National Institute for Health and Care Excellence

Final

Pancreatic cancer in adults:

diagnosis and management

Appendix L

Health economics evidence tables

February 2018

Final

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.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

Contents

Appendix L:Health economics evidence tables

L.1 Staging

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?

References to included studies:

Morris S, Gurusamy KS, Sheringham J et al. 'Cost-effectiveness of diagnostic laparoscopy for assessing resectability in pancreatic andperiampullary cancer'. BMC Gastroenterol. (2015)

Ghaneh P, Wong WL, Titman A et al. 'PET-PANC: Multi-centre prospective diagnostic accuracy and clinical value study of PET/CT in the diagnosis and management of pancreatic cancer'. Pancreatology. (2016)

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
Study 1						
Author: Ghaneh Year: 2016 Country: UK	Type of analysis: Cost-utility Model structure: Economic Evaluation alongside prospective diagnostic accuracy study Cycle length:	Base case (population): Adults with potential PDAC defined by either: a focal lesion identified in the pancreas or pancreatic duct detected on MDCT.	1. Standard diagnosis and staging with MDCT (standard work-up differed between centres)[MDCT] 2. PET/CT following standard diagnosis and	Primary Model (all patients received resection) Incremental Effectiveness (LYs vs MDCT)a: Basecase PDAC PDAC+Resection	 0.0150 0.0110 0.0161	Funding: The National Institute for Health Research Health Technology Assessment programme Comments

[a] Given the way costs and outcomes were calculated between competing interventions only incremental values were reported by the study.
[3] Given the way costs and outcomes were calculated between competing interventions only incremental values were reported by the study.

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	N/A Time horizon: 1 year Perspective: UK NHS Source of base-line data: All sources of baseline data were taken from the accompanying prospective diagnostic accuracy study involving 550 patients, 261 of whom (44%) had PDAC with 216 receiving surgical resection at 18 NHS tertiary centres. The aim of the study was to investigate the changes in diagnostic accuracy and management of patients from the addition of PET/CT to standard	Jaundice from biliary obstruction defined as serum bilirubin>35 µmol/l Serum ca19.9 >37kU/l Patients who were pregnant or had poorly controlled diabetes were excluded. Subgroup analysis (relevant to this topic): PET/CT only in patients with a PDAC diagnosis by MDCT [PDAC] PET/CT only in patients with PDAC diagnosis by MDCT and indicated for surgical resection. [PDAC+resection]	staging. [PET/CT]	Incremental Effectiveness (QALYs vs MDCT)b: Basecase PDAC PDAC+Resection Incremental costs (per patient vs MDCT)[Nuclear medicine/Clinical Oncology costs]: Basecase PDAC PDAC+Resection ICER (cost per QALY) [Nuclear medicine/Clinical Oncology costs]): Basecase PDAC PDAC+Resection Secondary Model (bypass and open and shut laparotomy also included) Incremental Effectiveness (LYs vs MDCT)c: Basecase PDAC	0.0157 0.0119 0.0175 -£645/-£912 -£639/-£906 -£1275/-£1542 PET/CT Dominant PET/CT Dominant PET/CT Dominant 0.0092 0.0096 0.0108	Study also includes subgroup analyses (i.e. chronic pancreatitis) that are not within the scope of this guideline and consequently have not been reported here.

[c] Given the way costs and outcomes were calculated between competing interventions only incremental values were reported by the study.

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	diagnostic work-up. The study is described in detail in the accompanying clinical evidence review. Source of effectiveness data: All effectiveness data (sensitivity, specificity, change in management etc.) was collected from the prospective diagnostic accuracy study described above. Source of utility data: Utility data was collected from patients in the prospective diagnostic accuracy study described above. Quality of life was collected using the EQ-5D-3L questionnaire given to participants in the study at each 3 monthly review and			PDAC+Resection Incremental Effectiveness (QALYs vs MDCT)d: Basecase PDAC PDAC+Resection Incremental costs (per patient vs MDCT)[Nuclear medicine/Clinical Oncology costs]: Basecase PDAC PDAC+Resection ICER (cost per QALY) [Nuclear medicine/Clinical Oncology costs]): Basecase PDAC PDAC+Resection Uncertainty: Probabilistic Sensitivity Analysis Cost effectiveness Planes	0.0078 0.0060 0.0089 £419/£152 £447/£180 £308/£41 £53,677/£19,445 £75,069/£30,252 £34,654/£4,626 64% iterations cost	

[d] Given the way costs and outcomes were calculated between competing interventions only incremental values were reported by the study.

