MONASH University

Quantifying Quality of Care for Patients Diagnosed with Pancreatic Cancer

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"The end of wisdom is freedom. The end of culture is perfection. The end of knowledge is love. The end of education is character."

Sathya Sai Baba

Abstract

Background and aims: Pancreatic cancer (PC) is the tenth most commonly diagnosed cancer in Australian men and ninth most common in Australian women. It is the fourth leading cause of cancer-related death and the leading cause of death from a digestive organ neoplasm in Australia. Further, PC is associated with a high symptom and psychological burden. The disease often has a late clinical presentation and, to-date, no effective and efficient approach to screening has been identified.

This thesis aims to: (1) determine the measures that quantify the quality of care provided to patients diagnosed with PC; (2) map the patterns of treatment provided to patients diagnosed with PC in Victoria, Australia, and the impact on survival; (3) identify the extent to which care is delivered in accordance with developed quality of care indicators, predictors of performance on survival; (4) explore the barriers and enablers to implementing two quality of care indicators which have been associated with low adherence; and (5) identify strategies to improve quality of care.

Methods: A set of clinical quality indicators (QI) were developed using a modified Delphi consensus method. Quantitative methods were used to evaluate the patterns and quality of care using the data collected by the Upper Gastrointestinal Cancer Registry (UGICR), and the association between quality care and survival. Qualitative methods underpinned by the Theoretical Domains Framework (TDF) were used to explore the beliefs and attitudes of specialists who manage PC to understand the barriers and enablers for two QIs: (1) the implementation of protocol imaging of the pancreas; and (2) the discussion of all patients at multidisciplinary team (MDT) meetings. A systematic review was undertaken to identify and describe Patient Reported Outcome Measures (PROMs), used in studies of patients with PC.

Results: The Delphi consensus study identified 27 QIs deemed both important and feasible by the panel (7 diagnostic and staging, 5 surgical, 4 other treatment, 5 patient management and 6 outcome). These were recommended for inclusion into the UGICR and data was collected over three years. Twenty-two of the 27 indicators were evaluated for routine measurement to determine compliance with best practice and 18 QIs were further assessed for association with survival. Compliance with the following QIs was associated with improved patient survival in a multivariable analysis after adjusting for confounders: (1) imaging using a pancreatic protocol CT or MRI; (2) documented ECOG at presentation and/or diagnostic ASA; (3) disease management discussed at an MDT meeting; (4) being included in a clinical trial; (5) adjuvant chemotherapy administered following surgery or a reason documented; and (6) chemotherapy ± chemo-radiation offered to patients with locally advanced disease.

Interviews with 21 healthcare professionals involved in determining whether a patient receives protocol imaging of the pancreas identified the following major barriers: a gap in knowledge or awareness on the recommendations within clinical practice guidelines; motivation to undertake surgery without the necessary preoperative staging; access to radiologists specialising in pancreatic radiology; and the timeliness of referrals. Strategies to improve compliance with this practice suggested by healthcare workers included case presentations to MDT meetings as a reminder for undertaking PPCT or MRIs, providing access to a range of relevant disciplines, especially specialist radiologists and a forum for receiving feedback.

Interviews with 29 healthcare professionals to examine the practice of presentation of patients at an MDT meeting identified the following major barriers: lack of capacity to discuss large volumes within the given meeting time; lack of palliative care representation; burden on radiologists (and pathologists) for reporting at MDT meetings; number of different MDT

meetings and clinical commitments; dissenting views; and a healthcare professionals' confidence to voice their opinions at the meeting. MDT meetings are integral to the provision of quality care. The organisational structures internal and external to MDT meetings need to be strengthened with the development of agreed evidence-based protocols and referral pathways, a focus on resource allocation and capabilities and a culture that fosters widespread collaboration for all stages of PC.

Three multidimensional PROMs were recommended in PC as a result of the systematic review: the (1) FACT-HEP in unresectable PC; (2) QLQ-PAN26 (in conjunction with its core QLQ-C30 PROM) in resectable PC; and (3) MDASI-GI are recommended as instruments to capture quality of life in patients with PC.

Conclusion: This research developed a set of evidence-based indicators and evaluated the type of PROMs applied in PC as the initial step to assess quality of care from a clinical and patient perspective. Evaluation of the data collected by the UGICR were the next steps and two qualitative studies identified the barriers and enablers to indicator implementation. Meeting high quality care is associated with improved outcomes. It is yet to be determined whether ongoing monitoring of QIs is associated with improved quality of care and whether the collection and reporting of PROMs in these reports impacts survivorship. This thesis provides the foundation for this work to be undertaken.

Thesis Including Published Works General Declaration

I, hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes four original papers published in peer reviewed journals and three unpublished publications, two currently in submission and one in preparation for submission. The core theme of the thesis is 'Quantifying Quality of Care in Pancreatic Cancer'. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the Department of Epidemiology and Public Health under the supervision of Professor Sue Evans, Professor John Zalcberg and Dr Liane Ioannou.

The inclusion of numerous co-authors reflects the fact that the work came from active collaboration between researchers and clinicians. It acknowledges the input into team-based research.

In the case of *chapters 1, 2, 4, 5 and 6* my contribution to the work involved the following:

Thesis Chapter	Publication Title	Publication Status *	Nature and % of student contribution	Co-author name(s) Nature and % of Co-author's contribution*	Co-author(s), Monash student Y/N*
1	The Upper Gastrointestinal Cancer Registry (UGICR): A clinical quality registry to monitor and improve care in upper gastrointestinal cancers	Published	**55%.** Preparation of the first draft based on the protocol developed by UGICR's program manager and coordinator; literature searches; submission of manuscript including preparation of revisions and correction of proofs.	1) Jen Holland, input into initial protocol and manuscript 30% 2) Prof John Zalcberg, senior author, input into manuscript 10% 3) Multiple co-authors, review of final manuscript and feedback, *combined total* 5%	No No No
1	Quality of care indicators in pancreatic cancer *(book chapter)*	In Press	**85%.** Conceptualisation of paper; literature search strategy; literature searches; preparation of manuscript; preparation of revisions and correction of proofs.	1) Prof Sue Evans, senior author, input into manuscript 7% 2) Prof John Zalcberg, review of manuscript and feedback 3% 3) Dr Liane Ioannou, review of manuscript and feedback, 3% 4) Dr Daniel Croagh, review of manuscript and feedback 2%	No No No No
2	Monitoring quality of care for patients with pancreatic cancer: A modified Delphi consensus	Published	**75%.** Obtained ethics approval; study design and protocol; literature search strategy and search; recruitment of participants for Delphi panel; data collection; analysis; conceptualisation of paper; preparation of manuscript; submission; preparation of revisions and correction of proofs.	1) Prof Sue Evans, senior author, input into manuscript and methods 10% 2) Dr Liane Ioannou, review of indicator list and grouping, input into manuscript and feedback, 5% 3) Multiple co-authors, panel members, review of manuscript and feedback, *combined total* 10%	No No No
4	Barriers and enablers to the implementation of protocol-based imaging in pancreatic cancer: A qualitative study using the theoretical domains framework	Submitted	**72%.** Obtained ethics approval; study design and protocol; developed interview schedule; recruitment of participants; interviews; data collection; analysis; conceptualisation of paper; preparation of manuscript; submission of manuscript	1) Prof Sally Green, senior author, input into manuscript, interviews and method 10% 2) Prof Sue Evans, validation of analysis, input into manuscript 5% 3) Dr Marnie Graco, validation of analysis, input into manuscript 3%	No No No

				4) Multiple co-authors, focus group, review of manuscript and feedback, *combined total* 10%	No
5	Barriers and enablers to the implementation of multidisciplinary team meetings: A qualitative study using the theoretical domains framework	Submitted	**72%.** As per Thesis Chapter 4	As per Thesis Chapter 4	No
6	Patient-reported outcome measures in pancreatic cancer: A systematic review	Published	**75%.** Conceptualisation of study; developed systematic literature search strategy; literature search; full text review; data collection; synthesis of literature; conceptualisation of paper; preparation of manuscript; submission; preparation of revisions and correction of proofs	1) Prof Sue Evans, input into manuscript and method 10% 2) Dr Liane Ioannou, senior author and input into manuscript 7% 3) Dr Stella Samoborec, validation of analysis 3% 4) Multiple Co-authors, review of manuscript and feedback, *combined total* 5%	No No Yes No

** published, in press, accepted, returned for revision*

I have not renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author I have consulted with the responsible author to agree on the respective contributions of the authors.

Publications, Presentations and Leadership

Publications during enrolment:

1. **Maharaj AD,** Evans SM, Ioannou LJ, Croagh DG, Earnest A, Holland JF, Pilgrim CHC, Neale RE, Goldstein D, Kench JG, Merrett ND, White K, Burmeister EA, Evans PM, Hayes TM, Houli N, Knowles BPF, Leong T, Nikfarjam M, Philip J, Quinn M, Shapiro J, Smith MD, Spillane JB, Wong R, Zalcberg JR. *The association between quality care and outcomes for patients diagnosed with pancreatic ductal adenocarcinoma in an Australian population*. Manuscript in preparation.
2. **Maharaj AD,** Evans SM, Zalcberg JR, Ioannou LJ, Graco M, Croagh DG, Pilgrim CHC, Dodson T, Goldstein D, Philip J, Kench JG, Merrett ND, Neale RE, White K, Evans PM, Leong T, Green SE. *Barriers and enablers to the implementation of protocol-based imaging in pancreatic cancer: A qualitative study using the theoretical domains framework*. 2020. Submitted manuscript.
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7. **Maharaj AD**, Samoborec S, Evans SM, Zalcberg JR, Neale RE, Goldstein D, Merrett ND, White K, Croagh D, Pilgrim CHC, Evans PM, Knowles BPF, Leong T, Philip J, Smith M, Ioannou LJ. *Patient-Reported Outcome Measures (PROMs) in Pancreatic Cancer: A Systematic Review.* HPB 2019: https://doi.org/10.1016/j.hpb.2019.09.002

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9. Ruseckaite R, **Maharaj AD**, Krysinska K, Dean J, Ahern S. Developing a Preliminary Conceptual Framework for Guidelines on Inclusion of Patient Reported-Outcome Measures (PROMs) in Clinical Quality Registries. Dove Medical Press 2019. https://doi.org/10.2147/PROM.S229569

Invited Book Chapter

1. **Maharaj AD**, Zalcberg JR, Ioannou LJ, Croagh D, Evans SM. *Quality of Care Indicators in Pancreatic Cancer; Chapter 6; Textbook of Pancreatic Cancer. Principles and Practice of Surgical Oncology.* Ed Soreide K and Stättner S; 2020. Published Springer Nature.

Conference Abstracts

1. **Maharaj AD,** Samoborec S, Evans SM, Zalcberg JR, Neale RE, Goldstein D, Merrett ND, White K, Croagh D, Pilgrim CHC, Evans PM, Knowles BPF, Leong T, Philip J, Smith M, Ioannou LJ. October 2019, International Society of Quality of Life Conference, San Diego, United States of America. Oral Presentation.
2. **Maharaj AD**, Ioannou LJ, Croagh D, Zalcberg JR, Neale RE, Goldstein D, Merrett ND, Kench JG, White K, Pilgrim CHC, Chantrill L, Cosman P, Kneebone A, Lipton LR, Nikfarjam M, Philip J, Sandroussi C, Tagkalidis P, Chye R, Haghighi KS, Samra J, Evans SM. *Monitoring quality of care for patients with pancreatic cancer: a modified Delphi consensus*. May 2019, Victorian Integrated Cancer Services Conference, Melbourne, Australia. Oral Presentation.
3. **Maharaj AD**, Samoborec S, Evans SM, Zalcberg JR, Neale RE, Goldstein D, Merrett ND, White K, Croagh D, Pilgrim CHC, Evans PM, Knowles BPF, Leong T, Philip J, Smith M, Ioannou LJ. *Patient-Reported Outcome Measures (PROMs) in Pancreatic Cancer: A Systematic Review*. May 2019, Victorian Integrated Cancer Services Conference, Melbourne, Australia. Oral Presentation.
4. **Maharaj AD**, Ioannou LJ, Croagh D, Zalcberg JR, Neale RE, Goldstein D, Merrett ND, Kench JG, White K, Pilgrim CHC, Chantrill L, Cosman P, Kneebone A, Lipton LR, Nikfarjam M, Philip J, Sandroussi C, Tagkalidis P, Chye R, Haghighi KS, Samra J, Evans SM. *Monitoring quality of care for patients with pancreatic cancer:*

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6. **Maharaj AD**, Ioannou LJ, Croagh D, Zalcberg JR, Neale RE, Goldstein D, Merrett ND, Kench JG, White K, Pilgrim CHC, Chantrill L, Cosman P, Kneebone A, Lipton LR, Nikfarjam M, Philip J, Sandroussi C, Tagkalidis P, Chye R, Haghighi KS, Samra J, Evans SM. *Monitoring quality of care for patients with pancreatic cancer: a modified Delphi consensus*. September 2018, BMJ and IHI International Forum on Quality and Safety, Melbourne, Australia. Oral Poster Presentation.

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Dedication




This work is dedicated to my loving grandparents (*in pictorial order*), Mr Ram Dhani and Mrs Sushila Wati (paternal grandparents), Mr Ram Manohar and Mrs Raj Kuar (maternal grandparents).

In particular, to Mr Ram Manohar who was diagnosed with stage IV pancreatic cancer in April 2004, at the age of 77, and succumbed to the disease peacefully on 28th December 2004. Quality of care for him meant spending time in his home surrounded by the love of his extended family, listening to the verses and feeling the vibrations expounded by the *'Hanuman Chalisa' (devotional hymn composed by a 16th century poet, Tulsidas, and dedicated to the embodiment of courage, Lord Hanuman)* from which he drew immense strength.

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operational management and complexities of clinical quality registries. I am also grateful to many people in the School of Public Health and Preventative Medicine for their support, guidance and encouragement throughout my candidature. These include Dr Liz Douglas, my first doctoral co-ordinator who experienced my grand entrance into her office with a cup of coffee that flew unknowingly out of my hands spilling with projectile force. I can only appreciate how calmly she undertook this entire experience. To Ms Kathryn Daly, who replaced Liz, thank you for your support, amazing grasp of language and sense of humour that am sure has kept many PhD students sane!

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Table of Contents

List of Tables

List of Figures

List of Abbreviations

CA 19-9	Carbohydrate Antigen 19-9
95% CI	95% Confidence Interval
CT	Computed Tomography
CQR	Clinical Quality Registry
HPB	Hepatopancreatobiliary
HR	Hazard Ratio
IOM	Institute of Medicine
MDT	Multidisciplinary team
MRI	Magnetic Resonance Imaging
PC	Pancreatic Cancer
PDAC	Pancreatic Ductal Adenocarcinoma
PPCT	Pancreatic Protocol Computed Tomography
PROM	Patient-Reported Outcome Measure
QI	Quality indicator
QoL	Quality of Life
RCT	Randomised Clinical Trial
TDF	Theoretical Domains Framework
UGICR	Upper Gastrointestinal Cancer Registry

"The roots of improvement are tactical. They lie in the quantitative sciences of systems and statistics but quality improvement has other roots, deeper roots, something more philosophical, something more emotional, and something more spiritual."

Dr Don Berwick

Social and Moral Determinants of Health, IHI Forum 2020

Chapter 1: Introduction

1.1 Overview of the Problem

Pancreatic cancer (PC) is associated with poor survival and a high symptom and psychological burden. The disease often has a late clinical presentation and there are no screening methods to date. Surgical resection is the only potentially curative treatment but the vast majority (~ 80%) of cases are inoperable at diagnosis. There is growing agreement that, even at early stages, PC is a systemic disease and management should include neo-adjuvant therapy prior to surgery and certainly adjuvant therapy following surgery to improve survival.[1] For the majority of patients diagnosed with advanced disease, palliative management results in a longer median overall and progression-free survival.[2]

In addition to aetiological factors, health services factors have also been associated with poor outcomes after a diagnosis of PC. Preconceived knowledge of its poor prognosis by clinicians can lead to a nihilistic approach to disease management. Differences in patient outcomes may be due to the variation in care provided by individual providers and/or institutions. For example, people living in rural regions in Australia can be less likely than their city counterparts to receive anti-cancer therapy.[3] Patients living in areas with higher socio-economic status are also more likely to receive access to more advanced medical care that is associated with improved survival and improved quality of life (QoL).[4]

Evaluating the quality of care delivered to patients diagnosed with PC is an essential step to understand the reasons behind the variations in care in PC. This thesis examines the performance measures that monitor quality of care provided to patients diagnosed with PC from a clinical and patient perspective using quality indicators and patient reported outcome measures, evaluates the measures to understand the variations in care and explores the barriers and enablers to indicator implementation.

1.2 The Pancreas

The pancreas is a flattened gland located deep within the upper abdomen *(Figure 1.1)*. It is composed of exocrine cells, whose primary role is to produce the enzymes required for the digestion of food, and the endocrine cells that secretes hormones such as insulin and glucagon to regulate blood sugar.[5] The location of the pancreas allows it to be protected from trauma, but it also makes it inaccessible to physical examination and for diseases such as cancer to progress, sometimes in the absence of symptoms such pain or disability.[6] The pancreas is divided into the head, body and tail regions with 75% of all PCs arising in the head of the pancreas, 15-20% in the body and 5-10% in the tail region.[7] The majority (90 – 95%) of the tumours develop from within the exocrine cells. Pancreatic neuroendocrine tumours which account for the other 5 – 10% have a different pathogenesis.[8] The research conducted in this thesis is confined to exocrine PC.

