Suspected Cancer:

recognition and management of suspected cancer in children, young people and adults

Update of clinical guideline 27

Appendix F: Evidence review

Developed for NICE by the National Collaborating Centre for Cancer

This document is an update of the Evidence Review which accompanies NICE clinical guideline 27 (published June 2005) and will replace it.

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. You are invited to comment on this evidence only. Appendix J contains content from the 2005 Evidence Review which is being deleted as it has been updated.

The original NICE guideline and supporting documents are available from
http://www.nice.org.uk/guidance/CG27

Contents

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

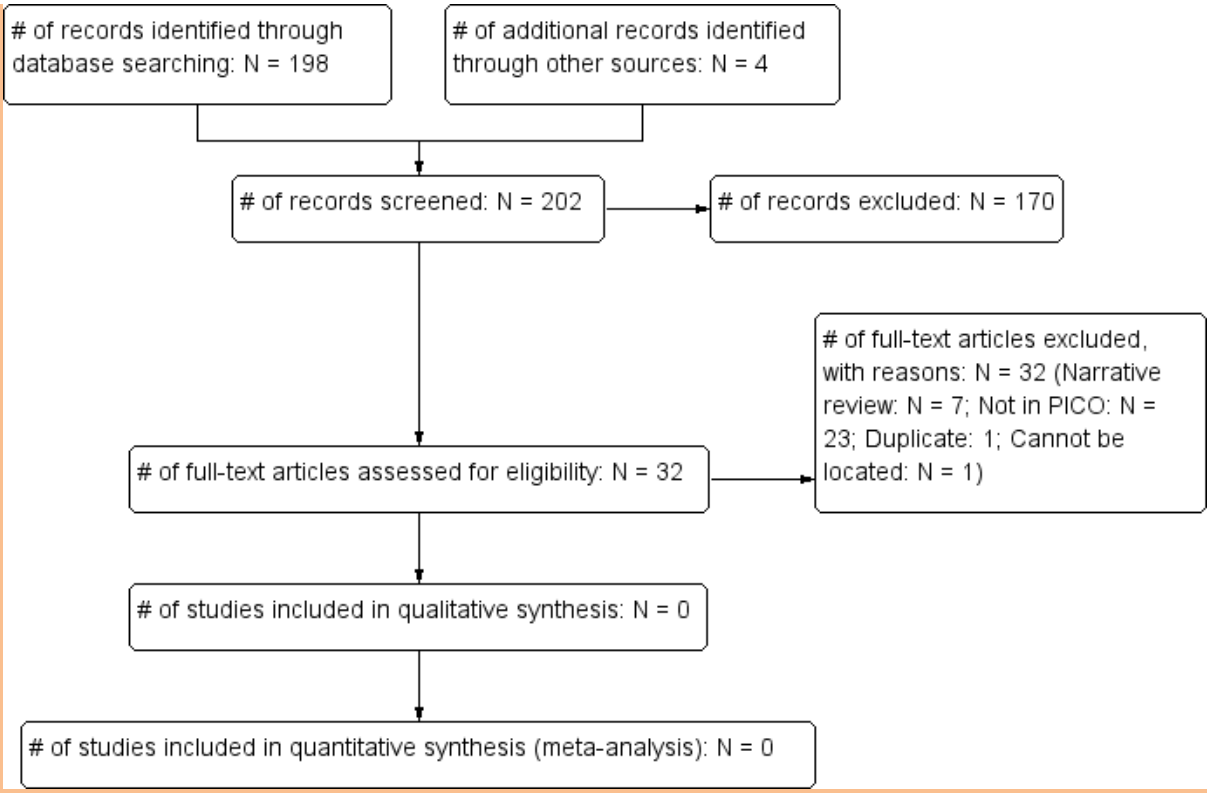
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	1575	93	11/07/2013
Premedline	1980-2013	95	3	11/07/2013
Embase	1980-2013	799	33	09/09/2013
Cochrane Library	1980-2013	874	0	09/09/2013
Psychinfo	1980-2013	133	3	09/09/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	38	0	09/09/2013
Websites etc			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
Medline	2013-27/082014	70	24	27/082014
Premedline	2013-27/082014	89	22	27/082014
Embase	2013-27/082014	125	31	27/082014
Cochrane Library	2013-27/082014	279	1	27/082014
Psychinfo	2013-27/082014	22	7	27/082014
Web of Science (SCI & SSCI) and ISI Proceedings	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%200%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., 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

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., Torring, 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., Torring, 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. & McIlfatrick, 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. & Prynn, 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 preferrences 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
Marenghi, 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., Tinmouth, 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., Ruszat, 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. & Knifsund, 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. & Ruszat, 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. & Holtedahl, 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 >=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 ofSystematic 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

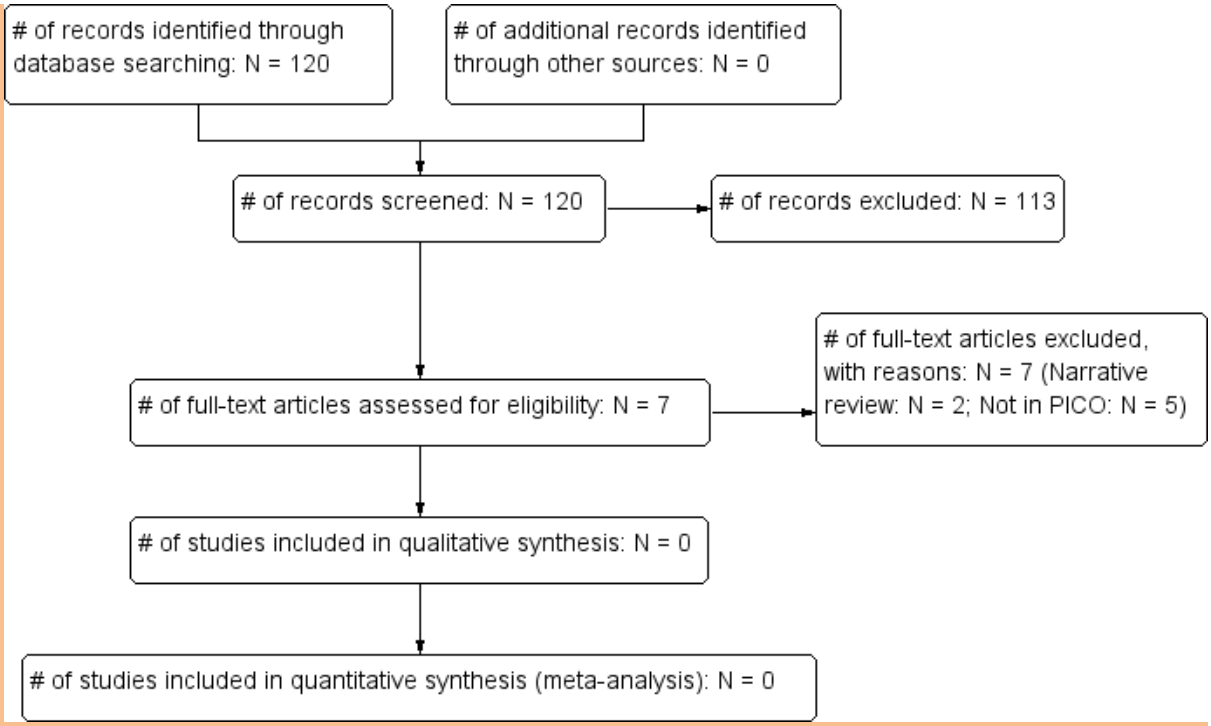
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	362	51	03/07/2013
Premedline	1980-2013	79	9	04/07/2013
Embase	1980-2013	548	21	04/07/2013
Cochrane Library	1980-2013	27	1	04/07/2013
Psychinfo	1980-2013	35	3	04/07/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	567	8	04/07/2013
Websites, Cancer networks			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
Medline	2013-27/08/2014	49	5	27/08/2014
Premedline	2013-27/08/2014	67	5	27/08/2014
Embase	2013-27/08/2014	98	10	27/08/2014
Cochrane Library	2013-27/08/2014	4	0	27/08/2014
Psychinfo	2013-27/08/2014	13	3	27/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	2013-27/08/2014	132	24	27/08/2014
Websites, Cancer networks			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., Eliott, 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. *Onkologe,* 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 Chesire 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
Houzard, S., Dubot, C., Fridmann, S., Dagousset, I., Rousset-Jablonski, C., Callet, N., Nos, C., Villet, R., Thoury, A., Delaloge, 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., Merkx, 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 safetynetting 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

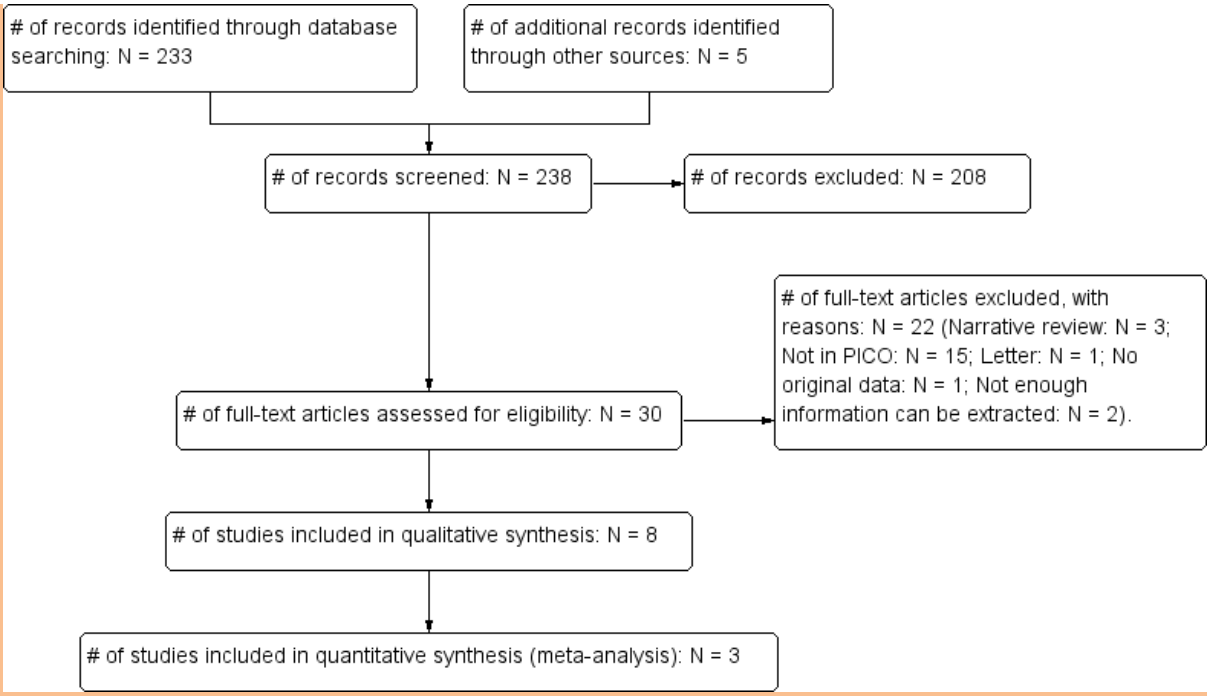
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	1520	57	06/02/2013
Premedline	All-2012	19	3	06/02/2013
Embase	All-2012	4958	100	12/02/2013
Cochrane Library	All-2012	419	3	12/02/2013
Psychinfo	All-2012	21	3	12/02/2013
Web of Science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

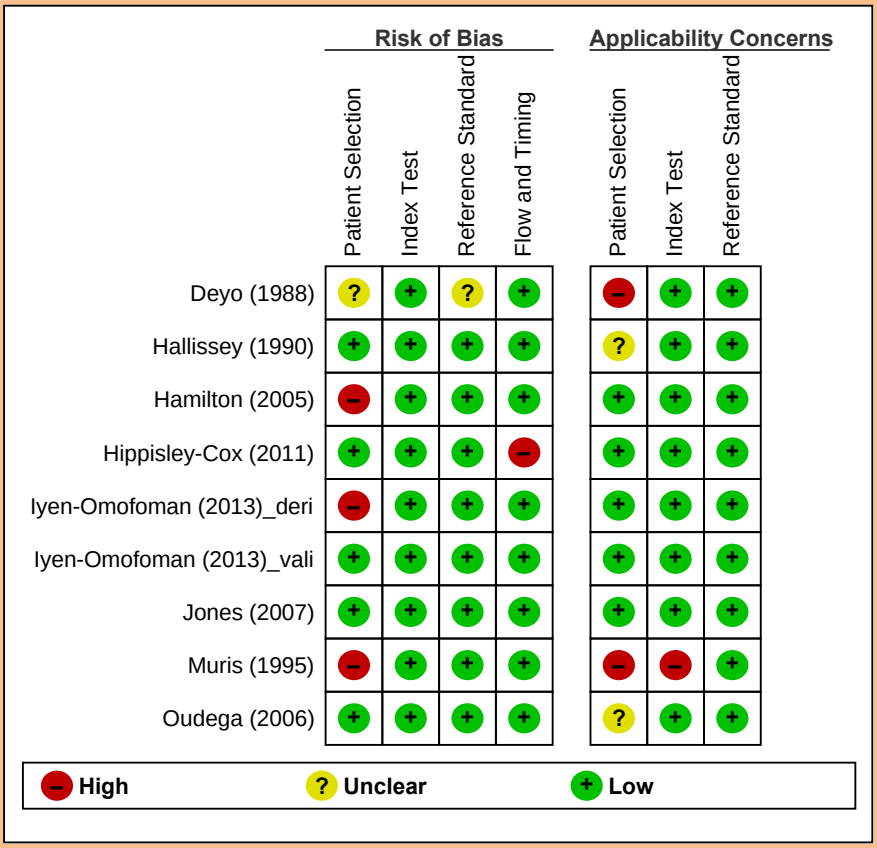
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	2013-19/08/2014	109	2	19/08/2014
Premedline	2013-19/08/2014	195	9	19/08/2014
Embase	2013-19/08/2014	298	13	19/08/2014
Cochrane Library	2013-19/08/2014	140	0	19/08/2014
Web of Science (SCI & SSCI)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



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 included patients	0.05 (0.003-0.3) 1/1975
Muris (1995)	Non-acute abdominal complaints	All included patients	0.2 (0.04-0.9) 2/933
Oudega (2006)	Deep vein thrombosis	All included 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)
Jones (2007)	Haemoptysis	Men (all ages) at 3 years	7.5 (6.6-8.5)
Jones (2007)	Haemoptysis	Men < 45 years at 3 years	0.21 (0.03-7.55)
Jones (2007)	Haemoptysis	Men 45-54 years at 3 years	1.65 (0.67-3.37)
Jones (2007)	Haemoptysis	Men 55-64 years at 3 years	8.37 (6.12-11.1)
Jones (2007)	Haemoptysis	Men 65-74 years at 3 years	14.86 (12-18.1)
Jones (2007)	Haemoptysis	Men 75-84 years at 3 years	17.05 (13.5-21.1)
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)
Jones (2007)	Haemoptysis	Women (all ages) at 3 years	4.3 (3.4-5.3)
Jones (2007)	Haemoptysis	Women < 45 years at 3 years	0.36 (0.04-1.3)
Jones (2007)	Haemoptysis	Women 45-54 years at 3 years	1.84 (0.6-4.24)
Jones (2007)	Haemoptysis	Women 55-64 years at 3 years	4.12 (2.32-6.71)
Jones (2007)	Haemoptysis	Women 65-74 years at 3 years	8.38 (5.73-11.8)
Jones (2007)	Haemoptysis	Women 75-84 years at 3 years	10.47 (7.01-14.9)
Jones (2007)	Haemoptysis	Women ≥ 85 years at 3 years	2.6 (0.32-9.07) 2/77
Hamilton (2005)	Haemoptysis	All included patients	2.4 (1.4-4.1)
Hamilton (2005)	Haemoptysis	All smokers	4.5 (NR)
Hamilton (2005)	Haemoptysis (reported twice)	All included patients	17 (NR)

Hamilton (2005)	Haemoptysis (reported twice)	All smokers	12 (NR)
Hamilton (2005)	Haemoptysis	Patients ≥ 70 years	7.1 (NR)
Hamilton (2005)	Cough	All included patients	0.4 (0.3-0.5)
Hamilton (2005)	Cough	All smokers	0.9 (NR)
Hamilton (2005)	Cough (reported twice)	All included 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 included patients	0.77 (0.54-1.1)
Iyen-Omofoman (2013)	Cough	Validation cohort	0.24 (0.2-0.3)
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)
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 included patients	0.43 (0.3-0.6)
Hamilton (2005)	Fatigue	All smokers	0.8 (NR)
Hamilton (2005)	Fatigue (reported twice)	All included patients	0.57 (0.4-0.9)
Hamilton (2005)	Fatigue (reported twice)	All smokers	1.2 (NR)
Hamilton (2005)	Dyspnoea	All included patients	0.66 (0.5-0.8)
Hamilton (2005)	Dyspnoea	All smokers	1.2 (NR)
Hamilton (2005)	Dyspnoea (reported twice)	All included 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)
Iyen-Omofoman (2013)	Dyspnoea 4-12 months prior to diagnosis	Derivation cohort	Cases: 1091/12074 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 included patients	0.82 (0.6-1.1)

Hamilton (2005)	Chest pain	All smokers	1.3 (NR)
Hamilton (2005)	Chest pain (reported twice)	All included 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)
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 included patients	1.1 (0.8-1.6)
Hamilton (2005)	Weight loss	All smokers	2.1 (NR)
Hamilton (2005)	Weight loss (reported twice)	All included 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)
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 included patients	0.87 (0.6-1.3)
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 included 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 diagnosis	Derivation cohort	Cases: 421/12074 Controls: 1848/120731
Hamilton (2005)	Thrombocytosis	All included patients	1.6 (0.8-3.1)
Hamilton (2005)	Thrombocytosis	All smokers	4.2 (NR)
Hamilton (2005)	Thrombocytosis	Patients 40-69 years	3 (NR)
Hamilton (2005)	Abnormal spirometry	All included patients	1.6 (0.9-2.9)
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 ≥ 40 years	9.7 (8.9-10.7)
Hamilton (2005)	Haemoptysis + cough	All included patients	2 (1.1-3.5)
Hamilton (2005)	Haemoptysis + cough	All smokers	3.9 (NR)
Hamilton (2005)	Haemoptysis + fatigue	All included patients	3.3 (NR)
Hamilton (2005)	Haemoptysis + fatigue	All smokers	6.1 (NR)

Hamilton (2005)	Haemoptysis + dyspnoea	All included patients	4.9 (NR)
Hamilton (2005)	Haemoptysis + dyspnoea	All smokers	6.9 (NR)
Hamilton (2005)	Haemoptysis + chest pain	All included patients	5 (NR)
Hamilton (2005)	Haemoptysis + chest pain	All smokers	4.1 (NR)
Hamilton (2005)	Haemoptysis + weight loss	All included patients	9.2 (NR)
Hamilton (2005)	Haemoptysis + weight loss	All smokers	*
Hamilton (2005)	Haemoptysis + appetite loss	All included patients	> 10 (NR)
Hamilton (2005)	Haemoptysis + appetite loss	All smokers	*
Hamilton (2005)	Haemoptysis + thrombocytosis	All included patients	> 10 (NR)
Hamilton (2005)	Haemoptysis + thrombocytosis	All smokers	NR
Hamilton (2005)	Haemoptysis + abnormal spirometry	All included patients	> 10 (NR)
Hamilton (2005)	Haemoptysis + abnormal spirometry	All smokers	*
Hamilton (2005)	Fatigue + cough	All included patients	0.63 (0.5-0.9)
Hamilton (2005)	Fatigue + cough	All smokers	1 (NR)
Hamilton (2005)	Fatigue + dyspnoea	All included patients	0.89 (0.6-?)
Hamilton (2005)	Fatigue + dyspnoea	All smokers	1.4 (NR)
Hamilton (2005)	Fatigue + chest pain	All included patients	0.84 (0.5-1.3)
Hamilton (2005)	Fatigue + chest pain	All smokers	1.3 (NR)
Hamilton (2005)	Fatigue + weight loss	All included patients	1 (0.6-1.7)
Hamilton (2005)	Fatigue + weight loss	All smokers	2 (NR)
Hamilton (2005)	Fatigue + appetite loss	All included patients	1.2 (0.7-2.1)
Hamilton (2005)	Fatigue + appetite loss	All smokers	2.3 (NR)
Hamilton (2005)	Fatigue + thrombocytosis	All included patients	1.8 (NR)
Hamilton (2005)	Fatigue + thrombocytosis	All smokers	2.4 (NR)
Hamilton (2005)	Fatigue + abnormal spirometry	All included patients	4 (NR)
Hamilton (2005)	Fatigue + abnormal spirometry	All smokers	>10 (NR)
Hamilton (2005)	Cough + dyspnoea	All included patients	0.79 (0.6-1)
Hamilton (2005)	Cough + dyspnoea	All smokers	1.4 (NR)
Hamilton (2005)	Cough + chest pain	All included patients	0.76 (0.6-1)
Hamilton (2005)	Cough + chest pain	All smokers	0.9 (NR)
Hamilton (2005)	Cough + weight loss	All included patients	1.8 (1.1-2.9)
Hamilton (2005)	Cough + weight loss	All smokers	2.3 (NR)
Hamilton (2005)	Cough + appetite loss	All included patients	1.6 (0.9-2.7)
Hamilton (2005)	Cough + appetite loss	All smokers	2.8 (NR)
Hamilton (2005)	Cough + thrombocytosis	All included patients	2 (1.1-3.5)
Hamilton (2005)	Cough + thrombocytosis	All smokers	6.5 (NR)

Hamilton (2005)	Cough + abnormal spirometry	All included patients	1.2 (0.6-2.6)
Hamilton (2005)	Cough + abnormal spirometry	All smokers	3.6 (NR)
Hamilton (2005)	Dyspnoea + chest pain	All included patients	1.2 (0.9-1.8)
Hamilton (2005)	Dyspnoea + chest pain	All smokers	2.2 (NR)
Hamilton (2005)	Dyspnoea + weight loss	All included patients	2 (1.2-3.8)
Hamilton (2005)	Dyspnoea + weight loss	All smokers	3.1 (NR)
Hamilton (2005)	Dyspnoea + appetite loss	All included patients	2 (1.2-3.8)
Hamilton (2005)	Dyspnoea + appetite loss	All smokers	5.5 (NR)
Hamilton (2005)	Dyspnoea + thrombocytosis	All included patients	2 (NR)
Hamilton (2005)	Dyspnoea + thrombocytosis	All smokers	2.4 (NR)
Hamilton (2005)	Dyspnoea + abnormal spirometry	All included patients	2.3 (NR)
Hamilton (2005)	Dyspnoea + abnormal spirometry	All smokers	>10 (NR)
Hamilton (2005)	Chest pain + weight loss	All included patients	1.8 (1-3.4)
Hamilton (2005)	Chest pain + weight loss	All smokers	4.4 (NR)
Hamilton (2005)	Chest pain + appetite loss	All included patients	1.8 (0.9-3.9)
Hamilton (2005)	Chest pain + appetite loss	All smokers	7.6 (NR)
Hamilton (2005)	Chest pain + thrombocytosis	All included patients	2 (NR)
Hamilton (2005)	Chest pain + thrombocytosis	All smokers	>10 (NR)
Hamilton (2005)	Chest pain + abnormal spirometry	All included patients	1.4 (NR)
Hamilton (2005)	Chest pain + abnormal spirometry	All smokers	>10 (NR)
Hamilton (2005)	Weight loss + appetite loss	All included patients	2.3 (1.2-4.4)
Hamilton (2005)	Weight loss + appetite loss	All smokers	5 (NR)
Hamilton (2005)	Weight loss + thrombocytosis	All included patients	6.1 (NR)
Hamilton (2005)	Weight loss + thrombocytosis	All smokers	>10 (NR)
Hamilton (2005)	Weight loss + abnormal spirometry	All included patients	1.5 (NR)
Hamilton (2005)	Weight loss + abnormal spirometry	All smokers	>10 (NR)
Hamilton (2005)	Appetite loss + thrombocytosis	All included patients	0.9 (NR)
Hamilton (2005)	Appetite loss + thrombocytosis	All smokers	*

Hamilton (2005)	Appetite loss + abnormal spirometry	All included patients	2.7 (NR)
Hamilton (2005)	Appetite loss + abnormal spirometry	All smokers	*
Hamilton (2005)	Thrombocytosis + abnormal spirometry	All included 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 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	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%). Inclusion criteria: 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. Exclusion criteria: Neck pain. Clinical setting: 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**
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)

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 and old patients with investigated dyspepsia. Inclusion criteria: All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia Exclusion criteria: None listed. Clinical setting: 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	**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	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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	**Yes**
For diagnostic case-control studies: 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: 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. Controls: 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. Inclusion criteria:

	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. Exclusion criteria: 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.
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**
For diagnostic case-control studies: 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 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	**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	

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 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). Current symptoms and symptoms in the preceding year: 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). Incident cases of lung cancer during the 2-year follow up period: N = 2196. Inclusion criteria: 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 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. *The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.* Exclusion criteria: 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. Clinical setting: 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	'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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	**Yes**
For diagnostic case-control studies: 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	Cases: 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. Controls: 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. Validation cohort: N = 1826293 (886994 males/939299 females). Age: Not reported. Incident cases of lung cancer during the 1-year follow up: N = 1728. Inclusion criteria: 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. 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**
For diagnostic case-control studies:	**Yes**

Investigators were kept 'blind' to other important confounding and prognostic factors?	
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	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.

