diagnoses by age, sex, and location. *AJR.American Journal of Roentgenology*, 164: 395-402.

Not in PICO

Kurth, W. & Gillet, P. (2006) [Lumps and bumps. Diagnosis and management of soft-tissue tumors]. [Review] [11 refs] [French]. *Revue Medicale de Liege*, 61: 763-770.

Narrative review

Leinung, S., Schonfelder, M. & Wurl, P. (2004) [Differential diagnosis of soft tissue sarcomas]. [German]. *Chirurg*, 75: 1159-1164.

Not in PICO

Leinung, S., Mobius, C., Udelnow, A., Hauss, J. & Wurl, P. (2007) Histopathological outcome of 597 isolated soft tissue tumors suspected of soft tissue sarcoma: a single-center 12-year experience. *European Journal of Surgical Oncology*, 33: 508-511.

Not in PICO

Leithner, A. & Windhager, R. (2007) Bone and soft tissue tumors: Diagnostic principles. [German]. *Wiener Medizinische Wochenschrift*, 157: 21-26.

Narrative review

Lewis, C. & Cutts, S. (2004) Managing soft tissue tumours. *Practitioner*, 248: 828-834.

Narrative review

Leyvraz, S. & Costa, J. (1988) [Interdisciplinary detection of soft tissue sarcomas. Diagnosis, grading and staging]. [Review] [44 refs] [German]. *Orthopade*, 17: 121-127.

Narrative review

Lopez-Terrada, D. (2006) Integrating the diagnosis of childhood malignancies. [Review] [77 refs]. *Advances in Experimental Medicine & Biology*, 587: 121-137.

Narrative review

Luba, M. C., Bangs, S. A., Mohler, A. M. & Stulberg, D. L. (2003) Common benign skin tumors. [Review] [36 refs]. *American Family Physician*, 67: 729-738.

Narrative review

MacIntyre, J. (2007) Pharmacologic application of sunitinib malate in the management of gastrointestinal stromal tumors. [Review] [23 refs]. *Clinical Journal of Oncology Nursing*, 11: 237-241.

Narrative review

Malik, A., Wigney, L., Murray, S. & Gerrand, C. H. (2007) The effectiveness of "two-week" referrals for suspected bone and soft tissue sarcoma. *Sarcoma*, 2007: 23870.

Not in PICO

Mastrangelo, G., Fadda, E., Cegolon, L., Montesco, M. C., Ray-Coquard, I., Buja, A., Fedeli, U., Frasson, A., Spolaore, P. & Rossi, C. R. (2010) A European project on incidence, treatment, and outcome of sarcoma. *BMC Public Health*, 10: 188.

Not in PICO

Mendez, M. C., Muinos, Y., Blanco, G., Saornil, M. A., Garcia-Alvarez, C., Sarasa, J. L. & Valbuena, C. (2012) Embryonal rhabdomyosarcoma of the caruncle in a 4 year-old boy: case report. *Arquivos Brasileiros de Oftalmologia*, 75: 207-209.

Not in PICO

Merchant, S., Cheifetz, R., Knowling, M., Khurshed, F. & McGahan, C. (2012) Practice referral patterns and outcomes in patients with primary retroperitoneal sarcoma in British Columbia.

American Journal of Surgery, 203: 632-638.

Not in PICO

Miettinen, M. (2006) From morphological to molecular diagnosis of soft tissue tumors. [Review] [70 refs]. *Advances in Experimental Medicine & Biology*, 587: 99-113.

Narrative review

Miron, I., Miron, L., Dumitras, S., Aprodu, G., Ciobanu, A. & Tansanu, I. (2007) [Statistical study of the evolution over ten years of the clinical and therapeutic approach in childhood soft tissue sarcoma]. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 111: 358-362.

Not in PICO

Myhre-Jensen, O. (1981) A consecutive 7-year series of 1331 benign soft tissue tumours.

Clinicopathologic data. Comparison with sarcomas. *Acta Orthopaedica Scandinavica*, 52: 287-293.

Not in PICO

Nijhuis, P. H., Schaapveld, M., Otter, R. & Hoekstra, H. J. (2001) Soft tissue sarcoma--compliance with guidelines. *Cancer*, 91: 2186-2195.

Not in PICO

Patel, S. R., Zagars, G. K. & Pisters, P. W. (2003) The follow-up of adult soft-tissue sarcomas. [Review] [15 refs]. *Seminars in Oncology*, 30: 413-416.

Narrative review

Pencavel, T. D., Strauss, D. C., Thomas, G. P., Thomas, J. M. & Hayes, A. J. (2010) Does the two-week rule pathway improve the diagnosis of soft tissue sarcoma? A retrospective review of referral patterns and outcomes over five years in a regional sarcoma centre. *Annals of the Royal College of Surgeons of England*, 92: 417-421.

Not in PICO

Penel, N., Valentin, F., Giscard, S., Vanseymortier, L. & Beuscart, R. (2007) General practitioners assessment of a structured report on medical decision making by a regional multidisciplinary cancer committee. *Bulletin du Cancer*, 94: E23-E26.

Not in PICO

Perrier, L., Buja, A., Mastrangelo, G., Vecchiato, A., Sandona, P., Ducimetiere, F., Blay, J. Y., Gilly, F. N., Siani, C., Biron, P., Ranchere-Vince, D., Decouvelaere, A. V., Thiesse, P., Bergeron, C., Dei Tos, A. P., Coindre, J. M., Rossi, C. R. & Ray-Coquard, I. (2012) Clinicians' adherence versus non adherence to practice guidelines in the management of patients with sarcoma: a cost-effectiveness assessment in two European regions. *BMC Health Services Research*, 12: 82.

Not in PICO

Persson, B. M. & Rydholm, A. (1986) Soft-tissue masses of the locomotor system. A guide to the clinical diagnosis of malignancy. *Acta Orthopaedica Scandinavica*, 57: 216-219.

Not in PICO

Pignolo, R. J., Shore, E. M. & Kaplan, F. S. (2011) Fibrodysplasia ossificans progressiva: clinical and genetic aspects. [Review]. *Orphanet Journal Of Rare Diseases*, 6: 80.

Narrative review

Pinkerton, R., Sommelet, D., Brunat-Mentigny, M., Farsi, F., Martel, I., Philip, T., Ranchere-Vince, D. & Thiesse, P. (1998) Standards, Options and Recommendations (SOR) for clinical care of rhabdomyosarcoma (RMS) and other soft tissue sarcoma in children. *Bulletin du Cancer*, 85: 1015-1042.

Guideline

Pitcher, M. E., Fish, S. & Thomas, J. M. (1994) Management of soft tissue sarcoma. *British Journal of Surgery*, 81: 1136-1139.

Not in PICO

- Plate, A. M., Steiner, G. & Posner, M. A. (2006) Malignant tumors of the hand and wrist. *The Journal of the American Academy of Orthopaedic Surgeons*, 14: 680-692.
Narrative review
- Prakash, P. K. & Hanna, F. W. (2006) Differential diagnosis of neck lumps. [Review] [2 refs]. *Practitioner*, 246: 252-254.
Narrative review
- Qadir, I., Umer, M., Umer, H., Uddin, N., Karsan, F. & Rabbani, S. (2012) Managing soft tissue sarcomas in a developing country: are prognostic factors similar to those of developed world? *World Journal of Surgical Oncology*, 10: 188.
Not in PICO
- Raees-Karami, S. R., Jafarieh, H., Ziyayi, V., Foumani, R. S. & Aghighi, Y. (2012) Evaluation of 20 years experience of fibrodysplasia ossificans progressiva in Iran: Lessons for early diagnosis and prevention. *Clinical Rheumatology*, 31: 1133-1137.
Not in PICO
- Ramos-Pascua, L. R., Sanchez-Herraez, S., Casas-Ramos, P., Izquierdo-Garcia, F. J. & Maderuelo-Fernandez, J. A. (2014) - [Health care circuit for patients with soft tissue sarcomas of the extremities. A tortuous and slow road to referral units]. [Spanish]. - *Revista Espanola de Cirugia Ortopedica y Traumatologia*, 58: 160-170.
Not in PICO
- Randall, R. L., Mann, J. A. & Johnston, J. O. (1996) Orthopedic soft-tissue tumors. Concepts for the primary care physician. [Review] [51 refs]. *Primary Care; Clinics in Office Practice*, 23: 241-261.
Narrative review
- Randall, R. L., Bruckner, J. D., Papenhausen, M. D., Thurman, T. & Conrad, E. U., III (2004) Errors in diagnosis and margin determination of soft-tissue sarcomas initially treated at non-tertiary centers. *Orthopedics*, 27: 209-212.
Not in PICO
- Ray-Coquard, I., Thiesse, P., Ranchere-Vince, D., Chauvin, F., Bobin, J. Y., Sunyach, M. P., Carret, J. P., Mongodin, B., Marec-Berard, P., Philip, T. & Blay, J. Y. (2004) Conformity to clinical practice guidelines, multidisciplinary management and outcome of treatment for soft tissue sarcomas. *Annals of Oncology*, 15: 307-315.
Not in PICO
- Rigor, B. M., Sr. (2000) Pelvic cancer pain. [Review] [46 refs]. *Journal of Surgical Oncology*, 75: 280-300.
Narrative review
- Romanus, B., Lindahl, S. & Stener, B. (1986) Accessory soleus muscle. A clinical and radiographic presentation of eleven cases. *Journal of Bone & Joint Surgery - American Volume*, 68: 731-734.
Not in PICO
- Rooser, B., Rydholm, A. & Alvegard, T. (1987) Centralization of soft tissue sarcoma. Status in Sweden in 1982. *Acta Orthopaedica Scandinavica*, 58: 641-644.
Not in PICO
- Rose, C., Stovall, E., Ganz, P. A., Desch, C. & Hewitt, M. (2008) Cancer Quality Alliance: Blueprint for a better cancer care system. *CA: A Cancer Journal for Clinicians*, 58: 266-292.
Narrative review/not in PICO
- Rougraff, B. T., Lawrence, J. & Davis, K. (2012) Length of symptoms before referral: prognostic variable for high-grade soft tissue sarcoma? *Clinical Orthopaedics & Related Research*, 470: 706-711.
Not in PICO
- Rydholm, A. (1992) Soft tissue lesions in adults: biopsy--yes or no? *Annals of Oncology*, 3: Suppl-8.
Not in PICO

- Rydholm, A. (1997) Centralization of soft tissue sarcoma. The southern Sweden experience. *Acta Orthopaedica Scandinavica.Supplementum*, 273: 4-8.
Not in PICO
- Seleye-Fubara, D., Nwosu, S. O. & Yellowe, B. E. (2005) Soft tissue sarcomas in the Niger Delta Region of Nigeria (a referral hospital's study).[Erratum appears in Niger J Med. 2005 Oct-Dec;14(4):461 Note: Bob-Yellowe, E [corrected to Yellowe, BE]]. *Nigerian Journal of Medicine: Journal of the National Association of Resident Doctors of Nigeria*, 14: 188-194.
Not in PICO
- Shah, H., Bhurgri, Y. & Pervez, S. (2005) Malignant Smooth Muscle Tumours of Soft Tissue - A demographic and clinicopathological study at a tertiary care hospital. *Journal of the Pakistan Medical Association*, 55: 138-143.
Not in PICO
- Sharif, M. A. & Hamdani, S. N. (2010) Second opinion and discrepancy in the diagnosis of soft tissue lesions at surgical pathology. *Indian journal of pathology & microbiology*, 53: 460-464.
Not in PICO
- Sinha, S. & Peach, A. H. (2010) Diagnosis and management of soft tissue sarcoma. [Review]. *BMJ*, 341: c7170.
Narrative review
- Stachowicz-Stencel, T. & Bien, E. (2007) Bone pains in malignant disorders in children. *Family Medicine and Primary Care Review*, 9: 859-861.
Narrative review
- Strauss, D. C., Qureshi, Y. A., Hayes, A. J., Thway, K., Fisher, C. & Thomas, J. M. (2010) The role of core needle biopsy in the diagnosis of suspected soft tissue tumours. *Journal of Surgical Oncology*, 102: 523-529.
Not in PICO
- Styring, E., Billing, V., Hartman, L., Nilbert, M., Seinen, J. M., Veurink, N., Vult von, S. F. & Rydholm, A. (2012) Simple guidelines for efficient referral of soft-tissue sarcomas: a population-based evaluation of adherence to guidelines and referral patterns. *Journal of Bone & Joint Surgery - American Volume*, 94: 1291-1296.
Not in PICO
- Thway, K. & Fisher, C. (2009) Histopathological diagnostic discrepancies in soft tissue tumours referred to a specialist centre. *Sarcoma*, 2009.
Not in PICO
- Trishkin, V. A. & Stoliarov, V. I. (1988) [Difficulties and errors in the ambulatory diagnosis of soft tissue sarcomas]. [Russian]. *Khirurgiia.(11):100-3, 1988 Nov.*, 100-103.
Russian. Looks like narrative review
- Trishkin, V. A., Vesnin, A. G., Stoliarov, V. I., Semenov, I. I., Novikov, A. I. & Chibisova, M. A. (1994) [A comparative analysis of the current methods for the outpatient diagnosis of soft tissue tumors]. [Russian]. *Vestnik Khirurgii Imeni i - i - Grekova*, 152: 93-98.
Not in PICO
- Tsel', E. A. (1986) [Complex diagnosis of soft tissue tumors under ambulatory conditions]. [Russian]. *Voprosy Onkologii*, 32: 68-71.
Not in PICO
- Tunn, P.-U. & Schlag, P. M. (1995) Early detection of soft tissue and limbs tumours. [German]. *Onkologie*, 18: 61-63.
Narrative review
- Venkatesan, M., Richards, C. J., McCulloch, T. A., Perks, A. G., Raurell, A., Ashford, R. U. & East Midlands Sarcoma Service (2012) Inadvertent surgical resection of soft tissue sarcomas. *European Journal of Surgical Oncology*, 38: 346-351.
Not in PICO

Vogt, T. (249) [Angiosarcoma]. [Review] [27 refs] [German]. *Hautarzt*, 59: 237-248.

Narrative review

Warzecha, J., Kamand, A., Daecke, W. & Meurer, A. (2010) [Benign soft tissue tumors in orthopedics]. [Review] [German]. *Orthopade*, 39: 1171-1180.

Narrative review

Weber, R., Knaup, P., Knietitg, R., Haux, R., Merzweiler, A., Mludek, V., Schilling, F. H. & Wiedemann, T. (2001) Object-oriented business process analysis of the cooperative soft tissue sarcoma trial of the german society for paediatric oncology and haematology (GPOH). *Studies in Health Technology & Informatics*, 84: 1-62.

Not in PICO

Williams, J. E., Kuo, P. Y., Yen, J. T. C., Parker, G. M., Chapman, S., Kandikattu, S., Sohanpal, I. & Barbachano, Y. (2011) The prevalence of pain in patients attending sarcoma outpatient clinics. *Sarcoma*, 2011.

Not in PICO

Williams, K. J. & Hayes, A. J. (2014) - A guide to oncological management of soft tissue tumours of the abdominal wall. - *Hernia*, 18: 91-97.

Narrative review/Not in PICO

Zacherl, M., Kastner, N., Glehr, M., Scheipl, S., Schwantzer, G., Koch, H., Leithner, A. & Windhager, R. (2012) Influence of prereferral surgery in soft tissue sarcoma: 10 years' experience in a single institution. *Orthopedics*, 35: e1214-e1220.

Not in PICO

Review question:

Which investigations of symptoms of suspected soft tissue sarcoma should be done with clinical responsibility retained by primary care?

Results

Literature search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	164	33	20/06/2013
Premedline	1980-2013	14	3	24/06/2013
Embase	1980-2013	145	51	24/06/2013
Cochrane Library	1980-2013	34	3	24/06/2013
Psychinfo	1980-2013	0	0	24/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	47	10	24/06/2013

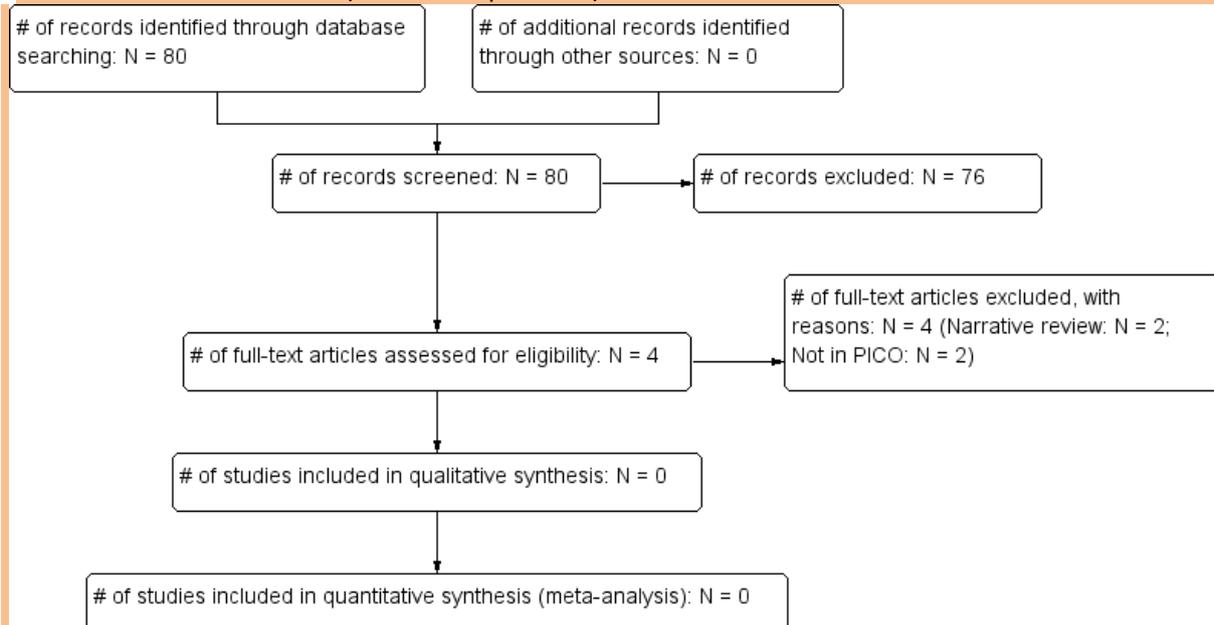
Total References retrieved (after de-duplication): 74

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	6/2013-26/08/2014	3	0	26/08/2014
Premedline	6/2013-26/08/2014	17	2	26/08/2014
Embase	6/2013-26/08/2014	21	3	26/08/2014
Cochrane Library	6/2013-26/08/2014	10	0	26/08/2014

Web of Science (SCI & SSCI) and ISI Proceedings	6/2013-26/08/2014	11	1	26/08/2014
--	-------------------	----	---	------------

Total References retrieved (after de-duplication): 6



Study results

No evidence was identified pertaining to the diagnostic accuracy of ultrasound in patients with suspected soft tissue sarcoma where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

Abellan, J. F., Lamo De Espinosa, J. M., Duart, J., Patino-Garcia, A., Martin-Algarra, S., Martinez-Monge, R. & San-Julian, M. (2009) Nonreferral of possible soft tissue sarcomas in adults: A dangerous omission in policy. *Sarcoma*, 2009.

Not in PICO

Aboulafia, A. J., Levin, A. M. & Blum, J. (2002) Prereferral evaluation of patients with suspected bone and soft tissue tumors. *Clinical Orthopaedics and Related Research*, 83-88.

Not in PICO

Adams, S. C., Potter, B. K., Pitcher, D. J. & Temple, H. T. (2010) Office-based core needle biopsy of bone and soft tissue malignancies: an accurate alternative to open biopsy with infrequent complications. *Clinical Orthopaedics and Related Research*, 468: 2774-2780.

Not in PICO

Akerman, M., Idvall, I. & Rydholm, A. (1980) Cytodiagnosis of soft tissue tumors and tumor-like conditions by means of fine needle aspiration biopsy. *Archives of Orthopaedic and Traumatic Surgery*, 96: 61-67.

Not in PICO

Andreou, D. & Tunn, P. U. (2009) Sentinel node biopsy in soft tissue sarcoma. *Recent Results in Cancer Research*, Fortschritte: 25-36.

Narrative review

- Arya, S., Nagarkatti, D. G., Dudhat, S. B., Nadkarni, K. S., Joshi, M. S. & Shinde, S. R. (2000) Soft tissue sarcomas: Ultrasonographic evaluation of local recurrences. *Clinical Radiology*, 55: 193-197.
Not in PICO
- Bastiaannet, E., Groen, H., Jager, P. L., Cobben, D. C., Graaf, W. T., Vaalburg, W. & Hoekstra, H. J. (2004) The value of FDG-PET in the detection, grading and response to therapy of soft tissue and bone sarcomas: a systematic review and meta-analysis (DARE structured abstract). *Cancer Treatment Reviews*, 30: 83-101.
Not in PICO
- Bennis, M., Dalsing, M., Sawchuck, A. & Wurtz, L. D. (2006) Soft tissue sarcomas may present with deep vein thrombosis. *Journal of Vascular Surgery*, 43: 788-793.
Not in PICO
- Benson, C. & Judson, I. (2014) Role of expert centres in the management of sarcomas - A UK perspective. *European Journal of Cancer*, 50: 1951-1956.
Narrative review
- Bredella, M. A., Caputo, G. R. & Steinbach, L. S. (2002) Value of FDG positron emission tomography in conjunction with MR imaging for evaluating therapy response in patients with musculoskeletal sarcomas. *American Journal of Roentgenology*, 179: 1145-1150.
Not in PICO
- Bui, B. N., Blay, J. Y., Bonichon, F., Bonvalot, S., Chevalier-Place, A., Coindre, J. M., Delannes, M., Le Cesne, A., Morice, P., Ray-Coquard, I., Pautier, P., Le Pechoux, C., Stoeckle, E., Taieb, S. & Bosquet, L. (2007) Clinical practice guidelines: 2006. Update of recommendations for the management of patients with soft tissue sarcoma (sarcoma of the extremity, uterine sarcoma and retroperitoneal sarcoma). *Oncologie*, 9: 173-177.
Not in PICO
- Bui, N. B., Stockle, E., Coindre, J. M., Kantor, G., Kind, M. & Thomas, L. (1996) Locally advanced soft tissue sarcoma of the thoracic wall. *Bulletin du Cancer*, 83: 335-343.
Not in PICO
- Coates, M. (2003) Ultrasound and soft-tissue mass lesions - A note of caution. *New Zealand Medical Journal*, 116.
Narrative review
- Coffin, C. M. & Dehner, L. P. (1998) Pathologic evaluation of pediatric soft tissue tumors. *American Journal of Clinical Pathology*, 109: S38-S52.
Narrative review
- Comandone, A., Berno, E., Boglione, A., Oliva, C., Ingui, M., Linari, A., Giubellino, E., Gino, G., Del Prever, E. M. B., Faletti, C., Piana, R., Turbiglio, M., Monasterolo, G., Pochettino, P., Dal, C. O., Cutin, S. C. & Bergnolo, P. (2012) Delay in diagnosis and treatment of soft tissue sarcomas (STS): Causes of late intervention and their role in prognosis-A prospective, multidisciplinary group study. *Journal of Clinical Oncology*, 30.
Not in PICO
- Datir, A., James, S. L. J., Ali, K., Lee, J., Ahmad, M. & Saifuddin, A. (2008) MRI of soft-tissue masses: the relationship between lesion size, depth, and diagnosis. *Clinical Radiology*, 63: 373-378.
Not in PICO
- Didolkar, M. M., Anderson, M. E., Hochman, M. G., Rissmiller, J. G., Goldsmith, J. D., Gebhardt, M. G. & Wu, J. S. (2013) Image guided core needle biopsy of musculoskeletal lesions: Are nondiagnostic results clinically useful? *Clinical Orthopaedics and Related Research*, 471: 3601-3609.
Not in PICO
- Domett, R., Stevens, M., Redaniel, T., Hamilton, W. & Martin, R. (2013) Features of cancer in teenagers and young adults (TYA) presenting to primary care in the uk: A population-based nested case-control study. *Pediatric Blood and Cancer*, 60: 3.
Already included

- Elliott, R. S., Flint, M. & French, G. (2012) Refer prior to biopsy of suspected appendicular soft tissue sarcoma. *New Zealand Medical Journal*, 125: 12-19.
Not in PICO
- Eyesan, S. U., Idowu, O. K. & Mbah, O. (2014) Referral for bone and soft tissue tumors: New pathway for resource constrained health care systems. *Journal of Clinical Oncology*, 32.
Not in PICO
- Fisher, C. & Thway, K. (2006) Pathology of tumours of soft tissue. *Surgery*, 24: 402-406.
Narrative review
- Fleming, J. B., Cantor, S. B., Varma, D. G. K., Holst, D., Feig, B. W., Hunt, K. K., Patel, S. R., Benjamin, R. S., Pollock, R. E. & Pisters, P. W. T. (2001) Utility of chest computed tomography for staging in patients with T1 extremity soft tissue sarcomas. *Cancer*, 92: 863-868.
Not in PICO
- Fletcher, C. D. M. (2014) The evolving classification of soft tissue tumours - an update based on the new 2013 WHO classification. *Histopathology*, 64: 2-11.
Narrative review
- Hayes, A. J., Alexander, N., Clark, M. A. & Thomas, J. M. (2004) Elastofibroma: A rare soft tissue tumour with a pathognomonic anatomical location and clinical symptom. *European Journal of Surgical Oncology*, 30: 450-453.
Not in PICO
- Heim-Hall, J. & Yohe, S. L. (2008) Application of immunohistochemistry to soft tissue neoplasms. *Archives of Pathology and Laboratory Medicine*, 132: 476-489.
Narrative review
- Hoglund, M., Muren, C. & Brattstrom, G. (1997) A statistical model for ultrasound diagnosis of soft-tissue tumours in the hand and forearm. *Acta radiologica (Stockholm, Sweden : 1987)*, 38: 355-358.
Not in PICO
- Ioannidis, J. P. & Lau, J. (2002) Positron emission tomography (FDG) for soft tissue sarcoma (STS) (DARE structured abstract). *Database of Abstracts of Reviews of Effects.*, 57.
Not in PICO
- Jager, P. L., Plaat, B. E., de Vries, E. G., Molenaar, W. M., Vaalburg, W., Piers, D. A. & Hoekstra, H. J. (2000) Imaging of soft-tissue tumors using L-3-[iodine-123]iodo-alpha-methyl-tyrosine single photon emission computed tomography: comparison with proliferative and mitotic activity, cellularity, and vascularity. *Clinical Cancer Research*, 6: 2252-2259.
Not in PICO
- Joshi, A., Magar, S. R., Chand, P., Panth, R. & Khatri Chhetri, B. R. (2013) Tru-cut biopsy as the initial method of tissue diagnosis in bone tumors with soft tissue extension. *Indian Journal of Orthopaedics*, 47: 195-199.
Not in PICO
- Karpeh, M. S., Brennan, M. F., Cance, W. G., Woodruff, J. M., Pollack, D., Casper, E. S., Dudas, M. E., Latres, E., Drobnjak, M. & Cordon-Cardo, C. (1995) Altered patterns of retinoblastoma gene product expression in adult soft-tissue sarcomas. *British Journal of Cancer*, 72: 986-991.
Not in PICO
- Kaufman, M., Pinkenson, M., Krigmont, M. & Weissberg, D. (1980) Fine needle aspiration for cytologic diagnosis. [Hebrew]. *Harefuah*, 98: 105-106+148.
Not in PICO
- Kind, M., Stock, N. & Coindre, J. M. (2009) Histology and imaging of soft tissue sarcomas. *European Journal of Radiology*, 72: 6-15.
Narrative review
- Lakkaraju, A., Sinha, R., Garikipati, R., Edward, S. & Robinson, P. (2009) Ultrasound for initial evaluation and triage of clinically suspicious soft-tissue masses. *Clinical Radiology*, 64: 615-621.
Not in PICO

- Le Bleu, P. T. & Steffes, J. (2014) Malignant fibrous histiocytoma: An evaluation of what lies beneath. *Journal of the American Academy of Dermatology*, 70: AB48.
Not in PICO
- Lewis, C. & Cutts, S. (2004) Managing soft tissue tumours. *Practitioner*, 248: 828-834.
Narrative review
- Leyvraz, S. & Costa, J. (1988) Interdisciplinary detection of soft tissue sarcomas. Diagnosis, grading and staging. [German]. *Der Orthopade*, 17: 121-127.
Narrative review
- Leyvraz, S. & Costa, J. (1988) Histological diagnosis and grading of soft-tissue sarcomas. *Seminars in Surgical Oncology*, 4: 3-6.
Narrative review
- Liu, J. C., Chiou, H. J., Chen, W. M., Chou, Y. H., Chen, T. H., Chen, W., Yen, C. C., Chiu, S. Y. & Chang, C. Y. (2004) Sonographically guided core needle biopsy of soft tissue neoplasms. *Journal of Clinical Ultrasound*, 32: 294-298.
Not in PICO
- Lucas, J. D., O'Doherty, M. J., Cronin, B. F., Marsden, P. K., Lodge, M. A., McKeet, P. H. & Smith, M. A. (1999) Prospective evaluation of soft tissue masses and sarcomas using fluorodeoxyglucose positron emission tomography. *British Journal of Surgery*, 86: 550-556.
Not in PICO
- Marcantonio, D. R., Weatherall, P. T. & Berrey Jr, B. H. (1998) Practical considerations in the imaging of soft tissue tumors. *Orthopedic Clinics of North America*, 29: 1-17.
Narrative review
- Marzano, L., Failoni, S., Gallazzi, M. & Garbagna, P. (2004) The role of diagnostic imaging in synovial sarcoma. Our experience. [Italian, English]. *Radiologia Medica*, 107: 533-540.
Not in PICO
- Mastrangelo, G., Fadda, E., Cegolon, L., Montesco, M. C., Ray-Coquard, I., Buja, A., Fedeli, U., Frasson, A., Spolaore, P. & Rossi, C. R. (2010) A European project on incidence, treatment, and outcome of sarcoma. *BMC Public Health*, 10: 188.
Not in PICO
- Mende, U., Ewerbeck, V., Krempien, B., Ludwig, R., Peichardt, P., Troger, J., Zoller, J. & Braun, A. (1992) Sonography in the therapy-related diagnosis and follow-up of primary bone and soft tissue tumors. [German]. *Bildgebung/Imaging*, 59: 4-14.
Not in PICO
- Miron, I., Miron, L., Dumitras, S., Aprodu, G., Ciobanu, A. & Tansanu, I. (2007) Statistical study of the evolution over ten years of the clinical and therapeutic approach in childhood soft tissue sarcoma. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 111: 358-362.
Not in PICO
- Mohr, Z., Hirche, C., Klein, T., Kneif, S. & Hunerbein, M. (2012) Vacuum-assisted minimally invasive biopsy of soft-tissue tumors. *Journal of Bone and Joint Surgery - Series A*, 94: 103-109.
Not in PICO
- Myhre-Jensen, O. (1981) A consecutive 7-year series of 1331 benign soft tissue tumours. Clinicopathologic data. Comparison with sarcomas. *Acta Orthopaedica Scandinavica*, 52: 287-293.
Not in PICO
- Narvani, A. A., Tsiridis, E., Saifuddin, A., Briggs, T. & Cannon, S. (2009) Does image guidance improve accuracy of core needle bio in diagnosis of soft tissue tumours? *Acta Orthopaedica Belgica*, 75: 239-244.
Not in PICO

- Neeff, H. & Imdahl, A. (2005) Soft-tissue tumors: primary excision or wait and see?. [German]. *MMW Fortschritte der Medizin*, 147: 41-43.
Narrative review
- Nishimura, H. (2001) Diagnosis of soft tissue tumors: 10 checkpoints. [Japanese]. *Nihon Igaku Hoshasen Gakkai zasshi*, Nippon: 275-291.
Narrative review
- Nobauer-Huhmann, I. M. (2014) - [Soft tissue tumors : Imaging strategy for local primary diagnostics - manifestation, pearls and pitfalls in MRI]. [German]. - *Radiologe*, 54: 803-818.
Narrative review
- Noebauer-Huhmann, I., Krssak, M., Amann, G., Panotopoulos, J., Funovics, P., Fruehwald-Pallamar, J., Weber, M., Kainberger, F. & Trattnig, S. (2011) Soft tissue tumours at 3 Tesla MRI: Influence of a myxoid matrix on diffusion weighted imaging. *Skeletal Radiology*, 40: 811.
Not in PICO
- Papandreou, I., Moschouris, H., Papadopoulos, G., Papadaki, E., Gerle, Z. & Papadaki, M. (2011) Ultrasound and color doppler imaging in the evaluation of soft tissue lumps in infants and children. *Acta Paediatrica, International Journal of Paediatrics*, 100: 52.
Not in PICO
- Pedersen, L., Balslev, I., Guldhammer, B. & Rose, C. (1988) Repeated fine needle aspirations in the diagnosis of soft tissue metastases in breast cancer. *European Journal of Cancer and Clinical Oncology*, 24: 1039-1040.
Not in PICO
- Pencavel, T. D., Strauss, D. C., Thomas, G. P., Thomas, J. M. & Hayes, A. J. (2010) Does the two-week rule pathway improve the diagnosis of soft tissue sarcoma? A retrospective review of referral patterns and outcomes over five years in a regional sarcoma centre. *Annals of the Royal College of Surgeons of England*, 92: 417-421.
Not in PICO
- Penel, N., Valentin, F., Giscard, S., Vanseymortier, L. & Beuscart, R. (2007) General practitioners assessment of a structured report on medical decision making by a regional multidisciplinary cancer committee. *Bulletin du Cancer*, 94: E23-E26.
Not in PICO
- Perek-Polnik, M., Filipek, I., Dembowska-Baginska, B., Owsik, A., Drogosiewicz, M., Jurkiewicz, E. & Perek, D. (2006) [Children with neurofibroma type 1 treated in the Children's Memorial Health Institute]. [Polish]. *Medycyna Wieku Rozwojowego*, 10: 699-709.
Not in PICO
- Pinkerton, R., Sommelet, D., Brunat-Mentigny, M., Farsi, F., Martel, I., Philip, T., Ranchere-Vince, D. & Thiesse, P. (1998) Standards, Options and Recommendations (SOR) for clinical care of rhabdomyosarcoma (RMS) and other soft tissue sarcoma in children. *Bulletin du Cancer*, 85: 1015-1042.
Guideline
- Porter, G. A., Cantor, S. B., Ahmad, S. A., Lenert, J. T., Ballo, M. T., Hunt, K. K., Feig, B. W., Patel, S. R., Benjamin, R. S., Pollock, R. E. & Pisters, P. W. (2002) Cost-effectiveness of staging computed tomography of the chest in patients with T2 soft tissue sarcomas (Structured abstract). *Cancer*, 94: 197-204.
Not in PICO
- Qureshi, Y., Strauss, D., Hayes, A. & Thomas, J. (2009) Accuracy of core needle biopsy in the diagnosis of soft tissue tumours. *European Journal of Surgical Oncology*, 35: 1210-1211.
Not in PICO
- Rahim, R. R., Schenker, M., Barry, R. B. M. & Langtry, J. A. A. (2011) Lack of consensus in the surgical treatment of cutaneous granular cell tumours. *British Journal of Dermatology*, 165: 102.
Not in PICO

- Randall, R. L., Mann, J. A. & Johnston, J. O. (1996) Orthopedic soft-tissue tumors - Concepts for the primary care physician. *Primary Care*, 23: 241-&. Narrative review
- Randall, R. L., Bruckner, J. D., Papenhausen, M. D., Thurman, T. & Conrad III, E. U. (2004) Errors in diagnosis and margin determination of soft-tissue sarcomas initially treated at non-tertiary centers. *Orthopedics*, 27: 209-212. Not in PICO
- Ray-Coquard, I., Thiesse, P., Ranchere-Vince, D., Chauvin, F., Bobin, J. Y., Sunyach, M. P., Carret, J. P., Mongodin, B., Marec-Berard, P., Philip, T. & Blay, J. Y. (2004) Conformity to clinical practice guidelines, multidisciplinary management and outcome of treatment for soft tissue sarcomas. *Annals of Oncology*, 15: 307-315. Not in PICO
- Roic, G., Ercegovic, S., Vlahovic, T., Cop, S., Bumci, I. & Visnjic, S. (1999) Sonographic diagnosis of soft-tissue foreign bodies in children. *Radiology and Oncology*, 33: 189-192. Not in PICO
- Rosenthal, T. C. & Kraybill, W. (1999) Soft tissue sarcomas: Integrating primary care recognition with tertiary care center treatment. *American Family Physician*, 60: 567-572. Narrative review
- Rowbotham, E., Bhuva, S., Gupta, H. & Robinson, P. (2012) Assessment of referrals into the soft tissue sarcoma service: Evaluation of imaging early in the pathway process. *Sarcoma*, 2012. Not in PICO
- Rydholm, A., Akerman, M., Idvall, I. & Persson, B. M. (1982) Aspiration cytology of soft tissue tumours. A prospective study of its influence on choice of surgical procedure. *International Orthopaedics*, 6: 209-214. Not in PICO
- Rydholm, A. (1983) Management of patients with soft-tissue tumors. Strategy developed at a regional oncology center. *Acta Orthopaedica Scandinavica*, 54. Not in PICO
- Sakata, K., Johnson, F. E., Beitler, A. L., Kraybill, W. G. & Virgo, K. S. (2003) Extremity soft tissue sarcoma patient follow-up: tumor grade and size affect surveillance strategies after potentially curative surgery. *International Journal of Oncology*, 22: 1335-1343. Not in PICO
- Schatz, J., Soper, J., McCormack, S., Healy, M., Deady, L. & Brown, W. (2008) Imaging of tumors in the ankle and foot. *Techniques in Foot and Ankle Surgery*, 7: 208-223. Narrative review
- Schmitt, R., Warmuth-Metz, M., Lanz, U., Lucas, D., Feyerabend, T. & Schindler, G. (1990) [Computed tomography of soft tissue tumors of the hand and the forearm]. [German]. *Radiologe*, 30: 185-192. Not in PICO
- Schulte, M., Brecht-Krauss, D., Heymer, B., Guhlmann, A., Hartwig, E., Sarkar, M. R., Diederichs, C. G., Schultheiss, M., Kotzerke, J. & Reske, S. N. (1999) Fluorodeoxyglucose positron emission tomography of soft tissue tumours: is a non-invasive determination of biological activity possible? *European Journal of Nuclear Medicine*, 26: 599-605. Not in PICO
- Seleye-Fubara, D., Nwosu, S. O. & Yellowe, B. E. (2005) Soft tissue sarcomas in the Niger Delta Region of Nigeria (a referral hospital's study). *Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria*, 14: 188-194. Not in PICO
- Silk, A. W. & Schuetze, S. M. (2012) Histology-specific therapy for advanced soft tissue sarcoma and benign connective tissue tumors. *Current Treatment Options in Oncology*, 13: 285-298. Not in PICO

- Strauss, D. C., Qureshi, Y. A., Hayes, A. J., Thway, K., Fisher, C. & Thomas, J. M. (2010) The role of core needle biopsy in the diagnosis of suspected soft tissue tumours. *Journal of Surgical Oncology*, 102: 523-529.
Not in PICO
- Suresh, S., Saifuddin, A. & O'Donnell, P. (2008) Lymphoma presenting as a musculoskeletal soft tissue mass: MRI findings in 24 cases. *European Radiology*, 18: 2628-2634.
Not in PICO
- Thunnissen, F. B. J. M., Kroese, A. H., Ambergen, A. W., Peterse, J. L., Jansen, J. W., Ladde, B. E., vanPel, R., Tiebosch, A. T. M. G. & Schaafsma, W. (1997) Which cytological criteria are the most discriminative to distinguish carcinoma, lymphoma, and soft-tissue sarcoma? A probabilistic approach. *Diagnostic Cytopathology*, 17: 333-338.
Not in PICO
- Thway, K. & Fisher, C. (2009) Histopathological diagnostic discrepancies in soft tissue tumours referred to a specialist centre. *Sarcoma*, 2009.
Not in PICO
- Trishkin, V. A. & Bykov, S. A. (1988) [Direct angioscintigraphy of soft tissue sarcomas in outpatient diagnosis]. [Russian]. *Voprosy Onkologii*, 34: 1374-1378.
Not in PICO
- Trishkin, V. A., Vesnin, A. G., Stoliarov, V. I., Semenov, I. I., Novikov, A. I. & Chibisova, M. A. (1994) [A comparative analysis of the current methods for the outpatient diagnosis of soft tissue tumors]. [Russian]. *Vestnik Khirurgii Imeni i - i - Grekova*, 152: 93-98.
Narrative review
- Tsukushi, S., Nishida, Y., Wasa, J., Urakawa, H. & Ishiguro, N. (2011) Clinicopathological assessment of T1 soft tissue sarcomas. *Archives of Orthopaedic and Trauma Surgery*, 131: 695-699.
Not in PICO
- Wainwright, K. & Wegner, E. (2013) Incidental finding of a soft tissue sarcoma on bone scan. *Internal Medicine Journal*, 43: 26-27.
Not in PICO
- Waldt, S., Rechl, H., Rummeny, E. J. & Woertler, K. (2003) Imaging of benign and malignant soft tissue masses of the foot. [Review] [34 refs]. *European Radiology*, 13: 1125-1136.
Narrative review

CHILDHOOD CANCERS

NEUROBLASTOMA, RETINOBLASTOMA, WILM'S TUMOUR

Review question:

What is the risk of neuroblastoma, retinoblastoma and Wilm's tumour in children presenting in primary care with symptom(s)?