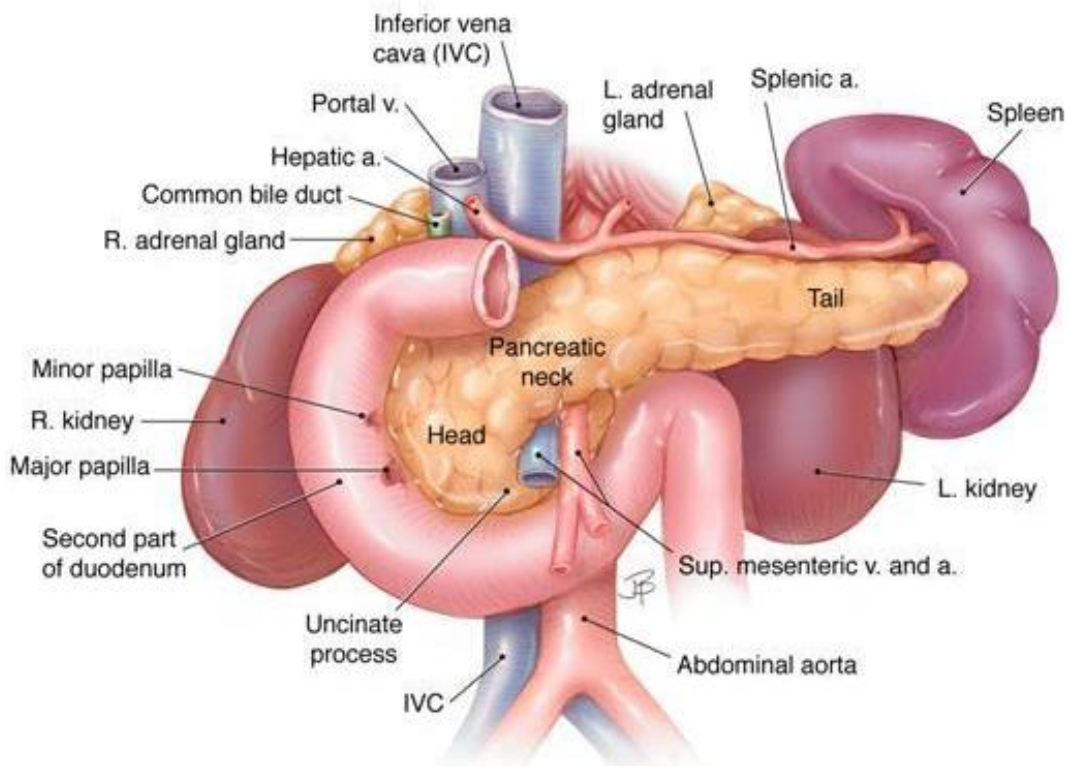

Figure 1.1: *Anatomic relationships of the pancreas with surrounding organs and structures. Source: Pancreapedia*[9]

1.3 Risk Factors

Although the cause for PC is unknown, there are known risk factors. The incidence and death rates of PC increase with advancing age, with a steep increase after 55 years. Men are also more likely to be diagnosed than women.[10] Individuals with a family history of PC, especially of Ashkenazi Jewish ancestry, generally have a 2 to 3-fold increased risk and this risk increases with the diagnosis of first-degree relatives.[11] Those living in the lowest socioeconomic zone have one of the highest age-standardised incidence and death rates for PC.[12] Risk factors include smoking, obesity and both type I and II diabetes mellitus. Smoking is the most well-known modifiable risk factor; people who smoke have twice the risk of a non-smoker of being diagnosed with PC. A recent Australian study estimated that approximately 22% of future PCs are attributable to current and recent smoking.[13] Long-standing diabetes has modest risk for PC, while new-onset diabetes, especially at advanced age, may be a manifestation of the disease.[14] Further aetiological and protective factors identified in a review of meta-analytical studies are described in *Figure 1.2*.[15] In Australia, indigenous Australians are at 1.6 times higher risk than non-indigenous of being diagnosed with PC.[16]

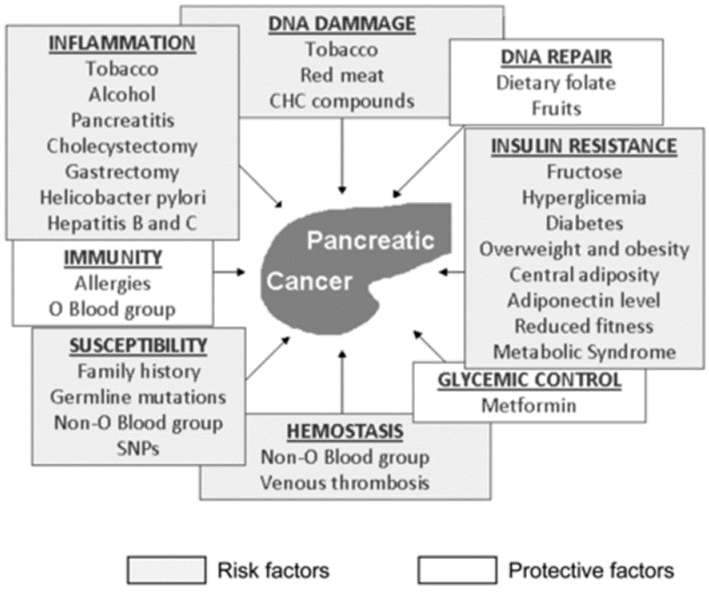

Figure 1.2: *Aetiological Risk Factors.*[15]

1.4 Diagnosis

The accurate and timely diagnosis of PC is dependent on the initial clinician associating the presenting symptoms to a suspicion of PC, followed by timely specialist referral and the use of a multimodal approach to diagnosis as outlined below.

1.4.1 Symptoms

Symptoms of PC are often non-specific and can include asthenia, anorexia, weight loss, abdominal pain and choluria. Jaundice is the main specific symptom that can present in advanced disease and is the result of obstruction by the tumour at the head of the common bile duct.[17] Due to the lack of specific symptoms, the suspicion of PC can go undetected and result in a late diagnosis.

1.4.2 Imaging modalities

High definition radiological imaging combined with expertise in interpretation is the cornerstone for accurate staging. The primary diagnostic modalities for PC are imaging with modern computed tomography (CT) or magnetic resonance imaging (MRI). A pancreatic protocol multiphase CT that includes an arterial phase and a venous or portal phase is recommended in the workup of a pancreatic mass to view the anatomical relationship between the tumour and the vascular anatomy of the pancreas, the lymph nodes and the potential sites of metastases.[17,18] The MRI is considered equivalent in sensitivity and specificity to the PPCT and is an option in characterising liver lesions. However, the use of MRI is generally restricted by cost, patient factors (such as anxiety) and availability.[19]

1.4.3 Biopsy

A biopsy is not always indicated prior to surgery in patients with a suspected, clinically resectable pancreatic head tumour. However, histologic confirmation is necessary prior to neo-adjuvant therapy and in those with locally advanced or metastatic disease. The preferred

method to achieve this is by the endoscopic ultrasound-guided fine needle aspirate for fluid and tissue acquisition.[20]

1.4.4 Tumour biomarkers

Although numerous biomarkers have been researched in PC, the most widely used biomarker for diagnosis and management is the Sialyl Lewis^{A} antigen or better known as the carbohydrate antigen (CA) 19-9. A CA19-9 level of <100 U/ml correlates with potentially operable disease whereas a level above 100 U/ml suggests advanced or metastatic PC. It is not useful as a screening tool in the asymptomatic population but baseline CA 19-9 serum levels correlates with tumour stage and holds prognostic significance for overall survival when levels are measured before or after surgery or chemotherapy. The CA 19-9 has several limitations which include a sensitivity of approximately 80% and specificity between 80 and 90%. Approximately, 5-10% of the population do not produce CA 19-9 as genetically they may have a Lewis negative phenotype and this may contribute to a false negative result. False positive results can occur in the presence of obstructive jaundice and other inflammatory conditions such as pancreatitis. These factors limit the clinical application of CA 19-9 as a screening mechanism.[21-23]

1.5 Staging and Treatment

Accurate staging determines the optimal treatment pathway in PC. The American Joint Committee on Cancer (AJCC) TNM (tumour, node, metastasis) staging system is the most widely used method for staging cancers. The tumour is categorised into stages based on size and invasion of nearby vessels, lymph node involvement and distant metastasis. These are important prognostic indicators for patient survival.[24] The criteria for staging is presented in *Table 1.1*.

Where clinical staging is not possible in the absence of surgery or a biopsy, operability can be categorised into *resectable, borderline resectable, locally advanced* and *metastatic* disease based on the best possible imaging.[18]

T Category	T Criteria
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma *in situ*
	This includes high-grade pancreatic intraepithelial neoplasia (PanIn-3), intraductal papillary mucinous neoplasm with high-grade dysplasia, intraductal tubulopapillary neoplasm with high-grade dysplasia, and mucinous cystic neoplasm with high-grade dysplasia
T1	Tumour ≤ 2 cm in greatest dimension
T1a	Tumour ≤ 0.5 cm in greatest dimension
T1b	Tumour > 0.5 cm and < 1cm in greatest dimension
T1c	Tumour 1 – 2 cm in greatest dimension
T2	Tumour > 2 cm and ≤ 4 cm in greatest dimension
T3	Tumour > 4cm in greatest dimension
T4	Tumour involves celiac axis, superior mesenteric artery, and/or common hepatic artery, regardless of size
N Category	**N Criteria**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastasis in 1 to 3 regional lymph nodes
N2	Metastasis in 4 or more regional lymph nodes
M Category	**M Criteria**
M0	No distant metastasis
M1	Distant metastasis

Table 1.1: *AJCC TNM Staging. Source: American Joint Committee on Cancer. The AJCC TNM Cancer Staging Manual. 8th Edition ed. Chicago 2016*

More than 50% of patients have metastatic disease at diagnosis. This means that the cancer has spread from the pancreas to other organs. A further 30% are locally advanced, where there is no distant metastasis but the tumour has encased surrounding structures such as the

major portal veins or superior mesenteric artery. Approximately 10 -15% of people diagnosed with PC are potentially curable and able to undergo surgery with curative intent.[25] For the other 85-90% of patients who cannot have a surgical resection, chemotherapy with or without radiotherapy is an option. A detailed treatment algorithm stratified by tumour stage and performance status is displayed in *Figure 1.3*. It is recommended that patients who cannot have surgery participate in clinical trials to test new approaches to disease management and help determine the optimal management pathway.[26] However, recruitment numbers are often low or there are insufficient trials for involvement.[27]

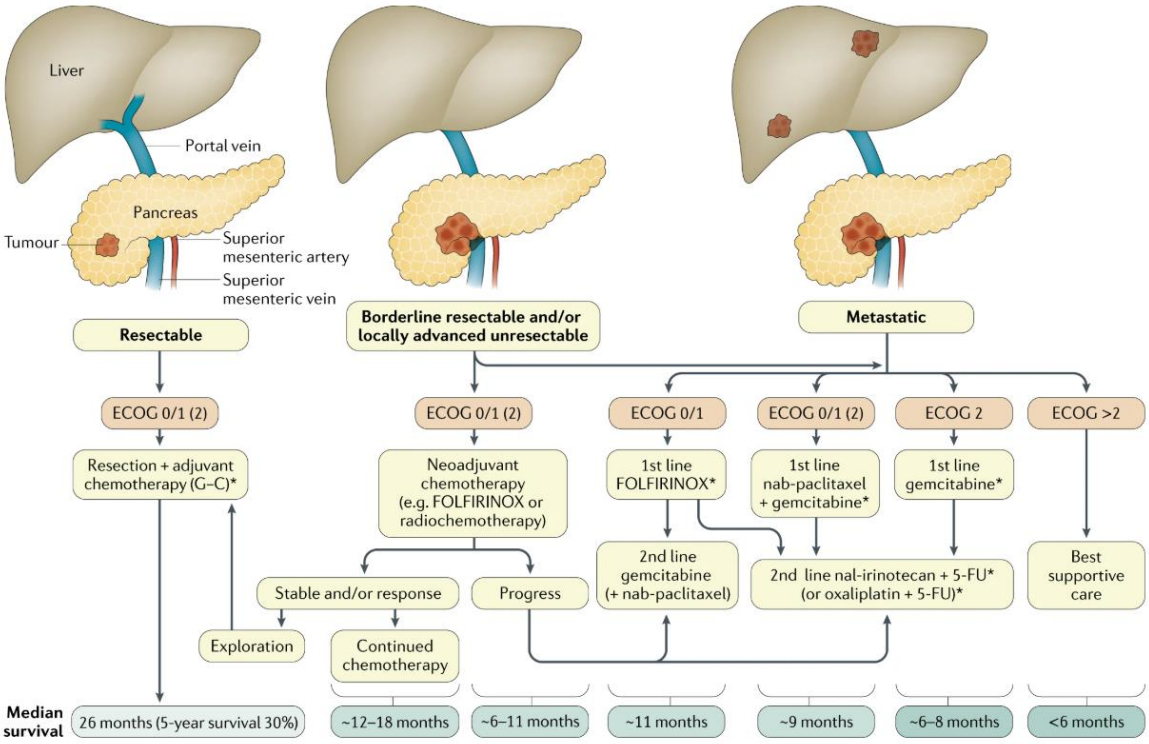

Figure 1.3: *Treatment algorithm stratified by tumour stage and performance status*[28]

1.6 Epidemiology

PC is the seventh leading cause of cancer deaths in both males and females globally. The highest incidence rates have been reported in Europe, North America, and Australia/New Zealand.[29] PC was estimated to be the fourth leading cause of death in Australia in 2019.[30]

1.6.1 Incidence and mortality

The incidence of PC is almost equivalent to mortality. The global incidence of PC in 2018 was 458,918 (2.5% of all cancers) and the number of deaths was 432,242 (4.5% of all cancers) in the same year.[29] The incidence of PC has increased over the last three decades. The Global Burden of Disease Study (GBD) has estimated that the age-standardised incidence rate increased from 5.0 per 100,000 person-years in 1990 to 5.7 per 100,000 per person-years in 2017. Within the same period the age-standardised death rate increased by 10.4% from 5.1 to 5.6 per 100,000 person-years and the disease-adjusted life-years (DALYs) doubled from 4.4 million in 1990 to 9.1 million in 2017.[31] A similar gradual rise in the age-adjusted incidence rate is observed in Australia from 1982 to 2015 as seen in *Figure 1.4*. The age-standardised incidence rate in Australia is approximately double the global statistics in comparison by 2015.

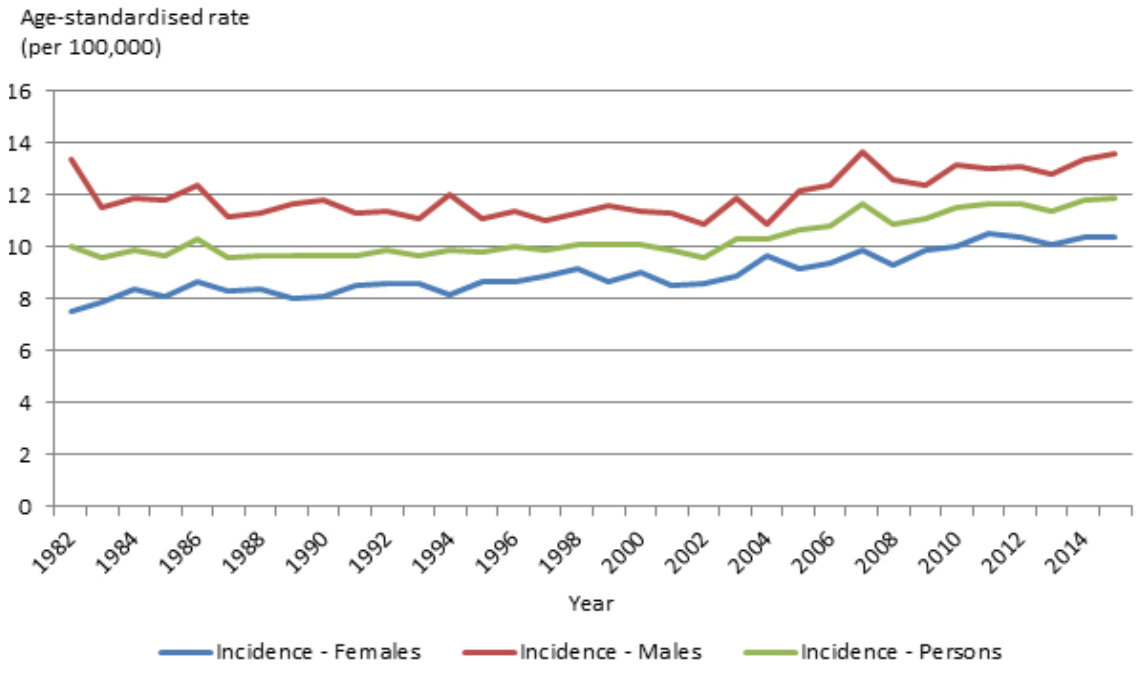

Figure 1.4: *PC Age-Adjusted Incidence Rates by Sex. Source: Australia Cancer Incidence and Mortality (ACIM) workbook Data 1968-2016*

1.6.2 Survival

Relative five-year overall survival following the diagnosis of PC remains poor and is estimated to be from 5 to 9% globally, with the differences in mortality rates potentially due to the lack of appropriate diagnosis, treatment and documentation of cancer cases.[31,32] The relative five-year survival in Australia is 9.8% based on 2011-2015 national data.[30] *Table 1.2* provides a breakdown of five-year overall survival by stage based on international statistics.