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	at baseline following consent. Responses were scored using UK population weightings. At least one questionnaire was completed by 452 patients. The difference in QALYs for the economic evaluation were calculated by calculating the difference in mean patient QALYs between patients whose management had been modified by the addition of PET/CT to that of MDCT alone. <u>Source of cost data:</u> Complete NHS contact with NHS secondary and primary, care including all investigations, treatments and palliation, was recorded for 279 patients within the study and was used to calculate resource			Primary Model [Nuclear Medicine costs] Secondary Model [Nuclear Medicine Costs] <u>Cost Effectiveness Acceptability Curves</u> <u>Probability PET/CT cost-effective at a WTP=</u> [Primary Model-Nuclear Medicine Costs] £20,000 £30,000 [Primary Model-Clinical Oncology Costs] £20,000 £30,000 [Secondary Model-Nuclear Medicine Costs] £20,000 £30,000 [Secondary Model-Clinical Oncology Costs] £20,000 £30,000	saving/health improving 2% iterations cost saving/health improving 82% 85% 88% 90% 18% 28% 50% 60%	

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	use for the economic model. All secondary care costs were estimated from NHS reference costs apart from pharmacological interventions which were costed using Prescription Cost Analysis. Primary care costs were taken from the Unit Costs of Health and Social Care. Two costs for CT and PET/CT were investigated in the model, those sourced from nuclear medicine and clinical oncology services in the NHS reference costs. Currency unit: UK Sterling (£) Cost year: 2012-2013 Discounting:					

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	Not appropriate for a one year time horizon.					
Study 2						
Author: Morris Year: 2015 Country: UK	<u>Type of analysis:</u> Cost-utility <u>Model structure:</u> Decision Tree <u>Cycle length:</u> N/A <u>Time horizon:</u> 6 months <u>Perspective:</u> UK NHS <u>Source of base-line data:</u> Not reported Source of effectiveness data: The majority of the probabilities used in the decision tree were taken from A Cochrane Review Considering the same subject.	<u>Base case (population):</u> People with pancreatic or periampullary cancer which has been identified as resectable through CT scanning. No population demographics were reported. <u>Subgroup analysis:</u> Pancreatic Cancer only Periampullary Cancer only	1. Direct Laparotomy with no further diagnostic work up. 2. Diagnostic laparoscopy, to assess resectability of tumour, prior to laparotomy.	<u>Effectiveness (QALYs):</u> Direct Laparotomy Diagnostic Laparoscopy <u>Total costs (per patient):</u> Direct Laparotomy Diagnostic Laparoscopy <u>ICER (cost per QALY):</u> 1 vs 2 Uncertainty: <u>Deterministic Sensitivity Analysis</u> Diagnostic laparoscopy schedules prior to surgery Subgroup pancreatic cancer only <u>Threshold Analysis (Direct Laparoscopy be preferred choice)</u>	0.337 0.346 £7480 £7470 Diagnostic Laparoscopy dominant Direct laparotomy preferred Diagnostic Laparoscopy Preferred	<u>Funding:</u> National Institute for Health Research Cochrane Programme grants scheme (reference number 10/4001/11) <u>Comments</u> Pancreatic cancer only model run, results not reported in detail so reported as a sensitivity analysis

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	This was based on 16 diagnostic accuracy studies (N=1146). Source of utility data: Utility data was taken from one previous economic evaluation comparing laparoscopy to laparotomy for the treatment of hepatic colorectal metastases. <u>Source of cost data:</u> All costs in the model were taken from NHS reference costs Currency unit: UK Sterling (£) <u>Cost year:</u> 2011 <u>Discounting:</u> Not appropriate for a six month time horizon.			Probability of non-resectable disease Post test probability of unresectable disease <u>Probabilistic Sensitivity Analysis</u> Probability diagnostic laparoscopy cost-effective at a WTP= £20,000 £30,000	<36% >22% 63.2% 66.2%	

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L.21 Biliary Obstruction

What is the optimal treatment of biliary obstruction in adults with newly diagnosed or recurrent pancreatic cancer?