Results

Literature search

Neuroblastoma:

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	384	29	14/11/2012
<i>Premedline</i>	All-2012	19	0	14/11/2012
<i>Embase</i>	All-2012	198	28	14/11/2012
<i>Cochrane Library</i>	All-2012	59	1	14/11/2012
<i>Psychinfo</i>	All-2012	14	0	14/11/2012
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	All-2012	33	5	14/11/2012
<i>Biomed Central</i>	All-2012	166	1	14/11/2012

Total References retrieved (after de-duplication): 45

Neuroblastoma: Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	11/2012-27/08/2014	8	1	27/08/2014
<i>Premedline</i>	11/2012-27/08/2014	49	1	27/08/2014
<i>Embase</i>	11/2012-27/08/2014	62	2	27/08/2014
<i>Cochrane Library</i>	11/2012-27/08/2014	21	0	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	11/2012-27/08/2014	6	1	27/08/2014

Total References retrieved (after de-duplication): 5

Retinoblastoma:

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	All-2012	576	62	15/11/2012
<i>Premedline</i>	All-2012	13	3	14/11/2012
<i>Embase</i>	All-2012	386	62	15/11/2012
<i>Cochrane Library</i>	All-2012	67	0	15/11/2012
<i>Psychinfo</i>	All-2012	1	0	15/11/2012
<i>Web of Science (SCI</i>	All-2012	30	8	15/11/2012

& SSCI) and ISI Proceedings				
Biomed Central	All-2012	75	0	15/11/2012

Total References retrieved (after de-duplication): 83

Retinoblastoma: Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	11/2012-27/08/2014	28	4	27/08/2014
Premedline	11/2012-27/08/2014	31	1	27/08/2014
Embase	11/2012-27/08/2014	51	2	27/08/2014
Cochrane Library	11/2012-27/08/2014	64	1	27/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	11/2012-27/08/2014	10	0	27/08/2014

Total References retrieved (after de-duplication): 4

Wilm's tumour:

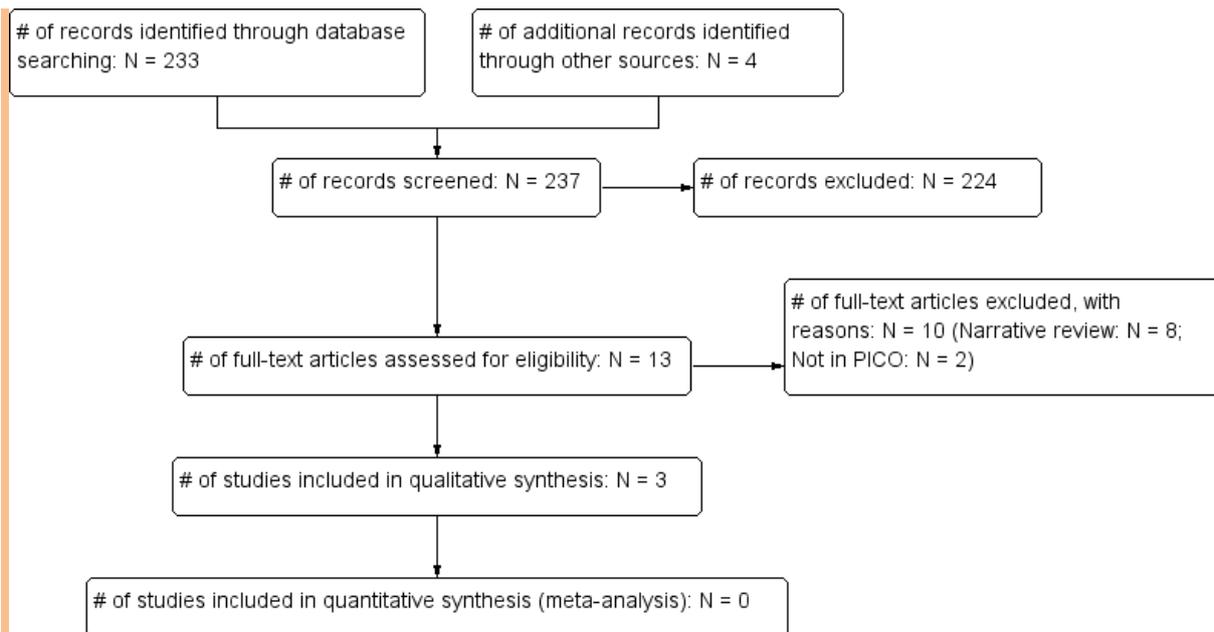
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	281	53	13/11/2012
Premedline	All-2012	20	3	13/11/2012
Embase	All-2012	311	55	14/11/2012
Cochrane Library	All-2012	34	0	14/11/2012
Psychinfo	All-2012	0	0	13/11/2012
Web of Science (SCI & SSCI) and ISI Proceedings	All-2012	7	3	14/11/2012
Biomed Central	All-2012	4	0	14/11/2012

Total References retrieved (after de-duplication): 93

Wilm's tumour: Update Search

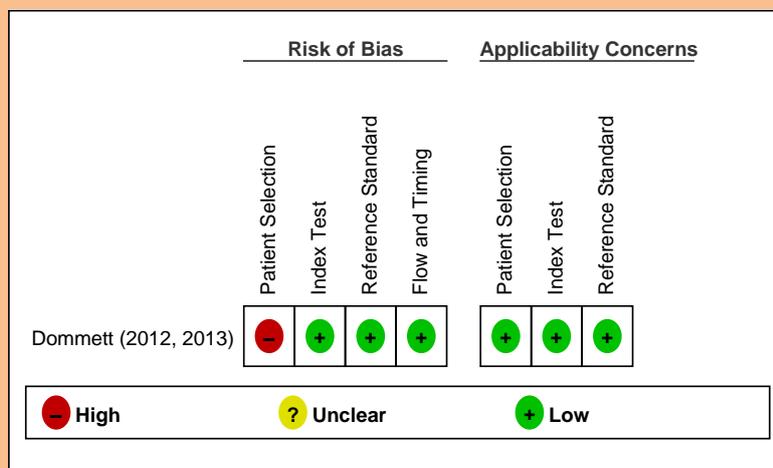
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	11/2012-27/08/2014	20	3	27/08/2014
Premedline	11/2012-27/08/2014	45	2	27/08/2014
Embase	11/2012-27/08/2014	33	0	27/08/2014
Cochrane Library	11/2012-27/08/2014	22	0	27/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	11/2012-27/08/2014	2	0	27/08/2014

Total References retrieved (after de-duplication): 3



Risk of bias in the included studies

The risk of bias and applicability concerns are summarised for the included study in the figure below. The main issue to note is that the study employed a case-control design which has been shown to inflate the test accuracy characteristics. However, the statistical analyses employed by the authors may have gone some way in counteracting this influence.



Study results

Table 1: Childhood cancers (neuroblastoma, retinoblastoma, Wilm’s tumour): Positive predictive values for any childhood cancer: Patients aged 0-14 years

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2012)	Any NICE alert symptom 0-3 months before diagnosis	All patients	0.055 (0.047-0.065) Cases: 342/1267 Control: 211/15318
Dommett (2012)	Any NICE alert symptom 0-12 months before	All patients	0.07 (0.064-0.078) Cases: 427/1267

	diagnosis		Control: 829/15318
Dommett (2012)	Neurological symptoms 0-12 months before diagnosis	All patients	0.083 (0.067-0.105) Cases: 108/1267 Control: 207/15318
Dommett (2012)	Headache 0-12 months before diagnosis	All patients	0.064 (0.051-0.082) Cases: 90/1267 Control: 224/15318
Dommett (2013a)	Headache 0-3 months before diagnosis	All patients	0.06 (0.04-0.08) Cases: 73/1267 Control: 55/15318
Dommett (2013a)	Headache 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.13 (0.08-0.22)
Dommett (2012)	Lymphadenopathy 0-12 months before diagnosis	All patients	0.096 (0.074-0.126) Cases: 82/1267 Control: 136/15318
Dommett (2013a)	Lymphadenopathy 0-3 months before diagnosis	All patients	0.09 (0.06-0.13) Cases: 69/1267 Control: 33/15318
Dommett (2013a)	Lymphadenopathy 0-3 months before diagnosis and ≤ 3 consultations	All patients	0.2 (0.1-0.39)
Dommett (2012)	Lump/mass/swelling 0-12 months before diagnosis	All patients	0.172 (0.119-0.25) Cases: 56/1267 Control: 52/15318
Dommett (2013a)	Lump/mass/swelling below neck excluding abdomen 0-3 months before diagnosis	All patients	0.11 (0.06-0.2) Cases: 42/1267 Control: 16/15318
Dommett (2013a)	Lump/mass/swelling below neck excluding abdomen 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.3 (0.09-0.99)
Dommett (2012)	Fatigue 0-12 months before diagnosis	All patients	0.085 (0.06-0.121) Cases: 47/1267 Control: 88/15318
Dommett (2013a)	Fatigue 0-12 months before diagnosis	All patients	0.07 (0.04-0.12) Cases: 42/1267 Control: 24/15318
Dommett (2013a)	Fatigue 0-12 months before diagnosis and ≥ 3 consultations	All patients	0.12 (0.06-0.23)
Dommett (2012)	Back pain 0-12 months before diagnosis	All patients	0.088 (0.06-0.128) Cases: 40/1267 Control: 73/15318
Dommett (2012)	Bruising 0-12 months before diagnosis	All patients	0.08 (0.054-0.118) Cases: 38/1267 Control: 76/15318
Dommett (2013a)	Bruising 0-3 months before diagnosis	All patients	0.08 (0.05-0.13) Cases: 33/1267

			Control: 18/15318
Dommett (2013a)	Bruising 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.38 (0.09-1.64)
Dommett (2013a)	Pallor 0-3 months before diagnosis	All patients	0.41 (0.12-1.34) Cases: 33/1267 Control: 18/15318
Dommett (2013a)	Pallor 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.76 (0.1-5.7)
Dommett (2013a)	Lump mass swelling head and neck 0-3 months before diagnosis	All patients	0.3 (0.1-0.84) Cases: 28/1267 Control: 4/15318
Dommett (2013a)	Lump mass swelling head and neck 0-3 months before diagnosis and ≤ 3 consultations	All patients	0.76 (0.1-5.7)
Dommett (2013a)	Abnormal movement 0-3 months before diagnosis	All patients	0.08 (0.04-0.14) Cases: 49/1267 Control: 26/15318
Dommett (2013a)	Abnormal movement 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.15 (0.07-0.32)
Dommett (2013a)	Bleeding 0-3 months before diagnosis	All patients	0.06 (0.03-0.1) Cases: 28/1267 Control: 21/15318
Dommett (2013a)	Bleeding 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.11 (0.04-0.31)
Dommett (2013a)	Visual symptoms 0-3 months before diagnosis	All patients	0.06 (0.03-0.1) Cases: 28/1267 Control: 21/15318
Dommett (2013a)	Visual symptoms 0-3 months before diagnosis and ≤ 3 consultations	All patients	0.23 (0.07-0.77)
Dommett (2013a)	Pain 0-3 months before diagnosis	All i patients	0.04 (0.03-0.06) Cases: 42/1267 Control: 41/15318
Dommett (2013a)	Pain 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.14 (0.07-0.31)
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All patients	0.04 (0.03-0.07) Cases: 107/1267 Control: 102/15318
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis and ≥ 3 consultations	All patients	0.13 (0.08-0.19)
Dommett (2012)	Urinary symptoms 0-12 months before diagnosis	All patients	0.266 (0.117-0.609) Cases: 15/1267

			Control: 9/15318
Dommett (2013a)	≥ 3 consultations	All patients	0.02
Dommett (2013a)	Childhood infection 0-3 months before diagnosis	All patients	Cases: 54/1267 Control: 236/15318
Dommett (2013a)	Upper respiratory tract infection 0-3 months before diagnosis	All patients	Cases: 143/1267 Control: 942/15318
Dommett (2013a)	Vomiting 0-3 months before diagnosis	All patients	Cases: 86/1267 Control: 105/15318
Dommett (2013a)	Cough 0-3 months before diagnosis	All patients	Cases: 77/1267 Control: 654/15318
Dommett (2013a)	Rash 0-3 months before diagnosis	All patients	Cases: 63/1267 Control: 555/15318
Dommett (2013a)	Abdominal pain 0-3 months before diagnosis	All patients	Cases: 60/1267 Control: 137/15318
Dommett (2013a)	Abdominal mass 0-3 months before diagnosis	All patients	Cases: 48/1267 Control: 0/15318
Dommett (2013a)	Fever 0-3 months before diagnosis	All patients	Cases: 49/1267 Control: 166/15318
Dommett (2013a)	Eye swelling 0-3 months before diagnosis	All patients	Cases: 39/1267 Control: 238/15318
Dommett (2013a)	Shortness of breath 0-3 months before diagnosis	All patients	Cases: 35/1267 Control: 221/15318
Dommett (2013a)	Constipation 0-3 months before diagnosis	All patients	Cases: 26/1267 Control: 61/15318
Dommett (2012)	Hepatosplenomegaly 0-12 months before diagnosis	All patients	2.19 (0.295-17.034) Cases: 14/1267 Control: 1/15318

The positive predictive values are calculated using Bayesian statistics.

Table 2: Childhood cancers (neuroblastoma, retinoblastoma, Wilm's tumour): Positive predictive values for any childhood cancer: Patients aged 0-4 years

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2012)	Any NICE alert symptom 0-3 months before diagnosis	Patients aged 0-4 years	0.081 (0.059-0.112) Cases: 96/436 Control: 55/4802
Dommett (2012)	Any NICE alert symptom 0-12 months before diagnosis	Patients aged 0-4 years	0.093 (0.077-0.113) Cases: 124/436 Control: 248/4802
Dommett (2012)	Neurological symptoms 0-12 months before diagnosis	Patients aged 0-4 years	0.076 (0.054-0.107) Cases: 43/436 Control: 105/4802
Dommett (2012)	Headache 0-12 months before diagnosis	Patients aged 0-4 years	0.135 (0.055-0.335) Cases: 8/436 Control: 11/4802
Dommett (2012)	Lymphadenopathy 0-12 months before diagnosis	Patients aged 0-4 years	0.061 (0.037-0.1) Cases: 20/436 Control: 61/4802
Dommett (2012)	Lump/mass/swelling 0-	Patients aged 0-4 years	0.198 (0.099-0.399)

	12 months before diagnosis		Cases: 16/436 Control: 15/4802
Dommett (2012)	Fatigue 0-12 months before diagnosis	Patients aged 0-4 years	0.087 (0.048-0.16) Cases: 15/436 Control: 32/4802
Dommett (2012)	Back pain 0-12 months before diagnosis	Patients aged 0-4 years	0.186 (0.047-0.742) Cases: 4/436 Control: 4/4802
Dommett (2012)	Bruising 0-12 months before diagnosis	Patients aged 0-4 years	0.155 (0.086-0.279) Cases: 20/436 Control: 24/4802
Dommett (2012)	Urinary symptoms 0-12 months before diagnosis	Patients aged 0-4 years	0.739 (0.159-3.496) Cases: 8/436 Control: 2/4802
Dommett (2012)	Hepatosplenomegaly 0-12 months before diagnosis	Patients aged 0-4 years	1.286 (0.161-10.569) Cases: 7/436 Control: 1/4802

The positive predictive values are calculated using Bayesian statistics.

Table 3: Childhood cancers (neuroblastoma, retinoblastoma, Wilm's tumour): Positive predictive values for any childhood cancer: Patients aged 5-14 years

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2012)	Any NICE alert symptom 0-3 months before diagnosis	Patients aged 5-14 years	0.056 (0.047-0.068) Cases: 246/831 Control: 156/10516
Dommett (2012)	Any NICE alert symptom 0-12 months before diagnosis	Patients aged 5-14 years	0.075 (0.066-0.084) Cases: 303/831 Control: 581/10561
Dommett (2012)	Neurological symptoms 0-12 months before diagnosis	Patients aged 5-14 years	0.091 (0.067-0.123) Cases: 65/831 Control: 102/10516
Dommett (2012)	Headache 0-12 months before diagnosis	Patients aged 5-14 years	0.055 (0.043-0.07) Cases: 82/831 Control: 213/10516
Dommett (2012)	Lymphadenopathy 0-12 months before diagnosis	Patients aged 5-14 years	0.118 (0.085-0.164) Cases: 62/831 Control: 75/10516
Dommett (2012)	Lump/mass/swelling 0-12 months before diagnosis	Patients aged 5-14 years	0.154 (0.099-0.24) Cases: 40/831 Control: 37/10516
Dommett (2012)	Fatigue 0-12 months before diagnosis	Patients aged 5-14 years	0.082 (0.053-0.125) Cases: 32/831 Control: 56/10516
Dommett (2012)	Back pain 0-12 months before diagnosis	Patients aged 5-14 years	0.075 (0.05-0.111) Cases: 36/831 Control: 69/10516
Dommett (2012)	Bruising 0-12 months before diagnosis	Patients aged 5-14 years	0.049 (0.029-0.084) Cases: 18/831 Control: 52/10516

Dommett (2012)	Urinary symptoms 0-12 months before diagnosis	Patients aged 5-14 years	0.143 (0.05-0.407) Cases: 7/831 Control: 7/10516
Dommett (2012)	Hepatosplenomegaly 0-12 months before diagnosis	Patients aged 5-14 years	Cases: 7/831 Control: 0/10516

The positive predictive values are calculated using Bayesian statistics.

Table 4: Childhood cancers (neuroblastoma, retinoblastoma, Wilm's tumour): Positive predictive values for leukaemia/lymphoma childhood cancer

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)
Dommett (2013a)	Bruising 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.53 (0.07-3.91)
Dommett (2013a)	Pallor 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.43 (0.06-3.15)
Dommett (2013a)	Lump mass swelling head and neck 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.35 (0.05-2.65)
Dommett (2013a)	Fatigue 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.07 (0.03-0.15)
Dommett (2013a)	Lymphadenopathy 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.06 (0.04-0.11)
Dommett (2013a)	Lump mass swelling below neck excluding abdomen 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.05 (0.02-0.13)
Dommett (2013a)	Bleeding 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.03 (0.01-0.08)
Dommett (2013a)	Pain 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.03 (0.01-0.06)
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.02 (0.01-0.03)
Dommett (2013a)	Fever 0-3 months before diagnosis	All leukemia/lymphoma patients and controls aged 0-14 years	0.01 (0.01-0.01)

		years	
Dommett (2013a)	Abdominal pain 0-3 months before diagnosis	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01 (0-0.01)
Dommett (2013a)	≥ 3 consultations	All leukemia/ lymphoma patients and controls aged 0-14 years	0.01 (0.01-0.01)

The positive predictive values are calculated using Bayesian statistics.

Table 5: Childhood cancers (neuroblastoma, retinoblastoma, Wilm's tumour): Positive predictive values for teenage and young adult leukaemia

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)
Dommett (2013b)	Bruising	All leukaemia patients and controls aged 15-24 years	0.0117 (0.004-0.0343) Cases: 9/143 Controls: 5/1799
Dommett (2013b)	Fatigue	All leukaemia patients and controls aged 15-24 years	0.0121 (0.0052-0.0282) Cases: 15/143 Controls: 8/1799
Dommett (2013b)	Lymphadenopathy	All leukaemia patients and controls aged 15-24 years	0.0151 (0.004-0.0578) Cases: 7/143 Controls: 3/1799
Dommett (2013b)	≥ 3 consultations	All leukaemia patients and controls aged 15-24 years	0.0038 (0.003-0.0048) Cases: 74/143 Controls: 125/1799

The positive predictive values are calculated using Bayesian statistics.

Table 6: Childhood cancers (neuroblastoma, retinoblastoma, Wilm's tumour): Positive predictive values for teenage and young adult lymphoma

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2013b)	Lump mass swelling head and neck	All lymphoma patients and controls aged 15-24 years	0.5034 (0.0696-3.68) Cases: 35/270 Controls: 1/3350
Dommett (2013b)	Lump mass swelling below neck excluding abdomen	All lymphoma patients and controls aged 15-24 years	0.0279 (0.0152-0.0515) Cases: 29/270 Controls: 15/3350
Dommett (2013b)	Lymphadenopathy	All lymphoma patients and controls aged 15-24 years	0.278 (0.1-0.75) Cases: 77/270 Controls: 4/3350
Dommett (2013b)	'Lump mass swelling head and neck', 'lymphadenopathy' and	All lymphoma patients and controls aged 15-24 years	0.0903 (0.057-0.1425)

	'lump mass swelling below neck excluding abdomen' combined as a single symptom		
Dommett (2013b)	≥ 3 consultations	All lymphoma patients and controls aged 15-24 years	0.0086 (0.0075-0.0099) Cases: 175/270 Controls: 294/3350

The positive predictive values are calculated using Bayesian statistics.

Table 7: Childhood cancers (neuroblastoma, retinoblastoma, Wilm's tumour): Positive predictive values for central nervous system (CNS) child- or young adulthood cancer tumour

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2013a)	Abnormal movement 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.11 (0.03-0.35)
Dommett (2013a)	Visual symptoms 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.07 (0.02-0.24)
Dommett (2013a)	Vomiting 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.04 (0.02-0.07)
Dommett (2013a)	Headache 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.03 (0.02-0.06)
Dommett (2013a)	Pain 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.03 (0.01-0.08)
Dommett (2013a)	Seizure 0-3 months before diagnosis	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.02 (0.01-0.06)
Dommett (2013a)	≥ 3 consultations	All CNS childhood cancer tumour patients and controls aged 0-14 years	0.01 (0-0.01)
Dommett (2013b)	Seizure	All CNS patients and controls aged 15-24 years	0.0238 (0.0082-0.0695) Cases: 18/154 Controls: 4/1906
Dommett (2013b)	Headache	All CNS patients and controls aged 15-24 years	0.0145 (0.0077-0.0276) Cases: 33/154 Controls: 12/1906

Dommett (2013b)	Vomiting	All CNS patients and controls aged 15-24 years	0.0116 (0.0041-0.031) Cases: 11/154 Controls: 5/1906
Dommett (2013b)	Pain	All CNS patients and controls aged 15-24 years	0.0029 (0.0014-0.006) Cases: 11/154 Controls: 20/1906
Dommett (2013b)	Visual symptoms	All CNS patients and controls aged 15-24 years	Cases: 8.4% Controls: 0%
Dommett (2013b)	≥ 3 consultations	All CNS patients and controls aged 15-24 years	0.0023 (0.0019-0.0029) Cases: 73/154 Controls: 165/1906

The positive predictive values are calculated using Bayesian statistics.

Table 8: Childhood cancers (neuroblastoma, retinoblastoma, Wilm's tumour): Positive predictive values for child- or young adulthood bone cancer tumour/soft tissue sarcoma

Study	Symptom(s)	Patient group	Positive predictive value (95% CI) Frequency
Dommett (2013a)	Lump mass swelling below neck excluding abdomen 0-3 months before diagnosis	All bone cancer tumour/soft tissue sarcoma patients and controls aged 0-14 years	0.03 (0.01-0.14)
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All bone cancer tumour/soft tissue sarcoma patients and controls aged 0-14 years	0.01 (0-0.01)
Dommett (2013a)	Trauma 0-3 months before diagnosis	All bone cancer tumour/soft tissue sarcoma patients and controls aged 0-14 years	0 (0-0)
Dommett (2013a)	≥ 3 consultations	All bone cancer tumour/soft tissue sarcoma patients and controls aged 0-14 years	0 (0-0)
Dommett (2013b)	Lump mass swelling	All bone cancer tumour/soft tissue sarcoma patients and controls aged 15-24 years	0.0415 (0.0124-0.1392) Cases: 19/196 Controls: 3/2438
Dommett (2013b)	Musculoskeletal symptoms	All bone cancer tumour/soft tissue sarcoma patients and	0.0093 (0.0058-0.0151) Cases: 37/196

		controls aged 15-24 years	Controls: 26/2438
Dommett (2013b)	Chest pain	All bone cancer tumour/soft tissue sarcoma patients and controls aged 15-24 years	0.0027 (0.001-0.0077) Cases: 5/196 Controls: 12/2438
Dommett (2013b)	≥ 3 consultations	All bone cancer tumour/soft tissue sarcoma patients and controls aged 15-24 years	0.003 (0.0024-0.0037) Cases: 86/196 Controls: 189/2438

The positive predictive values are calculated using Bayesian statistics.

Table 9: Childhood cancers (neuroblastoma, retinoblastoma, Wilm's tumour): Positive predictive values for childhood abdominal cancer tumour

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)
Dommett (2013a)	Bleeding 0-3 months before diagnosis	All abdominal cancer patients and controls aged 0-14 years	0.03 (0.01-0.12)
Dommett (2013a)	Lump mass swelling below neck excluding abdomen 0-3 months before diagnosis	All abdominal cancer patients and controls aged 0-14 years	0.03 (0.00-0.23)
Dommett (2013a)	Weight loss 0-3 months before diagnosis	All abdominal cancer patients and controls aged 0-14 years	0.02 (0.00-0.1)
Dommett (2013a)	Abdominal pain 0-3 months before diagnosis	All abdominal cancer patients and controls aged 0-14 years	0.01 (0.01-0.02)
Dommett (2013a)	Musculoskeletal symptoms 0-3 months before diagnosis	All abdominal cancer patients and controls aged 0-14 years	0.01 (0.00-0.01)
Dommett (2013a)	Childhood infection 0-3 months before diagnosis	All abdominal cancer patients and controls aged 0-14 years	0 (0-0)
Dommett (2013a)	≥ 3 consultations	All abdominal cancer patients and controls aged 0-14 years	0 (0-0)

Evidence statement(s):

The positive predictive values of having any childhood cancer ranged from 0.04% (for pain and musculoskeletal symptoms) to 2.19% (for hepatosplenomegaly) in all included patients aged 0-14 years, and from 0.061% (for lymphadenopathy) to 1.286% (for hepatosplenomegaly) for patients aged 0-4 years old, and from 0.049% (for bruising) to 0.154% (for 'lump/mass/swelling' [the PPV for hepatosplenomegaly could not be calculated as none of the controls experienced this symptom]) for

patients aged 5-14 years old (all from 1 study, N = 16585). The evidence quality is somewhat compromised by the case-control design of the study (see also Tables 1-3).

The positive predictive values of having leukaemia/lymphoma childhood cancer ranged from 0.01% (for fever and abdominal pain) to 0.53% (for bruising) for patients aged 0-14 years old; the positive predictive values of having young adulthood leukaemia ranged from 0.0117% (for bruising) to 0.0151% (for lymphadenopathy) for patients aged 15-24 years; and the positive predictive values of having young adulthood lymphoma ranged from 0.0279% (for 'lump mass swelling below the neck excluding the abdomen') to 0.5034% (for 'lump mass swelling head and neck') for patients aged 15-24 years (1 study, N = 30855). The evidence quality is somewhat compromised by the case-control design of the study (see also Tables 4-6).

The positive predictive values of having central nervous system childhood or young adulthood cancer tumours ranged from 0.02% (for seizure) to 0.11 (for abnormal movement) for patients aged 0-14 years old, and from 0.0029% (for pain) to 0.0238% (for seizure) for patients aged 15-24 years (1 study, N = 30855). The evidence quality is somewhat compromised by the case-control design of the study (see also Table 7).

The positive predictive values of having childhood or young adulthood bone cancer tumour/soft tissue sarcoma ranged from 0% (for trauma) to 0.03% (for 'lump mass swelling below neck excluding abdomen') for patients aged 0-14 years old, and from 0.0027% (for chest pain) to 0.0415% (for 'lump mass swelling') for patients aged 15-24 years (1 study, N = 30855). The evidence quality is somewhat compromised by the case-control design of the study (see also Table 8).

The positive predictive values of having childhood abdominal cancer tumours ranged from 0% (for childhood infection) to 0.03% (for bleeding and 'lump mass swelling below neck excluding abdomen') for patients aged 0-15 years old (1 study, N = 16585). The evidence quality is somewhat compromised by the case-control design of the study (see also Table 9).

Evidence tables

Dommett (2012; 2013a,b)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based nested case-control study using data from the General Practice Research Database (GPRD)
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and	<u>Cases:</u> 1267 children; aged 0-4 years: N = 436; aged 5-14 years: N = 831; 703

setting	<p>males/564 females.</p> <p>Cancer type: Leukemia: N = 368; brain: N = 270; lymphoma: N = 142; bone: N = 107; soft tissue sarcoma: N = 91; renal: N = 82; neuroblastoma: N = 75; other ICD codes: N = 132.</p> <p>1064 teenagers and young adults (TYA): 15-24 years: Gender not reported.</p> <p>Cancer type: Leukemia: N = 143; brain: N = 154; lymphoma: N = 270; bone: N = 96; soft tissue sarcoma: N = 100; other ICD codes: N = 301 (including testis: N = 60; skin: N = 49; ovary: N = 20 and thyroid: N = 17).</p> <p><u>Controls:</u> 15318 children; aged 0-4 years: N = 4802; aged 5-14 years: N = 10516; 8461 males/6857 females. 13206 TYA. Gender not reported</p> <p><u>Inclusion criteria:</u> The sample comprised all children and TYU aged 0–24 years, inclusive, drawn from all general practices contributing research-standard data to the GPRD between 1 January 1988 and 31 December 2010. To be included, the practices had to have been contributing research-standard data for a minimum of 1 year before each child’s date of cancer diagnosis or the index date (see below) for matched controls.</p> <p>Cases: Patients diagnosed with the following cancers: leukaemia, lymphoma, neuroblastoma, soft tissue sarcoma, hepatic, renal, bone and central nervous system tumours, using pre-defined medical codes used in the GPRD. The date of diagnosis for cases was defined as the date of pathological diagnosis, but if this was unavailable, the date of the first cancer code entered in the GPRD was used.</p> <p>Controls: Up to 13 controls (children with no diagnosis of cancer at any time) were selected per case, using a computer-generated random sequence, matched on age (within 1 year), sex and practice, and had to be currently registered on the date of diagnosis of their matched case (the index date).</p> <p><u>Exclusion criteria:</u> None listed</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	The GPRD uses just over 100 000 medical codes to encompass all primary care events, including both symptoms and diagnoses. From this list, libraries of codes were assembled representing individual alert symptoms derived from the NICE referral guidelines for suspected cancer in children. <i>No more information reported.</i>
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or	Low concern

interpretation differ from the review question?		
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Cancer diagnosis in the UK's General Practice Research Database.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	This study is published in three papers.	

References

Included studies

- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of childhood cancer in primary care: A population-based nested case-control study. *British Journal of Cancer* 106[5], 982-987. 2012.
- Dommett, R. M., Redaniel, T., Stevens, M. C. G., Martin, R. M., and Hamilton, W. Risk of childhood cancer with symptoms in primary care: A population-based case-control study. *British Journal of General Practice*; DOI:10.3399/bjgp13X660742. 2013a.
- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W., and Martin, R. M. Features of cancer in teenagers and young adults in primary care: A population-based nested case-control study. *British Journal of Cancer* 2329-2333. 2013b.