Stage at Diagnosis	% at Diagnosis	5-year Overall Survival, %
Localised / Potentially Resectable	10	37
Regional / Locally Advanced	29	12
Distant / Metastatic Disease	52	3

Table 1.2: *Five-year relative survival rates by stage at diagnosis, US, 2009 – 2015. Source: Siegel et al, Cancer statistics 2020*[25]

Figure 1.5 shows that, in comparison to other cancers, PC has the lowest survival of all known cancer diagnoses in Australia.

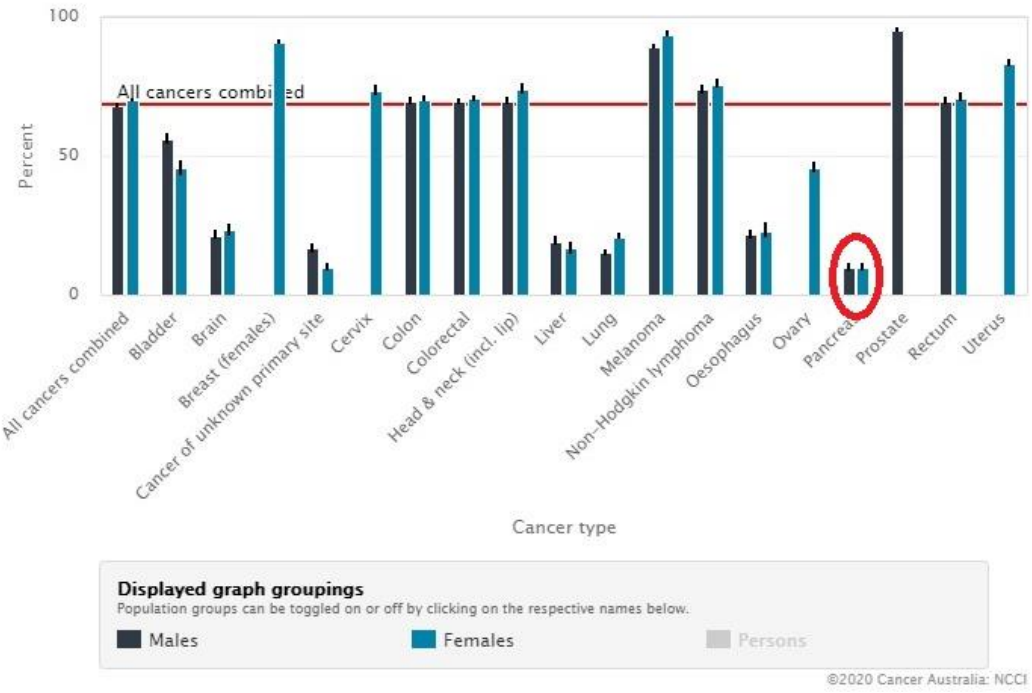

Figure 1.5: *Five-year relative survival for all cancers combined and selected cancer types, by sex, 2011 – 2015. Source: National Cancer Control Indicators (NCCI), Australia*

1.7 The burden of PC

1.7.1 Quality-adjusted life years (QALYs)

PC is projected to surpass breast, prostate and colorectal cancers to become the second leading cause of cancer-related death by 2030, following lung cancer.[33] A systematic review on the burden of PC in Europe compared survival, QoL and costs amongst the general population and those diagnosed with PC. This study highlighted that at 71 years of age, the general population can expect an additional 11.78 years of healthy life compared with only 0.25 years for patients diagnosed with PC.[34]

1.7.2 The economic burden

The economic burden of PC is large, both in terms of direct and indirect costs. Hospitalisation accounts for the majority of direct costs per residual lifetime, followed by interventions such as radiology, surgery with or without chemotherapy, and chemotherapy alone. Indirect costs include short-term and mean loss of productivity due to premature mortality.[34] The cost of surgery include not only the related expenses or charges, but also the costs associated with post-operative complications.[35] In Australia in 2016-17, PC accounted for approximately 3% of additional diagnoses for hospitalisations where a chemotherapy procedure was performed, and 5.5% of the ten most common principal diagnoses for cancer-related hospitalisations where palliative care was provided.[30]

1.7.3 The symptom and psychosocial burden

Compared to most other cancers, patients with PC have a high symptom burden that includes intractable pain, jaundice, cachexia, gastrointestinal effects, septic episodes and treatment-related morbidity.[36] Added to this physical burden is the psychological effects of depression and anxiety for both the patients and carers. One study of 136 patients and carers, reported that 15% of patients and 39% of carers suffered from clinical levels of anxiety, and

approximately 15% in both groups showed signs of clinical depression within three months of diagnosis. Further, 70% of patients had a QoL score below the population average.[37]

1.8 Evaluating quality of healthcare for patients with PC

PC has poor survival and QoL outcomes; and in the absence of screening and novel treatments, quality plays an important role in ensuring all patients receive optimal care.

1.8.1 The components and dimensions of healthcare quality

Avedis Donabedian first proposed using the triad of structure, process and outcome to evaluate the quality of healthcare in 1966.[38] He defined structure as the setting or the environment where care is provided, including organisation culture, information systems, services and supply, policies and procedures and workforce. Process assesses the effectiveness of systems of care and the implementation of policies, procedures and guidelines. Outcome is defined as the 'consequences of care' that may be influenced directly or indirectly by the structure or process components.[39] Termed the 'lasting framework', it provided the foundations for the Institute of Medicine (IOM) to build on Donabedian's work to further define quality and highlight the six core aims known as the dimensions of quality.[40]

The IOM defines healthcare quality as *"the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge."*[41] The six core aims of healthcare is to deliver *safe, effective, efficient, timely, patient-centered and equitable care* and the components of healthcare described by Donabedian are the conceptual frameworks which underpin the evaluation of the quality of PC care (*Figure 1.6*).[38,42]

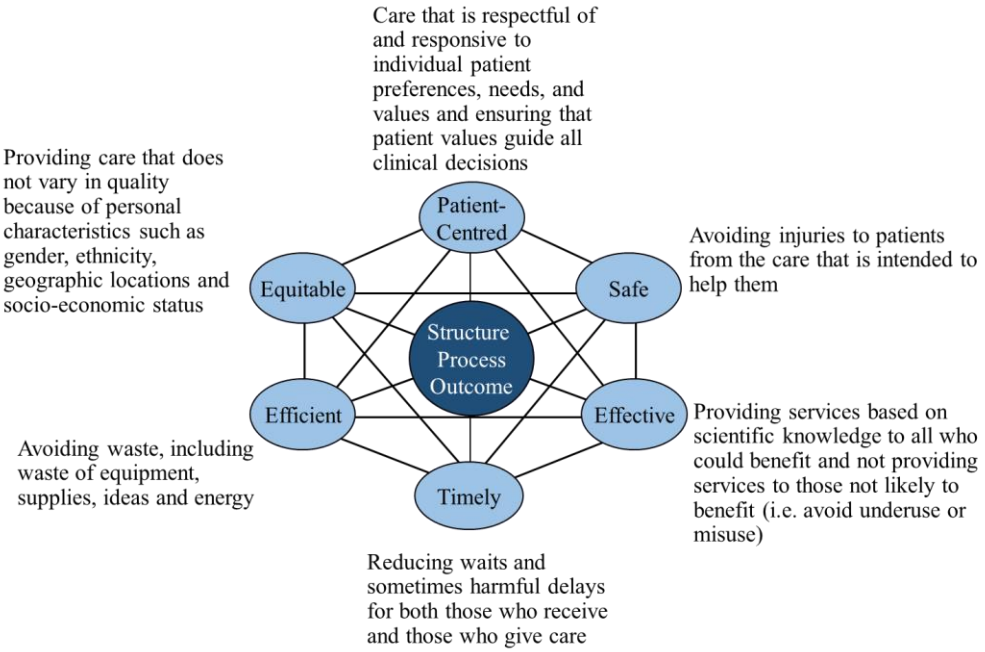

Figure 1. 6: *The dimensions and components of healthcare quality*

1.8.2 Assessing quality of care in patients with PC

There is evidence that clinical practice often does not meet evidence-based guidelines for PC. The following excerpt is taken from a chapter written for a book published by Springer titled chapter titled 'Quality of Care Indicators in PC' and highlights the current variations in care in the context of the dimensions of quality. The book chapter is attached as *Appendix 1.1*.

Is care safe? There is accumulating evidence that patients undergoing surgery in hospitals managing low volumes of patients have higher mortality rates than those treating high volumes of patients with PC.[43,44] Improved survival in high volume centres is possibly the result of increased ability to deliver safe care in hospitals resourced to manage these complex patients. A call has recently been made in a number of United States (US) health services to limit pancreatic surgery privileges to surgeons performing at least five cases per year and facilities with at least 20 cases per year.[45] However, the optimal surgeon and hospital volume remains to be determined as highlighted in recent reviews. For example, the criteria for high volume centres range from 20 - 40 cases annually in the literature.[46,47] Further, in comparison to overseas studies, Australian hospitals have a relatively low volume of pancreatic surgery,

yet comparable inpatient mortality and it has been suggested that resource availability may be more important that volume.[48] In addition to using mortality to assess safety of care, other markers of unsafe care include iatrogenic injuries and complications such as infection, haemorrhage, pressure ulcers, adverse drug events, and wound dehiscence.

Is care effective? There are cases where planned procedures (e.g. diagnostic laparoscopy) or a planned surgery for potentially resectable disease is abandoned intraoperatively. An abandoned surgery may indicate that the patient has not been effectively staged. In addition, surgery should ideally result in clear margins (margin-negative or R0). Unfortunately, around 20% of cases have microscopically positive (R1) or macroscopically positive (R2) margins resulting in poorer clinical outcomes.[49] R1 margins may be a marker of ineffective pre-operative staging before undertaking surgery.

Is care timely? PC is an aggressive disease with the majority of patients diagnosed at an advanced stage. The pathway to early diagnosis is complicated by the onset of generalised gastrointestinal symptoms, comorbidities and delays in referral. Patients can experience significant delays from referral to diagnosis when undergoing investigations for generalised gastrointestinal symptoms. A study researching delays caused by pre-diagnostic gastrointestinal investigations identified a median delay from referral to diagnosis of 64.5 days.[50]

Is care equitable? Differences in complications and mortality may be due to disparity in quality of care provided by individual providers or institutions. People living in regional or rural locations can be less likely than their city counterparts to receive anti-cancer therapy.[3] Patients living in areas with higher socio-economic status are also more likely to receive access to more advanced medical care that is associated with improved survival and improved QoL.[4]

Is care efficient? Structured reporting of surgical pathology increases the accuracy, accessibility, completeness and uniformity of surgical pathology diagnosis. However, there is variable quality of pathological reporting with some evidence that up to 44% of free text reports do not contain sufficient information for disease stage to be inferred. In one study margin status was recorded in only 11% of reports.[51]

Is care patient-centred? Current expert opinion and international recommendations state that management decisions, certainly for early PC should be made within the framework of a multidisciplinary team (MDT) meeting to ensure that the full range of available and appropriate treatment options are considered.[52] Yet, only a third of patients diagnosed with PC are presented to MDT meetings.[4]

1.9 The Role of Clinical Quality Registries in Improving Quality of Care in PC

In order to understand the reasons behind the variation in care described above, evaluating the current quality of care delivered to patients diagnosed with PC is an essential step. Disease-specific registries and audit databases provide vital evidence on the clinical management of patients with PC. Numerous cancer databases exist collecting incidence, demographic, treatment and mortality data on patients with PC. These include large datasets such as the SEER database (*Surveillance, Epidemiology, and End Results*) that collect information from 20 registries across the United states of America (USA) and are able to report on demographics, tumour site and morphology, stage at diagnosis, primary treatment and survival.[53]

Table 1.3 below provides examples of international registries that are collecting data prospectively for patients diagnosed with PC with the intention to improve care through regular reporting and feedback.

Name of registry / database	Year initiated	Type of Registry, Country	Purpose
EURECCA Pancreas[54] (*European Registration of Cancer Care*)	2007	International cancer registry with ability to report on PC. Registry is held in Leiden, Netherlands	A platform supporting the collection of cancer information across European countries. A shared items list was developed to enable data comparison on a large scale[55]
Nationella Pankreasregistret[56] (*National Quality Registry for Pancreatic and Periampullary Cancer*)	2010	National disease-specific (PC) registry - Sweden	Sweden has established over 100 clinical quality registries. The PC registry contains data on diagnosis, interventions, inpatient care, risk factors, QoL and follow-up data
PACAP[57] (*Dutch PAncreatic CAncer Project)*	2013	National disease-specific (PC) registry - Netherlands	The PACAP originated from a surgical audit, and extended over time to include all patients diagnosed with PC, and is now overseen by an expert panel.
Japan Pancreatic cancer Registry[58]	1981	National disease-specific (PC) registry - Japan	Established for over 3 decades with over 350 institutions contributing data on PC voluntarily with periodic follow-up[59]

Table 1.3: *International registries collecting prospective data on PC*

In Australia, the Upper Gastrointestinal Cancer Registry (UGICR) was established in 2015 to capture information from patients with oesophagus, stomach, liver, biliary and pancreas cancer. Clinical quality registries such as UGICR are recognised as important tools with the purpose of monitoring quality of care, providing feedback to the relevant clinical community and wider stakeholder groups, benchmarking performance, describing patterns of treatment, and identifying variation. The UGICR will act as an enabler to understanding reasons behind the variations in quality of care for patients with PC and provides the environment within which to conduct this research. The following publishing provides a background to the registry and its role in quality of care for PC.

BMJ Open

The Upper Gastrointestinal Cancer Registry (UGICR): a clinical quality registry to monitor and improve care in upper gastrointestinal cancers

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ABSTRACT

Purpose The Upper Gastrointestinal Cancer Registry (UGICR) was developed to monitor and improve the quality of care provided to patients with upper gastrointestinal cancers in Australia.

Participants It supports four cancer modules: pancreatic, oesophagogastric, biliary and primary liver cancer. The pancreatic cancer (PC) module was the first module to be implemented, with others being established in a staged approach. Individuals are recruited to the registry if they are aged 18 years or older, have received care for their cancer at a participating public/private hospital or private clinic in Australia and do not opt out of participation.

Findings to date The UGICR is governed by a multidisciplinary steering committee that provides clinical governance and oversees clinical working parties. The role of the working parties is to develop quality indicators based on best practice for each registry module, develop the minimum datasets and provide guidance in analysing and reporting of results. Data are captured from existing data sources (population-based cancer incidence registries, pathology databases and hospital-coded data) and manually from clinical records. Data collectors directly enter information into a secure web-based Research Electronic Data Capture (REDCap) data collection platform. The PC module began with a pilot phase, and subsequently, we used a formal modified Delphi consensus process to establish a core set of quality indicators for PC. The second module developed was the oesophagogastric cancer (OGC) module. Results of the 1 year pilot phases for PC and OGC modules are included in this cohort profile.

Future plans The UGICR will provide regular reports of risk-adjusted, benchmarked performance on a range of quality indicators that will highlight variations in care and clinical outcomes at a health service level. The registry has also been developed with the view to collect patient-reported outcomes (PROs), which will further add to our understanding of the care of patients with these cancers.

Strengths and limitations of this study

- The Upper Gastrointestinal Cancer Registry is the first clinical quality registry (CQR) in Australia, designed to capture information on upper gastrointestinal (UGI) cancers with the aim to improve practice by monitoring and providing benchmarked reports to participating sites.
- We describe the development of a CQR for UGI cancers, including the establishment of governance, recruitment framework, clinical quality indicators, minimum data set, data access policy and reporting structure.
- This registry was developed as per the Australian Commission on Quality and Safety in Health Care's (ACSQHC) Framework for Australian CQRs and follows ACSQHC's Australian Operating Principles for CQRs and can be used as a model for researchers developing CQRs.
- The time-consuming and labour-intensive site governance approval process in Australia is a major limitation for rollout of the registry.

