National Institute for Health and Care Excellence

Version 1.0

Pancreatic Cancer in adults:

diagnosis and management

Appendix C

Review protocols

31 July 2017

Draft for Consultation

Developed by the National Guideline Alliance, hosted by the Royal College of Obstetricians and Gynaecologists

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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1 Appendix C: Review protocols

C.1 2 People with jaundice

Item	Details
Area in Scope	Diagnosing Suspected Pancreatic Cancer
Review question in Scope	What is the most effective diagnostic pathway (including CA 19–9, histology, cytology and imaging investigations) for people with suspected pancreatic cancer in secondary care who have obstructive jaundice?
Review Question in Guideline	What is the most effective diagnostic pathway (imaging +/-CA 19–9, biopsy (cytology or histology)) for adults with suspected pancreatic cancer in secondary care who have jaundice?
Economic Priority	Moderate

PICO Table

Population	Index Test	Reference Standard	Outcomes

Adults suspected of having pancreatic cancer who have jaundice	• Imaging +/- CA 19–9
	• (Ultrasound , CT, MRI, PET-CT)
	• Biopsy (cytology or histology)
	  ○ endoscopic ultrasound +/- FNA
	  ○ ERCP+/- biliary brushings,
	  ○ EUS +/- core biopsy
	  ○ Percutaneous liver biopsy
	  ○ laparoscopy + biopsy
	  ○ percutaneous pancreatic biopsy
		• Definitive diagnosis (preferably Pathological diagnosis)
		• Each other
			• Diagnostic Accuracy including:
			  ○ Sensitivity
			  ○ Specificity
			  ○ Positive Predictive Value
			  ○ Negative Predictive Value
			  ○ Adverse events

Setting	Adults (18 and over) referred to secondary care with suspected pancreatic cancer.		
Additional Comments on PICO	If evidence on MRCP – report it		

	Details	Additional Comments
Type of review	Diagnostic	
Language	English	
Study design	• Diagnostics test accuracy studies • Systematic reviews of diagnostic test accuracy studies	
Status	Published	
	Details	**Additional Comments**
Other	Non-English Language Studies, conference	

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Item	Details	
criteria for inclusion / exclusion of studies	abstracts, narrative reviews and non-comparative case series will not routinely be included.	
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 2000 onwards	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised in a narrative format using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. Meta-analysis will of individual study data will be performed if possible. • As this is a diagnostic topic, the quality of the evidence will be assessed using QUADAS II checklists.	
Identified papers	• Pancreatic tumors: role of imaging in the diagnosis, staging, and treatment. Delbeke D, Pinson CW. J Hepatobiliary Pancreat Surg. 2004;11(1):4-10. Review. • A clinical algorithm for the assessment of pancreatic lesions: utilization of 16- and 64-section multidetector CT and endoscopic ultrasound. Rafique A, Freeman S, Carroll N. Clin Radiol. 2007 Dec;62(12):1142-53. Epub 2007 Sep 25. Review. PMID: 17981161 • The diagnosis of pancreatic cancer. Brand R. Cancer J. 2001 Jul-Aug;7(4):287-97. Review. PMID: 11561605 • Radiologic diagnosis and staging of pancreatic ductal adenocarcinoma. Balci NC, Semelka RC. Eur J Radiol. 2001 May;38(2):105-12. Review. PMID: 11335092 • Staging of pancreatic adenocarcinoma by imaging studies. Wong JC, Lu DS. Clin Gastroenterol Hepatol. 2008 Dec;6(12):1301-8. doi: 10.1016/j.cgh.2008.09.014. Epub 2008 Sep 27. Review. PMID: 18948228	

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C.21 People without jaundice but with a pancreatic abnormality

Item	Details
Area in Scope	Diagnosing Suspected Pancreatic Cancer
Review question in Scope	What is the most effective diagnostic pathway (including CA 19–9, histology, cytology and imaging investigations) for people with suspected pancreatic cancer in secondary care who have no jaundice with pancreatic lump(s)?
Review Question in Guideline	What is the most effective diagnostic pathway (imaging +/- CA 19–9, biopsy (cytology or histology)) for adults with suspected pancreatic cancer in secondary care who do not have jaundice but have a pancreatic abnormality on imaging?
Economic Priority	Moderate

PICO Table

Population	Index Test	Reference Standard	Outcomes

Adults in secondary care suspected of having pancreatic cancer who do not have jaundice but with a pancreatic abnormality on imaging	• Imaging +/- CA 19–9
	• (Ultrasound , CT, MRI, PET-CT)
	• Biopsy (cytology or histology)
	  ○ endoscopic ultrasound +/- FNA
	  ○ EUS +/- core biopsy
	  ○ Percutaneous liver biopsy
	  ○ laparoscopy + biopsy
	  ○ percutaneous pancreatic biopsy
		• Definitive diagnosis (preferably Pathological diagnosis)
		• Each other
			• Diagnostic Accuracy including:
			• Sensitivity
			• Specificity
			• Positive Predictive Value
			• Negative Predictive Value
			• Adverse events

Setting	Adults (18 and over) referred to secondary care with suspected pancreatic cancer.		
Additional Comments on PICO	• Record initial imaging that was undertaken to identify the abnormality • Record whether papers say patient has jaundice or not		

	Details	Additional Comments
Type of review	Diagnostic	
Language	English	
Study design	• Diagnostic accuracy studies • Systematic reviews of diagnostic accuracy studies	
Status	Published	
	Details	**Additional Comments**
Other criteria for inclusion / exclusion of studies	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.	
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR,	

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Item	Details	
	DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 2000 onwards	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised in a narrative format using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. Meta-analysis of individual study data will be performed where possible. • As this is a diagnostic topic, the quality of the evidence will be assessed using QUADAS II checklists.	
Identified papers	• Pancreatic tumors: role of imaging in the diagnosis, staging, and treatment. Delbeke D, Pinson CW .J Hepatobiliary Pancreat Surg. 2004;11(1):4-10. Review. • A clinical algorithm for the assessment of pancreatic lesions: utilization of 16- and 64-section multidetector CT and endoscopic ultrasound. Rafique A, Freeman S, Carroll N. Clin Radiol. 2007 Dec;62(12):1142-53. Epub 2007 Sep 25. Review. • The diagnosis of pancreatic cancer. Brand R. Cancer J. 2001 Jul-Aug;7(4):287-97. Review. • Radiologic diagnosis and staging of pancreatic ductal adenocarcinoma. Balci NC, Semelka RC. Eur J Radiol. 2001 May;38(2):105-12. Review. • Staging of pancreatic adenocarcinoma by imaging studies. Wong JC, Lu DS. • Clin Gastroenterol Hepatol. 2008 Dec;6(12):1301-8. doi: 10.1016/j.cgh.2008.09.014. Epub 2008 Sep 27. Review. • Advances in diagnosis, treatment and palliation of pancreatic carcinoma: 1990-2010. Sharma C, Eltawil KM, Renfrew PD, Walsh MJ, Molinari M. World J Gastroenterol. 2011 Feb 21;17(7):867-97. doi: 10.3748/wjg.v17.i7.867. Review. • Tumor markers in pancreatic cancer: a European Group on Tumor Markers (EGTM) status report. Duffy MJ, Sturgeon C, Lamerz R, Haglund C, Holubec VL, Klapdor R, Nicolini A, Topolcan O, Heinemann V. Ann Oncol. 2010 Mar;21(3):441-7. doi: 10.1093/annonc/mdp332. Epub 2009 Aug 18. Review.	

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Item	Details
	• Systematic review of carbohydrate antigen (CA 19-9) as a biochemical marker in the diagnosis of pancreatic cancer. Goonetilleke KS, Siriwardena AK. Eur J Surg Oncol. 2007 Apr;33(3):266-70. Epub 2006 Nov 9. Review.

C.31 Pancreatic Cysts

Item	Details
Area in Scope	Diagnosing Suspected Pancreatic Cancer
Review question in Scope	What is the most effective diagnostic pathway (including CA 19–9, histology, cytology and imaging investigations) for people with suspected pancreatic cancer in secondary care who have pancreatic cysts?
Review Question in Guideline	In adults with a pancreatic cyst, what is the diagnostic pathway to identify the cyst(s) at high risk of pancreatic malignancy?
Economic Priority	High

PICO Table

Population	Index Test	Reference Standard	Outcomes
• Adults with pancreatic cysts	• CA 19–9, CEA – in serum and cyst fluid • Histology • Cytology • Imaging (MRI/MRCP, PET-CT, CT, Ultrasound, needle Confocal Laser Endomicroscopy, EUS+/-FNA)	• Definitive diagnosis (preferably pathological diagnosis) • Each Other	• Diagnostic Accuracy including: ○ Sensitivity ○ Specificity ○ Positive Predictive Value ○ Negative Predictive Value ○ Adverse events
Setting	• Adults (18 and over) referred to secondary care with suspected pancreatic cancer. • Adults (18 and over) with newly diagnosed or recurrent pancreatic ductal adenocarcinoma.		
Additional Comments on PICO	• Exclude evidence on pseudocysts • Clinical features of potentially suspicious cysts include irregularity of the margin, septation, enhancement of the wall and calcification as well as associated features such as associated pancreatic duct dilatation • Only those with more than 50 participants		

	Details	Additional Comments
Type of review	Diagnostic	
Language	English	
Study design	• Diagnostic accuracy studies • Systematic reviews of diagnostic accuracy studies	
Status	Published	
	Details	**Additional Comments**
Other criteria for inclusion / exclusion of studies	• Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.	