Excluded studies (with excl reason)

- (1999) Doctor-patient relationships in primary care. Doctor, help! My child has cancer. [Review] [0 refs]. *BMJ*, 319: 554-556.
Not in PICO
- (2006) New report on childhood cancer shows early detection can save thousands of children's lives. *European Journal of Oncology*, 11: 65-67.
Narrative review
- (2007) Erratum: Retinoblastoma (*American Family Physician* (2006) (1039-1041)). *American Family Physician*, 75: 980.
Erratum

- Abdu, L. & Malami, S. (2011) Clinicopathological pattern and management of retinoblastoma in Kano, Nigeria. *Annals of African Medicine*, 10: 214-219.
Not in PICO
- Abramson, D. H., Notterman, R. B., Ellsworth, R. M. & Kitchin, F. D. (1983) Retinoblastoma treated in infants in the first six months of life. *Archives of Ophthalmology*, 101: 1362-1366.
Not in PICO
- Abramson, D. H., Beaverson, K., Sangani, P., Vora, R. A., Lee, T. C., Hochberg, H. M., Kirsztrot, J. & Ranjithan, M. (2003) Screening for retinoblastoma: presenting signs as prognosticators of patient and ocular survival. *Pediatrics*, 112: t-55.
Not in PICO
- Adegboye, V. O., Ogunseyinde, A. O., Obajimi, M. O., Ogunbiyi, O., Brimmo, A. I. & Adebo, O. A. (2003) Presentation of primary mediastinal masses in Ibadan. *East African Medical Journal*, 80: 484-487.
Not in PICO
- Agrons, G. A., Kingsman, K. D., Wagner, B. J. & Sotelo-Avila, C. (1997) Rhabdoid tumor of the kidney in children: a comparative study of 21 cases. *AJR.American Journal of Roentgenology*, 168: 447-451.
Not in PICO
- Ahmed, S., Goel, S., Khandwala, M., Agrawal, A., Chang, B. & Simmons, I. G. (2006) Neuroblastoma with orbital metastasis: ophthalmic presentation and role of ophthalmologists. *Eye*, 20: 466-470.
Not in PICO
- Ahrensberg, J. M., Fenger-Gron, M. & Vedsted, P. (2013) Use of primary care during the year before childhood cancer diagnosis: a nationwide population-based matched comparative study. *PLoS ONE [Electronic Resource]*, 8: e59098.
Not in PICO
- Alkatan, H., Al-Amry, M., Al-Hussain, H., Al-Dhibi, H. & al-Mesfer, S. (2011) Medulloepithelioma of the ciliary body: The delay in diagnosis and frequent initial mismanagement. *Canadian Journal of Ophthalmology*, 46: 431-438.
Not in PICO
- Almeida, C., Machado, I., Aguiar, L. & Almeida, F. (2009) Early diagnosis in childhood cancer: The shortest way for the cure. *Pediatric Blood and Cancer*, 53: 846.
Not in PICO
- Anastassiou, G., Bornfeld, N., Schueler, A. O., Schilling, H., Weber, S., Fluehs, D., Jurklies, B., Vij, O. & Sauerwein, W. (2006) Ruthenium-106 plaque brachytherapy for symptomatic vasoproliferative tumours of the retina. *British Journal of Ophthalmology*, 90: 447-450.
Not in PICO
- Anderson, B. D., Mason, S. & Cheson, B. D. (1986) Clinical trials referral resource. Current clinical trials in neuroblastoma. *Oncology (Williston Park)*, 16: 82-84.
Not in PICO
- Anderson, P. (2000) Taking care to the child. *Nursing Times*, 96: 51-53.
Not in PICO
- Angelini, P., Plantaz, D., De, B. B., Passagia, J. G., Rubie, H. & Pastore, G. (2011) Late sequelae of symptomatic epidural compression in children with localized neuroblastoma. *Pediatric blood & cancer*, 57: 473-480.
Not in PICO
- Antoneli, C. B., Steinhorst, F., Ribeiro, K. C., Chojniak, M. M., Novaes, P. E., Arias, V. & Bianchi, A. (2004) The Pediatrician's ability to recognize the presenting signs and symptoms of retinoblastoma. [Portuguese]. *Revista da Associacao Medica Brasileira (1992)*, 50: 400-402.
Not in PICO

- Antunes, N. L. & De Angelis, L. M. (1999) Neurologic consultations in children with systemic cancer. *Pediatric Neurology*, 20: 121-124.
Not in PICO
- Aston, J. W., Jr. (1990) Pediatric update #16. The orthopaedic presentation of neuroblastoma. *Orthopaedic Review*, 19: 929-932.
Not in PICO
- Atkins, L. A., Forbes, L. J. L., Austoker, J., Bankhead, C., Martin, F., Robb, K., Wardle, J. & Ramirez, A. J. (2010) Interventions to increase cancer awareness and promote early presentation: A systematic review. *Psycho-Oncology*, 19: S12.
Not in PICO
- Auber, F., Jeanpierre, C., Denamur, E., Jaubert, F., Schleiermacher, G., Patte, C., Cabrol, S., Leverger, G., Nihoul-Fekete, C. & Sarnacki, S. (2009) Management of Wilms tumors in Drash and Frasier syndromes. *Pediatric blood & cancer*, 52: 55-59.
Not in PICO
- Augsburger, J. J. (1983) Ocular tumors in children. *Pediatric Clinics of North America*, 30: 1071-1086.
Narrative review
- Aung, L., Chan, Y. H., Sabai, S. M., Khaing, T., Yeoh, E. J. & Quah, T. C. (2009) Retinoblastoma: A recent experience at the national university hospital, Singapore. *Pediatric Blood and Cancer*, 53: 811-812.
Not in PICO
- Austoker, J., Bankhead, C., Forbes, L. J., Atkins, L., Martin, F., Robb, K., Wardle, J. & Ramirez, A. J. (2009) Interventions to promote cancer awareness and early presentation: systematic review. [Review] [38 refs]. *British Journal of Cancer*, 101: Suppl-9.
Not in PICO
- Badalian, G. K., Kurbanmuradov, B. K., Nurgaliev, Z. B., Sharoev, T. A. & Khobbi, N. N. (1990) [The diagnostic and prognostic characteristics of nephroblastoma recurrences in children]. [Russian]. *Urologiia i Nefrologiia*.(2):23-6, 1990 Mar-Apr., 23-26.
Not in PICO
- Badhu, B., Sah, S. P., Thakur, S. K. D., Dulal, S., Kumar, S., Sood, A., Das, H. & Sah, R. P. (2005) Clinical presentation of retinoblastoma in Eastern Nepal. *Clinical and Experimental Ophthalmology*, 33: 386-389.
Not in PICO
- Baggesen, K., Flage, T. & Arnljot, H. M. (1999) [Leukocoria (white pupil) among children--mother is always right]. [Norwegian]. *Tidsskrift for Den Norske Laegeforening*, 119: 794-795.
Narrative review
- Bahakim, H. M. & el-Idrissy, I. M. (1989) Epidemiological observations of consanguinity and retinoblastoma in Arabia. A retrospective study. *Tropical & Geographical Medicine*, 41: 361-364.
Not in PICO
- Bai, S., Ren, R., Li, B., Xu, X., Zhao, B., Gao, F., Li, L. & Jonas, J. B. (2011) Delay in the diagnosis of retinoblastoma in China. *Acta Ophthalmologica*, 89: e72-e74.
Not in PICO
- Ballock, R. T., Wiesner, G. L., Myers, M. T. & Thompson, G. H. (1997) Hemihypertrophy. Concepts and controversies. [Review] [67 refs]. *Journal of Bone & Joint Surgery - American Volume*, 79: 1731-1738.
Narrative review
- Balmer, A., Zografos, L. & Munier, F. (2006) Diagnosis and current management of retinoblastoma. [Review] [60 refs]. *Oncogene*, 25: 5341-5349.
Narrative review
- Balmer, A. & Munier, F. (2007) Differential diagnosis of leukocoria and strabismus, first presenting signs of retinoblastoma. *Clinical Ophthalmology*, 1: 431-439.
Narrative review

- Barroca, H. & Bom-Sucesso, M. (2014) Fine needle biopsy with cytology in paediatrics: The importance of a multidisciplinary approach and the role of ancillary techniques. *Cytopathology*, 25: 6-20.
Narrative review
- Bernard, J. L., Gentet, J. C. & Raybaud, C. (1984) Detection and early diagnosis of solid tumors in children. [French]. *Medecine Infantile*, 91: 599-608.
Narrative review
- Bliznakova, D. (2003) Differential diagnosis of some kidney diseases in childhood. [Bulgarian]. *Bulgarian Medicine*, 11: 7-10.
Narrative review
- Boles, C. B., Vitale, B. F. & Porro, G. (1995) [The pediatric physician and consultation in ophthalmology]. [Review] [46 refs] [Italian]. *Minerva Pediatrica*, 47: 493-504.
Not in PICO
- Boranic, M. (2003) Solid malignant tumors in children. [Croatian]. *Paediatrica Croatica, Supplement*, 47: 19-24.
Narrative review
- Borer, J. G., Kaefer, M., Barnewolt, C. E., Elias, E. R., Hobbs, N., Retik, A. B. & Peters, C. A. (1999) Renal findings on radiological followup of patients with Beckwith- Wiedemann syndrome. *Journal of Urology*, 161: 235-239.
Not in PICO
- Boricean, I. D. & Barar, A. (2011) Understanding ocular torticollis in children. *Oftalmologia (Bucharest, Romania : 1990)*, 55: 10-26.
Narrative review
- Bornfeld, N., Schuler, A., Boloni, R., Jurklies, C., Wieland, R., Sauerwein, W. & Lohmann, D. (1977) [Retinoblastoma]. [Review] [39 refs] [German]. *Ophthalmologe*, 103: 59-76.
Narrative review
- Bove, K. E. (1999) Wilms' tumor and related abnormalities in the fetus and newborn. [Review] [59 refs]. *Seminars in Perinatology*, 23: 310-318.
Narrative review
- Brady, G. (2003) Retinoblastoma: Care and support of the pediatric patient and family. *Insight - Journal of the American Society of Ophthalmic Registered Nurses*, 28: 67-69.
Narrative review
- Brasme, J.-F., Morfouace, M., Grill, J., Martinot, A., Amalberti, R., Bons-Letouzey, C. & Chalumeau, M. (2012) Delays in diagnosis of paediatric cancers: A systematic review and comparison with expert testimony in lawsuits. *The Lancet Oncology*, 13: e445-e459.
Not in PICO
- Brasme, J.-F., Chalumeau, M., Doz, F., Lacour, B., Valteau-Couanet, D., Gaillard, S., Delalande, O., Aghakhani, N., Sainte-Rose, C., Puget, S. & Grill, J. (2012) Interval between onset of symptoms and diagnosis of medulloblastoma in children: Distribution and determinants in a population-based study. *European Journal of Pediatrics*, 171: 25-32.
Not in PICO
- Brown, B. J., Ajayi, S. O., Ogun, O. A. & Oladokun, R. E. (2009) Factors influencing time to diagnosis of childhood cancer in Ibadan, Nigeria.[Erratum appears in Afr Health Sci. 2010 Jun;10(2):137 Note: James, B O [corrected to Brown, B J]]. *African Health Sciences*, 9: 247-253.
Not in PICO
- Bursztyn, J. (2005) [New developments in 2005 for the management of visual deficit in the infant]. [French]. *Archives de Pediatrie*, 12: 357-360.
Not in PICO
- Butros, L. J., Abramson, D. H. & Dunkel, I. J. (2002) Delayed diagnosis of retinoblastoma: analysis of degree, cause, and potential consequences. *Pediatrics*, 109: E45.
Not in PICO

- Cabral, D. A. & Tucker, L. B. (1999) Malignancies in children who initially present with rheumatic complaints. *Journal of Pediatrics*, 134: 53-57.
Not in PICO
- Caiulo, V. A., Caiulo, S., Gargasole, C., Chiriaco, G., Latini, G., Cataldi, L. & Mele, G. (2012) Ultrasound mass screening for congenital anomalies of the kidney and urinary tract. *Pediatric Nephrology*, 27: 949-953.
Not in PICO
- Canadian Retinoblastoma Society (2009) National Retinoblastoma Strategy Canadian Guidelines for Care: Strategie therapeutique du retinoblastome guide clinique canadien. *Canadian Journal of Ophthalmology*, 44: Suppl-88.
Guideline
- Canty, C. A. (2009) Retinoblastoma: an overview for advanced practice nurses. [Review] [23 refs]. *Journal of the American Academy of Nurse Practitioners*, 21: 149-155.
Narrative review
- Canzano, J. C. & Handa, J. T. (1999) Utility of pupillary dilation for detecting leukocoria in patients with retinoblastoma. *Pediatrics*, 104: e44.
Not in PICO
- Castillo, B. V., Jr. & Kaufman, L. (2003) Pediatric tumors of the eye and orbit. [Review] [67 refs]. *Pediatric Clinics of North America*, 50: 149-172.
Narrative review
- Cepulic, M., Cizmic, A., Petkovic, I., Fattorini, I., Nakic, M. & Stepan, G. J. (2003) Nephroblastomas - Wilms' tumor (WT). [Croatian]. *Paediatrica Croatica, Supplement*, 47: 75-80.
Not in PICO
- Cerecedo, D. F., Lopez, A. E., Rivera, M. H., Arias, G. J., Ramirez, S. F. & Rodriguez, C. M. (2003) [Survival and clinical features of retinoblastoma]. [Spanish]. *Anales de Pediatria*, 58: 3-9.
Not in PICO
- Chantada, G., Fandino, A., Manzitti, J., Urrutia, L. & Schwartzman, E. (1999) Late diagnosis of retinoblastoma in a developing country. *Archives of Disease in Childhood*, 80: 171-174.
Not in PICO
- Chen, D. Y. & Uzzo, R. G. (2011) Evaluation and management of the renal mass. [Review]. *Medical Clinics of North America*, 95: 179-189.
Narrative review
- Chen, Y. F., Li, Y. W., Sheih, C. P. & Hsu, C. Y. (1999) Renal cell carcinoma: unusual pediatric renal tumors. *Journal of the Formosan Medical Association*, 98: 118-121.
Not in PICO
- Cheng, G. Y., Li, B., Li, L. Q., Gao, F., Ren, R. J., Xu, X. L. & Jonas, J. B. (2008) Review of 1375 enucleations in the TongRen Eye Centre, Beijing. *Eye*, 22: 1404-1409.
Not in PICO
- Choyke, P. L., Siegel, M. J., Craft, A. W., Green, D. M. & DeBaun, M. R. (1999) Screening for Wilms tumor in children with Beckwith-Wiedemann syndrome or idiopathic hemihypertrophy. *Medical & Pediatric Oncology*, 32: 196-200.
Not in PICO
- Chung, E. M., Specht, C. S. & Schroeder, J. W. (2007) From the archives of the AFIP: Pediatric orbit tumors and tumorlike lesions: neuroepithelial lesions of the ocular globe and optic nerve. [Review] [114 refs]. *Radiographics*, 27: 1159-1186.
Narrative review
- Claviez, A., Hero, B., Schneppenheim, R. & Berthold, F. (1996) [Hepatopathy in patients with stage 4S neuroblastoma]. [German]. *Klinische Padiatrie*, 208: 221-228.
Not in PICO

- Clericuzio, C. L. & Martin, R. A. (2009) Diagnostic criteria and tumor screening for individuals with isolated hemihyperplasia. *Genetics in Medicine*, 11: 220-222.
Narrative review
- Cook, A., Farhat, W. & Khoury, A. (2005) Update on Wilms' tumor in children. *Journal Medical Libanais*, 53: 85-90.
Narrative review
- Craft, A. W., Parker, L., Stiller, C. & Cole, M. (1995) Screening for Wilms' tumour in patients with Aniridia, Beckwith syndrome, or hemihypertrophy. *Medical and Pediatric Oncology*, 24: 231-234.
Narrative review
- Creutzig, U. & Graf, N. (1995) Early diagnosis of neoplastic diseases in childhood. [German]. *Onkologie*, 18: 24-27.
Narrative review
- Croft, D. & Dickerson, M. (1994) Ultrasound differentiation of two pediatric abdominal masses. *Journal of Diagnostic Medical Sonography*, 10: 12-17.
Narrative review
- D'Angio, G. J., Beckwith, J. B. & Breslow, N. E. (1980) Wilms' tumor: An update. *Cancer*, 45: 1791-1798.
Narrative review
- Davidson, A., Hartley, P., Desai, F., Daubenton, J., Rode, H. & Millar, A. (2006) Wilms tumour experience in a South African centre. *Pediatric blood & cancer*, 46: 465-471.
Not in PICO
- de la Briere, A. (2010) [The mission of nurses of patients with ocular cancers]. [French]. *Soins; La Revue de Reference Infirmiere.(744):46, 2010 Apr., 46.*
Not in PICO
- De, B. B., Conte, M., Nigro, M., Milanaccio, C. & Garaventa, A. (1994) [Neuroblastoma: update on clinical aspects and therapy]. [Review] [28 refs] [Italian]. *Pediatria Medica e Chirurgica*, 16: 7-14.
Narrative review
- DeBaun, M. R. & Tucker, M. A. (1998) Risk of cancer during the first four years of life in children from The Beckwith-Wiedemann Syndrome Registry. *Journal of Pediatrics*, 132: t-400.
Not in PICO
- Defachelles, A.-S., Rocourt, N., Branchereau, S. & Peuchmaur, M. (2012) Pancreatoblastoma in children: Diagnosis and therapeutic management. [French]. *Bulletin du Cancer*, 99: 793-799.
Narrative review
- Dehner, L. P. (1994) Pleuropulmonary blastoma is the pulmonary blastoma of childhood. *Seminars in Diagnostic Pathology*, 11: 144-151.
Narrative review
- Dhamija, R., Pittock, S., McKeon, A., Lachance, D., Mack, K., Patterson, M. & Lennon, V. (2010) Anti-neuronal nuclear antibody-type 1 in children. *Annals of Neurology*, 68: S98.
Not in PICO
- Diaconescu, S., Olaru, C., Mihaila, D., Aprodu, S. G. & Miron, I. (2013) Risk stratification and consecutive prognosis progresses in childhood Wilms tumors. Two cases report. *Chirurgia (Bucuresti)*, 108: 106-111.
Not in PICO
- Dimaras, H., Kimani, K., Dimba, E. A., Gronsdahl, P., White, A., Chan, H. S. & Gallie, B. L. (2012) Retinoblastoma. [Review]. *Lancet*, 379: 1436-1446.
Narrative review
- Dorransoro, M., I, Merino, M. R., Sastre-Urguelles, A., Garcia-Miguel Garcia-Rosado, P. & Garcia-Consuegra, M. J. (2004) [Malignant disease presenting as rheumatic manifestations]. [Spanish]. *Anales de Pediatria*, 61: 393-397.
Not in PICO

- Ell, C. & Schott, G. (1994) [Suspected kidney tumor--diagnostic-therapeutic procedure]. [German]. *Fortschritte der Medizin*, 112: 123-124.
Narrative review
- Epelman, S. (2012) Preserving vision in retinoblastoma through early detection and intervention. *Current Oncology Reports*, 14: 213-219.
Narrative review
- Erwenne, C. M. & Franco, E. L. (1989) Age and lateness of referral as determinants of extra-ocular retinoblastoma. *Ophthalmic Paediatrics & Genetics*, 10: 179-184.
Not in PICO
- Esquembre Menor, C. T. & Castel, S., V (1988) [Early diagnosis of cancer in children]. [Review] [0 refs] [Spanish]. *Anales Espanoles de Pediatria*, 29: Suppl-7.
Narrative review
- Essuman, V., Ntim-Amponsah, C. T., Akafo, S., Renner, L. & Edusei, L. (2010) Presentation of retinoblastoma at a paediatric eye clinic in ghana. *Ghana Medical Journal*, 44: 10-15.
Not in PICO
- Exelby, P. R. (1981) Retroperitoneal malignant tumors: Wilms' tumor and neuroblastoma. *Surgical Clinics of North America*, 61: 1219-1237.
Narrative review
- Exelby, P. R. (1991) Wilms' tumor 1991. Clinical evaluation and treatment. *Urologic Clinics of North America*, 18: 589-597.
Narrative review
- Fallat, M. E. & Donahoe, P. K. (2006) Intersex genetic anomalies with malignant potential. *Current Opinion in Pediatrics*, 18: 305-311.
Narrative review
- Ferris, I. T., Berbel, T. O., Ortega Garcia, J. A., Lopez Andreu, J. A., Garcia, I. C., Balaguer, G. J. & Aliaga, V. J. (2003) Risk factors for pediatric malignant renal tumors. [Spanish]. *Revista Espanola de Pediatria*, 59: 527-536.
Not in PICO
- Forgie, S. E. & Robinson, J. L. (2007) Pediatric malignancies presenting as a possible infectious disease. *BMC Infectious Diseases*, 7.
Not in PICO
- Fragkandrea, I., Nixon, J. A. & Panagopoulou, P. (2013) Signs and symptoms of childhood cancer: a guide for early recognition. *American Family Physician*, 88: 185-192.
Narrative review
- Fragkandrea, I., Nixon, J. A. & Panagopoulou, P. (2013) Signs and central nervous system (CNS): Early endocrine manifestations: A guide for early recognition. *American Family Physician*, 88: 185-192.
Narrative review
- Friedman, L. S. & Kaufman, L. M. (2003) Guidelines for pediatrician referrals to the ophthalmologist. *Pediatric Clinics of North America*, 50: 41-53.
Guideline
- Furtwangler, R., Schenk, J.-P., Reinhard, H., Leuschner, I., Rube, C., Von, S. D. & Graf, N. (2005) Nephroblastoma - Wilms' tumor. Genetics, radiological diagnostics and therapy concept - An overview. [German]. *Onkologe*, 11: 1077-1089.
Narrative review
- Furtwangler, R., Nourkami, N., Alkassar, M., Von, S. D., Stehr, M. & Graf, N. (2010) Syndromes and syndrome-like features in bilateral wilms tumor are associated with inferior outcome. *Pediatric Blood and Cancer*, 55: 885.
Not in PICO
- Garcia, H. B. (2008) Suspicion of cancer in pediatrics. [Spanish]. *Pediatria Integral*, 12: 537-544.
Narrative review

- Ghalayini, I. F. & Bani-Hani, I. H. (2003) Detection, staging and clinical implications of renal cell carcinoma. *Saudi Medical Journal*, 24: 79-83.
Not in PICO
- Gillan, T. L., Hughes, R., Godbout, R. & Grundy, P. E. (2003) The Simpson-Golabi-Behmel gene, GPC3, is not involved in sporadic Wilms tumorigenesis. *American Journal of Medical Genetics*, 122: 30-36.
Not in PICO
- Glick, R. D., Hicks, M. J., Nuchtern, J. G., Wesson, D. E., Olutoye, O. O. & Cass, D. L. (2004) Renal tumors in infants less than 6 months of age. [Review] [21 refs]. *Journal of Pediatric Surgery*, 39: 522-525.
Not in PICO
- Goddard, A. G., Kingston, J. E. & Hungerford, J. L. (1999) Delay in diagnosis of retinoblastoma: risk factors and treatment outcome. *British Journal of Ophthalmology*, 83: 1320-1323.
Not in PICO
- Goddard, K., Brown, T., Hukin, J., DeZorzi, P., Johnston, D., Punnett, A., Rassekh, S., Shaikh, F. & Olson, R. (2010) Case-based interactive e-learning programs for pediatric oncology: Rationale, development and user evaluation results. *Pediatric Blood and Cancer*, 55: 974.
Not in PICO
- Gogate, P., Gilbert, C. & Zin, A. (2011) Severe visual Impairment and blindness in infants: Causes and opportunities for control. *Middle East African Journal of Ophthalmology*, 18: 109-114.
Narrative review
- Gombos, D. S. & Diba, R. (2005) Estimating the incidence of retinoblastoma in Texas. *Texas Medicine*, 101: 70-72.
Not in PICO
- Gomez-Martinez, R., Silva-Padilla, N., Torres-Sauza, B. & Huerta-Rosas, J. (2005) [Solid malignant neoplasms in the first year of life]. [Spanish]. *Anales de Pediatría*, 62: 529-534.
Not in PICO
- Graf, N. (1996) Diagnosis and therapy of Wilms' tumor. [German]. *Praxis*, 85: 753-761.
Narrative review
- Graf, N. (1996) [Wilms' tumor]. [Review] [48 refs] [German]. *Praxis*, 85: 753-761.
Narrative review
- Gunes, D. (2010) Childhood cancers and bone pain: Review. [Turkish]. *Turkiye Klinikleri Pediatri*, 19: 216-222.
Narrative review
- Gutjahr, P. (1991) Congenital Wilms' tumors are mostly (benign) mesoblastic nephromas--significance of prenatally detected solid kidney tumors. [German]. *Geburtshilfe und Frauenheilkunde*, 51: 124-126.
Not in PICO
- Hadley, G. P., Govender, D. & Landers, G. (2002) Malignant solid tumours in neonates: An African perspective. *Pediatric Surgery International*, 18: 653-657.
Not in PICO
- Haider, S., Qureshi, W. & Ali, A. (2008) Leukocoria in children. *Journal of Pediatric Ophthalmology and Strabismus*, 45: 179-180.
Not in PICO
- Hammond, D. (1988) Opportunities for cancer prevention and early detection among children. *Cancer*, 62: 1829-1832.
Narrative review
- Hecht, F. (2007) Familial cancer syndromes: Catalog with comments. *Cytogenetic and Genome Research*, 118: 222-228.
Narrative review

- Hered, R. W. (2011) Effective vision screening of young children in the pediatric office. *Pediatric Annals*, 40: 76-82.
Narrative review
- Heuch, J. M., Heuch, I. & Kvale, G. (1996) Birth characteristics and risk of Wilms' tumour: A nationwide prospective study in Norway. *British Journal of Cancer*, 74: 1148-1151.
Not in PICO
- Hillbrand, M., Georg, D., Gadner, H., Potter, R. & Dieckmann, K. (2008) Abdominal cancer during early childhood: A dosimetric comparison of proton beams to standard and advanced photon radiotherapy. *Radiotherapy and Oncology*, 89: 141-149.
Narrative review
- Hormann, M. (2008) [Neuroblastoma in children]. [German]. *Radiologe*, 48: 940-945.
Narrative review
- Hu, V. H., Starling, A., Baynham, S. N., Wager, H. & Shun-Shin, G. A. (2012) Accuracy of referrals from an orthoptic vision screening program for 3- to 4-year-old preschool children. *Journal of AAPOS*, 16: 49-52.
Not in PICO
- Huang, S., Crawford, J. B., Porco, T. & Rutar, T. (2010) Clinicopathologic review of pediatric enucleations during the last 50 years. *Journal of AAPOS*, 14: 328-333.
Not in PICO
- Huh, J., Noh, C. I., Kim, Y. W., Choi, J. Y., Yun, Y. S., Shin, H. Y., Ahn, H. S. & Kim, Y. J. (1999) Secondary cardiac tumor in children. *Pediatric Cardiology*, 20: 400-403.
Not in PICO
- Hwang, S.-K., Paek, S.-H., Gyu, K. D., Jeon, Y.-K., Chi, J. G. & Jung, H.-W. (2002) Olfactory neuroblastomas: Survival rate and prognostic factor. *Journal of Neuro-Oncology*, 59: 217-226.
Not in PICO
- Ikpeme, E. E. & Dixon-Umo, O. T. (2013) Paediatric renal diseases in uyo, Nigeria : A 10 year review. *Pediatric Nephrology*, 28: 1411.
Not in PICO
- Israels, T., Ribeiro, R. C. & Molyneux, E. M. (2010) Strategies to improve care for children with cancer in Sub-Saharan Africa. [Review]. *European Journal of Cancer*, 46: 1960-1966.
Narrative review
- Jackson, C. & Glasson, W. (1998) Prevention of visual loss. Screening in general practice. *Australian Family Physician*, 27: 150-153.
Narrative review
- Jadresic, L., Leake, J., Gordon, I., Dillon, M. J., Grant, D. B., Pritchard, J., Risdon, R. A. & Barratt, T. M. (1990) Clinicopathologic review of twelve children with nephropathy, Wilms tumor, and genital abnormalities (Drash syndrome). *Journal of Pediatrics*, 117: 717-725.
Not in PICO
- James, B. O., Ajayi, S. O., Ogun, O. A. & Oladokun, R. E. (2009) Factors influencing time to diagnosis of childhood cancer in Ibadan, Nigeria. *African Health Sciences*, 9: 247-253.
Not in PICO
- Januszkiewicz, D., Lastowska, M. & Zielinski, W. (1990) Neuroblastoma in children. Results of the treatment and analysis of selected prognostic factors. [Polish]. *Nowotwory*, 40: 143-148.
Not in PICO
- Jett, J. R. (2010) Mediastinal tumors. *Respirology*, 15: 18.
Narrative review
- Joseph, B., Madhavan, J., Mamatha, G., Ramprasad, V. L., Gopal, L. & Kumaramanickavel, G. (2006) Retinoblastoma: a diagnostic model for India. *Asian Pacific Journal of Cancer Prevention: Apjcp*, 7: 485-488.
Not in PICO

- Junuzovic, D., Kerleta, A. & Masic, I. (2013) The frequency of renal cell carcinoma in population of patients with kidney tumors. *Medicinski Arhiv*, 67: 27-30.
Not in PICO
- Kaimbo, W. K., Mvitu, M. M. & Missotten, L. (2002) Presenting signs of retinoblastoma in Congolese patients. *Bulletin de la Societe Belge d Ophthalmologie*.(283):37-41, 2002., 37-41.
Not in PICO
- Kamath, V. B., Sowmya, V., Ballal, C. K. & Mendonca, N. (2013) Esthesioneuroblastoma as an unusual cause for dystopia. *Orbit*, 32: 392-394.
Not in PICO
- Kehrer-Sawatzki, H. & Cooper, D. N. (2008) Mosaicism in sporadic neurofibromatosis type 1: variations on a theme common to other hereditary cancer syndromes?. [Review] [136 refs]. *Journal of Medical Genetics*, 45: 622-631.
Narrative review
- Khalifa, N. M., Maximous, D. W. & Abd-Elseyed, A. A. (2008) Fetus in fetu: a case report. *Journal of Medical Case Reports [Electronic Resource]*, 2: 2.
Not in PICO
- Kim, H. J., McLawhorn, A. S., Goldstein, M. J. & Boland, P. J. (2012) Malignant Osseous Tumors of the Pediatric Spine. *Journal of the American Academy of Orthopaedic Surgeons*, 20: 646-656.
Narrative review
- Kumar, H. R., Sandoval, J. A., Lovell, M. A., Fenton, L. Z. & Bealer, J. F. (2010) Primary pancreatic neuroblastoma: an unusual tumor in infancy. *Journal of Pediatric Surgery*, 45: 642-646.
Not in PICO
- Kushner, B. H. & Cheung, N. K. (2005) Neuroblastoma--from genetic profiles to clinical challenge. *New England Journal of Medicine*, 353: 2215-2217.
Comment
- Lai, H., Ma, F. & Lai, S. (2003) Identification of the novel role of pRB in eye cancer. [Review] [38 refs]. *Journal of Cellular Biochemistry*, 88: 121-127.
Narrative review
- Leal, C. A., Rivera-Luna, R., Martinez, A., Cardenas, R. S., Salazar, A., Lanche, M. T. & Ridaura, S. C. (1995) Retinoblastoma in initial stages. Clinical experience at the Instituto Nacional de Pediatria. [Spanish]. *Revista del Instituto Nacional de Cancerologia*, 41: 192-195.
Not in PICO
- Lebedev, V. I., Pashkov, I. V., Boichenko, E. I., Sharov, T. A., Zaeva, G. E., Sokolova, I. N., Glekov, I. V., Mentkevich, G. L. & Ordukhian, Z. S. (1996) [Experience in treating Nephroblastomas]. [Review] [10 refs] [Russian]. *Vestnik Rossiiskoi Akademii Meditsinskikh Nauk*.(10):13-7, 1996., 13-17.
Narrative review
- Levecq, L., De, P. P. & Guagnini, A. P. (2005) [Epidemiology of ocular and orbital lesions referred to an ocular oncology center]. [French]. *Journal Francais d Ophthalmologie*, 28: 840-844.
Not in PICO
- Levitt, G. (2012) Renal tumours: Long-term outcome. *Pediatric Nephrology*, 27: 911-916.
Narrative review
- Levy, D., Aerts, I., Michon, J., Lumbroso-Le, R. L., Cellier, C. & Orbach, D. (2014) Childhood cancer: Progress but prognosis still very unequal. Example of Retinoblastoma and high-risk Neuroblastoma. [French]. *Bulletin du Cancer*, 101: 250-257.
Narrative review
- Lewis, G. & Maxwell, A. P. (2002) Early diagnosis improves survival in kidney cancer. *Practitioner*, 256: 13-16.
Narrative review
- Licata, B. & Turazzi, S. (210) Bleeding cerebral neoplasms with symptomatic hematoma. *Journal of Neurosurgical Sciences*, 47: 201-210.
Not in PICO

- Lin, Y. C. (2003) Early recognition of infant malignancy: the five most common infant cancers. *Neonatal network : NN*, 22: 11-19.
Narrative review
- Ling, R. E., Capsomidis, A. & Patel, S. R. (2014) Identifying childhood cancer: How is the urgent suspected cancer referral pathway performing? *Archives of Disease in Childhood*, 99: A108.
Not in PICO
- Long, J. A., Descotes, J. L. & Rambeaud, J. J. (2007) [Kidney cancer diagnosis]. [Review] [10 refs] [French]. *Revue du Praticien*, 57: 603-612.
Narrative review
- Ludick, A. (2013) Taking the early warning signs of childhood cancer to the rural areas of gauteng in south africa: Training health professionals. *Pediatric Blood and Cancer*, 60: 228.
Not in PICO
- Lueder, G. T. (2005) The effect of initial recognition of abnormalities by physicians on outcome of retinoblastoma. *Journal of Aapos: American Association for Pediatric Ophthalmology & Strabismus*, 9: 383-385.
Not in PICO
- Lyons, C. J. & Hungerford, J. (1990) Detection of ocular malignancies. *Journal of the Royal Society of Medicine*, 83: 165-167.
Not in PICO
- Makdoui, K. & Crafoord, S. (2011) Vasoproliferative retinal tumours in a Swedish population. *Acta Ophthalmologica*, 89: 91-94.
Not in PICO
- Maki, J. L., Marr, B. P. & Abramson, D. H. (2009) Diagnosis of retinoblastoma: how good are referring physicians? *Ophthalmic Genetics*, 30: 199-205.
Not in PICO
- Malkani, I., Warriar, R. P., Yu, L. C. & Ode, D. L. (1993) Retinoblastoma: a review. [Review] [31 refs]. *Indian Journal of Pediatrics*, 60: 227-236.
Narrative review
- Marsh-Tootle, W. L., McGwin, G., Kohler, C. L., Kristofco, R. E., Datla, R. V. & Wall, T. C. (2011) Efficacy of a web-based intervention to improve and sustain knowledge and screening for amblyopia in primary care settings. *Investigative Ophthalmology and Visual Science*, 52: 7160-7167.
Not in PICO
- Matejovsky, Z. & Povysil, C. (1986) Ewing's sarcoma. New clinico-pathological aspects. [German]. *Zentralblatt fur Allgemeine Pathologie und Pathologische Anatomie*, 132: 11-24.
Narrative review
- Maxwell, P. (2013) Identifying signs of retinoblastoma. *Nursing Times*, 109: 17-23.
Narrative review
- Mazur, K. A. (2010) Neuroblastoma: What the nurse practitioner should know. *Journal of the American Academy of Nurse Practitioners*, 22: 236-245.
Narrative review
- McHugh, K. (2007) Renal and adrenal tumours in children. [Review] [19 refs]. *Cancer Imaging*, 7: 41-51.
Narrative review
- McNeil, D. E., Brown, M., Ching, A. & DeBaun, M. R. (2001) Screening for Wilms tumor and hepatoblastoma in children with Beckwith-Wiedemann syndromes: a cost-effective model. *Medical & Pediatric Oncology*, 37: 349-356.
Not in PICO
- Meel, R., Radhakrishnan, V. & Bakhshi, S. (2012) Current therapy and recent advances in the management of retinoblastoma. *Indian journal of medical and paediatric oncology : official*

Journal of Indian Society of Medical & Paediatric Oncology, 33: 80-88.

Narrative review

Melamud, A., Palekar, R. & Singh, A. (2006) Retinoblastoma. [Review] [21 refs][Erratum appears in *Am Fam Physician*. 2007 Apr 1;75(7):980]. *American Family Physician*, 73: 1039-1044.

Narrative review

Memon, F., Rathi, S. L. & Memon, M. H. (2007) Pattern of solid paediatric malignant neoplasm at Lumhs, Jamshoro, Pakistan. *Journal of Ayub Medical College, Abbottabad: JAMC*, 19: 55-57.

Not in PICO

Mierzwa, D. M. & Romanowska, D. B. (2012) Assessment of the influence of one's education on early diagnosis of multiple primary cancer in patients with uveal melanoma. *Klinika. oczna*, 114: 111-114.

Not in PICO

Millar, A. J., Davidson, A., Rode, H., Numanoglu, A., Hartley, P. S., Daubenton, J. D. & Desai, F. (2005) Bilateral Wilms' tumors: a single-center experience with 19 cases. *Journal of Pediatric Surgery*, 40: 1289-1294.

Not in PICO

Miron, I., Miron, L., Dumitras, S., Aprodu, G., Ciobanu, A. & Tansanu, I. (2007) Statistical study of the evolution over ten years of the clinical and therapeutic approach in childhood soft tissue sarcoma. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 111: 358-362.

Not in PICO

Mitchell, W. G., Davalos-Gonzalez, Y., Brumm, V. L., Aller, S. K., Burger, E., Turkel, S. B., Borchert, M. S., Hollar, S. & Padilla, S. (2002) Opsoclonus-ataxia caused by childhood neuroblastoma: developmental and neurologic sequelae.[Erratum appears in *Pediatrics* 2002 Oct;110(4):853-4]. *Pediatrics*, 109: 86-98.

Not in PICO

Mohanna, M. A. & Sallam, A. K. (2014) - Idiopathic hemihypertrophy. - *Saudi Medical Journal*, 35: 403-405.

Not in PICO

Mott, M. G. (1995) Neoplasia in Childhood - 25 Years of Progress. *Annals of Oncology*, 6: 3-9.