	Haemoptysis: 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. Dysphagia: 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. Rectal bleeding: 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. Inclusion criteria: 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. Exclusion criteria: 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. Clinical setting: 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: Haematuria: Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs. Haemoptysis: Respiratory tract neoplasms. Dysphagia: Oesophageal neoplasms. Rectal bleeding: 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	**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 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: Haematuria: 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. Dysphagia: 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. *Estimates based on the pre-specified cancers may be thus conservative for these symptoms.* Haemoptysis: Extension of the diagnostic criteria yielded 6 additional cancers. Rectal bleeding: 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.

	Inclusion criteria: 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. Exclusion criteria: None listed. Clinical setting: 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. Inclusion criteria: 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. Exclusion criteria: Patients with a known malignancy or a malignancy detected within 2 weeks of deep vein thrombosis diagnosis. Clinical setting: 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

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-Scmidt, 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

Demetrious, J., Demetrious, G. J., Demetrious, J. & Demetrious, 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 ncreased 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 extact 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 Laeger,* 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 >=5% in primary care for cancer: systematic review. [Review]. *British Journal of General Practice,* 60: e366-e377.
Systematic Review. Theincluded 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 Associacao Medica 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
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
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? *Zdravniski 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., 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
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

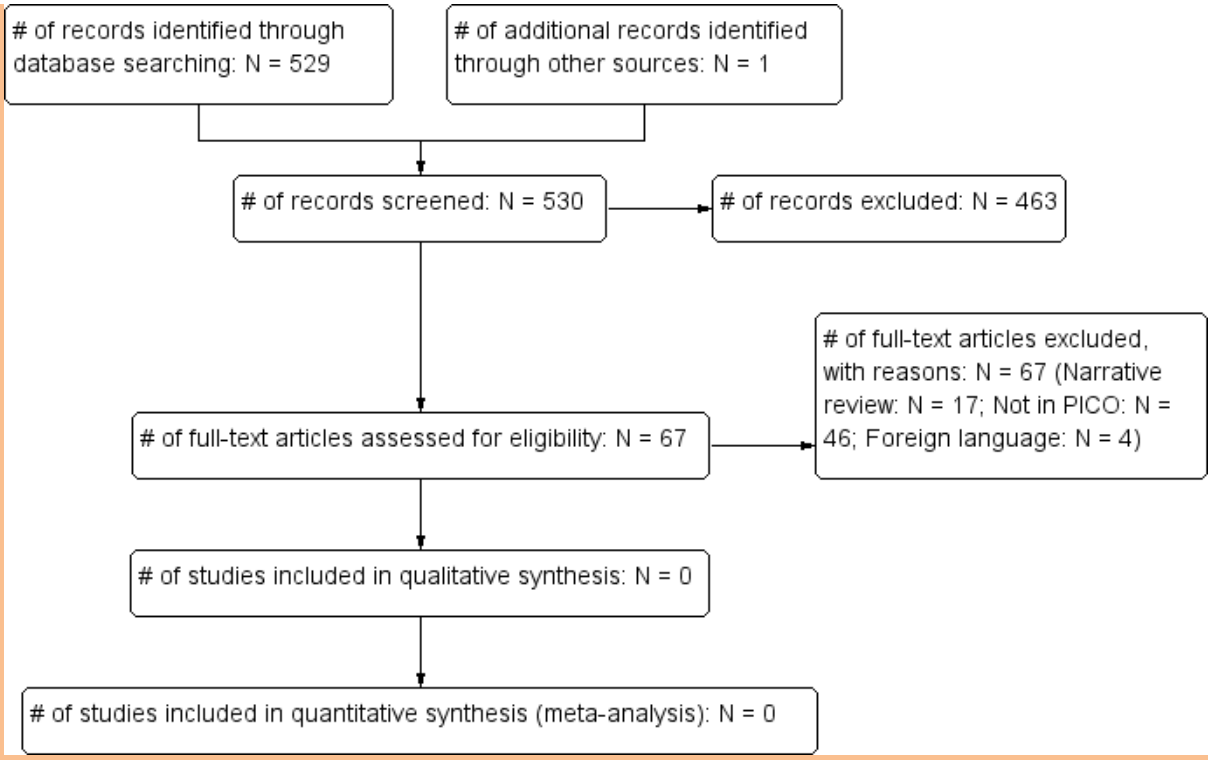
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	958	180	28/02/2013
Premedline	1980-2013	136	25	28/02/2013
Embase	1980-2013	1481	339	06/03/2013
Cochrane Library	1980-2013	175	2	06/03/2013
Psychinfo	1980-2013	14	4	06/03/2013
Web of Science (SCI & SSCI) and ISI Proceedings	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
Medline	2013-19/08/2014	105	6	19/08/2014
Premedline	2013-19/08/2014	133	14	19/08/2014
Embase	2013-19/08/2014	164	31	19/08/2014
Cochrane Library	2013-19/08/2014	70	0	19/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	2013-19/08/2014	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., Terzibasioglu, 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 Tuberculosi 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-observervariation 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-Scmidt, 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. (133) 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., Moscovitcz, 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

Gimenez, 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 bioloski 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 contributuions 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., Muche, 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 extact 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., Patrinou-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., Shvetz, 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 fibreoptic 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

Lyall, 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 Lungenkrankheiten,* 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,* Fortschritte: 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 Otology, 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 biomaker 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., Gribaudi, 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., Mojzisik, 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) Possibilites 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 expediates 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 Merkuriusz 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., Koksal, 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., Roufosse, 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 anaesthesis. *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]. *Przeglad Lekarski,* 63: 62-64.
Not in PICO

Wilde, J. (1981) Early detection of lung cancer. Possibilities--limits--organization. [German]. *Archiv fur 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., 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., 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

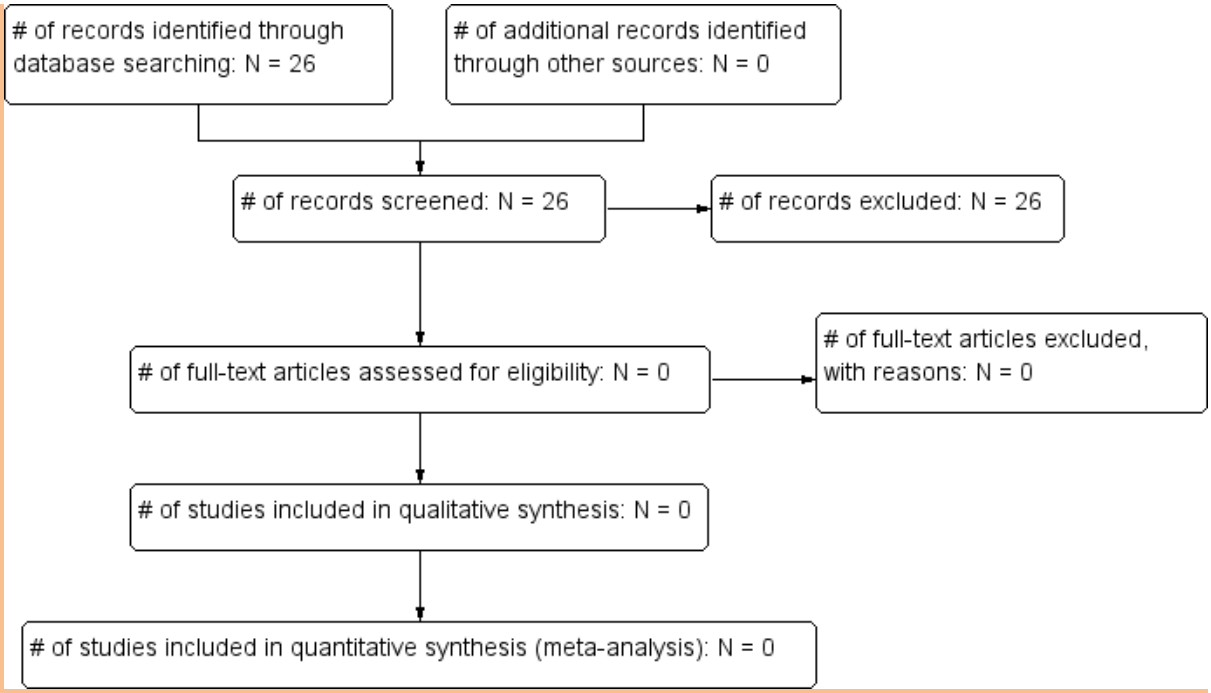
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	185	6	22/04/2013
Premedline	1980-2013	4	0	22/04/2013
Embase	1980-2013	301	15	22/04/2013
Cochrane Library	1980-2013	17	0	22/04/2013
Psychinfo	1980-2013	2	0	22/04/2013
Web of Science (SCI & SSCI) and ISI Proceedings	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
Medline	4/2013-20/08/2014	120	0	20/08/2014
Premedline	4/2013-20/08/2014	22	2	20/08/2014
Embase	4/2013-20/08/2014	37	2	20/08/2014
Cochrane Library	4/2013-20/08/2014	4	0	20/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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 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. & Kohlhaufl, 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. *Il 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. & Pairon, 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. *Kardiologiia,* 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

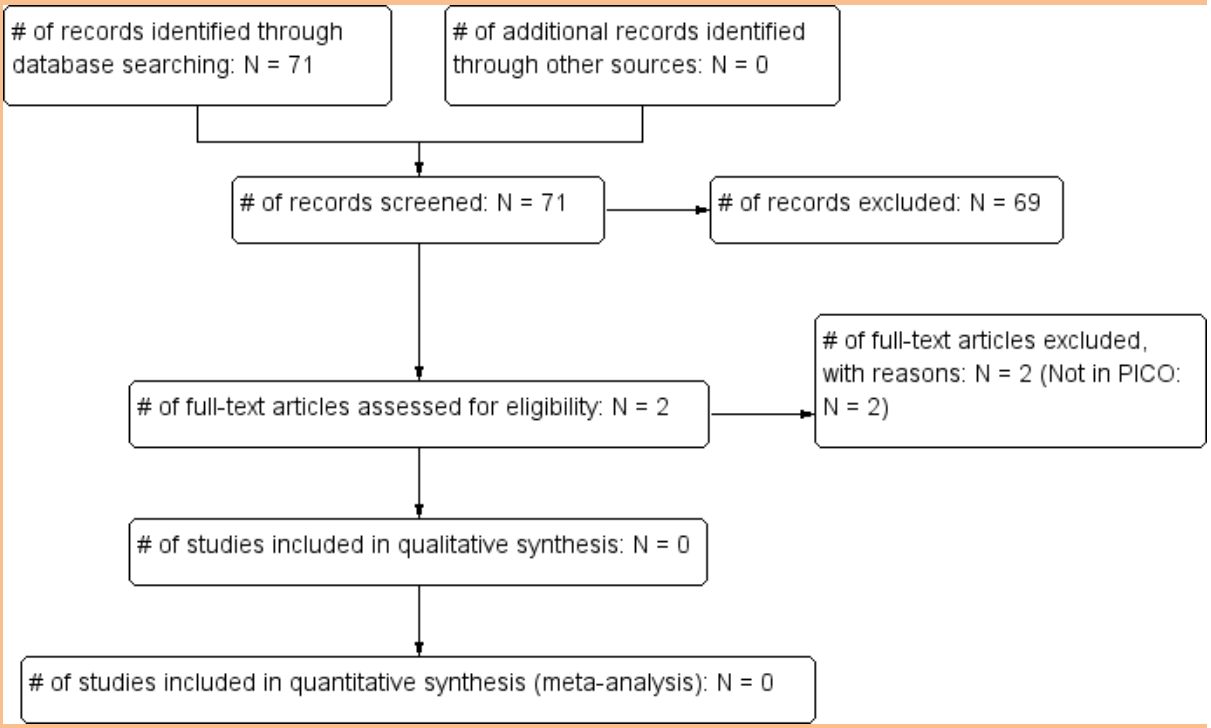
Psychinfo	1980-2013	1	0	14/05/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	24	0	14/05/2013

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
Medline	5/2013-20/08/2014	7	0	20/08/2014
Premedline	5/2013-20/08/2014	17	3	20/08/2014
Embase	5/2013-20/08/2014	37	4	20/08/2014
Cochrane Library	5/2013-20/08/2014	4	0	20/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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. & Kohlhaufl, 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. & Szilai, 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. & Reznek, 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--thoracoscopic biopsy and tumor marker. [Japanese]. *Nippon Geka Gakkai zasshi,* 110: 333-337.
Narrative review
Szubert, Z., Stankiewicz-Choroszucha, 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., Ksiazkiewicz, 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., Irngartinger, 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

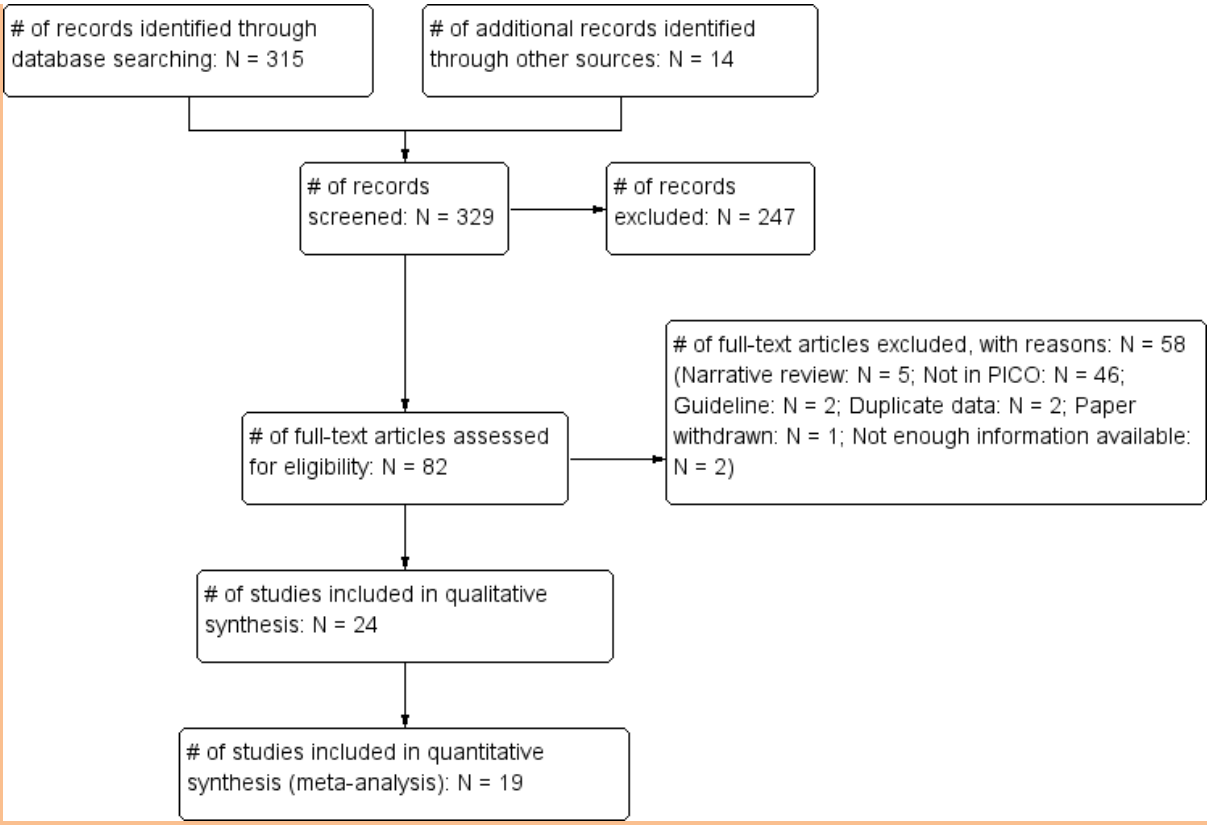
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	1593	122	08/05/2013
Premedline	All-2012	72	17	08/05/2013
Embase	All-2012	1831	182	09/05/2013
Cochrane Library	All-2012	483	5	10/05/2013
Psychinfo	All-2012	6	2	08/05/2013
Web of Science (SCI & SSCI) and ISI Proceedings	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
Medline	5/2013-20/08/2014	429	8	20/08/2014
Premedline	5/2013-20/08/2014	76	1	20/08/2014
Embase	5/2013-20/08/2014	458	11	20/08/2014
Cochrane Library	5/2013-20/08/2014	31	0	20/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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.

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. Inclusion criteria: "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." Exclusion criteria: None listed Clinical setting: 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	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; 4563 men, 13792 women). Incident cases of gastro-oesophageal cancer during the 2-year follow up period: N = 1766 (1184 men, 582 women; 32% gastric cancer, 68% oesophageal cancer). 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 (see below), the date of the first recorded onset within the study period. Exclusion criteria: Patients with a prior diagnosis of gastro-oesophageal cancer, registration with the general practice < 12 months, or with invalid dates. 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: 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. Inclusion criteria: 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). Exclusion criteria: Patients with a known history of iron-deficiency anaemia in the previous 2 years, a history of gastrointestinal malignancy or congenital haemoglobinopathy. Clinical setting: 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. Inclusion criteria: 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. Exclusion criteria: 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. 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	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. Inclusion criteria: 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. Exclusion criteria: None listed Clinical setting: 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

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: Neurologial 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		**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	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. Inclusion criteria: 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). 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. 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	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. Inclusion criteria: All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia Exclusion criteria: None listed. Clinical setting: Primary care, England.
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. Inclusion criteria: "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. Exclusion criteria: 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 contyraindicated. Clinical setting: 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 olkder 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, rangfe = 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. Inclusion criteria: 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). Exclusion criteria: 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 Clinical setting: 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 phosphatise, 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

	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 lasy year (N = 218862. Incident cases of gastro-oseophageal cancer during the 2-year follow up period: N = 1343 (776 oesophageal and 567 gastric). Inclusion criteria: 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. *The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.* Exclusion criteria: 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. 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: 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 ≥ 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. Inclusion criteria: "participants who were treated for dyspeptic complaints such as epigastric pain, heartburn, post-prandial pain and bloating, vomiting or nausea wiuth 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 caercinoma." 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 wiuth 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.

	Haemoptysis: 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. Dysphagia: 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. Rectal bleeding: 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. Inclusion criteria: 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. Exclusion criteria: 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. Clinical setting: 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: Haematuria: Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs. Haemoptysis: Respiratory tract neoplasms. Dysphagia: Oesophageal neoplasms. Rectal bleeding: 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: Haematuria: 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. Dysphagia: 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. *Estimates based on the pre-specified cancers may be thus conservative for these symptoms.* Haemoptysis: Extension of the diagnostic criteria yielded 6 additional cancers. Rectal bleeding: Extension of the diagnostic criteria yielded 2 additional cancers.

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. Inclusion criteria: "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." Exclusion criteria: 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. Clinical setting: 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 ≥ 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 withion 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. Inclusion criteria: "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. Exclusion criteria: 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. Clinical setting: 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	**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	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 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	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. Inclusion criteria: Patients who during a 3-month period consulted one of the participating GPs for abdominal complaints. Exclusion criteria: Patients aged < 18 years and patients with a condition necessitating immediate referral or admission to hospital. Clinical setting: 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. Inclusion criteria: 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%). Exclusion criteria: Patients who had been examined for any of the above symptoms within the last 6 months. Clinical setting: 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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	**Yes**
For diagnostic case-control studies: 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 years: N = 1712; 70-84 years: N = 2230; ≥ 85 years: N = 532. Gastric cancer cases: 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) Controls: Oesophageal cancer controls: 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. Gastric cancer controls: 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) Inclusion criteria: 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.

	Exclusion criteria: Oesophago-gastric cancer (controls), no consultations in the year before diagnosis. 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 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 analtomical description, whereas the variable 'abdominal pain' incorporated all other abdominal pain variables without a precise analtomical 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).
Were the index test results interpreted without knowledge of the results of the reference standard?	**Yes**
For diagnostic case-control studies: 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. Inclusion criteria: All patients aged > 50 years found to have iron deficiency anaemia between January 1989 and March 1994. Exclusion criteria: None listed. Clinical setting: 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. Inclusion criteria: Patients ≥ 18 years with a primary complaint of ≥ 3 months intermittent or continuous dyspepsia. Patients could not have used proton pump inhibitiors within 30 days or prokinetics or prescription H_2-receptor antagonists (H_2RAS) within 14 days of enrolment. Exclusion criteria: 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. Clinical setting: 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 endoscoy (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	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%). Inclusion criteria: "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." Exclusion criteria: "Patients with either previous or recurrent complaints or previously investigated for UGI symptoms were not included". Clinical setting: 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 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	N = 2741, mean (range) age = not reported (not reported) years, numbers of females/males: Not reported. Inclusion criteria: 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). Exclusion criteria: 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. Clinical setting: 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. Inclusion criteria: 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. Exclusion criteria: History of anaemia within previous 12 months, known

	haematological abnormalities (e.g., haemoglobinopathy), unavailable notes at follow up. *That is, patients with a history of cancer were not excluded.* 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 ≤ 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.

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., 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-effectiveeness 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., 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.
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., Nouraie, M., Razjouyan, H., Lee, E. E., Dowlati, E., El-Seyed, 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 lugoul 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. l. 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. Achalaslia-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 assosiated 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., 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
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., 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: 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]. *Paediatria 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 Diease 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 practitionner. 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

Olithselvan, 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., Jeen, 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. & Robaszkiewicz, 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 gastro-intestinal 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.
Nasrrative 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 reviewSchlansky, 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., Blaszak, A., Gil, J., Dyrla, P. & Jalocha, L. (2009) [The importance of functional tests in gastroesophageal reflux disease diagnosing, monitoring and treatment]. [Review] [20 refs] [Polish]. *Polski Merkuriusz 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

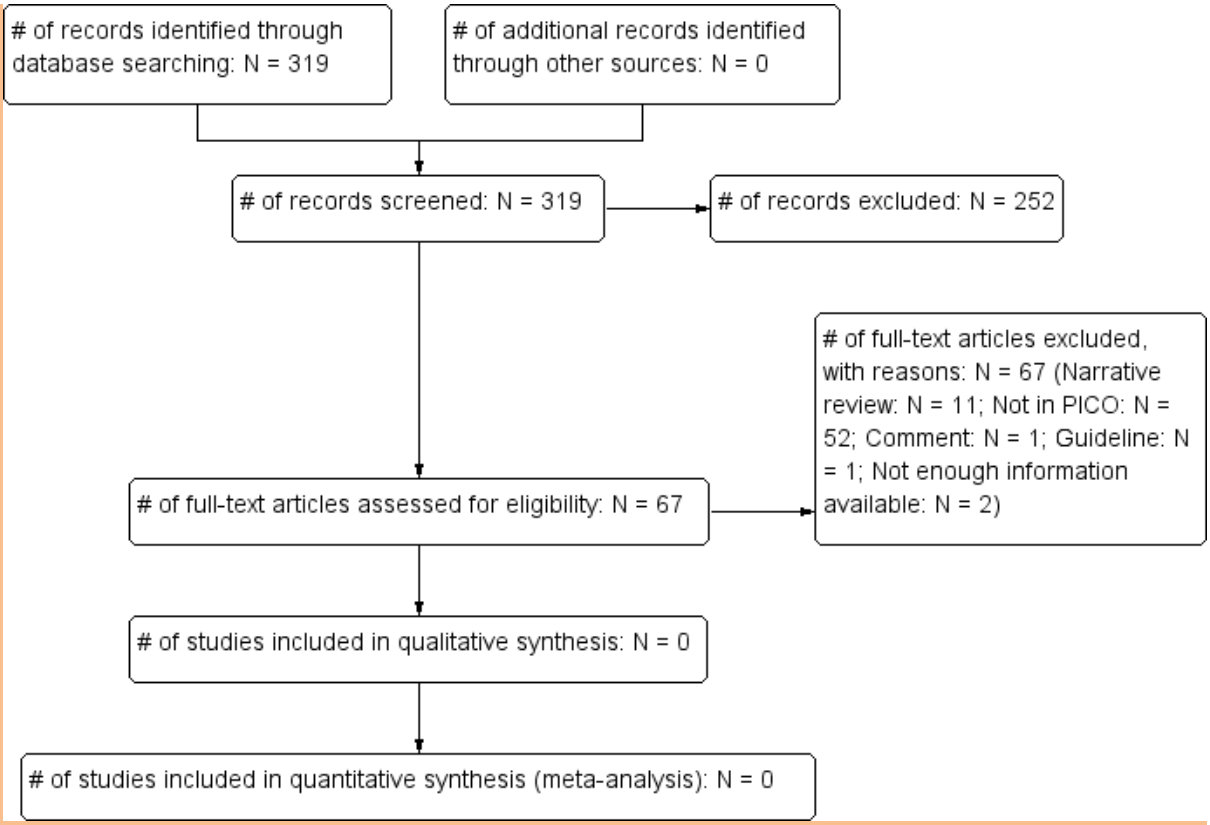
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	339	136	04/06/2013
Premedline	1980-2013	46	16	04/06/2013
Embase	1980-2013	675	142	05/06/2013
Cochrane Library	1980-2013	29	7	05/06/2013
Psychinfo	1980-2013	1	0	05/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	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
Medline	5/2013-20/08/2014	9	0	20/08/2014
Premedline	5/2013-20/08/2014	73	19	20/08/2014
Embase	5/2013-20/08/2014	34	10	20/08/2014
Cochrane Library	5/2013-20/08/2014	4	1	20/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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., Ragunath, 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., Tucat, 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 lugoul 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., Ragunath, 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., Ragunath, 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., Shakhatreh, 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 Wewnetrznej,* 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. & Ragunath, K. (2006) Acetic acid-enhanced magnification endoscopy in the diagnosis of specialized intestinal metaplasia, dysplasia and early cancer in Barrett's oesophagus. *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., Kruel, 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. & Iafrate, 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 acn 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]. *Paediatria Croatica, Supplement,* 50: 93-102.
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
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
Lecleire, 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
Masclee, 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
Ormeci, 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: I27-I32.
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-esophagoscopic 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-bioptic 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]. *Przeglad 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., Piscioli, F., Pozzato, F., Ronzani, G., Rugge, M., Saggioro, 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