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Item	Details
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 2000 onwards
Useful Search Terms	
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is a diagnostic topic, the quality of the evidence will be assessed using QUADAS II checklists.
Identified papers	• Pancreatic Cyst Disease: A Review. Stark A, Donahue TR, Reber HA, Hines OJ. JAMA. 2016 May 3;315(17):1882-93. doi: 10.1001/jama.2016.4690. • Cystic lesions of the pancreas. Karoumpalis I, Christodoulou DK. Ann Gastroenterol. 2016 Apr-Jun;29(2):155-61. doi: 10.20524/aog.2016.0007. Review. • Current perspectives on pancreatic serous cystic neoplasms: Diagnosis, management and beyond. Zhang XP, Yu ZX, Zhao YP, Dai MH. World J Gastrointest Surg. 2016 Mar 27;8(3):202-11. doi: 10.4240/wjgs.v8.i3.202. Review. • Clinical approach to incidental pancreatic cysts. Chiang AL, Lee LS. World J Gastroenterol. 2016 Jan 21;22(3):1236-45. doi: 10.3748/wjg.v22.i3.1236. Review. • Pancreatic Solid and Cystic Neoplasms: Diagnostic Evaluation and Intervention. Al-Hawary MM, Francis IR, Anderson MA. Radiol Clin North Am. 2015 Sep;53(5):1037-48. doi: 10.1016/j.rcl.2015.05.005. Review. • Management of pancreatic cysts: a review of the current guidelines. Hol L, Signoretti M, Poley JW. Minerva Gastroenterol Dietol. 2015 Jun;61(2):87-99. Epub 2015 Feb 5. Review. • Imaging of pancreatic neoplasms. Balachandran A, Bhosale PR, Charnsangavej C, Tamm EP. Surg Oncol Clin N Am. 2014 Oct;23(4):751-88. doi:

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Item	Details
	10.1016/j.soc.2014.07.002. Review. • Imaging of indeterminate pancreatic cystic lesions: a systematic review. Jones MJ, Buchanan AS, Neal CP, Dennison AR, Metcalfe MS, Garcea G. Pancreatology. 2013 Jul-Aug;13(4):436-42. doi: 10.1016/j.pan.2013.05.007. Epub 2013 Jun 4. Review. • Management of pancreatic cysts: a multidisciplinary approach. Law JK, Hruban RH, Lennon AM. Curr Opin Gastroenterol. 2013 Sep;29(5):509-16. doi: 10.1097/MOG.0b013e328363e3b3. Review. • Diagnostic and radiological management of cystic pancreatic lesions: important features for radiologists. Buerke B, Domagk D, Heindel W, Wessling J. Clin Radiol. 2012 Aug;67(8):727-37. doi: 10.1016/j.crad.2012.02.008. Epub 2012 Apr 18. • Pancreatic cystic neoplasms: diagnosis and management. Yoon WJ, Brugge WR. Gastroenterol Clin North Am. 2012 Mar;41(1):103-18. doi: 10.1016/j.gtc.2011.12.016. Epub 2012 Jan 20. • Diagnostic evaluation of pancreatic cystic malignancies. Hutchins G, Draganov PV. Surg Clin North Am. 2010 Apr;90(2):399-410. doi: 10.1016/j.suc.2010.01.003.

C.41 People with inherited high risk of pancreatic cancer

Item	Detail
Area in Scope	Diagnosing Suspected Pancreatic Cancer
Review question in Scope	What is the most effective diagnostic pathway (including CA 19–9, histology, cytology and imaging investigations) for people with suspected pancreatic cancer in secondary care who are from other high risk groups, for example, familial pancreatic cancer and hereditary pancreatitis (PRSS1 mutations)?
Review Question in Guideline	What is the most effective monitoring protocol for adults with an inherited high risk of pancreatic cancer in secondary care to ensure early diagnosis
Economic Priority	Low

PICO Table

Population	Index Test	Reference Standard	Outcomes
• Adults who have a history of: • familial pancreatic cancer (FPC) • associated with chronic inflammation of the pancreas, namely cystic fibrosis and hereditary chronic pancreatitis • hereditary tumour predisposition syndromes, namely • ataxia-telangiectasia • familial atypical multiple mole melanoma (FAMMM) • familial adenomatous polyposis (FAP) • hereditary breast and ovarian cancer syndrome (HBOC)	• Biomarkers in blood, serum or pancreatic juice (CA19-9, CEA, Kras, GNAS, p53, p16) • Imaging • (Ultrasound , CT, MRI/MRCP, PET-CT) • Biopsy (cytology or histology) ○ endoscopic ultrasound +/- FNA ○ EUS +/- core biopsy ○ ERCP ○ laparoscopy + biopsy ○ percutaneous pancreatic biopsy	• Definitive diagnosis (preferably pathological diagnosis) • Each Other; alone and in combination	• Early diagnosis • Survival • Diagnostic Accuracy including: • Sensitivity • Specificity • Positive Predictive Value • Negative Predictive Value • Adverse events of interventions • HRQoL

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Item	Detail			
• Li-Fraumeni syndrome • Lynch syndrome (HNPCC) • Peutz-Jeghers syndrome				
Setting	Adults (18 and over) referred to secondary care with suspected pancreatic cancer.			
Additional Comments on PICO				
	Details		**Additional Comments**	
Type of review	Diagnostic			
Language	English			
Study design	• Diagnostic test accuracy studies • Systematic reviews of diagnostic test accuracy studies			
Status	Published			
	Details		**Additional Comments**	
Other criteria for inclusion / exclusion of studies	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.			
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 2000 onwards			
Useful Search Terms				
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised in a narrative			

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Item	Detail	
	format using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. Meta-analysis of individual study data will be performed where possible. • As this is a diagnostic topic, the quality of the evidence will be assessed using QUADAS II checklists. • For surveys on HRQoL outcomes related to screening/surveillance studies, the GATE checklist will be used.	
Identified papers	• NATHAN HOWES,MARKUS M. LERCH,WILLIAM GREENHALF, Clinical and Genetic Characteristics of Hereditary Pancreatitis in Europe CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2004;2:252–261 • Christopher J Grocock, Vinciane Rebours, Myriam N Delhaye et al. The variable phenotype of the p.A16V mutation of cationic trypsinogen (PRSS1) in pancreatitis families Gut 2010;59:357e363 • James A. Nicholson, William Greenhalf, Richard Jackson, et al. Incidence of Post-ERCP Pancreatitis From Direct Pancreatic Juice Collection in Hereditary Pancreatitis and Familial Pancreatic Cancer Before and After the Introduction of Prophylactic Pancreatic Stents and Rectal Diclofenac. Pancreas 2015;44: 260–265 • Marcia Irene Canto, Femme Harinck, Ralph H Hruban. International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. Gut 2013;62:339–347 • Hans Vasen, Isaura Ibrahim, Carmen Guillen Ponce, et al. Benefit of Surveillance for Pancreatic Cancer in High-Risk Individuals: Outcome of Long-Term Prospective Follow-Up Studies From Three European Expert Centers. J Clin Oncol 2016; 34:2010-2019. • Al-Sukhni W, Borgida A, Rothenmund H, et al: Screening for pancreatic cancer in a high-risk cohort: An eight-year experience. J Gastrointest Surg 16: 771-783, 2012 • Canto MI, Goggins M, Yeo CJ, et al: Screening for pancreatic neoplasia in high-risk individuals: An EUS-based approach. Clin Gastroenterol Hepatol 2: 606-621, 2004 • Canto MI, Goggins M, Hruban RH, et al: Screening for early pancreatic neoplasia in high-risk individuals: A prospective controlled study. Clin Gastroenterol Hepatol 4:766-781, 2006 • Harinck F, Konings IC, Kluijt I, et al: A multicentre comparative prospective blinded analysis of EUS and MRI for screening of pancreatic cancer in high-risk individuals. Gut pii:gutjnl-2014-308008, 2015 • Langer P, Kann PH, Fendrich V, et al: Five years of prospective screening of high-risk individuals from families with familial pancreatic cancer. Gut 58: 1410-1418, 2009 • Brentnall TA: Pancreatic cancer surveillance: Learning as we go. Am J Gastroenterol 106:955-956, 2011 • Canto MI, Hruban RH, Fishman EK, et al: Frequent detection of pancreatic lesions in asymptomatic high-risk individuals. Gastroenterology 142: 796-804, 2012 • Del Chiaro M, Verbeke CS, Kartalis N, et al: Short-term results of a magnetic resonance imaging based Swedish screening program for individuals at risk for pancreatic cancer. JAMA Surg 150:512-518, 2015 • Kimmey MB, Bronner MP, Byrd DR, et al: Screening and surveillance for hereditary pancreatic cancer. Gastrointest Endosc 56:S82-S86, 2002 (suppl 4) • Poley JW, Kluijt I, Gouma DJ, et al: The yield of first-time endoscopic ultrasonography in screening individuals at a high risk of developing pancreatic	

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Item	Detail
	cancer. Am J Gastroenterol 104:2175-2181, 2009 • Verna EC, Hwang C, Stevens PD, et al: Pancreatic cancer screening in a prospective cohort of high-risk patients: A comprehensive strategy of imaging and genetics. Clin Cancer Res 16:5028-5037, 2010

C.51 Referral to specialist multidisciplinary teams

Item	Description
Area in Scope	Referral to Specialist Teams
Review question in Scope	Does referral of all adults with suspected pancreatic cancer to a regional centre or multidisciplinary team for review improve patient management and outcomes?
Review Question in Guideline	Does referral of all adults with suspected pancreatic cancer to a specialist MDT for review improve patient management and outcomes
Economic Priority	

PICO Table

Population	Intervention	Comparison	Outcomes

• Adults with suspected pancreatic cancer
• Stage
  ○ I
  ○ II
  ○ III
  ○ IV
	• Referral by region to
	• Specialist pancreatic MDT
	• Local MDT
		Each Other	• Survival Outcomes
			• Proportion receiving chemotherapy
			• Entry into clinical trials
			• Resection rates
			• Post-operative mortality
			• Patient Satisfaction
			• Quality of Life

Setting	Adults 18 years and older referred to secondary care with suspected pancreatic cancer.

Additional Comments on PICO	• Consider
	  ○ Models of MDT (presumption that a model is dominated by specialist MDT and refer all cases in for discussion/LMDT screens out some patients who may not need to be discussed to by the MDT)
	  ○ Staffing (levels, experience etc)
	  ○ Centre size/specialism (number of patients treated, specialist expertise available
	  ○ Do all patients get referred to SMDT or not
	  ○ Data from NCIN (2010-2015)
	  ○ Number of pancreatic cancer patients newly diagnosed each year by region
	  ○ The regional population for the years reported on
	  ○ Number of pancreatic cancer patients discussed by the MDTs per year (split by diagnosed or suspected if possible)
	  ○ The number of the newly diagnosed patients that had a resection
	  ○ The number of patients that dies within 30 days following the resection date
	  ○ The overall 1 year survival rate for the years reported on (all cases)
	  ○ Any demographic data available for the years reported on (age, gender, stage etc)

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Item	Description	
	○ Resection rates as a surrogate marker for who is being seen by a specialist MDT. ○ Regions, no. of patients with pancreas cancer, no. of resections	
	Details	**Additional Comments**
Type of review	Interventional	
Language	English	
Study design	• Systematic reviews, • Randomised Control Trial, • Cohort, • Case-control, • cross-sectional, • audit	• RCT's not likely to be available • Case series with one intervention or case reports will not be included due to no comparison to the reference standard/ other interventions.
Status	Peer reviewed journals	
Other criteria for inclusion / exclusion of studies	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.	Could consider surveying clinicians/patients to get their views
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate.	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is an interventional topic, GRADE	

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Item	Description	
	methodology will be used to assess study quality for the outcomes. • Relevant subgroups for analysis will be identified upfront where appropriate	
Identified papers	None identified	