References to included studies:

Arguedas MR, Heudebert GH, Stinnett AA et al. 'Biliary stents in malignant obstructive jaundice due to pancreatic carcinoma: a cost-effectiveness analysis' AM J Gastroenterol 97(4) (2002) p898-904

Morris S, Gurusamy KS, Sheringham J et al. 'Cost-effectiveness of preoperative biliary drainage for obstructive jaundice in pancreatic and periampullary cancer. J Surg Res 193(1) (2014) p202-209

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
Study 1						
Author: Arguedas Year: 2002 Country: US	Type of analysis: Cost Utility Model structure: Markov Model Cycle length: 1 Month Time horizon: Until all the model cohort had transitioned to the death state. Perspective: US Societal Source of base-line data:	Base case (population): Hypothetical cohort of people with pancreatic cancer and obstructive jaundice presenting for palliative biliary stenting. No population demographics were reported. Subgroup analysis: None performed	1. Initial stenting with plastic stent 2. Initial stenting with metal stent	Effectiveness (QALMs): Plastic Metal Total costs (per patient): Plastic Metal ICER Metal vs Plastic Uncertainty: Deterministic Sensitivity Analysis(cost per QALM) Survival (metal vs plastic) 1 Months 3 Months 12 Months	 $13,879 $13,446 1.799 1.832 Metal Dominant $248,083 $70,521	Funding: Not reported Comments Reported as societal perspective but no societal costs reported in paper.

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	Not reported <u>Source of effectiveness data:</u> Probability of stent occlusion was taken from three RCTs comparing plastic to metal stenting. Procedure related complications and mortality were taken from one US prospective observational study. The probability of disease specific complications were estimated from various sources identified through a MEDLINE literature search. <u>Source of utility data:</u> Health state utilities were estimated using the standard gamble technique from 14 healthcare workers working at the authors' healthcare institution. <u>Source of cost data:</u> All diagnosis, procedure and other treatment costs were taken from Medicare reimbursement rates at the University of Alabama. <u>Currency unit:</u> US Dollar($)			<u>Cost Metal Stent (basecase=$899)</u> $500 $1000 $1500 $2000 <u>Cost Plastic Stent (basecase=$110)</u> $50 $250 Deterministic Sensitivity Analysis(cost per QALM) Probability of occlusion of both metal and plastic Probability metal occlusion vs probability stent replacement following occlusion	Metal Dominant Metal Dominant Metal Dominant $6026 $16,332 Metal Dominant Metal Dominant Metal preferred when occlusion rate less than half that of plastic Metal preferred in >80% iterations	

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	Cost year: 1999 Discounting: Not performed given the short life expectancy of the model cohort					
Study 2						
Author: Morris Year: 2014 Country: UK	Type of analysis: Cost-utility Model structure: Decision Tree Cycle length: N/A Time horizon: 6 months Perspective: UK NHS perspective Source of base-line data: No base-line characteristics reported Source of effectiveness data: Probabilities of receiving the intervention, the	Base case (population): People with pancreatic or periampullary cancer and obstructive jaundice who are potential candidates for resection. Subgroup analysis: None performed	1)Preoperative Biliary Drainage (PBD) prior to surgery. 2)Direct Surgery with no biliary drainage	Effectiveness (QALYs): PBD Direct Surgery Total costs (per patient): PBD Direct Surgery ICER (cost per QALY): Direct Surgery vs PBD Uncertainty: Deterministic Sensitivity Analysis (cost per QALY) Performed across high and low range for all parameters. Probabilistic Sensitivity Analysis (cost per QALY)	0.337 0.343 £10,775 £8221 Direct Surgery Dominant Direct Surgery always the dominant strategy	Funding: National Institute of Health Research (Programme Grant Scheme; reference number 10/4001/11) Comments

