National Institute for Health and Care Excellence

Version 1.0

Pancreatic Cancer in adults:

diagnosis and management

Appendix L

Health economics evidence tables

31 July 2017

Draft for Consultation

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

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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.

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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)

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
Study 1						
Author: Morris Year: 2015 Country: UK	Type of analysis: Cost-utility Model structure: Decision Tree Cycle length: N/A Time horizon: 6 months Perspective: UK NHS	Base case (population): People with pancreatic or periampullary cancer which has been identified as resectable through CT scanning. No population demographics were reported. Subgroup analysis: Pancreatic Cancer	1. Direct Laparotomy with no further diagnostic work up. 2. Diagnostic laparoscopy, to assess resectability of tumour, prior to laparotomy.	Effectiveness (QALYs): Direct Laparotomy Diagnostic Laparoscopy Total costs (per patient): Direct Laparotomy Diagnostic Laparoscopy ICER (cost per QALY): 1 vs 2 Uncertainty:	0.337 0.346 £7480 £7470 Diagnostic Laparoscopy dominant	Funding: National Institute for Health Research Cochrane Programme grants scheme (reference number 10/4001/11) Comments Pancreatic cancer only model run,

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	Source of base-line data: 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. 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. Source of cost data: All costs in the model were taken from NHS reference costs Currency unit: UK Sterling (£) Cost year: 2011 Discounting: Not appropriate for a six	only Periampullary Cancer only		Deterministic Sensitivity Analysis Diagnostic laparoscopy schedules prior to surgery Subgroup pancreatic cancer only Threshold Analysis (Direct Laparoscopy be preferred choice) Probability of non-resectable disease Post test probability of unresectable disease Probabilistic Sensitivity Analysis Probability diagnostic laparoscopy cost-effective at a WTP= £20,000 £30,000	Direct laparotomy preferred Diagnostic Laparoscopy Preferred <36% >22% 63.2% 66.2%	results not reported in detail so reported as a sensitivity analysis

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	month time horizon.					

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	Base case (population): Hypothetical cohort of people with pancreatic cancer and obstructive jaundice presenting for palliative biliary stenting. No population demographics were	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	 $13,879 $13,446 1.799 1.832 Metal Dominant	Funding: Not reported Comments Reported as societal perspective but no societal costs reported in paper.

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	death state. Perspective: US Societal Source of base-line data: Not reported Source of effectiveness data: 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. Source of utility data: Health state utilities were estimated using the standard gamble technique from 14 healthcare workers working at the authors' healthcare institution. Source of cost data: All diagnosis, procedure	reported. Subgroup analysis: None performed		per QALM) Survival (metal vs plastic) 1 Months 3 Months 12 Months Cost Metal Stent (basecase=$899) $500 $1000 $1500 $2000 Cost Plastic Stent (basecase=$110) $50 $250 Deterministic Sensitivity Analysis(cost per QALM) Probability of occlusion of both metal and plastic	 $248,083 $70,521 Metal Dominant Metal Dominant Metal Dominant $6026 $16,332 Metal Dominant Metal Dominant Metal preferred when occlusion rate less than half that of plastic	

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	and other treatment costs were taken from Medicare reimbursement rates at the University of Alabama. Currency unit: US Dollar($) Cost year: 1999 Discounting: Not performed given the short life expectancy of the model cohort			Probability metal occlusion vs probability stent replacement following occlusion	Metal preferred in >80% iterations	
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:	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)	0.337 0.343 £10,775 £8221 Direct Surgery Dominant	Funding: National Institute of Health Research (Programme Grant Scheme; reference number 10/4001/11) Comments

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	No base-line characteristics reported <u>Source of effectiveness data:</u> Probabilities of receiving the intervention, the 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>			Performed across high and low range for all parameters. Probabilistic Sensitivity Analysis (cost per QALY) Probability PBD cost effective (Willingness to per QALY) £20,000 £30,000	Direct Surgery always the dominant strategy 9.5% 8.9%	

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	UK Sterling (£) Cost year: 2011 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:	Base case (population): People with resectable pancreatic head cancer. Population characteristics not	1.Surgery First 2.Neoadjuvant therapy: Either 4 cycles gemcitabine (750mg/m^2) and	Effectiveness (QALYs[a]): Surgery First Surgery First (high-volume centre) Neoadjuvant Therapy (ITT) Neoadjuvant Therapy (Completed, Surgery) Neoadjuvant Therapy (Completed, no	 0.73 0.80 1.60 1.95 0.64	Funding: National Institute for Health through MD Anderson's Cancer Center

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

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	N/A Time horizon: Lifetime 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	reported. Subgroup analysis: None performed	cisplatin (30mg/m^2)followed by 4 cycles of gemcitabine (400 mg/m_2) with concurrent external-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) Neoadjuvant Therapy (Unresectable Disease at surgery) Total costs (per patient): 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]	0.59 $46,830 $45,721 $36,538 $45,673 $12,401 $20,380 Dominant Dominant Dominant Dominant Dominant	Support Grant. 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

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	from a prospective pancreas database at one US hospital (2002-2008). 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			Perioperative Mortality Rate=1% Perioperative Mortality Rate=5% Perioperative Mortality Rate=15% Perioperative Mortality Rate=20% Complication Rate Surgery First=41% Complication Rate Surgery First=61% Adding Erlotinib to Adjuvant Therapy Elimination Adjuvant Radiotherapy	Dominant Dominant Dominant Dominant Dominant Dominant Dominant	analysis performed. Patient groups for each intervention unlikely to be comparable.

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

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

3 References to included studies:

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

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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. These were not reported in	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 CA 19-9 and routine CT/CXR	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

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	the paper. Source of effectiveness data: 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 Source of utility data: PDAC assigned a QALY weighting of 0.66 during QOL analysis. It was not reported how this value was derived. Source of cost data: Resource use was taken from the one centre's surveillance program records explained above. All costs for the model were taken from 2011 medicare payments.		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	ICER (cost per QALY[b]): Strategy 2 vs Strategy 1 Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2 Uncertainty: Deterministic Sensitivity Analysis (cost per Life Month) Chemotherapy for half of recurrence time Strategy 2 vs Strategy 1 Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2 Probability of treatment at 6 months=30% Strategy 2 vs Strategy 1 Strategy 3 vs Strategy 2 Strategy 4 vs Strategy 2 Strategy 5 vs Strategy 2 Probability of treatment at 6 months=70% 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 sme key outcomes not adequately reported.

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

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	<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	

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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

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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 the model were based on these		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

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	responses and the number of grade III and IV adverse events. Source of cost data: 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. Currency unit: Canadian Dollar(CA$) Cost year: 2010			Drug Cost increased 50% GEM-CAP GEM-E FOLFIRINOX Drug Cost decreased 50% GEM-CAP GEM-E FOLFIRINOX Probability FOLFIRINOX cost effective at willingness to pay threshold. 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	

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	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 evidence review. (Gourgou-Bourgade 2013)	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 of between 0 and 1.	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 patients receive GEM	Effectiveness (Life Years)[c]: 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 ICER (cost per QALY):	 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.

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

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	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 specific to the Ontario region of Canada. Resource use for	Subgroup analysis: None performed	as second line chemotherapy.	*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 Analysis 2	 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 CA$57,975	

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Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
	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			 <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 Analysis 2	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 CA$38,420	

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

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