C.61 Staging

Item	Description		
Area in Scope	Staging of Pancreatic Cancer		
Review question in Scope	What is the most effective investigative pathway (for example, combinations of CA19-9, endoscopic ultrasound, CT, MRI, positron emission tomography (PET)-CT, tissue diagnosis, laparoscopy with or without ultrasound) for staging pancreatic cancer as resectable, borderline resectable, locally advanced and metastatic disease?		
Review Question in Guideline	What is the most effective investigative pathway for staging adults with newly diagnosed pancreatic cancer or a non-definitive diagnostic result as resectable, borderline resectable, locally advanced and metastatic disease?		
Economic Priority	High		
PICO Table			
Population	**Index Test**	**Reference Standard**	**Outcomes**
Adults with newly diagnosed pancreatic cancer or a non-definitive diagnostic result	Investigative pathways including combinations of: • Imaging (MRI/MRCP, PET-CT, CT, Ultrasound, EUS) • Laparoscopy (with or without ultrasound) • CA 19–9 • Histology • cytology	• Each Other • Histological TNM classification • Surgery	• Diagnostic Accuracy • Sensitivity • Specificity • Positive Predictive Value • Negative Predictive Value • Resectability • Adverse events
Setting	Adults (18 and over) with newly diagnosed or recurrent pancreatic ductal adenocarcinoma.		
Additional Comments on PICO	Record whether: histology and cytology of the metastasis or the primary tumour; TNM classification used by papers (e.g. UICC 5th, 6th or 7th edition or AJCC classification)		
	Details		**Additional Comments**
Type of review	Diagnostic		
Language	English		
Study design	• Prospective diagnostic test accuracy studies • Retrospective reviews of prospective databases if no prospective studies Systematic reviews of diagnostic test accuracy studies		

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Item	Description	
Status	Published	
	Details	**Additional Comments**
Other criteria for inclusion / exclusion of studies	• Foreign Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included. • ≥50 participants	
Search strategies	Date limit of 2000	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised in a narrative format using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. Meta-analysis of individual study data will be performed where possible. • As this is a diagnostic topic, the quality of the evidence will be assessed using QUADAS II checklists.	
Identified papers	• The Role of Positron Emission Tomography/Computed Tomography in Management and Prediction of Survival in Pancreatic Cancer. Nunna P, Sheikhbahaei S, Ahn S, Young B, Subramaniam RM. J Comput Assist Tomogr. 2016 Jan-Feb;40(1):142-5 • Pearls and pitfalls of imaging metastatic disease from pancreatic adenocarcinoma: a systematic review. Zaheer A, Wadhwa V, Oh J, Fishman EK Clin Imaging. 2015 Sep-Oct;39(5):750-8 • Multimodality imaging of pancreatic cancer-computed tomography, magnetic resonance imaging, and positron emission tomography. Raman SP, Horton KM, Fishman EK. Cancer J. 2012 Nov-Dec;18(6):511-22. • Staging cancer of the pancreas. Morana G, Cancian L, Pozzi Mucelli R, Cugini C. Cancer Imaging. 2010 Oct 4;10 • Pancreatic tumors: role of imaging in the diagnosis, staging, and treatment. Delbeke D, Pinson CW. J Hepatobiliary Pancreat Surg. 2004;11(1):4-10 • Cancer of the pancreas: the best image for early detection--CT, MRI, PET or US? Hanbidge AE. Can J Gastroenterol. 2002 Feb;16(2):101-5	

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Item	Description
	• Radiological evaluation of focal pancreatic lesions. Putzer D, Jaschke W. • Dig Dis. 2015;33(1):91-8

C.71 Psychological support needs

Item	Detail
Area in Scope	Information and support
Review question in Scope	What are the specific information and support needs of people or their carers who are diagnosed with pancreatic cancer and their families or carers (as appropriate) throughout the care pathway?
Review Question in Guideline	What are the specific psychological support needs (including information) of adults with newly diagnosed or recurrent pancreatic cancer and their families or carers (as appropriate) throughout the care pathway?
Economic Priority	Low

PICO Table

Population	Context	Outcomes
• Adults with pancreatic cancer • And their carers or family members	• Psychological support needs/information and/or interventions designed to meet patient needs in areas including: • Pain • Bowel/digestive problems • Nutritional concerns • Anxiety • Depression • Fatigue • Timing	• Health Related Quality of Life • Patient satisfaction • Patient/family/ carer understanding of disease impact • Patient reported outcomes • Patient experience
Setting	• Adults (18 and over) referred to secondary care with suspected pancreatic cancer. • Adults (18 and over) with newly diagnosed or recurrent pancreatic ductal adenocarcinoma.	
Additional Comments on PICO	• Report by stage if available • Prioritise patient reported evidence	

	Details	Additional Comments
Type of review	• Qualitative Evidence • Mixed Methods (including quantitative and qualitative analysis) • Audits (patient experience survey)	Some level of quantitative evidence may be available from mixed methods studies though it is likely to be limited.
Language	English	
Study design	• Qualitative Studies • Mixed Methods studies	RCT's not likely to be available
Status		
	Details	**Additional Comments**
Other criteria for inclusion / exclusion of	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included	

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Item	Detail	
studies		
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 1990 onwards	
Useful Search Terms	• Information cancer patients • Unmet needs cancer patients • psychosocial distress, • health literacy • psycho-social support • holistic needs	
Review strategies	• The evidence for this topic will be qualitative and therefore risk of bias will be assessed using the NICE qualitative checklists included in the guidelines manual 2014. • Themes in the evidence will be identified and reported where relevant.	Themes: • Themes will be identified from the literature, but possible themes are expected to centre around psychosocial support, patient carer information and content of information: • Specific themes might include: • Psychosocial support: • Support groups/programmes and frequency of meetings • Dietetic input/advice and counselling • Psychological support/counselling • Timing of support • Frequency of support or assessments • Community based support • Secondary or Tertiary care support • Named individual or specialist nurse for point of contact Patient/carer information: • Support groups and organisations • Format and provision of information leaflets • Information prescription (list of potentially useful leaflets as determined by healthcare professional for a particular patient) • Personalised care plans (holistic needs assessment) • Availability and format of dietetic support

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Item	Detail	
		• Format and provision of communication or leaflets/information • Respite care • Support and benefits available to carers • Content • Access to various sources of information • Quality of information available • Specialist Palliative care services • Lifestyle, leisure, work, finances and social issues • Use or understanding of jargon and terminology • Treatments received or available and their associated complications • End of life care planning • Advance care planning
Identified papers	• Ziebland, S. Chapple A, Evans J (2015) Health Expect. Barriers to shared decisions in the most serious of cancers: a qualitative study of patients with pancreatic cancer treated in the UK 2015 Dec;18(6):3302-12. Epub 2014 Dec 11. • Chapple, A., Evans J., Ziebland S. (2012) An alarming prognosis: How people affected by pancreatic cancer use (and avoid) Internet information. Policy and Intent • Otani, H., Morita, T., Esaki,T., Ariyama, H., Tsukasa, K., Oshima, A., and Shiraisi, K. (2011). "Burden on Oncologists When Communicating the Discontinuation of Anticancer Treatment" Japanese Journal of Clinical Oncology. From a nursing perspective this paper highlight the provision of emotional and symptomatic support from a nurse specialist at the time of, or after giving bad news as essential. • Fine, E., Reid, C., Shengelia, R., and Adelman, R. (2010) "Directly Observed Patient–Physician Discussions in Palliative and End-of-Life Care: A Systematic Review of the Literature." Journal of Palliative Medicine. 13(5), p – 595 603 • Friis, L.S., Elverdam, B., and Schmidt K, G.(2003) " The patient's perspective: a qualitative study of acute myeloid leukaemia patients' need for information and their information-seeking behaviour". Supportive Care Cancer. 11, p 162–170. • Friedrichsen, M.J., Strang, P.M., and Carlsson,. M.E. (2000)" Breaking bad news in the transition to curative to palliative care-patient's view of the doctor giving the information" . Supportive Care Cancer. 8, p 472–478. • Aitini, E., and Aleotti, P (2006) . "Breaking bad news in oncology: like a walk in the twilight?" Annals of Oncology. 17(3), p 359–360 (suggest that as a patient's cancer advance further it becomes more difficult to understand what a patient really wants to know.) • Beesley et al (2016a) A tsunami of unmet needs: pancreatic and ampullary cancer patients' supportive care needs and use of community and allied health services in Psycho-Oncology 25: 150–157. • Beesley et al (2016b) Risk factors for current and future unmet supportive care needs of people with pancreatic cancer. A longitudinal study in Supportive Care in Cancer DOI 10.1007/s00520-016-3212-4 • Akizuki et al (2016) Prevalence and predictive factors of depression and anxiety in patients with pancreatic cancer: a longitudinal study in Japanese Journal of Clinical Oncology, 2016, 46(1) 71–77.	

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Item	Detail
	• ESMO (2015) Cancer of the pancreas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up in Annals of Oncology 26 (Supplement 5): v56–v68. • Polakowski et al (2015) Caring for the Continuum of Patients With Pancreatic Cancer: The Importance of Survivorship Care Planning in Clinical Journal of Oncology Nursing, Volume 19, Number 1. • Castellanos & Merchant (2014) Intensity of Follow-up after Pancreatic Cancer Resection in Ann Surg Oncol. 2014 March ; 21(3): 747–751. doi:10.1245/s10434-013-3289-7. • De La Cruz et al (2014) Diagnosis and Management of Pancreatic Cancer in Am Fam Physician. 2014;89(8):626-632. • Gooden & White (2013) Pancreatic cancer and supportive care—pancreatic exocrine insufficiency negatively impacts on quality of life in Supportive Care in Cancer 21:1835–1841. • Heiberg et al (2013) Development and preliminary validation of the pancreatic cancer disease impact score in Supportive Care in Cancer 21:1677–1684. • Torgerson & Wiebe (2013) Supportive Care of the Patient With Advanced Pancreatic Cancer - http://www.cancernetwork.com/oncology-journal/supportive-care-patient-advanced-pancreatic-cancer [Accessed online] • Boyd et al (2012) Screening for Depression, Sleep-Related Disturbances, and Anxiety in Patients with Adenocarcinoma of the Pancreas: A Preliminary Study in The Scientific World Journal, Article ID 650707, doi: 10.1100/2012/650707. • Petzel et al (2012) Fear of Cancer Recurrence after Curative Pancreatectomy: A Cross-sectional Study in Survivors of Pancreatic and Periampullary Tumors in Ann Surg Oncol 19:4078–4084. http://www.healthtalk.org/peoples-experiences/cancer/pancreatic-cancer/topics

C.81 Pain

Item	Detail		
Topic in Scope	Management of pancreatic cancer		
Review question in Scope	What is the role of sympathectomy or neurolytic l techniques in the management of pain from locally advanced and metastatic pancreatic cancer?		
Review Question in Guideline	What is the role of interventional techniques (e.g. sympathectomy or neurolytic techniques) in the management of pain in adults with newly diagnosed or recurrent pancreatic ductal adenocarcinoma?		
Economic Priority	Low		
PICO Table			
Population	**Intervention**	**Comparison**	**Outcomes**
• Adults with pancreatic cancer	• Sympathectomy (splanchnicectomy) • Neurolytic Techniques (nerve block/ablation, celiac plexus block/ablation, coeliac ganglion block/ablation, superior hypogastric block/ablation)	• Each Other • Other methods of pain management	• Reduction in opioid medication • Pain Relief/ improved analgesia (pain scores) • Duration of effect/ duration of relief • Adverse Events (Diarhoea, reduction in