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	intervention being successful and any complications from the interventions were taken from five prospective randomised trials. Probabilities not calculable in those studies were taken from one previous economic evaluation comparing laparoscopy to laparotomy for the treatment of hepatic colorectal metastases. <u>Source of utility data:</u> Utility data was taken from one previous economic evaluation comparing laparoscopy to laparotomy for the treatment of hepatic colorectal metastases. <u>Source of cost data:</u> All costs in the model were taken from NHS reference costs. <u>Currency unit:</u> UK Sterling (£) <u>Cost year:</u> 2011			Probability PBD cost effective (Willingness to per QALY) £20,000 £30,000	 9.5% 8.9%	

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	Discounting: Not appropriate for 6 month time horizon					

L.3 Neo-adjuvant treatment

Is neoadjuvant therapy for people with resectable and borderline resectable pancreatic adenocarcinoma an effective treatment?

References to included studies:

Abbott DE, Tzeng CW, Merkow RP et al. 'The cost-effectiveness of neoadjuvant chemoradiation is superior to a surgery-first approach in the treatment of pancreatic head adenocarcinoma.'Ann Surg Oncol 20 (2013): Suppl 3: s500-503

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
Study 1						
Author: Abbott Year: 2013 Country: USA	Type of analysis: Cost-utility Model structure: Decision tree Cycle length: N/A Time horizon: Lifetime	Base case (population): People with resectable pancreatic head cancer. Population characteristics not reported. Subgroup analysis: None performed	1.Surgery First 2.Neoadjuvant therapy: Either 4 cycles gemcitabine (750mg/m^2) and cisplatin (30mg/ m^2)followed by 4 cycles of gemcitabine (400 mg/m$_2$) with concurrent external-	Effectiveness (QALYs[e]): Surgery First Surgery First (high-volume centre) Neoadjuvant Therapy (ITT) Neoadjuvant Therapy (Completed, Surgery) Neoadjuvant Therapy (Completed, no surgery) Neoadjuvant Therapy (Unresectable Disease at surgery) Total costs (per patient): $46,830	0.73 0.80 1.60 1.95 0.64 0.59	Funding: National Institute for Health through MD Anderson's Cancer Center Support Grant.

[e] Reported as Quality Adjusted Life Months(QALM) but converted to QALYs using the formulae QALY=QALM/12

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	Perspective: US Healthcare Payer Source of base-line data: NCDB and NSQIP databases described below. Source of effectiveness data: Effectiveness data for the surgery first group was taken from 2922 patients in the American College of Surgeons National cancer database (NCDB) (2003-2005) and the National Surgical Improvement Program (NSQIP) (2005-2007). Data from other literature were used to populate nodes in the model not covered by the database. All effectiveness data for the chemoradiation group were taken from 164 patients from a prospective pancreas database at one US hospital (2002-2008).		beam radiotherapy (30 Gy, 10 fractions). OR gemcitabine (750 mg/m$_2$) or capecitabine (800 mg/m^2 twice daily, 28 days) OR capecitabine-based chemoradiation	Surgery First Surgery First (high-volume centre) Neoadjuvant Therapy (ITT) Neoadjuvant Therapy (Completed, Surgery) Neoadjuvant Therapy (Completed, no surgery) Neoadjuvant Therapy (Unresectable Disease at surgery) ICER (cost per QALY): [Neoadjuvant vs Surgery First] ITT Analysis ITT (high-volume centre) As Treated As treated (high-volume centre) Uncertainty: Deterministic Sensitivity Analysis One-way sensitivity analysis (cost per QALY) [Neoadjuvant vs Surgery First, ITT Approach, only performed around Surgery first] Perioperative Mortality Rate=1% Perioperative Mortality Rate=5% Perioperative Mortality Rate=15% Perioperative Mortality Rate=20%	$45,721 $36,538 $45,673 $12,401 $20,380 Dominant Dominant Dominant Dominant Dominant Dominant Dominant Dominant	Various Donor Fund for Pancreatic Cancer Research. Career Development Award from the Health Services Research and Development Service of the Department of Veterans Affairs Nathan and Isabel Miller Family Foundation (DJB). Comments No probabilistic sensitivity analysis performed.