Narrative review

Motzer, R. J., Bolger, G. B., Boston, B., Carducci, M. A., Fishman, M., Hancock, S. L., Hauke, R. J., Hudes, G. R., Jonasch, E., Kantoff, P., Kuzel, T. M., Lange, P. H., Levine, E. G., Logothetis, C., Margolin, K. A., Pohar, K., Redman, B. G., Robertson, C. N., Samlowski, W. E., Sheinfeld, J. & National Comprehensive, C. N. (2006) Kidney cancer. Clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network*, 4: 1072-1081.

Guideline

Moukheiber, A. K., Nicollas, R., Roman, S., Coze, C. & Triglia, J. M. (2001) Primary pediatric neuroblastic tumors of the neck. *International Journal of Pediatric Otorhinolaryngology*, 60: 155-161.

Not in PICO

Mouratova, T. (2005) Trilateral retinoblastoma: a literature review, 1971-2004. [Review] [92 refs]. *Bulletin de la Societe Belge d Ophthalmologie*.(297):25-35, 2005., 25-35.

Narrative review

Mullaney, P. B., Karcioğlu, Z. A., al-Mesfer, S. & Dowaidi, M. (1996) Retinoblastoma referral patterns in Saudi Arabia. *Ophthalmic Epidemiology*, 3: 35-46.

Not in PICO

Musarella, M. A., Chan, H. S., DeBoer, G. & Gallie, B. L. (1984) Ocular involvement in neuroblastoma: prognostic implications. *Ophthalmology*, 91: 936-940.

Not in PICO

- Nabie, R., Taheri, N., Fard, A. M. & Fouladi, R. F. (2012) Characteristics and clinical presentations of pediatric retinoblastoma in North-western Iran. *International Journal of Ophthalmology*, 5: 510-512.
Not in PICO
- Nakamura, L. & Ritchey, M. (2010) Current management of wilms' tumor. [Review] [58 refs]. *Current Urology Reports*, 11: 58-65.
Narrative review
- Narukawa, T., Naitoh, Y., Taniguchi, H., Ueno, A., Nakagawa, H., Suzuki, K., Fujihara, A., Okihara, K. & Miki, T. (2014) - [A pediatric wilms' tumor presenting with a right renal injury]. [Japanese]. - *Hinyokika Kyo - Acta Urologica Japonica*, 60: 329-331.
Not in PICO
- Naseripour, M., Nazari, H., Bakhtiari, P., Modarres-Zadeh, M., Vosough, P. & Ausari, M. (2009) Retinoblastoma in Iran: Outcomes in terms of patients' survival and globe survival. *British Journal of Ophthalmology*, 93: 28-32.
Not in PICO
- Nathan, N. R. & Donahue, S. P. (2011) Modification of Plusoptix referral criteria to enhance sensitivity and specificity during pediatric vision screening. *Journal of AAPOS*, 15: 551-555.
Not in PICO
- Nathrath, M. & Teichert, V. L., I (2009) Oncologic causes of bone pain. [German]. *Monatsschrift fur Kinderheilkunde*, 157: 655-660.
Narrative review
- Nishimura, O. & Ohata, M. (1994) [Neuroblastoma]. [Review] [10 refs] [Japanese]. *Ryoikibetsu Shokogun Shirizu.(4):440-1, 1994., 440-441.*
Narrative review?
- Nucci, P. & Curiel, B. (2009) Abnormal head posture due to ocular problems: A review. *Current Pediatric Reviews*, 5: 105-111.
Narrative review
- O'Doherty, M., Lanigan, B., Breathnach, F., O'Meara, A., Gallie, B., Chan, H. & O'Keefe, M. (2005) A retrospective review of visual outcome and complications in the treatment of retinoblastoma. *Irish Medical Journal*, 98: 17-20.
Not in PICO
- Osman, Y., Haraz, A., El-Mekresh, M., Gomha, A. M., El-Ghar, M. A. & Eraky, I. (2011) Adrenal tumors with venous thrombosis: a single-institution experience. *Urologia Internationalis*, 87: 182-185.
Not in PICO
- Ott, J. J., Ullrich, A. & Miller, A. B. (2009) The importance of early symptom recognition in the context of early detection and cancer survival. *European Journal of Cancer*, 45: 2743-2748.
Narrative review
- Ozdemir, H., Tacyildiz, N., Unal, E., Yavuz, G., Ugur, H. & Gunduz, K. (2007) Clinical and epidemiological characteristics of retinoblastoma: Correlation with prognosis in a Turkish Pediatric Oncology Center. *Pediatric Hematology and Oncology*, 24: 221-231.
Not in PICO
- Pakakasama, S. & Tomlinson, G. E. (2002) Genetic predisposition and screening in pediatric cancer. *Pediatric Clinics of North America*, 49: 1393-1413.
Narrative review
- Palazzi, M. A., Stephan, C., Brandalise, S. R. & Aguiar, S. D. S. (2013) Retinoblastoma diagnosis: A proposal based on the experience of Centro Infantil Boldrini, Brazil. *Pediatric Hematology and Oncology*, 30: 379-385.
Not in PICO
- Paltiel, H. J. (2007) Sonography of Pediatric Renal Tumors. *Ultrasound Clinics*, 2: 89-104.
Narrative review

- Paradies, G., Zullino, F., Orofino, A. & Leggio, S. (2013) Mediastinal teratomas in children. Case reports and review of the literature. *Annali Italiani di Chirurgia*, 84(4):395-403, -403, 2013.
Not in PICO
- Park, C. S., Ha, H. G., Lee, S. D. & Chung, M. K. (2009) Clinical characteristics of Wilms' tumor according to age. [Korean]. *Korean Journal of Urology*, 50: 1188-1192.
Not in PICO
- Paulino, A. C. (1999) Trilateral retinoblastoma: is the location of the intracranial tumor important?. [Review] [45 refs]. *Cancer*, 86: 135-141.
Not in PICO
- Peng, X., Wang, G., Zhang, F., Meng, S. & Lu, N. (2002) [Clinical features of 48 cases with retinal angioma]. [Chinese]. *Chung-Hua Yen Ko Tsa Chih [Chinese Journal of Ophthalmology]*, 38: 550-552.
Not in PICO
- Petrus, L. V., Hall, T. R., Boechat, M. I., Westra, S. J., Curran, J. G., Steckel, R. J. & Kangarloo, H. (1992) The pediatric patient with suspected adrenal neoplasm: which radiological test to use? *Medical & Pediatric Oncology*, 20: 53-57.
Not in PICO
- Pollock, B. H., Krischer, J. P. & Vietti, T. J. (1991) Interval between symptom onset and diagnosis of pediatric solid tumors. *Journal of Pediatrics*, 119: 725-732.
Not in PICO
- Priest, J. R., McDermott, M. B., Bhatia, S., Watterson, J., Manivel, J. C. & Dehner, L. P. (1997) Pleuropulmonary blastoma: A clinicopathologic study of 50 cases. *Cancer*, 80: 147-161.
Not in PICO
- Provenzi, M., Saettini, F., Conter, V., Chinaglia, D., Vai, P., Bruno, A., Cavalleri, L., Foglia, C., Giraldi, E., Collini, P. & Spreafico, F. (2013) Is there a role for FDG-PET for the assessment of treatment efficacy in Wilms' tumor? A case report and literature review. *Pediatric Hematology & Oncology*, 30(7):633-9, -9, 2013.
Not in PICO
- Pujol, J. F., Perel, Y., Fayon, M., Dossantos, P., Cazauran, J. M., Bucco, P. & Guillard, J. M. (1992) Malignant Systemic Hypertension-Related Cardiac-Failure in A Child with Nephroblastoma. *Pediatric*, 47: 441-444.
Not in PICO
- Raab, C. P. & Gartner, J. C., Jr. (2009) Diagnosis of childhood cancer. [Review] [33 refs]. *Primary Care; Clinics in Office Practice*, 36: 671-684.
Narrative review
- Rahi, J. S. & Lynn, R. (1998) A survey of paediatricians' practice and training in routine infant eye examination. *Archives of Disease in Childhood*, 78: 364-366.
Not in PICO
- Reinhard, H., Aliani, S., Ruebe, C., Stockle, M., Leuschner, I. & Graf, N. (2004) Wilms' tumor in adults: Results of the Society of Pediatric Oncology (SIOP) 93-01/Society for Pediatric Oncology and Hematology (GPOH) Study. *Journal of Clinical Oncology*, 22: 4500-4506.
Not in PICO
- Rezaimehr, Y. & Bhargava, R. (2013) Neuroblastoma presenting as persistent postprandial emesis in a neonate. *Pediatric Emergency Care*, 29(12):1273-5, -5, 2013.
Not in PICO
- Riley, R. D., Burchill, S. A., Abrams, K. R., Heney, D., Lambert, P. C., Jones, D. R., Sutton, A. J., Young, B., Wailoo, A. J. & Lewis, I. J. (2003) A systematic review and evaluation of the use of tumour markers in paediatric oncology: Ewing's sarcoma and neuroblastoma (Structured abstract). *Health Technology Assessment Database*, 1.
Not in PICO

- Ritchey, M., Daley, S., Shamberger, R. C., Ehrlich, P., Hamilton, T., Haase, G. & Sawin, R. (2008) Ureteral extension in Wilms' tumor: a report from the National Wilms' Tumor Study Group (NWTSG). *Journal of Pediatric Surgery*, 43: 1625-1629.
Not in PICO
- Rodrigues, K. E. & de, C. B. (2003) Early diagnosis of childhood cancer: a team responsibility. [Portuguese]. *Revista da Associação Médica Brasileira (1992)*, 49: 29-34.
Narrative review
- Roganovic, J. (2006) Hepatic tumours. [Croatian]. *Paediatrica Croatica, Supplement*, 50: 260-264.
Narrative review
- Ross, G., Lipper, E. G., Abramson, D. & Preiser, L. (2001) The development of young children with retinoblastoma. *Archives of Pediatrics & Adolescent Medicine*, 155: 80-83.
Not in PICO
- Roth, A. (1981) The role of the general practitioner and the family in the initial diagnosis and treatment of the squinting child. [French]. *Therapeutische Umschau*, 38: 228-234.
Narrative review
- Royer-Pokora, B., Beier, M., Henzler, M., Alam, R., Schumacher, V., Weirich, A. & Huff, V. (2004) Twenty-four new cases of WT1 germline mutations and review of the literature: genotype/phenotype correlations for Wilms tumor development. *American Journal of Medical Genetics.Part A*, 127A: 249-257.
Not in PICO
- Royer-Pokora, B. (2007) Genetic predisposition to Wilms tumor. [German]. *Medizinische Genetik*, 19: 234-238.
Narrative review
- Ruccione, K. S. (1992) Wilms' tumor: a paradigm, a parallel, and a puzzle. [Review] [67 refs]. *Seminars in Oncology Nursing*, 8: 241-251.
Narrative review
- Sampson, V. B., Gorlick, R., Kamara, D. & Anders, K. E. (2013) A review of targeted therapies evaluated by the pediatric preclinical testing program for osteosarcoma. *Frontiers in Oncology*, 3:132.
Narrative review
- Sasaki, H., Sato, Y., Kondo, S., Fukai, I., Kiriya, M., Yamakawa, Y. & Fuji, Y. (2002) Expression of the periostin mRNA level in neuroblastoma. *Journal of Pediatric Surgery*, 37: 1293-1297.
Not in PICO
- Schenk, J.-P., Engelmann, D., Rohrschneider, W., Zieger, B., Semler, O., Graf, N. & Troger, J. (2004) Rhabdoid tumors of the kidney in childhood - A retrospective radiomorphologic analysis of 22 patients as part of the nephroblastoma study SIOP 93/01-GPOH registered cases. [German]. *RoFo Fortschritte auf dem Gebiet der Röntgenstrahlen und der Bildgebenden Verfahren*, 176: 965-971.
Not in PICO
- Schilling, F. H. (2002) [Neuroblastoma Early Detection Model Project. Background and results]. [German]. *Kinderkrankenschwester*, 21: 295-296.
Narrative review
- Schmidt, D. (2005) [Retinal angiomas]. [Review] [176 refs] [German]. *Klinische Monatsblätter für Augenheilkunde*, 222: 90-109.
Narrative review
- Schmidt, D., Anderson, L., Bingen, K., Hoag, J., Kupst, M. J. & Warwick, A. B. (2010) Late effects in adult survivors of childhood cancer: Considerations for the general practitioner. *Wisconsin Medical Journal*, 109: 98-108.
Narrative review
- See, W. A. & Williams, R. D. (1992) Tumors of the kidney, ureter, and bladder. *Western Journal of Medicine*, 156: 523-534.
Narrative review

- Seregard, S., Ek, U., Preisler, G., af, T. E., Jacobson, L., Oskar, K., Illerstahl, I. & Kock, E. (1996) [A study of children with retinoblastoma. Diagnosis is often delayed]. [Swedish]. *Lakartidningen*, 93: 1133-1135.
Not in PICO
- Servodidio, C. A., Abramson, D. H. & Romanella, A. (1991) Retinoblastoma. [Review] [19 refs]. *Cancer Nursing*, 14: 117-123.
Narrative review
- Shamberger, R. C., Haase, G. M., Argani, P., Perlman, E. J., Cotton, C. A., Takashima, J., Green, D. M. & Ritchey, M. L. (652) Bilateral Wilms' tumors with progressive or nonresponsive disease. *Journal of Pediatric Surgery*, 41: 652-657.
Not in PICO
- Shi, G. H., Chen, Y., Yao, X. D., Zhang, S. L., Dai, B., Feng, L. Q., Zhang, H. L., Shen, Y. J., Zhu, Y., Zhu, Y. P., Xiao, W. J., Ma, C. G., Wen, L. G., Qin, X. J., Yang, L. F. & Ye, D. W. (2013) Individualized renal mass biopsy strategy for Chinese patients with different subtypes and necrosis area. *Urologic Oncology*, 31(6):920-3, -3, 2013.
Not in PICO
- Shields, J. A., Shields, C. L., Gunduz, K. & Eagle, R. C., Jr. (1999) Neoplasms of the retinal pigment epithelium: the 1998 Albert Ruedemann, Sr, memorial lecture, Part 2. *Archives of Ophthalmology*, 117: 601-608.
Not in PICO
- Simon, J. W. & Kaw, P. (2001) Commonly missed diagnoses in the childhood eye examination. [Review] [16 refs]. *American Family Physician*, 64: 623-628.
Narrative review
- Simon, T. (555) [Neuroblastoma]. [Review] [7 refs] [German]. *Urologe (Auszg.A)*, 44: 543-554.
Narrative review
- Somashekhar, M., Kadamba, P. S. & Wakodkar, M. (2008) Chronic disseminated intravascular coagulation presenting as renal mass. *Journal of Indian Association of Pediatric Surgeons*, 13: 144-146.
Not in PICO
- Sovinz, P., Urban, C., Lackner, H., Benesch, M. & Langmann, G. (2006) Retinoblastoma: a proposal for a multimodal treatment concept for intraocular retinoblastoma in Austria. *Wiener Klinische Wochenschrift*, 118: 22-30.
Not in PICO
- Stepan, J., Cepulic, M., Petkovic, I., Cizmic, A. & Nakic, M. (2007) Nephroblastomas - Wilm's tumor (WT). [Croatian]. *Paediatrica Croatica, Supplement*, 51: 92-97.
Narrative review
- Stricker, S. J. & Hunt, T. (2004) Evaluation of leg length discrepancy in children. *International Pediatrics*, 19: 134-142+144.
Narrative review
- Suita, S. (2002) Stephen L. Gans overseas lecture. Mass screening for neuroblastoma in Japan: lessons learned and future directions. *Journal of Pediatric Surgery*, 37: 949-954.
Not in PICO
- Teplick, A., Kowalski, M., Biegel, J. A. & Nichols, K. E. (2011) Educational paper : Screening in cancer predisposition syndromes: Guidelines for the general pediatrician. *European Journal of Pediatrics*, 170: 285-294.
Narrative review
- Van Den Heuvel-Eibrink, M. M., Grundy, P., Graf, N., Pritchard-Jones, K., Bergeron, C., Patte, C., Van, T. H., Rey, A., Langford, C., Anderson, J. R. & De, K. J. (2008) Characteristics and survival of 750 children diagnosed with a renal tumor in the first seven months of life: A collaborative study by the SIOP/GPOH/SFOP, NWTSG, and UKCCSG Wilms tumor study groups. *Pediatric Blood and*

- Cancer*, 50: 1130-1134.
Not in PICO
- Varan, A. (2008) Wilms' tumor in children: An overview. *Nephron - Clinical Practice*, 108: c83-c90.
Narrative review
- Vemuganti, G. K., Jalali, S., Honavar, S. G. & Shekar, G. C. (2001) Enucleation in a tertiary eye care centre in India: prevalence, current indications and clinicopathological correlation. *Eye*, 15: 6-5.
Not in PICO
- Verma, N., Fromberg, G., Ghose, S. & Chandershekhar, G. (1987) Ultrasonography in orbital retinoblastoma. *Orbit*, 6: 37-41.
Not in PICO (referred population)
- Vingtain, P., Negrel, A. D., Ginoux, J., Cozette, P., Rivaud, C., Queguiner, P., Feuillerat, J. & Chovet, M. (1986) [Orbital and ocular tumors in the Republic of Mali]. [French]. *Medecine Tropicale*, 46: 147-153.
Not in PICO
- Vujanic, G. M. (2006) Renal tumours in early life. *Current Diagnostic Pathology*, 12: 210-219.
Narrative review
- Wakamb, G. K., Nkashama, G. M., Mbuli, R. L., Borasisi, G. C. & Nikulu, J. I. (2013) [Problematic of the management of childhood cancer: experience of retinoblastoma in Lubumbashi (DR Congo) and the importance of early diagnosis]. [French]. *The Pan African medical journal*, 14: 64.
Not in PICO
- Wallach, M., Balmer, A., Munier, F., Houghton, S., Pampallona, S., von der, W. N., Beck-Popovic, M., Swiss Pediatric Oncology Group & Swiss Childhood, C. R. (2006) Shorter time to diagnosis and improved stage at presentation in Swiss patients with retinoblastoma treated from 1963 to 2004. *Pediatrics*, 118: e1493-e1498.
Not in PICO
- Wayte, N., Da, S. L., Chenevix-Trench, G. & Lakhani, S. R. (2008) What's in a cancer syndrome? Genes, phenotype and pathology. *Pathology*, 40: 247-259.
Narrative review
- Weng, E. Y., Mortier, G. R. & Graham, J. (1995) Beckwith-Wiedemann syndrome: An update and review for the primary pediatrician. *Clinical Pediatrics*, 34: 317-326.
Narrative review
- White, J. & Gole, G. (2012) Delay in the diagnosis of retinoblastoma: An update. *Clinical and Experimental Ophthalmology*, 40: 37.
Not in PICO
- Wiesbauer, P. (2008) [Nephrogenic tumors]. [German]. *Radiologe*, 48: 932-939.
Narrative review
- Wirix, M., Parys-Vanginderdeuren, R., Casteels, I. & Uyttendaele, A. (2000) Delayed diagnosis of retinoblastoma. *Bulletin de la Societe Belge d Ophthalmologie*.(278):37-41, 2000., 37-41.
Not in PICO
- Wolf, W. J. & Bancroft, B. (1980) Early detection of childhood malignancies. *Pediatric Nursing*, 6: 43-46.
Narrative review
- Young, G., Toretsky, J. A., Campbell, A. B. & Eskenazi, A. E. (2000) Recognition of common childhood malignancies. *American Family Physician*, 61: 2144-2154.
Narrative review
- Zawitkowska-Klaczynska, J., Katski, K., Nurzynska-Flak, J. & Kowalczyk, J. (2003) Primary chest tumours in children. *Annales Universitatis Mariae Curie-Sklodowska - Sectio d - Medicina*, 58: 106-110.
Not in PICO

Zeller, G. X. & De, S. E. (1991) [A numerical overview of various forms of retinoblastoma]. [Review] [14 refs] [German]. *Klinische Monatsblätter für Augenheilkunde*, 198: 81-82.

Narrative review

Zintl, E. & Deufrains, A. (1989) [Contribution of the pediatrician in the early diagnosis of eye diseases. 2]. [Review] [10 refs] [German]. *Kinderärztliche Praxis*, 57: 263-270.

Narrative review

Zoller, G., Lakomek, M. & Ringert, R. H. (1992) [Wilm's tumor 1992. State of research and results of current therapeutic concepts]. [Review] [20 refs] [German]. *Urologe (Auszg.A)*, 31: 360-367.

Narrative review

Review question:

Which investigations of symptoms of suspected retinoblastoma, neuroblastoma and Wilm's tumour in children should be done with clinical responsibility retained by primary care?

Results

Literature search

Retinoblastoma:

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	341	42	26/06/2013
<i>Premedline</i>	1980-2013	15	2	26/06/2013
<i>Embase</i>	1980-2013	240	21	26/06/2013
<i>Cochrane Library</i>	1980-2013	19	0	26/06/2013
<i>Psychinfo</i>	1980-2013	1	0	26/06/2013
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	1980-2013	34	9	26/06/2013

Total References retrieved (after de-duplication): 66

Retinoblastoma: Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	6/2013-27/08/2014	8	1	27/08/2014
<i>Premedline</i>	6/2013-27/08/2014	11	1	27/08/2014
<i>Embase</i>	6/2013-27/08/2014	11	2	27/08/2014
<i>Cochrane Library</i>	6/2013-27/08/2014	7	0	27/08/2014
<i>Web of Science (SCI & SSCI) and ISI Proceedings</i>	6/2013-27/08/2014	8	0	27/08/2014

Total References retrieved (after de-duplication): 2

Neuroblastoma:

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
<i>Medline</i>	1980-2013	220	16	25/06/2013
<i>Premedline</i>	1980-2013	21	5	25/06/2013

Embase	1980-2013	135	14	25/06/2013
Cochrane Library	1980-2013	4	1	25/06/2013
Psychinfo	1980-2013	4	0	25/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	26	2	25/06/2013

Total References retrieved (after de-duplication): 33

Neuroblastoma: Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	6/2013-27/08/2014	6	0	27/08/2014
Premedline	6/2013-27/08/2014	26	4	27/08/2014
Embase	6/2013-27/08/2014	18	2	27/08/2014
Cochrane Library	6/2013-27/08/2014	17	0	27/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	6/2013-27/08/2014	5	0	27/08/2014

Total References retrieved (after de-duplication): 6

Wilm's tumour:

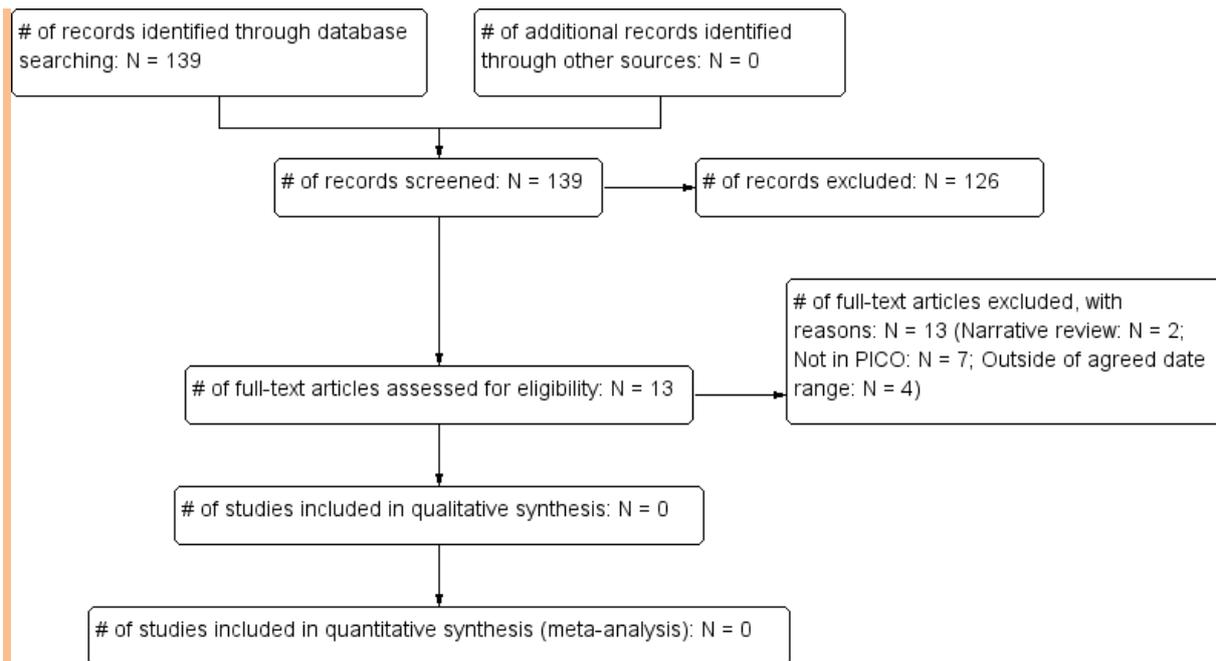
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	266	23	26/06/2013
Premedline	1980-2013	22	2	26/06/2013
Embase	1980-2013	219	11	26/06/2013
Cochrane Library	1980-2013	40	0	26/06/2013
Psychinfo	1980-2013	1	0	26/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	5	1	26/06/2013

Total References retrieved (after de-duplication): 28

Wilm's tumour: Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	6/2013-27/08/2014	9	1	27/08/2014
Premedline	6/2013-27/08/2014	28	2	27/08/2014
Embase	6/2013-27/08/2014	29	3	27/08/2014
Cochrane Library	6/2013-27/08/2014	13	0	27/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	6/2013-27/08/2014	1	0	27/08/2014

Total References retrieved (after de-duplication): 4



Study results

No evidence was identified pertaining to the diagnostic accuracy of tests in children with suspected retinoblastoma, neuroblastoma and Wilm's tumour where the clinical responsibility was retained by primary care.

References

Included studies

None

Excluded studies (with excl reason)

- Ahmed, S., Goel, S., Khandwala, M., Agrawal, A., Chang, B. & Simmons, I. G. (2006) Neuroblastoma with orbital metastasis: ophthalmic presentation and role of ophthalmologists. *Eye*, 20: 466-470. Not in PICO
- Ahrensberg, J. M., Fenger-Gron, M. & Vedsted, P. (2013) Use of primary care during the year before childhood cancer diagnosis: a nationwide population-based matched comparative study. *PLoS ONE [Electronic Resource]*, 8: e59098. Not in PICO
- Alkatan, H., Al-Amry, M., Al-Hussain, H., Al-Dhibi, H. & al-Mesfer, S. (2011) Medulloepithelioma of the ciliary body: The delay in diagnosis and frequent initial mismanagement. *Canadian Journal of Ophthalmology*, 46: 431-438. Not in PICO
- Aston, J. W., Jr. (1990) Pediatric update #16. The orthopaedic presentation of neuroblastoma. *Orthopaedic Review*, 19: 929-932. Not in PICO
- Augsburger, J. J. & Shields, J. A. (1984) Fine needle aspiration biopsy of solid intraocular tumors: indications, instrumentation and techniques. *Ophthalmic Surgery*, 15: 34-40. Not in PICO
- Augsburger, J. J., Shields, J. A., Folberg, R., Lang, W., O'Hara, B. J. & Claricci, J. D. (1985) Fine needle aspiration biopsy in the diagnosis of intraocular cancer. Cytologic-histologic correlations.

- Ophthalmology*, 92: 39-49.
Not in PICO
- Augsburger, J. J. (1988) Fine needle aspiration biopsy of suspected metastatic cancers to the posterior uvea. *Transactions of the American Ophthalmological Society*, 86: 499-560.
Not in PICO
- Badhu, B., Sah, S. P., Thakur, S. K. D., Dulal, S., Kumar, S., Sood, A., Das, H. & Sah, R. P. (2005) Clinical presentation of retinoblastoma in Eastern Nepal. *Clinical and Experimental Ophthalmology*, 33: 386-389.
Not in PICO
- Bai, S., Ren, R., Li, B., Xu, X., Zhao, B., Gao, F., Li, L. & Jonas, J. B. (2011) Delay in the diagnosis of retinoblastoma in China. *Acta Ophthalmologica*, 89: e72-e74.
Not in PICO
- Balmer, A., Zografos, L. & Munier, F. (2006) Diagnosis and current management of retinoblastoma. [Review] [60 refs]. *Oncogene*, 25: 5341-5349.
Narrative review
- Balmer, A. & Munier, F. (2007) Differential diagnosis of leukocoria and strabismus, first presenting signs of retinoblastoma. *Clinical Ophthalmology*, 1: 431-439.
Narrative review
- Barroca, H. & Bom-Successo, M. (2014) Fine needle biopsy with cytology in paediatrics: The importance of a multidisciplinary approach and the role of ancillary techniques. *Cytopathology*, 25: 6-20.
Narrative review
- Bilal, M. M. & Brown, J. J. (1997) MR imaging of renal and adrenal masses in children. *Magnetic Resonance Imaging Clinics of North America*, 5: 179-197.
Narrative review
- Bliznakova, D. (2003) Differential diagnosis of some kidney diseases in childhood. [Bulgarian]. *Bulgarian Medicine*, 11: 7-10.
Narrative review
- Boubaker, A. & Bischof, D. A. (2003) Nuclear medicine procedures and neuroblastoma in childhood. Their value in the diagnosis, staging and assessment of response to therapy. [Review] [55 refs]. *Quarterly Journal of Nuclear Medicine*, 47: 31-40.
Narrative review
- Brasme, J. F., Morfouace, M., Grill, J., Martinot, A., Amalberti, R., Bons-Letouzey, C. & Chalumeau, M. (2012) Delays in diagnosis of paediatric cancers: a systematic review and comparison with expert testimony in lawsuits. [Review]. *Lancet Oncology*, 13: e445-e459.
Not in PICO
- Brink, H. M., Pinckers, A. J. & Verbeek, A. M. (1990) The electro-oculogram in uveal melanoma. A prospective study. *Documenta Ophthalmologica*, 75: 329-334.
Not in PICO
- Butros, L. J., Abramson, D. H. & Dunkel, I. J. (2002) Delayed diagnosis of retinoblastoma: analysis of degree, cause, and potential consequences. *Pediatrics*, 109: E45.
Not in PICO
- Cabral, D. A. & Tucker, L. B. (1999) Malignancies in children who initially present with rheumatic complaints. *Journal of Pediatrics*, 134: 53-57.
Not in PICO
- Canty, C. A. (2009) Retinoblastoma: an overview for advanced practice nurses. [Review] [23 refs]. *Journal of the American Academy of Nurse Practitioners*, 21: 149-155.
Narrative review
- Canzano, J. C. & Handa, J. T. (1999) Utility of pupillary dilation for detecting leukocoria in patients with retinoblastoma. *Pediatrics*, 104: e44.
Not in PICO

- Chen, K. S., Lai, M. K., Huang, C. C., Chu, S. H. & Leu, M. L. (1995) Urologic cancers in uremic patients. *American Journal of Kidney Diseases*, 25: 694-700.
Not in PICO
- Ciocalteu, A. M., Ardeleanu, S. & Checherita, I. A. (2011) [The role of ultrasonography exam in orbital-ocular tumors]. [Romanian]. *Revista Medico-Chirurgicala a Societatii de Medici Si Naturalisti Din Iasi*, 115: 1113-1118.
Narrative review
- Clericuzio, C. L. & Martin, R. A. (2009) Diagnostic criteria and tumor screening for individuals with isolated hemihyperplasia. *Genetics in Medicine*, 11: 220-222.
Narrative review
- Cozzi, D. A., Mele, E., Ceccanti, S., Natale, F., Clerico, A., Schiavetti, A. & Dominici, C. (2013) Long-term follow-up of the "wait and see" approach to localized perinatal adrenal neuroblastoma. *World Journal of Surgery*, 37: 459-465.
Not in PICO
- Croft, D. & Dickerson, M. (1994) Ultrasound differentiation of two pediatric abdominal masses. *Journal of Diagnostic Medical Sonography*, 10: 12-17.
Narrative review
- Damato, B. (2001) Time to treatment of uveal melanoma in the United Kingdom. *Eye*, 15: 2-8.
Not in PICO
- Damato, E. M. & Damato, B. E. (2012) Detection and time to treatment of uveal melanoma in the United Kingdom: an evaluation of 2,384 patients. *Ophthalmology*, 119: 1582-1589.
Not in PICO
- Damgaard-Pedersen, K. (1980) CT and IVU in the diagnosis of Wilms' tumour. A comparative study. *Pediatric Radiology*, 9: 207-211.
Not in PICO
- DE, F. G. (1956) [Early diagnosis and treatment of Wilms' tumor in infancy]. [Portuguese]. *Revista Brasileira de Cirurgia*, 31: 375-383.
Outside of agreed date range (pre 1980)
- Diaconescu, S., Olaru, C., Mihaila, D., Aprodu, S. G. & Miron, I. (2013) Risk stratification and consecutive prognosis progresses in childhood Wilms Tumors. Two cases report. *Chirurgia (Bucuresti)*, 108: 106-111.
Not in PICO
- Diaconescu, S., Olaru, C., Mihaila, D., Aprodu, S. G. & Miron, I. (2013) Risk stratification and consecutive prognosis progresses in childhood Wilms tumors. Two cases report. *Chirurgia (Bucuresti)*, 108: 106-111.
Not in PICO
- Dieckhues, B. (1986) [Value of serologic tumor tests in malignant melanoma of the choroid]. [German]. *Klinische Monatsblätter für Augenheilkunde*, 188: 114-117.
Not in PICO
- Diniz, G., Aktas, S., Turedi, A., Ortac, R. & Vergin, C. (2010) Telomerase activity in wilms tumor. *Pediatric Blood and Cancer*, 55: 884-885.
Not in PICO
- Dommett, R. M., Redaniel, M. T., Stevens, M. C. G., Hamilton, W. & Martin, R. M. (2012) Features of childhood cancer in primary care: A population-based nested case-control study. *British Journal of Cancer*, 106: 982-987.
Not in PICO
- Drlicek, G., Hayder, W. & Kratochwil, A. (1987) [Use of sonography at the peripheral hospital in the diagnosis of kidney tumors]. [German]. *Wiener Klinische Wochenschrift*, 99: 835-838.
Not in PICO
- Dubashi, B., Cyriac, S. & Tenali, S. G. (2009) Clinicopathological analysis and outcome of primary mediastinal malignancies - A report of 91 cases from a single institute. *Annals of Thoracic*

- Medicine*, 4: 140-142.
Not in PICO
- Edeling, C.-J., Frederiksen, P. B., Kamper, J. & Jeppesen, P. (1987) Diagnosis and treatment of neuroblastoma using metaiodobenzylguanidine. *Clinical Nuclear Medicine*, 12: 632-637.
Not in PICO
- Edeling, C. J. (1983) Ga-67 imaging in pediatric oncology. *Clinical Nuclear Medicine*, 8: 205-209.
Not in PICO
- Edeling, C. J., Buchler, F. P., Kamper, J. & Jeppesen, P. (1986) Diagnosis and treatment of neuroblastoma using 131I-meta-iodobenzylguanidine. *Nuclear-Medizin*, 25: 172-175.
Not in PICO
- Ell, C. & Schott, G. (1994) [Suspected kidney tumor--diagnostic-therapeutic procedure]. [German]. *Fortschritte der Medizin*, 112: 123-124.
Narrative review
- Esquembre Menor, C. T. & Castel, S., V (1988) [Early diagnosis of cancer in children]. [Review] [0 refs] [Spanish]. *Anales Espanoles de Pediatria*, 29: Suppl-7.
Narrative review
- Faulkner-Jones, B. E., Foster, W. J., Harbour, J. W., Smith, M. E. & Davila, R. M. (2005) Fine needle aspiration biopsy with adjunct immunohistochemistry in intraocular tumor management. *Acta Cytologica*, 49: 297-308.
Not in PICO
- Fitz, C. R., Chuang, S. H. & Harwood-Nash, D. C. (1985) Computed tomography diagnoses of eye tumors and anomalies in early childhood and infancy. *Annales de Radiologie*, 28: 235-240.
Not in PICO
- Fragkandrea, I., Nixon, J. A. & Panagopoulou, P. (2013) Signs and central nervous system (CNS): Early endocrine manifestations: A guide for early recognition. *American Family Physician*, 88: 185-192.
Narrative review
- Gallagher, R. P., Elwood, J. M., Rootman, J., Threlfall, W. J. & Davis, J. (1988) Symptoms and time to presentation and treatment in ocular melanoma: the Western Canada Melanoma Study. *Canadian Journal of Ophthalmology*, 23: 11-13.
Not in PICO
- Gao, L., Lin, W. H., Gong, Z. J., Liu, Y., Liu, Y. M. & Zhu, M. H. (2004) [Fine needle aspiration cytology of eyelid sebaceous gland carcinoma and its differential diagnosis]. [Chinese]. *Chung-Hua Ping Li Hsueh Tsa Chih - Chinese Journal of Pathology*, 33: 36-39.
Not in PICO
- Garcia, H. B. (2008) Suspicion of cancer in pediatrics. [Spanish]. *Pediatrics Integral*, 12: 537-544.
Narrative review
- George, J. L. & Marchal, J. C. (2010) Orbital tumors in children: Clinical examination, imaging, specific progression. [French]. *Neurochirurgie*, 56: 244-248.
Narrative review
- Gillmore, R., Xue, S.-A., Holler, A., Kaeda, J., Hadjiminias, D., Healy, V., Dina, R., Parry, S. C., Bellantuono, I., Ghani, Y., Coombes, R. C., Waxman, J. & Stauss, H. J. (2006) Detection of Wilms' tumor antigen-specific CTL in tumor-draining lymph nodes of patients with early breast cancer. *Clinical Cancer Research*, 12: 34-42.
Not in PICO
- Gombos, D. S. & Diba, R. (2005) Estimating the incidence of retinoblastoma in Texas. *Texas Medicine*, 101: 70-72.
Not in PICO
- Griffiths, D. F. R. & Vujanic, G. M. (2002) Cystic lesions of the kidney - Selected topics. *Current Diagnostic Pathology*, 8: 94-101.
Narrative review