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Item	Detail		
			Opioid induced side effects) • Health Related Quality of Life (functional domains) • Patient experience • PROMS • Overall survival
Setting	Adults (18 and over) with newly diagnosed or recurrent pancreatic ductal adenocarcinoma.		
Additional Comments on PICO	• Prioritise RCTs but no filter • Record detail of how the interventions are performed • Report timing of intervention if available		
	Details		**Additional Comments**
Type of review	Interventional		
Language	English		
Study design	• Systematic Reviews/Meta-analysis • Randomised Trials • Large comparative studies		Only include large comparative studies for interventions where there are no randomised trials
Status	Published		
Other criteria for inclusion / exclusion of studies	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.		
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 1966 onwards		
Useful Search Terms			
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a		

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Item	Detail
	minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is an interventional topic, GRADE methodology will be used to assess study quality for the outcomes. • Relevant subgroups for analysis will be identified upfront where appropriate
Possibly relevant papers (indentified by GC members and during initial scoping search)	• Arcidiacono PG. Celiac plexus block for pancreatic cancer pain in adults. [Review]. Cochrane Database of Systematic Reviews 2011;(3). • Yan BM. Neurolytic celiac plexus block for pain control in unresectable pancreatic cancer. [Review] [21 refs]. Am J Gastroenterol 2007 February;102(2):430-8. • Zhong W. Celiac plexus block for treatment of pain associated with pancreatic cancer: a meta-analysis. Pain Practice 2014 January;14(1):43-51. • Kaufman M. Efficacy of endoscopic ultrasound-guided celiac plexus block and celiac plexus neurolysis for managing abdominal pain associated with chronic pancreatitis and pancreatic cancer. [Review] [39 refs]. J Clin Gastroenterol 2010 February;44(2):127-34. • Mercadante S et al Sympathetic blocks for visceral cancer pain management : a systematic review and EAPC recommendations – suggest look at the references used which underpinned these recommendations? • Fujuii-Lau et al Impact of celiac neruolysis on survival in patients with pancreatic cancer. J Am Coll Surg 2015 Apr 220(4) • Lavu H a prospective randomised, double-blind placebo controlled trial on the efficacy of ethanol celiac plexus neurolysis in patients with operable pancreatic and periampullary & adenoca. World J of gastrointest Oncol 2014; 15;6(9): 360-8 • Leblanc J et al A prospective randomised study of EUS guided celiac plexus neurolysis for pancreatic cancer, one injection or two? Gastrointest ENdosc 2011; 74(6): 1300-7 • Arcidiano PG et al Celiac plexus block for pancreatic cancer pain in adults Cochrane database systematic review 2011 – not sure if this meets NICE criteria – can we look at the papers they used if we cant include this? • Allen PJ et al Prospective evaluation of laprascopic celiac plexus block in patients with unresectable pancreatic adenocarcinoma Ann Surg Oncol 2011 18;(3): 636-41 • Johnson CD et al An open randomised comparison of clinical effectiveness of protocol driven opioid nalgesia celiac plexus block or thorascopic splannicectomy for pain management in patients with pancreatic and other abdominal malignancies Pancreatology 2009;9(6):755-63 • O'Toole complication rates of EUS guided celiac plexus blockade & neurolysis results of a large case series Endoscopy 2009;41(7):593-7 • Mercadente S Celiac plexus bloc for pancreatic cancer pain: factors influencing pain, symptoms & quality of life J of pain & symptom management 2003; 26(6) 1140-7

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C.91 Nutritional interventions

Item	Detail
Topic in Scope	Management of Pancreatic Cancer
Review question in scope	What nutritional interventions (e.g. pancreatic enzyme replacement therapy, liquid nutritional supplements, dietetic assessment) improve outcomes for patients with pancreatic cancer?
Review Question in Guideline	What nutritional interventions (e.g. pancreatic enzyme replacement therapy, oral nutritional supplements, dietary manipulation, omega 3 fatty acids) are effective for patients with newly diagnosed or recurrent pancreatic cancer?
Economic Priority	Low

PICO Table

Population	Intervention	Comparison	Outcomes
• Patients with • Resectable pancreatic cancer (pre and post-operative) • Unresectable or metastatic pancreatic cancer	• Pancreatic Enzyme replacement therapy +/- Proton Pump Inhibitors • Information on taking PERT • Oral nutritional supplements • Dietary manipulation from specialist dietitian • Fish oils (Omega 3 fatty acids, DHA, EPA) • Glycaemic control • Enteral/ parenteral/oral nutrition	• No intervention • Each other	• Overall Survival • Treatment related morbidity • Health Related Quality of Life • Symptom control • Nutritional status (weight, BMI, lean body mass, strength test/ muscle function, sarcopenia, percentage weight change) • Adverse events • Patient experience • recurrence • tolerance to treatment (as in chemo/ surgery) • Ability to carry out normal activities

Additional Comments on PICO	• Subgroup analysis: Different stages of disease (1. Resectable pancreatic cancer; 2. Borderline resectable pancreatic cancer. 3. Unresectable pancreatic cancer)
Setting	• Adults (18 years and older) with newly diagnosed or recurrent ductal adenocarcinoma of the pancreas.

	Details	Additional Comments
Type of review	Interventional	
Language	English	
Study design	• Systematic Reviews/Meta-analysis of RCTs • Randomised Trials • Large comparative studies	
Status	Published and peer reviewed	

	Details	Additional Comments
Other criteria for	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.	

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Item	Detail	
inclusion / exclusion of studies		
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: None initially, possibly 1995 depending on the volume of literature found.	
Useful Search Terms		• Pancreatic Enzyme replacement therapy +/- Proton Pump Inhibitors – PERT, Creon, Nutrizym, Pancrease, Pancreatin, PPI, Pancreatic exocrine insufficiency/ exocrine pancreatic insufficiency, PEI/EPI • Information on taking PERT – PERT, Creon, Nutrizym, Pancrease, Pancreatin, Pancreatic exocrine insufficiency/ exocrine pancreatic insufficiency, PEI/EPI, literature • Oral nutritional supplements – enteral nutritional supplements, liquid food preparations, dietary supplements, artificial nutritional supplements, food replacement • Dietary manipulation from specialist dietitian – dietary input/ management, dietetic support, nutritional support, dietary modification, diet therapy, dietetic intervention, dietary advice, nutritional management (not sure if there are too many here, I'm just trying to think of things people call this) • Fish oils (Omega 3 fatty acids, DHA, EPA), Eicosapentaenoic acid, Docosahexaenoic acid, n3/n-3 fats/ fatty acids • Glycaemic control - blood glucose control/ management, blood sugar control/ management, diabetes, type 3c diabetes • Enteral/ parenteral/oral nutrition – artificial feeding/ artificial nutrition support, tube feeding, nasogastric feeding, nasojejunal feeding, jejunal feeding, PEG/ Percutanious Endoscopic Gastrostomy, gastrostomy, TPN, PN, parenteral nutrition

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Item	Detail
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. Evidence synthesis will take the form of a meta-analysis where possible. • As this is an interventional topic, GRADE methodology will be used to assess quality of the individual outcomes across the included studies. Relevant subgroups for analysis will be identified upfront where appropriate
Possibly relevant papers (identified by GC members and during initial scoping search)	• Bartel MJ, Asbun H, Stauffer J, Raimondo M. Pancreatic exocrine insufficiency in pancreatic cancer: A review of the literature. Dig Liver Dis. 2015;47(12):1013-20. • Landers A, Muircroft W, Brown H. Pancreatic enzyme replacement therapy (PERT) for malabsorption in patients with metastatic pancreatic cancer. BMJ Support Palliat Care. 2014 • Pericleous M, Rossi RE, Mandair D, Whyand T, Caplin ME. Nutrition and pancreatic cancer. Anticancer Res. 2014;34(1):9-21. • Bye A, Jordhøy MS, Skjegstad G, Ledsaak O, Iversen PO, et al. Symptoms in advanced pancreatic cancer are of importance for energy intake. Support Care Cancer. 2013;21(1):219-27. • Reid J, Mills M, Cantwell M, Cardwell CR, Murray LJ, et al. Thalidomide for managing cancer cachexia. Cochrane Database Syst Rev. 2012 18;4:CD008664. (Cochrane review 2012) • Domínguez-Muñoz JE. Pancreatic enzyme replacement therapy for pancreatic exocrine insufficiency: when is it indicated, what is the goal and how to do it?. Adv Med Sci. 2011;56(1):1-5. • Dewey A, Baughan C, Dean T, Higgins B, Johnson I. Eicosapentaenoic acid (EPA, an omega-3 fatty acid from fish oils) for the treatment of cancer cachexia. Cochrane Database Syst Rev. 2007 (Cochrane review 2007) • Davidson W, Ash S, Capra S, Bauer J, Cancer Cachexia Study G: Weight stabilisation is associated with improved survival duration and quality of life in unresectable pancreatic cancer. Clinical nutrition 2004; 23: 239-247. • Bachmann J, Heiligensetzer M, Krakowski-Roosen H, Buchler MW, Friess H, Martignoni ME: Cachexia worsens prognosis in patients with resectable pancreatic cancer. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract 2008; 12: 1193-1201.

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Item	Detail
	• Peng P, Hyder O, Firoozmand A, Kneuertz P, Schulick RD, Huang D et al.: Impact of sarcopenia on outcomes following resection of pancreatic adenocarcinoma. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract 2012; 16: 1478-1486. • Keller J, Layer P: Human pancreatic exocrine response to nutrients in health and disease. Gut 2005; 54 Suppl 6: vi1-28 • Barber MD: Cancer cachexia and its treatment with fish-oil-enriched nutritional supplementation. Nutrition 2001; 17: 751-755.Gooden & White, 2013. Pancreatic cancer and supportive care-pancreatic exocrine insufficiency negatively impacts on quality of life. • McCallum et al., 2014, Pancreatic Malignancy and Nutrition: a study of clinical practice. Annals of Oncology. Volume 25, Issue suppl 4 Pp. iv535.