INTRODUCTION

The five most common upper gastrointestinal (UGI) cancers in Australia are pancreas, oesophagus, stomach, liver (hepatocellular carcinoma) and biliary cancers; the combined incidence is approximately 10 000, and there are around 7500 deaths annually.[1] The 5-year relative survival rates of UGI cancers are among the worst of all tumour types: 9.8% in pancreas; 18.5% in liver; 20.1% in biliary; 22% in oesophagus; and 30.3% in stomach.[1] The dismal prognosis of these cancers can be largely attributed to their presentation at an

advanced disease stage. Additionally, older age is a risk factor for mortality from these tumours, and significant cardiac and respiratory comorbidities may limit treatment options. As a result, only 15% of pancreas, 43% of liver, 20% of oesophagus and 50% of stomach cancers are potentially resectable at diagnosis.[2 3]

Resection, with radical lymph node dissection where appropriate, remains the principal potentially curative therapy for all localised UGI cancers. Disease management is almost invariably multimodal and may include chemotherapy and radiotherapy as neoadjuvant, adjuvant or palliative therapy and the provision of optimal supportive care.[4–8]

The aggressive nature of these cancers and the complexity of treatment often decrease health-related quality of life.[9] Advances in surgical techniques and perioperative care have resulted in operative mortality falling to less than 5% in major centres.[10] However, surgery remains a morbid procedure with postoperative complications resulting in prolonged hospital admission, adversely impacting on overall quality of life and the ability to undergo any adjuvant therapies.[11] In those surviving 1–2 years following curative treatment, health-related quality of life generally recovers to baseline. However, there are still major challenges faced by survivors. For those having palliative or supportive therapy only, quality of life frequently deteriorates throughout the disease trajectory.[9]

Local or distant cancer recurrence occurs frequently following resection for all UGI cancers. A third of patients diagnosed with stomach[12] and half of all patients diagnosed with oesophageal[13] cancer develop recurrent disease within 2 years. In pancreatic cancer (PC), where only 10%–15% of tumours are considered resectable, the local recurrence rate ranges from 10% to 40% and distant recurrence is as high as 88%.[14]

There is evidence that variability exists in the management and outcomes of UGI cancers. For example, not all patients are presented to a multidisciplinary team meeting[15]; there are disparities in the utilisation of surgical resection and associated disease-specific survival based on where patients live[16]; there is wide variation in histopathological assessment of margins and the proportion that have clear margins[14]; the duration of surgery, postoperative complication rates and their management differ between public and private hospitals[17 18]; administration of adjuvant chemotherapy or radiotherapy is variable, often due to morbidity associated with postoperative complications[19]; and the 30-day postoperative mortality is lower in hospitals performing more resections each year.[20 21] Patients with UGI cancers have significant unmet needs pertaining to quality of life, finance, relationships and family or caregiver distress; these are often exacerbated by a lack of understanding of the health system.[22 23] In PC, over 50% of participants (n=136) in an Australian-based study reported moderate to high unmet physical or psychological needs.[24]

Measuring quality of care with clinical quality registries (CQRs)

To identify, understand and reduce unwarranted clinical variation and ensure that all patients receive optimal care, it is important to collect high-quality disease-specific data. CQRs support continuous improvements in patient outcomes by monitoring quality of care and providing risk-adjusted feedback to the relevant clinical community. These data describe patterns of treatment in order to identify variation and can provide a framework for research.[25] Successful implementation of CQRs has been achieved in a range of disciplines include trauma, cardiac, transplant and bariatric surgery,[26] joint replacement[27] and cancer care (eg, prostate).[28]

The Australian Commission on Safety and Quality in Health Care (ACSQHC) supports the development of CQRs in Australia through the provision of the national framework for CQRs.[29] The framework details the necessary principles, guidelines and standards for best practice design, build, operation and security of CQRs. A recent evaluation of the cost-effectiveness of CQRs determined that when funded sufficiently with robust operating procedures, CQRs provide a substantial return on investment.[30] In prioritising the development of CQRs in Australia, the ACSQHC ranked the development of registries for high-burden cancers only behind those monitoring ischaemic heart disease and musculoskeletal disorders.[31] PC is ranked fourth as a high-burden cancer in terms of its impact on disability-adjusted life years behind lung, bowel and breast cancer.[32] It was predicted to be the third leading cause of cancer deaths in the USA in 2018 and by 2030 is predicted to be the second most common cause of cancer associated mortality.[2]

Although a number of generic population-based cancer registries exist, there are no CQRs specific to the five aforementioned UGI cancers. Disease-specific registries[33 34] and audit databases[35] provide much needed evidence about the management of patients with these cancers. However, little prospective data have been published from multi-institution databases and/or registries regarding the quality of UGI cancer care across the disease trajectory.

Rationale for the Upper Gastrointestinal Cancer Registry (UGICR)

Improvements in cancer outcomes for patients with UGI cancer will understandably come through establishment of models of care that are informed by close attention to clinical and patient-reported quality measures and standardisation of treatment that comply with agreed best practice. Given the lack of Australian population-level data regarding patient outcomes from UGI cancers, it was considered that a registry established to monitor treatment and outcomes of patients with cancers arising in the oesophagus, stomach, pancreas, liver and biliary system will improve management of these diseases. Furthermore, while detailed guidelines exist for each of these cancers,

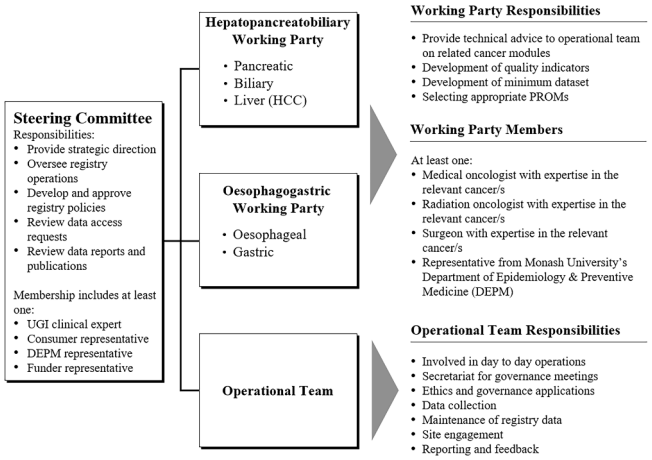

Figure 1 UGICR governance structure. HCC, hepatocellular carcinoma; PROMs, patient reported outcome measures; UGI, upper gastrointestinal.

gaps remain regarding optimal care and management of these patient groups.[4–8 36]

The UGICR is a CQR established with the aims to:

1. Assess patterns of care and identify variations in clinical and patient reported outcomes.
2. Benchmark performance and provide feedback to service providers using a targeted quality improvement approach to drive improvements in current practice.
3. Provide confidence to public, clinician and wider stakeholders on the delivery of high-quality service.
4. Advance knowledge of best treatment protocols by facilitating future clinical, health service, psychosocial and biomedical research.

COHORT DESCRIPTION

Overview

The UGICR is a multicentre, population-based, non-interventional prospective cohort study.

It was established in 2015 in Victoria and has since expanded to the state of New South Wales, Australia.

Governance

The UGICR is governed by a Steering Committee and, currently, two clinical working parties with the responsibility of each outlined in figure 1. The Steering Committee performs in accordance with the Australian Framework for CQRs.[29]

A central research team provides operational oversights. A principal investigator at each participating hospital is responsible for ensuring that research activities undertaken at their site are conducted in accordance with the human research ethics committee (HREC) approval, the research protocol, site registry agreements and related policy documentation. At each site, patients are identified for recruitment and data collection occurs.

Registry design

The UGICR has a multimodular design with pancreatic, oesophagogastric (OG), liver and biliary cancer modules.

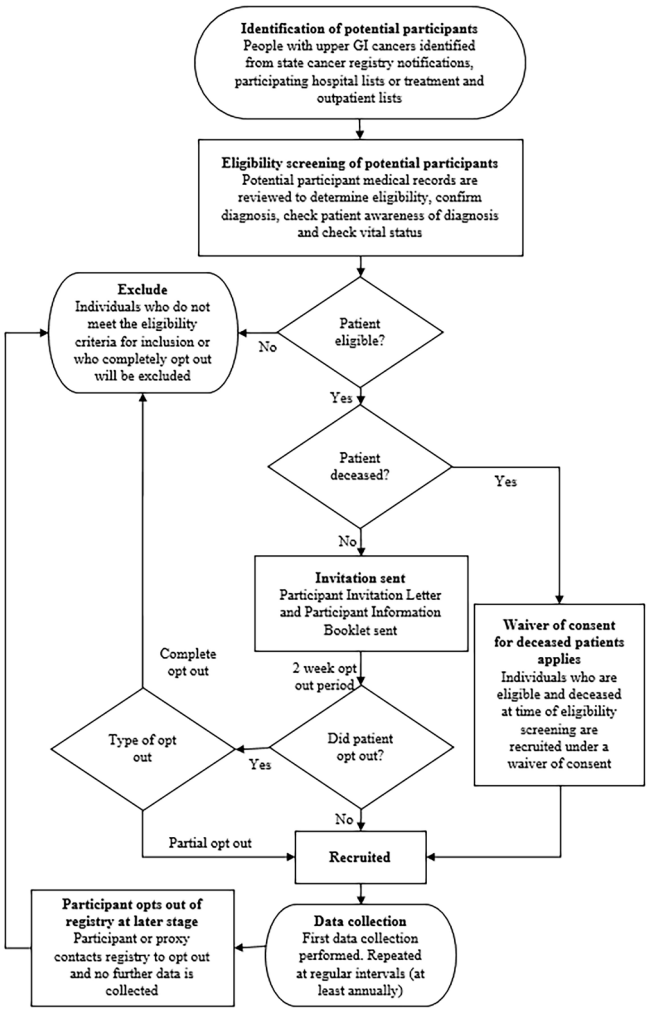

Figure 2 Registry recruitment schema. GI, gastrointestinal.

Data are entered into Research Electronic Data Capture (REDCap), a secure web-based application, hosted and managed by Helix (Monash University).[37] The registry was developed in REDCap, and all data are held securely on a Monash University server that has been accredited under the information security standard ISO27001.[38]

Participant recruitment and consent

The full recruitment schema is outlined in figure 2. Eligible patients are identified within each jurisdiction through state-based cancer registries or by individual health services. Eligibility criteria are listed in table 1. The UGICR uses an opt-out approach to minimise selection bias.[39]

Eligible participants are mailed an introductory letter explaining the study and an information booklet outlining details of the registry, its purpose, possible outcomes of the research and the opt-out process. Participants are given 2 weeks to opt out of the registry before their participation is assumed, after which we commence collection of clinical and personal data covering diagnosis to end-of-life care. Patients can withdraw their consent from participation in the registry at any point by telephoning or emailing the UGICR office, as outlined in the participant information booklet. A waiver of consent applies

Table 1 Eligibility criteria

All modules			
Inclusion	1. Patient has a confirmed primary pancreatic, oesophageal, gastric, liver, biliary or gall bladder cancer with some limited exclusions specified in each module (see below). 2. Patient has been assessed or received care at a participating public or private hospital or private clinician rooms. 3. Patient is 18 years of age or older at time of diagnosis. 4. Patient has a diagnosis date on or after 1 January 2016 (apart from one centre that commenced recruitment in November 2015).		
Module specific			
Modules		**Tumour sites**	**Tumour cell types**
Pancreatic	*Inclusion*	Pancreas. Periampullary region Ampulla of Vater. Biliary origin. Intestinal origin. Distal bile duct.	Ductal adenocarcinoma. Cholangiocarcinoma. Acinar cell carcinoma. Acinar cell cystadenocarcinoma. IPMN (invasive). Pancreatoblastoma. Serous cystadenocarcinoma.
	Exclusion	Non-distal bile duct	Neuroendocrine neoplasms. Premalignant lesions. Mesenchymal tumours. Solid pseudopapilliary carcinoma. IPMN (non-invasive).
Oesophagogastric	*Inclusion*	Oesophagus (lower two-thirds). Gastro-oesophageal junction. Stomach.	Carcinoma Adenocarcinoma. Squamous cell carcinoma. Other subtypes.
	Exclusion	Upper third of oesophagus.	Neuroendocrine neoplasms. Lymphomas. Mesenchymal tumours.
Biliary	*Inclusion*	Perihilar (hilar) bile duct. Intrahepatic bile duct. Gall bladder.	Carcinoma. Cholangiocarcinoma. Adenosquamous carcinoma. Squamous cell carcinoma. Cholangiosarcoma.
	Exclusion	Distal bile duct.	Neuroendocrine neoplasms. Mesenchymal tumours.
Liver*	*Inclusion*	Liver.	Hepatocellular carcinoma.
	Exclusion	Intrahepatic bile duct.	Cholangiocarcinoma. Mesenchymal tumours. Germ cell tumours. Lymphomas.

*Liver module eligibility criteria still to be finalised.
IPMN, intraductal papillary mucinous neoplasm.

where patients deemed eligible require an interpreter, have significant cognitive impairment or where there is evidence that the patient is deceased.

FINDINGS TO DATE

Data set

The first module developed was the PC module, which began with a pilot phase of approximately 1 year, during which we collected data for a provisional set of quality indicators in three Victorian sites from 2016 to 2017. The second module developed using a similar pilot phase was the OG module. Subsequently, we used a formal modified Delphi consensus process to establish a core set of quality indicators for PC. This process involved 19 PC care experts from three states in Australia. A detailed description of the methods of the modified Delphi process and the selected indicators has been published separately.[40] In addition, a review was undertaken of the Australian Optimal Care Pathways (OCP) for PC[41] and OGC[42] to ensure that indicators are aligned with the seven themes described in the OCP (prevention and early detection; presentation, initial investigations and referral; diagnosis,

Table 2 PC Optimal Care Pathway (OCP) mapped to modified Delphi quality indicators

PC OCP	OCP elements	Mapped quality indicators from modified Delphi consensus[40]
Step 1: Prevention and early detection	1.1 Prevention. 1.2 Risk factors. 1.3 Early detection.	Nil
Step 2: Presentation, initial investigations and referral	2.1 Signs and symptoms. 2.2 Assessments by general practitioner or medical practitioner. 2.3 Referral.	► Documented baseline CA19-9 level before treatment. ► Documented ECOG and/or ASA at presentation. ► Time from referral to definitive treatment within 60 days.
	2.4, 3.5, 4.6, 5.4, 6.6 and 7.3 Support and communication	Nil
Step 3: Diagnosis, assessment and treatment planning	3.1 Diagnostic workup. 3.2 Staging. 3.3 Treatment planning.	► Documented pancreatic protocol CT or MRI scan for diagnosis and/or staging. ► Operability of tumour is clearly defined and documented as either operable/resectable, borderline resectable, locally advanced (unresectable) or metastatic (unresectable). ► Disease management for all patients discussed at an MDT meeting.
	3.4, 4.4, 5.3, 6.5 and 7.2 Research and clinical trials	► Number of patients included in a clinical trial.
	3.1 and 3.2 Timeframe	► Time from referral to definitive treatment within 60 days.
Step 4: Treatment	4.1 Treatment intent	Nil
	4.2.1 Surgery (curative)	► All patients who did not undergo surgery should have a valid reason documented. ► Number of patients undergoing PC surgery in a level 1–4 hospital.
	4.2.1 Chemotherapy or chemoradiation.	► Adjuvant chemotherapy administered following surgery or a reason documented for not undergoing treatment.
	4.2.2 and 4.3 Treatment of unresectable PC/ palliative care.	► Chemotherapy±chemoradiation offered to patients with locally advanced disease, or a reason documented for not undergoing treatment. ► Number of patients who saw a medical or radiation oncologist or a reason documented for not doing so.
	4.5 Complementary or alternative therapies.	Nil
Step 5: Care after initial treatment and recovery Step 6: Managing recurrent, residual and metastatic disease	5.1 Survivorship. 5.2 Post-treatment care planning. 6.1 Signs and symptoms of recurrent, residual or metastatic disease.	► All patients having completed treatment followed up by a specialist every 3–6 months for up to 2 years.
Step 7: End-of-life-care	6.4 Palliative care. 7.1 Multidisciplinary palliative care.	► All patients with metastatic disease referred to (or seen by) palliative care specialist.

Some elements in each step of the pathway are overlapping. Elements 6.2 and 6.3 readdress steps 3 and 4. Please note: the purpose of this document is to provide a broad overview of the areas within the OCP that the developed PC quality indicators measure. Only the key indicators that map to the elements are listed.
ASA, American Society of Anesthesiologists (performance status); ECOG, Eastern Cooperative Oncology Group (performance status); MDT, Multidisciplinary Team.

staging and treatment planning; treatment; care after initial treatment and recovery; managing recurrent, residual or metastatic disease; and end-of-life care). An outline of this process for PC is provided in table 2. There are currently no clinical quality indicators in the UGICR that measure care for the prevention and early detection

of PC. However, the UGICR is participating in a collaborative project, Symptom-UGI: Upper Gastrointestinal Cancer Symptom Study, to map the patient pathways from onset of symptoms to cancer diagnosis. Details of this study can be found within the UGICR website (https://ugicr.org.au/associated-studies/).

The minimum data set was established to enable quality indicators to be calculated. Data items and definitions were aligned with national specifications where appropriate, and a comprehensive data dictionary was developed for each module. The core data items are outlined in table 3.

The OGC module has been developed by the OGC working party following a literature review, and a consensus method was used to agree on the quality indicator set. The registry has future plans to begin the collection of patient-reported outcomes (PROs) and patient-reported experiences (PREs) to provide valuable patient perspectives. As an initial step, a systematic review evaluating patient-reported outcome measures (PROMs) in PC has been undertaken by the UGICR team to define which PROMs are most appropriate for this group of patients.

Data collection

If the participant has not opted out of the registry, data collectors abstract diagnosis, surgical, pathology and treatment data directly from the participant's electronic and/or hard copy medical records from participating sites or from clinician rooms. Data collection begins close to the time of recruitment with at least annual follow-up until end of life.

Results from the pilot studies from the PC and OGC modules

The results of the pilot phase for both PC and OGC modules are displayed in table 4. Of the 123 participants eligible for the PC module and 189 for the OGC module, 8 (6.5%) and 9 (4.8%) opted out of the registry, respectively. Clinical stage at diagnosis was not well documented in both the PC module (n=80, 70%) and OGC cancer module (n=82, 46%) and is an area for future quality improvement. Around 20% of the pancreatic cohort received surgery as first treatment, which is broadly representative of surgical treatment in patients with PC.[43] Furthermore, 73 participants in the PC and 94 participants in the OGC module had documented reasons for no surgery. The pilot results for both modules identified areas for improving data completeness, definitions, items and structure of data collection forms. Following the pilot phase, the registry focused on improving these areas before expanding to other participating hospitals.