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	Source of utility data: QoL weightings were taken from two previous economic evaluations for treatments of pancreatic cancer. Source of cost data: Resource use was taken from the NCDB and NSQIP databases described above. All costs were based on Medicaid payment estimates. Costs of readmission after surgery, readmission after complications of radiotherapy or chemotherapy and hospice care were not included. Currency unit: US Dollar($) Cost year: 2011 Discounting: Costs: 3% per annum QALYs: 3% per annum			Complication Rate Surgery First=41% Complication Rate Surgery First=61% Adding Erlotinib to Adjuvant Therapy Elimination Adjuvant Radiotherapy	Dominant Dominant Dominant Dominant	Patient groups for each intervention unlikely to be comparable.

L.41 Follow up for people with resected pancreatic cancer.

What is the optimal follow-up protocol for people with resected pancreatic adenocarcinoma?

References to included studies:

Tzeng CW, Abbott DE, Cantor SB et al. 'Frequency and intensity of postoperative surveillance after curative treatment of pancreatic cancer: a cost-effectiveness analysis.' Ann Surg Oncol 20 (2013): Suppl 3: 2197-203

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
Study 1						
Author: Tzeng Year: 2013 Country: USA	Type of analysis: Cost-utility Model structure: Markov Model Cycle length: N/A Time horizon: Lifetime Perspective: US Healthcare Payer Source of base-line data: Baseline data were taken from one centre's surveillance program records described below.	Base case (population): Hypothetical cohort who completed neoadjuvant therapy and pancreaticoduodenectomy for PDAC. No population demographics were reported. Subgroup analysis: None performed	1. No scheduled surveillance, patient-initiated clinical evaluation for symptoms with computed tomography (CT) of the abdomen/pelvis and posterior-anterior/lateral chest X-ray 2. Scheduled clinical evaluation every 6 months with carbohydrate antigen (CA) 19-9 assay 3. Scheduled clinical evaluation every 6 months with	Effectiveness (Life Months): Strategy 1 Strategy 2 Strategy 3 Strategy 4 Strategy 5 Total costs (per patient): Strategy 1 Strategy 2 Strategy 3 Strategy 4 Strategy 5 ICER (cost per Life Year): Strategy 2 vs Strategy 1 Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2	 24.6 32.8 32.8 33.8 34.1 $3,837 $7,496 $10,961 $18,523 $24,775 $5,364 Dominated $127,680 $294,696	Funding: Khalifa Bin Zayed Al Nahyan Foundation and the Various Donor Pancreatic Research Fund at The University of Texas MD Anderson Cancer Center. Comments Outcome measure of Life Years in primary analysis not

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	These were not reported in the paper. <u>Source of effectiveness data:</u> Health related probabilities for populating the model were taken from a review of prospectively recorded follow-up data of 254 patients with potentially or borderline resectable PDAC treated with pancreaticoduodenectomy. The data was from one cancer centre's surveillance program between 1998 and 2008 <u>Source of utility data:</u> PDAC assigned a QALY weighting of 0.66 during QOL analysis. It was not reported how this value was derived. <u>Source of cost data:</u> Resource use was taken from the one centre's surveillance program records explained above. All costs for the model		CA 19-9 and routine CT/CXR 4. Scheduled clinical evaluation every 3 months with CA 19-9 5. Scheduled clinical evaluation every 3 months with CA 19-9 and routine CT/CXR	<u>ICER (cost per QALY[f]):</u> Strategy 2 vs Strategy 1 Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2 <u>Uncertainty:</u> Deterministic Sensitivity Analysis (cost per Life Month) <u>Chemotherapy for half of recurrence time</u> Strategy 2 vs Strategy 1 Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2 <u>Probability of treatment at 6 months=30%</u> Strategy 2 vs Strategy 1 Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2 <u>Probability of treatment at 6 months=70%</u> Strategy 2 vs Strategy 1	$421 Dominated Dominated Dominated $271 Dominated $5,601 $18,922 $133 Dominated $9,509 $24,558 $732	adjusted for quality of life. No probabilistic sensitivity analysis performed. Patient groups for each intervention unlikely to be comparable. Source of some key outcomes not adequately reported.