C.10 1 Biliary obstruction

Item	Detail
Topic in Scope	Management of Pancreatic Cancer
Review question in scope	What is the optimal management of biliary obstruction?
Review Question in Guideline	What is the optimal treatment of biliary obstruction in adults with newly diagnosed or recurrent pancreatic cancer?
Economic Priority	High

PICO Table

Population	Intervention	Comparison	Outcomes
• Patients with biliary obstruction • Resectable pancreatic cancer • Borderline resectable pancreatic cancer • Unresectable or metastatic pancreatic cancer	• Biliary stent placement • plastic stents • Self-expandable metallic/metal stents (fully covered, partially covered, uncovered) • Preoperative biliary drainage followed by resection • Biliary bypass Surgery • Surgical resection without stenting	• Best supportive care • Each Other	• Relief of obstruction • Relief of symptoms • Treatment-related mortality • Treatment related morbidity • Treatment-related complications • Overall Survival • Time to definitive treatment • Health Related Quality of Life • Patient experience • PROMS

Setting	Adult (18 years and older) with newly diagnosed or recurrent ductal adenocarcinoma of the pancreas
Additional Comments on PICO	• Record method of stent placement (endoscopic (ERCP); percutaneous (PTHC/PTBD); EUS/trans duodenal/trans gastric) • Record if bypass surgery is open or laparoscopic • Was bilirubin level a criteria for going straight to surgery or stenting • Relief of symptoms: different studies have used differing definitions. Would include normalisation or near normalisation of bilirubin. Resolution of visible skin and sclera discolouration. Resolution of itch and return of urine to a normal colour.

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Item	Detail	
	• Treatment related morbidity: it's important that we dig out all the outcomes related to this topic, many of which are used in the van der Gaag study NEJM 2010, such as time to surgery, complications, hospital stay etc • Subgroup analysis: • Different types of endoscopy treatments (E.G. 1.metal stents VS Self-expandable metallic stents; 2. covered versus uncovered stents) • Different types of surgical treatments (E.G. open VS laparoscopic) • Different types of surgical treatments (E.G. 1. Choledochoduodenostomy; 2. choledochojejunostomy 3. Hepaticojejunostomy) • Include studies on covered or partially-covered SEMS vs uncovered SEMS; Exclude studies on plastic stent vs another type of plastic stent, one type of SEMS vs another type of SEMS.	
	Details	**Additional Comments**
Type of review	Interventional	
Language	English	
Study design	• Systematic Reviews/Meta-analysis of RCTs • RCTs • Comparative cohort studies • Qualitative Studies for PROMS?	
Status	Published and peer reviewed	
	Details	**Additional Comments**
Other criteria for inclusion / exclusion of studies	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.	
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 1995 onwards	
Useful Search Terms		None to be added
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary	

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Item	Detail	
	according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. Evidence synthesis will take the form of a meta-analysis where possible • As this is an interventional topic, GRADE methodology will be used to assess quality of the individual outcomes across the included studies. • Relevant subgroups for analysis will be identified upfront where appropriate	
Possibly relevant papers (indentified by GC members and during initial scoping search)	• Glazer ES, Hornbrook MC, Krouse RS. A meta-analysis of randomized trials: immediate stent placement vs surgical bypass in the palliative management of malignant biliary obstruction. J Pain Symptom Manage 2014;47(2):307-14. • Moss AC, Morris E, Leyden J, MacMathuna P. Malignant distal biliary obstruction: a systematic review and meta-analysis of endoscopic and surgical bypass results. Cancer Treat Rev 2007;33(2):213-21. • Artifon EL, Sakai P, Cunha JE, Dupont A, Filho FM, et al. Surgery or endoscopy for palliation of biliary obstruction due to metastatic pancreatic cancer. Am J Gastroenterol 2006;101(9):2031-7. • Moss AC, Morris E, Mac Mathuna P. Palliative biliary stents for obstructing pancreatic carcinoma. Cochrane Database Syst Rev 2006 (Cochrane review 2006) • Andtbacka RH, Evans DB, Pisters PW. Surgical and endoscopic palliation for pancreatic cancer. Minerva Chir 2004;59(2):123-36. • Fang Y, Gurusamy KS, Wang Q, Davidson BR, Lin H, Xie X, et al. Pre-operative biliary drainage for obstructive jaundice. Cochrane database Syst Rev. 2012 Jan;9:CD005444. • van der Gaag NA, Rauws EAJ, van Eijck CHJ, Bruno MJ, van der Harst E, Kubben FJGM, et al. Preoperative biliary drainage for cancer of the head of the pancreas. N Engl J Med. 2010 Jan 14;362(2):129–37.	

C.11 1 Duodenal obstruction

Item	Description
Topic in Scope	Management of Pancreatic Cancer
Review question in scope	What is the optimal management of duodenal obstruction?
Review Question in Guideline	What is the optimal treatment of adults with newly diagnosed or recurrent resectable pancreatic cancer, borderline resectable pancreatic cancer and unresectable/metastatic pancreatic cancer who have duodenal obstruction?
Economic Priority	Low

PICO Table

Population	Intervention	Comparison	Outcomes
• Adults with duodenal obstruction	• Duodenal stent placement	• Each Other	• Relief of obstruction

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Item	Description		
• Resectable pancreatic cancer • Borderline resectable pancreatic cancer • Unresectable or metastatic pancreatic cancer	• Gastric/duodenal bypass surgery (gastrojejunostomy/gastroenterostomy) • Venting gastrostomy • Resectional surgery	• Pharmacological management • Best supportive care	• Change in symptoms • Nutritional status • Adverse events • Overall Survival • Health Related Quality of Life • Patient experience • PROMS
Setting	Adults (18 and over) with newly diagnosed or recurrent pancreatic ductal adenocarcinoma.		
Additional Comments on PICO	• Stratify according to open or laparoscopic procedures • Subgroup analysis: • Different types of endoscopy treatments (E.G. 1.metal stents VS Self-expandable metallic stents; 2. covered versus uncovered stents) • Different types of gastrojejunostomy (open VS laparoscopic) • Whether obstructive jaundice can be treated successfully following duodenal stent placement vs gastroenterostomy.		

	Details	Additional Comments
Type of review	Interventional	
Language	English	
Study design	• Systematic Reviews/Meta-analysis of RCTs • RCTs • cohort studies (20+ participants)	
Status	Published	
	Details	**Additional Comments**
Other criteria for inclusion / exclusion of studies	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.	
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 2000 onwards for metal stents	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded	

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Item	Description
	by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is an interventional topic, GRADE methodology will be used to assess study quality for the outcomes. • Relevant subgroups for analysis will be identified upfront where appropriate
Possibly relevant papers (indentified by GC members and during initial scoping search)	• Gurusamy KS, Kumar S, Davidson BR. Prophylactic gastrojejunostomy for unresectable periampullary carcinoma. Cochrane Database Syst Rev. 2013 Feb 28;2:CD008533. (Cochrane Review 2013) • Maire F, Sauvanet A. Palliation of biliary and duodenal obstruction in patients with unresectable pancreatic cancer: endoscopy or surgery?. J Visc Surg 2013 Jun;150(3 Suppl):S27-31. • Lyons JM, Karkar A, Correa-Gallego CC, D'Angelica MI, DeMatteo RP, et al. Operative procedures for unresectable pancreatic cancer: does operative bypass decrease requirements for postoperative procedures and in-hospital days?. HPB (Oxford) 2012 Jul;14(7):469-75. • Jeurnink SM, Polinder S, Steyerberg EW, Kuipers EJ, Siersema PD. Cost comparison of gastrojejunostomy versus duodenal stent placement for malignant gastric outlet obstruction. J Gastroenterol 2010 May;45(5):537-43. • Köninger J, Wente MN, Müller MW, Gutt CN, Friess H, et al. Surgical palliation in patients with pancreatic cancer. Langenbecks Arch Surg 2007 Jan;392(1):13-21. • Maire F, Hammel P, Ponsot P, Aubert A, O'Toole D, et al. Long-term outcome of biliary and duodenal stents in palliative treatment of patients with unresectable adenocarcinoma of the head of pancreas. Am J Gastroenterol 2006 Apr;101(4):735-42. • Aware of Dutch study (Marco Bruno Rotterdam) comparing duodenal stent to surgery may still be recruiting

C.121 Neo-adjuvant treatment

Item	Detail
Topic in Scope	Management of Pancreatic Cancer
Review question in scope	Is neoadjuvant therapy for people with newly diagnosed or recurrent resectable and borderline resectable pancreatic adenocarcinoma an effective treatment?
Review question in	Is neoadjuvant therapy for adults with resectable and borderline resectable pancreatic adenocarcinoma an effective treatment?

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Item	Detail
guideline	
Economic Priority	Moderate

PICO Table

Population	Intervention	Comparison	Outcomes
• Adults with • Resectable pancreatic cancer • Borderline resectable pancreatic cancer	• Chemotherapy + resectional Surgery • Radiotherapy (stereotactic) + resectional Surgery • Chemoradiotherapy + resectional Surgery • Sequential chemotherapy + chemoradiotherapy + resectional Surgery	Resectional surgery	• Response to neoadjvuant treatment pre-surgery • Disease-free interval • Relapse-free survival • Overall Survival • Resection rate • Time from initiating treatment to Surgery • Adverse Events • Health Related Quality of Life • Patient experience • PROMS

Setting	Adults (18 and over) with newly diagnosed or recurrent pancreatic ductal adenocarcinoma.
Additional Comments on PICO	• Resection rate – record as a proportion of the total cohort • Adverse events – need to include surgical morbidity/mortality • All comparisons with or without adjuvant therapy • Chemotherapy regimens – gemcitabine, 5FU-based therapies, irinotecan, oxaliplatin, cisplatin, capecitabine, paclitaxel

	Details	Additional Comments
Type of review	Interventional	
Language	English	
Study design	• Systematic Reviews/Meta-analysis • Randomised Trials • Large comparative studies • Non comparative studies (50+ participants)	
Status	Published	

	Details	Additional Comments
Other criteria for inclusion / exclusion of studies	Non- English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.	
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to	

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Item	Detail	
	subject specific databases and used as appropriate. • Date Limit: 2000 onwards	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is an interventional topic, GRADE methodology will be used to assess study quality for the outcomes. • Relevant subgroups for analysis will be identified upfront where appropriate	
Possibly relevant papers (indentified by GC members and during initial scoping search)	• Andriulli A. Neoadjuvant/preoperative gemcitabine for patients with localized pancreatic cancer: a meta-analysis of prospective studies. [Review]. Ann Surg Oncol 2012 May;19(5):1644-62. • Chua TC. Preoperative chemoradiation followed by surgical resection for resectable pancreatic cancer: a review of current results. [Review]. Surg Oncol 2011 December;20(4):e161-e168. • Festa V. Neoadjuvant chemo-radiotherapy for patients with borderline resectable pancreatic cancer: a meta-analytical evaluation of prospective studies. Jop: Journal of the Pancreas [Electronic Resource] 2013 November;14(6):618-25. • Laurence JM, Tran PD, Morarji. A systematic review and meta-analysis of survival and surgical outcomes following neoadjuvant chemoradiotherapy for pancreatic cancer. [Review]. J Gastrointest Surg 2011 November;15(11):2059-69. • Petrelli F. FOLFIRINOX-based neoadjuvant therapy in borderline resectable or unresectable pancreatic cancer: a meta-analytical review of published studies. Pancreas 2015 May;44(4):515-21. • Xu CP, Xue XJ, Liang. Effect of chemoradiotherapy and neoadjuvant chemoradiotherapy in resectable pancreatic cancer: a systematic review and meta-analysis. [Review]. Journal of Cancer Research & Clinical Oncology 2014 April;140(4):549-59. • Gillen S et al. Preoperative/Neoadjuvant Therapy in Pancreatic Cancer: A Systematic Review and Meta-analysis of Response and Resection Percentages. PLOS 2010 • Assifi et al. Neoadjuvant Therapy in Pancreatic Adenocarcinoma: A Meta-Analysis	