Population coverage

Population coverage in Victoria is based on data from the Victorian Cancer Registry. The population coverage in the pilot phase was 19% for the PC module and 11% for the OGC module. Current coverage is 73% for PC and 55% for the OGC module. In New South Wales, data are currently only being collected on the PC module with an estimated population coverage of 55%.

Reporting

The registry will produce risk-adjusted benchmarked reports that will feed back deidentified data to participating sites on the associated quality indicators. To provide fair and meaningful benchmarked reports, we have undertaken a review of risk models to identify demographic and baseline clinical variables (focusing on those over which clinicians have no control, for example, age, sex and disease stage) that predict patient outcomes for the purposes of risk adjustment. The data from the registry will also permit validation of current predictive risk models and enable further refinement of these tools. Publicly available annual reports that provide an overview of quality of care and the registry's activities will be published. A UGICR website (https://ugicr.org.au/) has been developed to provide information about the registry to patients, clinicians and other stakeholders. This will be updated to include results as they become available.

STRENGTHS AND LIMITATIONS

The UGICR is Australia's first UGI cancer CQR. The aims of the registry are to monitor quality of care, benchmark clinical and patient-reported outcomes against best practice and provide high-quality population-based data for clinical research. Registries such as the UGICR provide much needed real-world evidence outside the context of randomised control trials about disease epidemiology, treatment patterns, burden of illness, survival outcomes, clinical variation and treatment safety.[44]

In recent decades, there has been increasing integration of PROMs into cancer registries to collect outcomes such as overall quality of life, functional and psychosocial well-being, lifestyle behaviours and supportive care needs.[45] Clinicians and patients may place different emphasis on symptom impacts and expectations from their treatment.[46] The collection of PROMs is an important step in understanding patients' experience of their symptoms and management and the impact of the disease and its treatment on their quality of life. The UGICR will determine and integrate the most relevant PROMs for each UGI cancer type following thorough examination of the literature.

Through the accumulation of significant and consistent data on UGI cancers, the registry will assess how clinical management compares with best practice and communicate this to clinicians through the PIs or relevant hospital departments. Furthermore, the UGICR provides a platform for longer term clinical follow-up, randomised clinical trials and substudies exploring treatment outcomes and linking outcomes to tumour tissue characteristics.

An important consideration is the maturity of each module before useful quality indicator reports can be provided to participating hospitals, as some UGI cancers have a relatively low incidence in comparison with other

Table 3 UGICR minimum dataset*

Participant details
Title
First name
Middle name(s)
Surname
Recruiting hospital
Medical record number
Date of birth
Sex
Medicare number
Department of Veteran Affairs number
Country of birth
Preferred language
Interpreter required
Indigenous status
Contact details
- Phone number(s)
- Email address
- Postal address
- Residential address at diagnosis

Next of kin and contact details
General practitioner details
Deceased status
Date of death
Cause of death

Diagnosis and staging (prior to antitumour treatment)
Diagnosis date
Date mass first seen on imaging
Diagnostic imaging tests completed†
Pathology testing prior to anti-tumour treatment
- Cytology date
- Histology date

Primary site of tumour
Tumour morphology
Clinical disease stage (TNM)
Resectability of tumour at diagnosis
CA 19–9 measured
Discussion at a multidisciplinary team meeting
Date earliest multidisciplinary team meeting discussion
Diagnosing hospital

Surgery
Date of operation
Type of resection
Surgical approach
Reason resection surgery abandoned
Date of return to theatre
Readmitted to hospital within 90 days of surgery (excluding same day chemotherapy)
Date of readmission
Died in surgical admission
Name of consultant surgeon
Hospital where surgery was performed
Resection pathology
- Maximum dimension of tumour
- Number of lymph nodes examined
- Number of lymph nodes positive
- Closest reported margin
- Pathologic staging (pTNM)
- Histology

Chemotherapy
Treatment intent (Neoadjuvant/adjuvant/curativetive/palliative)‡
Date chemotherapy commenced
- Chemotherapy agent(s) administered
- Name of medical oncologist
- Hospital providing chemotherapy

Radiotherapy
Treatment intent (Neoadjuvant/adjuvant/curativetive/palliative)‡
- Date radiotherapy commenced
- Radiation oncologist
- Radiotherapy technique
- Body sites treated
- Total dose given (Gy)
- Number of fractions
- Name of radiation oncologist
- Hospital providing radiotherapy

Restaging after neoadjuvant therapy
Date neoadjuvant therapy completed
Resectability of tumour
Clinical disease (TNM)

Other treatment and end-of-life care
Referral to or contact with palliative care
Date of referral to palliative care
≥2 ED presentations in the last 30 days prior to death
≥14 days in acute hospital during last 30 days of life
Died within 30 days of dose of chemotherapy

*More detailed, module specific data dictionaries have been developed.
†Varies between modules.
‡All related data items collected for first cycle of each type of treatment intent.
ED, Emergency Department; TNM (staging), Tumour, Node, Metastasis ; UGICR, Upper Gastrointestinal Cancer Registry.

Table 4 PC and OGC module data from pilot data collection

Variable	PC module n (%)	OGC module n (%)
Recruited	**115**	**180**
Recruited via invitation letter	88 (76.5)	120 (66.7)
Recruited via waiver of consent (deceased)	27 (23.5)	60 (33.3)
Sex		
Male	56 (48.7)	132 (73.3)
Female	59 (51.3)	48 (26.7)
Age at diagnosis (years)		
<50	6 (5.2)	11 (6.1)
50–59	14 (12.2)	22 (12.2)
60–69	30 (26.1)	54 (30.0)
70–79	38 (33.0)	54 (30.0)
≥80	22 (19.1)	33 (18.3)
Missing	5 (4.3)	6 (3.3)
Resectability at diagnosis		
Resectable	25 (21.7)	58 (32.2)
Borderline resectable	3 (2.6)	11 (6.1)
Unresectable	67 (58.3)	64 (35.6)
Locally advanced (LA)	*24 (20.9)*	*6 (3.3)*
Metastatic (Mets)	*43 (37.4)*	*58 (32.2)*
Not documented	14 (12.2)	–
Unknown	–	41 (22.8)
Missing	6 (5.2)	6 (3.3)
Clinical stage at diagnosis		
I or II	5 (4.3)	33 (18.3)
III	–	7 (3.9)
IV	18 (15.7)	50 (27.8)
Complete TNM* not documented	80 (69.6)	82 (45.6)
Missing	12 (10.4)	8 (4.4)
First treatment		
Neoadjuvant therapy	4 (3.5)	60 (33.3)
Attempted or completed resection surgery	27 (23.5)	13 (7.2)
Curative intent ChemoTx and/or RT	–	7 (3.9)
Palliative intent ChemoTx and/or RT	37 (32.2)	55 (30.6)
No treatment	29 (25.2)	23 (12.8)
Unknown	–	16 (8.9)
Missing	18 (15.7)	6 (3.3)
Reasons for no surgery†		
LA or Mets	62	60
Advanced age	1	6
Comorbidities	7	9
Patient declined	1	12
Patient died prior to surgery	0	7

Continued

Table 4 Continued

Variable	PC module n (%)	OGC module n (%)
Performance status	–	4
Other reason	1	–
Reason not documented	4	3
Participant data collection status		
Complete	51 (44.3)	107 (59.4)
Incomplete	64 (55.7)	73 (40.6)
Data entry subform completeness		
Demographics	113 (98.2)	180 (100.0)
Vital status and tumour recurrence	58 (50.4)	145 (80.6)
Diagnosis details	97 (84.3)	165 (91.7)
Biliary stents	94 (81.7)	–
Surgery	102 (88.7)	168 (93.3)
Pathology of resection sample	102 (88.7)	–
Neoadjuvant therapy	104 (90.4)	–
Adjuvant therapy	98 (85.2)	–
Therapy for locally advanced disease	95 (82.6)	–
Therapy for metastatic disease	77 (67.0)	–
Other treatment and trials	80 (70.0)	–
Treatment summary	–	167 (92.8)
Restaging after neoadjuvant therapy	–	167 (92.8)
Chemotherapy details	–	162 (90.0)
Radiotherapy details	–	163 (90.6)
End-of-life details	–	81 (45.0)

*TNM system of classification of cancer.
†Reason for no surgery: participants may have more than one reason documented.
ChemoTX, chemotherapy; RT, radiotherapy.

cancers.[1] The working groups in collaboration with statisticians will determine an analysis plan for each indicator with due consideration to data completeness and risk adjustment methods.

Identified challenges

The UGICR has faced some key challenges affecting its establishment and implementation. The introduction of the National Mutual Acceptance (NMA) scheme has significantly streamlined the ethics process for all public hospitals in Australia, except in the Northern Territory, making the process to gain approval for CQRs more manageable. However, obtaining governance approval at each site continues to be both labour intensive and time consuming.[47 48] Furthermore, separate HREC approval is frequently required to access data from private hospitals and clinics.

Funding is another challenge faced by CQRs. As with many healthcare initiatives, the financial burden can be a major impediment.[25] Data from CQRs are held in positive regard by clinicians, health managers and government. However, further funding will be required to progress national rollout of the registry.

Other identified barriers include reluctance of some healthcare providers to supply source data, and poor interoperability between clinical information systems leading to duplication of data entry. Where data are of high quality, such as for diagnosis and procedure codes, administrative data is appropriate, but there are limited data for comorbidities and risk factors.[49] While automation of data collection from existing data sources would be ideal, this is hampered by inconsistent documentation and a lack of standardisation.[50]

Collaboration

The UGICR aims to capture whole of population, real-world data that monitors and aspires to improve the quality of care provided to patients with UGI cancers. The registry is currently recruiting hospitals to increase population capture and selecting the most relevant instruments for measuring PROs and PREs for inclusion in each module. The biliary module is entering its pilot

phase, and the liver module is to be developed. Monash University is the UGICR's data custodian and is accountable for the privacy, security and integrity of patient information held within the registry. Participating sites can request a copy of their own patient-level data. Researchers may access registry data following a formal submission to the UGICR data custodian and approval by the UGICR Steering Committee. They are required to complete a request form detailing their research aims and methods, potential impact on healthcare, and provide evidence relevant HREC approval before deidentified data will be released. The registry will harness new opportunities for data linkage with technologies such as the electronic medical records and collaborate with existing data repositories (eg, biomedical) to evolve and fulfil its aim of providing quality evidence.

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1.10 Thesis Aims, Research Questions, and Hypotheses

1.10.1 Overall PhD aim

The purpose of this thesis is to: (1) determine the measures that quantify the quality of care provided to patients diagnosed with PC, from a clinical and patient perspective (2) map the patterns of treatment provided to patients diagnosed with PC in Victoria, Australia, and the impact on survival; (3) identify the extent to which care is delivered in accordance with developed quality of care indicators, as predictors of performance on survival; (4) explore the barriers and enablers to implementing two quality of care indicators which have been associated with low adherence; and (5) identify strategies to improve quality of care.

1.10.2 Objectives, research questions and hypotheses

The following objectives and hypotheses were defined for this thesis in concordance with the overall aim:

<u>Aim 1:</u> Determine the measures that quantify the quality of care provided to patients diagnosed with PC, from a clinical and patient perspective

Research Question: How should quality of care be measured by a clinical quality registry established for patients diagnosed with pancreatic cancer (PC)?

Objective 1: To determine the measures that quantify quality of care from a clinical perspective by developing a core, consensus-set of evidence-based clinical quality indicators (QIs) that monitor the care provided to patients with PC.

Hypothesis: That quality of care metrics can be agreed upon by a multidisciplinary group of experts and successfully incorporated into a PC clinical quality registry to monitor care across the disease trajectory (from referral to death)

Objective 2: To determine the measures that quantify quality of care from a patient perspective by examining patient-reported outcome measures (PROMs), their attributes and application in patients with PC.

Hypothesis: A systematic review will identify the best validated PROMs that can be applied in patients diagnosed with PC

<u>Aim 2:</u> To map the patterns of care and identify unwarranted variation in quality of care provided to patients diagnosed with PC

Research Question: What patient, provider and health system factors are associated with compliance with processes and outcomes of care for patients with PC?

Objective 3: To assess compliance with the agreed set of QIs that reflect best practice using the data collected by the UGICR.

Hypothesis: QIs that meet high and low compliance will be identified warranting further investigation as to the cause of this variation

Objective 4: To assess the association between compliance with the QIs and outcomes such as survival.

Hypothesis: High quality care will be associated with improved outcomes for patients with PC

<u>Aim 3:</u> To explore the barriers and enablers to providing quality care to patients with PC

Research Question: What are the barriers and enablers to quality improvement implementation using QIs in PC care?

Objective 5: To understand the barriers and enablers to the implementation of QIs in healthcare in at least two areas that define optimal care.

Hypothesis: The facilitation of improvement will be achieved by identifying the modifiable barriers and enhancing the identified enablers

1.10.3 Overview of thesis Chapters

In the first Chapter, a general overview of PC, its risk factors, diagnosis, staging and treatment, epidemiology and the burden of a diagnosis of PC is presented. In the absence of screening and novel treatments, the importance of monitoring quality of care to improve survival and QoL outcomes are discussed in the context of clinical quality registries. A cohort profile on the UGICR provides further background and has been published in the *BMJ Open*.[60]

In Chapter 2, the development of clinical QIs using a modified Delphi method are outlined as the primary step towards monitoring quality of care in PC. This has been published in the *Hepatopancreatobiliary (HPB) Oxford Journal*.[61]

In Chapter 3, the patterns and quality of care are evaluated and the association of patient factors and the clinical QIs to patient survival using a univariable and multivariable analysis. The manuscript for this study is currently in preparation.

In Chapters 4 and 5, two qualitative studies using semi-structured interviews with clinicians, explore the barriers and enablers to the implementation of protocol imaging and all patients discussed at multidisciplinary team meetings. The two manuscripts are currently under review.

In chapter 6, a systematic review explores the numerous patient-reported outcome measures (PROMs) applied in PC with recommendations proposed based on the findings of this review. The study has been published in the *Hepatopancreatobiliary (HPB) Oxford Journal.*[62]

Chapter 7 summarises the findings. There is also a discussion of the issues, further questions that have arisen and future directions for the registry that can be undertaken for further research.

“Knowing is not enough; we must apply. Willing is not enough; we must do. Without haste, but without rest.

Few people have the imagination for reality. Whatever you can do or dream you can, begin it. The soul that sees beauty may sometimes walk alone.

Doubt can only be removed by action.

Boldness has genius, power and magic in it. As soon as you trust yourself, you will know how to live. Magic is believing in yourself, if you can do that, you can make anything happen ”

Nothing is worth more than this day.

Johann Wolfgang von Goethe

Chapter 2: Monitoring Quality of Care for Patients with PC

Variations in care for patients diagnosed with PC were described in Chapter 1 within the context of the dimensions of quality. In this Chapter we address the first aim and objective 1 of this thesis, to understand and measure quality of care through the development of a core set of evidence-based clinical QIs.

This research outlines the development of a core set of PC clinical QIs by an expert panel. These indicators form the basis for benchmark reports to be developed by the UGICR. These benchmark reports will compare, at a hospital level, performance against these QIs. Further, the QIs informed the data fields that needed to be captured by UGICR to evaluate quality of care on an ongoing basis for benchmark reports to be generated. Important considerations for the panel were the feasibility of data collection and the extent to which QIs will need to be risk-adjusted and/or stratified.

Ethics approval was gained from Monash University HREC (*Appendix 2.1*). A preliminary list of indicators were identified following a literature review, which was collated into an extensive supplementary document, provided as *Appendix 2.2*.

A modified, three round Delphi survey was performed with a diverse range of clinical experts with experience in managing patients diagnosed with PC. The experts used a scale ranging from 1 (not important) to 9 (very important) to rank the importance of including the proposed indicator. Prior to the first online survey, the aforementioned supplementary document was provided to each panellist. Following round one, an executive summary provided details of the agenda for the second face-to-face round, statistical calculations and the results from round one. Excerpts of the executive summary are attached as *Appendix 2.3*. Each panellist was also provided with a summary document that highlighted their individual score in relation to the median group score. A template of this document is provided as *Appendix 2.4*.

In round two, the panellists were asked to rank not only importance of the proposed indicator but also the feasibility of data collection. A summary of the importance and feasibility scores following round two are provided as *Appendix 2.5*. The full publication of this study is provided below.

2.1 Published Journal Article

Maharaj AD, Ioannou LJ, Croagh D, Zalcberg JR, Neale RE, Goldstein D, Merrett ND, Kench JG, White K, Pilgrim CHC, Chantrill L, Cosman P, Kneebone A, Lipton LR, Nikfarjam M, Philip J, Sandroussi C, Tagkalidis P, Chye R, Haghighi KS, Samra J, Evans SM. Monitoring quality of care for patients with pancreatic cancer: a modified Delphi consensus. HPB (Oxford) 2018; 21: 444-455. https://doi.org/10.1016/j.hpb.2018.08.016

ORIGINAL ARTICLE

Monitoring quality of care for patients with pancreatic cancer: a modified Delphi consensus

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Abstract

Background: Best practise care optimises survival and quality of life in patients with pancreatic cancer (PC), but there is evidence of variability in management and suboptimal care for some patients. Monitoring practise is necessary to underpin improvement initiatives. We aimed to develop a core set of quality indicators that measure quality of care across the disease trajectory.

Methods: A modified, three-round Delphi survey was performed among experts with wide experience in PC care across three states in Australia. A total of 107 potential quality indicators were identified from the literature and divided into five areas: diagnosis and staging, surgery, other treatment, patient management and outcomes. A further six indicators were added by the panel, increasing potential quality indicators to 113. Rated on a scale of 1–9, indicators with high median importance and feasibility (score 7–9) and low disagreement (<1) were considered in the candidate set.