[f] QALYs not reported disaggregated from ICER and unable to be calculated from information reported in the paper

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	were taken from 2011 medicare payments. <u>Currency unit:</u> US Dollar($) <u>Cost year:</u> 2011 <u>Discounting:</u> Costs: 3% per annum QALYs: 3% per annum			Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2 <u>Effectiveness of chemotherapy increased to 36 months overall survival</u> Strategy 2 vs Strategy 1 Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2 <u>Effectiveness of chemotherapy increased to 60 months overall survival</u> Strategy 2 vs Strategy 1 Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2	Dominated $13,186 $24,558 $480 Dominated $6,990 $14,634 $1,006 Dominated $5,155 $10,930	

L.5 Management of metastatic pancreatic cancer.

What are the most effective interventions (excluding relevant NICE TAs) for adults with newly diagnosed or recurrent metastatic pancreatic cancer (chemotherapy, surgery, biological therapy, immunotherapy, radiotherapy, ablative techniques, low molecular weight heparin)?

References to included studies:

Tam VC, Ko YJ, Mittmann N, Cheung MC, Kumar K, Hassan S, Chan KK. 'Cost-effectiveness of systemic therapies for metastatic pancreatic cancer' Curr Oncol 20 (2013) e90-e106

Attard CL, Brown S, Alloul K et al. 'Cost-effectiveness of folfirinox for first-line treatment of metastatic pancreatic cancer' Curr Oncol 21 (2014) e41-51

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
Study 1						
Author: Tam Year: 2013 Country: Canada	Type of analysis: Cost-utility Model structure: Markov Model Cycle length: 1 month Time horizon: 2 years (although this covered life expectancy for the majority of the model cohort) Perspective:	Base case (population): Hypothetical cohort of people with metastatic pancreatic cancer undergoing chemotherapy No population demographics were reported. Subgroup analysis: None performed	1. Gemcitabine Alone (GEM) 1000/mg m^2 IV once weekly for 7 of 8 weeks for first cycle and then 3 of 4 weeks thereafter. 2. Gemcitabine and capecitabine (GEM-CAP). GEM 1000/mg m^2 IV once weekly 3 of every 4 weeks. CAP 1660/mg m^2 orally in divided doses twice daily for 3 of every 4 weeks.	Effectiveness (QALYs): GEM GEM-CAP GEM-E FOLFIRINOX Total costs (per patient): GEM GEM-CAP GEM-E FOLFIRINOX ICER [vs GEM] (cost per QALY): GEM-CAP	 0.487 0.536 0.564 0.703 CA$29,423 CA$33,572 CA$41,239 CA$58,243 CA$84,299	Funding: Funding source not reported. One author received an honorarium and another author a honorarium and research funding from Sanofi–Aventis Canada Inc. Comments