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Item	Detail
	of Phase II Trials. Surgery 2011 • Heinemann V, Haas M, Boeck S (2013) Neoadjuvant treatment of borderline resectable and non-resectable pancreatic cancer. Ann Oncol 24: 2484–2492

C.131 Resectable and borderline resectable pancreatic cancer

Item	Detail		
Topic in Scope	Management of Pancreatic Cancer		
Review question in scope	What is the most effective surgery (type and extent) for adults with newly diagnosed or recurrent resectable and borderline resectable pancreatic cancer?		
Review Question in Guideline	What is the most effective surgery (type and extent) for adults with newly diagnosed resectable and borderline resectable pancreatic cancer?		
Economic Priority	Moderate		
PICO Table			
Population	**Intervention**	**Comparison**	**Outcomes**
• Adults with • Resectable pancreatic cancer • Borderline resectable pancreatic cancer	• Minimally invasive surgery • Laparoscopic • robotic • Extended surgery (e.g. venous arterial, extent of lymph nodes resection, other organs to be removed)	• Open surgery • Standard surgery	• Local Recurrence • Distant Recurrence • Overall Survival • Post operative death (30 day/90 day) • Treatment related morbidity • Treatment related mortality • Lymph node harvest • Health Related Quality of Life • Patient experience • PROMS
Setting	Adults (18 and over) with newly diagnosed pancreatic ductal adenocarcinoma.		
Additional Comments on PICO	• Types of surgery are • Pylorus Preserving Pancreatoduodectomy • Whipples Procedure • Distal Pancreatectomy • Total Pancreatectomy • Include papers of surgery plus adjuvant therapy • Report stage where available		
	Details	**Comments**	
Type of review	Interventional		
Language	English		
Study design	• Systematic Reviews/Meta-analysis • Randomised Trials • Large cohort studies		
Status	Published		
Other criteria for inclusion / exclusion of	Non-English Language Studies, conference abstracts, narrative		

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Item	Detail	
studies	reviews and non-comparative case series will not routinely be included.	
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 1995 onwards • RCT/SR filters to be applied to the searches	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is an interventional topic, GRADE methodology will be used to assess study quality for the outcomes. • Relevant subgroups for analysis will be identified upfront where appropriate	
Possibly relevant papers (indentified by GC members and during initial scoping search)	• Diener MK, Fitzmaurice C, Schwarzer G, Seiler CM, Hüttner FJ, Antes G, Büchler MW Pylorus-preserving pancreaticoduodenectomy (pp Whipple) versus pancreaticoduodenectomy (classic Whipple) for surgical treatment of periampullary and pancreatic carcinoma	

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Item	Detail
	10.1002/14651858.CD006053.pub5 (Cochrane Review 2014) • Diener MK, Knaebel HP, Heukaufer. A systematic review and meta-analysis of pylorus-preserving versus classical pancreaticoduodenectomy for surgical treatment of periampullary and pancreatic carcinoma. [Review] [59 refs]. Ann Surg 2007 February;245(2):187-200. • Karanicolas PJ, Davies E, Kunz. The pylorus: take it or leave it? Systematic review and meta-analysis of pylorus-preserving versus standard whipple pancreaticoduodenectomy for pancreatic or periampullary cancer. [Review] [36 refs]. Ann Surg Oncol 2007 June;14(6):1825-34. • Hartwig W, et al. Extended pancreatectomy in pancreatic ductal adenocarcinoma: definition and consensus of the International Study Group for Pancreatic Surgery (ISGPS) Surgery. 2014 Jul;156(1):1-14. doi: 10.1016/j.surg.2014.02.009. Epub 2014 Feb 20. • Bockhorn M, et al. Borderline resectable pancreatic cancer: A consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2014 Jun;155(6):977-88. doi: 10.1016/j.surg.2014.02.001. Epub 2014 Feb 7. • Tol JA, et al Definition of a standard lymphadenectomy in surgery for pancreatic ductal adenocarcinoma: a consensus statement by the International Study Group on Pancreatic Surgery (ISGPS). Surgery. 2014 Sep;156(3):591-600.

C.141 Adjuvant treatment

Item	Detail
Topic in Scope	Management of Pancreatic Cancer
Review question in Scope	What is the most effective adjuvant therapy (chemotherapy, chemoradiotherapy or radiotherapy) for people who have undergone surgical resection of pancreatic adenocarcinoma?
Review Question in Guideline	What is the most effective adjuvant therapy (chemotherapy, chemoradiotherapy, biological therapy, immunotherapy, combinations of therapies) for adults who have undergone surgical resection of pancreatic adenocarcinoma?
Economic Priority	Low

PICO Table

Population	Intervention	Comparison	Outcomes
• Patients who have undergone resection of primary pancreatic cancer	• Chemotherapy • combination chemotherapy with chemoradiotherapy • Immunotherapy • Biological therapy	• Different Chemo types/combination regimens • chemoradiotherapy • No adjuvant therapy • Combination chemotherapy with chemoradiothery • Chemotherapy Alone • Chemoradiotherapy Alone • No Adjuvant Treatment • Other adjuvant therapy • No Adjuvant treatment • Other adjuvant therapy • No Adjuvant treatment	• Disease-free interval • Relapse-free survival • Overall Survival • Adverse Events • Health Related Quality of Life • Patient experience • PROMS

Settings	• Adults (18 and over) referred to secondary care with suspected pancreatic cancer.

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Item	Detail	
	• Adults (18 and over) with newly diagnosed or recurrent pancreatic ductal adenocarcinoma.	
Additional Comments on PICO	• Exclude surgery in cases of benign disease and in non-pancreatic cancer populations (e.g. pancreatitis) • Chemotherapy regimens – gemcitabine, 5FU-based therapies, irinotecan, oxaliplatin, cisplatin, capecitabine, paclitaxel, S-1 • Immunotherapy – interferon, vaccine, K-Ras, antibody	
	Details	**Additional Comments**
Type of review	Interventional	
Language	English	
Study design	• Systematic Reviews/Meta-analysis • Randomised Trials	
Status	Published	
	Details	**Additional Comments**
Other criteria for inclusion / exclusion of studies	• Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.	
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 2000 onwards • RCT/SR filters to be applied to the searches	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is an interventional topic, GRADE methodology will be used to assess study	

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Item	Detail
	quality for the outcomes. • Relevant subgroups for analysis will be identified upfront where appropriate
Possibly relevant papers (identified by GC members and during initial scoping search)	• Boeck S, Ankerst DP, Heinemann. The role of adjuvant chemotherapy for patients with resected pancreatic cancer: systematic review of randomized controlled trials and meta-analysis. [Review] [30 refs]. Oncology 2007;72(5-6):314-21. • Khanna A. Is adjuvant 5-FU-based chemoradiotherapy for resectable pancreatic adenocarcinoma beneficial? A meta-analysis of an unanswered question. J Gastrointest Surg 2006 May;10(5):689-97. • Stocken DD, Buchler MW, Dervenis. Meta-analysis of randomised adjuvant therapy trials for pancreatic cancer. Br J Cancer 2005 April 25;92(8):1372-81. • Adjuvant chemotherapy with gemcitabine vs observation in patients undergoing curative-intent resection of pancreatic cancer: a randomized controlled trial. • Oettle H, Post S, Neuhaus P, Gellert K, Langrehr J, Ridwelski K, Schramm H, Fahlke J, Zuelke C, Burkart C, Gutberlet K, Kettner E, Schmalenberg H, Weigang-Koehler K, Bechstein WO, Niedergethmann M, Schmidt-Wolf I, Roll L, Doerken B, Riess H JAMA. 2007;297(3):267 • Fluorouracil vs gemcitabine chemotherapy before and after fluorouracil-based chemoradiation following resection of pancreatic adenocarcinoma: a randomized controlled trial. Regine WF, Winter KA, Abrams RA, Safran H, Hoffman JP, Konski A, Benson AB, Macdonald JS, Kudrimoti MR, Fromm ML, Haddock MG, Schaefer P, Willett CG, Rich TA JAMA. 2008;299(9):1019 • Adjuvant 5-fluorouracil and folinic acid vs observation for pancreatic cancer: composite data from the ESPAC-1 and -3(v1) trials. Neoptolemos JP, Stocken DD, Tudur Smith C, Bassi C, Ghaneh P, Owen E, Moore M, Padbury R, Doi R, Smith D, Büchler MW Br J Cancer. 2009;100(2):246 • A randomised phase III trial comparing gemcitabine with surgery-only in patients with resected pancreatic cancer: Japanese Study Group of Adjuvant Therapy for Pancreatic Cancer. Ueno H, Kosuge T, Matsuyama Y, Yamamoto J, Nakao A, Egawa S, Doi R, Monden M, Hatori T, Tanaka M, Shimada M, Kanemitsu K Br J Cancer. 2009;101(6):908 • Adjuvant chemoradiation for pancreatic adenocarcinoma: the Johns Hopkins Hospital-Mayo Clinic collaborative study. Hsu CC, Herman JM, Corsini MM, Winter JM, Callister MD, Haddock MG, Cameron JL, Pawlik TM, Schulick RD, Wolfgang CL, Laheru DA, Farnell MB, Swartz MJ, Gunderson LL, Miller RC Ann Surg Oncol. 2010;17(4):981 • Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: a randomized controlled trial. Neoptolemos JP, Stocken DD, Bassi C, Ghaneh P, Cunningham D, Goldstein D, Padbury R, Moore MJ, Gallinger S, Mariette C, Wente MN, Izbicki JR, Friess H, Lerch MM, Dervenis C, Oláh A, Butturini G, Doi R, Lind PA, Smith D, Valle JW, Palmer DH, Buckels JA, Thompson J, McKay CJ, Rawcliffe CL, Büchler MW, European Study Group for Pancreatic Cancer JAMA. 2010;304(10):1073. • Fluorouracil-based chemoradiation with either gemcitabine or fluorouracil chemotherapy after resection of pancreatic adenocarcinoma: 5-year analysis of the U.S. Intergroup/RTOG 9704 phase III trial. Regine WF, Winter KA, Abrams R, Safran H, Hoffman JP, Konski A, Benson AB, Macdonald JS, Rich TA, Willett CG Ann Surg Oncol. 2011;18(5):1319 • Adjuvant chemotherapy with gemcitabine and long-term outcomes