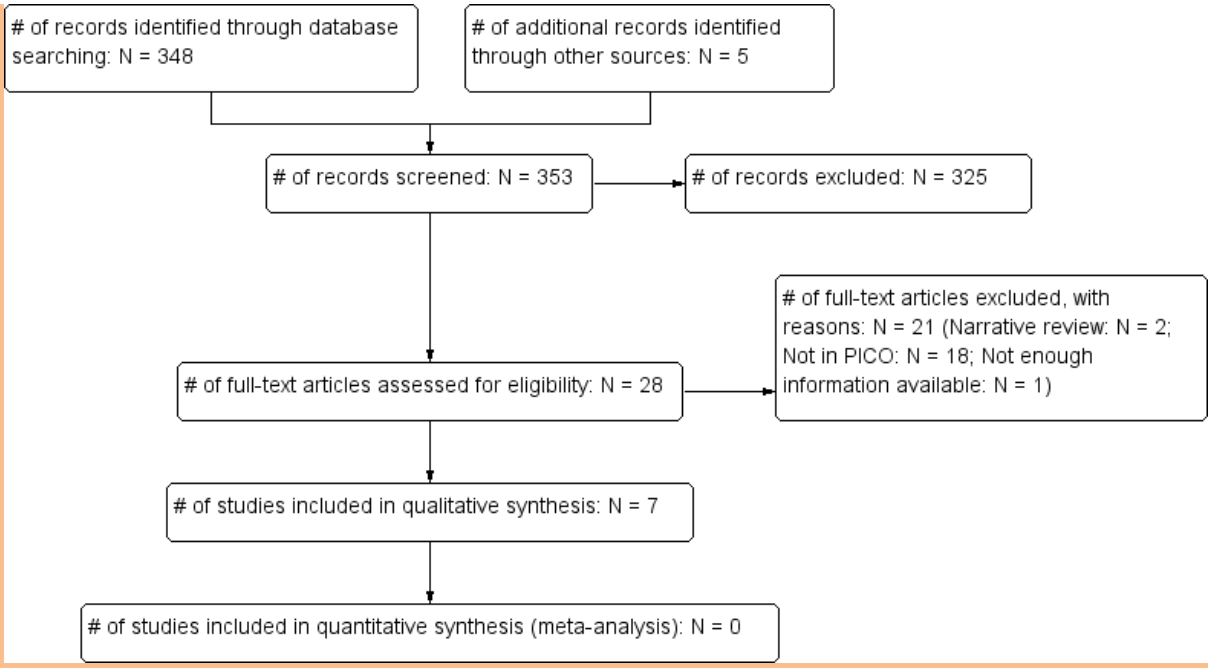
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	973	152	31/05/2013
Premedline	All-2012	130	19	31/05/2013
Embase	All-2012	1396	245	07/06/2013
Cochrane Library	All-2012	191	0	07/06/2013
Psychinfo	All-2012	29	6	31/05/2013
Web of Science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

Total References retrieved (after de-duplication): 331

Update Search

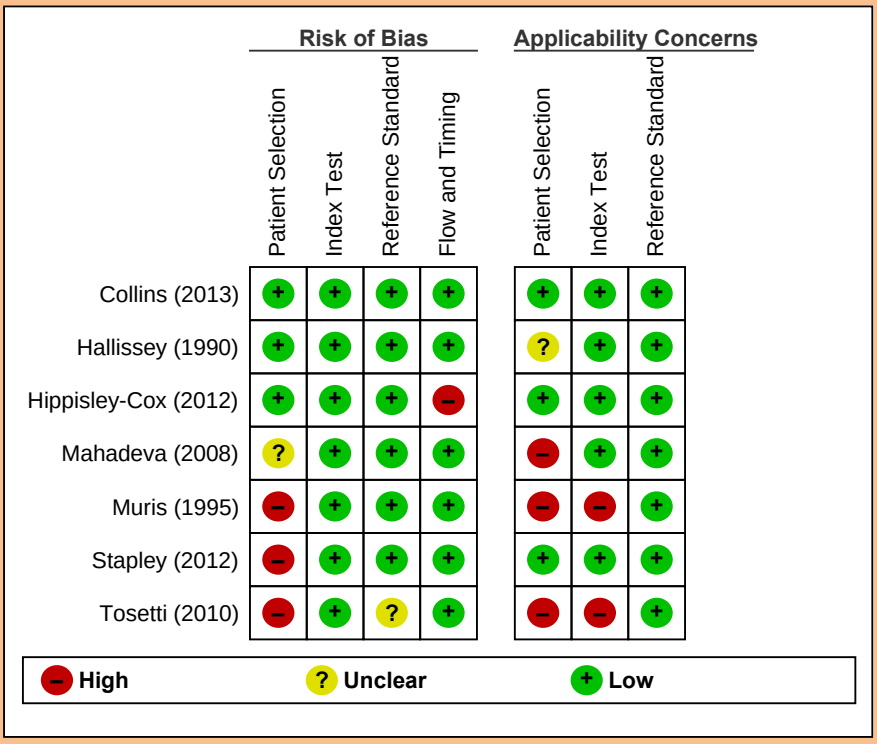
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	5/2013-20/08/2014	48	2	20/08/2014
Premedline	5/2013-20/08/2014	90	4	20/08/2014
Embase	5/2013-20/08/2014	151	11	20/08/2014
Cochrane Library	5/2013-20/08/2014	60	0	20/08/2014
Web of Science (SCI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



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)
		Women	0.1 (0.09-0.12)
		Men	0.19 (0.16-0.22)
Hippisley-Cox (2012)	Abdominal pain	All patients	0.3 (0.3-0.4)
Stapley (2012)	Abdominal pain	All patients	0.2 (0.19-0.22)
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)
Collins (2013)	Abdominal distension	Women	0.16 (0.07-0.34)
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)
Collins (2013)	Dysphagia	Men	0.1 (0.05-0.19)
Collins (2013)	Appetite loss	All patients	0.39 (0.26-0.59)
		Women	0.32 (0.17-0.59)
		Men	0.49 (0.27-0.86)
Hippisley-Cox (2012)	Appetite loss	All patients	0.8 (0.5-1.2)
Collins (2013)	Weight loss	All patients	0.28 (0.22-0.35)
		Women	0.16 (0.11-0.24)
		Men	0.42 (0.32-0.54)
Hippisley-Cox (2012)	Weight loss	All patients	0.6 (0.5-0.8)
Stapley (2012)	Weight loss	All patients	0.44 (0.36-0.55)
Stapley (2012)	Weight loss	Patients ≥ 60 years	0.8 (0.7-1)
Stapley (2012)	Nausea/vomiting	All patients	0.19 (0.17-0.21)
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)
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)
Stapley (2012)	Constipation	Patients ≥ 60 years	0.2 (0.2-0.2)
Collins (2013)	Constipation	Males	0.21 (0.11-0.38)
Stapley (2012)	Diarrhoea	All patients	0.09 (0.08-0.11)
Stapley (2012)	Diarrhoea	Patients ≥ 60 years	0.2 (0.2-0.2)
Stapley (2012)	Malaise	All patients	0.12 (0.1-0.15)
Stapley (2012)	Malaise	Patients ≥ 60 years	0.2 (0.2-0.3)
Stapley (2012)	Jaundice	All patients	12.9 (7.89-27.1)
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)
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)
Stapley (2012)	Low haemoglobin	All patients	0.1 (0.09-0.11)
Stapley (2012)	Raised inflammatory markers	All patients	0.16 (0.15-0.17)
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	A total of 2150322 patients were identified from 364 practices. Symptoms: 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). Incident cases of pancreatic cancer during the 2-year follow up period: N = 618 (331 men, 287 women). 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 (see below), the date of the first recorded onset within the study period. Exclusion criteria: Patients with a prior diagnosis of pancreatic cancer, registration < 12 months with the general practice, or invalid dates. 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: 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. Inclusion criteria: All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia Exclusion criteria: None listed. Clinical setting: 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	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). Current symptoms and symptoms in the preceding year: 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). Incident cases of pancreatic cancer during the 2-year follow up period: N = 781.

	Inclusion criteria: 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. *The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.* Exclusion criteria: 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. Clinical setting: 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	'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 ≥ 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	

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. Inclusion criteria: "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. Exclusion criteria: 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. Clinical setting: 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.

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	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.

setting	Inclusion criteria: 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. Exclusion criteria: None listed. 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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	**Yes**
For diagnostic case-control studies: 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: 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. Controls: 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. Inclusion criteria: 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. Exclusion criteria: Pancreatic cancer (controls), no consultations in the year before diagnosis. Clinical setting: 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	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**
For diagnostic case-control studies: 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%). Inclusion criteria: "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." Exclusion criteria: "Patients with either previous or recurrent complaints or previously investigated for UGI symptoms were not included". Clinical setting: 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 oesophageal (1/275).

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 QCancer(®) (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-effectiveeness 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 pronostic 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) Uselfulness 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., Delhaye, 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., Kantsevoy, 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., Piciucchi, 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. & DiMagno, 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 recommanded 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]. *Vnitrni Lekarstvi,* 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., Suciu, O., Grad, C. & Gheban, D. (2010) Thrombotic complications of pancreatic cancer: classical knowledge revisited. [Review]. *Digestive Diseases,* 28: 350-354.
Narrative review
Efeovbokhan, N., Makol, A., Cuison, 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., Eltoum, 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]. *Przeglad 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 GeneralPractice,* 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-demograpic 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 Lekaru 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. & Bastanhagh, 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 thromboembolismand 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., Ehehalt, 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., Chijiiwa, 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

Piciucchi, 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

Piciucchi, M., Capurso, G., Valente, R., Barrucca, V., Carnuccio, A., Romiti, A., Pilozzi, 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]. *Przeglad 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 Societes & 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., McMahon, 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., Delhaye, 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., Stroszczynski, 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 anhidrase 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 Interdisziplinar,* 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
Steegmueller, 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 Merkuriusz 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 Shokakibyo 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. l., 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

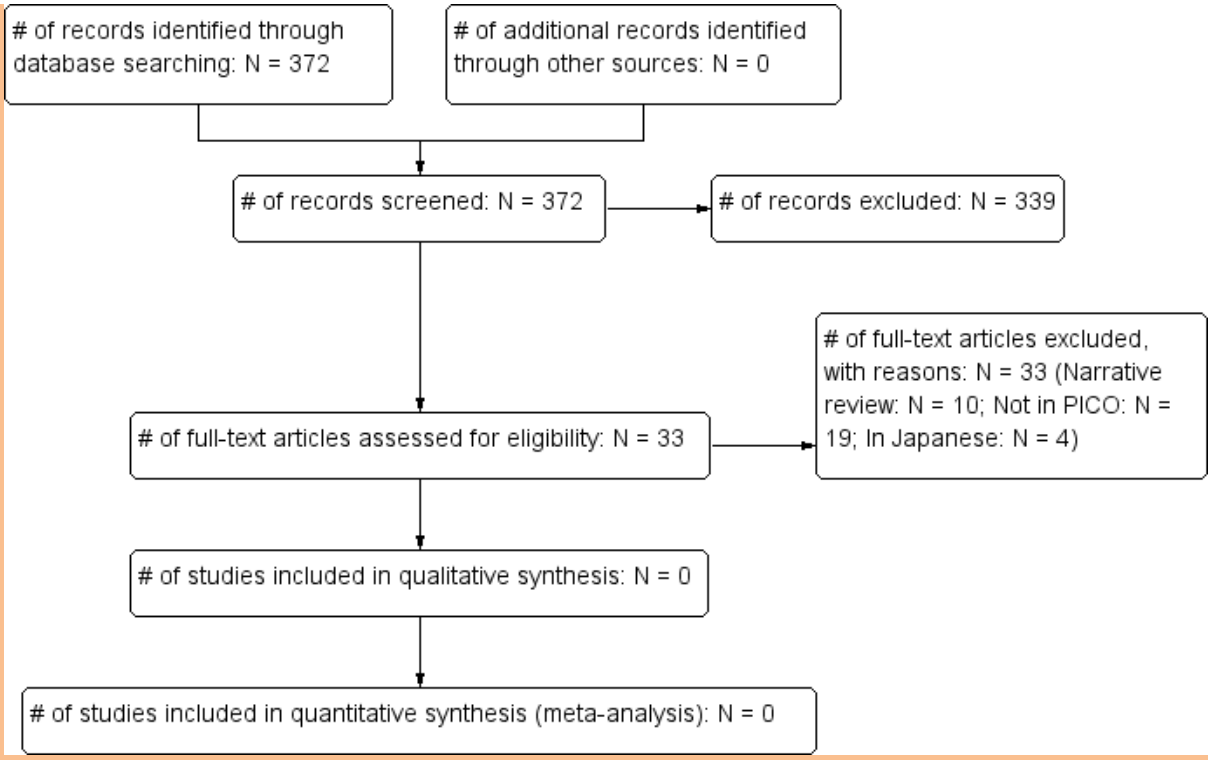
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	951	257	14/06/2013
Premedline	1980-2013	81	3	14/06/2013
Embase	1980-2013	1407	132	14/06/2013
Cochrane Library	1980-2013	67	12	14/06/2013
Psychinfo	1980-2013	1	0	14/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	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
Medline	6/2013-20/08/2014	42	12	20/08/2014
Premedline	6/2013-20/08/2014	93	16	20/08/2014
Embase	6/2013-20/08/2014	24	6	20/08/2014
Cochrane Library	6/2013-20/08/2014	9	1	20/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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 Sohwagi 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

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

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 extrtacted, 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 Merkuriusz 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., Kalff, 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. & Chevallier, 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., Eltoum, 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., Eltoum, 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., Eltoum, 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., Kluijt, 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
Iiboshi, 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., Ekbom, 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-demograpic 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) Cholangiopancreatoscopy 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 fur 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 panreatic 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., Stroszczynski, 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 CXC 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., Etzkorn, 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., Kitamra, 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., Bozdag, 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. & Rajszys, R. (1980) Advances in the diagnosis of pancreatic tumours. Diagnostic efficacy of the presently used examination methods. Optimal tactics of diagnostic management. [Polish]. *Polski Przeglad Radiologii i Medycyny Nuklearnej,* 44: 485-489.
Not in PICO
Queneau, P. E., Adessi, G. L., Thibault, P., Cleau, D., Heyd, B., Mantion, 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. (127) 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 Pancreatoscopy 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. & Reznek, 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., Tyrvainen, 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., Morandeau, 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

Seregni, 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., Greenson, 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

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 Merkuriusz 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., Lluis, 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 periampullary carcinomas. [Review] [61 refs]. *Surgical Endoscopy,* 17: 1514-1520.
Narrative review
Wang, G., Lipert, R. J., Jain, M., Kaur, S., Chakraboty, 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 periampullary 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., Burrig, 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., Holzknecht, 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 Biomark. 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 fur 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

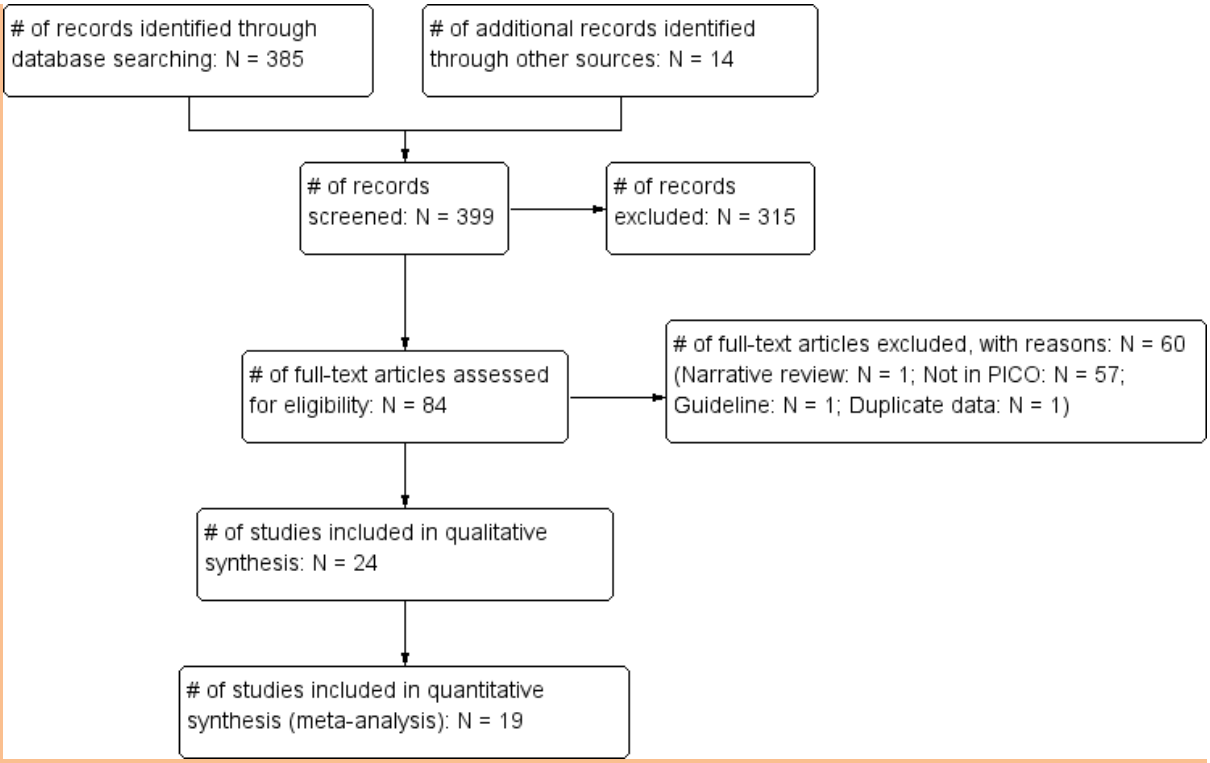
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	965	199	20/05/2013
Premedline	All-2012	108	33	21/05/2013
Embase	All-2012	1500	227	24/05/2013
Cochrane Library	All-2012	215	0	28/05/2013
Psychinfo	All-2012	13	2	21/05/2013
Web of Science (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
Medline	5/2013-26/08/2014	43	5	26/08/2014
Premedline	5/2013-26/08/2014	82	10	26/08/2014
Embase	5/2013-26/08/2014	109	5	26/08/2014
Cochrane Library	5/2013-26/08/2014	88	0	26/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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.

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. Inclusion criteria: "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." Exclusion criteria: None listed Clinical setting: 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	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; 4563 men, 13792 women). Incident cases of gastro-oesophageal cancer during the 2-year follow up period: N = 1766 (1184 men, 582 women; 32% gastric cancer, 68% oesophageal cancer). 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 (see below), the date of the first recorded onset within the study period.

	Exclusion criteria: Patients with a prior diagnosis of gastro-oesophageal cancer, registration with the general practice < 12 months, or with invalid dates. 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: 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. Inclusion criteria: 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). Exclusion criteria: Patients with a known history of iron-deficiency anaemia in the previous 2 years, a history of gastrointestinal malignancy or congenital haemoglobinopathy. Clinical setting: 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. Inclusion criteria: 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. Exclusion criteria: 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. 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	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. Inclusion criteria: 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. Exclusion criteria: None listed Clinical setting: 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 Clkeveland Clinic Foundation outpatient clinic by their primary care physician. Exclusion criteria: Neurologial 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)	Copmpleted 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	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. Inclusion criteria: 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). 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. 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	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 and old patients with investigated dyspepsia. Inclusion criteria: All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia Exclusion criteria: None listed. Clinical setting: 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).	

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. Inclusion criteria: "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. Exclusion criteria: 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 contyraindicated. Clinical setting: 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 olkder 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, rangfe = 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. Inclusion criteria: 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). Exclusion criteria: 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 Clinical setting: 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 phosphatise, 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	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 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 lasy year (N = 218862. Incident cases of colorectal cancer during the 2-year follow up period: N = 1343 (776 oesophageal and 567 gastric). Inclusion criteria: 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. *The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.* Exclusion criteria: 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. 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: 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 ≥ 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. Inclusion criteria: "participants who were treated for dyspeptic complaints such as epigastric pain, heartburn, post-prandial pain and bloating, vomiting or nausea wiuth 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 caercinoma." 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 wiuth 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	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. Haemoptysis: 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. Dysphagia: 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. Rectal bleeding: 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. Inclusion criteria: 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. Exclusion criteria: 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. Clinical setting: 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: Haematuria: Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs. Haemoptysis: Respiratory tract neoplasms. Dysphagia: Oesophageal neoplasms. Rectal bleeding: 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: Haematuria: 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.

	Dysphagia: 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. *Estimates based on the pre-specified cancers may be thus conservative for these symptoms.* Haemoptysis: Extension of the diagnostic criteria yielded 6 additional cancers. Rectal bleeding: Extension of the diagnostic criteria yielded 2 additional cancers.

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. Inclusion criteria: "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." Exclusion criteria: 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. Clinical setting: 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 ≥ 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 withion 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. Inclusion criteria: "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. Exclusion criteria: 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. Clinical setting: 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. 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 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. Inclusion criteria: Patients who during a 3-month period consulted one of the participating GPs for abdominal complaints. Exclusion criteria: Patients aged < 18 years and patients with a condition necessitating immediate referral or admission to hospital. Clinical setting: 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. Inclusion criteria: 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%). Exclusion criteria: Patients who had been examined for any of the above symptoms within the last 6 months. Clinical setting: 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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	**Yes**
For diagnostic case-control studies: 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

	years: N = 1712; 70-84 years: N = 2230; ≥ 85 years: N = 532. Gastric cancer cases: 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) Controls: Oesophageal cancer controls: 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. Gastric cancer controls: 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) Inclusion criteria: 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. Exclusion criteria: Oesophago-gastric cancer (controls), no consultations in the year before diagnosis. 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 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 analtomical description, whereas the variable 'abdominal pain' incorporated all other abdominal pain variables without a precise analtomical 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).

Were the index test results interpreted without knowledge of the results of the reference standard?	**Yes**
For diagnostic case-control studies: 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. Inclusion criteria: All patients aged > 50 years found to have iron deficiency anaemia between January 1989 and March 1994. Exclusion criteria: None listed. Clinical setting: 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. Inclusion criteria: Patients ≥ 18 years with a primary complaint of ≥ 3 months intermittent or continuous dyspepsia. Patients could not have used proton pump inhibitiors within 30 days or prokinetics or prescription H_2-receptor antagonists (H_2RAS) within 14 days of enrolment. Exclusion criteria: 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. Clinical setting: 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 endoscoy (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	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%). Inclusion criteria: "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." Exclusion criteria: "Patients with either previous or recurrent complaints or previously investigated for UGI symptoms were not included". Clinical setting: 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 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	N = 2741, mean (range) age = not reported (not reported) years, numbers of females/males: Not reported. Inclusion criteria: 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). Exclusion criteria: 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. Clinical setting: 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 cacer: 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. Inclusion criteria: 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. Exclusion criteria: History of anaemia within previous 12 months, known haematological abnormalities (e.g., haemoglobinopathy), unavailable notes at follow up. *That is, patients with a history of cancer were not excluded.* 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 ≤ 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.

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., 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-effectiveeness 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., 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.