- Gutjahr, P. (1991) [Congenital Wilms' tumors are mostly (benign) mesoblastic nephromas--significance of prenatally detected solid kidney tumors]. [German]. *Geburtshilfe und Frauenheilkunde*, 51: 124-126.
Not in PICO
- Holden, R. & Damato, B. E. (1996) Preventable delays in the treatment of intraocular melanoma in the UK. *Eye*, 10: 127-129.
Not in PICO
- Hsu, W. M., Lee, H., Juan, H. F., Shih, Y. Y., Wang, B. J., Pan, C. Y., Jeng, Y. M., Chang, H. H., Lu, M. Y., Lin, K. H., Lai, H. S., Chen, W. J., Tsay, Y. G., Liao, Y. F. & Hsieh, F. J. (2008) Identification of GRP75 as an independent favorable prognostic marker of neuroblastoma by a proteomics analysis. *Clinical Cancer Research*, 14: 6237-6245.
Not in PICO
- Ikpeme, E. E. & Dixon-Umo, O. T. (2013) Paediatric renal diseases in uyo, Nigeria : A 10 year review. *Pediatric Nephrology*, 28: 1411.
Not in PICO
- Israels, T., Ribeiro, R. C. & Molyneux, E. M. (2010) Strategies to improve care for children with cancer in Sub-Saharan Africa. [Review]. *European Journal of Cancer*, 46: 1960-1966.
Narrative review
- Jakobiec, F. A., Yeo, J. H., Trokel, S. L., Abbott, G. F., Anderson, R., Citrin, C. M. & Alper, M. G. (1982) Combined clinical and computed tomographic diagnosis of primary lacrimal fossa lesions. *American Journal of Ophthalmology*, 94: 785-807.
Not in PICO
- Januszkiewicz, D., Lastowska, M. & Zielinski, W. (1990) [Neuroblastoma in children. Results of the treatment and analysis of selected prognostic factors]. [Polish]. *Nowotwory*, 40: 143-148.
Not in PICO
- Junuzovic, D., Kerleta, A. & Masic, I. (2013) The frequency of renal cell carcinoma in population of patients with kidney tumors. *Medicinski Arhiv*, 67: 27-30.
Not in PICO
- Kamaleshwaran, K. K., Shibu, D. K., Mohanan, V. & Shinto, A. S. (2014) - Rare case of trilateral retinoblastoma with spinal canal drop metastasis detected with fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography imaging. - *Indian Journal of Nuclear Medicine*, 29: 115-116.
Not in PICO
- Kamath, V. B., Sowmya, V., Ballal, C. K. & Mendonca, N. (2013) Esthesioneuroblastoma as an unusual cause for dystopia. *Orbit*, 32: 392-394.
Not in PICO
- Kato, K., Kubota, T., Ikeda, M., Tadokoro, M., Abe, S., Nakano, S., Nishino, M., Kobayashi, H. & Ishigaki, T. (2006) Low efficacy of 18F-FDG PET for detection of uveal malignant melanoma compared with 123I-IMP SPECT. *Journal of Nuclear Medicine*, 47: 404-409.
Not in PICO
- Kersten, R. C., Ewing-Chow, D., Kulwin, D. R. & Gallon, M. (1997) Accuracy of clinical diagnosis of cutaneous eyelid lesions. *Ophthalmology*, 104: 479-484.
Not in PICO
- Kostopoulou, O., Delaney, B. C. & Munro, C. W. (2008) Diagnostic difficulty and error in primary care - A systematic review. *Family Practice*, 25: 400-413.
Not in PICO
- Kreft, B., Flacke, S., Conrad, R., Pauleit, D., Bachmann, R., Wardelmann, E., Albers, P. & Schild, H. (1999) [The pathological/MR tomographic correlation and differential diagnosis of malignant kidney tumors]. [German]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin*, 171: 106-112.
Not in PICO

- Kumar, H. R., Sandoval, J. A., Lovell, M. A., Fenton, L. Z. & Bealer, J. F. (2010) Primary pancreatic neuroblastoma: an unusual tumor in infancy. *Journal of Pediatric Surgery*, 45: 642-646.
Not in PICO
- Lau, D. T., Norris, M. D., Marshall, G. M., Haber, M. & Ashton, L. J. (2011) HLA-G polymorphisms, genetic susceptibility, and clinical outcome in childhood neuroblastoma. *Tissue Antigens*, 78: 421-427.
Not in PICO
- Law, C., Krema, H. & Simpson, E. R. (2012) Referral patterns of intraocular tumour patients to a dedicated Canadian ocular oncology department. *Canadian Journal of Ophthalmology*, 47: 254-261.
Not in PICO
- Lewis, G. & Maxwell, A. P. (2002) Early diagnosis improves survival in kidney cancer. *Practitioner*, 256: 13-16.
Narrative review
- Ling, R. E., Capsomidis, A. & Patel, S. R. (2014) Identifying childhood cancer: How is the urgent suspected cancer referral pathway performing? *Archives of Disease in Childhood*, 99: A108.
Not in PICO
- Long, J. A., Descotes, J. L. & Rambeaud, J. J. (2007) [Kidney cancer diagnosis]. [Review] [10 refs] [French]. *Revue du Praticien*, 57: 603-612.
Narrative review
- Ludick, A. (2013) Taking the early warning signs of childhood cancer to the rural areas of gauteng in south africa: Training health professionals. *Pediatric Blood and Cancer*, 60: 228.
Not in PICO
- Lueder, G. T. (2005) The effect of initial recognition of abnormalities by physicians on outcome of retinoblastoma. *Journal of Aapos: American Association for Pediatric Ophthalmology & Strabismus*, 9: 383-385.
Not in PICO
- Lyons, C. J. & Hungerford, J. (1990) Detection of ocular malignancies. *Journal of the Royal Society of Medicine*, 83: 165-167.
Not in PICO
- Maaita, J. F., Sunna, L. F., Al-Madani, M. V. & Horrani, S. M. (2003) Eye diseases in children in Southern Jordan. *Saudi Medical Journal*, 24: 154-156.
Not in PICO
- Machekhin, V. A. (1980) [Reliability of ultrasonic diagnosis in suspected intraocular tumor]. [Russian]. *Vestnik Oftalmologii*.(2):58-61, 1980 Mar-Apr., 58-61.
Not in PICO
- Maki, J. L., Marr, B. P. & Abramson, D. H. (2009) Diagnosis of retinoblastoma: how good are referring physicians? *Ophthalmic Genetics*, 30: 199-205.
Not in PICO
- Margolis, R., Brasil, O. F., Lowder, C. Y., Singh, R. P., Kaiser, P. K., Smith, S. D., Perez, V. L., Sonnie, C. & Sears, J. E. (2007) Vitrectomy for the diagnosis and management of uveitis of unknown cause. *Ophthalmology*, 114: 1893-1897.
Not in PICO
- Martin, K., Rossi, V., Ferrucci, S. & Pian, D. (2010) Retinal astrocytic hamartoma. *Optometry-Journal of the American Optometric Association*, 81: 221-233.
Not in PICO
- Maxwell, P. (2013) Identifying signs of retinoblastoma. *Nursing Times*, 109: 17-23.
Narrative review
- Mazur, K. A. (2010) Neuroblastoma: What the nurse practitioner should know. *Journal of the American Academy of Nurse Practitioners*, 22: 236-245.
Narrative review

- McBride, D. (2010) Identification of proteins may lead to urinary test for kidney cancer. *ONS Connect*, 25: 17.
Narrative review
- Melamud, A., Palekar, R. & Singh, A. (2006) Retinoblastoma. *American Family Physician*, 73: 1039-1044.
Narrative review
- Melzer, H. I., Coppenrath, E., Schmid, I., Albert, M. H., Von, S. D., Tudball, C., Bartenstein, P. & Pfluger, T. (2011) 123I-MIBG scintigraphy/SPECT versus 18F-FDG PET in paediatric neuroblastoma. *European Journal of Nuclear Medicine and Molecular Imaging*, 38: 1648-1658.
Not in PICO
- Messmer, E. M., Mackert, M. J., Zapp, D. M. & Kampik, A. (2006) In vivo confocal microscopy of pigmented conjunctival tumors. *Graefes Archive for Clinical & Experimental Ophthalmology*, 244: 1437-1445.
Not in PICO
- Midena, E. & Parrozzani, R. (2012) Biopsies in Uveal Melanoma. *Current Concepts in Uveal Melanoma*, 49: 81-95.
Narrative review
- Mierzwa, D. M. & Romanowska, D. B. (2012) Assessment of the influence of one's education on early diagnosis of multiple primary cancer in patients with uveal melanoma. *Klinika.oczn*, 114: 111-114.
Not in PICO
- Morgan-Followell, B. & Reyes, E. L. (2013) Child Neurology: Diagnosis of Lambert-Eaton myasthenic syndrome in children. *Neurology*, 80: e220-e222.
Not in PICO
- Morrissey, J. J., London, A. N., Luo, J. & Kharasch, E. D. (2010) Urinary biomarkers for the early diagnosis of kidney cancer. *Mayo Clinic Proceedings*, 85: 413-421.
Not in PICO
- Mullaney, P. B., Karcioğlu, Z. A., al-Mesfer, S. & Dowaidi, M. (1996) Retinoblastoma referral patterns in Saudi Arabia. *Ophthalmic Epidemiology*, 3: 35-46.
Not in PICO
- Musumeci, R. & Botturi, M. (1978) [The radiological symptomatology of primary malignant neoplasia of the kidney (author's transl)]. [Italian]. *Radiologia Medica*, 64: 753-768.
Narrative review
- Nabie, R., Taheri, N., Fard, A. M. & Fouladi, R. F. (2012) Characteristics and clinical presentations of pediatric retinoblastoma in North-western Iran. *International Journal of Ophthalmology*, 5: 510-512.
Not in PICO
- Nadel, H. R. (2014) - SPECT/CT in pediatric patient management. - *European Journal of Nuclear Medicine & Molecular Imaging*, 41 Suppl 1: S104-S114.
Narrative review
- Nathrath, M. & Teichert, V. L., I (2009) Oncologic causes of bone pain. [German]. *Monatsschrift für Kinderheilkunde*, 157: 655-660.
Narrative review
- Nozaki, C., Horibe, K., Iwata, H., Ishiguro, Y., Hamaguchi, M. & Takahashi, M. (2000) Prognostic impact of telomerase activity in patients with neuroblastoma. *International Journal of Oncology*, 17: 341-345.
Not in PICO
- Palazzi, M. A., Stephan, C., Brandalise, S. R. & Aguiar, S. D. S. (2013) Retinoblastoma diagnosis: A proposal based on the experience of Centro Infantil Boldrini, Brazil. *Pediatric Hematology and Oncology*, 30: 379-385.
Not in PICO

- Palko, A., Kun, E., Greksa, E. & Khertelendi, A. (1991) [The role of computerized tomography in the diagnosis and evaluation of the dissemination of malignant kidney tumors]. [Russian]. *Vestnik Rentgenologii i Radiologii*.(2):37-40, 1991 Mar-Apr., 37-40.
Not in PICO
- Paradies, G., Zullino, F., Orofino, A. & Leggio, S. (2013) Mediastinal teratomas in children. Case reports and review of the literature. *Annali Italiani di Chirurgia*, 84(4):395-403, -403, 2013.
Not in PICO
- Parmar, R., Wadia, F., Yassa, R. & Zenios, M. (2013) Neuroblastoma: a rare cause of a limping child. How to avoid a delayed diagnosis? *Journal of Pediatric Orthopedics*, 33: e45-e51.
Not in PICO
- Patel, N., Salchow, D. J. & Materin, M. (2013) Differentials and approach to leukocoria. *Connecticut Medicine*, 77: 133-140.
Narrative review
- Petrus, L. V., Hall, T. R., Boechat, M. I., Westra, S. J., Curran, J. G., Steckel, R. J. & Kangarloo, H. (1992) The pediatric patient with suspected adrenal neoplasm: which radiological test to use? *Medical & Pediatric Oncology*, 20: 53-57.
Not in PICO
- Pickuth, D., Heywang-Kobrunner, S. H. & Spielmann, R. P. (1999) Computed tomography and magnetic resonance imaging features of olfactory neuroblastoma: An analysis of 22 cases. *Clinical Otolaryngology and Allied Sciences*, 24: 457-461.
Not in PICO
- Pollock, B. H., Krischer, J. P. & Vietti, T. J. (1991) Interval between symptom onset and diagnosis of pediatric solid tumors. *Journal of Pediatrics*, 119: 725-732.
Not in PICO
- Provenzi, M., Saettini, F., Conter, V., Chinaglia, D., Vai, P., Bruno, A., Cavalleri, L., Foglia, C., Girdali, E., Collini, P. & Spreafico, F. (2013) Is there a role for FDG-PET for the assessment of treatment efficacy in Wilms' tumor? A case report and literature review. *Pediatric Hematology & Oncology*, 30(7):633-9, -9, 2013.
Not in PICO
- Psooy, K. (2007) Long-term urological follow-up of multicystic dysplastic kidneys: Is it still indicate in 2007? *Cuaj-Canadian Urological Association Journal*, 1: 113-116.
Not in PICO
- Qian, Y. (1994) Visual acuity test of children in the strabismus clinic. [Chinese]. *Zhonghua hu li za zhi = Chinese journal of nursing*, 29: 92-93.
Not in PICO
- Raab, C. P. & Gartner, J. C., Jr. (2009) Diagnosis of childhood cancer. [Review] [33 refs]. *Primary Care: Clinics in Office Practice*, 36: 671-684.
Narrative review
- Reiman, T. A., Siegel, M. J. & Shackelford, G. D. (1986) Wilms tumor in children: abdominal CT and US evaluation. *Radiology*, 160: 501-505.
Not in PICO
- Reither, M., Schumacher, R. & Klingmuller, V. (1983) [Sonographic diagnosis of abdominal tumors in childhood]. [German]. *Ultraschall in der Medizin*, 4: 139-146.
Not in PICO
- Rezaimehr, Y. & Bhargava, R. (2013) Neuroblastoma presenting as persistent postprandial emesis in a neonate. *Pediatric Emergency Care*, 29(12):1273-5, -5, 2013.
Not in PICO
- Rice, M. L., Leske, D. A., Smestad, C. E. & Holmes, J. M. (2008) Results of ocular dominance testing depend on assessment method. *Journal of AAPOS*, 12: 365-369.
Not in PICO

- Riley, R. D., Burchill, S. A., Abrams, K. R., Heney, D., Lambert, P. C., Jones, D. R., Sutton, A. J., Young, B., Wailoo, A. J. & Lewis, I. J. (2003) A systematic review and evaluation of the use of tumour markers in paediatric oncology: Ewing's sarcoma and neuroblastoma (Structured abstract). *Health Technology Assessment.Database.*, 1.
Not in PICO
- Ritchey, M., Daley, S., Shamberger, R. C., Ehrlich, P., Hamilton, T., Haase, G., Sawin, R. & National Wilms' Tumor Study Group (2008) Ureteral extension in Wilms' tumor: a report from the National Wilms' Tumor Study Group (NWTSG). *Journal of Pediatric Surgery*, 43: 1625-1629.
Not in PICO
- Rosati, P., Jenkner, A., De, V. R., Boldrini, R., Chiodi, P., Celesti, L. & Giampaolo, R. (2011) 'Tell me about your pain': abdominal pain and a history of bullying. *BMJ Case Reports*, 2011, 2011.
Not in PICO
- Rossi, E., Imbach, P., Kaser, H. & Wagner, H. P. (1978) [The malignant neoplasm in pediatrics]. [German]. *Schweizerische Medizinische Wochenschrift.Journal Suisse de Medecine*, 108: 513-517.
Narrative review
- Roth, A. (1981) The role of the general practitioner and the family in the initial diagnosis and treatment of the squinting child. [French]. *Therapeutische Umschau*, 38: 228-234.
Narrative review
- Saeed, P., van Furth, W. R., Tanck, M., Kooremans, F., Freling, N., Streekstra, G. I., Regensburg, N. I., van der Sprenkel, J. W., Peerdeman, S. M., van Overbeeke, J. J. & Mourits, M. P. (2011) Natural history of sphenoidal meningiomas. *Acta Neurochirurgica*, 153: 395-402.
Not in PICO
- Sampson, V. B., Gorlick, R., Kamara, D. & Anders, K. E. (2013) A review of targeted therapies evaluated by the pediatric preclinical testing program for osteosarcoma. *Frontiers in Oncology*, 3:132.
Narrative review
- Schmechel, C. & Raatzsch, H. (1965) [Prognosis and early diagnosis of primary kidney tumors]. [German]. *Landarzt*, 41: 139-142.
Outside of agreed date range (pre 1980)
- Schmidt, D., Anderson, L., Bingen, K., Hoag, J., Kupst, M. J. & Warwick, A. B. (2010) Late effects in adult survivors of childhood cancer: Considerations for the general practitioner. *Wisconsin Medical Journal*, 109: 98-108.
Narrative review
- Seregard, S., Ek, U., Preisler, G., af, T. E., Jacobson, L., Oskar, K., Illerstahl, I. & Kock, E. (1996) [A study of children with retinoblastoma. Diagnosis is often delayed]. [Swedish]. *Lakartidningen*, 93: 1133-1135.
Not in PICO
- Servodidio, C. A., Abramson, D. H. & Romanella, A. (1991) Retinoblastoma. *Cancer Nursing*, 14: 117-123.
Narrative review
- Shakoor, K. A. & Phil, M. (1989) Fine needle aspiration cytology in advanced pediatric tumors. *Pediatric Pathology*, 9: 713-718.
Not in PICO
- Shi, G. H., Chen, Y., Yao, X. D., Zhang, S. L., Dai, B., Feng, L. Q., Zhang, H. L., Shen, Y. J., Zhu, Y., Zhu, Y. P., Xiao, W. J., Ma, C. G., Wen, L. G., Qin, X. J., Yang, L. F. & Ye, D. W. (2013) Individualized renal mass biopsy strategy for Chinese patients with different subtypes and necrosis area. *Urologic Oncology*, 31(6):920-3, -3, 2013.
Not in PICO
- Shields, J. A., Shields, C. L., Ehya, H., Eagle, R. C., Jr. & De, P. P. (1993) Fine-needle aspiration biopsy of suspected intraocular tumors. The 1992 Urwick Lecture. *Ophthalmology*, 100: 1677-1684.
Not in PICO

- Skoldenberg, E., Soderberg, M., Wangberg, J. & Ljungman, G. (2011) Cutting needle biopsies in the management of childhood tumors. *Pediatric Blood and Cancer*, 57: 747.
Not in PICO
- Sumarac, Z. & Petronic, V. (1973) [Varieties in the symptomatology and diagnosis of malignant kidney tumors]. [Serbian]. *Srpski Arhiv Za Celokupno Lekarstvo*, 100: 627-637.
Outside of agreed date range (pre 1980)
- Taupitz, A. (1969) [Early diagnosis of urologic tumors]. [German]. *Zeitschrift fur Allgemeinmedizin*, 45: 1417-1423.
Outside of agreed date range (pre 1980)
- Temming, P., Lohmann, D., Bornfeld, N., Sauerwein, W., Goericke, S. L. & Eggert, A. (2012) Current Concepts for Diagnosis and Treatment of Retinoblastoma in Germany: Aiming for Safe Tumor Control and Vision Preservation. *Klinische Padiatrie*, 224: 339-347.
Narrative review
- Valverde, A. S., Martin, R. J., Alvarez, V. H. & Encinas Martin, J. L. (2000) [Posterior uveal pseudomelanoma. Clinical differential diagnosis at the referral hospital]. [Spanish]. *Archivos de la Sociedad Espanola de Oftalmologia*, 75: 529-534.
Not in PICO
- Van Den Heuvel-Eibrink, M. M., Grundy, P., Graf, N., Pritchard-Jones, K., Bergeron, C., Patte, C., Van, T. H., Rey, A., Langford, C., Anderson, J. R. & De, K. J. (2008) Characteristics and survival of 750 children diagnosed with a renal tumor in the first seven months of life: A collaborative study by the SIOP/GPOH/SFOP, NWTSG, and UKCCSG Wilms tumor study groups. *Pediatric Blood and Cancer*, 50: 1130-1134.
Not in PICO
- Vogel, M. & Meyer-Schwickerath, G. (1982) [Diagnostic considerations and measures in suspected malignant melanoma of the choroid]. [German]. *Bucherei des Augenarztes*.(89):98-105, 1982., 98-105.
Not in PICO
- Wakamb, G. K., Nkashama, G. M., Mbuli, R. L., Borasisi, G. C. & Nikulu, J. I. (2013) [Problematic of the management of childhood cancer: experience of retinoblastoma in Lubumbashi (DR Congo) and the importance of early diagnosis]. [French]. *The Pan African medical journal*, 14: 64.
Not in PICO
- Wallach, M., Balmer, A., Munier, F., Houghton, S., Pampallona, S., von der, W. N., Beck-Popovic, M., Swiss Pediatric Oncology Group & Swiss Childhood, C. R. (2006) Shorter time to diagnosis and improved stage at presentation in Swiss patients with retinoblastoma treated from 1963 to 2004. *Pediatrics*, 118: e1493-e1498.
Not in PICO
- Warnecke, M. U. & Bartels, H. (1986) [The significance of nephrosonography for the early recognition of kidney tumors]. [German]. *Ultraschall in der Medizin*, 7: 3-6.
Not in PICO
- Wende, S., Kazner, E. & Grumme, T. (1980) The diagnostic value of computed tomography in orbital diseases. A cooperative study of 520 cases. *Neurosurgical Review*, 3: 43-49.
Not in PICO
- White, J. & Gole, G. (2012) Delay in the diagnosis of retinoblastoma: An update. *Clinical and Experimental Ophthalmology*, 40: 37.
Not in PICO
- White, J. & Gole, G. (2012) Delay in the diagnosis of retinoblastoma: An update. *Clinical and Experimental Ophthalmology*, 40: 37.
Not in PICO
- Wirix, M., Parys-Vanginderdeuren, R., Casteels, I. & Uyttebrouck, A. (2000) Delayed diagnosis of retinoblastoma. *Bulletin de la Societe Belge d Ophthalmologie*.(278):37-41, 2000., 37-41.
Not in PICO

Xu, G., Hu, J., Wu, Y., Xiao, Y. & Xu, M. (2013) Botryoid Wilms' tumor: a case report and review of the literature. *World Journal of Surgical Oncology*, 11: 102.

Not in PICO

Zagorski, Z., Lang, G. & Naumann, G. (1991) [Eye tumors in children. Histopathological aspects of differential diagnosis]. [Polish]. *Klinika Oczna*, 93: 59-62.

Narrative review

Zhang, C. H., Zhang, T. C., Zhong, J. S., Li, Y. W. & Zhang, C. M. (2004) [Early diagnosis of the tumors in orbital apex and optic nerve]. [Chinese]. *Chung-Hua Yen Ko Tsa Chih [Chinese Journal of Ophthalmology]*, 40: 34-36.

Not in PICO

NON-SITE SPECIFIC SYMPTOMS

ABDOMINAL PAIN

Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main validity issues to note is that patient sampling was not clearly consecutive or random in some of the studies, with some studies also conducted in populations that are not clearly directly relevant to the current question and the quality of others suffering from missing data. Studies employing non-consecutive/random sampling are at risk of bias because, for example, case-control studies have been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection. Studies conducted in other settings than UK-based primary care are only applicable to the extent that the study populations and settings are comparable to a UK GP population as defined for the current purposes. Other issues to note concern missing data, the influence of which on the results is difficult to determine.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Bellentani (1990)	+	+	+	+	?	?	+
Collins (2012)	+	+	+	+	+	+	+
Collins (2012a)	+	+	+	+	+	+	+
Collins (2013)	+	+	+	+	+	+	+
Collins (2013a)	+	+	+	+	+	+	+
Hamilton (2005)	-	+	+	+	+	+	+
Hippisley-Cox (2011)	+	+	+	?	+	+	+
Hippisley-Cox (2012)	+	+	+	-	+	+	+
Hippisley-Cox (2012a)	+	+	+	+	+	+	+
Hippisley-Cox (2012b)	+	+	+	-	+	+	+
Moellmann (1981)	+	+	?	-	?	+	+
Panzuto (2003)	-	+	+	?	?	+	+
Stapley (2012)	-	+	+	+	+	+	+

- High
 ? Unclear
 + Low

Table 1: Non-site specific symptoms of concern: Calculation of overall positive predictive value of abdominal pain for cancer

Cancer site	Study	Lower age limit	Upper age limit	PPV (95% CI), prevalence
Bladder/renal	Hippisley-Cox (2012)	30	84	0.2 (0.2-0.2)
Colorectal	Various*	30	84	1.524
Oesophagus/stomach	Meta-analysis	varied	varied	0.34 (0.16-0.71)
Pancreatic	Hippisley-Cox (2012)	30	84	0.3 (0.3-0.4)
Sum				2.364

* Not sure which one to pick, so used average.

Table 2: Non-site specific symptoms of concern: Positive predictive values for abdominal pain

Cancer site	Comment/relevant recs	Study	Symptom	Patient group	Positive predictive value% (95% CI)	Sex	Age inclusion, lower limit	Age inclusion, upper limit
Bladder/renal		Collins (2013)	Abdominal pain	All patients	0.11 (0.1-0.13)	both	30	84
Bladder/renal		Collins (2013)	Abdominal pain	Men	0.2 (0.2-0.21)	men	30	84
Bladder/renal		Collins (2013)	Abdominal pain	Women	0.1 (0.1-0.1)	women	30	84
Bladder/renal		Hippisley-Cox (2012)	Abdominal pain	All patients	0.2 (0.2-0.2)	both	30	84
Colorectal		Hamilton (2005)	Abdominal pain (reported once)	All patients	1.1 (0.9-1.3)	both	40	no upper limit
Colorectal		Hamilton (2005)	Abdominal pain	Patients 40-69 years	0.65 (NR)	both	40	69
Colorectal		Hamilton (2005)	Abdominal pain	Patients ≥ 70 years	2 (NR)	both	70	no upper limit
Colorectal		Hamilton (2005)	Abdominal pain (reported twice)	All patients	3 (1.8-5.2)	both	40	no upper limit
Colorectal		Hamilton (2005)	Abdominal pain and	All patients	1.4 (0.3-2.2)	both	40	no upper limit

			abdominal tenderness					
Colorectal		Hamilton (2005)	Abdominal tenderness (reported once)	All patients	1.1 (0.8-1.5)	both	40	no upper limit
Pancreatic		Collins (2013a)	Abdominal pain	All patients	0.14 (0.12-0.15)	both	30	84
Pancreatic		Collins (2013a)	Abdominal pain	Women	0.1 (0.09-0.12)	women	30	84
Pancreatic		Collins (2013a)	Abdominal pain	Men	0.19 (0.16-0.22)	men	30	84
Pancreatic		Hippisley-Cox (2012b)	Abdominal pain	All patients	0.3 (0.3-0.4)	both	30	84
Pancreatic		Stapley (2012)	Abdominal pain	All patients	0.2 (0.19-0.22)	both	40	no upper limit
Pancreatic		Stapley (2012)	Abdominal pain	Patients ≥ 60 years	0.3 (0.3-0.4)	both	60	no upper limit
Pancreatic		Stapley (2012)	Abdominal pain (attended ≥ twice)	Patients ≥ 60 years	1 (0.8-1.2)	both	60	no upper limit
META-ANALYSES (1) Colorectal								
Colorectal		Meta-analysis	Abdominal pain	All patients	2.04 (0.53-7.55)	both	2 studies 30-84, 1 study 18-87, 1 study NR Individual study details provided below	
Colorectal		Meta-analysis	Abdominal pain	All patients; w/o Panzuto (2003)	1.02 (0.38-2.69)	both	2 studies 30-84, 1 study NR Individual study details provided below	
The 4 studies below are those included in the meta-analysis reported in the cells above:								
Colorectal		Bellentani (1990)	Abdominal pain	All patients	3.9 (2-7.3)	both	NR	NR

Colorectal		Collins (2012)	Abdominal pain	All patients	0.5 (0.5-0.5)	both	30	84
Colorectal		Hippisley-Cox (2012a)	Abdominal pain	All patients	0.7 (0.6-0.7)	both	30	84
Colorectal		Panzuto (2003)	Abdominal pain	All patients	13.5 (9.4-18.8)	both	18	87
The following results are any extra analyses reported by the studies included in the above meta-analysis:								
Colorectal		Collins (2012)	Abdominal pain	Men 30-84 years	0.6 (0.6-0.7)	men	30	84
Colorectal		Collins (2012)	Abdominal pain	Women 30-84 years	0.4 (0.4-0.5)	women	30	84
META-ANALYSES (2) Oesophageal								
Oesophagus/stomach	2 combining gastro-oesophageal and 1 reporting on oesophageal cancer separately	Meta-analyses	Abdominal pain	All patients	0.23 (0.14-0.36)	both	2 studies 30-84, 1 study 40- >90 Individual study details provided below.	
The 3 studies below are those included in the meta-analysis reported in the cell above (Please note the same data from Collins (2012a) and Hippisley-Cox (2011) appear both here and under stomach, avoid double counting it):								
Oesophageal/stomach		Collins (2012a)	Abdominal pain	All patients	0.2 (0.2-0.2)	both	30	84
Oesophageal/stomach		Hippisley-Cox (2011)	Abdominal pain	All patients	0.3 (0.3-0.4)	both	30	84
Oesophageal		Møllmann (1981)	Upper abdominal pain > 2 weeks	All patients	0 (0-0.8)	both	40	>90
The following results are any extra analyses reported by the studies included in the above meta-								

analysis:								
Oesophageal/stomach		Collins (2012a)	Abdominal pain	Women	0.1 (0.1-0.1)	women	30	84
Oesophageal/stomach		Collins (2012a)	Abdominal pain	Men	0.3 (0.3-0.3)	men	30	84
META-ANALYSES (3) Stomach								
Oesophagus/stomach	2 combining gastro-oesophageal and 1 reporting on stomach cancer separately	Meta-analyses	Abdominal pain	All patients	0.34 (0.16-0.71)	both	2 studies 30-84, 1 study 40- >90	
The 3 studies below are those included in the meta-analysis reported in the cell above (Please note the same data from Collins (2012a) and Hippisley-Cox (2011) appear both here and under oesophageal, avoid double counting it):								
Oesophageal/stomach		Collins (2012)	Abdominal pain	All patients	0.2 (0.2-0.2)	both	30	84
Oesophageal/stomach		Hippisley-Cox (2011)	Abdominal pain	All patients	0.3 (0.3-0.4)	both	30	84
Stomach		Møllmann (1981)	Upper abdominal pain > 2 weeks	All patients	1 (0.4-2.4)	both	40	>90

Evidence statement(s):

Abdominal pain (9 studies, N = 6248014) presenting in a primary care setting is associated with an overall positive predictive value of 2.364% for cancer. The studies were associated with 0-3 bias/applicability concerns (see also Table 1).

Evidence tables

Bellentani (1990)

PATIENT SELECTION

A. risk of bias	
Patient sampling	Prospective consecutive patient series
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 254 (103 males/151 females); mean (SD) age of patients = Not reported; N = 140 were studied in primary care, N = 114 were referred to the gastroenterology services. It is unclear from the publication whether the patients who were referred to secondary care were a subset of "254 consecutive patients who presented to their GP during the study period for chronic abdominal pain" or whether they are recruited directly from secondary care (see Inclusion criteria).</p> <p><u>Inclusion criteria:</u> All consecutive patients consulting 14 GPs of the local health district, taking care of 14000 citizens, or referred to the outpatient clinic of the Gastroenterology Unit, either complaining of recurrent abdominal pain or having intestinal problems (as judged by the GP), between January 1987 and March 1988.</p> <p><u>Exclusion criteria:</u> Patients with acute abdomen, acute gastroenteritis or a clear cut diagnosis of upper gastrointestinal tract disease (gastritis, oesophagitis, peptic ulcer, or dyspepsia).</p> <p><u>Clinical setting:</u> Primary/secondary care, Italy.</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Recurrent abdominal pain or intestinal problems (as judged by the GP; not further specified)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Double-contrast barium enema or colonoscopy no more than 2 months after the enrolment in the study.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients are accounted for in the results but the number of true negatives and false negatives could not be ascertained from the reported results.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk
NOTES		
Collins (2012)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective patient series using the THIN database.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>A total of 2135540 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Rectal bleeding (N = 56234; 28423 men, 27811 women), abdominal pain (N = 245989; 102192 men, 143797 women), appetite loss (N = 5776; 2481 men, 3295 women), weight loss (N = 28289; 12891 men, 15398 women), anaemia (N = 18125; 4466 men, 13659 women), change in bowel habit (men only, N = 1670).</p> <p><u>Incident cases of colorectal cancer during the 2-year follow up period:</u> N = 3712 (2036 men, 1676 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of colorectal cancer at baseline, and patients with a recorded 'red-flag' symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	'Red-flag' symptoms: Rectal bleeding, loss of appetite, weight loss, abdominal pain, change in bowel habit (men only), and anaemia.	

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	The is very large, if not complete, overlap of the data used in this study with those used in Hamilton (2008 [for anaemia], 2009)

Collins (2012a)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	A total of 2135540 patients were identified from 364 practices. Symptoms: Dysphagia (N = 19237; 8846 men, 10391 women), abdominal pain (N = 246998; 102732 men, 144266 women), appetite loss (N = 5838; 2521 men, 3317 women), weight loss (N = 28403; 12938 men, 15465 women), haematemesis (N = 10792; 6162 men, 4630 women), anaemia (N = 18355;

	<p>4563 men, 13792 women).</p> <p><u>Incident cases of gastro-oesophageal cancer during the 2-year follow up period:</u> N = 1766 (1184 men, 582 women; 32% gastric cancer, 68% oesophageal cancer).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of gastro-oesophageal cancer, registration with the general practice < 12 months, or with invalid dates.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Haematemesis, dysphagia, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes

Could the patient flow have introduced bias?	Low risk
NOTES	The study did not distinguish between gastric and oesophageal cancer
Collins (2013)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2145133 patients (1063355 men, 1081778 women) were identified from 364 practices.</p> <p><u>Symptoms:</u> Haemoglobin < 11 g/dl recorded in the last year (N = 16961; 3969 men, 12992 women), abdominal pain (N = 253344; 105247 men, 148097 women), appetite loss (N = 6097; 2616 men, 3481 women), weight loss (N = 29369; 13332 men, 16037 women), haematuria (N = 37810; 22810 men, 15000 women), previous diagnosis of cancer apart from renal tract cancer at study entry (N = 49303; 18130 men, 31173 women).</p> <p><u>Incident cases of renal tract cancer during the 2-year follow up period:</u> N = 2283 (1685 men, 598 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (e.g., haematuria, abdominal pain, weight loss, appetite loss, and anaemia), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of renal tract cancer, registered less than 12 months with the general practice, had invalid dates, < 30 years old or ≥ 85 years old.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Renal tract cancer, which was defined as incident diagnosis of cancer of the bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes. Patients without the outcome were censored at the earliest of the date of death, date of leaving the practice study of 2 years of follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	It is unclear why no data has been presented for men for the symptoms of appetite loss and weight loss.