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Item	Detail
	among patients with resected pancreatic cancer: the CONKO-001 randomized trial. Oettle H, Neuhaus P, Hochhaus A, Hartmann JT, Gellert K, Ridwelski K, Niedergethmann M, Zülke C, Fahlke J, Arning MB, Sinn M, Hinke A, Riess H JAMA. 2013;310(14):1473 • Adjuvant treatments for resected pancreatic adenocarcinoma: a systematic review and network meta-analysis. Liao WC, Chien KL, Lin YL, Wu MS, Lin JT, Wang HP, Tu YK Lancet Oncol. 2013;14(11):1095 • Adjuvant gemcitabine alone versus gemcitabine-based chemoradiotherapy after curative resection for pancreatic cancer: a randomized EORTC-40013-22012/FFCD-9203/GERCOR phase II study. Van Laethem JL, Hammel P, Mornex F, Azria D, Van Tienhoven G, Vergauwe P, Peeters M, Polus M, Praet M, Mauer M, Collette L, Budach V, Lutz M, Van Cutsem E, Haustermans K J Clin Oncol. 2010;28(29):4450. • Fukutomi A, Uesaka K, Boku N, et al. JASPAC 01: Randomized phase III trial of adjuvant chemotherapy with gemcitabine versus S-1 for patients with resected pancreatic cancer (abstract). J Clin Oncol 31,2013 (suppl; abstr 4008). http://meetinglibrary.asco.org/content/116237-132 (Accessed on June 10, 2013). • Gemcitabine Adjuvant Therapy for Resected Pancreatic Cancer: A Meta-analysis. Yu Z, Zhong W, Tan ZM, Wang LY, Yuan YH Am J Clin Oncol. 2015;38(3):322 • ESPAC-1: A European, randomized controlled study of adjuvant chemoradiation and chemotherapy in resectable pancreatic cancer. Neoptolemos JP, Dunn JA, Moffitt DD, et al, for the members of the European Study Group for Pancreatic Cancer (ESPAC). Lancet 2001;358:1576-85. • A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer. Neoptolemos JP, Stocken DD, Friess H, et al, for the members of the European Study Group for Pancreatic Cancer (ESPAC). N Engl J Med 2004;350:1200-10. • Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. Oettle H, Neuhaus P, Hochhaus A, et al. JAMA 2013;310:1473-81. • Adjuvant 5-fluorouracil and folinic acid vs observation for pancreatic cancer: composite data from the ESPAC-1 and -3(v1) trials. Neoptolemos JP, Stocken DD, Tudur Smith C, et al. Br J Cancer 2009;100:246-50. • Optimal duration and timing of adjuvant chemotherapy after definitive surgery for ductal adenocarcinoma of the pancreas: ongoing lessons from the ESPAC-3 study. Valle JW, Palmer D, Jackson R, et al. J Clin Oncol 2014;32:504-512. • Fluorouracil vs gemcitabine chemotherapy before and after fluorouracil-based chemoradiation following resection of pancreatic adenocarcinoma: a randomized controlled trial. Regine WF, Winter KA, Abrams RA, et al. JAMA 2008;299:1019-26. • Adjuvant chemoradiation for pancreatic cancer: few good data, much debate. Twombly R. J Natl Cancer Inst 2008;100:1670-1. • Open-label, multicenter, randomized phase III trial of adjuvant chemoradiation plus interferon Alfa-2b versus fluorouracil and folinic acid for patients with resected pancreatic adenocarcinoma. Schmidt J, Abel U, Debus J, et al. J Clin Oncol 2012;30:4077-83. • Adjuvant treatments for resected pancreatic adenocarcinoma: a systematic review and network meta-analysis. Liao WC, Chien KL, Lin YL, et al. Lancet Oncol 2013; 14:1095-103.

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Item	Detail
	• Bayesian analysis unravels pancreas cancer adjuvant therapy. Neoptolemos JP, T Cox. Lancet Oncol 2013; 14:1034-5. • European Study Group for Pancreatic Cancer. Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: a randomized controlled trial. Neoptolemos JP, Stocken DD, Bassi C, et al; JAMA. 2010; 304(10): 1073-81. 2010; 304(10): 1073-81. 2010;304:1073-81. • Classification of R1 resections for pancreatic cancer: the prognostic relevance of tumour involvement within 1 mm of a resection margin. Campbell F, Smith RA, Whelan P, et al. Histopathology 2009;55:277-83. • TNM classification of malignant tumours Sobin LH, Gospodarowicz, MK, Wittekind C, eds. 7th edition. UICC 7th Edition 2009. Oxford, England: Wiley-Blackwell, 2010:132-5. • TAME: development of a new method for summarising adverse events of cancer treatment by the Radiation Therapy Oncology Group. Trotti A, Pajak TF, Gwede CK, et al. Lancet Oncol 2007;8:613-24. • JASPAC 01: Randomized phase III trial of adjuvant chemotherapy with gemcitabine versus S-1 for patients with resected pancreatic cancer. Fukutomi A, Uesaka K, Boku N, et al. J Clin Oncol. 2013;31: supplement, abstract 4008. • CONKO-005: Adjuvant therapy in R0 resected pancreatic cancer patients with gemcitabine plus erlotinib versus gemcitabine for 24 weeks—A prospective randomized phase III study. Sinn M, Liersch T, Gellert K, et al. J Clin Oncol 2015;33: supplement, abstract 4007. • European Study Group for Pancreatic Cancer. Pancreatic cancer hENT1 expression and survival from gemcitabine in patients from the ESPAC-3 Trial. Greenhalf W, Ghaneh P, Neoptolemos JP, et al; J Natl Cancer Inst 2014;106(1):djt347.

C.151 Follow-up for people with resected pancreatic cancer

Item	Detail
Area in Scope	Follow Up
Review question in Scope	What is the most effective follow-up protocol for people with resected pancreatic cancer?
Review Question in Guideline	What is the optimal follow-up protocol for people with resected pancreatic adenocarcinoma?
Economic Priority	High

PICO Table

Population	Intervention	Comparison	Outcomes
Patients who have undergone surgical resection for pancreatic adenocarcinoma with curative intent	• GI/endocrine • Psychological • Oncological • Follow-up packages (including combinations of follow-up elements such as clinical assessment (including Holistic Needs Assessment	No active/ scheduled follow-up or one of the interventions listed	• Survival • Time to detection of recurrence • Proportion of asymptomatic recurrence (imaging) • Fitness for further intervention • HRQL • Adverse events

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Item	Detail		
	(HNA) and clinical examination), imaging, blood tests including CA19.9, including the frequency of follow up)		• Risk of increased radiation (following repeated imaging) • PROMS • Patient acceptability
Setting	Adults (18 years and older) with newly diagnosed or recurrent ductal adenocarcinoma of the pancreas.		
Additional Comments on PICO	• Follow up setting primary or secondary care – Active follow up would be in secondary care (surgical / oncology / CNS reviews) • Look at whether follow up should be at specialist centre or local hospital • Some conference abstracts may give good insight into HCP role in follow up		

	Details	Additional Comments
Type of review	Management	
Language	English	
Study design	• Systematic reviews / meta-analysis • Case series • Published studies of unit/centre experiences and outcomes (retrospective audits) • Comparative studies • Articles in press	
Status		
	Details	**Additional Comments**
Other criteria for inclusion / exclusion of studies	Non-English Language Studies, conference abstracts, narrative reviews will not routinely be included.	
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: Suggest 1995 onwards (as per some of the previous questions)	
Useful Search Terms		• Follow-up, surveillance, survivorship, post-operative supportive care and PDAC • Nurse led/ nurse led follow up" , • "recurrence" or " diagnosis of recurrence and PDAC"
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through	

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Item	Detail
	systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is an interventional topic, GRADE methodology will be used to assess study quality for the outcomes. Evidence synthesis will be in the form of a meta-analysis where appropriate though in the case of this topic, it is likely to take the form of a narrative review due to a lack of evidence. • Relevant subgroups for analysis will be identified upfront where appropriate
Identified papers	• Suufferlin, T., et al (2012) “Pancreatic Adenocarcinoma: ESMO-ESDO clinical practice guidelines for diagnosis , treatment and follow up”. Annals of Oncology. 23 (7) • Tjaden , C et al (2005) “Clinical Impact of Structured follow up after Pancreatic Surgery”. Pancreas. • Ploakowski et al (2015) “Caring for the continuum of patients with pancreatic cancer. Importance of survivorship care planning. Clinical Journal of Oncology Nursing. 19, 1. • Parikh, A., et al (2015) “ Adjuvant therapy in Pancreas Cancer: Does it influence patterns of recurrence?” American College of Surgeons • Tzeng CW et al (2013) “Frequency and intensity of postoperative surveillance after curative treatment of pancreatic cancer: a cost-effectiveness analysis” . Annals of Surgical Oncology • Beeseley et al (2016) “A tsunmi of unmet needs: pancreatic and ampu8llary cancer patients supportive care needs and use of community and allied health services. Psycho oncology, 25, pp 150 – 157. • Visser, B.C, May, Y et al (2012) “Failure to comply with NCCN guidelines for the management of pancreatic cancer compromises patient outcomes. HPB. 14, pp 5390547. • O’Reilly, EM, Lowery, M.A (2012) “Post resection status for pancreatic cancer: performance status, imaging and serum markers. Cancer Journal, 18, pp 609-613.

C.161 Management of locally advanced pancreatic cancer

Item	Detail
Topic in Scope	Management of Pancreatic Cancer
Review question in	What is the most effective treatment (chemotherapy,

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Item	Detail		
Scope	chemoradiotherapy, or other local therapies) for people with unresectable locally advanced pancreatic cancer?		
Review Question in Guideline	What is the most effective treatment (chemotherapy, chemoradiotherapy, radiotherapy, combinations of chemotherapy and chemoradiotherapy, biological therapies, immunotherapy or other local therapies) for adults with newly diagnosed or recurrent unresectable locally advanced non-metastatic pancreatic cancer?		
Economic Priority			
PICO Table			
Population	**Intervention**	**Comparison**	**Outcomes**
Patients with unresectable non-metastatic locally advanced pancreatic cancer	• Chemotherapy • Radiotherapy/ SBRT +/- chemotherapy • Immunotherapy • Biological therapies • Other local therapies (RFA, microwave • Chemoradiotherapy +/- chemotherapy (either sequence)	• Chemotherapy • different types/regimens/combinations of chemotherapy • best supportive care • Chemoradiotherapy • Best supportive care • chemotherapy	• Objective Response (CR/PR/PD/SD/) • Resection rate • Progression Free Survival (local, distant) • Overall Survival • Adverse Events • Health Related Quality of Life • pain control • Patient experience • PROMS
Setting	• Adults (18 and over) referred to secondary care with suspected pancreatic cancer. • Adults (18 and over) with newly diagnosed or recurrent pancreatic ductal adenocarcinoma.		
Additional Comments on PICO			
	Details		**Comments**
Type of review	Interventional		
Language	English		
Study design	• Systematic Reviews/Meta-analysis • Randomised Trials • Large comparative studies • Non-comparative prospective (50+ participants)		
Status	Published		
Other criteria for inclusion / exclusion of studies	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.		
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science.		