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., Ibrahimi, 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) Uselfulness 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 Concensus 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
Bazaldua, 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., Zumtobel, 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. & 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
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* -

Gastrenterologia 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-erB-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-Lamptey, 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 gastaro 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. l. 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 cardial 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., Colatruglio, 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.
Narative review

Guirguis, E. M. (1989) Gastric cancer in primary care: how hard should you look? *Canadian Family Physician,* 35: 243-248.
Narative 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., Chijiiwa, 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., Tanii, 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 Interdisziplinaren Gesprachen,* 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., 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
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., 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
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., Hirono, 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., Ohsone, 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 thromboembolismand 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., Rosentzwig, 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. *Changgeng 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
Loyd, 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]. *Klinicheskaia 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., 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. & Kemona, 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. (230) 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., Ulacia, 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., Jeen, 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 Interdisziplinar,* 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., Charatcharoenwitthaya, 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 disection 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
Medline	1980-2013	2648	137	23/05/2013
Premedline	1980-2013	143	20	23/05/2013
Embase	1980-2013	3279	120	23/05/2013
Cochrane Library	1980-2013	151	7	23/05/2013
Psychinfo	1980-2013	1	0	23/05/2013
Web of Science (SCI &	1980-2013	147	34	23/05/2013

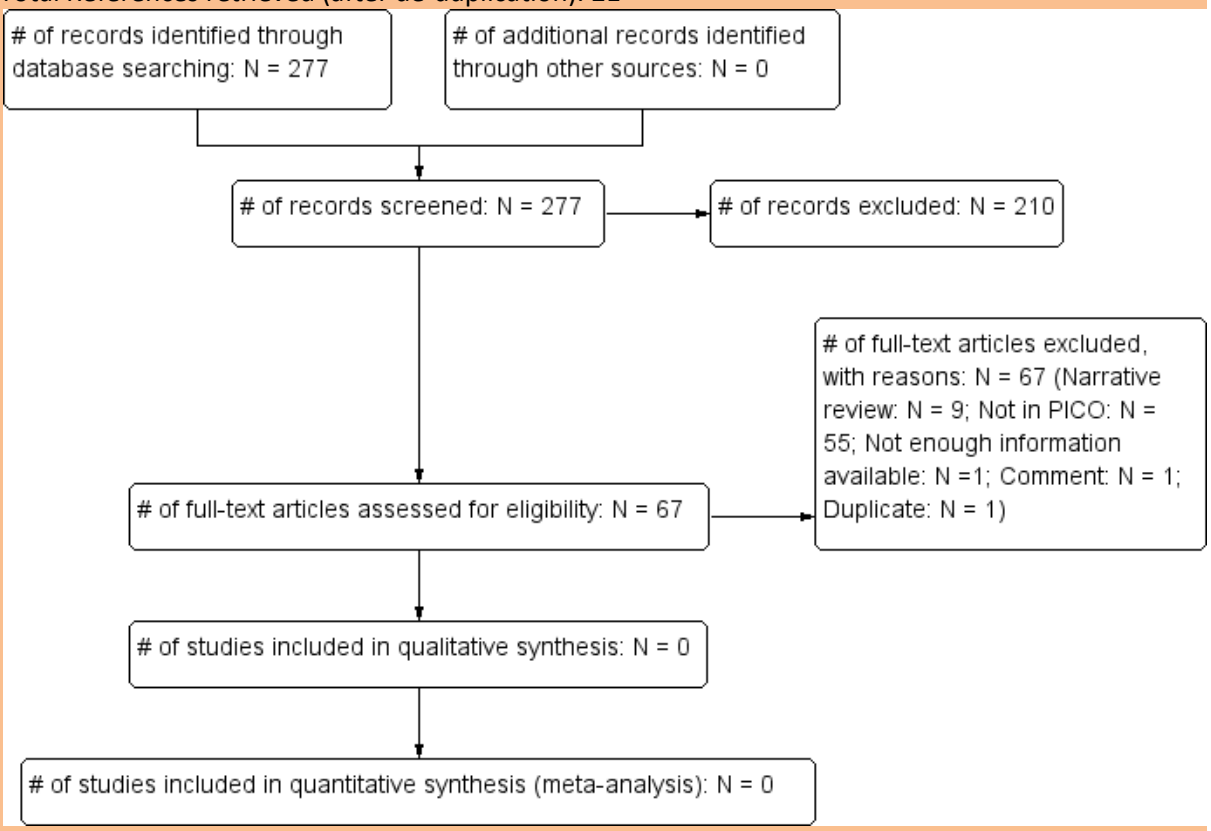
SSCI) and ISI Proceedings				

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., 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

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 fur Arztliche 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., Hosseinnezhad, 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-Lamptey, 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

Dettori, 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 evluation. 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.
Narative 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., Chijiiwa, 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., Chijiiwa, 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., Toyoizumi, 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., Toyoizumi, 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. & Kemona, 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., Jeen, 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., Tripatkhi, 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., Tripatkhi, 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 hydrosonography 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,* I.: 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, biut 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
Worlicek, 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., Piscioli, F., Pozzato, F., Ronzani, G., Rugge, M., Saggioro, 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 PICOYagi, 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 Ko 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

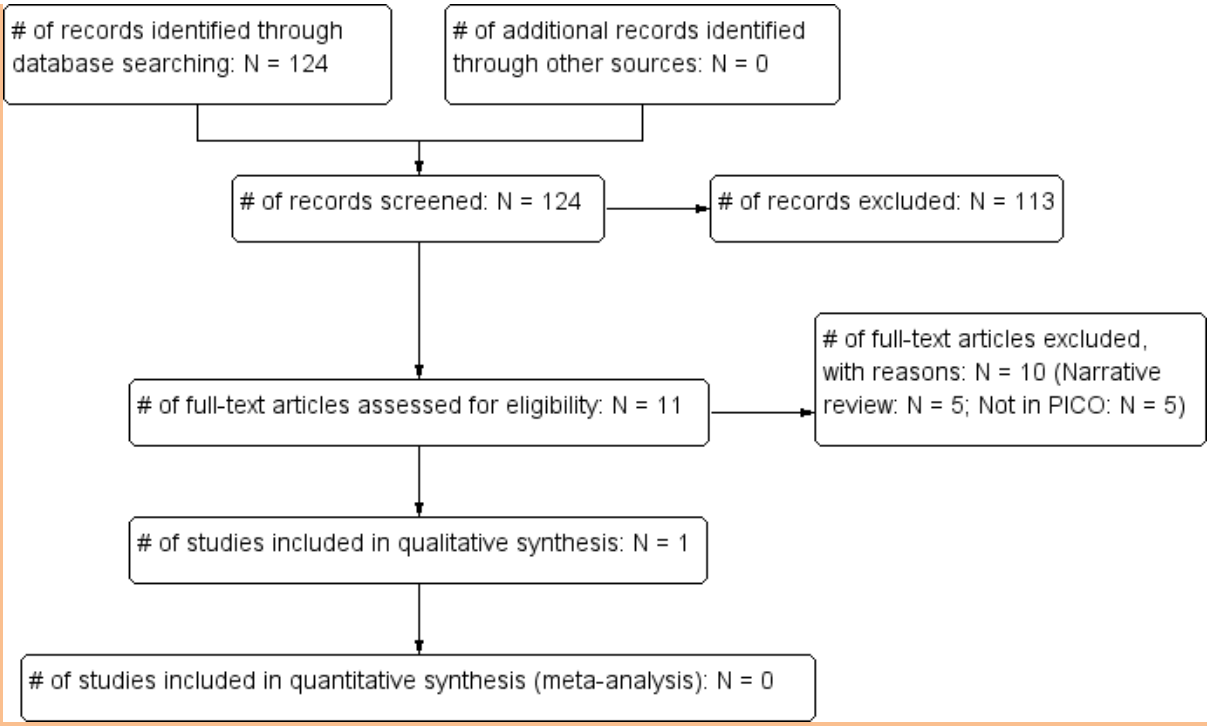
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	344	68	29/10/2012
Premedline	All-2012	2	1	29/10/2012
Embase	All-2012	398	53	01/11/2012
Cochrane Library	All-2012	172	0	01/11/2012
Psychinfo	All-2012	0	0	01/11/2012
Web of Science (SCI & SSCI) and ISI Proceedings	All-2012	211	3	01/11/2012
Biomed Central	All-2012	217	5	05/11/2012

Total References retrieved (after de-duplication): 117

Update Search

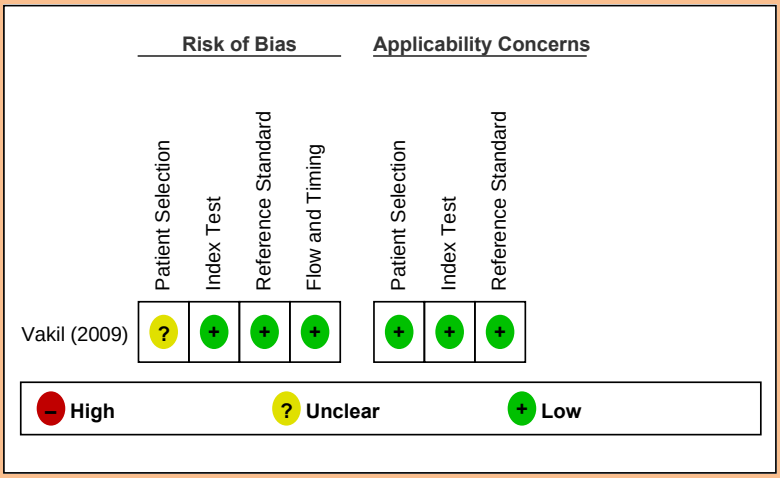
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	11/2012-26/08/2014	25	2	26/08/2014
Premedline	11/2012-26/08/2014	4	3	26/08/2014
Embase	11/2012-26/08/2014	40	2	26/08/2014
Cochrane Library	11/2012-26/08/2014	155	0	26/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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. Inclusion criteria: 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). Exclusion criteria: 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. Clinical setting: 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".

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, Biffl, 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]. Pathologe 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.; Chijiiwa,K.; Shimoda,K. (2014). A case report of gastrointestinal stromal tumor of the small intestine presenting with liver abscesses caused by Streptococcus constellatus. *Nippon Shokakibyo 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 fur 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 fur alle Gebiete der operativen Medizen 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 Matsuhashi, 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

Ugurlu, 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

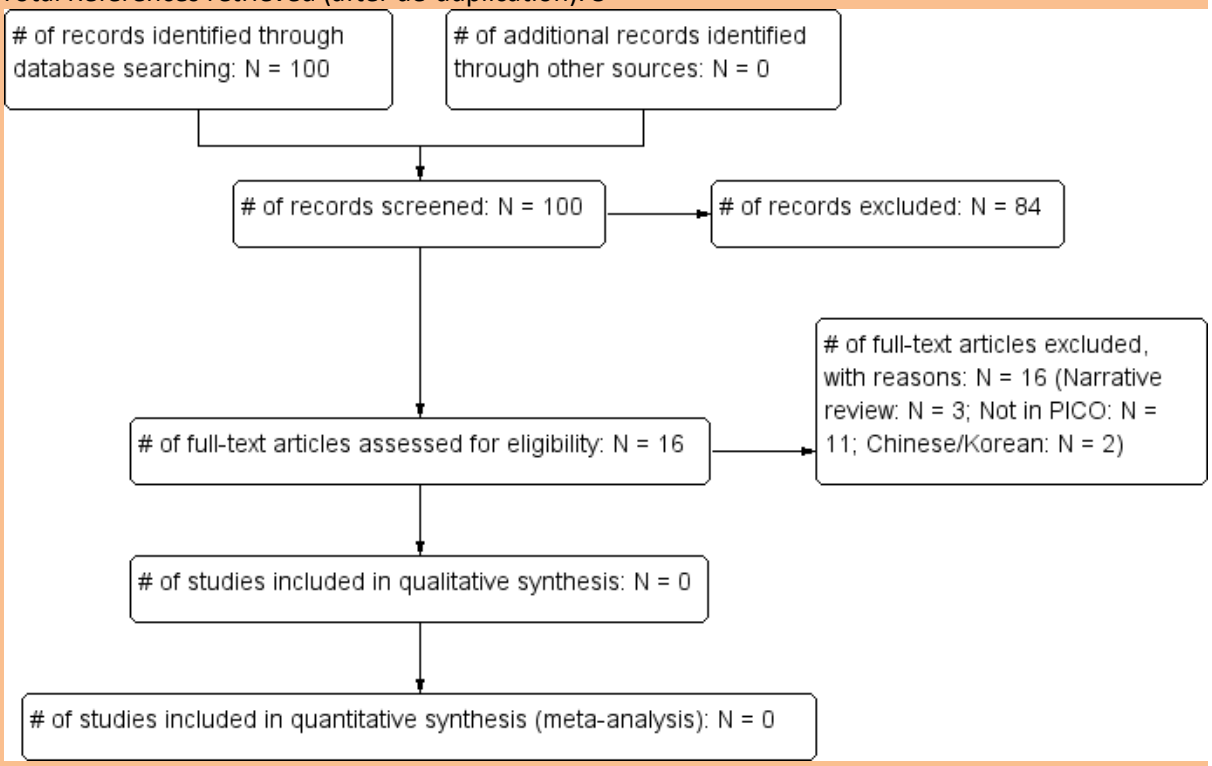
Total References retrieved (after de-duplication): 95

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., Giannakoulopoulou, 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

Cichoz-Lach, H. & Celinnski, K. (2007) Modern methods of endoscopic diagnosis of gastrointestinal tract. [Review] [53 refs]. *Journal of Physiology & Pharmacology,* 58: Suppl-31.
Narrative review

Clemencon, 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

Cwikiel, 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

Galmiche, 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., 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

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 Sohwagi 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. & Rheinwalt, 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 reiew

Maruyama, M. (2003) Early gastrointestinal cancers. [Review] [40 refs]. *Abdominal Imaging,* 28: 456-463.
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

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 inforamtion 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]. *Klinicheskaia 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 ampula 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. & Matsuhashi, 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

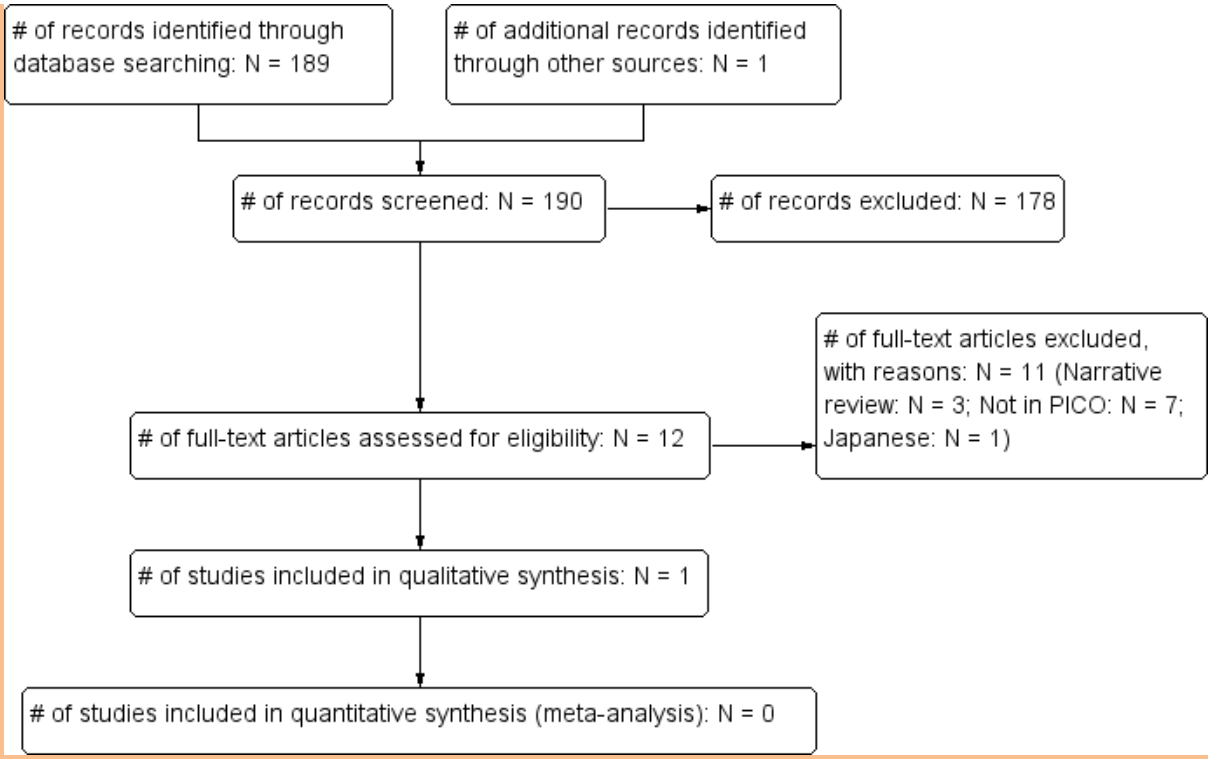
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	691	113	05/11/2012
Premedline	All-2012	24	6	05/11/2012
Embase	All-2012	1010	94	07/11/2012
Cochrane Library	All-2012	160	0	07/11/2012
Psychinfo	All-2012	1	1	05/11/2012
Web of Science (SCI & SSCI) and ISI Proceedings	All-2012	75	7	07/11/2012
Biomed Central	All-2012	82	0	07/11/2012

Total References retrieved (after de-duplication): 182

Update Search

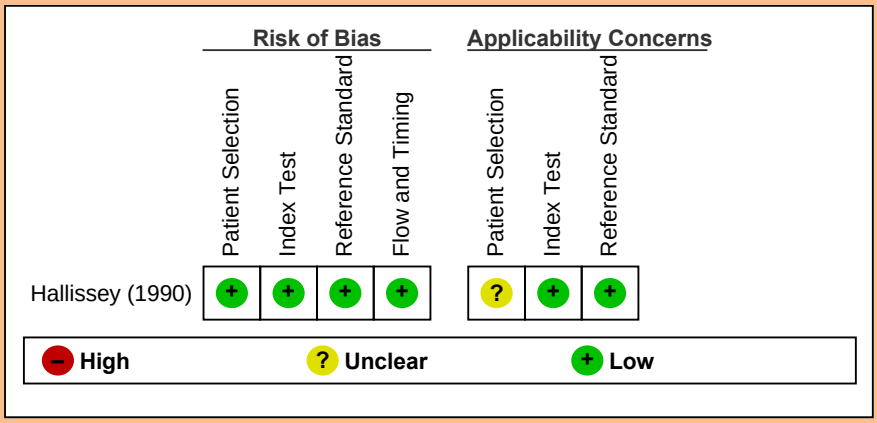
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	11/2012-26/08/2014	35	1	26/08/2014
Premedline	11/2012-26/08/2014	59	2	26/08/2014
Embase	11/2012-26/08/2014	200	4	26/08/2014
Cochrane Library	11/2012-26/08/2014	38	0	26/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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.



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 and old patients with investigated dyspepsia. Inclusion criteria: All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia Exclusion criteria: None listed. Clinical setting: 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), circinomatosis 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
Chijiiwa, 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, andtreatment. 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 specifity 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
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,* 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 choledocholitiasis! *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., Fraguela, 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 Shokakibyo 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) Gallbllader 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 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
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., Valimuhammad, 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 thromboembolismand 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., Eltoum, 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., Chijiiwa, 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 Shokakibyo 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,* I.: 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

Sirisinha, 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 accidently 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., Yamaguc, h. 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
Medline	1980-2013	348	100	08/05/2013
Premedline	1980-2013	19	4	08/05/2013
Embase	1980-2013	509	69	09/05/2013
Cochrane Library	1980-2013	31	0	09/05/2013
Psychinfo	1980-2013	0	0	09/05/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	21	5	09/05/2013

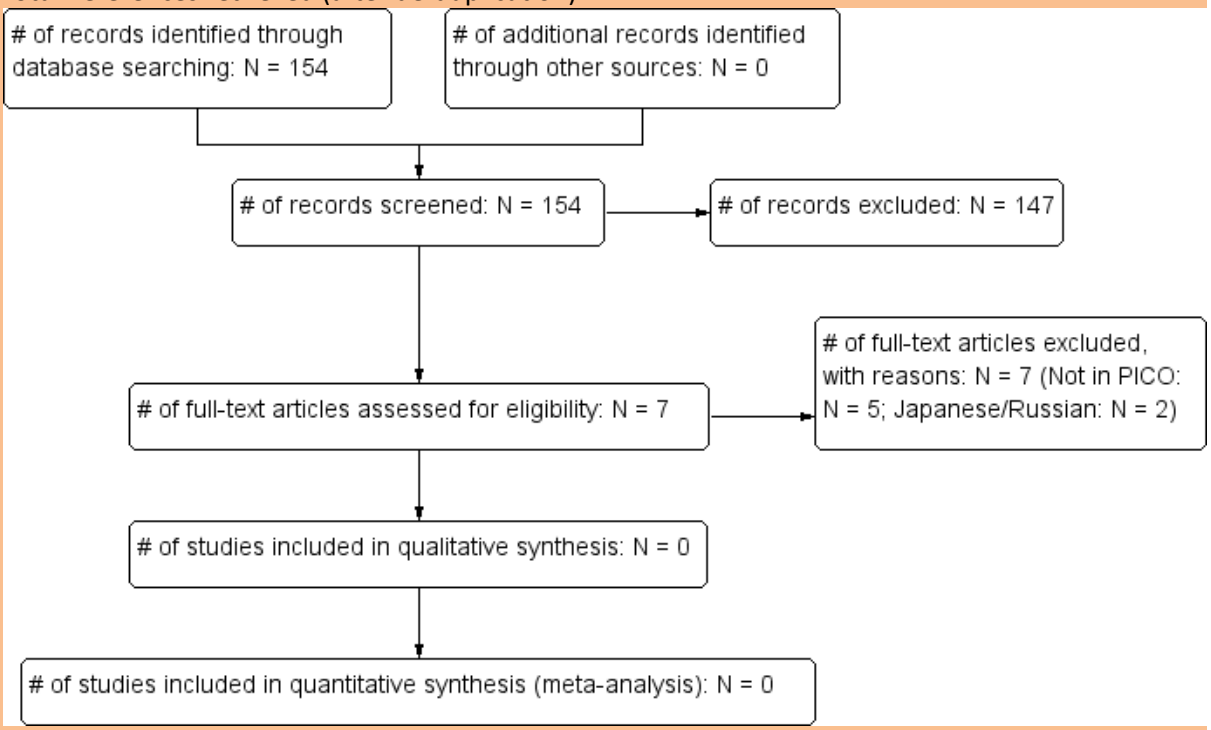
Total References retrieved (after de-duplication): 142

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	5/2013-26/08/2014	9	0	26/08/2014
Premedline	5/2013-26/08/2014	16	3	26/08/2014

Embase	5/2013-26/08/2014	75	11	26/08/2014
Cochrane Library	52013-26/08/2014	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, andtreatment. 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., Eltoum, 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. & Eltoum, 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 specifity 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., Voegtle, 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) Cholangiopancreatoscopy 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) Gallbllader cancer: 10 years of experience at an Amazon reference hospital. *Revista do Colegio Brasileiro de Cirurgioes,* 38: 100-104.
Not in PICO
Iwama, A., Tadatoshi, 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 Societes & 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 Shokakibyo 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 gallblader and biliary ducts - What is the value of CT, MRI, and magnetic resonance cholangiography?. [German]. *Chirurgische Gastroenterologie Interdisziplinar,* 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]. *Wiadomosci 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., Vetruccio, 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., Eltoum, 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 Shokakibyo 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 of18F-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

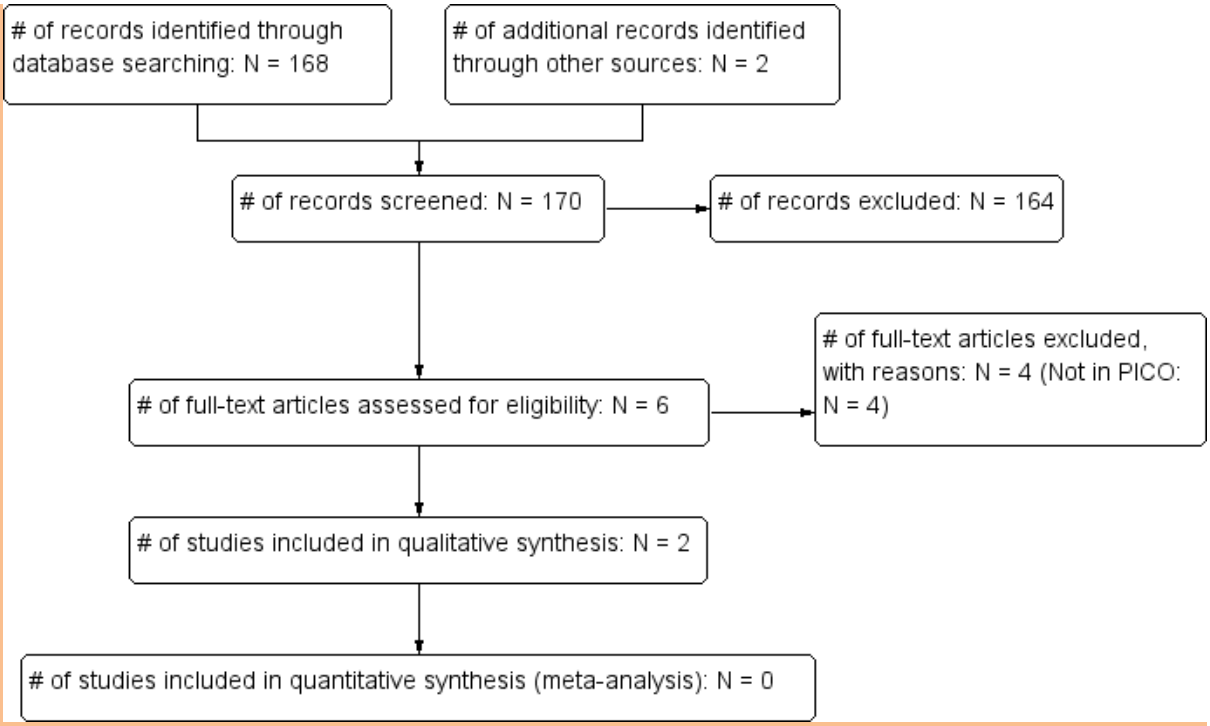
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	1073	71	30/04/2013
Premedline	All-2012	155	9	01/05/2013
Embase	All-2012	1305	93	02/05/2013
Cochrane Library	All-2012	459	0	03/05/2013
Psychinfo	All-2012	20	2	30/04/2013
Web of Science (SCI & SSCI) and ISI Proceedings	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
Medline	5/2013-19/08/2014	28	1	19/08/2014
Premedline	5/2013-19/08/2014	101	2	19/08/2014
Embase	5/2013-19/08/2014	163	2	19/08/2014
Cochrane Library	5/2013-19/08/2014	202	0	19/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	5/2013-19/08/2014	139	0	19/08/2014

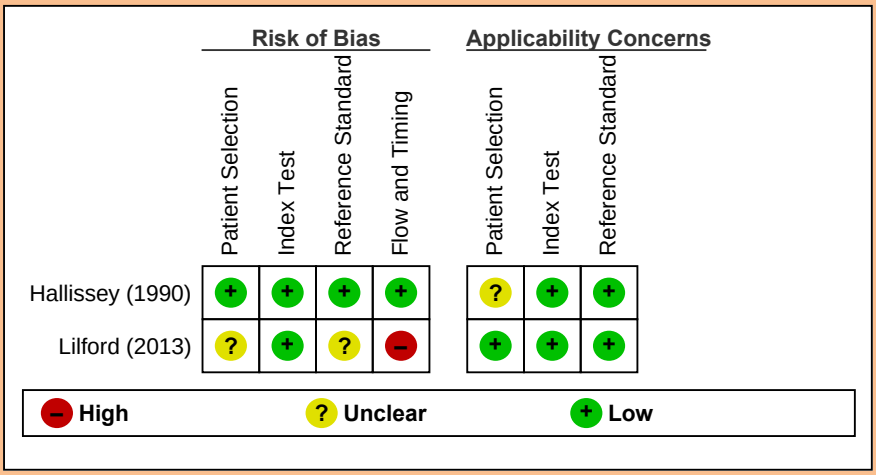
Total References retrieved (after de-duplication): 4



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.