Results: From 113 potential quality indicators, 34 indicators met the inclusion criteria and 27 (7 diagnosis and staging, 5 surgical, 4 other treatment, 5 patient management, 6 outcome) were included in the final set.

Conclusions: The developed indicator set can be applied as a tool for internal quality improvement, comparative quality reporting, public reporting and research in PC care.

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Introduction

Pancreatic cancer (PC) has poor survival and quality of life (QoL) outcomes. Currently, it is the fourth leading cause of cancer death in Western society and recently overtook breast cancer to become the third leading cause of cancer death in the United States.[1] Approximately 3000 people are diagnosed in Australia each year with an overall five-year survival of 6–8%.[2] Despite a significant decline in mortality across almost all neoplasms over the past 15 years, the age-adjusted mortality rate from PC has largely remained unchanged.[3]

There is some evidence that clinical practise may not always be concordant with evidence-based guidelines in PC care. For

example, the literature has identified underutilisation of surgery in patients with localised disease,[4] surgery being abandoned in one out of four cases,[5] eligible patients not receiving chemotherapy or radiotherapy,[5] a high proportion of patients with positive surgical margins,[6] patients undergoing surgical resections at low volume or in regional centres with potential impact on outcomes,[7,8] variable quality of pathological reporting,[9] a low percentage of patients participating in clinical trials[10] or being discussed at a multidisciplinary meetings,[11] and inadequate palliative or supportive care.[12] A preconceived impression of poor outcomes can lead to a nihilistic approach to disease management, especially in the use of surgery as a treatment option in older patients.[13] Differences in complications and mortality may be due to disparity in the quality of care provided by individual providers and institutions. In Australia, people living in rural regions have been shown to receive less anti-cancer therapy than their city counterparts[8,14] and those living in areas with higher socio-economic status are more likely to access advanced medical care, which is associated with improved survival and improved QoL.[15]

To better understand the reasons behind the variability in quality of care, the Upper Gastrointestinal Cancer Registry (UGICR) was established in 2014 to capture information about patients with oesophagus, stomach, liver, biliary system and pancreas cancer. Clinical Quality Registries (CQR) such as the UGICR are recognised as important tools for monitoring quality of care, providing feedback to the relevant clinical community and wider stakeholder groups, benchmarking performance, describing patterns of treatment, reducing variation, and for conducting research. Studies that have evaluated the impact of CQRs as an intervention have found a positive correlation with healthcare outcomes[16] and that they provide excellent return on investment.[17] The aims of the PC module of the UGICR are to: (i) identify patterns of care to inform policy development, with a particular focus on gaps in care; (ii) improve compliance with best practise guidelines through the feedback of benchmark reports and targeted quality improvement activities; (iii) provide a tool for future clinical, health service and biomedical research to advance knowledge of best treatment protocols; (iv) interact with and provide confidence to the public that there is a robust quality improvement system to optimize management of PC.

Quality indicators provide a quantitative basis for assessing aspects of the structure, process, or outcomes of healthcare. They can be evidence based, derived from academic literature or, where scientific evidence is lacking, determined by an expert panel of health professionals in a consensus process.[18] A modified Delphi approach,[19] which blends both scientific rigour and the consensus process, was used to identify important and measurable indicators across all areas of PC care: diagnosis and staging, surgery, other treatment, patient management and outcomes.

The aim of this study was to develop a consensus set of PC quality indicators via a Delphi process that can be tested within the framework of the UGICR to provide regular audit and feedback reports to clinicians and hospitals, benchmarking their performance on evidence-based care indicators and health outcomes.

Methods

Participants

A three-round modified Delphi survey was performed among experts with experience in the care of PC. Eligible experts from a broad range of disciplines were identified through various sources from New South Wales (NSW), Victoria and Queensland, and received an electronic invitation to be involved in the study. Commitment to contribute to all rounds was requested when agreeing to participate in this process. The majority of the experts were identified from NSW and Victoria as the registry was initially being piloted in these states.

Ethics

This study was approved by the Monash University Human Research Ethics Committee (MUHREC #9943).

Selection of quality indicators

A quality indicator is a measure of clinical management and/or outcome of care which screens or draws attention to a specific clinical issue, resulting in identification of variations in care.[18] To determine a preliminary list of indicators, an extensive literature review was undertaken using Medline, Embase and Cochrane databases. A total of 1081 articles published between January 2005 and February 2017 were identified, with an additional 12 articles identified from other sources (Fig. 1). Following title and abstract screening of studies that investigated factors affecting quality of care in patients with PC and reviewing domestic and international guidelines, 26 full text articles and guidelines were assessed for indicator development. Indicator selection was based on guideline recommendations and studies that had previously developed measures in pancreatic cancer. All indicators and indicator targets were proposed to the panel of experts to determine their importance. Eight guidelines[20–27] and 10 articles[15,28–36] were used and an additional article[37] was added for round three of this study based on panel recommendation. Members of the study team (AM, LI) grouped the quality indicators into five categories: diagnosis and staging; surgery; other treatment; patient management (focus on communication and supportive measures e.g. multidisciplinary team meetings, palliative care support); and outcomes.

Delphi consensus rounds

A modified Delphi approach consisting of three rounds was undertaken (Fig. 2). Surveys were designed online for rounds 1 and 3 using secure online survey software. Non-responders received up to two reminders prior to the date of closure.

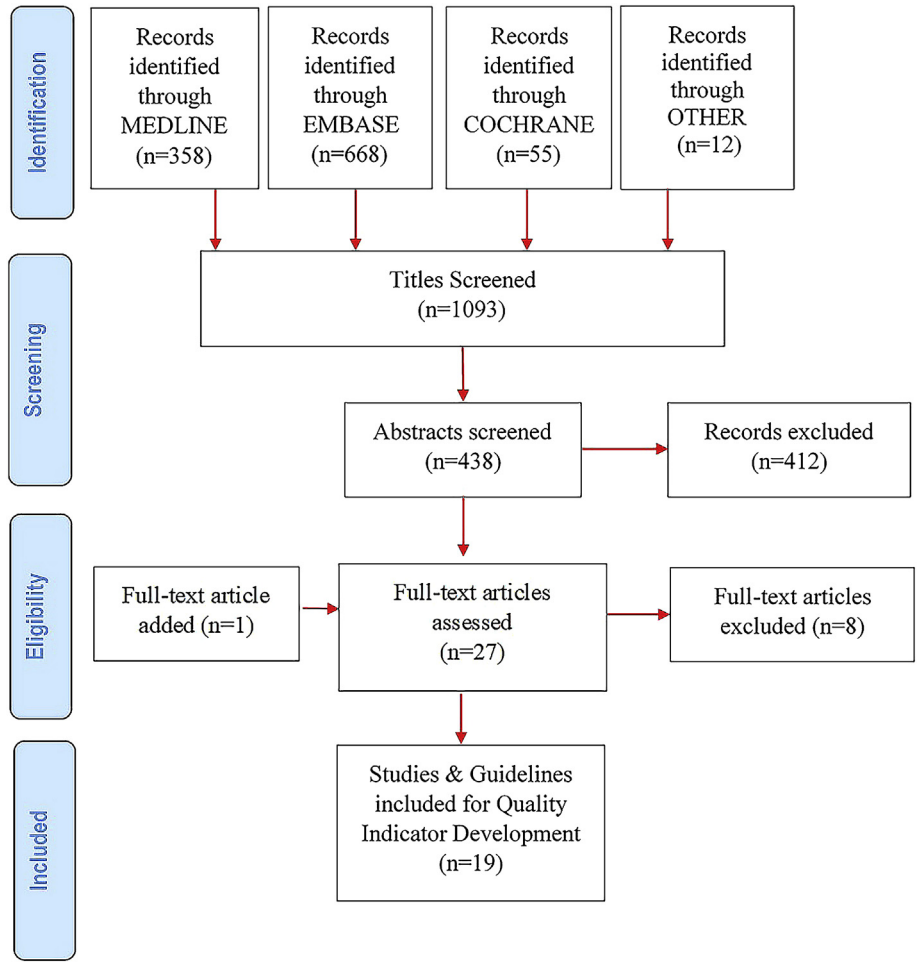

Figure 1 Prisma Flow Diagram. Ref: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7)

In the first round, 19 experts were presented with a list of 107 quality indicators, accompanied by a supplementary document that included indicator source, grade of evidence and measurement construct (numerator and denominator). Experts were asked to use a scale ranging from 1 (not important) to 9 (very important) to rank the *importance* of including the proposed indicator in the PC module of the UGICR. When making this decision, experts were asked to consider the literature from where the indicator was taken and its grade of evidence or recommendation.[38] Experts were also asked to compare similar indicators, grouped by the same indicator reference number, take their differences into consideration and to score the preferred indicator with a significantly higher rating. There was also the option of 'unable to comment' if they felt that they had inadequate knowledge or experience to rate a proposed indicator.

Prior to the second round, the results were analysed from the first round using Excel 2013 to calculate the median importance (MI) ranging from 1 to 9 and disagreement index (DI). The DI is a continuous scale that measures the variation in expert ratings. Based on the RAND method,[39] a DI of 0 represents complete agreement whereas DI $\geq$ 1 indicates significant disagreement or lack of consensus. An 'unable to comment' response was excluded from the calculations. Indicators with a median value of $\geq$7 and a DI < 1 progress to a set of candidate indicators. These results were sent to the Delphi panel.

The second round consisted of a full day face-to-face meeting in Sydney, NSW. Real-time scoring via a personalised online form, took place following thorough discussion about each of the 107 indicators, regardless of whether they were rated as important or not in the first round. Panel members were required to rate both *importance* and *feasibility* using the earlier scale (from 1 to 9). The expert panel was able to refine the wording of indicators and to propose new indicators, supported by evidence, that were felt to be important for quality care in PC.

Following analysis of round two results to calculate MI, median feasibility (MF) and DI, four indicators deemed to be important by the panellists had disagreement on feasibility. Two more indicators were proposed for inclusion as these indicators

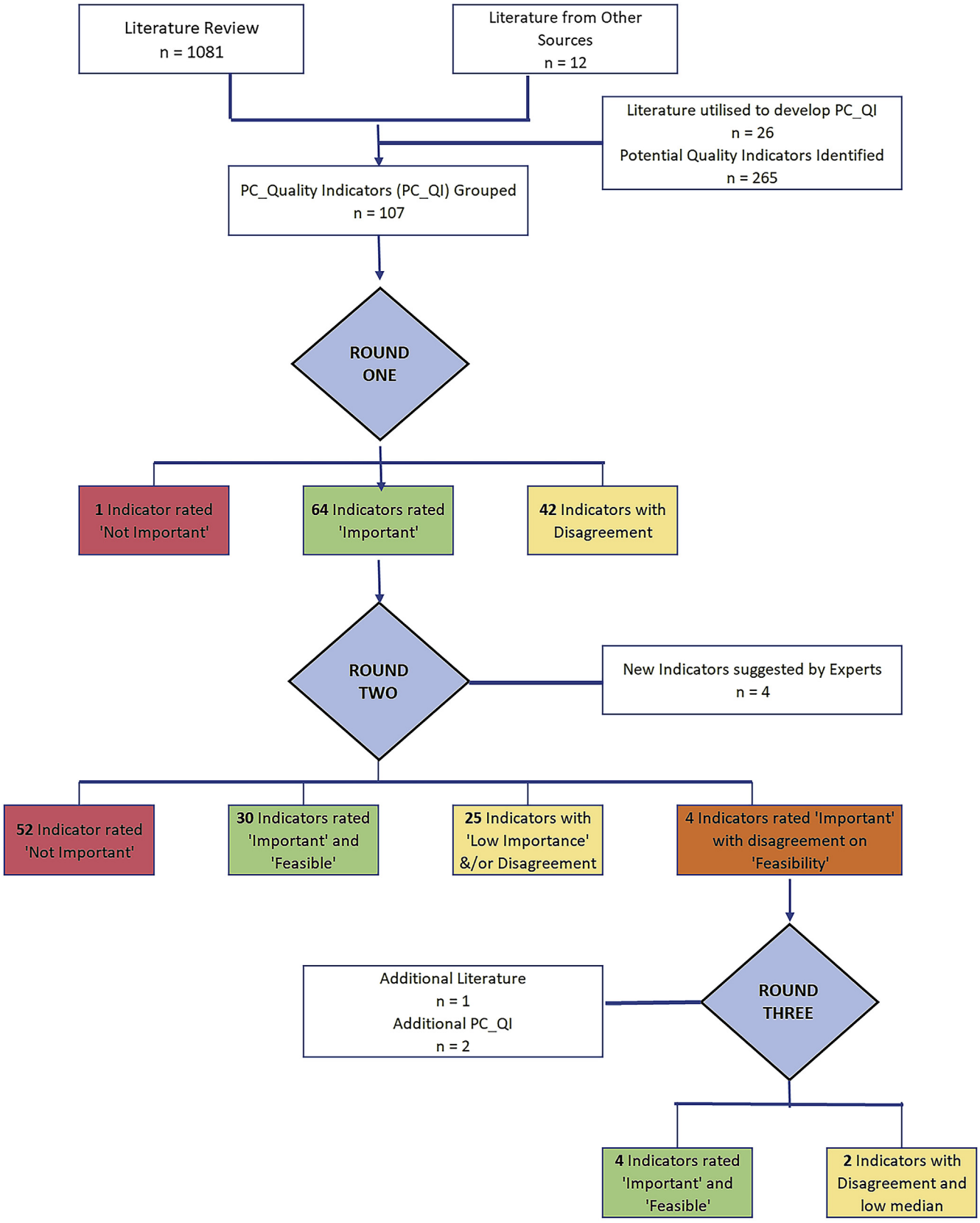

Figure 2 Quality Indicator Development Flow Diagram: An overview of the modified Delphi process for development of quality indicators in PC

formed part of a suite of end of life (EoL) indicators. These six indicators went to a third round via a short online survey using the same criteria as round one.

Selection of final indicator set

To ensure capture of the most important indicators while minimizing the burden of data collection thresholds for MI and MF were set. Only indicators at or above both thresholds were proposed to the panel for inclusion in the final set.

Results

Of the 22 experts invited to participate in this study, 19 (five female) agreed to undertake the first online survey (round one). Eleven were from NSW, seven from Victoria and one from Queensland. These had a minimum of 17 years practise and comprised eight surgeons, four medical oncologists, two palliative care specialists, one pathologist, one gastroenterologist, one radiation oncologist, one nurse specialist and one epidemiologist. Thirteen of the initial 19 were available to meet for the face-to-face expert panel meeting (round two) and all of whom completed the online survey for round three (final).

Round 1: online survey

The literature review identified 265 possible indicators (40 diagnosis & staging, 51 surgery, 61 treatment, 88 management, 17 outcome indicators and 8 others). Of these, 149 indicators were amalgamated within the proposed indicators as they were clearly alike and nine were excluded as they related to screening for disease. Of the 107 potential indicators (Supplementary document) presented to panel experts in round one, one indicator (0.9%) was rated unimportant, 64 (59.8%) as very important (MI $\geq$ 7) and there were 42 (39.2%) indicators with disagreement (DI $\geq$ 1) on importance.