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	Ministry of health and long term care (MOHLTC) of Ontario, Canada. (Healthcare payer perspective) <u>Source of base-line data:</u> Base line data reported is identical to those reported in the trials to inform effectiveness. Base-line data reported as similar for GEM, GEM-CAP and GEM-E trials. FOLFIRINOX trial patients were also similar but had a higher baseline performance score. <u>Source of effectiveness data:</u> Overall, progression free survival, drug dosage and adverse events were taken from published phase III randomised clinical trials of metastatic cancer for all four interventions considered. <u>Source of utility data:</u> Utility was obtained from an EQ-5D survey of 60 medical oncologists across Canada. Utility values in		3. Gemcitabine and erlotinib (GEM-E). GEM 1000/mg m^2 IV once weekly for 7 of 8 weeks for first cycle and then 3 of 4 weeks thereafter. Erlotinib 150mg orally daily for duration of each cycle 4. FOLFIRINOX. Oxaliplatin IV 85mg/m^2 , Irinotecan IV 180mg/m^2, 5-Fluorouracil 400mg/m^2 IV bolus then 2400mg/m^2 IV continuous infusion over 46 hours, folinic acid 400mg/m^2 IV once every 2 weeks.	GEM-E FOLFIRINOX <u>Uncertainty:</u> Deterministic Sensitivity Analysis [vs GEM] (cost per QALY) <u>Discount Rate=5%</u> GEM-CAP GEM-E FOLFIRINOX <u>Discount Rate=0%</u> GEM-CAP GEM-E FOLFIRINOX <u>Relative Dose Intensity GEM=90%</u> GEM-CAP GEM-E FOLFIRINOX <u>Relative Dose Intensity FOLFIRINOX=90%</u> FOLFIRINOX <u>Relative Dose Intensity FOLFIRINOX=70%</u> FOLFIRINOX	CA$153,631 CA$133,184 CA$84,674 CA$154,506 CA$133,800 CA$83,770 CA$152,323 CA$132,258 CA$87,604 CA$155,754 CA$133,939 CA$148,634	Potential conflict of interest as the authors received honorarium and research funding from a manufacturer of oxaliplatin

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	the model were based on these responses and the number of grade III and IV adverse events. <u>Source of cost data:</u> Resource use was estimated from one retrospective chart review of metastatic pancreatic cancer patients from one hospital in Canada. Management costs were taken from the same retrospective chart review described above. Palliative care costs were taken from one Canadian costing study of palliative care in cancer. The costs of drugs and administration were taken from one Canadian pharmacy centre. Costs of treating adverse events were based on either the Ontario Case Costing Initiative, a costing study of febrile neutropenia or estimated from clinicians. <u>Currency unit:</u> Canadian Dollar(CA$) <u>Cost year:</u>			<u>Drug Cost increased 50%</u> GEM-CAP GEM-E FOLFIRINOX <u>Drug Cost decreased 50%</u> GEM-CAP GEM-E FOLFIRINOX <u>Probability FOLFIRINOX cost effective at willingness to pay threshold.</u> CA$100,000 Range Willingness pay intervention is preferred GEM GEM-CAP GEM-E FOLFIRINOX	CA$117,732 CA$137,980 CA$231,725 CA$194,991 CA$30,604 CA$75,546 CA$71,376 <5% <CA$80,000 CA$80,000-CA$130,000 Always Dominated >CA$130,000	

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	2010 Discounting: Cost: 3% per annum QALYs: 3% per annum					
Study 2						
Author: Attard Year: 2014 Country: Canada	Type of analysis: Cost-utility Model structure: Markov Model Cycle length: 1 week Time horizon: Lifetime Perspective: Ontario Public Payer Source of base-line data: Base-line data was taken from the ACCORD 11/0402 trial, comparing FOLFIRINOX to Gemcitabine, as discussed in detail in the accompanying clinical	Base case (population): The cohort for the model was populated from that of the ACCORD 11/0402 trial as discussed in detail in the accompanying clinical evidence review. (Gourgou-Bourgade 2013) Briefly the patient population consisted of patients with metastatic pancreatic cancer. Patients were between 18 and 75 years old and had an ECOG performance score	1.Gemcitabine Alone (GEM) 1000/mg m^2 IV once weekly for 7 of 8 weeks for first cycle and then 3 of 4 weeks thereafter. A proportion of patients receive second line platinum-based chemotherapy (analysis 1) or best supportive care [BSC] (analysis 2) 2.FOLFIRINOX. Oxaliplatin IV 85mg/m^2 , Irinotecan IV 180mg/m^2, 5-Fluorouracil 400mg/m^2 IV bolus then 2400mg/m^2 IV continuous infusion over 46 hours, folinic acid 400mg/m^2 IV once every 2 weeks. A proportion of	Effectiveness (Life Years)[g]: GEM FOLFIRINOX Effectiveness (QALYs): GEM FOLFIRINOX Total costs (per patient): *Analysis 1* GEM FOLFIRINOX *Analysis 2* GEM FOLFIRINOX ICER (cost per Life Year): *FOLFIRINOX vs GEM* Analysis 1 Analysis 2	 0.670 0.974 0.510 0.752 CA$7,207 CA$21,103 CA$2,995 CA$19,118 CA$45,877 CA$53,623	Funding: Sanofi Canada Comments Potential conflict of interest as the study was funded by a manufacturer of Oxiplatin.