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 phosphatise; 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. Inclusion criteria: All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia Exclusion criteria: None listed. Clinical setting: 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. Inclusion criteria: 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. Exclusion criteria: None listed. Clinical setting: 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

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.

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]. *Przeglad 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., Eltoum, 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. & Zurrida, 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., Benvegnu, 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 gallblader and biliary ducts - What is the value of CT, MRI, and magnetic resonance cholangiography?. [German]. *Chirurgische Gastroenterologie Interdisziplinar,* 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]. *Intervirology,* 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 thromboembolismand 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

Lertpipopmetha, 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]. *Paediatria 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., Benvegnu, 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., Benvegnu, 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., Benvegnu, 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 Diease 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., Aytekin, 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., Koufuji, 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 Steenbergen, 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 fur 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., Chijiiwa, 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'Keeffe, 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 Diease 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

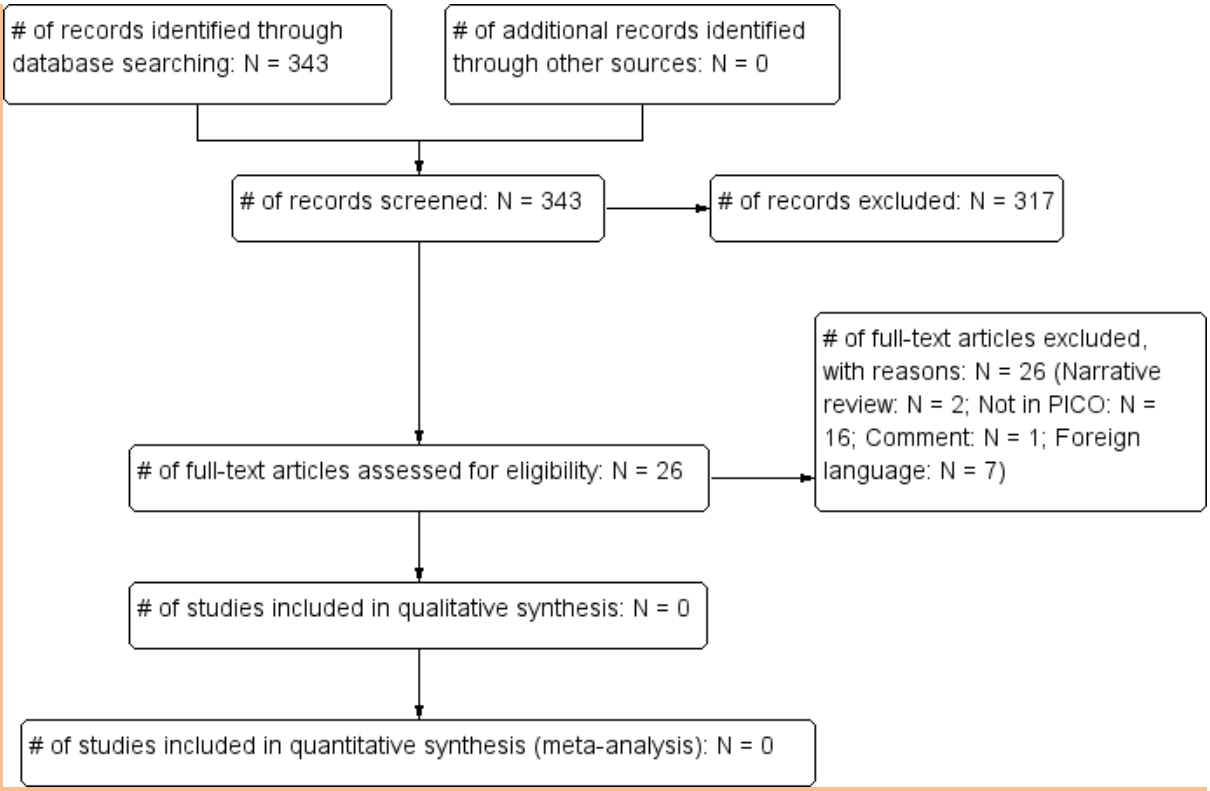
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	992	190	21/05/2013
Premedline	1980-2013	75	19	22/05/2013
Embase	1980-2013	1742	176	22/05/2013
Cochrane Library	1980-2013	182	2	22/05/2013
Psychinfo	1980-2013	1	0	22/05/2013
Web of Science (SCI & SSCI) and ISI Proceedings	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
Medline	5/2013-19/08/2014	23	2	19/08/2014
Premedline	5/2013-19/08/2014	73	5	19/08/2014
Embase	5/2013-19/08/2014	70	5	19/08/2014
Cochrane Library	5/2013-19/08/2014	92	0	19/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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) Corelation 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]. *Przeglad 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. & Pfannenberg, 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. & Gedgaudas-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) Hepatocellualar 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., Nejdet, 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., Trere, 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., Chammas, 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., Chammas, 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., Chammas, 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., Benvegnu, 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 alphafetoprotein. *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. & Eltoum, 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 coinfected 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 Daigahu 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., Belhadjbrik, 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 gallblader and biliary ducts - What is the value of CT, MRI, and magnetic resonance cholangiography?. [German]. *Chirurgische Gastroenterologie Interdisziplinar,* 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., Dhillon, 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., Heinernann, V. & Schafer, C. (2008) Interdisciplinary diagnosis of and therapy for cholangiocarcinoma. *Zeitschrift fur 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 Shokakibyo 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 biospy. *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]. *Intervirology,* 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., Veiseh, 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., Ladep, 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]. *Vnitrni Lekarstvi,* 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 gadoxetic 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

Shaalan, 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., Ioanitescu, 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]. *Intervirology,* 47: 199-208.
Narrative review

Tanaka, H., Nouso, 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., Benevegnu, 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., Pattanapraphapan, 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 diagonosis 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., Blanchi, 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-arterioportography (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

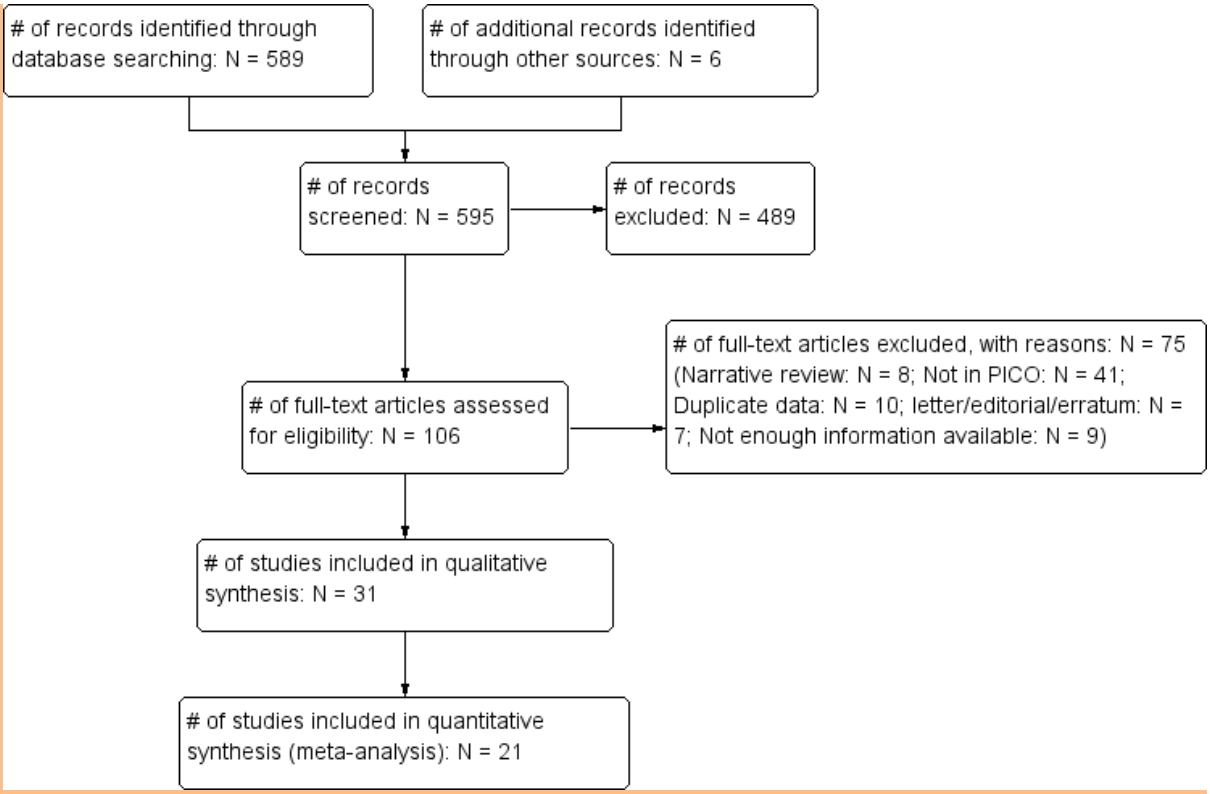
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All - 2012	3575	329	10/08/2012
Premedline	All - 2012	16	12	11/07/2012
Embase	All - 2012	4169	279	18/07/2012
Cochrane Library	All - 2012	725	5	18/07/2012
Psychinfo	All - 2012	12	4	18/07/2012
Web of Science (SCI & SSCI) and ISI Proceedings	All - 2012	1207	53	18/07/2012
Biomed Central	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
Medline	7/2012-13/08/2014	172	24	13/08/2014
Premedline	7/2012-13/08/2014	98	20	13/08/2014
Embase	7/2012-13/08/2014	655	31	13/08/2014
Cochrane Library	7/2012-13/08/2014	23	0	13/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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 (N = 56234)	2.4 (2.3-2.6)
Du Toit (2006)	Rectal bleeding	All patients (N = 265)	5.7 (3.3-9.4)
Ellis (2005),	Rectal bleeding	All patients (N = 319)	3.4 (1.8-6.3)
Fijten (1995),	Rectal bleeding	All patients (N = 269)	3.3 (1.6-6.5)
Heintze (2005)	Rectal bleeding	All patients (N = 400)	4.3 (2.6-6.9)
Helfand (1997)	Rectal bleeding	All patients (N = 201)	6.5 (3.6-11.1)
Hippisley-Cox (2012)	Rectal bleeding	All patients (N = 28952)	2.9 (2.7-3.1)
Jones (2007, at 6 months)	Rectal bleeding	All patients (N = 15289)	1.7 (1.5-1.9)
Jones (2007, at 3 years)	Rectal bleeding	All patients (N = 15289)	2.2 (2-2.5)
Mant (1989)	Rectal bleeding	All patients (N = 145)	11.7 (7.2-18.4)
Metcalf (1996)	Rectal bleeding	All patients (N = 99)	8.1 (3.8-15.8)
Nørrelund (1996)	Rectal bleeding	All patients (N = 417)	13.7 (10.6-17.4)
Panzuto (2003)	Rectal bleeding	All patients (N = 114)	15.8 (9.9-24.1)
Parker (2007)	Rectal bleeding	All patients (N = 29007)	2.2 (2.1-2.4)
Robertson (2006)	Rectal bleeding	All patients (N = 604)	3.6 (2.4-5.6)
Wauters (2000)	Rectal bleeding	All patients (N = 386)	7 (4.7-10.1)
Bellentani (1990)	Abdominal pain	All patients (N = 254)	3.9 (2-7.3)
Collins (2012)	Abdominal pain	All patients (N = 245989)	0.5 (0.5-0.5)
Hippisley-Cox (2012)	Abdominal pain	All patients (N = 125237)	0.7 (0.6-0.7)
Panzuto (2003)	Abdominal pain	All patients (N = 223)	13.5 (9.4-18.8)
Collins (2012)	Anaemia	All patients (N = 18125)	1.7 (1.5-1.9)
Droogendijk (2011)	Anaemia	All patients (N = 287)	8.4 (5.5-12.3)
Farrus Palou (2000)	Anaemia	All patients (N = 58)	3.4 (0.6-13)
Hippisley-Cox (2012)	Anaemia	All patients (N = 16823)	1.5 (1.3-1.7)
Lucas (1996)	Anaemia	All patients (N = 130)	6.9 (3.4-13.1)
Panzuto (2003)	Anaemia	All patients (N = 69)	40.6 (29.1-53.1)
Stellon (1997)	Anaemia	All patients (N = 26)	7.7 (1.3-26.6)

Yates (2004)	Anaemia	All patients (N = 431)	8.6 (6.2-11.7)
Collins (2012)	Weight loss	All patients (N = 28289)	0.8 (0.7-0.9)
Hippisley-Cox (2012)	Weight loss	All patients (N = 14007)	0.8 (0.7-0.9)
Panzuto (2003)	Weight loss	All patients (N = 42)	35.7 (22-52)
Hallissey (1990)	Dyspepsia	All patients	0.5 (0.3-0.9) 14/2585
Heikkinen (1995)	Dyspepsia	All patients	0/400
Meineche-Schmidt (2002)	Dyspepsia	All patients	1.14 (0.7-1.9)

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)
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)
Hippisley-Cox (2012)	Loss of appetite	All patients	0.9 (0.6-1.2)
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)
Muris (1995)	Non-acute abdominal complaints	All patients	0.43 (0.1-1.2)
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)
Hamilton (2008)	Haemoglobin 10-12.9 g dl^{-1}	All patients	0.3 (0.2-0.3)
Hamilton (2005)	Haemoglobin < 10 g dl^{-1} (reported once)	All patients	2.3 (1.6-3.1)
Hamilton (2008)	Haemoglobin < 9.9 g dl^{-1}	All patients	2 (1.7-2.3)
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 pattern rectal bleeding and change in bowel habit	All patients	26.85 (19-36.4) 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)
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)
Robertson (2006)	Rectal bleeding and no 'increased frequency/loose motions'	All patients	2.8 (1.4-5.5)
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/	1.97 (0.6-5.3) 4/203

		questionnaire data	
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)
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)
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)
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:	All patients	9 (NR)

	Blood seen on paper		
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
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)
Metcalf (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)
Fijten (1995)	Rectal bleeding: Others or combinations apart from “blood on stool or mixed with stool	All patients	1 (NR) Total positives N = 122

	only"		
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)
Robertson (2006)	Rectal bleeding: Blood neither dark nor mixed with stool	All patients	1.9 (0.7-4.7)
Robertson (2006)	Rectal bleeding: Not 'blood neither dark nor mixed with stool'	All patients	4.9 (3-7.9)
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)
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)
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)
Nørrelund (1996)	New onset or changed pattern rectal bleeding and no abdominal pain	All patients	11.7 (8.2-16.3)
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)
Fijten (1995)	Rectal bleeding and weight loss	All patients	10 (NR) Total positives N = 42
Hamilton (2005)	Rectal bleeding and weight loss	All patients	4.7 (NR)
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)
Metcalf (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)
Nørrelund (1996)	New onset or changed pattern rectal bleeding and no weight loss	All patients	13.07 (9.6-17.5)
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	All patients	14 (NR)

	anal itch		
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)
Robertson (2006)	Rectal bleeding and haemorrhoids and bright red blood not mixed with stools	All patients	1.9 (0.5-5.8)
Robertson (2006)	Rectal bleeding and haemorrhoids and no other symptoms except bright non-mixed bleeding	All patients	3.3 (0.9-10.1) 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)
Robertson (2006)	Rectal bleeding and no 'haemorrhoids and bright red blood not mixed with stools'	All patients	4.5 (2.8-7.2)
Robertson (2006)	Rectal bleeding and no 'haemorrhoids and no other symptoms except bright non-mixed bleeding'	All patients	3.8 (2.4-6.1)
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	All patients	0 (0-4.8) Total positives N = 96

	bleeding		
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)
Metcalf (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 syndrome	All patients	0 (0-4.8) 0/96
Robertson (2006)	Rectal bleeding and no history of irritable bowel syndrome	All patients	4.4 (2.8-6.7)
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)
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 (NR)
		Patients 55-64 years	1.3 (NR)
		Patients 65-74 years	9.5 (NR)
		Patients ≥ 75 years	7.9 (NR)
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)
		Patients 70-79 years	34.12 (24.4-45.3)
		Patients 80+ years	20 (7.6-41.3)
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)
		Patients 55-64 years	2.8 (2.3-3.3)
		Patients 65-74 years	4.3 (3.7-5)
		Patients 75-84 years	5.5 (4.7-6.3)
		Patients ≥ 85 years	3.7 (2.8-4.8)
Robertson (2006)	Rectal bleeding	Patients < 50 years	1.1 (0.3-3.5)

		Patients 50-69 years	4.8 (2.6-8.7)
		Patients ≥ 70 years	7.5 (3.5-14.6)
Wauters (2000)	Rectal bleeding	Patients < 50 years	0.7 (0-4.9)
		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)
Jones (2007)	Rectal bleeding at 6 months	Men (all ages)	1.8 (15-2.2)
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)
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)
Robertson (2006)	Rectal bleeding	Men (all ages)	4.8 (2.7-8.2)
Jones (2007)	Rectal bleeding at 3 years	Men < 45 years	0.07 (0.01-0.27)
		Men 45-54 years	1.56 (1-2.31)
		Men 55-64 years	3.38 (2.47-4.51)
		Men 65-74 years	4.8 (3.65-6.17)
		Men 75-84 years	7.74 (5.78-10.1)
		Men ≥ 85 years	5.1 (2.23-9.79)
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)
Hippisley-Cox (2012)	Change in bowel habit	Men 30-84 years	2.8 (1.8-4.2)
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)
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)
Collins (2012)	Weight loss	Men 30-84 years	1 (0.8-1.1)
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	Men 60-69 years	12 (3.1-37)
		Men 70-79 years	16 (6.3-35)

	deficiency**	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)
Yates (2004)	Anaemia	Men > 20 years	18.2 (12.6-25.4)
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)
Jones (2007)	Rectal bleeding at 6 months	Women (all ages)	1.5 (1.3-1.8)
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)
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)
Robertson (2006)	Rectal bleeding	Women (all ages)	2.7 (1.3-5.3)
Jones (2007)	Rectal bleeding at 3 years	Women < 45 years	0.22 (0.08-0.47)
		Women 45-54 years	0.63 (0.27-1.24)
		Women 55-64 years	2.75 (1.9-3.84)
		Women 65-74 years	2.42 (1.62-3.48)
		Women 75-84 years	7.2 (5.63-9.06)
		Women > 85 years	2.79 (1.45-4.82)
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)
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 graph)	Women < 60 years	0.1 (0.1-0.1)
		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)
Collins (2012)	Weight loss	Women 30-84 years	0.6 (0.5-0.7)
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 dl^{-1} + indicators of iron deficiency	Women 30-59 years	0.2 (0.1-0.4)
		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)
Collins (2012)	Anaemia	Women 30-84 years	1.3 (1.1-1.5)
Yates (2004)	Anaemia	Women > 50 years	3.2 (1.6-6.3)
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	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). Inclusion criteria: 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 judges by the GP), between January 1987 and March 1988. Exclusion criteria: Patients with acute abdomen, acute gastroenteritis or a clear cut diagnosis of upper gastrointestinal tract disease (gastritis, oesophagitis, peptic ulcer, or dyspepsia). Clinical setting: Primary/secondary 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	Recurrent abdominal pain or intestinal problems (as judges 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	A total of 2135540 patients were identified from 364 practices.

characteristics and setting	Symptoms: 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). Incident cases of colorectal cancer during the 2-year follow up period: N = 3712 (2036 men, 1676 women). 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 (see below), the date of the first recorded onset within the study period. Exclusion criteria: 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
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	**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	The is ***very large, if not complete, overlap*** 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. Inclusion criteria: 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). Exclusion criteria: Patients with a known history of iron-deficiency anaemia in the previous 2 years, a history of gastrointestinal malignancy or congenital haemoglobinopathy. Clinical setting: 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. Inclusion criteria: Patients aged ≥ 45 years reporting new onset rectal bleeding with or without diarrhoea, during a 10-year period. 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	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	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). Inclusion criteria: 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. 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	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)	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	

1

2 **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	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. Inclusion criteria: 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). 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	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. Inclusion criteria: 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. Exclusion criteria: 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. Clinical setting: Primary care, 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	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 and old patients with investigated dyspepsia. Inclusion criteria: All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia Exclusion criteria: None listed. Clinical setting: 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	**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)	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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	**Yes**
For diagnostic case-control studies: The groups were comparable at baseline, including all	**Yes**

major confounding and prognostic factors?	
Could the selection of patients have introduced bias?	**High risk**
B. Concerns regarding applicability	
Patient characteristics and setting	Cases: 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. Controls: 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. Inclusion criteria: 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. Exclusion criteria: 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. 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	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**
For diagnostic case-control studies: 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		

1

2 **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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?		**Yes**
For diagnostic case-control studies: 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: 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. 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) Controls: 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 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) Inclusion criteria: 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). 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	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**
For diagnostic case-control studies: 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	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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	**Yes**
For diagnostic case-control studies: 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: 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 = 626/11.4%; Obesity: N = 510/9.3%. Controls: 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. 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 ≥ 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%. Inclusion criteria: 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). 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	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: ≥ 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. < 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.
Were the index test results interpreted without knowledge of the results of the reference standard?	**Yes**
For diagnostic case-control studies: 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 characteristics and setting	N = 400; 152 males, 248 females; 77% were > 44 years. Inclusion criteria: 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). Exclusion criteria: 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 Clinical setting: 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 phosphatise, 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		**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	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). Inclusion criteria: 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. Exclusion criteria: ≤ minimum level of data entry for each patient by the participating physician. Clinical setting: 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 where 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	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. Inclusion criteria: 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. Exclusion criteria: Patients with no data available at 6 and 12 months follow up. Clinical setting: Walk-in and general medical clinics of the Veterans Affairs Medical Center, Palo Alto, California
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 (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	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). Symptoms: 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). Incident cases of colorectal cancer during the 2-year follow up period: N = 2603 (1562 colon and 1041 rectum). Inclusion criteria: 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. *The relevant data for the present purposes is only available for the validation cohort, therefore only information pertaining to these patients will be reported.* Exclusion criteria: 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
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)

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. Haemoptysis: 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. Dysphagia: 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. Rectal bleeding: 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. Inclusion criteria: 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. Exclusion criteria: 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. Clinical setting: 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: Haematuria: Urinary tract neoplasms, including neoplasms of the urethra, bladder, ureter, and kidney but excluding neoplasms of the prostate and other reproductive organs. Haemoptysis: Respiratory tract neoplasms. Dysphagia: Oesophageal neoplasms. Rectal bleeding: 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: Haematuria: 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. Dysphagia: 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. *Estimates based on the pre-specified cancers may be thus conservative for these symptoms.* Haemoptysis: Extension of the diagnostic criteria yielded 6 additional cancers. Rectal bleeding: Extension of the diagnostic criteria yielded 2 additional cancers.	

1

1 **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	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 Inclusion criteria: 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. Exclusion criteria: Patients with colorectal cancer, or a diagnosis of colorectal 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	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. Inclusion criteria: 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. Exclusion criteria: None listed. Clinical setting: UK primary and beyond	
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	N = 145; 77 males, 68 females; mean age (SD, range) = 57.7 (11.9, 40-95) years.

	Inclusion criteria: All patients aged ≥ 40 years who consulted the GP with rectal bleeding. Exclusion criteria: 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 melenic, or (5) who refused investigation. Clinical setting: General practice in New South Wales, Australia.
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.

1

1 **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 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.

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 characteristics and setting	N = 99, 42 males, 57 females; median age (range) = 58 (40-86) years. Inclusion criteria: Patients aged > 40 years presenting with rectal bleeding of recent onset (< 1 year). Exclusion criteria: Patients refusing colonoscopy. 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	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	

1

2 **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. Inclusion criteria: Patients who during a 3-month period consulted one of the participating GPs for abdominal complaints. Exclusion criteria: Patients aged < 18 years and patients with a condition necessitating immediate referral or admission to hospital. Clinical setting: 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	Follow up for 15 months.