Round 2: face-to-face meeting

The expert panel meeting was conducted in one session over seven hours with 13 members participating. Round two voting was undertaken, following in-depth discussion of indicators within each area of care. The number of indicators with

Table 1 Results and full indicator list considered in each round

		Rd 1	Round 2		Round 3	
		IMPT	IMPT	FEAS	IMPT	FEAS
DIAGNOSIS AND STAGING (n = 35)	Documented Eastern Cooperative Oncology Group (ECOG) and/or American Society of Anesthesiologists (ASA) performance status at presentation	7	9	8		
	Documented pancreatic protocol computed tomography (CT) or magnetic resonance imaging (MRI) scan for diagnosis and/or staging	8	9	9		
	Documented baseline carbohydrate antigen (CA)19-9 level before treatment	8	9	9		
	Endoscopic ultrasound (EUS) services available on site where pancreatic cancer (PC) surgery performed	7	8	8		
	Operability of tumour is clearly defined and documented as either operable/resectable, borderline resectable, locally advanced (unresectable) or metastatic (unresectable)	9	9	8		
	Time from referral to definitive treatment within 60 days (relief of biliary obstruction is not definitive treatment)	9	9	8		
	Tissue biopsy attempted prior to chemotherapy or radiotherapy	7	9	9		
	MRI, CT or positron emission tomography (PET) completed following neo-adjuvant treatment	8	9	8		8
	Documented referral to genetic counsellor for patients with Ashkenazi Jewish ancestry	6	6	6		
	Documented pre-operative risk assessment	6	5	6.5		
	Documented CA19-9 level assessing treatment response	8	4	3		
	Documented pancreatic protocol CT for diagnosis or staging	8	3.5	9		
	Documented multiphase CT of chest, abdomen and pelvis	7	2	9		
	Tissue biopsy confirming advanced, unresectable disease prior to palliative therapy	8	3	8		
	In patients with jaundice, documented results of liver function tests (LFTs), abdominal ultrasound (US) ± CT is present	8	2	8		
	Staging completed and documented within one week of presentation	7	1	5		
	Documented CT of chest, abdomen and pelvis; or PET scan	6	3	9		
	EUS ± biopsy of the tumour confirming diagnosis and/or staging of PC	6	2	8		
	Documented history & physical examination	6	2	7		
	Documented history & physical examination with pre-operative risk assessment	7	2	4		
	Documented comorbidity profile prior to surgery or treatment	6	3	4		
	Documented referral to genetic counsellor for young patients	5	2	4		
	In patients with jaundice, documented results of LFTs and abdominal US is present	7	2	8		
	EUS confirming PC	6	2	8		
	EUS ± fine needle aspiration (FNA) confirming disease in patients with clinical suspicion of PC	6	2	7.5		
	EUS ± biopsy or contrast enhanced MRI confirming PC	6	1	8		
	EUS ± biopsy or magnetic resonance cholangiopancreatography (MRCP) confirming PC	5	1.5	8		
	Staging completed and documented following high quality dedicated imaging at presentation	6	2	5		
	Staging completed and documented within four weeks of surgery	6	1	6		
	Documented tumour, node, metastasis (TNM) clinical stage in patients who do not undergo surgical resection	7	2	5		
	Documented physical status, geriatric assessment if elderly, comorbidities and performance status prior to surgery or treatment	8	2	2		
	In patients with resectable disease, stage, patent superior mesenteric vein (SMV), portal vein and definable tissue plane between the tumour and regional structures documented	8	2.5	2		
	Documented geriatric assessment prior to surgery or treatment	5	1	3		
	Documented referral to genetic counsellor for patients with a family history of cancer	6	2	3		
	Documented CA19-9 level in patients presenting with ongoing epigastric or back pain	5	1	2		
SURGERY (n = 16)	All patients who did not undergo surgery should have a valid reason documented	8	9	8		
	Number of patients undergoing pancreatic cancer surgery in a level 1-4 hospital (check private hospital)	8	9	9		
	Number of R1 resections (positive < 1mm margin) for those that have a synoptic report. Number of R1 resections for those that do not have a synoptic report	9	9	9		
	Royal College of Pathologists Australasia (RCPA) or equivalent synoptic reporting used to document findings for patients undergoing surgical resection	9	9	9		
	Standard lymphadenectomy with the removal of ≥ 10 lymph nodes pathologically examined and documented	7	9	9		
	All patients defined operable with adequate performance status offered surgery or a valid reason documented for not undergoing surgery	9	2	7		
	Patients with stage IV disease who underwent surgical resection	7	1	7		
	Standard lymphadenectomy with the removal of ≥ 15 lymph nodes pathologically staged and documented	8	2	8		
	Surgery is undertaken by surgeons who perform ≥ 5 resections per year	8	1	4.5		
	Surgery performed at a high volume institution with an annual case load of ≥ 12 resections per year	7	2	8		
	Time from diagnosis to surgery or first treatment less than 2 months	8	1	7		
	Patients potentially resectable do not have a tissue biopsy prior to surgery	5.5	1	5		
	Suspicious adenopathy evaluated by frozen section	5	1	6		
	Surgery performed at a high volume institution with an annual case load of ≥ 15 resections per year	6	2	8		
	Time from final multidisciplinary team (MDT) meeting to surgery is 3 weeks	7	2	8		
	Coeliac plexus block discussed and documented prior to surgical procedure	5	1	2		

		Rd 1	Round 2		Round 3	
		IMPT	IMPT	FEAS	IMPT	FEAS
OTHER TREATMENT (n = 15)	Adjuvant chemotherapy administered following surgery or a reason documented for not undergoing treatment	9	9	9		
	Neo-adjuvant chemotherapy ± chemo-radiation (CRT) administered to patients with borderline resectable disease, or a valid reason documented for not undergoing treatment	8	9	8		
	All patients should see a medical or radiation oncologist or a reason documented for not doing so	8	9	8		
	* Chemotherapy ± CRT administered to patients with locally advanced disease, or a reason documented for not undergoing treatment		9	9		
	Adjuvant chemotherapy administered following surgery with minimum Gemcitabine or 5-Flurouracil, or a valid reason documented for not undergoing treatment	7.5	1	8		
	Patients with metastatic disease and good performance status offered chemotherapy with Folfirinox or Gemcitabine ± Nab-paclitaxel, or a valid reason documented	7.5	1	5		
	CRT offered to patients with microscopically positive (R1) resection, or valid reason documented for not receiving CRT	6	2	7.5		
	Patients with locally advanced PC (LAPC) and poor performance status offered chemotherapy with Gemcitabine as a minimum, or a valid reason documented for not doing so	6	1	5		
	Patients with metastatic disease and poor performance status offered chemotherapy with Gemcitabine as a minimum, or a valid reason documented for not doing so	6.5	1	5		
	Patients with LAPC offered CRT or stereotactic body radiation therapy (SBRT), or a valid reason documented for not doing so	4.5	1	5		
	Patients with LAPC offered CRT or SBRT following initial chemotherapy, or a valid reason documented for not doing so	5	1	5		
	Surgery and chemotherapy or CRT (neo-adjuvant or adjuvant) provided to all patients with Stage I – III disease	6	2	7.5		
	Surgery and chemotherapy or CRT (neo-adjuvant or adjuvant) provided to all patients with Stage I disease	5	1	6		
	Surgery and chemotherapy or CRT (neo-adjuvant or adjuvant) provided to all patients with Stage II disease	6	1	5.5		
	Surgery and chemotherapy or CRT (neo-adjuvant or adjuvant) provided to all patients with Stage III disease	5	1	7		
PATIENT MANAGEMENT (n = 29)	All patients with metastatic disease referred to (or seen by) palliative care specialist	9	9	8		
	All patients having completed treatment followed up by specialist every three to six months for up to 2 years	7	9	8		
	Disease management for all patients discussed at a MDT meeting	9	9	9		
	All patients with biliary obstruction managed surgically or by stent	7	9	8		
	Number of patients who undergo biliary stenting that receive a self-expandable metallic stent (SEMs)	8	8	8		
	All patients seen by a dietician	6	8	8		
	Number of patients included in a clinical trial	8	9	6		8
	Patients with potentially resectable disease referred to a Hepatopancreatobiliary (HPB) surgeon	9	9	2		
	Patients with LAPC having completed treatment followed up every three to four months	7	1	5		
	Resectability discussed at a MDT	9	2	8		
	All patients with a documented treatment or clinical plan	8	2	3		
	All patients with a documented treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems	7	2	2		
	All patients with a HPB surgeon as the primary specialist in non-metastatic pancreatic cancer	7	3	2.5		
	All patients offered psychosocial support following diagnosis	8	2	2		
	Baseline performance status, symptom burden and comorbidity profile evaluated and documented for all patients	8	2	2		
	Cachexia, anorexia and weight loss managed with nutritional supplements and appetite stimulants	7	1	3		
	Pain managed with opioid analgesics, palliative radiation or nerve blocks or reason for not treating pain documented	8.5	2	2		
	Patients with borderline resectable disease included in a clinical trial, or a valid reason documented for not being included	8	2	2		
	Patients with LAPC included in a clinical trial, or a valid reason documented for not being included	7	1	2		
	Patients with resectable disease not stented prior to surgery or reason for stenting documented	7	1	2.5		
	Treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems documented and discussed with patients & caregivers	8	2	2		
	All patients assigned a care coordinator	7	6	2		
	All patients referred to palliative care services following diagnosis	5	2	8		
	All patients treated with pancreatic enzyme replacement therapy	6	1	5		
	Patients with locally advanced disease referred to palliative care services following diagnosis	8	2	8		
	Patients with metastatic disease on active cancer-directed therapy followed up every 2 – 3 months	8	1	4.5		
	Baseline symptom burden evaluated and documented for all patients	6	1	2		
	Biliary or gastric outlet obstruction managed surgically in patients with good performance status	6	2	3		
	SEM used for biliary drainage prior to surgery	6	1	4		

		Rd 1	Round 2		Round 3	
		IMPT	IMPT	FEAS	IMPT	FEAS
OUTCOME (n = 18)	30-day and 90-day mortality rate following surgical resection (level of risk adjustment to be determined	8	9	8		
	2 year and 5 year survival rates for patients who underwent a surgical resection	8	9	8.5		
	Institution monitors their 30 day readmission rate following a surgical resection	7	8	8		
	Number of patients requiring a re-operation following surgical resection	8	9	9		
	Patients requiring radiological or endoscopic intervention following surgical resection	6	8	8		
	* Number of patient that died within 30-days of last dose of chemotherapy		9	9		
	* Number of patients with >2 emergency department (ED) presentations in the last 30-days before death		9	9		
	* Number of patients with ≥14 days in acute hospital in the last 30 days before death		9	8.5		
	Number of patients receiving transfusion during admission	6	8	7.5		7
	Patients who developed pancreatic fistula following surgical resection	8	8.5	6.5		8
	Institution monitors their margin-negative resection rate	7.5	1	6		
	Patients who developed a pulmonary embolism following surgical resection	7	1.5	4.5		
	Institution monitors their risk-adjusted perioperative mortality following surgical resection	8	2	2		
	Patients who developed a portal vein thrombosis following surgical resection	7	2	3		
	Institution monitors their median operative time for surgical resections	6	2	2.5		
	Patients who developed delayed gastric emptying following surgical resection	6	1.5	3		
	* Number of PC patient deaths in hospital				4.5	8
	* Number of intensive care unit (ICU) presentations in the last 30 days before death				6.5	8

FOOTNOTE:

* New Indicator, Rd = round, IMPT = importance, FEAS = feasibility

RATING
Median 7-9 with Agreement <1 = Green
Median 7-9 with Disagreement >1 = Yellow
Median 4-6 with Agreement <1 = Yellow
Median 4-6 with Disagreement >1 = Yellow
Median 1-3 with Agreement <1 = Red **(Round 1)**
Median 1-3 with disagreement >1 = Yellow **(Round 1)**
Median 1-3 with Agreement <1 or Disagreement >1 = Red **(Round 2)**

disagreement reduced from 42 to 25 (22.5%) in this round, many with low MI. At the conclusion of round two, 52 indicators (46.8%) were rated not important and 30 indicators (27%) were deemed very important (MI $\geq$ 7) and feasible (MF $\geq$ 7) with low disagreement (DI < 1). Of the 30 indicators rated important and feasible, 21 had the wording refined to reflect the systems in use in Australia or to phrase as a measurable indicator. A further four new indicators were introduced and rated by the experts at this meeting.

Round 3: Online Survey

Four indicators (3.6%) that were judged to be very important by the experts had disagreement on feasibility requiring an additional voting round (round three) for feasibility only.

Table 2 Final consensus pancreatic cancer quality indicators identified by Delphi process

INDICATORS		VALID (median value)	FEASIBLE (median value)	OVERALL RATING
Diagnosis & Staging				
1.3.2	Documented pancreatic protocol CT or MRI scan for diagnosis and/or staging	9	9	18
1.4.1a	Tissue biopsy attempted prior to chemotherapy or radiotherapy	9	9	18
1.5.1a	Documented baseline CA19-9 level before treatment	9	9	18
1.1.2c	Documented ECOG and/or ASA at presentation	9	8	17
1.6.1b	Time from referral to definitive treatment within 60 days (relief of biliary obstruction is not definitive treatment)	9	8	17
1.6.3	MRI, CT or PET completed following neoadjuvant treatment	9	8	17
1.6.4b	Operability of tumour is clearly defined and documented as either operable/resectable, borderline resectable, locally advanced (unresectable) or metastatic (unresectable)	9	8	17
1.4.6	EUS services available on site where PC surgery performed	8	8	16
Surgery				
2.1.7	Royal College of Pathologists Australasia (RCPA) or equivalent synoptic reporting used to document findings for patients undergoing surgical resection	9	9	18
2.2.1a	Standard lymphadenectomy with the removal of ≥ 10 lymph nodes pathologically examined and documented	9	9	18
2.3.1	Number of R1 resections (positive < 1mm margin) for those that have a synoptic report Number of R1 resections (positive < 1mm margin) for those that do not have a synoptic report	9	9	18
2.4.2	Number of patients undergoing pancreatic cancer surgery in a level 1-4 hospital	9	9	18
2.1.1a	All patients who did not undergo surgery should have a valid reason documented	9	8	17
Other Treatment				
3.2.1a	Adjuvant chemotherapy administered following surgery or a reason documented for not undergoing treatment	9	9	18
3.4.1	Chemotherapy ± chemo-radiation administered to patients with locally advanced disease, or a reason documented for not undergoing treatment	9	9	18
3.1.1	Neo-adjuvant chemotherapy ± chemo-radiation administered to patients with borderline resectable disease, or a valid reason documented for not undergoing treatment	9	8	17
3.3.1a	All patients should see a medical or radiation oncologist or a reason documented for not doing so	9	8	17

INDICATORS		VALID (median value)	FEASIBLE (median value)	OVERALL RATING
Patient Management				
4.5.1	Disease management for all patients discussed at a MDT meeting	9	9	18
4.6.1	All patients with biliary obstruction managed surgically or by stent	9	8	17
4.8.1	All patients with metastatic disease referred to (or seen by) palliative care specialist	9	8	17
4.9.1	All patients having completed treatment followed up specialist every three to six months for up to 2 years	9	8	17
4.2.1	Number of patients included in a clinical trial	9	8	17
4.3.1	All patients seen by a dietician	8	8	16
4.6.1	Number of patients who undergo biliary stenting that receive a SEMs (metal stent)	8	8	16
Outcome				
5.2.6	Number of patients requiring a re-operation following surgical resection	9	9	18
5.3.1	Number of patient that died within 30-days of last dose of chemotherapy	9	9	18
5.3.2	Number of patients with ≥2 ED presentations in the last 30-days before death	9	9	18
5.1.2	2 year and 5 year survival rates for patients who underwent a surgical resection	9	8.5	17.5
5.3.3	Number of patients with ≥14 days in acute hospital in the last 30 days before death	9	8.5	17.5
5.1.1	30-day and 90-day mortality rate following surgical resection	9	8	17
5.2.1	Patients who developed pancreatic fistula following surgical resection	8.5	8	16.5
5.1.6	Institution monitors their 30 day readmission rate following a surgical resection	8	8	16
5.2.2	Patients requiring radiological or endoscopic intervention following surgical resection	8	8	16
5.1.4	Number of patients receiving transfusion during admission	8	7	15

PC indicators excluded from final set

Furthermore, two indicators were added to round three to complete voting on a suite of EoL indicators, increasing the total potential indicators that underwent voting to 113.

Of the six indicators voted on in round three, all indicators requiring rating on feasibility gained agreement on feasibility (MF $\geq$ 7). The final two EoL additional indicators had significant disagreement and were not deemed highly important.

The results for each round are displayed in Table 1. A total of 34 indicators gained consensus with MI and MF $\geq$ 7, and DI < 1. An arbitrary cut point was used to decrease the number of indicators to a manageable set for the registry. Hence, 27 indicators (Table 2) with MI (=9) and MF (≥8) were proposed for inclusion into the UGICR.

Discussion

This study provides a core set of evidence-based indicators that measure the quality of care provided to patients with PC, with the ultimate aim of optimising QoL and survival. From 113 potential indicators, 27 are proposed for inclusion in the UGICR which will enable monitoring of quality for surgery and staging, assess the appropriateness of treatments, assess compliance with

guidelines, identify potential areas for improvement and provide feedback to participating sites.

In 1999, the Institute of Medicine (IOM) outlined the ideal state of cancer care and recommended that the first step was to establish the attributes of care linked to optimal outcomes followed by observations of current medical practise.[40] Following this, two exemplary bodies of work have developed measures to monitor quality of care in PC. Bilimoria and colleagues[30] identified 29 quality indicators as highly valid and 14 with moderate validity. Of the 29 highly valid indicators, 27 related to surgery and surgical outcomes, which do not fully reflect the PC population, as only 10–15% have resectable disease at diagnosis. More recently, the study by Burmeister and colleagues[29] developed care statements that included a broader range of management indicators. However, a number of indicators did not reach consensus, an opportunity was not provided for discussion, and the study did not address the feasibility of collecting information routinely. The core set of indicators developed in this study measure all areas of the disease trajectory for PC (*seven* diagnosis and staging, *five* surgical, *four* other treatment, *five* patient management and *six* outcome measures) and all are considered feasible to collect.

From the 113 proposed indicators, the panel rated 79 from low to moderate importance and/or feasibility. This was due to factors such as the difficulty or reliability of measurement, multiplicative nature of many indicators and the need for breadth of quality indicators across the care continuum. For example, in the case of lymphadenectomy, two indicators were proposed with the removal of either $\geq$10 or 15 lymph nodes. The panellists were required to make a judgement between these similar indicators and choose the most appropriate one that corresponds to good care. Proposed indicators such as 'time from final MDT meeting to surgery within 3 weeks' or 'documented CA19-9 level in patients presenting with ongoing epigastric or back pain' did not meet the feasibility criteria. Indicators such as 'patients assigned a care coordinator' lacked agreement on importance and upon discussion were considered infeasible to collect.