[g] The assumptions of the model mean that effectiveness outcomes are identical for Analysis 1 and Analysis 2

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	evidence review. (Gourgou-Bourgade 2013) Source of effectiveness data: Effectiveness data was populated from the ACCORD 11/0402 trial as discussed in detail in the accompanying clinical evidence review. (Gourgou-Bourgade 2013) Source of utility data: Utility data was taken from one survey of 267 patients taking part in one randomised phase III trial comparing gemcitabine with placebo to gemcitabine with bevacizumab at multiple sites across the US. Utility values for stable disease and disease progression were collected using the EQ-5D and scored using values derived from the US general population Source of cost data: Chemotherapy costs were taken from publicly available healthcare costs	of between 0 and 1. Subgroup analysis: None performed	patients receive GEM as second line chemotherapy.	ICER (cost per QALY): *FOLFIRINOX vs GEM* Analysis 1 Analysis 2 Uncertainty: Deterministic Sensitivity Analysis (cost per QALY) Discount Rate=0% Analysis 1 Analysis 2 Discount Rate=3% Analysis 1 Analysis 2 Relative Dose Intensity FOLFIRINOX=100% Analysis 1 Analysis 2 Relative Dose Intensity FOLFIRINOX=70% Analysis 1 Analysis 2 Relative Dose Intensity GEM=90% Analysis 1	 CA$57,858 CA$67,626 CA$57,600 CA$67,289 CA$57,756 CA$67,493 CA$69,604 CA$81,666 CA$51,985 CA$60,606	

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	specific to the Ontario region of Canada. Resource use for chemotherapy was based on the regimens as given in the ACCORD trial. Adverse events were assumed to only incur costs if they required hospitalisation. Again these were costed using publicly available unit costs. <u>Currency unit:</u> Canadian Dollar(CA$) <u>Cost year:</u> 2013 <u>Discounting:</u> Cost: 5% per annum QALYs: 5% per annum			Analysis 2 <u>Relative Dose Intensity GEM=80%</u> Analysis 1 Analysis 2 <u>Max Cycles First line FOLFIRINOX=12 & GEM=26</u> Analysis 1 Analysis 2 <u>Max second line GEM cycles =9</u> Analysis 1 Analysis 2 <u>Max second line GEM cycles =6</u> Analysis 1 Analysis 2 <u>Proportion receiving second line=50%</u> Analysis 1 Analysis 2 <u>Proportion receiving second line=40%</u> Analysis 1 Analysis 2 <u>Hazard ratio overall survival=0.45</u> Analysis 1	CA$57,975 CA$67,727 CA$58,092 CA$67,828 CA$52,004 CA$61,741 CA$57,847 CA$67,229 CA$56,372 CA$66,039 CA$58,077 CA$54,624 CA$60,460 CA$56,320	

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
				Analysis 2 <u>Hazard ratio overall survival=0.73</u> Analysis 1 Analysis 2 <u>Health State Utilities Stable disease=0.65 & progressed disease=0.58</u> Analysis 1 Analysis 2 <u>Adverse Event Utilities +20%</u> Analysis 1 Analysis 2 <u>Adverse Event Utilities -20%</u> Analysis 1 Analysis 2 <u>Duration of G-CSF administration=11 days</u> Analysis 1 Probabilistic Sensitivity Analysis <u>Probability FOLFIRINOX cost effective at threshold of CA$100,000</u> Analysis 1 Analysis 2	CA$38,420 CA$44,928 CA$105,004 CA$122,678 CA$64,192 CA$75,029 CA$57,763 CA$67,515 CA$57,954 CA$67,738 CA$56,180 >85% >80%	

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