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	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	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. Inclusion criteria: 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. Exclusion criteria: None listed. 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	**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?	**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. Inclusion criteria: Patients aged ≥ 40 years who between August 1989 and October 1992 presented to the participating GPs with rectal bleeding. Exclusion criteria: Known inflammatory bowel disease, colonic polyps, polyposis coli, colorectal cancer, predisposition to haemorrhage, and melaena stool. Clinical setting: 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	

1

2 **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. Inclusion criteria: 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. Exclusion criteria: Patients with a known malignancy or a malignancy detected within 2 weeks of deep vein thrombosis diagnosis. Clinical setting: 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.	

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. Inclusion criteria: 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]. Exclusion criteria: Patients with previous diagnoses of colorectal disorders or a recent large bowel examination. Clinical setting: 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		**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)	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	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. Inclusion criteria: 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. Exclusion criteria: Previous record of colorectal cancer (for patients presenting with rectal bleeding) and endometrial cancer (for patients presenting with post-menopausal bleeding) 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	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	N = 604, 273 males, 331 females; median age (range) = 52 (18-97) years. Inclusion criteria: Patients who between September 1996 and June 1999 presented to the participating GPs with rectal bleeding. Exclusion criteria: Patients with ulcerative colitis, current warfarin treatment or missing data for the kind of bleeding. 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	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 characteristics and setting	N = 26; 5 males, 21 females; age range = 51-87 years. Inclusion criteria: All patients aged > 50 years found to have iron deficiency anaemia between January 1989 and March 1994. Exclusion criteria: None listed. Clinical setting: 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. Inclusion criteria: All patients who in 1993-4 presented with rectal bleeding. Exclusion criteria: None listed. Clinical setting: 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	18-30 months follow up.

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	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		

1

2 **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. Inclusion criteria: 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. Exclusion criteria: History of anaemia within previous 12 months, known haematological abnormalities (e.g., haemoglobinopathy), unavailable notes at follow up. *That is, patients with a history of cancer were not excluded.* 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 ≤ 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.

Metcalf, 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]. *Vnitrni Lekarstvi,* 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., Greenamyer, 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
Barraclough, 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]. *Pediatria 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. & 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

Brandenbarg, 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 practioner - 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., Mpofu, 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., Neirot, 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 featurers 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 Isere 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., Karczmarski, 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 extact 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., Nogueras, 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
Kozlowska, E., Szewczyk, M. T., Banaszkiewicz, Z., Jawien, A., Cierzniakowska, 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. & Szmitkowski, 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 Ko 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.
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

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., Lawence, 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 Shokakibyo 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. & Sjodahl, 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 Przeglad 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
Osoba, 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., Jeen, 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., Findler, 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. & Kouloulias, 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 pathogical 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 irondeficiency 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-Torrejon, 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
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

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., Iriondo, 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., 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

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 Interdisziplinar,* 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 >=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 Steenbergen, 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
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
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
Tolwinska, A., Kisielewski, R. & Laudanski, P. (2012) Chronic pelvic pain in menopausal women. *Przeglad 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. *Bristish 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., Bjelogrlic, 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., Bjelogrlic, 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 fur Arztliche Fortbildung und Qualitatssicherung,* 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 fur 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. & Ragunath, 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
Medline	1980-2013	1321	136	10/01/2013
Premedline	1980-2013	35	4	14/01/2013
Embase	1980-2013	896	132	14/01/2013
Cochrane Library	1980-2013	116	3	14/01/2013
Psychinfo	1980-2013	4	1	14/01/2012
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	79	21	14/01/2013
Biomed Central	1980-2013	68	0	14/01/2013

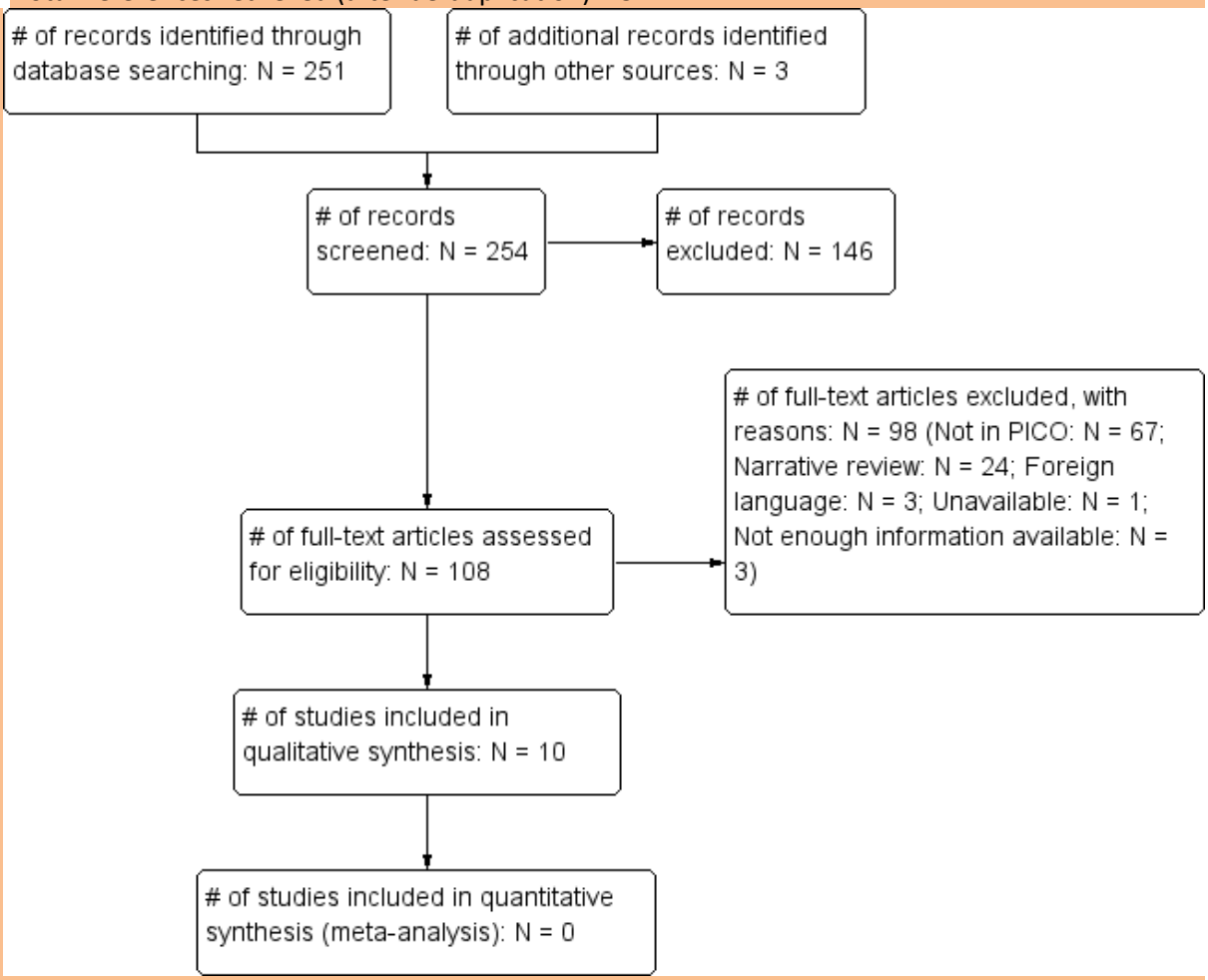
Total References retrieved (after de-duplication): 226

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	2013-13/08/2014	48	9	13/08/2014
Premedline	2013-13/08/2014	37	4	13/08/2014
Embase	2013-	131	26	13/08/2014

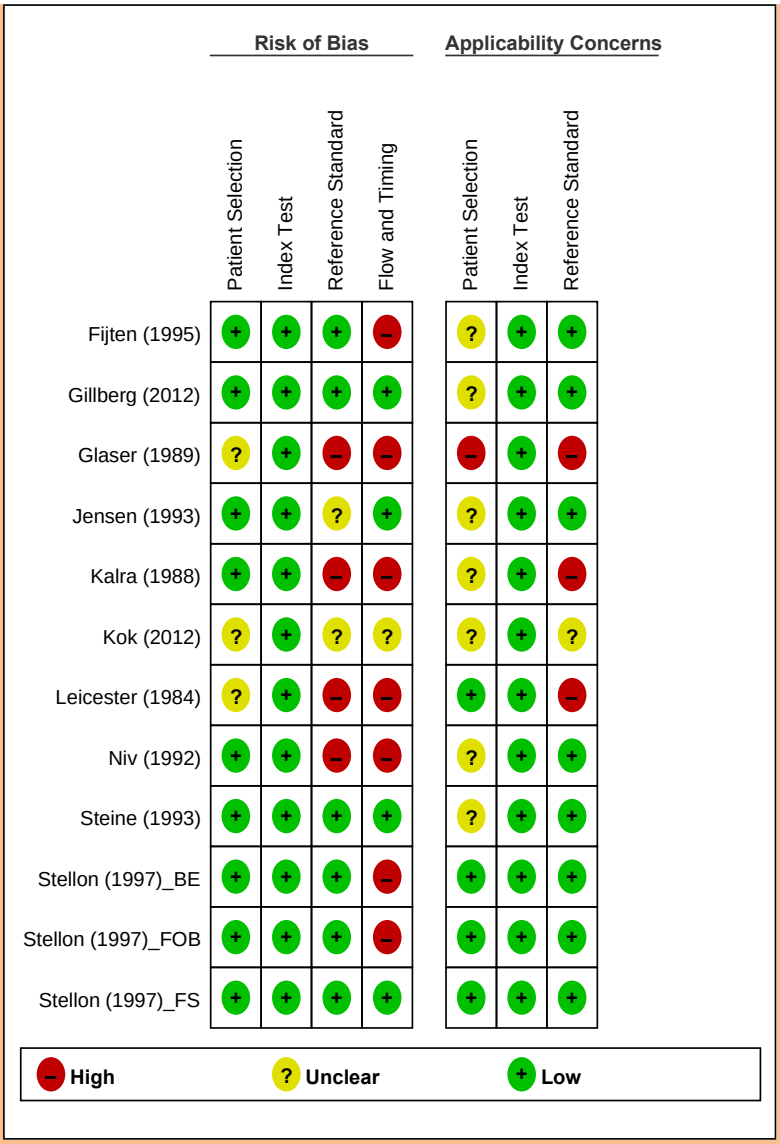
	13/08/2014			
Cochrane Library	2013-13/08/2014	15	1	13/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	2013-13/08/2014	118	1	13/08/2014

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.



Study results

Table 1: Colorectal cancer: Faecal occult blood

Study	Test	Prevalence	Sensi-tivity	Speci-ficity	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-by2 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 abnormnal 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-by2 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%

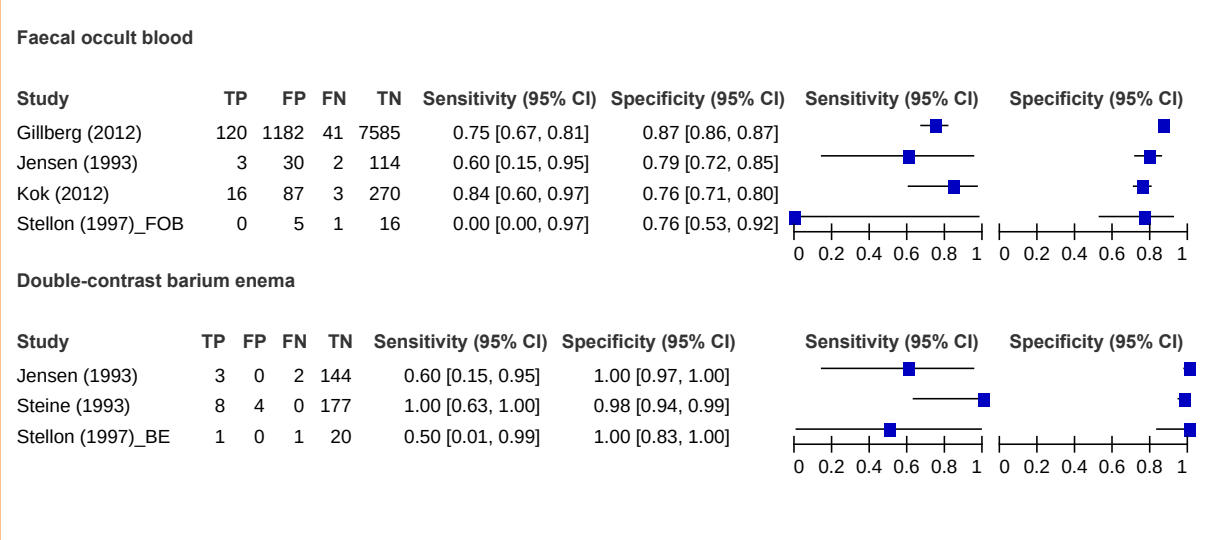
The data were not meta-analysed due to concerns about differences in the tests employed and missing data. TP = true positives, FP = false positives, TN = true negatives, FN = false negatives.

Table 3: Colorectal cancer: Double-contrast barium enema

Study	Test	Prevalence	Sensi-tivity	Speci-ficity	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



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	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. Inclusion criteria: 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. Exclusion criteria: 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. Clinical setting: Primary care, 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	Faecal occult blood (Haemoccult test, 3 X, with a diet low of perioxidase 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. Inclusion criteria: All patients who between 2000-2005 had undergone faecal occult blood testing in one of the participating primary care centres. Exclusion criteria: Repeat faecal occult blood testing for the same individual. Clinical setting: 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 (Haemoccult 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 ademona 984), colorectal cancer dioagnosis > 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. Inclusion criteria: 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. Exclusion criteria: None listed. Clinical setting: 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. Inclusion criteria: All patients referred with symptoms of colorectal disease by general practitioners to the Department of Radiology, Varberg Hospital, Sweden, for a double-contrast enema. Exclusion criteria: None listed. Clinical setting: 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**
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? All test		**Yes**
Could the patient flow have introduced bias? All tests		**Low risk**
NOTES		

Kalra (1988)

PATIENT SELECTION		
A. risk of bias		
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**
B. Concerns regarding applicability		
Patient characteristics and setting	N = 541; male:female ratio = 35:65. Abdominal pain was the commonest cause of open access referreal followed by diarrhoea, rectal bleeding and constipation. Inclusion criteria: All patients referred for fibresigmoidoscopy for the first time during 1982-6. Open access referreals were defined as patients seen for the first time during the procedure and in whom no examination or investigations had previously been undertaken. Exclusion criteria: Hospital inpatients, patients attending the outpatient department for colorectal symptoms in whom results of other investigations were available. Clinical setting: 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. Inclusion criteria: 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 eldeely, or findings at physical examination suggestive or organic bowel disease (palpable abdominal or rectal mass). Exclusion criteria: Patients aged < 18 years, unable to give informed consent, previously diagnosed with organic bowel disease, or positive on triple faeces test (testing for intestinal paracites) not requiring endoscopy. Clinical setting: 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)/sigmoidoiscopy (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	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. Inclusion criteria: Patients aged > 40 years presenting in general practice with any abdominal or bowel complaints. Exclusion criteria: None listed. Clinical setting: 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	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)	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.
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

1

2 **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). Inclusion criteria: All patients referred for open-access flexible sigmoidoscopy by general practitioners. Exclusion criteria: Bad state of health, referral error. Clinical setting: 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 negitive 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	
A. risk of bias	
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**
B. Concerns regarding applicability	
Patient characteristics and setting	N = 190; age range = 45-79 years. Inclusion criteria: Random sample (9%) of patients referred by GPs for double-contrast barium enema at the Central Roentgen Institute. Exclusion criteria: Patients not aged 45-79. Clinical setting: Norwegian roentgen institute.
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	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. Inclusion criteria: 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. Exclusion criteria: None listed. Clinical setting: 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 faecel 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: I23.
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., Greenamyer, 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., 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

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

Castioglione, G., Pacini, F., Palli, D., Fucini, C., Ciani, P., D'Albasio, G. & Falorni, P. (1987) Haemoccult test and a self-administered quistionnaire in the early diagnosis of colorectal cancer. *Italian Journal of Gastoenterology,* 19: 83-86.
Mixed symptomatic/asymptomatic population; cannot extract the information fopr symptomatixc patients only; large number did not receive referecne 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 laiety 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 extact 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. & Prynn, 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., 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
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 fibreoptic 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., Ilangovan, 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 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.
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 Bristish 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. & Ekbom, 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., Jeen, 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

Petruzziello, 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., Filliettaz, 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]. *Eksperimental'Naia i Klinicheskaia Gastroenterologiia.(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., Iriondo, 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., Nogueras, 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 Interdisziplinar,* 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 >= 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 Steenbergen, 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. (2222) [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?
Tolwinska, A., Kisielewski, R. & Laudanski, P. (2012) Chronic pelvic pain in menopausal women. *Przeglad 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

Viiala, 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 fibreoptic 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 usefullness and the accuracy of GP's refferals. [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

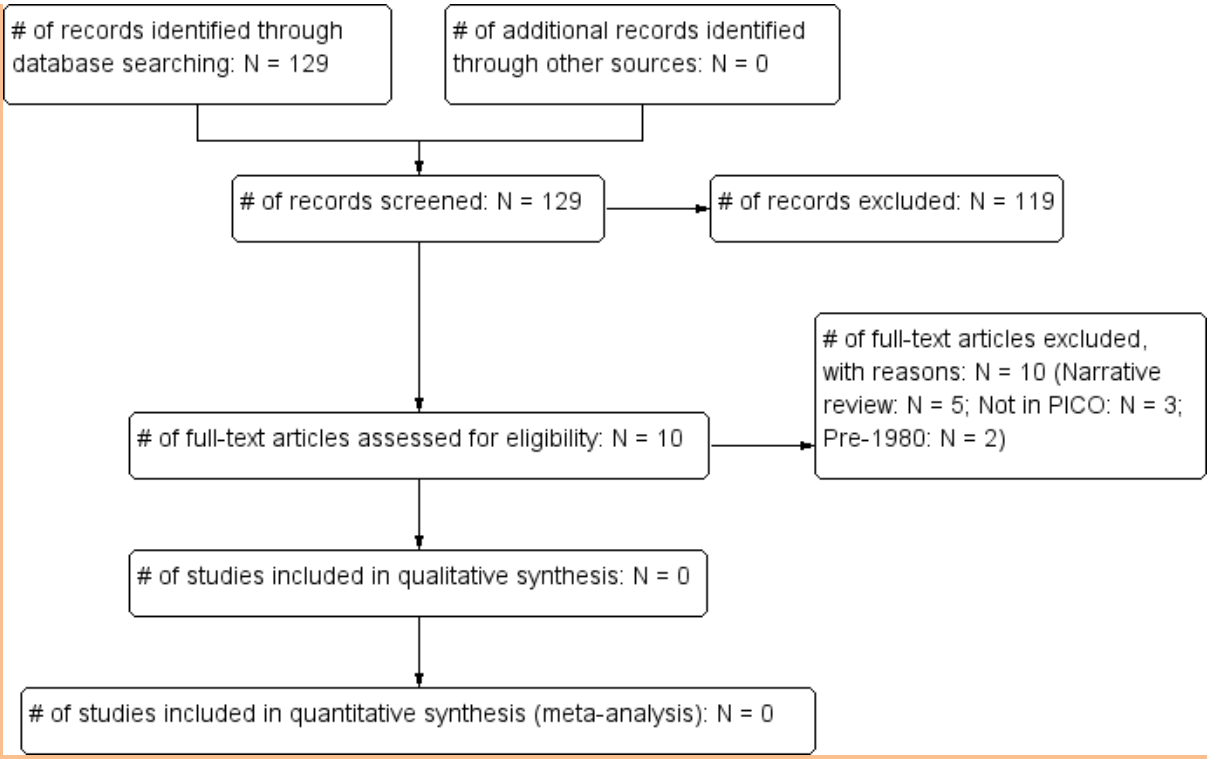
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	217	99	04/09/2012
Premedline	All-2012	8	1	04/09/2012
Embase	All-2012	264	61	04/09/2012
Cochrane Library	All-2012	132	2	12/09/2012
Psychinfo	All-2012	6	0	12/09/2012
Web of Science (SCI & SSCI) and ISI Proceedings	All-2012	85	11	12/09/2012
Biomed Central	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
Medline	9/2012-26/08/2014	7	0	26/08/2014
Premedline	9/2012-26/08/2014	38	0	26/08/2014
Embase	9/2012-26/08/2014	61	1	26/08/2014
Cochrane Library	9/2012-26/08/2014	58	0	26/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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 Schwartsmann, 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 [et[3], 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., Nogueras, 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

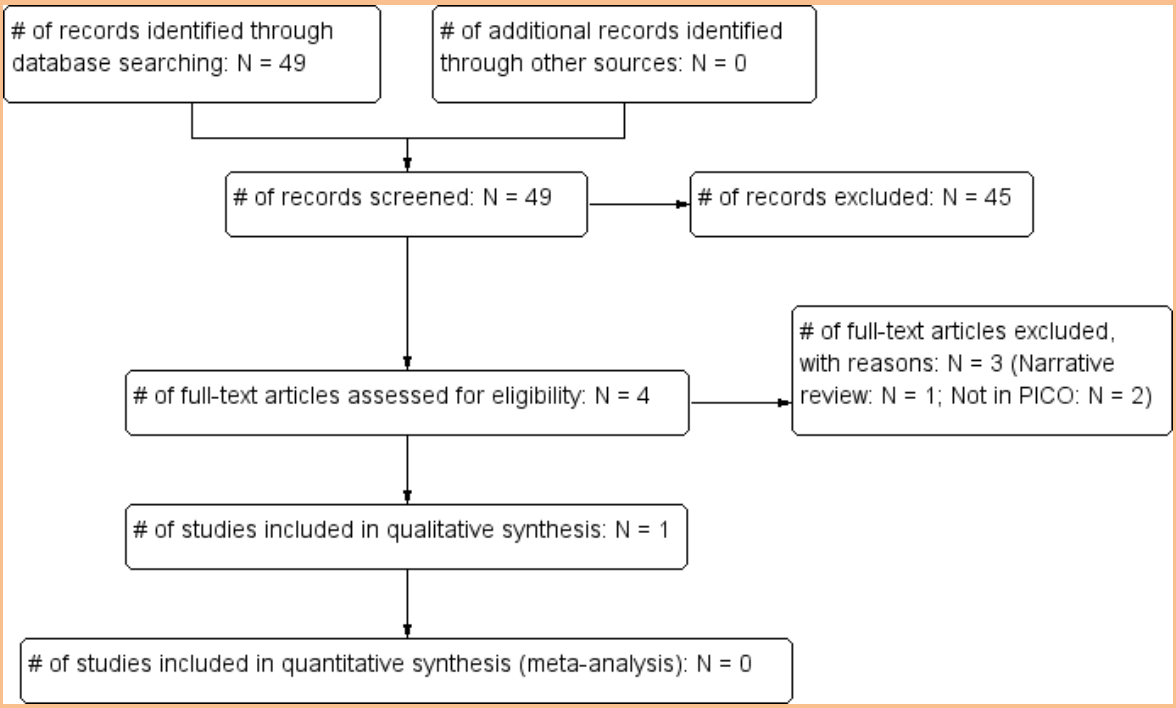
		found	retrieved	search
Medline	1980-2013	146	19	11/06/2013
Premedline	1980-2013	19	2	11/06/2013
Embase	1980-2013	196	29	12/06/2013
Cochrane Library	1980-2013	57	0	12/06/2013
Psychinfo	1980-2013	5	0	11/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	93	9	13/06/2013

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
Medline	6/2013-26/08/2014	5	0	26/08/2014
Premedline	6/2013-26/08/2014	13	1	26/08/2014
Embase	6/2013-26/08/2014	38	4	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	12	0	26/08/2014

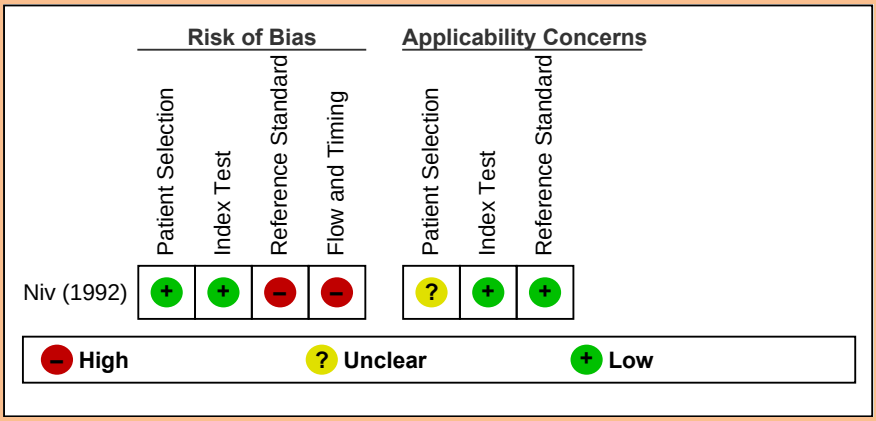
Total References retrieved (after de-duplication): 5



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.