Collins (2013a)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	A total of 2150322 patients were identified from 364 practices. <u>Symptoms:</u> Dysphagia (men only: N = 9326), abdominal pain (N = 255058; 106768 men, 148290 women), appetite loss (N = 6102; 2658 men, 3444 women), weight loss (N = 29464; 13484 men, 15980 women), abdominal distension (women only: N = 4457), constipation (men only, N = 5326). <u>Incident cases of pancreatic cancer during the 2-year follow up period:</u> N = 287 (331 men, 287 women). <u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the

	study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <u>Exclusion criteria:</u> Patients with a prior diagnosis of pancreatic cancer, registration < 12 months with the general practice, or invalid dates. <u>Clinical setting:</u> Primary care, UK
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Dysphagia (men only), loss of appetite, weight loss, abdominal pain, abdominal distension (women only), and constipation (men only).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Hamilton (2005)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based matched case-control study involving all 21 general

	practices in Exeter, Devon, UK.	
Was a consecutive or random sample of patients enrolled?		No
Was a case-control design avoided?		No
Did the study avoid inappropriate exclusions?		Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?		Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?		Yes
Could the selection of patients have introduced bias?		High risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p><u>Cases:</u> N = 349 (177 males/172 females), age at diagnosis: < 60 years: N = 45, 60-69 years: N = 97, 70-79 years: N = 113, 80+ years: N = 94. 210/349 had tumours at or distal to the splenic flexure, and 126/349 had tumours proximal to the splenic flexure, the remaining 13/349 has tumours in multiple or unknown sites. Duke's staging was known for 305/349: 170/305 were Duke's A or B, and 135/305 were Duke's C or D.</p> <p><u>Controls:</u> N = 1744 (885 males/859 females), age at diagnosis: < 60 years: N = 225, 60-69 years: N = 487, 70-79 years: N = 555, 80+ years: N = 477.</p> <p><u>Inclusion criteria:</u> Cases: All patients aged ≥ 40 years with a primary colorectal cancer, diagnosed from 1998 to 2002, were identified from the cancer registry at the Royal Devon and Exeter Hospital combined with computerised searches at every practice in Devon to identify any cases missing from the cancer register. Controls: Five controls were matched to each case on sex, general practice, and age (to 1-year bands if possible, increased in 1-year multiples to a maximum of 5 years). Controls were eligible if they were alive at the time of diagnosis of their case.</p> <p><u>Exclusion criteria:</u> Cases and controls: Unobtainable records; no consultations in the 2 years before diagnosis; previous colorectal cancer; or residence outside Exeter at the time of diagnosis.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	Anonymised photocopies of the full primary care records for 2 years before diagnosis were coded (blinded to case/control status) for all entries using the International Classification of Primary Care-2. Additional codes were created to incorporate all possible clinical features. Only variables occurring in ≥ 2.5% of cases or controls were analysed.	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes

<i>For diagnostic case-control studies:</i>	
Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Colorectal cancer diagnosis in the cancer registry at the Royal Devon and Exeter Hospital or practice notes.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Hippisley-Cox (2011)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	A total of 1238971 patients were identified from 189 practices (621478 males, 617493 females), mean (SD) age = 50.1 (15) years, mean (SD) Townsend score = -0.2 (3.6). <u>Symptoms:</u> Current dysphagia (N = 8165), current haematemesis (N = 7119), current

	<p>abdominal pain (N = 126161), current appetite loss (N = 6133), current weight loss (N = 5377), tiredness in the last year (N = 14119), haemoglobin recorded in the last year (N = 12638, haemoglobin < 11 g/dl in the last year (N = 218862).</p> <p><u>Incident cases of gastro-oesophageal cancer during the 2-year follow up period:</u> N = 1343 (776 oesophageal and 567 gastric).</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000); 12 months after the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of gastro-oesophageal cancer at baseline, and patients with a recorded ‘red-flag’ symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	‘Red-flag’ symptoms: Incident dysphagia, haematemesis, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	A total of 1342329 patients were initially identified of whom 103358 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of gastro-oesophageal cancer (N = 538), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 31973), leaving 1238971 patients. However, data is presented for 963040/1238971 patients for all symptoms. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Could the patient flow have introduced bias?	Unclear risk	
NOTES	Results not presented separately for gastric and oesophageal cancer	
Hippisley-Cox (2012)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>A total of 1240722 patients were identified from 189 practices (622166 males, 618556 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Current symptoms and symptoms in the preceding year:</u> Current haematuria (N = 25553), current abdominal pain (N = 128721), current appetite loss (N = 5531), current weight loss (N = 14464), constipation in the last year (N = 8472), diarrhoea in the last year (N = 12171), tiredness in the last year (N = 12669), haemoglobin recoded in the last year (N = 216201), haemoglobin < 11 g/dl in the last year (N = 16169).</p> <p><u>Incident cases of renal tract cancer during the 2-year follow up period:</u> N = 1622; mean age at diagnosis = 70 years, 1187 males/ 435 females; Type of cancer: Bladder: N = 1292; Kidney: N = 307; Ureter: N = 21; Urethra: N = 2.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for \geq a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from</p>	

	<p>patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months' registration prior to study entry. For patients with incident haematuria, appetite loss, weight loss, or abdominal pain, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of renal tract cancer at baseline, and patients with a recorded 'red-flag' (see "Definition of symptom" below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Renal tract cancer, which was defined as incident diagnosis of cancer of the bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 codes (188 or 189) or ICD-10 diagnostic codes (C64–67).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 101607 patients

	<p>were excluded for the following reasons: No recorded Townsend score (N = 70847), history of renal tract cancer (N = 1506), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 29254), leaving 1240722 patients. However, data is presented for 967681 / 1240722 patients. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.</p>
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	
Hippisley-Cox (2012a)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1236601 patients were identified from 189 practices (620240 males, 616361 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Symptoms:</u> Current rectal bleeding (N = 29118), current abdominal pain (N = 125816), current appetite loss (N = 5358), current weight loss (N = 14065), recent change in bowel habit (N = 1821).</p> <p><u>Incident cases of colorectal cancer during the 2-year follow up period:</u> N = 2603 (1562 colon and 1041 rectum).</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for \geq a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000); 12 months after the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of colorectal cancer at baseline, and patients with a recorded 'red-flag' symptom in the 12 months prior to the study entry date.</p>

	Clinical setting: Primary care, UK
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: First onset rectal bleeding, first onset loss of appetite, first onset weight loss, first onset abdominal pain, first onset change in bowel habit (in the past 12 months), and anaemia (recorded haemoglobin < 11 g/dl in the past 12 months).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 105728 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of colorectal cancer (N = 2908), and ≥ one 'red flag' symptom recorded in the 12 months prior to study entry (N = 31973), leaving 1236601 patients. However, data is presented for 1235547/1236601 patients for all symptoms apart from change in bowel habit, which is only presented for 619651/620240 of the male patients. The missing data does not appear to include any of the cancer cases (although this cannot be ascertained for change in bowel habit), but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Low risk
NOTES	Please note there is some overlap between this patient sample and that of Parker (2007)

Hippisley-Cox (2012b)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1243740 patients were identified from 189 practices (624352 males, 619388 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Current symptoms and symptoms in the preceding year:</u> Current dysphagia (N = 8507), current abdominal pain (N = 129924), current abdominal distension (N = 4929), current appetite loss (N = 5567), current weight loss (N = 14686), constipation in the last year (N = 8476), diarrhoea in the last year (N = 12233), tiredness in the last year (N = 12688), itching in the last year (N = 1454), haemoglobin recoded in the last year (N = 214497), haemoglobin < 11 g/dl in the last year (N = 16172).</p> <p><u>Incident cases of pancreatic cancer during the 2-year follow up period:</u> N = 781.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months’ registration prior to study entry. For patients with incident haematuria, appetite loss, weight loss, or abdominal pain, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of pancreatic cancer at baseline, and patients with a recorded ‘red-flag’ (see “Definition of symptom” below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	‘Red-flag’ symptoms were defined as symptoms that might alarm the patient

	and also indicate the presence of pancreatic cancer; that is, symptoms of dysphagia, loss of appetite, weight loss, abdominal distension or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Pancreatic cancer, which was defined as incident diagnosis of pancreatic cancer during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 code (157) or ICD-10 diagnostic codes (C25).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 98589 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of pancreatic cancer (N = 96), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 27646), leaving 1243740 patients. However, data is presented for 971706 / 1243740 patients. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	
Møllmann (1981)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from an open-access gastroscopy clinic in

	Denmark.	
Was a consecutive or random sample of patients enrolled?		Yes
Was a case-control design avoided?		Yes
Did the study avoid inappropriate exclusions?		Yes
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 1480; gender not reported; 40-44 years: N = 144; 45-49 years: N = 186; 50-69 years: N = 882; 70-74 years: N = 130; 75-79 years: N = 83; 80-89 years N = 47; 90- years: N = 8.</p> <p><u>Inclusion criteria:</u> All patients who, for a 2-year period, presented to their GP with (any of) the following symptoms were referred to the open access gastroscopy clinic: Upper abdominal pain > 2 weeks, nausea and/or vomiting > 2 weeks, weight loss and/or anorexia, gastrointestinal bleeding, and anaemia (i.e., Hb < 80%).</p> <p><u>Exclusion criteria:</u> Patients who had been examined for any of the above symptoms within the last 6 months.</p> <p><u>Clinical setting:</u> GPs in Denmark</p>	
Are there concerns that the included patients and setting do not match the review question?		Unclear concern
INDEX TEST		
A. Risk of bias		
Index test	Upper abdominal pain > 2 weeks, nausea and/or vomiting > 2 weeks, weight loss and/or anorexia, gastrointestinal bleeding, and anaemia (i.e., Hb < 80%).	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	2-stage process: Gastroscopy with photography, using a gastroscope, performed with only local anaesthesia of the pharynx. If this investigation disclosed abnormal conditions, the next stage was gastroscopy, possibly with biopsy, using diazepam sedation.	
Is the reference standard likely to correctly classify the target condition?		Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?		No
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		

A. risk of bias	
Flow and timing	177/1480 patients declined endoscopy, 2/1480 did not show up for endoscopy, and it was unsuccessful in a further 24 patients, leaving 1277 patients. However, the paper reports that only 1273 had primary endoscopy, and then reports the results for between 1181 and 1297 patients.
Was there an appropriate interval between index test and reference standard?	Yes probably
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	There were a total of 18 gastric cancers confirmed in the study. No oesophageal cancers were reported. This research was published in 2 papers.

Panzuto (2003)

PATIENT SELECTION

A. risk of bias

Patient sampling	Prospective 8-week study of patients presenting to 159 primary care physicians (approximately 63600 patient visits during the study period in total) in Italy.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability

Patient characteristics and setting	N = 280; 120 males, 160 females; median age (range) = 61 (18-87) years. <u>Inclusion criteria:</u> Consecutive patients who consulted their GP "with symptoms considered suspicious for the presence of a colon disease to rule out the presence of colorectal cancer" and who were investigated with a colonoscopy or double-contrast barium enema [The decision of how (colonoscopy or double-contrast barium enema) and when to investigate the colon was made only by the physicians on the basis of the clinical evaluation during the visit]. <u>Exclusion criteria:</u> Patients with previous diagnoses of colorectal disorders or a recent large bowel examination. <u>Clinical setting:</u> Primary care, Italy.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern

INDEX TEST

A. Risk of bias

Index test	Abdominal pain, bloating, constipation, rectal bleeding, diarrhoea, iron-deficiency anaemia (haemoglobin levels < 14 g/dl for males and < 12 g/dl for females, in the presence of ferritin < 30 µg/l and a median corpuscular value < 80 fl), change in bowel habits (onset of diarrhoea or constipation or altered stool in the previous 3 months) and weight loss (decrease of ≥ 3 kg in the 3 months prior to the visit).
Were the index test results interpreted without knowledge	Yes

of the results of the reference standard?	
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Histology
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	56/332 patients were excluded due to lack of mandatory fields (age, sex, clinical history, presenting symptoms and procedure results) in the database (N = 35) or violation of exclusion criteria (N = 18)
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	
Stapley (2012)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Matched case-control study using patients in the UK's General Practice Research Database (GPRD).
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> N = 3635, 1743 males / 1892 females; median number of consultations = 18 (IQR = 11-27); aged 40-49 years: N = 107; 50-59 years: N = 529; 60-69 years: N = 829; 70-79 years: N = 1212; ≥ 80 years: N = 958; UK.</p> <p><u>Controls:</u> N = 16459, gender not reported; median number of consultations = 9 (IQR = 4-15); aged 40-49 years: N = 422; 50-59 years: N = 2239; 60-69 years: N = 3755; 70-79 years: N = 5702; ≥ 80 years: N = 4341; UK.</p> <p><u>Inclusion criteria:</u> Cases: Patients with a record of one of 25 GPRD pancreatic cancer codes between January 2000 and December 2009 inclusive, aged ≥ 40 years, with min. 1 year of data before diagnosis. The first instance of a pancreatic cancer code was assigned the data of diagnosis/index date. Controls: Up to 5 controls were matched to cases on sex, general practice, and to 1 year of age of the case. The index date was the index date of the matched case.</p> <p><u>Exclusion criteria:</u> Pancreatic cancer (controls), no consultations in the year before diagnosis.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	All symptoms, physical signs or abnormal investigations compiled from the pancreatic cancer literature were studied, and supplemented by discussion with two pancreatic cancer charities. Libraries of codes relating to these were collated. All codes for fractures were also identified, as a test for any recording bias between cases and controls (making the assumption that the fracture rate would be approximately equal). Occurrences of these features in the year before the index date were identified. Features were only retained for further study if they occurred in ≥5% of cases or controls. Repeat attendances with the same symptom were also retained if the subsequent consultation also occurred in ≥5% of cases or controls. New-onset diabetes was defined as a code for diabetes, or a random blood glucose above the local laboratory's normal range, without similar codes more than 1 year before the index date. For laboratory tests, patients without a test were considered to be the same status as those with a normal result, making our binary variable abnormal result/ no abnormal result. Abnormal liver function was defined as any liver enzyme above the normal range, and raised inflammatory markers as either abnormal erythrocyte sedimentation rate or C-reactive protein, as there were too few plasma viscosity results.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Pancreatic cancer code in the UK's General Practice Research Database.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 21624 patients were identified, 17977 controls and 3647 cases. Of the controls the following exclusions were applied: pancreatic cancer (N = 64), case excluded (N = 40), and no data in year pre-index date (N = 1414). Of the cases the following exclusions were applied: No controls (N = 2), and cancer not of pancreatic origin (N = 10).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	

References

Included studies

- Bellentani, S., Baldoni, P., Petrella, S., Tata, C., Armocida, C., Marchegiano, P., Saccoccio, G., and Manenti, F. A simple score for the identification of patients at high risk of organic diseases of the colon in the family doctor consulting room. *The Local IBS Study Group. Family Practice* 7[4], 307-312. 1990.
- Collins, G.S., Altman, D.G. Identifying patients with undetected colorectal cancer: An independent validation of QCancer (Colorectal). *British Journal of Cancer* 107, 260-265. 2012.
- Collins, G.S., Altman, D.G. Identifying patients with undetected gastro-oesophageal cancer in primary care: External validation of QCancer (Gastro-Oesophageal). *European Journal of Cancer*, <http://dx.doi.org/10.1016/j.ejca.2012.10.023>. 2012a.
- Collins, G.S., and Altman, D.G. Identifying patients with undetected renal tract cancer in primary care: An independent and external validation of QCancer (renal) prediction model. *Cancer Epidemiology*, 37, 115-120. 2013.
- Collins, G.S.; Altman, D.G. (2013a). Identifying patients with undetected pancreatic cancer in primary care: an independent and external validation of QCancer^(®) (Pancreas). *British Journal of General Practice*, 63: 636-642.

- Hamilton, W., Round, A., Sharp, D., and Peters, T. J. Clinical features of colorectal cancer before diagnosis: a population-based case-control study. *British Journal of Cancer* 93[4], 399-405. 22-8-2005.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected gastro-oesophageal cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice*; DOI: 10.3399/bjgp11X606609. 2011.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected renal tract cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice* 62[597], e251-e260. 2012.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected colorectal cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice* 62[594], e29-e37. 2012a.
- Hippisley-Cox, J. & Coupland, C. (2012b) Identifying patients with suspected pancreatic cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice*, 62: e38-e45.
- Møllmann, K.-M. Early diagnosis of gastric cancer: The possibility of delimiting high risk groups. *Danish Medical Bulletin* 28, 89-92. 1981.
- Panzuto, F., Chiriatti, A., Bevilacqua, S., Giovannetti, P., Russo, G., Impinna, S., Pistilli, F., Capurso, G., Annibale, B., Delle, Fave G., and Digestive and Liver Disease and Primary Care Medicine Lazio Group. Symptom-based approach to colorectal cancer: survey of primary care physicians in Italy. *Digestive & Liver Disease* 35[12], 869-875. 2003.
- Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M. & Hamilton, W. (2012) The risk of pancreatic cancer in symptomatic patients in primary care: a large case-control study using electronic records. *British Journal of Cancer*, 106: 1940-1944.

APPETITE LOSS

Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The body of evidence was generally of high quality. The main validity issues to note is that patient sampling was not clearly consecutive or random in one of the studies, and that some of studies suffered from missing data. Studies employing non-consecutive/random sampling are at risk of bias because, for example, case-control studies have been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection. The statistical analyses employed by this study are however likely to have gone some way in addressing this issue.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Collins (2012)	+	+	+	+	+	+	+
Collins (2012a)	+	+	+	+	+	+	+
Collins (2013)	+	+	+	+	+	+	+
Collins (2013a)	+	+	+	+	+	+	+
Hamilton (2005)	-	+	+	+	+	+	+
Hippisley-Cox (2011)	+	+	+	?	+	+	+
Hippisley-Cox (2012)	+	+	+	-	+	+	+
Hippisley-Cox (2012a)	+	+	+	+	+	+	+
Hippisley-Cox (2012b)	+	+	+	-	+	+	+

- High
 ? Unclear
 + Low

Table 1: Non-site specific symptoms of concern: Calculation of overall positive predictive value of appetite loss for cancer

Cancer site	Study	Lower age limit	Upper age limit	PPV (95% CI), prevalence
Bladder/renal	Hippisley-Cox (2012)	30	84	0.18 (0.07-0.4)
Colorectal	Hippisley-Cox (2012)	30	84	0.9 (0.6-1.2)
Lung	Hamilton* (2005)	40	no upper limit	1.285
Oesophagus/stomach	Hippisley-Cox (2011)	30	84	1.1 (0.8-1.5)

Pancreatic	Hippisley-Cox (2012)	30	84	0.8 (0.5-1.2)
Sum				4.65

* Not sure which one to pick, so used average.

Table 2: Non-site specific symptoms of concern: Positive predictive values for appetite loss

Cancer site	Comment/relevant recs	Study	Symptom	Patient group	Positive predictive value% (95% CI)	Sex	Age inclusion, lower limit	Age inclusion, upper limit
Bladder/renal		Collins (2013)	Appetite loss	Women	0.1 (0.04-0.3)	Women	30	84
Bladder/renal		Hippisley-Cox (2012)	Appetite loss	All patients	0.18 (0.07-0.4)	both	30	84
Colorectal		Hippisley-Cox (2012a)	Loss of appetite	All patients	0.9 (0.6-1.2)	both	30	84
Colorectal		Collins (2012)	Loss of appetite	All patients	0.8 (0.6-1.1)	both	30	84
Colorectal		Collins (2012)	Loss of appetite	Men 30-84 years	1 (0.6-1.5)	men	30	84
Colorectal		Collins (2012)	Loss of appetite	Women 30-84 years	0.6 (0.4-1)	women	30	84
Lung		Hamilton (2005)	Appetite loss	All included patients	0.87 (0.6-1.3)	both	40	No upper limit
Lung		Hamilton (2005)	Appetite loss (reported twice)	All included patients	1.7 (NR)	both	40	No upper limit
Lung		Hamilton (2005)	Appetite loss	Patients 40-69 years	1.1 (NR)	both	40	69
Lung		Hamilton (2005)	Appetite loss	All smokers	1.8 (NR)	both	40	No upper limit
Lung		Hamilton	Appetite loss	All smoke	2.7 (NR)	both	40	No upper limit

		(2005)	(reported twice)	rs				
Oesophagus/stomach		Collins (2012a)	Appetite loss	All patients	0.6 (0.5-0.9)	both	30	84
Oesophagus/stomach		Collins (2012a)	Appetite loss	Women	0.4 (0.2-0.7)	women	30	84
Oesophagus/stomach		Collins (2012a)	Appetite loss	Men	1 (0.7-1.5)	men	30	84
Oesophagus/stomach		Hippisley-Cox (2011)	Appetite loss	All patients	1.1 (0.8-1.5)	both	30	84
Pancreatic		Collins (2013a)	Appetite loss	All patients	0.39 (0.26-0.59)	both	30	84
Pancreatic		Collins (2013a)	Appetite loss	Women	0.32 (0.17-0.59)	women	30	84
Pancreatic		Collins (2013a)	Appetite loss	Men	0.49 (0.27-0.86)	women	30	84
Pancreatic		Hippisley-Cox (2012b)	Appetite loss	All patients	0.8 (0.5-1.2)	both	30	84

Evidence statement(s):

Appetite loss (5 studies, N = 4961516) presenting in a primary care setting is associated with an overall positive predictive value of 4.65% for cancer. The studies were associated with 0-1 bias/applicability concern (see also Table 1).

Evidence tables

Collins (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	

Patient characteristics and setting	<p>A total of 2135540 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Rectal bleeding (N = 56234; 28423 men, 27811 women), abdominal pain (N = 245989; 102192 men, 143797 women), appetite loss (N = 5776; 2481 men, 3295 women), weight loss (N = 28289; 12891 men, 15398 women), anaemia (N = 18125; 4466 men, 13659 women), change in bowel habit (men only, N = 1670).</p> <p><u>Incident cases of colorectal cancer during the 2-year follow up period:</u> N = 3712 (2036 men, 1676 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of colorectal cancer at baseline, and patients with a recorded 'red-flag' symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	'Red-flag' symptoms: Rectal bleeding, loss of appetite, weight loss, abdominal pain, change in bowel habit (men only), and anaemia.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	2-year follow up	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients seem to be accounted for	

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	The is <i>very large, if not complete, overlap</i> of the data used in this study with those used in Hamilton (2008 [for anaemia], 2009)
Collins (2012a)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2135540 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Dysphagia (N = 19237; 8846 men, 10391 women), abdominal pain (N = 246998; 102732 men, 144266 women), appetite loss (N = 5838; 2521 men, 3317 women), weight loss (N = 28403; 12938 men, 15465 women), haematemesis (N = 10792; 6162 men, 4630 women), anaemia (N = 18355; 4563 men, 13792 women).</p> <p><u>Incident cases of gastro-oesophageal cancer during the 2-year follow up period:</u> N = 1766 (1184 men, 582 women; 32% gastric cancer, 68% oesophageal cancer).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of gastro-oesophageal cancer, registration with the general practice < 12 months, or with invalid dates.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Haematemesis, dysphagia, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	The study did not distinguish between gastric and oesophageal cancer

Collins (2013)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	A total of 2145133 patients (1063355 men, 1081778 women) were identified from 364 practices. Symptoms: Haemoglobin < 11 g/dl recorded in the last year (N = 16961; 3969 men, 12992 women), abdominal pain (N = 253344; 105247 men, 148097 women), appetite loss (N = 6097; 2616 men, 3481 women), weight loss (N = 29369; 13332 men, 16037 women), haematuria (N = 37810; 22810 men, 15000 women), previous diagnosis of cancer apart from renal tract cancer at study entry (N = 49303; 18130 men, 31173 women). <u>Incident cases of renal tract cancer during the 2-year follow up period:</u> N = 2283 (1685 men, 598 women).

	<p>Inclusion criteria: Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (e.g., haematuria, abdominal pain, weight loss, appetite loss, and anaemia), the date of the first recorded onset within the study period.</p> <p>Exclusion criteria: Patients with a prior diagnosis of renal tract cancer, registered less than 12 months with the general practice, had invalid dates, < 30 years old or ≥ 85 years old.</p> <p>Clinical setting: Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Renal tract cancer, which was defined as incident diagnosis of cancer of the bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes. Patients without the outcome were censored at the earliest of the date of death, date of leaving the practice study of 2 years of follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes

Could the patient flow have introduced bias?		Low risk
NOTES	It is unclear why no data has been presented for men for the symptoms of appetite loss and weight loss.	
Collins (2013a)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective patient series using the THIN database.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?		Low risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>A total of 2150322 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Dysphagia (men only: N = 9326), abdominal pain (N = 255058; 106768 men, 148290 women), appetite loss (N = 6102; 2658 men, 3444 women), weight loss (N = 29464; 13484 men, 15980 women), abdominal distension (women only: N = 4457), constipation (men only, N = 5326).</p> <p><u>Incident cases of pancreatic cancer during the 2-year follow up period:</u> N = 287 (331 men, 287 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of pancreatic cancer, registration < 12 months with the general practice, or invalid dates.</p> <p><u>Clinical setting:</u> Primary care, UK</p>	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	'Red-flag' symptoms: Dysphagia (men only), loss of appetite, weight loss, abdominal pain, abdominal distension (women only), and constipation (men only).	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	2-year follow up	

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Hamilton (2005)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based matched case-control study involving all 21 general practices in Exeter, Devon, UK.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> N = 247 (170 males/77 females), age at diagnosis: < 60 years: N = 35, 60-69 years: N = 60, 70-79 years: N = 118, 80+ years: N = 34.</p> <p><u>Controls:</u> N = 1235 (850 males/385 females), age at diagnosis: < 60 years: N = 178, 60-69 years: N = 310, 70-79 years: N = 575, 80+ years: N = 174.</p> <p><u>Inclusion criteria:</u> Cases: All patients aged ≥ 40 years with a primary lung cancer, diagnosed from 1998 to 2002, were identified from the cancer registry at the Royal Devon and Exeter Hospital combined with computerised searches at every practice in Devon to identify any cases missing from the cancer register.</p>

	<p>Controls: Five controls were matched to each case on sex, general practice, and age. Controls were eligible if they were alive at the time of diagnosis of their case.</p> <p><u>Exclusion criteria:</u> Cases and controls: Unobtainable records; no consultations in the 2 years before diagnosis; previous lung cancer; or residence outside Exeter at the time of diagnosis.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
<u>A. Risk of bias</u>	
Index test	Anonymised photocopies of the full primary care records for 2 years before diagnosis were coded (blinded to case/control status) for all entries using the International Classification of Primary Care-2. Additional codes were created to incorporate all possible clinical features. Only variables occurring in $\geq 2.5\%$ of cases or controls were analysed.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
<u>A. risk of bias</u>	
Reference standard(s)	Lung cancer diagnosis in the cancer registry at the Royal Devon and Exeter Hospital or practice notes.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
<u>A. risk of bias</u>	
Flow and timing	All the patients are accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

NOTES	
Hippisley-Cox (2011)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1238971 patients were identified from 189 practices (621478 males, 617493 females), mean (SD) age = 50.1 (15) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Symptoms:</u> Current dysphagia (N = 8165), current haematemesis (N = 7119), current abdominal pain (N = 126161), current appetite loss (N = 6133), current weight loss (N = 5377), tiredness in the last year (N = 14119), haemoglobin recorded in the last year (N = 12638, haemoglobin < 11 g/dl in the last year (N = 218862).</p> <p><u>Incident cases of gastro-oesophageal cancer during the 2-year follow up period:</u> N = 1343 (776 oesophageal and 567 gastric).</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000); 12 months after the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of gastro-oesophageal cancer at baseline, and patients with a recorded 'red-flag' symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Incident dysphagia, haematemesis, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge	Yes

of the results of the reference standard?	
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 103358 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of gastro-oesophageal cancer (N = 538), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 31973), leaving 1238971 patients. However, data is presented for 963040/1238971 patients for all symptoms. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	Results not presented separately for gastric and oesophageal cancer
Hippisley-Cox (2012)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	

Patient characteristics and setting	<p>A total of 1240722 patients were identified from 189 practices (622166 males, 618556 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Current symptoms and symptoms in the preceding year:</u> Current haematuria (N = 25553), current abdominal pain (N = 128721), current appetite loss (N = 5531), current weight loss (N = 14464), constipation in the last year (N = 8472), diarrhoea in the last year (N = 12171), tiredness in the last year (N = 12669), haemoglobin recoded in the last year (N = 216201), haemoglobin < 11 g/dl in the last year (N = 16169).</p> <p><u>Incident cases of renal tract cancer during the 2-year follow up period:</u> N = 1622; mean age at diagnosis = 70 years, 1187 males/ 435 females; Type of cancer: Bladder: N = 1292; Kidney: N = 307; Ureter: N = 21; Urethra: N = 2.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months’ registration prior to study entry. For patients with incident haematuria, appetite loss, weight loss, or abdominal pain, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of renal tract cancer at baseline, and patients with a recorded ‘red-flag’ (see “Definition of symptom” below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	‘Red-flag’ symptoms were defined as symptoms that might alarm the patient and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference	Renal tract cancer, which was defined as incident diagnosis of cancer of the

standard(s)	bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 codes (188 or 189) or ICD-10 diagnostic codes (C64–67).	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	A total of 1342329 patients were initially identified of whom 101607 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of renal tract cancer (N = 1506), and ≥ one 'red flag' symptom recorded in the 12 months prior to study entry (N = 29254), leaving 1240722 patients. However, data is presented for 967681 / 1240722 patients. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Could the patient flow have introduced bias?	High risk	
NOTES		
Hippisley-Cox (2012a)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	A total of 1236601 patients were identified from 189 practices (620240 males, 616361 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6). <u>Symptoms:</u> Current rectal bleeding (N = 29118), current abdominal pain (N = 125816), current appetite loss (N = 5358), current weight loss (N = 14065), recent	

	<p>change in bowel habit (N = 1821). <u>Incident cases of colorectal cancer during the 2-year follow up period:</u> N = 2603 (1562 colon and 1041 rectum). <u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for \geq a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000); 12 months after the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i> <u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of colorectal cancer at baseline, and patients with a recorded ‘red-flag’ symptom in the 12 months prior to the study entry date. Clinical setting: Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	‘Red-flag’ symptoms: First onset rectal bleeding, first onset loss of appetite, first onset weight loss, first onset abdominal pain, first onset change in bowel habit (in the past 12 months), and anaemia (recorded haemoglobin < 11 g/dl in the past 12 months).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 105728 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of colorectal cancer (N = 2908), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 31973), leaving 1236601 patients. However, data is presented for 1235547/1236601 patients for all symptoms apart from change in bowel habit, which is only presented for 619651/620240 of the male patients. The missing data does not appear to include any of the cancer cases (although this cannot be ascertained for change in bowel habit), but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Low risk
NOTES	Please note there is some overlap between this patient sample and that of Parker (2007)

Hippisley-Cox (2012b)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1243740 patients were identified from 189 practices (624352 males, 619388 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Current symptoms and symptoms in the preceding year:</u> Current dysphagia (N = 8507), current abdominal pain (N = 129924), current abdominal distension (N = 4929), current appetite loss (N = 5567), current weight loss (N = 14686), constipation in the last year (N = 8476), diarrhoea in the last year (N = 12233), tiredness in the last year (N = 12688), itching in the last year (N = 1454), haemoglobin recoded in the last year (N = 214497), haemoglobin < 11 g/dl in the last year (N = 16172).</p> <p><u>Incident cases of pancreatic cancer during the 2-year follow up period:</u> N = 781.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for \geq a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from</p>

	<p>patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months' registration prior to study entry. For patients with incident haematuria, appetite loss, weight loss, or abdominal pain, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of pancreatic cancer at baseline, and patients with a recorded 'red-flag' (see "Definition of symptom" below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of pancreatic cancer; that is, symptoms of dysphagia, loss of appetite, weight loss, abdominal distension or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Pancreatic cancer, which was defined as incident diagnosis of pancreatic cancer during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 code (157) or ICD-10 diagnostic codes (C25).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 98589 patients

	were excluded for the following reasons: No recorded Townsend score (N = 70847), history of pancreatic cancer (N = 96), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 27646), leaving 1243740 patients. However, data is presented for 971706 / 1243740 patients. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	

References

Included studies

- Collins, G.S., Altman, D.G. Identifying patients with undetected colorectal cancer: An independent validation of QCancer (Colorectal). *British Journal of Cancer* 107, 260-265. 2012.
- Collins, G.S., Altman, D.G. Identifying patients with undetected gastro-oesophageal cancer in primary care: External validation of QCancer (Gastro-Oesophageal). *European Journal of Cancer*, <http://dx.doi.org/10.1016/j.ejca.2012.10.023>. 2012a.
- Collins, G.S., and Altman, D.G. Identifying patients with undetected renal tract cancer in primary care: An independent and external validation of QCancer (renal) prediction model. *Cancer Epidemiology*, 37, 115-120. 2013.
- Collins, G.S.; Altman, D.G. (2013a). Identifying patients with undetected pancreatic cancer in primary care: an independent and external validation of QCancer[®] (Pancreas). *British Journal of General Practice*, 63: 636-642.
- Hamilton, W., Peters, T. J., Round, A. & Sharp, D. (2005) What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. *Thorax*, 60: 1059-1065. The data split by smoking status is available from: <http://webarchive.nationalarchives.gov.uk/20130513211237/http://www.ncat.nhs.uk/sites/default/files/work-docs/ncl%20lung%20guide.pdf>
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected gastro-oesophageal cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice*; DOI: 10.3399/bjgp11X606609. 2011.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected renal tract cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice* 62[597], e251-e260. 2012.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected colorectal cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice* 62[594], e29-e37. 2012a.
- Hippisley-Cox, J. & Coupland, C. (2012b) Identifying patients with suspected pancreatic cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice*, 62: e38-e45.

WEIGHT LOSS AND APPETITE LOSS

Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main validity issues to note is that patient sampling was not based on a consecutive or random series of patients in one of the studies, while the other study was conducted in a population that is not necessarily directly relevant to the current question. Studies employing non-consecutive/random sampling are at high risk of bias because, for example, case-control studies have been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection. Studies conducted in other settings than UK-based primary care are only applicable to the extent that the study populations and settings are comparable to a UK GP population as defined for the current purposes. Other bias and applicability threats to the results concern missing data and a potentially suboptimal reference standard.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Hamilton (2005)	⊖	⊕	⊕	⊕	⊕	⊕	⊕
Moellmann (1981)	⊕	⊕	?	⊖	?	⊕	⊕

⊖ High ? Unclear ⊕ Low

Table 1: Non-site specific symptoms of concern: Calculation of overall positive predictive value of appetite loss with weight loss for cancer

Cancer site	Study	Lower age limit	Upper age limit	PPV (95% CI), prevalence
Lung	Hamilton (2005)	40	no upper limit	2.3 (1.2-4.4)
Oesophagus	Møllmann (1981)	40	>90	0 (0-8.9) 0/50
Stomach	Møllmann (1981)	40	>90	2 (0.1-12) 1/50
<u>Sum</u>				<u>4.3</u>

Table 2: Non-site specific symptoms of concern: Positive predictive values for weight loss + appetite loss

Cancer site	Comment/relevant recs	Study	Symptom	Patient group	Positive predictive value% (95% CI)	Sex	Age inclusion, lower limit	Age inclusion, upper limit
Lung	Rec: Offered FBC and xray	Hamilton (2005)	Weight loss + appetite loss	All included patients	2.3 (1.2-4.4)	both	40	no upper limit

Lung	Rec: Offered FBC and xray	Hamilton (2005)	Weight loss + appetite loss	All smokers	5 (NR)	both	40	no upper limit
Oesophagus		Møllmann (1981)	Weight loss and/or anorexia	All patients	0 (0-8.9)	both	40	>90
Stomach	Rec: UGI endoscopy	Møllmann (1981)	Weight loss and/or anorexia	All patients	2 (0.1-12)	both	40	>90

Evidence statement(s):

Appetite loss with weight loss (2 studies, N = 2962) presenting in a primary care setting is associated with an overall positive predictive value of 4.3% for cancer. The studies were associated with 1-3 bias/applicability concerns (see also Table 1).

Evidence tables

Hamilton (2005)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based matched case-control study involving all 21 general practices in Exeter, Devon, UK.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> N = 247 (170 males/77 females), age at diagnosis: < 60 years: N = 35, 60-69 years: N = 60, 70-79 years: N = 118, 80+ years: N = 34.</p> <p><u>Controls:</u> N = 1235 (850 males/385 females), age at diagnosis: < 60 years: N = 178, 60-69 years: N = 310, 70-79 years: N = 575, 80+ years: N = 174.</p> <p><u>Inclusion criteria:</u> Cases: All patients aged ≥ 40 years with a primary lung cancer, diagnosed from 1998 to 2002, were identified from the cancer registry at the Royal Devon and Exeter Hospital combined with computerised searches at every practice in Devon to identify any cases missing from the cancer register.</p>

	<p>Controls: Five controls were matched to each case on sex, general practice, and age. Controls were eligible if they were alive at the time of diagnosis of their case.</p> <p><u>Exclusion criteria:</u> Cases and controls: Unobtainable records; no consultations in the 2 years before diagnosis; previous lung cancer; or residence outside Exeter at the time of diagnosis.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
<u>A. Risk of bias</u>	
Index test	Anonymised photocopies of the full primary care records for 2 years before diagnosis were coded (blinded to case/control status) for all entries using the International Classification of Primary Care-2. Additional codes were created to incorporate all possible clinical features. Only variables occurring in $\geq 2.5\%$ of cases or controls were analysed.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
<u>A. risk of bias</u>	
Reference standard(s)	Lung cancer diagnosis in the cancer registry at the Royal Devon and Exeter Hospital or practice notes.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
<u>A. risk of bias</u>	
Flow and timing	All the patients are accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

NOTES	
Møllmann (1981)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from an open-access gastroscopy clinic in Denmark.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1480; gender not reported; 40-44 years: N = 144; 45-49 years: N = 186; 50-69 years: N = 882; 70-74 years: N = 130; 75-79 years: N = 83; 80-89 years N = 47; 90- years: N = 8. <u>Inclusion criteria:</u> All patients who, for a 2-year period, presented to their GP with (any of) the following symptoms were referred to the open access gastroscopy clinic: Upper abdominal pain > 2 weeks, nausea and/or vomiting > 2 weeks, weight loss and/or anorexia, gastrointestinal bleeding, and anaemia (i.e., Hb < 80%). <u>Exclusion criteria:</u> Patients who had been examined for any of the above symptoms within the last 6 months. <u>Clinical setting:</u> GPs in Denmark
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Upper abdominal pain > 2 weeks, nausea and/or vomiting > 2 weeks, weight loss and/or anorexia, gastrointestinal bleeding, and anaemia (i.e., Hb < 80%).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-stage process: Gastroscopy with photography, using a gastroscope, performed with only local anaesthesia of the pharynx. If this investigation disclosed abnormal conditions, the next stage was gastroscopy, possibly with biopsy, using diazepam sedation.
Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its	Unclear risk

interpretation have introduced bias?		
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	177/1480 patients declined endoscopy, 2/1480 did not show up for endoscopy, and it was unsuccessful in a further 24 patients, leaving 1277 patients. However, the paper reports that only 1273 had primary endoscopy, and then reports the results for between 1181 and 1297 patients.	
Was there an appropriate interval between index test and reference standard?		Yes probably
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		No
Could the patient flow have introduced bias?		High risk
NOTES	There were a total of 18 gastric cancers confirmed in the study. No oesophageal cancers were reported. This research was published in 2 papers.	