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Item	Detail	
	Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 2000 onwards, apart from no date limit for ablation.	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is an interventional topic, GRADE methodology will be used to assess study quality for the outcomes. • Relevant subgroups for analysis will be identified upfront where appropriate	
Possibly relevant papers (indentified by GC members and during initial scoping search)	• Ambe C. A Meta-analysis of Randomized Clinical Trials of Chemoradiation Therapy in Locally Advanced Pancreatic Cancer. Journal of Gastrointestinal Cancer 2015 September;46(3):284-90. • Earle CC. The treatment of locally advanced pancreatic cancer: a practice guideline. [Review] [20 refs]. Can J Gastroenterol 2003 March;17(3):161-7. • Huguet F. Chemoradiotherapy in the management of locally advanced pancreatic carcinoma: a qualitative systematic review. [Review] [31 refs]. J Clin Oncol 2009 May 1;27(13):2269-77. • Sultana A. Systematic review, including meta-analyses, on the management of locally advanced pancreatic cancer using	

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Item	Detail
	radiation/combined modality therapy. [Review] [40 refs]. Br J Cancer 2007 April 23;96(8):1183-90. • Sultana A. Meta-analyses of chemotherapy for locally advanced and metastatic pancreatic cancer. J Clin Oncol 2007 June 20;25(18):2607-15. • Hu J. A meta-analysis of gemcitabine containing chemotherapy for locally advanced and metastatic pancreatic adenocarcinoma. Journal of hematology & oncology 2011;4:11. • Ierardi AM. Systematic review of minimally invasive ablation treatment for locally advanced pancreatic cancer. [Review]. Radiol Med (Torino) 2014 July;119(7):483-98. • Fegrachi S, Besselink MG, van Santvoort HC, van Hillegersberg. Radiofrequency ablation for unresectable locally advanced pancreatic cancer: a systematic review. [Review]. HPB 2014 February;16(2):119-23. • Gurusamy KS, Kumar S, Davidson BR, Fusai G. Resection versus other treatments for locally advanced pancreatic cancer. Cochrane Database of Systematic Reviews 2014;(2). • Hammel P et al. Comparison of chemoradiotherapy (CRT) and chemotherapy (CT) in patients with a locally advanced pancreatic cancer (LAPC) controlled after 4 months of gemcitabine with or without erlotinib: Final results of the international phase III LAP 07 study. J Clin Oncol 31, 2013 (suppl; abstr LBA4003) • Huguet F et al. Impact of chemoradiotherapy (CRT) on local control and time without treatment in patients with locally advanced pancreatic cancer (LAPC) included in the international phase III LAP 07 study. J Clin Oncol 32:5s, 2014 (suppl; abstr 4001^) • Huguet F, Mukherjee S, Javle M. Locally Advanced Pancreatic Cancer: The Role of Definitive Chemoradiotherapy. Clin Oncol (R Coll Radiol). 2014 Jul 4. pii: S0936-6555(14)00235-0. doi: 10.1016/j.clon.2014.06.002. [Epub ahead of print] • Mukherjee S, Hurt CN, Bridgewater J, Falk S, Cummins S, Wasan H, Crosby T, Jephcott C, Rajarshi Roy, Radhakrishna G, McDonald A, Ray R, Joseph G, Staffurth J, Abrams RA, Griffiths G, Maughan T. Gemcitabine-based or capecitabine-based chemoradiotherapy for locally advanced pancreatic cancer (SCALOP): a multicentre, randomised, phase 2 trial. Lancet Oncol. 2013 Apr;14(4):317-26. doi: 10.1016/S1470-2045(13)70021-4. Epub 2013 Mar 6 • Loehrer P et al. Gemcitabine Alone Versus Gemcitabine Plus Radiotherapy in Patients With Locally Advanced Pancreatic Cancer: An Eastern Cooperative Oncology Group Trial. JCO November 1, 2011 vol. 29 no. 31 4105-4112 • Chauffert et al, Phase III trial comparing intensive induction chemoradiotherapy (60 Gy, infusional 5-FU and intermittent cisplatin) followed by maintenance gemcitabine with gemcitabine alone for locally advanced unresectable pancreatic cancer. Definitive results of the 2000–01 FFCD/SFRO study. Ann Oncol (2008) 19 (9): 1592-1599. doi: 10.1093/annonc/mdn281 • Hurt CN et al. Health-Related Quality of Life in SCALOP, a Randomized Phase 2 Trial Comparing Chemoradiation Therapy Regimens in Locally Advanced Pancreatic Cancer. Int J Radiat Oncol Biol Phys. 2015 Nov 15;93(4):810-8. doi: 10.1016/j.ijrobp.2015.08.026. Epub 2015 Aug 24. • Esnaola et al Phase 2 trail of induction gemcitabime, oxaliplatin, and cetuximab followed by selective capcitabine based chemoradiation in patients with borderline of unresetable LAPC – International Journal of Radiation Oncology – 2014, 88 (4), 837 – 44.

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C.171 Management of metastatic pancreatic cancer

Item	Detail		
Topic in Scope	Management of Pancreatic Cancer		
Review question in scope	What is the most effective method of management for people with metastatic pancreatic cancer (for example, chemotherapy [excluding interventions covered by NICE technology appraisals], symptom control, surgery for isolated metastases?		
Review Question in Guideline	What are the most effective interventions (excluding relevant NICE TAs) for adults with newly diagnosed or recurrent metastatic pancreatic cancer (chemotherapy, surgery, radiotherapy)?		
Economic Priority	High		
PICO Table			
Population	**Intervention**	**Comparison**	**Outcomes**
Patients with advanced and/or metastatic pancreatic cancer	• Chemotherapy (1st line, 2nd line) • Surgery for metastatic disease +/- chemotherapy • Radiotherapy	• Different Chemo types/regimens • Best supportive care • No surgery • Ablative techniques for metastases • Best supportive care • Best supportive care	• Response rate • Progression Free Survival • Overall Survival • Adverse Events • Health Related Quality of Life • Patient experience and PROMs • Symptom control
Setting	• Adults (18 and over) referred to secondary care with suspected pancreatic cancer. • Adults (18 and over) with newly diagnosed or recurrent pancreatic ductal adenocarcinoma.		
Additional Comments on PICO	Chemotherapy regimens: • FOLFIRINOX, • FOLFOX, • CAPOX, • capecitabine, • cisplatin, • paclitaxel, • immunotherapy, • other 5FU-based chemotherapy regimens, • GEMCAP irinotecan, • epirubicin In terms of the question as to the definition of 'best supportive care' helpfully there isn't an agreed one. Generally speaking it is usually meant to help patients & families cope with the condition from any point along their journey encompassing symptom control, information needs, psychological support, social needs EOLC, bereavement etc, it isn't specialist palliative care per se. Some sites - e.g. National Cancer Institute equate supportive care to palliative care. There are a few studies - e.g. in lung cancer where the absence of the definition of BSC for both clinical and economic comparators is pointed out and generally speaking it is considered to be the best care that is available excluding the intervention i.e. chemo, RT which is I suppose what we are trying to establish in this question and in which case if it is not a standard alternative should probably be listed separately.		

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Item	Detail	
	Details	**Additional Comments**
Type of review	Interventional	
Language	English	
Study design	• Systematic Reviews/Meta-analysis • Randomised Trials	
Status	Published	
	Details	**Additional Comments**
Other criteria for inclusion / exclusion of studies	Non-English Language Studies, conference abstracts, narrative reviews and non-comparative case series will not routinely be included.	
Search strategies	• The core databases as listed in the NICE Guidelines Manual will be searched as a minimum (i.e. Cochrane Library (CDSR, DARE, CENTRAL and HTA), Medline & Medline in Process and Embase). Additionally we may search Web of Science. Consideration will be given to subject specific databases and used as appropriate. • Date Limit: 2000 onwards, apart from no date limit for ablation and surgery for metastatic disease.	
Useful Search Terms		
Review strategies	• Evidence will be identified, assessed and synthesised according to the methods outlined in the Guidelines Manual (2014). • Relevant studies will be identified through systematic searches by the information specialist. Results will be sifted and irrelevant studies excluded by title and abstract in the first instance. A proportion of the studies will be dual sifted by a second reviewer/research assistant and any discrepancies will be recorded and discussed. The proportion sifted will vary according to the size of the topic with a minimum 15% of studies dual sifted. • Full text articles will be ordered and a further sift to exclude irrelevant studies will be carried out. • The remaining, relevant evidence will assessed and synthesised using the appropriate quality checklists according to the NICE Guideline Manual (2014) in order to assess the risk of bias. • As this is an interventional topic, GRADE methodology will be used to assess study quality for the outcomes. • Relevant subgroups for analysis will be identified upfront where appropriate	
Possibly relevant papers (identified by GC members and during initial scoping search)	• Moir J. Systematic review of irreversible electroporation in the treatment of advanced pancreatic cancer. [Review]. Eur J Surg Oncol 2014 December;40(12):1598-604. • Sultana A. Meta-analyses of chemotherapy for locally advanced and	

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Item	Detail
	metastatic pancreatic cancer. J Clin Oncol 2007 June 20;25(18):2607-15. • Sultana A. Meta-analyses of chemotherapy for locally advanced and metastatic pancreatic cancer: results of secondary end points analyses. Br J Cancer 2008 July 8;99(1):6-13. • Adler H. Pancreatectomy for metastatic disease: a systematic review. [Review]. Eur J Surg Oncol 2014 April;40(4):379-86. • Gounaris I. Options for the treatment of gemcitabine-resistant advanced pancreatic cancer. [Review] [69 refs]. Jop: Journal of the Pancreas [Electronic Resource] 2010;11(2):113-23. • FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer. Conroy et al. N Engl J Med 2011; 364:1817-1825 • Phase III randomized comparison of gemcitabine versus gemcitabine plus capecitabine in patients with advanced pancreatic cancer. Cunningham et al. J Clin Oncol 2009 Nov 20;27(33) 5513-8 • FRAGEM trial: Gemcitabine versus gemcitabine plus dalteparin • thromboprophylaxis in pancreatic cancer A. Maraveyas et al. Eur J Cancer 2012;48:1283-92 • Second-Line Oxaliplatin, Folinic Acid, and Fluorouracil Versus Folinic Acid and Fluorouracil Alone for Gemcitabine-Refractory Pancreatic Cancer: Outcomes From the CONKO-003 Trial Helmut Oettle et al. JCO 2014.

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