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). Inclusion criteria: All patients referred for open-access flexible sigmoidoscopy by general practitioners. Exclusion criteria: Bad state of health, referral error. Clinical setting: 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**

NOTES	

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

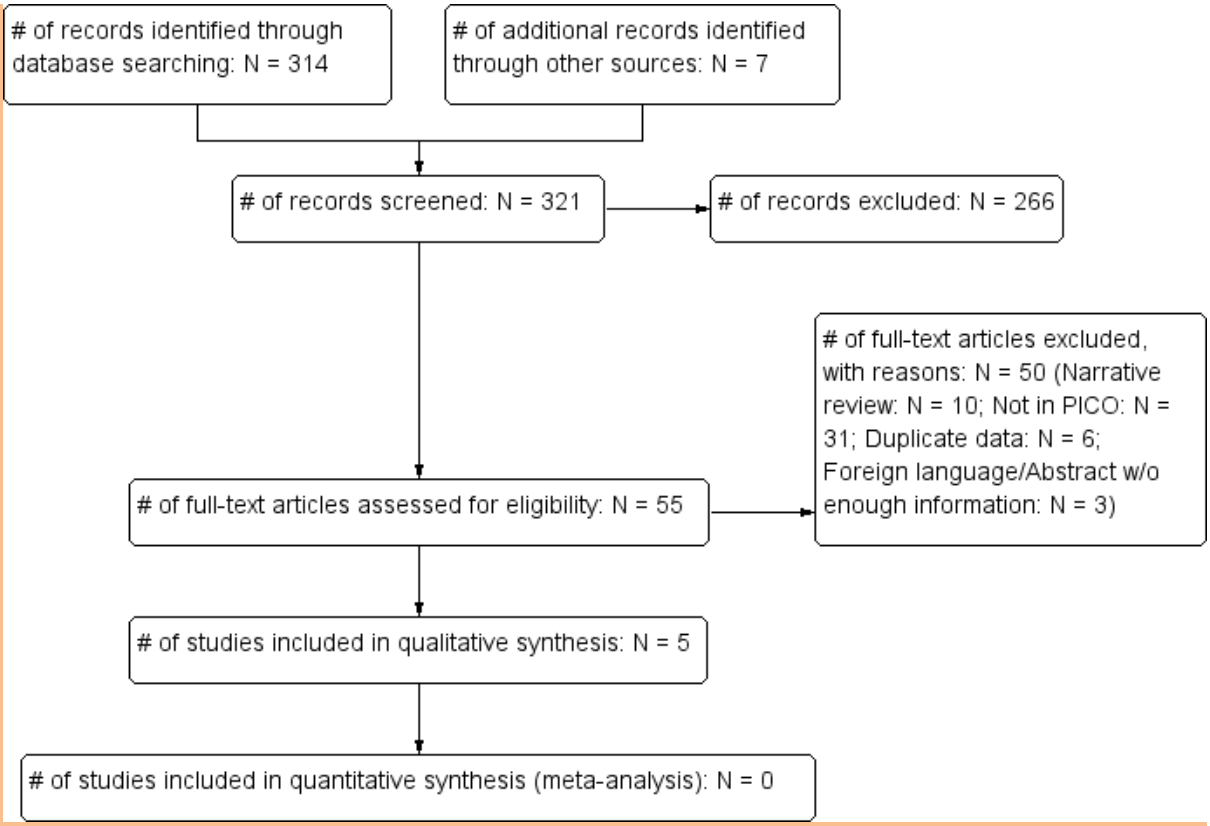
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-4/2013	1361	122	22/04/2013
Premedline	1980-4/2013	275	24	23/04/2013
Embase	1980-4/2013	1776	151	25/04/2013
Cochrane Library	1980-4/2013	426	4	25/04/2013
Psychinfo	1980-4/2013	385	23	23/04/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-4/2013	1541	84	26/04/2013

Total References retrieved (after de-duplication): 284

Update Search

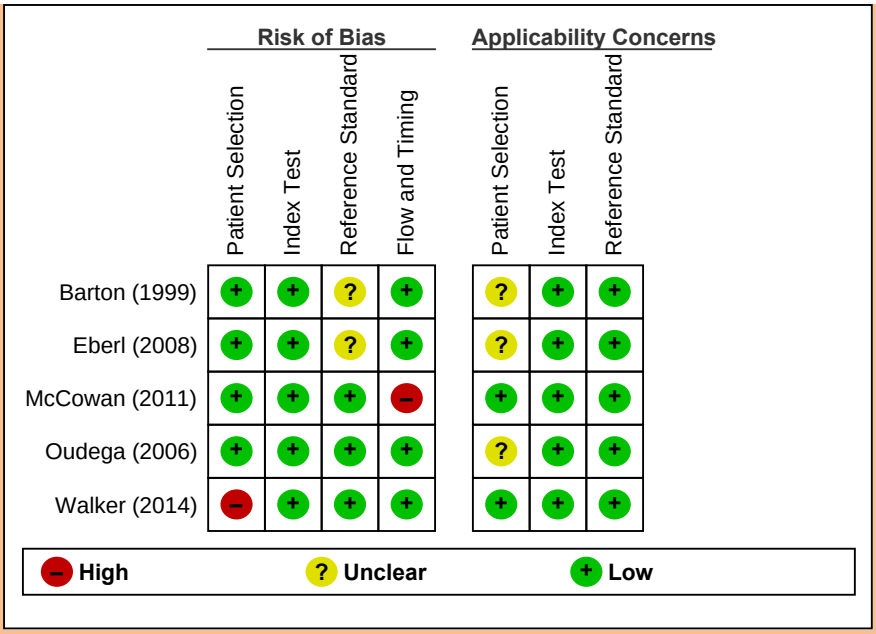
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	4/2013-12/08/2014	145	9	12/08/2014
Premedline	4/2013-12/08/2014	172	11	12/08/2014
Embase	4/2013-12/08/2014	578	13	12/08/2014
Cochrane Library	4/2013-12/08/2014	138	0	12/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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.



Study results

Table 1: Breast cancer: Single symptoms

Study	Symptom(s)	Patient group	Positive predictive value (95% CI)% Prevalence
Barton (1999) *Episode-based analysis*	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) *Episode-based analysis*	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) *Episode-based analysis*	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) *Episode-based analysis*	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) *Episode-based analysis*	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) *Episode-based analysis*	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) *Episode-based analysis*	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) *Episode-based analysis*	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) *Episode-based analysis*	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) *Episode-based analysis*	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	6.5 (NR)

	pain	years	
Walker (2014)	Breast lump and breast pain	Women aged 70+ years	> 5 (NR)
Barton (1999) *Episode-based analysis*	Breast pain and skin or nipple change	Women aged 40-79 years	0 (0-26.8) 0/14 *episodes in 372 women*
Barton (1999) *Episode-based analysis*	Breast pain and breast lumpiness	Women aged 40-79 years	0 (0-43.9) 0/7 *episodes in 372 women*
Barton (1999) *Episode-based analysis*	Breast mass and skin or nipple change	Women aged 40-79 years	100 (5.5-100) 1/1 *episodes in 372 women*
Barton (1999) *Episode-based analysis*	Breast mass and breast lumpiness	Women aged 40-79 years	20 (10.5-70.1) 1/5 *episodes in 372 women*
Barton (1999) *Episode-based analysis*	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 'irrregularly 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	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. Inclusion criteria: "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 ion 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." Exclusion criteria: 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). Clinical setting: Health maintenance organisation, 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	Patient symptoms were classified as follows: 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) Physical examination findings were recorded by using the same five categories. More than one symptom/finding could be documented. "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

	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**
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)	"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." 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 *last* 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.
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	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	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. 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.

1

1 **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	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. Inclusion criteria: 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 *International Classification of Primary Care (ICPC)*. The term *encounter* 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." Exclusion criteria: None reported. Clinical setting: Dutch primary care.
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. Inclusion criteria: "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." Exclusion criteria: "Patients were excluded if the consultation was related to issues around cosmetic surgery or breastfeeding problems." 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	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		

1

2 **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. Inclusion criteria: 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. Exclusion criteria: Patients with a known malignancy or a malignancy detected within 2 weeks of deep vein thrombosis diagnosis. Clinical setting: 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.

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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	**Yes**
For diagnostic case-control studies: 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: 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. Controls: 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. Inclusion criteria: 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. Exclusion criteria: 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. Clinical setting: 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	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 ≥1% of the cases or controls (this was invariably cases). We assembled a list of plausible laboratory abnormalities *a priori* 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**
For diagnostic case-control studies: 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 practictioners' 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]. *Bratislavske Lekarske 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-Lamptey, 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 Print,* 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., Firneno, 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., 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

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 extact 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]. *Przeglad 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., Mccready, 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/IS00 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., Marklun, 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

Meechan, 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

Meechan, 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., Haghighat, 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) T *he 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., 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
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., Wheeller, 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

Psyrri, 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 fur Arztliche Fortbildung und Qualitatssicherung,* 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 >=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

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

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
Torring, 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. (1111) 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

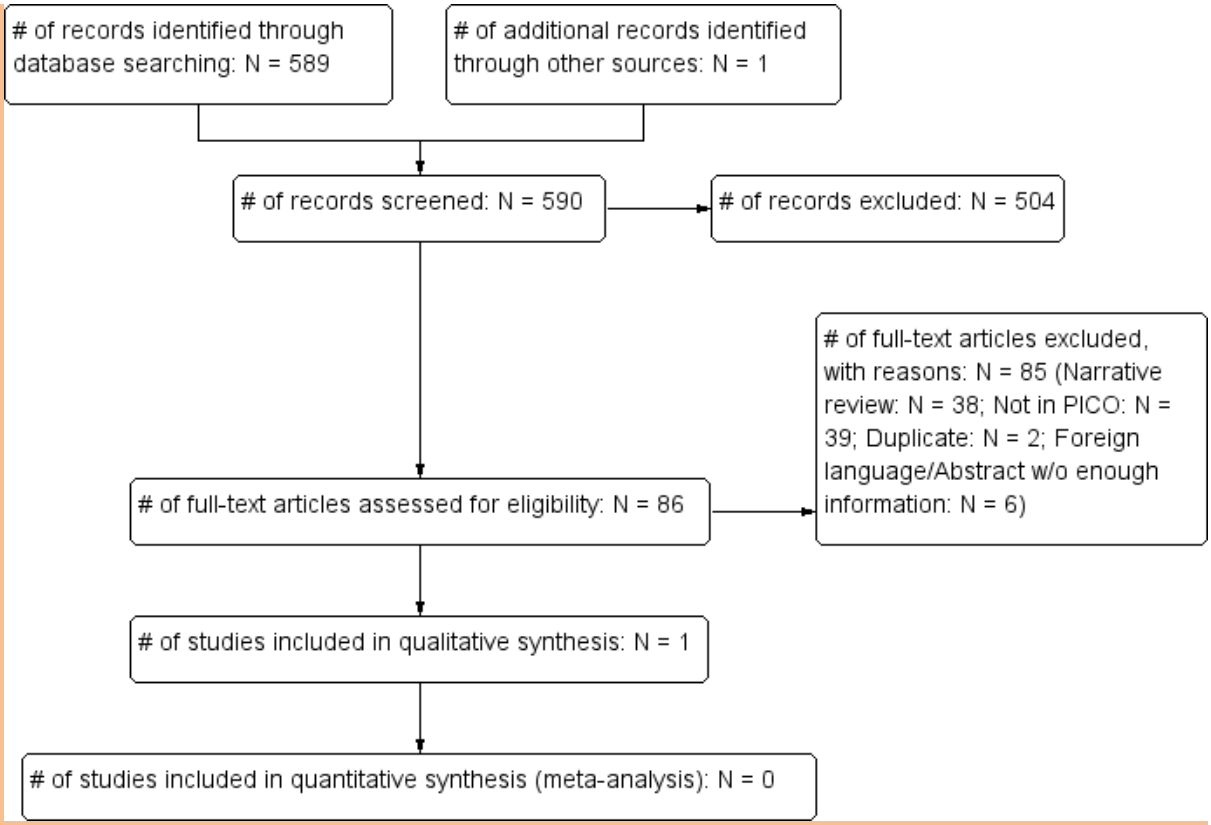
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-4/2013	1663	326	24/04/2013
Premedline	1980-4/2013	350	45	24/04/2013
Embase	1980-4/2013	1509	290	25/04/2013
Cochrane Library	1980-4/2013	274	22	25/04/2013
Psychinfo	1980-4/2013	67	4	24/04/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-4/2013	164	14	25/04/2013

Total References retrieved (after de-duplication): 553

Update Search

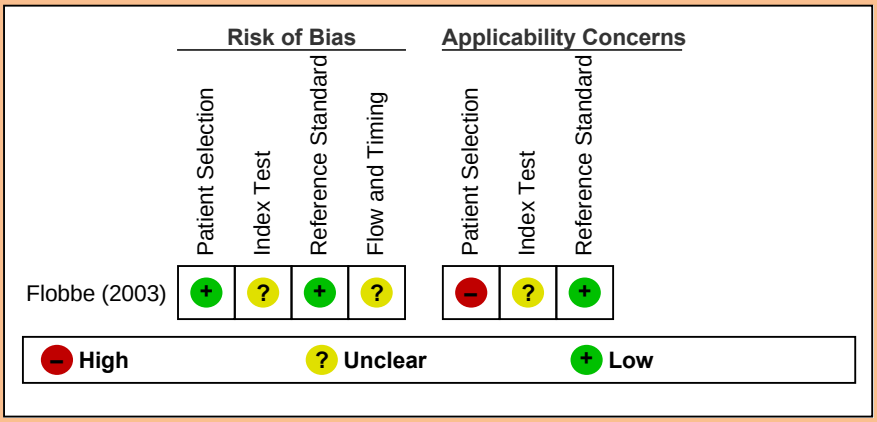
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	4/2013-12/08/014	349	17	12/08/014
Premedline	4/2013-12/08/014	180	11	12/08/014
Embase	4/2013-12/08/014	137	11	12/08/014
Cochrane Library	4/2013-12/08/014	77	0	12/08/014
Web of Science (SCI & SSCI) and ISI Proceedings	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.



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 ***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.*** 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	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). *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).* Inclusion criteria: "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]". Exclusion criteria: When ultrasound could not be performed because of logistic reasons or when no informed consent was given. Clinical setting: Unclear, the Ntherlands
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-iiv.
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'skii, 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]. *Klinicheskaia 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]. *Klinicheskaia 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., Launders, 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., Slonimskaia, 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 Societes & 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 malignat 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 multimedial 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. (410) Accuracy of mammography in an Australian community setting. *Medical Journal of Australia,* 149: 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 99mTc-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., Ostrovtsev, 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 99mTc-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., Ardeshna, 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. (970) 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 & Fertilite,* 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 Ginecologika,* 8: 81-86.
Not in PICO

Giuseppetti, G. M., Rizzatto, 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. & Ameeral, 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 Biopty-cut needle in diagnosis of early breast cancer. *Breast,* 4: 135-136.
Not in PICO
Hamy, A. S., Giacchetti, S., Albiter, 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 Rinkes, 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., Lehnherr, 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 Chiryo 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., Gunesekara, 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 extact 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]. *Przeglad 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., Walleser, 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. (1719) 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 ultrasoundguided 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., Winnnikow, 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 Chiryo 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., Hoefer, 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
Pfandzelter, 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) [Gammography 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) Radioisortropic 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., Giraldi, 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 practioners. [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 fur Arztliche Fortbildung und Qualitatssicherung,* 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. [Azerbaidzhani]. *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

Siziopikou, 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
Stoeckelhuber, 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., Kozlowska, 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 < or = 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

Torring, 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 Associacao Medica 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 & Fertilite,* 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 laplacion-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 fur 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

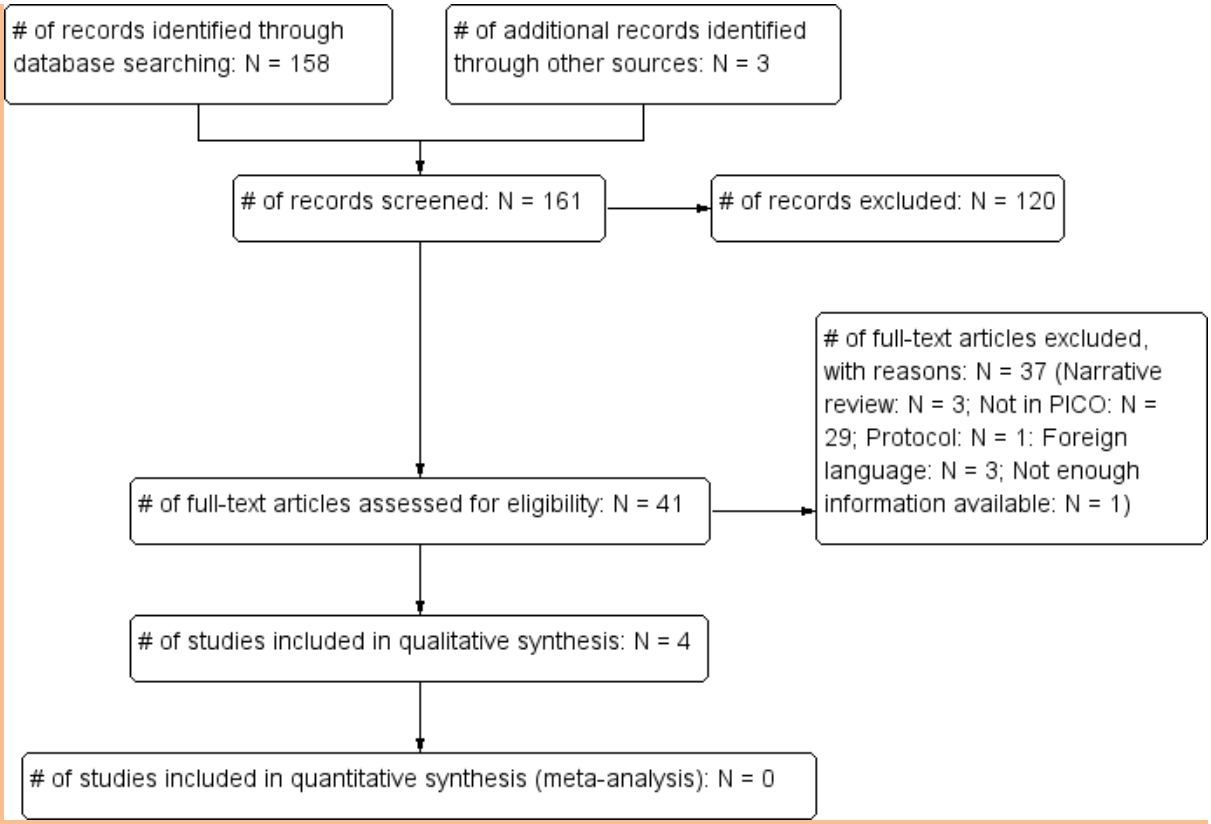
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	849	63	12/04/2013
Premedline	All-2012	24	3	12/04/2013
Embase	All-2012	2855	111	15/04/2013
Cochrane Library	All-2012	565	3	15/04/2013
Psychinfo	All-2012	5	0	12/04/2013
Web of Science (SCI & SSCI) and ISI Proceedings	All-2012	259	9	16/04/2013

Total References retrieved (after de-duplication): 144

Update Search

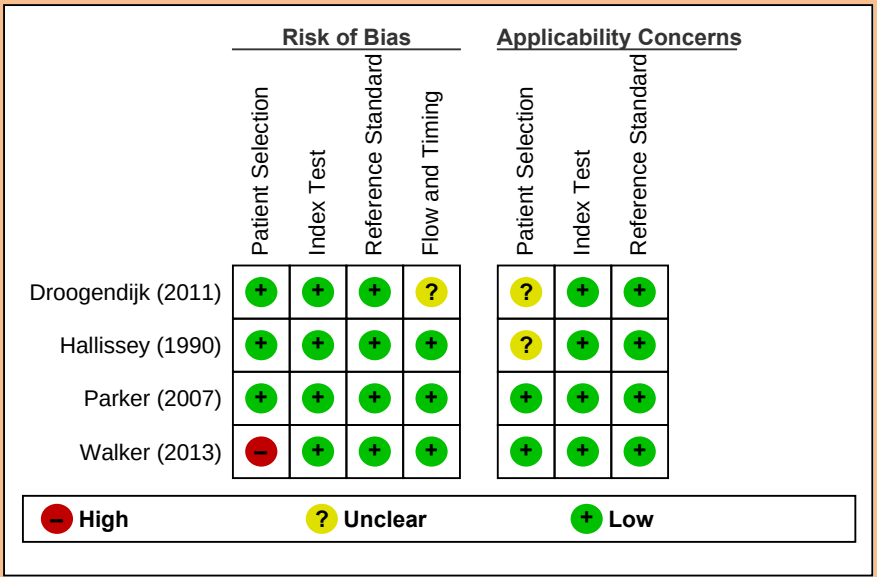
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	4/2013-13/08/2014	41	2	13/08/2014
Premedline	4/2013-13/08/2014	32	7	13/08/2014
Embase	4/2013-13/08/2014	196	6	13/08/2014
Cochrane Library	4/2013-13/08/2014	81	0	13/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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.



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) *As reported, but CI is not correct*
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)
		Women 40-44 years	0 (0-5.9) 0/77
		Women 45-54 years	0.3 (0.2-0.7)
		Women 55-64 years	1.1 (0.9-1.5)
		Women 65-74 years	3.1 (2.4-4.1)
		Women 75-84 years	5.4 (4-7.2)
		Women ≥ 85 years	3.7 (2-6.7)
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. Inclusion criteria: 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). Exclusion criteria: Patients with a known history of iron-deficiency anaemia in the previous 2 years, a history of gastrointestinal malignancy or congenital haemoglobinopathy. Clinical setting: 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. Inclusion criteria: All patients over 40 years making their first attendance during the study period (4 years and 9 months) with any degree of dyspepsia Exclusion criteria: None listed. Clinical setting: 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	**Low concern**

interpretation differ from the review question?	
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. Inclusion criteria: 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. Exclusion criteria: Previous record of colorectal cancer (for patients presenting with rectal bleeding) and endometrial cancer (for patients presenting with post-menopausal bleeding) 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	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**
For diagnostic case-control studies: Attempts were made within the design or analysis to balance the comparison groups for potential confounders?	**Yes**
For diagnostic case-control studies: 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: 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. Controls: 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. Inclusion criteria: 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. Exclusion criteria: 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 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. Clinical setting: Primary care UK
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	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 ≥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**
For diagnostic case-control studies: 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 by the reference standard does not match the question?	**Low concern**
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

Achilarre, 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 Obstetricia 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

Brogi, 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 reatins 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 reatins 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. & Pesssini, 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 Obstetricia et Gynecologica Scandinavica,* 82: 1112-1119.
Not in PICO (secondary care)
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
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 prevalance = 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 Ginekologiia,* 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-Sleczka, 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 Ginekologiia,* 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. (11111) 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 oupatient 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. Analyis 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. (1381) 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 - Uluslararasi 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., 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., 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-Maghami, 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 >=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 fur Gynakologie 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]. *Przeglad 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

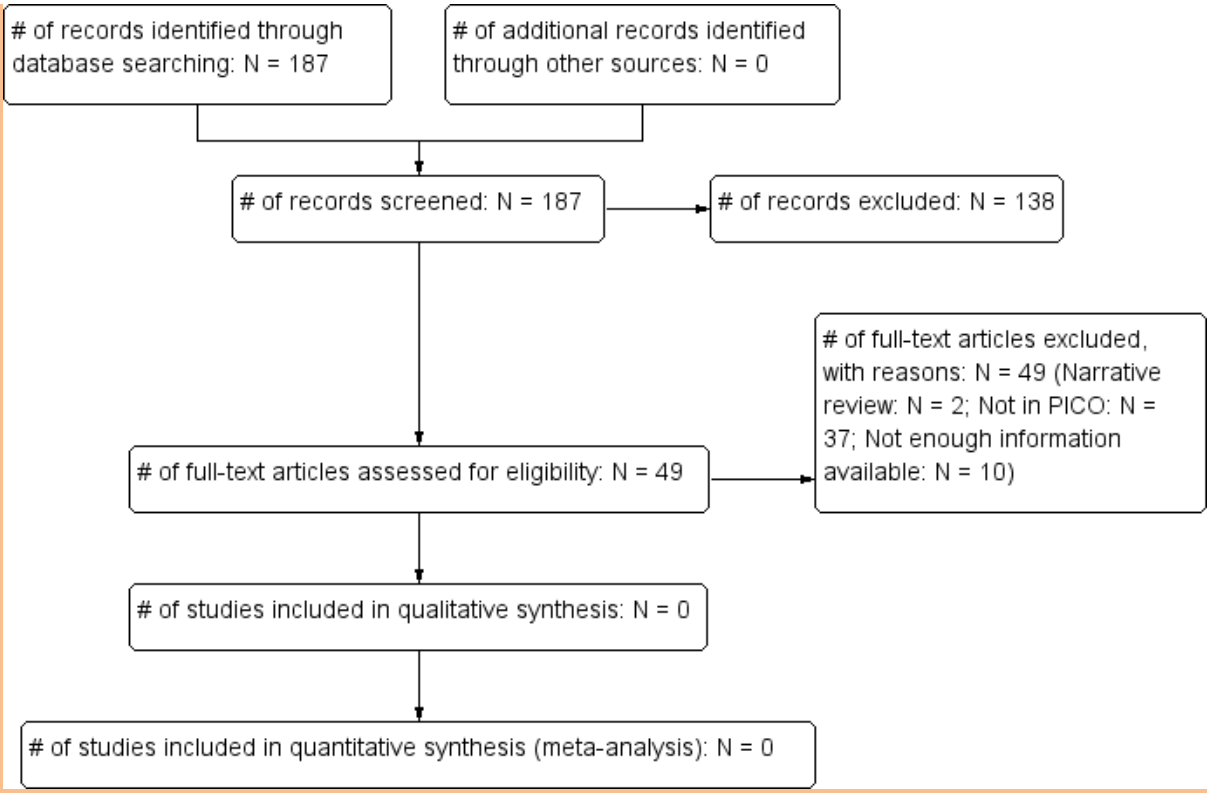
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	1107	80	19/06/2013
Premedline	1980-2013	66	6	19/06/2013
Embase	1980-2013	2720	101	20/06/2013
Cochrane Library	1980-2013	145	8	20/06/2013
Psychinfo	1980-2013	3	1	19/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	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
Medline	6/2013-13/08/2014	10	1	13/08/2014
Premedline	6/2013-13/08/2014	51	4	13/08/2014
Embase	6/2013-13/08/2014	45	4	13/08/2014
Cochrane Library	6/2013-13/08/2014	78	0	13/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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 Obstetricia 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., Delpech, 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 reveiw