References

Included studies

Hamilton, W., Peters, T. J., Round, A. & Sharp, D. (2005) What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. *Thorax*, 60: 1059-1065.

The data split by smoking status is available from:

<http://webarchive.nationalarchives.gov.uk/20130513211237/http://www.ncat.nhs.uk/sites/default/files/work-docs/ncl%20lung%20guide.pdf>

Møllmann, K.-M. Early diagnosis of gastric cancer: The possibility of delimiting high risk groups. *Danish Medical Bulletin* 28, 89-92. 1981.

Møllmann, K.-M. Endoscopic service for general practice. *Danish Medical Bulletin* 28, 96-99. 1981.

DEEP VEIN THROMBOSIS

Risk of bias in the included studies

The risk of bias and applicability concerns are summarised in the figure below. The main validity issue to note is that the study was conducted in the Netherlands and the findings are only applicable to the extent that the study population and setting are comparable to a UK GP population as defined for the current purposes.

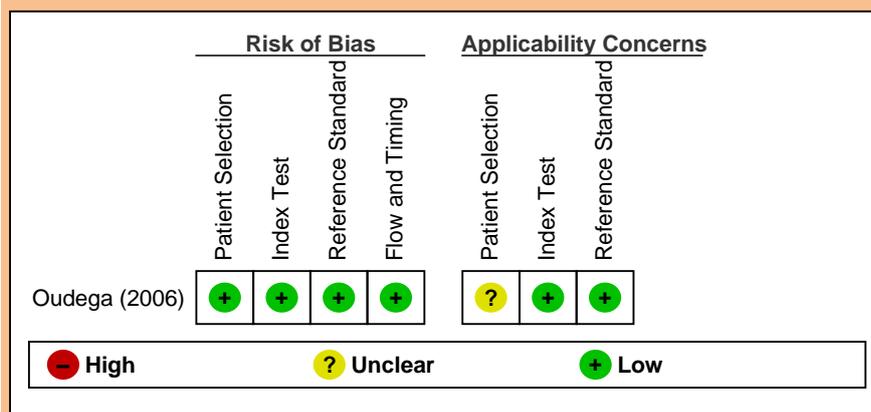


Table 1: Non-site specific symptoms of concern: Calculation of overall positive predictive value of deep vein thrombosis for cancer

Cancer site	Study	Lower age limit	Upper age limit	PPV (95% CI), prevalence
Colorectal	Oudega (2006)	No age incl/excl given, sample mean (SD) age = 60.7 (18.2) years		0.7 (0.2-2.2)
Urogenital	Oudega (2006)	No age incl/excl given, sample mean (SD) age = 60.7 (18.2) years		1.16 (0.4-2.9)
Breast	Oudega (2006)	No age incl/excl given, sample mean (SD) age = 60.7 (18.2) years		0.93 (0.3-2.53)
Lung	Oudega (2006)	No age incl/excl given, sample mean (SD) age = 60.7 (18.2) years		0.7 (0.2-2.2)
<u>Sum</u>				<u>3.49</u>

Table 2: Non-site specific symptoms of concern: Positive predictive values for deep vein thrombosis

Cancer site	Comment/relevant recs	Study	Symptom	Patient group	Positive predictive value% (95% CI)	Sex	Age inclusion, lower limit	Age inclusion, upper limit
Colorectal		Oudega (2006)	Deep vein thrombosis	All included patients	0.7 (0.2-2.2)	both	No age incl/excl given, sample mean (SD) age = 60.7 (18.2) years	
Urogenital		Oudega	Deep	All	1.16 (0.4-	both	No age incl/excl given, sample	

nital		a (2006)	vein thrombosis	included patients	2.9)		mean (SD) age = 60.7 (18.2) years
Breast		Oudega (2006)	Deep vein thrombosis	All included patients	0.93 (0.3-2.53)	women	No age incl/excl given, sample mean (SD) age = 60.7 (18.2) years
Lung		Oudega (2006)	Deep vein thrombosis	All included patients	0.7 (0.2-2.2)	both	No age incl/excl given, sample mean (SD) age = 60.7 (18.2) years
Other		Oudega (2006)	Deep vein thrombosis	All included patients	0.93 (0.3-2.53)	both	No age incl/excl given, sample mean (SD) age = 60.7 (18.2) years

Evidence statement(s):

Deep vein thrombosis (1 study, N = 430) presenting in a primary care setting is associated with an overall positive predictive value of 3.49% for cancer. The study was associated with 1 applicability concern (see also Table 1).

Evidence tables

Oudega (2006)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective study of all primary care physicians (N = 50) within a catchment area (ca 130000 inhabitants) of a non-teaching hospital in The Netherlands.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 430; 162 males, 268 females; mean age (SD) = 60.7 (18.2) years. <u>Inclusion criteria:</u> Consecutive patients who consulted their GP between January 1996 and July 2002 and who, after investigation (not referral) was confirmed to have deep vein thrombosis. <u>Exclusion criteria:</u> Patients with a known malignancy or a malignancy detected within 2 weeks of deep vein thrombosis diagnosis. <u>Clinical setting:</u> Primary care, The Netherlands.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern

INDEX TEST	
A. Risk of bias	
Index test	Deep vein thrombosis (suspicion based on painful swollen leg ≤ 30 days). Patients were classified as having secondary deep vein thrombosis if ≥ 1 of the following risk factors for deep vein thrombosis were present: Recent surgery, prolonged immobilisation, use of oral contraceptives or hormonal replacement therapy. If no risk factors were present patients were classified as having idiopathic deep vein thrombosis.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2 years follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 19 had cancer: 3 colorectal, 5 urogenital (not further subgrouped), 4 breast, 3 lung and 4 other. The urogenital data is added to the renal cancer evidence review.

References

Included studies

Oudega, R. (2006) Deep vein thrombosis in primary care: Possible malignancy? *British Journal of General Practice*, 56: 693-696.

DYSPEPSIA

Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The main validity issues to note is that patient sampling was not clearly consecutive or random in a number of the studies, and the vast majority of the studies were conducted in populations that are not clearly directly relevant to the current question. Studies employing non-consecutive/random sampling are at risk of bias because, for example, case-control studies have been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection. Studies conducted in other settings than UK-based primary care are only applicable to the extent that the study populations and settings are comparable to a UK GP population as defined for the current purposes. Other bias and applicability threats to the results concern missing data and a potentially suboptimal reference standard.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Brignoli (1997)	?	+	-	+	?	+	+
Duggan (2008)	?	+	+	+	+	+	+
Edenholm (1985)	?	+	+	-	?	+	+
Hallissey (1990)	+	+	+	+	?	+	+
Hansen (1998)	+	+	+	?	?	+	+
Heikkinen (1995)	+	+	+	+	?	+	+
Jaskiewicz (1991)	?	+	+	+	?	?	+
Kagevi (1989)	+	+	+	+	?	+	+
Meineche-Schmidt (2002)	+	+	+	+	?	+	+
Thomson (2003)	?	+	+	+	?	+	+
Vakil (2009)	?	+	+	+	+	+	+

- High
 ? Unclear
 + Low

Table 1: Non-site specific symptoms of concern: Calculation of overall positive predictive value of dyspepsia for cancer

Cancer site	Study	Lower age limit	Upper age limit	PPV (95% CI), prevalence
Liver	Hallissey (1990)	40	no upper limit	0.04 (0.002-0.25)
Pancreatic	Hallissey (1990)	40	no upper limit	0.23 (0.09-0.53)
Uterine	Hallissey (1990)	40	no upper limit	0.04 (0.002-0.25)

Leukaemia	Hallissey (1990)	40	no upper limit	0.04 (0.002-0.3)
Gall bladder	Hallissey (1990)	40	no upper limit	0.04 (0.002-0.3)
Prostate	Hallissey (1990)	40	no upper limit	0.08 (0.01-0.3)
Bronchial	Hallissey (1990)	40	no upper limit	0.3 (0.1-0.6)
Oesophagus/stomach	Meta-analysis	varied	varied	0.65 (0.33-1.3)
Colorectal	Meta-analysis	varied	varied	0.6 (0.27-1.35)
Sum				2.02

Table 2: Non-site specific symptoms of concern: Positive predictive values for dyspepsia

Cancer site	Comment/relevant recs	Study	Symptom	Patient group	Positive predictive value% (95% CI)	Sex	Age inclusion, lower limit	Age inclusion, upper limit
Liver		Hallissey (1990)	Dyspepsia	All patients	0.04 (0.002-0.25)	both	40	no upper limit
Pancreatic		Hallissey (1990)	Dyspepsia	All patients	0.23 (0.09-0.53)	both	40	no upper limit
Uterine		Hallissey (1990)	Dyspepsia	All patients	0.04 (0.002-0.25)	both	40	no upper limit
Leukaemia		Hallissey (1990)	Dyspepsia	All patients	0.04 (0.002-0.3)	both	40	no upper limit
Gall bladder		Hallissey (1990)	Dyspepsia	All patients	0.04 (0.002-0.3)	both	40	no upper limit
Prostate		Hallissey (1990)	Dyspepsia	All patients	0.08 (0.01-0.3)	both	40	no upper limit
Bronchial		Hallissey (1990)	Dyspepsia	All patients	0.3 (0.1-0.6)	both	40	no upper limit
Other		Hallissey (1990)	Dyspepsia	All patients	0.3 (0.1-0.6)	both	40	no upper limit
Other		Meinche-Schmidt (2002)	Dyspepsia	All patients	0.4 (0.16-0.92)	both	18	65+
META-ANALYSES (1) Oesophageal								
Oesophagus/stomach	2 combining gastro-	Meta-analyses	Dyspepsia	All patients	0.25 (0.13-0.5)	both	2 studies > 15, 2 studies > 18, 1 study > 40, 1 study 17-80, 2 studies 18-70, 1 study 19-87, 1 study 18- >65, 1 study NR but	

	oesophageal and 9 reporting on oesophageal cancer separately						mean (SD) = 41-42 (15-16) Individual study details provided below	
The 11 studies below are those included in the meta-analysis reported in the cell above (Please note the same data from Hansen (1998) and Meineche-Schmidt (2002) appear both here and under stomach, avoid double counting it):								
Oesophageal		Brignoli (1997)	Dyspepsia	All patients	0 (0-0.58)	both	Mean (SD) age = 41-42 (15-16) years	
Oesophageal		Duggan (2008)	Dyspepsia	All patients	0.27 (0.05-1.1)	both	18	70
Oesophageal		Edenholm (1985)	Persistent epigastric pain/ulcer-like dyspepsia	All patients who received an UGI endoscopy	0.61 (0.03-3.8)	both	17	80
Oesophageal		Hallisey (1990)	Dyspepsia	All patients	0.58 (0.33-0.98)	both	40	No upper limit
Oesophageal/stomach		Hansen (1998)	Dyspepsia	All patients	1 (0.4-2.2)	both	Mean age (SD) = 47 (16.8)	
Oesophageal		Heikkinen (1995)	Dyspepsia	All patients	0.5 (0.09-2)	both	77% were > 44 years.	
Oesophageal		Jaskiewicz (1991)	Dyspepsia	All patients	0 (0-0.8)	both	19	87
Oesophageal		Kagevi (1989)	Dyspepsia	All included patients	0 (0-2.7)	both	16	No upper limit
Oesophageal/stomach		Meineche-Schmidt (2002)	Dyspepsia	All patients	0.54 (0.25-1.1)	both	18	65+

Oesophageal		Thoms on (2003)	Dyspepsia	All patients	0.1 (0.01-0.6)	both	18	84
Oesophageal		Vakil (2009)	Dyspepsia without alarm symptoms	All patients	0.1 (0.03-0.35)	both	18	70
The following results are any extra analyses reported by the studies included in the above meta-analysis:								
Oesophageal		Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 45 years old	0.18 (0.03-0.71)	both	45	70
Oesophageal		Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 50 years old	0.24 (0.04-1)	both	50	70
Oesophageal		Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 55 years old	0.18 (0.01-1.16)	both	55	70
Oesophageal		Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 60 years old	0.3 (0.02-2)	both	60	70
Oesophageal/stomach		Hansen (1998)	Ulcer-like dyspepsia	All patients	0.6 (0.03-3.9)	both	Mean age (SD) = 47 (16.8)	
Oesophageal/stomach		Hansen (1998)	Dysmotility-like dyspepsia	All patients	0 (0-2.9)	both	Mean age (SD) = 47 (16.8)	
Oesophageal/stomach		Hansen (1998)	Reflux-like dyspepsia	All patients	1.16 (0.2-4.6)	both	Mean age (SD) = 47 (16.8)	
Oesophageal/stomach		Hansen (1998)	Unclassifiable dyspepsia	All patients	0.9 (0.05-5.8)	both	Mean age (SD) = 47 (16.8)	

META-ANALYSES (2) Stomach							
Oesophagus/stomach	2 combining gastro-oesophageal and 9 reporting on stomach cancer separately	Meta-analyses	Dyspepsia	All patients	0.65 (0.33-1.3)	both	2 studies > 15, 2 studies > 18, 1 study > 40, 1 study 17-80, 2 studies 18-70, 1 study 19-87, 1 study 18- >65, 1 study NR but mean (SD) = 41-42 (15-16) Individual study details provided below.
The 11 studies below are those included in the meta-analysis reported in the cell above (Please note the same data from Hansen (1998) and Meineche-Schmidt (2002) appear both here and under oesophageal, avoid double counting it):							
Stomach		Brignoli (1997)	Dyspepsia	All patients	0.4 (0.09-1.14)	both	Mean (SD) age = 41-42 (15-16) years
Stomach		Duggan (2008)	Dyspepsia	All patients	0.27 (0.05-1.1)	both	18 70
Stomach		Edenholm (1985)	Persistent epigastric pain/ulcer-like dyspepsia	All patients who received an UGI endoscopy	1.2 (0.21-4.77)	both	17 80
Stomach		Hallisey (1990)	Dyspepsia	All patients	2.28 (1.76-3)	both	40 No upper limit
Oesophageal/stomach		Hansen (1998)	Dyspepsia	All patients	1 (0.4-2.2)	both	Mean age (SD) = 47 (16.8)
Stomach		Heikkinen (1995)	Dyspepsia	All patients	1.75 (0.8-3.7)	both	77% were > 44 years.
Stomach		Jaskiewicz (1991)	Dyspepsia	All patients	2.7 (1.6-4.5)	both	19 87
Stomach		Kagevi (1989)	Dyspepsia	All patients	1.16 (0.2-4.6)	both	16 No upper limit
Oesophageal/stomach		Meineche-Schmidt	Dyspepsia	All patients	0.54 (0.25-1.1)	both	18 65+

		(2002)						
Stomach		Thoms on (2003)	Dyspeps ia	All patien ts	0.1 (0.01-0.6)	both	18	84
Stomach		Vakil (2009)	Dyspeps ia without alarm symptoms	All patien ts	0.1 (0.03-0.35)	both	18	70
The following results are any extra analyses reported by the studies included in the above meta-analysis:								
Stomach		Jaskiewicz (1991)	Dyspeps ia	Males	3.4 (1.8-6)	Males	19	87
Stomach		Jaskiewicz (1991)	Dyspeps ia	Females	1.7 (0.6-4.7)	Females	19	87
Oesophageal/stomach		Hansen (1998)	Ulcer-like dyspeps ia	All patien ts	0.6 (0.03-3.9)	Both	Mean age (SD) = 47 (16.8)	
Oesophageal/stomach		Hansen (1998)	Dysmotility-like dyspeps ia	All patien ts	0 (0-2.9)	Both	Mean age (SD) = 47 (16.8)	
Oesophageal/stomach		Hansen (1998)	Reflux-like dyspeps ia	All patien ts	1.16 (0.2-4.6)	Both	Mean age (SD) = 47 (16.8)	
Oesophageal/stomach		Hansen (1998)	Unclassifiable dyspeps ia	All patien ts	0.9 (0.05-5.8)	Both	Mean age (SD) = 47 (16.8)	
Stomach		Vakil (2009)	Dyspeps ia without alarm symptoms	Patien ts ≥ 45 years old	0.27 (0.07-0.84)	both	45	70
Stomach		Vakil (2009)	Dyspeps ia without alarm symptoms	Patien ts ≥ 50 years old	0.36 (0.09-1.15)	both	50	70
Stomach		Vakil (2009)	Dyspeps ia without	Patien ts ≥ 55 years	0 (0-0.86)	both	55	70

			alarm symptoms	old				
Stomach		Vakil (2009)	Dyspepsia without alarm symptoms	Patients ≥ 60 years old	0 (0-1.47)	both	60	70
META-ANALYSES (3) Colorectal								
Colorectal	1 study from 15, 1 study from 18-65+ and 1 study from 40.	Meta-analysis	Dyspepsia	All patients	0.6 (0.27-1.35)	both	15-18	65+
The 3 studies below are those included in the meta-analysis reported in the cell above:								
Colorectal		Hallisey (1990)	Dyspepsia	All patients	0.5 (0.3-0.9)	both	40	No upper limit
Colorectal		Heikkinen (1995)	Dyspepsia	All patients	0 (0-1.2)	both	77% were > 44 years.	
Colorectal		Meinche-Schmidt (2002)	Dyspepsia	All patients	1.14 (0.7-1.9)	both	18	65+

Evidence statement(s):

Dyspepsia (11 studies, N = 18464) presenting in a primary care setting is associated with an overall positive predictive value of 2.02% for cancer. The study was associated with 1-3 bias/applicability concerns (see also Table 1).

Evidence tables

Brignoli (1997)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from Switzerland.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	N = 828; 329 men, 499 women; mean (SD) age = 41-42 (15-16) years. <u>Inclusion criteria</u> : "Adult patients with epigastric complaints were admitted to the multicentre [omega]-project if their symptoms persisted for over 1 month and their clinical history and appearance did not suggest an organic disorder (i.e. absence of alarm features, such as gastrointestinal blood loss, palpable tumour mass, massive weight loss, etc.). The studies were conducted by general practitioners acting as primary care physicians." <u>Exclusion criteria</u> : None listed <u>Clinical setting</u> : Primary care, Switzerland
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Epigastric complaints (dyspepsia)
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy and 84-day follow up.
Is the reference standard likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	3 patients had gastric cancer, 0 patients had oesophageal cancer, and 2 patients had cancer outside the digestive tract.

Duggan (2008)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from 43 GP practices in the UK.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>N = 762; 411 men, 351 women; mean (range) age = 42 (18-73) years.</p> <p><u>Inclusion criteria:</u> Patients aged 18-70 with dyspepsia thought by the GP to arise from the upper GI tract and of sufficient severity to justify empirical treatment with an H₂ antagonist or PPI.</p> <p><u>Exclusion criteria:</u> Patients thought to be unfit for investigation, with alarm symptoms suggestive of malignancy (dysphagia, weight loss > 5 g, anaemia, haematemesis, melaena or jaundice), previous radiological or endoscopic diagnosis of peptic ulcer disease or reflux oesophagitis, investigation for dyspepsia in the previous 5 years with either procedure or symptom onset within 6 months of commencement of NSAID therapy, previous H. pylori eradication therapy or more than 3 prescriptions for acid suppression therapy in the previous 6 months.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy and 1-2-year follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined	Low concern

by the reference standard does not match the question?		
FLOW AND TIMING		
A. risk of bias		
Flow and timing	At 12-month follow up GP data were available for 753/762.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk
NOTES	2 patients had gastric cancer, 2 patients had oesophageal cancer (the authors report that these patients should not have been included as they had a history of dysphagia).	
Edenholm (1985)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series from the District General Clinic in Huskvarna, Sweden.	
Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?		Unclear risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 187; 96 men, 91 women; mean/median (range) age = 44 (17-80) years.</p> <p><u>Inclusion criteria:</u> Patients who between November 1982 and June 1984 called on the clinic because of abdominal pain and who were diagnosed by the general practitioner as having ulcer-like dyspepsia. The criterion used was persistent epigastric pain. Most patients also had additional symptoms such as acid regurgitation, nausea, belching or vomiting.</p> <p><u>Exclusion criteria:</u> None listed</p> <p><u>Clinical setting:</u> GPs in Sweden</p>	
Are there concerns that the included patients and setting do not match the review question?		Unclear concern
INDEX TEST		
A. Risk of bias		
Index test	Ulcer-like dyspepsia. The criterion used was persistent epigastric pain.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference	UGI endoscopy	

standard(s)	
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	20/187 patients declined endoscopy and it was unsuccessful in a further 2 patients. Thus the PPV is likely to be an over-estimate, calculated as 2/165.
Was there an appropriate interval between index test and reference standard?	Yes probably
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	There were a total of 3 cancers confirmed in the 165 patients who received UGI endoscopy: 1 oesophageal cancer, 1 stomach cancer, and 1 cancer of the duodenum, the latter of which was included with the stomach cancer
Hallissey (1990)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Propective consecutive patient series from a group of 10 general practices in England.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2585 aged > 40 years. No other information reported. The patient group was equally divided between new patients with dyspepsia, old patients with uninvestigated dyspepsia, and old patients with investigated dyspepsia. <u>Inclusion criteria:</u> All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, England.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia of any degree

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 4 weeks and follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	2659 patients were seen and 2585 attended for investigation
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 115 patients: Gastric adenocarcinoma (57), gastric lymphoma (1; added to the gastric adenocarcinoma data in the PPV), oesophageal cancer (15), colorectal (14), pancreatic (6), bronchial (8), prostatic (2), duodenal (1, also added to the gastric carcinoma data in the PPV), liver (1), gall bladder (1), carcinoid (1), uterine (1), leukaemia (1), carcinomatosis of unknown primary (7).

Hansen (1998)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series from general an open-access endoscopy clinic in Denmark.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient	N = 612 from 66 GPs; 288 males / 324 females; mean age (SD) = 47 (16.8)

characteristics and setting	<p>years.</p> <p><u>Inclusion criteria:</u> "All general practitioners (n = 108) in the city of Odense (population, 170,000) were invited to participate in the study. GPs were asked to refer all patients who consulted them with dyspepsia, regardless of the severity of the symptoms. To obtain compliance with this request the participating GPs were sent numerous reminders. Because of a limited endoscopy capacity not all GPs took part in the study at the same time." Study period was 11 March 1991-27 March 1992.</p> <p><u>Exclusion criteria:</u> Aged < 18 years, signs of UGI bleeding, abdominal emergency, jaundice, previous surgery in the UGI tract except for closure of an ulcer, supposed acute bacterial or viral infection, pregnancy, or endoscopy contraindicated.</p> <p><u>Clinical setting:</u> GPs in Denmark</p>
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Epigastric or retrosternal pain or discomfort, with or without heartburn, nausea, vomiting, and any other symptom considered to be referable to the proximal alimentary tract.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy within 1 week of referral and follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	56 eligible patients declined participation. These patients were older than the study group (mean age = 52 years versus 47 years) and they were characterised by a shorter dyspepsia history (median duration = 1 month, range = 4 days to 35 years versus 2 months, range = 4 days to 14 years). Fewer of the non-participating patients had had a previous endoscopy or UGI

	radiography (22% versus 43%, but identical proportions of the patients had an ulcer history (11% versus 14%).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	There were a total of 4 cancers histologically confirmed in the study. No subclassification of the cancers reported. Follow up of the 364 patients with normal endoscopy revealed missing data in 5% of the cases and 1 lymphoma and 1 rectal carcinoma. These 6 cancers (NOS) are included in the overall PPV for dyspepsia.

Heikkinen (1995)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Consecutive patient series from 11 GPs (from 3 rural health centres) and from the catchment area of 6 physicians in the health centre of an urban area (population [individuals > 14 years old] of study area = 24600) in Finland.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 400; 152 males, 248 females; 77% were > 44 years. <u>Inclusion criteria:</u> Consecutive patients who consulted their GP from January 11th 1993 to January 12 th 1994 for dyspepsia (defined as upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptoms considered to be referable to the proximal alimentary tract). <u>Exclusion criteria:</u> Patients with symptoms of an acute condition within the abdomen or who had had an upper intestinal endoscopy performed within the last 3 months or aged < 15 years <u>Clinical setting:</u> Primary care, Finland.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia (defined as upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptoms considered to be referable to the proximal alimentary tract).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or	Low concern

interpretation differ from the review question?		
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Upper gastrointestinal endoscopy, upper abdominal ultrasound, more detailed interview, blood count, serum screening (creatinine, alkaline phosphatase, alanine aminotransferase, amylase, and C-reactive protein), lactose intolerance test, and follow up of ≥ 1 month.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appear to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	In total N = 9 had cancer: 0 colorectal, 2 oesophageal and 7 stomach (of which 3 were lymphomas of the MALT type (Mucosa-associated lymphoid tissue)).	
Jaskiewicz (1991)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Patient series from a program aimed at screening patients with chronic gastric complaints for gastric carcinoma in the South and North-Western Cape Province of South Africa.	
Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
Could the selection of patients have introduced bias?	Unclear risk	
B. Concerns regarding applicability		
Patient characteristics and setting	N = 585, 355 males, 230 females; mean (range) age males = 45.1 (19-87) years, mean (range) age females = 47.2 (19-87) years. <u>Inclusion criteria:</u> "participants who were treated for dyspeptic complaints such as epigastric pain, heartburn, post-prandial pain and bloating, vomiting or nausea with a duration of at least 3 months. Patients represented various areas in the south-and north-western Cape province including Namaqualand, and formed part of a programme aimed at screening patients with chronic	

	gastric complaints for gastric carcinoma.” Exclusion criteria: None listed Clinical setting: Unclear, South Africa.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Unspecified dyspepsia (dyspeptic complaints such as epigastric pain, heartburn, post-prandial pain and bloating, vomiting or nausea with a duration of at least 3 months).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Endoscopy
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 16 had gastric cancer. No oesophageal cancers reported
Kagevi (1989)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Propective consecutive patient series from a primary care centre in Sweden.
Was a consecutive or random sample of patients enrolled?	Yes

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 172; 88 men, 84 women; mean (SD) age = 43 (16) years. <u>Inclusion criteria</u> : "All patients visiting the medical center with complaints referable to the digestive tract were considered for inclusion. Even when the patient consulted the primary care center because of another complaint and coincidentally mentioned gastrointestinal problem, the patient was considered for inclusion. The patient's gastrointestinal problem could have been reported in connection with an earlier visit at the primary care center." <u>Exclusion criteria</u> : Patients with jaundice, gastrointestinal bleeding or acute abdominal pain were excluded and so were patients judged to have a non-gastro-enterologic cause of their symptoms (gynaecologic problems, spondylosis deformans, etc), patients aged < 16 years and patients unwilling to participate. <u>Clinical setting</u> : Primary care Center, Sweden.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia defined as any pain, discomfort, or other symptoms referable to the digestive tract \geq 2 weeks. Symptoms could be intermittent or continuous.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Esophagogastroduodenoscopy within 1 week and 6 month follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	13/185 patients were excluded as they did not want to have an endoscopy

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	2 patients had gastric cancer, 0 patients had oesophageal cancer.
Meineche-Schmidt (2002)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Consecutive patient series from 82 GPs in Denmark.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1491; 688 males, 803 females; age groups: 18-37 years: N = 377; 38-50 years: N = 369; 51-64 years: N = 338; 65- years: N = 402. <u>Inclusion criteria:</u> Consecutive patients who consulted their GP between June 1991 and May 1993 for dyspepsia (defined as pain or discomfort in the abdomen judged by the GP to be related to the gastrointestinal tract). <u>Exclusion criteria:</u> None listed. <u>Clinical setting:</u> Primary care, Denmark.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia (defined as pain or discomfort in the abdomen judged by the GP to be related to the gastrointestinal tract).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	18 months-3 years and 10 months follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients appear to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	In total N = 31 had cancer: 17 colorectal, 8 gastro-oesophageal (no subgroup analyses presented for these patients) and 6 other.

Thomson (2003)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Propective patient series from a group of 49 family physician practices in Canada.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 1040, 520 males / 520 females; mean (range) age =45.6 (18-84) years. <u>Inclusion criteria:</u> Patients ≥ 18 years with a primary complaint of ≥ 3 months intermittent or continuous dyspepsia. Patients could not have used proton pump inhibitors within 30 days or prokinetics or prescription H ₂ -receptor antagonists (H ₂ RAS) within 14 days of enrolment. <u>Exclusion criteria:</u> Heartburn or acid regurgitation as their sole symptom; documented history of upper GI pathology/surgery; clinical investigation of dyspepsia by endoscopy or radiology in the previous 6 months or more than twice in the past 10 years; H. pylori eradication treatment in the previous 6 months; irritable bowel syndrome as assessed by the presence of ≥ manning criteria; or severe concurrent disease. <u>Clinical setting:</u> Family physician practice, Canada.
Are there concerns that the included patients and setting do not match the review question?	Unclear concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia defined as symptom complex of epigastric pain/discomfort in association with other upper GI symptoms, including heartburn and acid regurgitation.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes

Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Upper gastrointestinal endoscopy within 10 days and 6-months follow up.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients are accounted for. 1100/1171 enrolled patients consented to endoscopy, but 60/1100 did not received endoscopy (eligibility criteria not fulfilled [27], lost to follow up [3], withdrew consent [9], non-compliant with the protocol [1], endoscopy-intolerable [2], other [18]).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Malignancy was detected in 2 patients: Gastric (MALToma; 1), oesophageal cancer (1).

Vakil (2009)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes (probably)
Could the selection of patients have introduced bias?	Unclear risk
B. Concerns regarding applicability	
Patient characteristics and setting	N = 2741, mean (range) age = not reported (not reported) years, numbers of females/males: Not reported. <u>Inclusion criteria:</u> Patients aged 18-70 years who met Rome II criteria for dyspepsia (intermittent or continuous pain or burning centered in the upper

	<p>abdomen for ≥ 3 months).</p> <p><u>Exclusion criteria:</u> Past diagnosis of gastro-oesophageal reflux disease, predominant symptom of heartburn or regurgitation, history of heartburn or regurgitation > 2 days/week, treatment > 2 days/week with non-steroidal anti-inflammatory drugs or cyclooxygenase-2 selective inhibitors or aspirin (except for cardiovascular prophylaxis at doses ≤ 325 mg/day), concurrent alarm features (e.g., dysphagia, recurrent vomiting, unexplained anaemia, gastro-intestinal bleeding), H pylori eradication treatment within 12 months, maintenance therapy with either a proton pump or an H2-receptor antagonist within 6 months.</p> <p><u>Clinical setting:</u> The study was conducted in 190 primary care health centers in 17 countries (Argentina, Belgium, Brazil, Canada, Denmark, France, Germany, Greece, Iceland, Italy, Norway, Romania, Singapore, South Africa, Spain, Sweden, Switzerland). Patients were recruited from primary care clinics where flyers publicising the study were placed and the primary care physicians recruited patients presenting to their offices with dyspepsia [random or consecutive sampling unlikely].</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	Dyspepsia/ intermittent or continuous pain or burning centered in the upper abdomen for ≥ 3 months. Symptoms were evaluated using a scale validated in a number of languages
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	All patients received outpatient endoscopy
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No (but all patients had a positive index test)
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for in the results.
Was there an appropriate interval between index test and	Yes (probably)

reference standard?	
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	Supported by AstraZeneca R&D Sweden. The authors state that "The sponsor did not play any role in the calculations or in the writing of the manuscript". Six patients had cancer: 3 oesophagus and 3 stomach.

References

Included studies

- Brignoli, R., Watkins, P., Halter, F. The Omega-Project – a comparison of two diagnostic strategies for risk- and cost-oriented management of dyspepsia. *European Journal of Gastroenterology and Hepatology* 9, 337-343. 1997.
- Duggan, A.F., Elliott, C.A., Miller, P., Hawkey, C.J., Logan, R.F.A. Clinical trial: A randomized trial or early endoscopy, *Helicobacter pylori* testing and empirical therapy for the management of dyspepsia in primary care. *Alimentary Pharmacology and Therapeutics* 29, 55-68. 2008.
- Edenholm, M., Gustavsson, R., Jansson, O., et al. Endoscopic findings in patients with ulcer-like dyspepsia. *Scandinavian Journal of Gastroenterology* 20(suppl 109), 163-167. 1985.
- Hallissey, M.T., Allum, W.H., Jewkes, A.J., Ellis, A.J., Fielding, J.W.L. Early detection of gastric cancer. *British Medical Journal* 301, 513-515. 1990.
- Hansen, J.M., Bytzer, P., Schaffalitzky de Muckadell, O.B. Management of dyspeptic patients in primary care: Value of the unaided clinical diagnosis and of dyspepsia subgrouping. *Scandinavian Journal of Gastroenterology* 33, 799-805. 1998.
- Heikkinen, M., Pikkarainen, P., Takala, J., and Rasanen, H. Julkunen R. Etiology of dyspepsia: Four hundred unselected consecutive patients in general practice. *Scandinavian Journal of Gastroenterology* 30[6], 519-523. 1995.
- Jaskiewicz, K., Louwrens, H.D. Chronic atrophic gastritis in a population at risk for gastric carcinoma. *Anmticancer Research* 11, 835-840. 1991.
- Kagevi, I., Löfstedt, S., Persson, L.-G. Endoscopic findings and diagnoses in unselected dyspeptic patients at a primary health care center. *Scandinavian Journal of Gastroenterology* 24, 145-150. 1989.
- Meineche-Schmidt, V. and Jorgensen, T. 'Alarm symptoms' in patients with dyspepsia: a three-year prospective study from general practice. *Scandinavian Journal of Gastroenterology* 37[9], 999-1007. 2002.
- Thomson, A.B.R., Barkun, A.N., Armstrong, D., Chiba, N., White, R.J., Daniels, S., Escobedos, S., Chakraborty, B., Sinclair, S. The prevalence of clinically significant endoscopic findings in primary care patients with uninvestigated dyspepsia: The Canadian Adult Dyspepsia Empiric Treatment-Prompt Endoscopy (CADET-PE) study. *Alimentary Pharmacology and Therapeutics* 17, 1481-1491. 2003.
- Vakil, N., Talley, N., van Zanten, S. V., Flook, N., Persson, T., Bjorck, E., Lind, T., and Bolling-Sternevald, E. Cost of Detecting Malignant Lesions by Endoscopy in 2741 Primary Care Dyspeptic Patients Without Alarm Symptoms. *Clinical Gastroenterology and Hepatology* 7[7], 756-761. 2009.