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 reatins 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 reatins 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 reatins 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. & Pesssini, 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-cavital 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 reatins 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 hysteroscopical 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. & 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

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 Obstetricia et Gynecologica Scandinavica,* 81: 799-816.
Think it's not in PICO for endometrial as cancer prevalance = 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 Obstetricia 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 Ginekologiia,* 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 Ginekologiia,* 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 Ginekologiia,* 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 Obstetricia 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
Lynge, E. (1982) [Vaginal cytological examinations in Denmark]. [Danish]. *Ugeskrift for Laeger,* 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]. *Przeglad 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., Paraskevaidis, 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., 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
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. (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

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., 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.
Not in PICO

Zlatkov, V., Kostova, P., Barzakov, G., Tcholakova, A., Milochov, 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

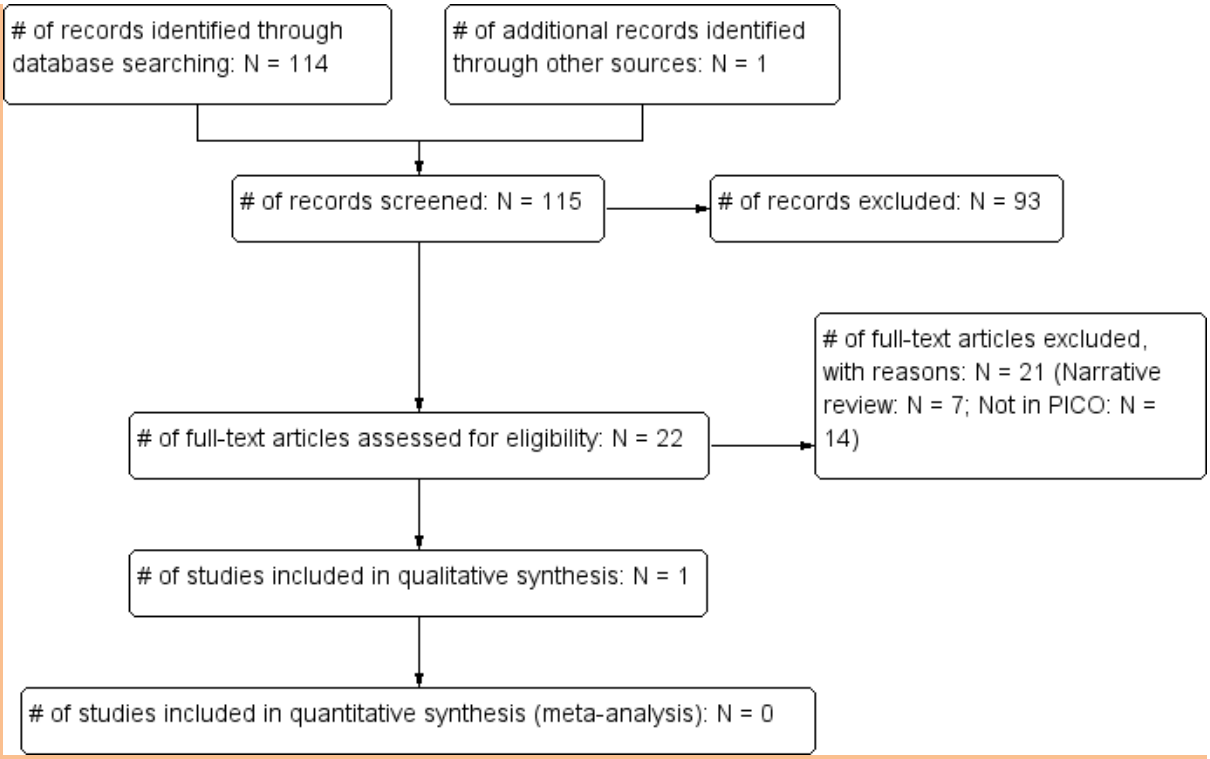
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	1076	34	17/04/2013
Premedline	All-2012	42	5	18/04/2013
Embase	All-2012	1532	44	18/04/2013
Cochrane Library	All-2012	529	3	19/04/2013
Psychinfo	All-2012	31	2	18/04/2013
Web of Science (SCI & SSCI) and ISI Proceedings	All-2012	539	16	19/04/2013

Total References retrieved (after de-duplication): 96

Update Search

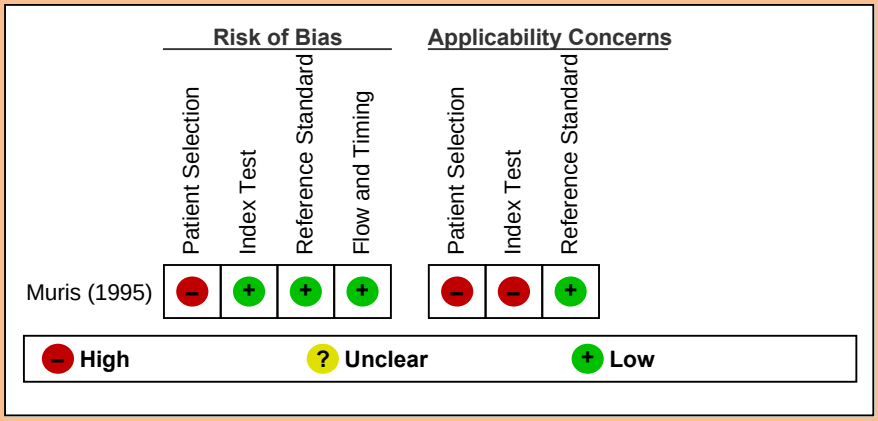
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	4/2013-13/08/2014	166	4	13/08/2014
Premedline	4/2013-13/08/2014	56	5	13/08/2014
Embase	4/2013-13/08/2014	315	9	13/08/2014
Cochrane Library	4/2013-13/08/2014	99	0	13/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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

system

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. Inclusion criteria: 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. Exclusion criteria: None listed. 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	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. & Matisic, 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 Obstetricia 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 Obstetricia 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 Laeger,* 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 - Uluslararasi 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., Tailor, 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
Winfree, 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
Medline	1980-2013	917	138	10/06/2013
Premedline	1980-2013	158	6	10/06/2013
Embase	1980-2013	2221	114	11/06/2013

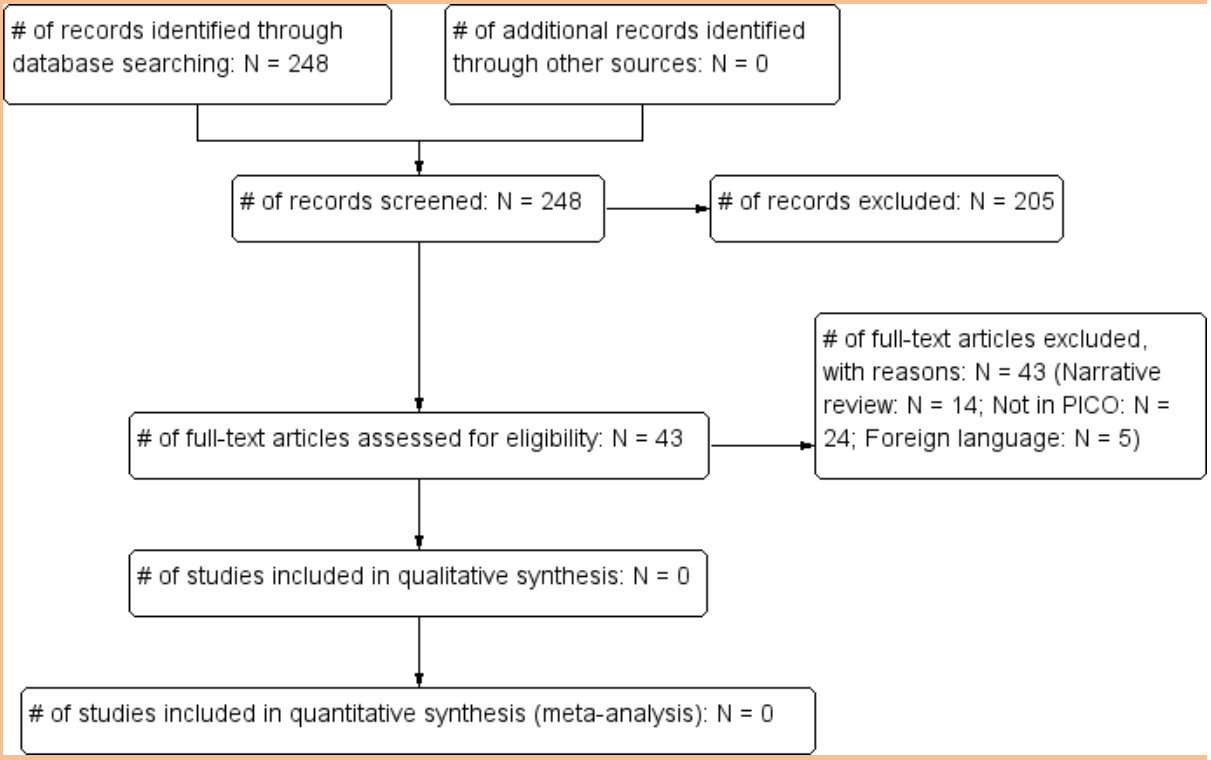
Cochrane Library	1980-2013	275	18	11/06/2013
Psychinfo	1980-2013	8	1	11/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	108	12	11/06/2013

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
Medline	6/2013-13/08/2014	170	2	13/08/2014
Premedline	6/2013-13/08/2014	44	1	13/08/2014
Embase	6/2013-13/08/2014	32	0	13/08/2014
Cochrane Library	6/2013-13/08/2014	34	0	13/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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

Afanas'eva, K. G., Ugriumova, 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., Eheman, 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., Dudhbhai, 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., Balfoort, 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]. *Przeglad 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 Obstetricia 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. & 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

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

Flannelly, 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

Flannelly, 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

Flannelly, 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
Igidbashian, 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 Ginekologiia,* 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. & Paraskevaidis, 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
McCrory, 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 oupatient 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., Chandrashekhar, 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., Fraschini, 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 cervices. *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., Bhamarapravati, 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., Eheman, 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-Vrscaj, 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., Tailor, 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

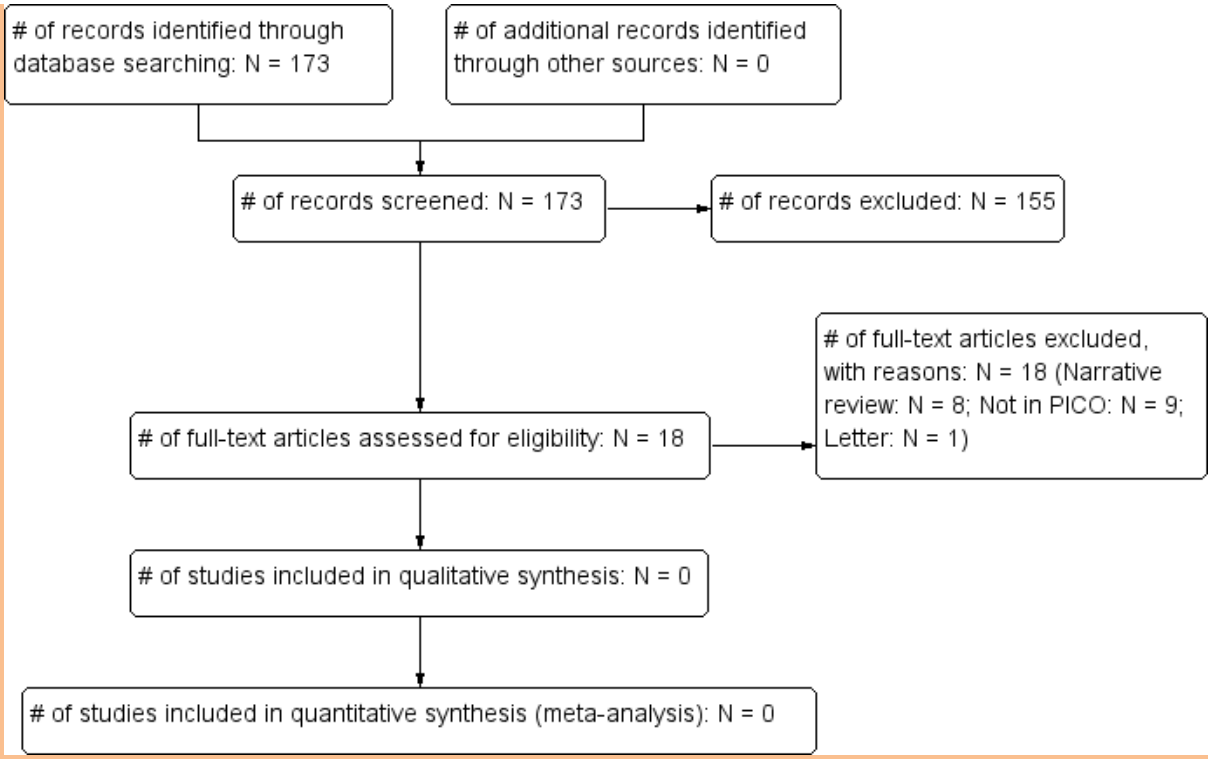
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	373	93	27/09/2012
Premedline	All-2012	9	2	27/09/2012
Embase	All-2012	474	125	01/10/2012
Cochrane Library	All-2012	23	0	27/09/2012
Psychinfo	All-2012	0	0	27/09/2012
Web of Science (SCI & SSCI) and ISI Proceedings	All-2012	3	2	27/09/2012
Biomed Central	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
Medline	9/2012-27/08/2014	42	0	27/08/2014
Premedline	9/2012-27/08/2014	36	4	27/08/2014
Embase	9/2012-27/08/2014	56	3	27/08/2014
Cochrane Library	9/2012-27/08/2014	17	0	27/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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]. Przeglad 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., Breitenecker, 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., Silvetti, 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., Schuuring, 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]. Onkologe 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. 592.
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
Medline	1980-2013	196	37	06/06/2013
Premedline	1980-2013	17	1	06/06/2013
Embase	1980-2013	212	57	06/06/2013
Cochrane Library	1980-2013	24	1	06/06/2013
Psychinfo	1980-2013	1	0	06/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	1980-2013	25	5	06/06/2013

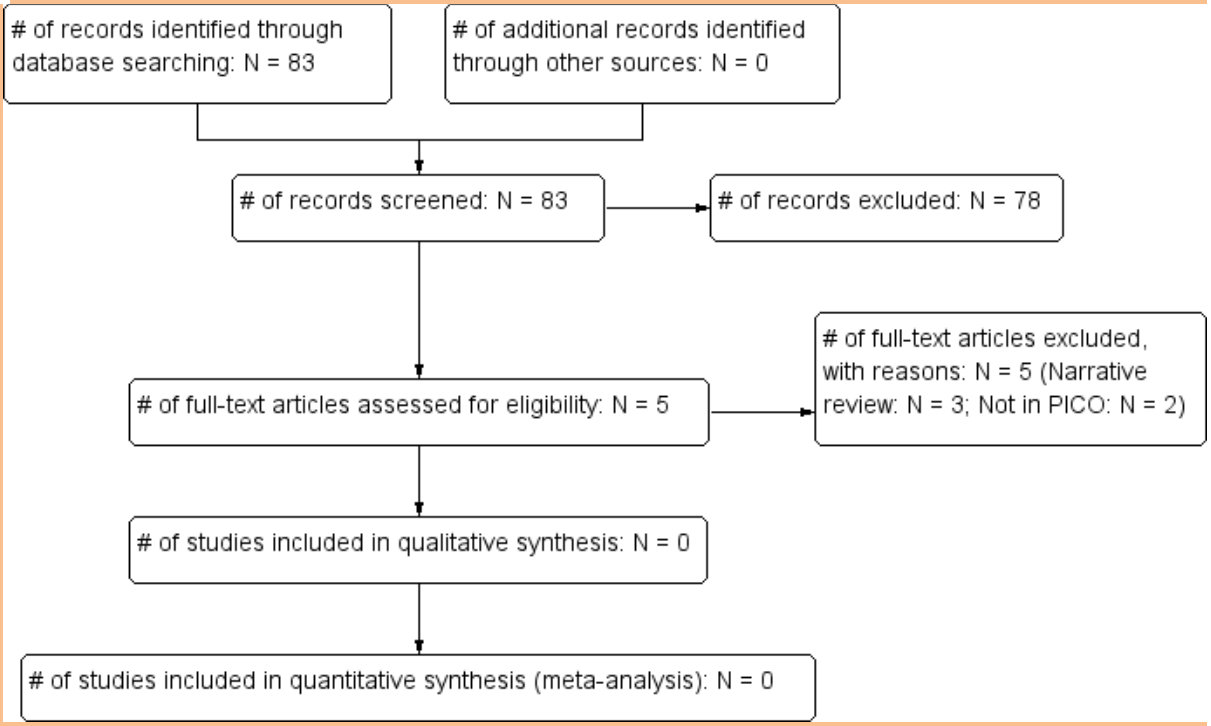
Total References retrieved (after de-duplication): 77

Update Search

Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	6/2013-27/08/2014	5	0	27/08/2014
Premedline	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 vulval 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., Breitenecker, 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., Anfuso, 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. & Brenan, J. (1995) Audit of 114 non-neoplastic vulvar biopsies. *British Journal of Obstetrics and Gynaecology,* 102: 780-786.
Not in PICO
Ouldamer, L., Chraibi, 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 vulval 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., Karelovic, 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

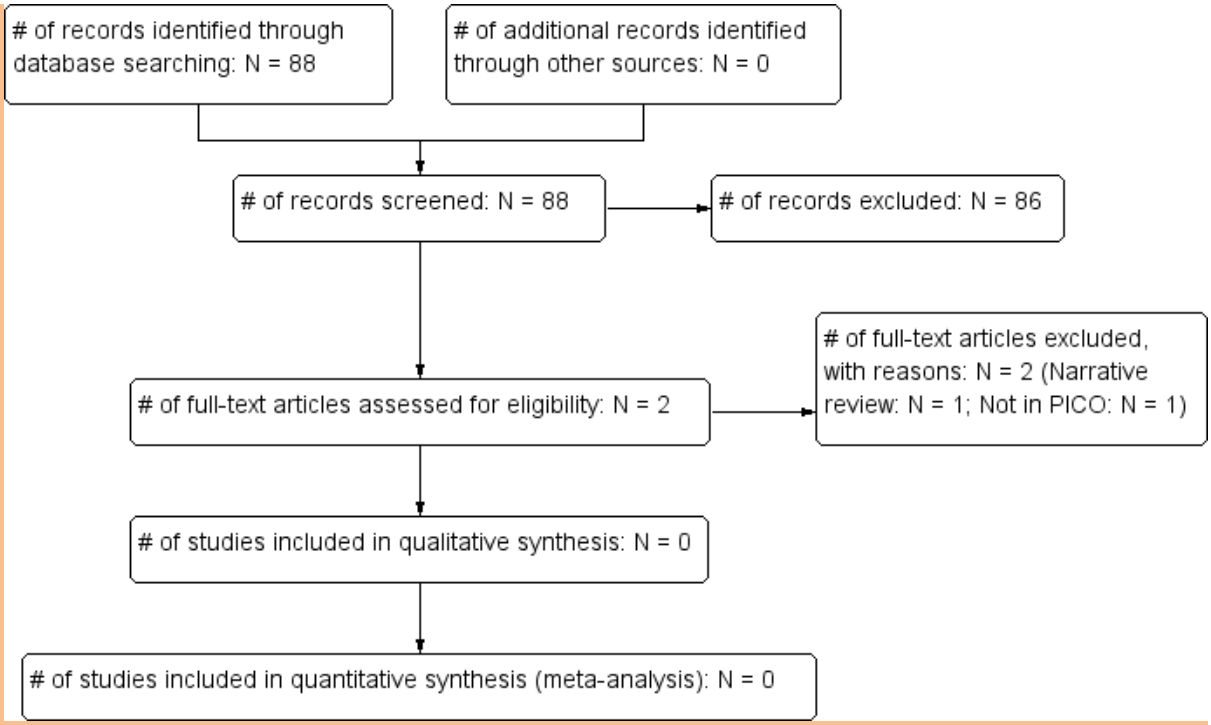
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	All-2012	248	50	24/09/2012
Premedline	All-2012	6	2	24/09/2012
Embase	All-2012	293	54	27/09/2012
Cochrane Library	All-2012	83	0	24/09/2012
Psychinfo	All-2012	3	0	24/09/2012
Web of Science (SCI & SSCI) and ISI Proceedings	All-2012	4	1	27/09/2012
Biomed Central	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
Medline	9/2012-27/08/2014	8	1	27/08/2014
Premedline	9/2012-27/08/2014	20	1	27/08/2014
Embase	9/2012-27/08/2014	36	2	27/08/2014
Cochrane Library	9/2012-27/08/2014	99	0	27/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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 Gebski, 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., Breitenecker, 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 Lekaru Ceskych 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 Lekaru Ceskych 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 Kiyo - 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 Ginekologiia,* 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 Obstetricia 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]. Onkologe 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

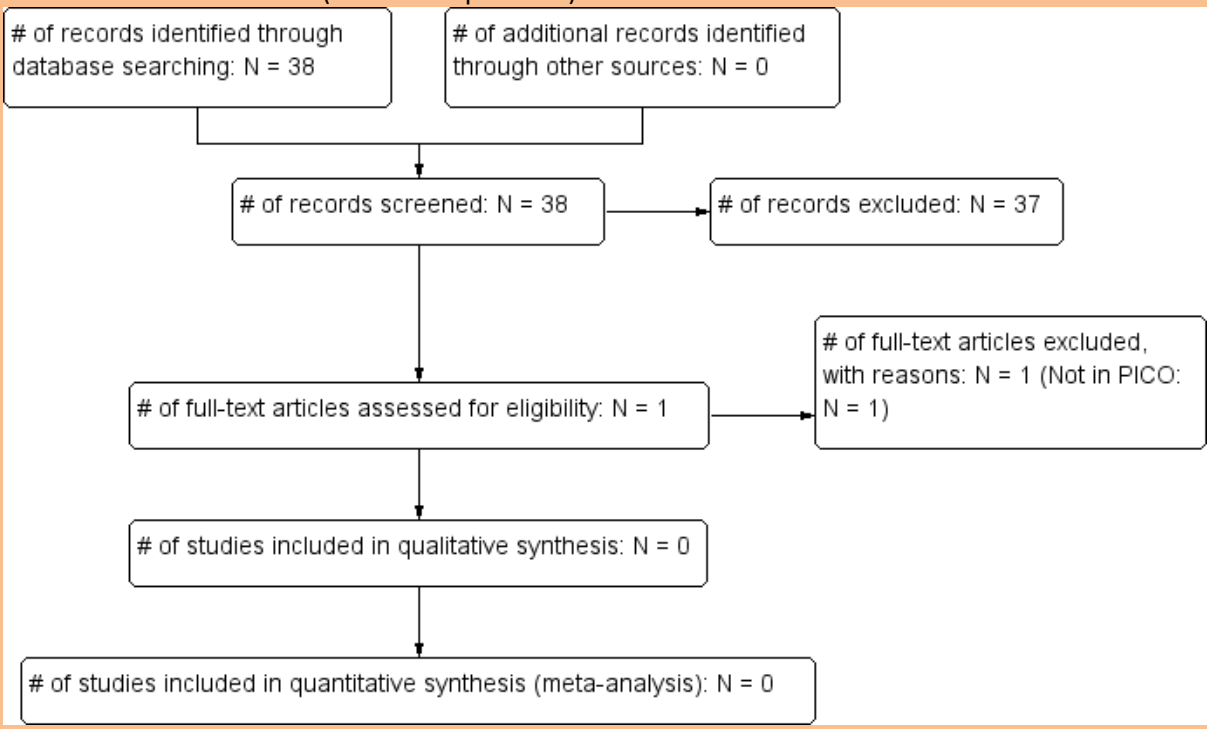
Database name	Dates Covered	No of references found	No of references retrieved	Finish date of search
Medline	1980-2013	151	16	05/06/2013
Premedline	1980-2013	10	1	05/06/2013
Embase	1980-2013	142	10	05/06/2013
Cochrane Library	1980-2013	104	0	05/06/2013
Psychinfo	1980-2013	4	0	05/06/2013
Web of Science (SCI & SSCI) and ISI Proceedings	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
Medline	6/2013-27/08/2014	6	0	27/08/2014
Premedline	6/2013-27/08/2014	10	0	27/08/2014
Embase	6/2013-27/08/2014	18	2	27/08/2014
Cochrane Library	6/2013-27/08/2014	75	0	27/08/2014
Web of Science (SCI & SSCI) and ISI Proceedings	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., Breitenecker, 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 Ginekologiia,* 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. (11111) 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 Obstetricia 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 (cervival 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