WEIGHT LOSS

Risk of bias in the included studies

The risk of bias and applicability concerns are summarised per study in the figure below. The body of evidence was generally of high quality. The main validity issues to note is that patient sampling was not clearly consecutive or random in a number of the studies, and that some of studies suffered from missing data. Studies employing non-consecutive/random sampling are at risk of bias because, for example, case-control studies have been shown to be associated with inflated test accuracy parameters compared to designs that incorporate random or consecutive patient selection. The statistical analyses employed by these studies are however likely to have gone some way in addressing this issue. One study was conducted in a setting that is unlikely to be directly applicable to UK-based primary care and, as a consequence, also seems to present inflated PPVs that may be more reflective of secondary care. Finally, some of the studies were compromised by missing data, the influence of which on the results is difficult to determine.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Collins (2012)	+	+	+	+	+	+	+
Collins (2012a)	+	+	+	+	+	+	+
Collins (2013)	+	+	+	+	+	+	+
Collins (2013a)	+	+	+	+	+	+	+
Hamilton (2005)	-	+	+	+	+	+	+
Hamilton (2005a)	-	+	+	+	+	+	+
Hamilton (2006)	-	+	+	+	+	+	+
Hippisley-Cox (2011)	+	+	+	?	+	+	+
Hippisley-Cox (2012)	+	+	+	+	+	+	+
Hippisley-Cox (2012a)	+	+	+	-	+	+	+
Hippisley-Cox (2012b)	+	+	+	-	+	+	+
Iyen-Omofoman (2013)	+	+	+	+	+	+	+
Panzuto (2003)	-	+	+	?	?	+	+
Stapley (2012)	-	+	+	+	+	+	+

- High
 ? Unclear
 + Low

Table 1: Non-site specific symptoms of concern: Calculation of overall positive predictive value of weight loss for cancer

Cancer site	Study	Lower age limit	Upper age limit	PPV (95% CI), prevalence
Bladder/renal	Hippisley-Cox (2012)	30	84	0.41 (0.3-0.6)
Colorectal	Meta-analysis	18	87	3 (0.32-22.89)
Lung	Hamilton (2005)	40	No upper limit	1.1 (0.8-1.6)
Oesophagus/stomach	Hippisley-Cox (2011)	30	84	1.2 (1-1.4)
Pancreatic	Hippisley-Cox (2012)	30	84	0.6 (0.5-0.8)
Prostate	Hamilton (2006)	40	No upper limit	0.75 (0.38-1.4)
Sum				7.06

Table 2: Non-site specific symptoms of concern: Positive predictive values for weight loss

Cancer site	Comment/relevant recs	Study	Symptom	Patient group	Positive predictive value% (95% CI)	Sex	Age inclusion, lower limit	Age inclusion, upper limit
Bladder/renal		Collins (2013a)	Weight loss	Women	0.1 (0.1-0.2)	Women	30	84
Bladder/renal		Hippisley-Cox (2012b)	Weight loss	All patients	0.41 (0.3-0.6)	both	30	84
Lung		Hamilton (2005a)	Weight loss	All patients	1.1 (0.8-1.6)	both	40	no upper limit
Lung		Hamilton (2005a)	Weight loss (reported twice)	All patients	1.2 (0.7-2.3)	both	40	no upper limit
Lung		Hamilton (2005a)	Weight loss	All smokers	2.1 (NR)	both	40	no upper limit
Lung		Hamilton (2005a)	Weight loss (reported twice)	All smokers	1.7 (NR)	both	40	no upper limit
Lung		Iyen-Omofoman (2013)	Weight loss	Validation cohort	0.34 (0.23-0.5)	both	40	no upper limit
Oesophagus/stomach		Collins (2012a)	Weight loss	All patients	0.8 (0.7-0.9)	both	30	84

Oesophagus/stomach		Collins (2012a)	Weight loss	Women	0.6 (0.4-0.7)	Women	30	84
Oesophagus/stomach		Collins (2012a)	Weight loss	Men	1 (0.9-1.2)	Men	30	84
Oesophagus/stomach		Hippisley-Cox (2011)	Weight loss	All patients	1.2 (1-1.4)	both	30	84
Pancreatic		Collins (2013)	Weight loss	All patients	0.28 (0.22-0.35)	both	30	84
Pancreatic		Collins (2013)	Weight loss	Women	0.16 (0.11-0.24)	women	30	84
Pancreatic		Collins (2013)	Weight loss	Men	0.42 (0.32-0.54)	men	30	84
Pancreatic		Hippisley-Cox (2012a)	Weight loss	All patients	0.6 (0.5-0.8)	both	30	84
Pancreatic		Stapley (2012)	Weight loss	All patients	0.44 (0.36-0.55)	both	40	no upper limit
Pancreatic		Stapley (2012)	Weight loss	Patients ≥ 60 years	0.8 (0.7-1)	both	60	no upper limit
Prostate		Hamilton (2006)	Loss of weight	All patients	0.75 (0.38-1.4)	men	40	no upper limit
Prostate		Hamilton (2006)	Loss of weight (reported twice)	All patients	2.1 (NR)	men	40	no upper limit
Colorectal		Hamilton (2005)	Loss of weight (reported once)	All patients	1.2 (0.9-1.6)	both	40	no upper limit
Colorectal		Hamilton (2005)	Loss of weight (reported twice)	All patients	1.4 (0.8-2.6)	both	40	no upper limit
Colorectal		Hamilton (2005)	Loss of weight	Patients 40-69 years	0.74 (NR)	both	40	69
Colore		Hamilt	Loss of	Patien	2.5 (NR)	both	70	no upper limit

ctal		on (2005)	weight	ts ≥ 70 years				
Colorectal		Hamilton (2005)	Weight loss 5-10% (read off graph)	Men aged < 60 years	0.1 (0.05-0.2)	Males	40	59
Colorectal		Hamilton (2005)	Weight loss 5-10% (read off graph)	Men aged 60-69 years	0.3 (0.2-0.4)	Males	60	69
Colorectal		Hamilton (2005)	Weight loss 5-10% (read off graph)	Men aged 70-79 years	0.7 (0.5-0.8)	Males	70	79
Colorectal		Hamilton (2005)	Weight loss 5-10% (read off graph)	Men aged ≥ 80 years	0.5 (0.3-0.8)	Males	80	no upper limit
Colorectal		Hamilton (2005)	Weight loss ≥ 10% (read off graph)	Men < 60 years	0.2 (0.1-0.3)	Males	40	59
Colorectal		Hamilton (2005)	Weight loss ≥ 10% (read off graph)	Men 60-69 years	0.7 (0.4-0.9)	Males	60	69
Colorectal		Hamilton (2005)	Weight loss ≥ 10% (read off graph)	Men 70-79 years	1.5 (1.2-1.8)	Males	70	79
Colorectal		Hamilton (2005)	Weight loss ≥ 10% (read off graph)	Men ≥ 80 years	0.8 (0.6-1.4)	Males	80	no upper limit
Colorectal		Hamilton (2005)	Weight loss 5-10% (read off graph)	Women < 60 years	0.05 (0.05-0.05)	Females	40	59
Colorectal		Hamilton (2005)	Weight loss 5-10% (read off graph)	Women 60-69 years	0.2 (0.1-0.3)	Females	60	69

			graph)					
Colorectal		Hamilton (2005)	Weight loss 5-10% (read off graph)	Women 70-79 years	0.4 (0.3-0.6)	Females	70	79
Colorectal		Hamilton (2005)	Weight loss 5-10% (read off graph)	Women ≥ 80 years	0.4 (0.3-0.6)	Females	80	no upper limit
Colorectal		Hamilton (2005)	Weight loss ≥ 10% (read off graph)	Women < 60 years	0.06 (0.06-0.08)	Females	40	59
Colorectal		Hamilton (2005)	Weight loss ≥ 10% (read off graph)	Women 60-69 years	0.5 (0.3-0.7)	Females	60	69
Colorectal		Hamilton (2005)	Weight loss ≥ 10% (read off graph)	Women 70-79 years	0.8 (0.6-1.1)	Females	70	79
Colorectal		Hamilton (2005)	Weight loss ≥ 10% (read off graph)	Women ≥ 80 years	0.8 (0.6-1.1)	Females	80	no upper limit
META-ANALYSES (1) Colorectal								
Colorectal		Meta-analyses	Weight loss	All patients	3 (0.32-22.89)	both	2 studies 30-84, 1 study 18-87 Individual study details below	
The 3 studies below are those included in the meta-analysis reported in the cell above:								
Colorectal		Collins (2012)	Weight loss	All patients	0.8 (0.7-0.9)	both	30	84
Colorectal		Hippisley-Cox (2012)	Weight loss	All patients	0.8 (0.7-0.9)	both	30	84
Colorectal		Panzuto (2003)	Weight loss	All patients	35.7 (22-52)	both	18	87
The following results are any extra analyses reported by the studies included in the above meta-analysis:								
Colorectal		Collins (2012)	Weight loss	Males	1 (0.8-1.1)	Males	30	84
Colorectal		Collins (2012)	Weight loss	Females	0.6 (0.5-0.7)	Females	30	84

Evidence statement(s):

Weight loss (8 studies, N = 3768550) presenting in a primary care setting is associated with an overall positive predictive value of 7.06% for cancer. The studies were associated with 0-3 bias/applicability concerns (see also Table 1).

Evidence tables**Collins (2012)**

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2135540 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Rectal bleeding (N = 56234; 28423 men, 27811 women), abdominal pain (N = 245989; 102192 men, 143797 women), appetite loss (N = 5776; 2481 men, 3295 women), weight loss (N = 28289; 12891 men, 15398 women), anaemia (N = 18125; 4466 men, 13659 women), change in bowel habit (men only, N = 1670).</p> <p><u>Incident cases of colorectal cancer during the 2-year follow up period:</u> N = 3712 (2036 men, 1676 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of colorectal cancer at baseline, and patients with a recorded 'red-flag' symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Rectal bleeding, loss of appetite, weight loss, abdominal pain, change in bowel habit (men only), and anaemia.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or	Low concern

interpretation differ from the review question?		
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	2-year follow up	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients seem to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES	The is very large, if not complete, overlap of the data used in this study with those used in Hamilton (2008 [for anaemia], 2009)	

Collins (2012a)

PATIENT SELECTION		
A. risk of bias		
Patient sampling	Retrospective patient series using the THIN database.	
Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of patients have introduced bias?	Low risk	
B. Concerns regarding applicability		
Patient characteristics and setting	<p>A total of 2135540 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Dysphagia (N = 19237; 8846 men, 10391 women), abdominal pain (N = 246998; 102732 men, 144266 women), appetite loss (N = 5838; 2521 men, 3317 women), weight loss (N = 28403; 12938 men, 15465 women), haematemesis (N = 10792; 6162 men, 4630 women), anaemia (N = 18355; 4563 men, 13792 women).</p> <p><u>Incident cases of gastro-oesophageal cancer during the 2-year follow up period:</u> N = 1766 (1184 men, 582 women; 32% gastric cancer, 68% oesophageal cancer).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January</p>	

	2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <u>Exclusion criteria:</u> Patients with a prior diagnosis of gastro-oesophageal cancer, registration with the general practice < 12 months, or with invalid dates. <u>Clinical setting:</u> Primary care, UK
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Haematemesis, dysphagia, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	The study did not distinguish between gastric and oesophageal cancer
Collins (2013)	
PATIENT SELECTION	
A. risk of bias	

Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2150322 patients were identified from 364 practices.</p> <p><u>Symptoms:</u> Dysphagia (men only: N = 9326), abdominal pain (N = 255058; 106768 men, 148290 women), appetite loss (N = 6102; 2658 men, 3444 women), weight loss (N = 29464; 13484 men, 15980 women), abdominal distension (women only: N = 4457), constipation (men only, N = 5326).</p> <p><u>Incident cases of pancreatic cancer during the 2-year follow up period:</u> N = 287 (331 men, 287 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of pancreatic cancer, registration < 12 months with the general practice, or invalid dates.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Dysphagia (men only), loss of appetite, weight loss, abdominal pain, abdominal distension (women only), and constipation (men only).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	

Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All patients seem to be accounted for
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Collins (2013a)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Retrospective patient series using the THIN database.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 2145133 patients (1063355 men, 1081778 women) were identified from 364 practices.</p> <p><u>Symptoms:</u> Haemoglobin < 11 g/dl recorded in the last year (N = 16961; 3969 men, 12992 women), abdominal pain (N = 253344; 105247 men, 148097 women), appetite loss (N = 6097; 2616 men, 3481 women), weight loss (N = 29369; 13332 men, 16037 women), haematuria (N = 37810; 22810 men, 15000 women), previous diagnosis of cancer apart from renal tract cancer at study entry (N = 49303; 18130 men, 31173 women).</p> <p><u>Incident cases of renal tract cancer during the 2-year follow up period:</u> N = 2283 (1685 men, 598 women).</p> <p><u>Inclusion criteria:</u> Patients aged 30–84 years and registered with practices between 1 January 2000 and 30 June 2008. Entry to the cohort was defined as the latest of the study start date; the date the patient registered with the practice; and for those patients with red flag symptoms (e.g., haematuria, abdominal pain, weight loss, appetite loss, and anaemia), the date of the first recorded onset within the study period.</p> <p><u>Exclusion criteria:</u> Patients with a prior diagnosis of renal tract cancer, registered less than 12 months with the general practice, had invalid dates, < 30 years old or ≥ 85 years old.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient

	and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Renal tract cancer, which was defined as incident diagnosis of cancer of the bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes. Patients without the outcome were censored at the earliest of the date of death, date of leaving the practice study of 2 years of follow up.	
Is the reference standard likely to correctly classify the target condition?		Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?		Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients seem to be accounted for	
Was there an appropriate interval between index test and reference standard?		Yes
Did all patients receive the same reference standard?		Yes
Were all patients included in the analysis?		Yes
Could the patient flow have introduced bias?		Low risk
NOTES	It is unclear why no data has been presented for men for the symptoms of appetite loss and weight loss.	
Hamilton (2005)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Population-based matched case-control study involving all 21 general practices in Exeter, Devon, UK.	
Was a consecutive or random sample of patients enrolled?		No
Was a case-control design avoided?		No
Did the study avoid inappropriate exclusions?		Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?		Yes

<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?		Yes
Could the selection of patients have introduced bias?		High risk
<u>B. Concerns regarding applicability</u>		
Patient characteristics and setting	<p><u>Cases:</u> N = 349 (177 males/172 females), age at diagnosis: < 60 years: N = 45, 60-69 years: N = 97, 70-79 years: N = 113, 80+ years: N = 94. 210/349 had tumours at or distal to the splenic flexure, and 126/349 had tumours proximal to the splenic flexure, the remaining 13/349 has tumours in multiple or unknown sites. Duke's staging was known for 305/349: 170/305 were Duke's A or B, and 135/305 were Duke's C or D.</p> <p><u>Controls:</u> N = 1744 (885 males/859 females), age at diagnosis: < 60 years: N = 225, 60-69 years: N = 487, 70-79 years: N = 555, 80+ years: N = 477.</p> <p><u>Inclusion criteria:</u> Cases: All patients aged ≥ 40 years with a primary colorectal cancer, diagnosed from 1998 to 2002, were identified from the cancer registry at the Royal Devon and Exeter Hospital combined with computerised searches at every practice in Devon to identify any cases missing from the cancer register.</p> <p>Controls: Five controls were matched to each case on sex, general practice, and age (to 1-year bands if possible, increased in 1-year multiples to a maximum of 5 years). Controls were eligible if they were alive at the time of diagnosis of their case.</p> <p><u>Exclusion criteria:</u> Cases and controls: Unobtainable records; no consultations in the 2 years before diagnosis; previous colorectal cancer; or residence outside Exeter at the time of diagnosis.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
<u>A. Risk of bias</u>		
Index test	Anonymised photocopies of the full primary care records for 2 years before diagnosis were coded (blinded to case/control status) for all entries using the International Classification of Primary Care-2. Additional codes were created to incorporate all possible clinical features. Only variables occurring in ≥ 2.5% of cases or controls were analysed.	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
<u>B. Concerns regarding applicability</u>		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern

REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Colorectal cancer diagnosis in the cancer registry at the Royal Devon and Exeter Hospital or practice notes.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	All the patients are accounted for.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Hamilton (2005a)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based matched case-control study involving all 21 general practices in Exeter, Devon, UK.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> N = 247 (170 males/77 females), age at diagnosis: < 60 years: N = 35, 60-69 years: N = 60, 70-79 years: N = 118, 80+ years: N = 34.</p> <p><u>Controls:</u> N = 1235 (850 males/385 females), age at diagnosis: < 60 years: N = 178, 60-69 years: N = 310, 70-79 years: N = 575, 80+ years: N = 174.</p> <p><u>Inclusion criteria:</u></p>

	<p>Cases: All patients aged ≥ 40 years with a primary lung cancer, diagnosed from 1998 to 2002, were identified from the cancer registry at the Royal Devon and Exeter Hospital combined with computerised searches at every practice in Devon to identify any cases missing from the cancer register.</p> <p>Controls: Five controls were matched to each case on sex, general practice, and age. Controls were eligible if they were alive at the time of diagnosis of their case.</p> <p><u>Exclusion criteria:</u> Cases and controls: Unobtainable records; no consultations in the 2 years before diagnosis; previous lung cancer; or residence outside Exeter at the time of diagnosis.</p> <p><u>Clinical setting:</u> Primary care, UK.</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
<u>A. Risk of bias</u>	
Index test	Anonymised photocopies of the full primary care records for 2 years before diagnosis were coded (blinded to case/control status) for all entries using the International Classification of Primary Care-2. Additional codes were created to incorporate all possible clinical features. Only variables occurring in $\geq 2.5\%$ of cases or controls were analysed.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
<u>A. risk of bias</u>	
Reference standard(s)	Lung cancer diagnosis in the cancer registry at the Royal Devon and Exeter Hospital or practice notes.
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
<u>B. Concerns regarding applicability</u>	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
<u>A. risk of bias</u>	
Flow and timing	All the patients are accounted for.
Was there an appropriate interval between index test and	Yes

reference standard?	
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	
Hamilton (2006)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Population-based case-control study, involving all 21 general practices in Exeter, Devon, UK.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> 217 male patients; age at diagnosis: < 60 years: N = 15 (7%); 60-69 years: N = 51 (24%); 70-79 years: N = 100 (46%); ≥ 80 years: N = 51 (24%); median number of consultations in the 2 years preceding diagnosis = 14 (IQR = 10-21).</p> <p><u>Controls:</u> 1080 male patients; age at diagnosis: < 60 years: N = 79 (7%); 60-69 years: N = 253 (23%); 70-79 years: N = 494 (46%); ≥ 80 years: N = 254 (24%); median number of consultations in the 2 years preceding diagnosis = 14 (IQR = 10-21).</p> <p><u>Inclusion criteria:</u> Cases: All patients aged 40 years or over with prostate cancer, diagnosed from 1998 to 2002 inclusive, were identified from the cancer registry at the Royal Devon and Exeter Hospital (the only hospital offering urological services to Exeter patients). Computerised searches at every practice identified any cases missing from the register. Cases without positive histology were included if the records contained a consultant urologist diagnosis of cancer based on strong clinical evidence. Controls: Five male controls were matched to each case on general practice and on age (to 1-year bands if possible, increased in 1-year multiples to a maximum of 5 years). Controls were eligible if they were alive at the time of diagnosis of their case.</p> <p><u>Exclusion criteria:</u> Unobtainable records; no consultations in the 2 years before diagnosis; previous prostate cancer; or residence outside Exeter at the time of diagnosis.</p>

	Clinical setting: Primary care, UK	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	All entries into the primary care records for 2 years before diagnosis were coded, blinded to case/control status, using the International Classification of Primary Care-2. Only variables occurring in >2.5% of cases or controls were analysed.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Prostate cancer code, from 1998 to 2002 inclusive, in the cancer registry at the Royal Devon and Exeter Hospital or the general practice records	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All patients appears to be accounted for	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES		
Hippisley-Cox (2011)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).	

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1238971 patients were identified from 189 practices (621478 males, 617493 females), mean (SD) age = 50.1 (15) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Symptoms:</u> Current dysphagia (N = 8165), current haematemesis (N = 7119), current abdominal pain (N = 126161), current appetite loss (N = 6133), current weight loss (N = 5377), tiredness in the last year (N = 14119), haemoglobin recorded in the last year (N = 12638, haemoglobin < 11 g/dl in the last year (N = 218862).</p> <p><u>Incident cases of gastro-oesophageal cancer during the 2-year follow up period:</u> N = 1343 (776 oesophageal and 567 gastric).</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000); 12 months after the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of gastro-oesophageal cancer at baseline, and patients with a recorded 'red-flag' symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms: Incident dysphagia, haematemesis, loss of appetite, weight loss, anaemia, and abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	

A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 103358 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of gastro-oesophageal cancer (N = 538), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 31973), leaving 1238971 patients. However, data is presented for 963040/1238971 patients for all symptoms. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	Results not presented separately for gastric and oesophageal cancer
Hippisley-Cox (2012)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	A total of 1236601 patients were identified from 189 practices (620240 males, 616361 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6). <u>Symptoms:</u> Current rectal bleeding (N = 29118), current abdominal pain (N = 125816), current appetite loss (N = 5358), current weight loss (N = 14065), recent change in bowel habit (N = 1821). <u>Incident cases of colorectal cancer during the 2-year follow up period:</u>

	<p>N = 2603 (1562 colon and 1041 rectum).</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000); 12 months after the patient registered with the practice; and for those patients with red flag symptoms (see below), the date of the first recorded onset within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of colorectal cancer at baseline, and patients with a recorded ‘red-flag’ symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care, UK</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	‘Red-flag’ symptoms: First onset rectal bleeding, first onset loss of appetite, first onset weight loss, first onset abdominal pain, first onset change in bowel habit (in the past 12 months), and anaemia (recorded haemoglobin < 11 g/dl in the past 12 months).
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	2-year follow up
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	

Flow and timing	A total of 1342329 patients were initially identified of whom 105728 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of colorectal cancer (N = 2908), and \geq one 'red flag' symptom recorded in the 12 months prior to study entry (N = 31973), leaving 1236601 patients. However, data is presented for 1235547/1236601 patients for all symptoms apart from change in bowel habit, which is only presented for 619651/620240 of the male patients. The missing data does not appear to include any of the cancer cases (although this cannot be ascertained for change in bowel habit), but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Low risk
NOTES	Please note there is some overlap between this patient sample and that of Parker (2007)

Hippisley-Cox (2012a)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1243740 patients were identified from 189 practices (624352 males, 619388 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Current symptoms and symptoms in the preceding year:</u> Current dysphagia (N = 8507), current abdominal pain (N = 129924), current abdominal distension (N = 4929), current appetite loss (N = 5567), current weight loss (N = 14686), constipation in the last year (N = 8476), diarrhoea in the last year (N = 12233), tiredness in the last year (N = 12688), itching in the last year (N = 1454), haemoglobin recoded in the last year (N = 214497), haemoglobin < 11 g/dl in the last year (N = 16172).</p> <p><u>Incident cases of pancreatic cancer during the 2-year follow up period:</u> N = 781.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for \geq a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1</p>

	<p>January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months' registration prior to study entry. For patients with incident haematuria, appetite loss, weight loss, or abdominal pain, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of pancreatic cancer at baseline, and patients with a recorded 'red-flag' (see "Definition of symptom" below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of pancreatic cancer; that is, symptoms of dysphagia, loss of appetite, weight loss, abdominal distension or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Pancreatic cancer, which was defined as incident diagnosis of pancreatic cancer during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 code (157) or ICD-10 diagnostic codes (C25).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 98589 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of pancreatic cancer (N = 96), and \geq one 'red flag' symptom

	recorded in the 12 months prior to study entry (N = 27646), leaving 1243740 patients. However, data is presented for 971706 / 1243740 patients. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	
Hippisley-Cox (2012b)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Prospective patient series using patients in the QResearch database (version 30).
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p>A total of 1240722 patients were identified from 189 practices (622166 males, 618556 females), mean (SD) age = 50.1 (14.9) years, mean (SD) Townsend score = -0.2 (3.6).</p> <p><u>Current symptoms and symptoms in the preceding year:</u> Current haematuria (N = 25553), current abdominal pain (N = 128721), current appetite loss (N = 5531), current weight loss (N = 14464), constipation in the last year (N = 8472), diarrhoea in the last year (N = 12171), tiredness in the last year (N = 12669), haemoglobin recoded in the last year (N = 216201), haemoglobin < 11 g/dl in the last year (N = 16169).</p> <p><u>Incident cases of renal tract cancer during the 2-year follow up period:</u> N = 1622; mean age at diagnosis = 70 years, 1187 males/ 435 females; Type of cancer: Bladder: N = 1292; Kidney: N = 307; Ureter: N = 21; Urethra: N = 2.</p> <p><u>Inclusion criteria:</u> All practices in England and Wales that had been using their Egton Medical Information Systems (EMIS) computer system for ≥ a year were included. Two-thirds of practices were randomly allocated to the derivation dataset and the remaining practices were allocated to the validation dataset. An open cohort of patients aged 30–84 years was identified, drawn from patients registered with practices between 1 January 2000 and 30 September 2010. Entry to the cohort was defined as the latest of the study start date (1 January 2000) and 12 months after the patient registered with the practice, ensuring that all patients had ≥ 12 months' registration prior to study entry. For patients with incident haematuria, appetite loss, weight loss, or abdominal pain, the entry date was the date of the first consultation with the symptom within the study period. <i>The relevant data for the present purposes is only available for the validation cohort, therefore only information</i></p>

	<p><i>pertaining to these patients will be reported.</i></p> <p><u>Exclusion criteria:</u> Patients without a postcode-related Townsend score, patients with a history of renal tract cancer at baseline, and patients with a recorded 'red-flag' (see "Definition of symptom" below) symptom in the 12 months prior to the study entry date.</p> <p><u>Clinical setting:</u> Primary care</p>
Are there concerns that the included patients and setting do not match the review question?	Low concern
INDEX TEST	
A. Risk of bias	
Index test	'Red-flag' symptoms were defined as symptoms that might alarm the patient and also indicate the presence of renal tract cancer; that is, symptoms of haematuria, loss of appetite, weight loss, or abdominal pain.
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
REFERENCE STANDARD	
A. risk of bias	
Reference standard(s)	Renal tract cancer, which was defined as incident diagnosis of cancer of the bladder, kidney, ureter, or urethra during the 2 years after study entry, recorded either on the patient's GP record using the relevant UK diagnostic Read Codes, or their linked Office for National Statistics cause-of-death record, using the relevant ICD-9 codes (188 or 189) or ICD-10 diagnostic codes (C64–67).
Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
FLOW AND TIMING	
A. risk of bias	
Flow and timing	A total of 1342329 patients were initially identified of whom 101607 patients were excluded for the following reasons: No recorded Townsend score (N = 70847), history of renal tract cancer (N = 1506), and ≥ one 'red flag' symptom recorded in the 12 months prior to study entry (N = 29254), leaving 1240722 patients. However, data is presented for 967681 / 1240722 patients. The missing data does not appear to include any of the cancer cases, but it is unclear whether some of the missing data includes symptomatic patients, i.e., false positives.
Was there an appropriate interval between index test and	Yes

reference standard?	
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk
NOTES	
Iyen-Omofoman (2013)	
PATIENT SELECTION	
A. risk of bias	
Patient sampling	Case-control study using The Health Improvement Network (THIN) database, which had data from 446 UK general practices with a total of 8.2 million patients.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No (for derivation cohort) Yes (for validation cohort)
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk (for derivation cohort) Low risk (for validation cohort)
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> N = 12074 (7154 males/4920 females), age at diagnosis: 40-45 years: N = 95, 45-50 years: N = 220, 50-55 years: N = 469, 55-60 years: N = 896, 60-65 years: N = 1488, 65-70 years: N = 1750, 70-75 years: N = 2212, 75-80 years: N = 2305, > 80 years: N = 2639.</p> <p><u>Controls:</u> N = 120731 (58034 males/62697 females), age at diagnosis (of cases): 40-45 years: N = 18969, 45-50 years: N = 16756, 50-55 years: N = 15963, 55-60 years: N = 15439, 60-65 years: N = 13475, 65-70 years: N = 11201, 70-75 years: N = 9940, 75-80 years: N = 8191, > 80 years: N = 10797.</p> <p><u>Validation cohort:</u> N = 1826293 (886994 males/939299 females). Age: Not reported. Incident cases of lung cancer during the 1-year follow up: N = 1728.</p> <p><u>Inclusion criteria:</u> Cases: All incident cases of lung cancer diagnosed between 1 January 2000 and 28 July 2009 in patients aged ≥ 40 years. Controls: Ten randomly selected controls aged ≥ 40 years with ≥ 1 year of active records were matched to each case on general practice. Validation cohort: All THIN patients aged > 39 years, free from lung cancer on 29 July 2009, and ≥ 1 year general practice follow up.</p> <p><u>Exclusion criteria:</u> Cases: Patients with < 1 year of active records prior to their first diagnosis of lung cancer.</p>

	Clinical setting: Primary care, UK.	
Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	Cough, chest/shoulder pain, dyspnoea, weight loss, hoarseness, upper and lower respiratory tract infections, non-specific chest infections, constipation, depressive disorders, and chronic obstructive pulmonary disease (COPD), recorded over the 2-year period before lung cancer diagnosis.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Lung cancer diagnosis in THIN database	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	All the patients are accounted for.	
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?	Low risk	
NOTES		
Panzuto (2003)		
PATIENT SELECTION		
A. risk of bias		
Patient sampling	Prospective 8-week study of patients presenting to 159 primary care physicians (approximately 63600 patient visits during the study period)	

	in total) in Italy.	
Was a consecutive or random sample of patients enrolled?		No
Was a case-control design avoided?		Yes
Did the study avoid inappropriate exclusions?		Unclear
Could the selection of patients have introduced bias?		High risk
B. Concerns regarding applicability		
Patient characteristics and setting	<p>N = 280; 120 males, 160 females; median age (range) = 61 (18-87) years.</p> <p><u>Inclusion criteria:</u> Consecutive patients who consulted their GP “with symptoms considered suspicious for the presence of a colon disease to rule out the presence of colorectal cancer” and who were investigated with a colonoscopy or double-contrast barium enema [The decision of how (colonoscopy or double-contrast barium enema) and when to investigate the colon was made only by the physicians on the basis of the clinical evaluation during the visit].</p> <p><u>Exclusion criteria:</u> Patients with previous diagnoses of colorectal disorders or a recent large bowel examination.</p> <p><u>Clinical setting:</u> Primary care, Italy.</p>	
Are there concerns that the included patients and setting do not match the review question?		Unclear concern
INDEX TEST		
A. Risk of bias		
Index test	Abdominal pain, bloating, constipation, rectal bleeding, diarrhoea, iron-deficiency anaemia (haemoglobin levels < 14 g/dl for males and < 12 g/dl for females, in the presence of ferritin < 30 µg/l and a median corpuscular value < 80 fl), change in bowel habits (onset of diarrhoea or constipation or altered stool in the previous 3 months) and weight loss (decrease of ≥ 3 kg in the 3 months prior to the visit).	
Were the index test results interpreted without knowledge of the results of the reference standard?		Yes
Could the conduct or interpretation of the index test have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Histology	
Is the reference standard likely to correctly classify the target condition?		Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?		No
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern

FLOW AND TIMING	
A. risk of bias	
Flow and timing	56/332 patients were excluded due to lack of mandatory fields (age, sex, clinical history, presenting symptoms and procedure results) in the database (N = 35) or violation of exclusion criteria (N = 18)
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk
NOTES	

Stapley (2012)

PATIENT SELECTION	
A. risk of bias	
Patient sampling	Matched case-control study using patients in the UK's General Practice Research Database (GPRD).
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
<i>For diagnostic case-control studies:</i> Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	Yes
<i>For diagnostic case-control studies:</i> The groups were comparable at baseline, including all major confounding and prognostic factors?	Yes
Could the selection of patients have introduced bias?	High risk
B. Concerns regarding applicability	
Patient characteristics and setting	<p><u>Cases:</u> N = 3635, 1743 males / 1892 females; median number of consultations = 18 (IQR = 11-27); aged 40-49 years: N = 107; 50-59 years: N = 529; 60-69 years: N = 829; 70-79 years: N = 1212; ≥ 80 years: N = 958; UK.</p> <p><u>Controls:</u> N = 16459, gender not reported; median number of consultations = 9 (IQR = 4-15); aged 40-49 years: N = 422; 50-59 years: N = 2239; 60-69 years: N = 3755; 70-79 years: N = 5702; ≥ 80 years: N = 4341; UK.</p> <p><u>Inclusion criteria:</u> Cases: Patients with a record of one of 25 GPRD pancreatic cancer codes between January 2000 and December 2009 inclusive, aged ≥ 40 years, with min. 1 year of data before diagnosis. The first instance of a pancreatic cancer code was assigned the data of diagnosis/index date. Controls: Up to 5 controls were matched to cases on sex, general practice, and to 1 year of age of the case. The index date was the index date of the matched case.</p> <p><u>Exclusion criteria:</u> Pancreatic cancer (controls), no consultations in the year before diagnosis.</p> <p><u>Clinical setting:</u> Primary care</p>

Are there concerns that the included patients and setting do not match the review question?		Low concern
INDEX TEST		
A. Risk of bias		
Index test	All symptoms, physical signs or abnormal investigations compiled from the pancreatic cancer literature were studied, and supplemented by discussion with two pancreatic cancer charities. Libraries of codes relating to these were collated. All codes for fractures were also identified, as a test for any recording bias between cases and controls (making the assumption that the fracture rate would be approximately equal). Occurrences of these features in the year before the index date were identified. Features were only retained for further study if they occurred in $\geq 5\%$ of cases or controls. Repeat attendances with the same symptom were also retained if the subsequent consultation also occurred in $\geq 5\%$ of cases or controls. New-onset diabetes was defined as a code for diabetes, or a random blood glucose above the local laboratory's normal range, without similar codes more than 1 year before the index date. For laboratory tests, patients without a test were considered to be the same status as those with a normal result, making our binary variable abnormal result/ no abnormal result. Abnormal liver function was defined as any liver enzyme above the normal range, and raised inflammatory markers as either abnormal erythrocyte sedimentation rate or C-reactive protein, as there were too few plasma viscosity results.	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
<i>For diagnostic case-control studies:</i> Investigators were kept 'blind' to other important confounding and prognostic factors?	Yes	
Could the conduct or interpretation of the index test have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern	
REFERENCE STANDARD		
A. risk of bias		
Reference standard(s)	Pancreatic cancer code in the UK's General Practice Research Database.	
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk	
B. Concerns regarding applicability		
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern	
FLOW AND TIMING		
A. risk of bias		
Flow and timing	A total of 21624 patients were identified, 17977 controls and 3647 cases. Of	

	the controls the following exclusions were applied: pancreatic cancer (N = 64), case excluded (N = 40), and no data in year pre-index date (N = 1414). Of the cases the following exclusions were applied: No controls (N = 2), and cancer not of pancreatic origin (N = 10).
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk
NOTES	

References

Included studies

- Collins, G.S., Altman, D.G. Identifying patients with undetected colorectal cancer: An independent validation of QCancer (Colorectal). *British Journal of Cancer* 107, 260-265. 2012.
- Collins, G.S., Altman, D.G. Identifying patients with undetected gastro-oesophageal cancer in primary care: External validation of QCancer (Gastro-Oesophageal). *European Journal of Cancer*, <http://dx.doi.org/10.1016/j.ejca.2012.10.023>. 2012a.
- Collins, G.S.; Altman, D.G. (2013). Identifying patients with undetected pancreatic cancer in primary care: an independent and external validation of QCancer[®] (Pancreas). *British Journal of General Practice*, 63: 636-642.
- Collins, G.S., and Altman, D.G. Identifying patients with undetected renal tract cancer in primary care: An independent and external validation of QCancer (renal) prediction model. *Cancer Epidemiology*, 37, 115-120. 2013a.
- Hamilton, W., Round, A., Sharp, D., and Peters, T. J. Clinical features of colorectal cancer before diagnosis: a population-based case-control study. *British Journal of Cancer* 93[4], 399-405. 22-8-2005.
- Hamilton, W., Peters, T. J., Round, A. & Sharp, D. (2005a) What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. *Thorax*, 60: 1059-1065.
The data split by smoking status is available from:
<http://webarchive.nationalarchives.gov.uk/20130513211237/http://www.ncat.nhs.uk/sites/default/files/work-docs/ncl%20lung%20guide.pdf>
- Hamilton, W., Sharp, D. J., Peters, T. J., and Round, A. P. Clinical features of prostate cancer before diagnosis: a population-based, case-control study. *British Journal of General Practice* 56[531], 756-762. 2006.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected gastro-oesophageal cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice*; DOI: 10.3399/bjgp11X606609. 2011.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected colorectal cancer in primary care: Derivation and validation of an algorithm. *British Journal of General Practice* 62[594], e29-e37. 2012.
- Hippisley-Cox, J. & Coupland, C. (2012a) Identifying patients with suspected pancreatic cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice*, 62: e38-e45.
- Hippisley-Cox, J. and Coupland, C. Identifying patients with suspected renal tract cancer in primary care: derivation and validation of an algorithm. *British Journal of General Practice* 62[597], e251-e260. 2012b.

Iyen-Omofoman, B., Tata, L. J., Baldwin, D. R., Smith, C. J. P. & Hubbard, R. B. (2013) Using socio-demographic and early clinical features in general practice to identify people with lung cancer earlier. *Thorax*, 68, 451-9.

Panzuto, F., Chiriatti, A., Bevilacqua, S., Giovannetti, P., Russo, G., Impinna, S., Pistilli, F., Capurso, G., Annibale, B., Delle, Fave G., and Digestive and Liver Disease and Primary Care Medicine Lazio Group. Symptom-based approach to colorectal cancer: survey of primary care physicians in Italy. *Digestive & Liver Disease* 35[12], 869-875. 2003.

Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M. & Hamilton, W. (2012) The risk of pancreatic cancer in symptomatic patients in primary care: a large case-control study using electronic records. *British Journal of Cancer*, 106: 1940-1944.