The provision for discussion in round two was useful in determining definitions, importance and feasibility of an indicator, a recognised advantage of a modified Delphi over other consensus processes. While the panel acknowledged the importance of indicators that measured the documentation of comorbidity profile and geriatric assessment, further discussion questioned the reliability of data and the burden of data collection. The Charlson Comorbidity Index (CCI) is only modestly predictive of survival.[41] This may be governed by its reliance on administrative data to capture the data items needed that can result in misclassification of the score.[42] Performance status at diagnosis as measured by Eastern Cooperative Oncology Group (ECOG) or American Society of Anesthesiologists (ASA) score was deemed a surrogate measure for capturing comorbidity profile[43] and rated highly by the panel. Additionally, timeliness of the diagnostic pathway (inclusive of referral and staging) to definitive treatment was discussed. While current evidence suggests that timeliness may not be a factor in survival outcomes for PC,[44] the panel felt that it was an important measure of patient-centred care as delay in treatment can cause psychological distress to patients and their families.[45]

Adequate staging of PC can be difficult and is often dependent on detailed pathological analysis. The usefulness of the Tumor/Node/Metastases (TNM) staging algorithm developed by the American joint committee on cancer (AJCC) was discussed in context of the registry's ability to collect this from clinical notes. Currently, there is limited level 1 evidence that supports the AJCC staging system in hepatobiliary cancers[46] and it was also recognised that collection of pathological stage in PC requires that the patient has undergone surgery. The panel agreed that the best definition is the documentation of the operability of the tumour in terms of resectable, borderline resectable, locally advanced or metastatic[47] which can be determined by clinical staging obtained by a pancreatic protocol CT or MRI scan and is supported by grade A evidence (Appendix, Supplementary document).

Recently, neo-adjuvant therapy has gained momentum as standard care for many gastrointestinal cancers such as oesophageal and gastric cancers. Two recent meta-analyses suggest that neo-adjuvant therapy has benefit in patients with borderline PC,[48,49] albeit based on small studies with lack of control groups. Both studies demonstrated a median survival in patients with borderline resectable disease that was comparable to patients with localised resectable disease. In the context of the registry, capture of neo-adjuvant therapy data will further provide a body of evidence on its contribution to survival outcome and was supported by the expert panel.

The addition of end-of-life quality indicators for rating in rounds two and three reflected the aggressive nature of PC and often the short timeframe from diagnosis to death. Indicators developed by Earle and colleagues[37] are widely accepted, with a number of studies using these measures for benchmarking and improvement.[50] The experts supported the majority of EoL indicators. The panel discussed the indicator relating to ICU presentation within 30 days of death but did not reach consensus that there was adequate evidence of its association with poor quality of care.

Arbitrary cut points for importance and feasibility were made to enable inclusion of the indicators with the highest importance and feasibility. As the registry pilots these indicators, it may be that for some indicators a ceiling effect is identified (i.e. that poor care is not identified across sites and clinicians). In this instance, they will be removed and replaced with lower scoring indicators. This will evolve over the next three years as the registry reaches maturity.

Limitations in this study include lack of grade A evidence for the majority of proposed indicators, purposive sampling to

identify panel experts, attrition bias due to the reduction in the number of experts from 19 to 13 in round two, and the difficulty in measuring crucial patient-centred indicators. Given the nature of PC, it would be difficult to ascertain grade A evidence across the full spectrum of care. Of the 107 initially proposed indicators, 10 were supported by grade A evidence. Seven of those indicators with grade A evidence were not endorsed by the panel, five because there were considered too narrow in their scope and two because they were considered difficult to collect.

Purposive sampling was used to identify panel members who had an excellent contemporary understanding of the literature; their opinions may not be representative of all clinicians treating patients with PC. To ensure some representativeness, the panel comprised clinicians working in metropolitan and regional hospitals across states and was inclusive of all speciality groups managing patients with PC. We did not include consumers as this study purposely focused on details of surgical, non-surgical management and treatment regimens. It is widely recommended that patients be involved in determining what good care looks like.[51] Future research is required to develop patient-centred indicators in PC. Proposed patient-centred indicators relating to pain control, psychosocial support, symptom burden and development of treatment plans failed the feasibility test due to the registry's inability to capture this data objectively. Judged as an important set of measures, the panel agreed that patient-reported outcome measures (PROMs) is a more feasible approach to capture patient-centred care and collection of PROMS is planned as part of the registry.

Strengths of this study include the use of an in-depth literature review using the most recent published guidelines and studies, inclusion of experts from different disciplines and regions, and a face-to-face meeting to enable robust discussion.

The 27 indicators developed to measure care in PC will provide clinicians and organisations the foundations to compare their practise with best practise standards. In the near future, extraction of data and feedback of findings based on these indicators will facilitate a change in practise and will contribute to the efforts to improve outcomes and prognosis for patients with PC.

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Contributors

AM, LI, JZ and SME designed the study. AM collated the data. AM, LI analysed and interpreted the data. All authors (except AM, LI and SME) participated in the Delphi survey in varying rounds. AM prepared the manuscript. Feedback was received from RE, DG, NM, JK, DC and JP. All authors reviewed the manuscript and gave final approval for submission of the final manuscript.

Conflicts of interest

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hpb.2018.08.016.

2.2 Chapter Summary

A core set of QIs to monitor quality of care was established after review of evidence-based guidelines and manuscripts describing QIs used to assess quality of PC care. Using a modified Delphi approach based on the RAND/UCLA Appropriateness method, a set of QIs was presented to a panel of clinical experts in the field of PC. Data was analysed in accordance with the RAND methodology using algorithms to assess importance and disagreement among panellists.[63]

A total of 113 potential QIs were identified from the literature and informed by the panel. The areas of care were defined into the following: diagnosis and staging, surgery, other treatment, patient management (focus on communication and supportive measures e.g. multidisciplinary team meetings, palliative care support) and outcomes. From the potential QIs, 27 were recommended for inclusion as the final set within the UGICR. *Appendix 2.6* outlines the data items and definitions related to the developed QIs. The QIs will be reviewed regularly following periodic evaluation to ensure that only the most relevant QIs are captured (i.e. retirement of QIs that reach a ceiling effect) and development of new QIs that are aligned with current best practice. Further, *Figure 2.1* shows that the final indicator set measures across the majority of the dimensions and components of healthcare quality. Structural indicators assessing the dimensions of patient-centeredness and equitability are lacking as is outcome indicators for equitability. These are best captured using PROMs and will be further discussed in chapter 6.

	Dimensions of Quality					
Components in Healthcare	**SAFE**	**EFFECTIVE**	**TIMELY**	**EFFICIENT**	**PATIENT-CENTERED**	**EQUITABLE**
STRUCTURE	✓	✓✓	✓	✓✓		
PROCESS	✓✓✓✓	✓✓✓✓✓✓ ✓✓✓✓✓✓ ✓✓✓✓✓	✓	✓✓✓	✓✓	✓✓
OUTCOME	✓✓✓✓	✓✓✓✓	✓	✓✓✓	✓✓	

Figure 2. 1: *Core indicator set in relation to the dimensions and components of healthcare quality*

"Systems awareness and systems design are important for health professionals, but they are not enough. They are enabling mechanisms only. It is the ethical dimensions of individuals that are essential to a system's success.

Ultimately, the secret of quality is love. You have to love your patient, you have to love your profession, you have to love your God. If you have love, you can then work backward to monitor and improve the system."

Prof Avedis Donabedian

Chapter 3: The Association Between Quality Care and Outcomes

Chapter 2 described the development of a core set of quality indicators (QIs) to enable the care of patients with PC to be monitored and ultimately improved. This Chapter addresses the second aim of this thesis which incorporate objectives 3 and 4: (1) to assesses compliance with the consensus set of QIs; and (2) evaluate the association between compliance with QIs and survival.

Ethics approval was gained from Monash University HREC (*Appendix 3.1*). Data were collected by the UGICR for patients diagnosed between 1 January 2016 and 31 December 2018. Twenty-two QIs were assessed for compliance. To achieve this, the numerator and denominator for each QI was formatted, taking into consideration inclusion and exclusion criteria. Calculations were then developed into STATA language using the relevant data items. The formatting of the QIs and the calculations are attached as *Appendix 3.2*.

Following the assessment of compliance, associations between 18 process QIs (excluding outcome-based QIs) and patient and health service characteristics were tested using linear regression, and survival analysed using Cox proportional hazard models.

The full study is provided in the following pages which include the background, full methods, results and discussion, followed by a chapter summary.

3.1 Background

The five-year relative survival for patients diagnosed with pancreatic ductal adenocarcinoma cancer (PDAC) in Australia has improved from 3.3% three decades ago to 9.8% reported in 2019.[64] However, PDAC continues to be a low survival cancer; while it represents approximately 2% of all cancer diagnoses, it was the fifth most common cause of cancer death in 2018.[64] In the State of Victoria with a population of 6.4 million people, 887 new cases of PDAC were diagnosed and 755 people died in 2018.[65]

A critical component of optimal care is accurately determining the patients with the potential to be cured. This requires identifying patients suitable for surgical resection, with subsequent consideration of adjuvant post-operative chemotherapy. Further, there is accumulating evidence that the addition of neo-adjuvant therapy may be associated with improved outcomes in resectable patients, as well as a reduction in the rate of positive resection margins in patients diagnosed with borderline resectable disease.[49,66]

In patients with unresectable disease and reasonable performance status, systemic chemotherapy has also shown a clear survival benefit.[67] In advanced disease, the early involvement of palliative care by clinicians trained in end of life management ensures best possible quality of life.[68] A recent study that analysed the treatment patterns and outcomes in PDAC from 2011-2015 in Victoria (n=3962) showed that 67% of patients had metastatic disease at diagnosis with 45% receiving some form of cancer-directed treatment such as chemo- and/or radiotherapy and 69% receiving palliative care. One-year overall survival in the metastatic group was 15%. Of the patients with non-metastatic disease, 1.5% were treated with neo-adjuvant therapy, and 31% underwent surgical resection of which 77% proceeded to adjuvant therapy. One-year overall survival in the non-metastatic group was 60%.[69]

The above findings were derived from administrative data and do not provide clinical insights into practices that may have influenced patient outcomes. Hence, we used findings from a clinical quality registry to understand quality of care at a population level. To monitor quality of care in patients diagnosed with PDAC, a core set of 27 quality indicators was developed using a modified, three-round Delphi study.[57] The plan was to monitor the care of patients captured in the Upper Gastrointestinal Cancer Registry (UGICR) using the 27 QIs and to benchmark institutions against these indicators. The UGICR is a clinical quality registry established in 2015 to prospectively capture whole of population, real-world data to monitor care for patients diagnosed with upper gastrointestinal cancers in Australia.[56] In other jurisdictions, this type of registry would be described as a prospective, observational cohort study of a population-based cohort with PDAC, This study aimed to: (1) assess compliance with the agreed set of QIs that reflect best practice for patients diagnosed with PDAC in Victoria using data collected by the UGICR over a three year period (from 2016 – 2018); and (2) assess the association between compliance with these QIs and survival. We hypothesised that high quality care would result in improved outcomes for patients diagnosed with PDAC.

3.2 Methods

The UGICR collects patient information on the diagnosis and staging, treatment and management of patients diagnosed with upper gastrointestinal cancers. Details of the registry's approval by a human research ethics Committee, governance, and operations have been previously published.[56] Based on data from the Victorian Cancer Registry (VCR; a registry that primarily captures incidence and mortality on every patient diagnosed with cancer in the State of Victoria), 32% (n=871/2699) of Victorian PC patients diagnosed from 2016 to 2018 have been included in this analysis.

3.2.1 Population

Patients with PDAC are mandatorily notified to the VCR by hospitals and pathology providers. Referring hospitals authorise the VCR to provide patient details to the UGICR to enable patient recruitment. To be eligible for data collection through the UGICR and for this analysis, patients must have been newly diagnosed with adenocarcinoma of the pancreas or of the periampullary region (ampulla of Vater or distal bile duct) between 1 January 2016 and 31 December 2018, aged 18 years or older, and have been diagnosed or managed at a participating hospital. In this study we further compared the demographic information of patients included and not included in the UGICR with data provided by VCR.

3.2.2 Recruitment into the UGICR

The UGICR used an opt-out approach to recruitment with a waiver of consent applied to enable capture of data on deceased patients. An invitation letter and participant information booklet about the registry was mailed to eligible patients with a two week opt-out period.[67]

3.2.3 Data collection

To supplement demographic data provided by the VCR, trained data collectors captured information about patients' diagnosis (including pathology) and disease management (surgery, radiotherapy, chemotherapy, palliative care) from electronic and/or hardcopy medical records from participating hospitals; data are entered into the registry's secure REDCap platform.[70] The VCR captures information about deaths through linkage with the Victorian Registry of Births Deaths and Marriages and the National Death Index; this is transmitted periodically to the UGICR.

3.2.4 Patient and hospital characteristics

Patient factors evaluated included age, sex, performance status as measured by the Eastern Cooperative Oncology Group (ECOG),[71] resectability of tumour at diagnosis, site of tumour, and socio-economic status (SES) grouped into quintiles using the Australian Socio-Economic Indexes for Areas (SEIFA), 2016.[72] Hospital characteristics evaluated included the geographical region of the diagnosing hospital within Victoria (regional/metropolitan), the hospital type (public/private), hospital capacity based on the number of beds (100-199, 200-500, >500), annual hospital PDAC case volume (<10, 10-29, >30), and the annual PDAC surgical volume (<5, 6-10, 11-15).

3.2.5 Compliance with quality indicators

Variables necessary to determine compliance with the core set of quality indicators were formatted and calculations for each indicator developed. Compliance was calculated on the number of patients who met the indicator (numerator) divided by the number of patients eligible for the procedure, treatment or disease management (denominator).

3.2.6 Statistical analysis

Patient and hospital characteristics, patterns of treatment, and proportions of eligible patients (with 95% confidence intervals) who met each indicator were calculated and reported as descriptive statistics. The difference between the registry population and those not captured by the registry according to their age group, sex and SES were assessed using Fishers exact and Chi-square (χ^2) tests.

We used univariable and multivariable Cox proportional hazards models to estimate hazard ratios for the association between risk of death and patient characteristics, hospital characteristics and quality indicators. In the multivariable analysis, compliance with quality indicators was adjusted for significant confounders from the univariable model. Survival time was calculated from the date of diagnosis recorded in the VCR to the date of death from all

causes or the date at which death data was last extracted (September 2019). A separate category was created for observations with missing data. Sensitivity analysis was undertaken for relevant QIs to identify any potential differences in results between pancreatic and periampullary cancers by analysing these groups separately. All analyses were undertaken using STATA 15.0 (StataCorp). A two-sided P value of < 0.05 was considered statistically significant.

3.2.7 Ethical approval

This study was approved by the Monash University Human Research Ethics Committee (MUHREC #15325).

3.3 Results

The recruitment pathway is displayed in *Figure 3.1*. The UGICR provided data on 1278 patients. Of these, 373 (29.2%) were excluded because they were identified at a hospital where patients were treated but not necessarily diagnosed (treating hospital) and either the diagnosing hospital: (1) was not contributing to the registry; (2) did not provide sufficient information to the treating hospital to verify the diagnosis for the patient; or (3) the diagnosis details were in the process of being obtained. In addition, 30 patients (2.3%) did not have their tumour site clearly specified and 4 (0.3%) were defined loosely as located within the periampullary region rather than a defined tumour site. Our final data set included 871 (68.1%) patients. The registry dataset was compared with 585 non-registry participants. Patients included in the registry were more likely to be younger (*p-value <0.001*) and from a higher socioeconomic group *(p-value <0.001*) compared to patients with PDAC not included within the registry.

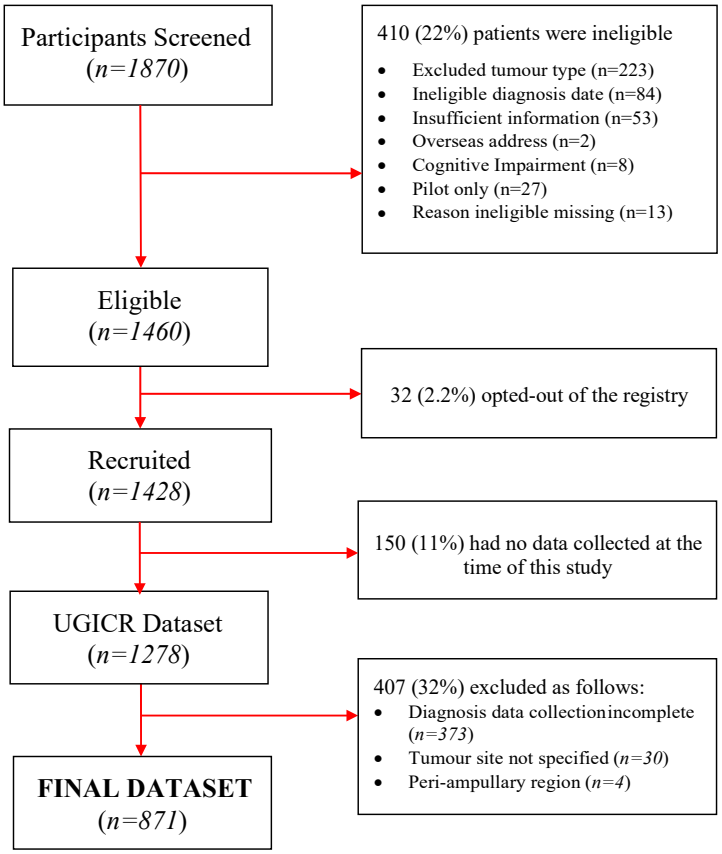


Figure 3.1: *Recruitment and final dataset*

3.3.1 Patient and hospital characteristics

The patient and hospital characteristics are summarised in *Table 3.1*. Approximately 73% of patients were over the age of 65 years at the time of diagnosis, with a median age of 72 years (range 42 – 95 years) and 53% were male. At diagnosis, 62% (n=538) of patients had locally advanced (15%) or metastatic (47%) disease, and 50% of tumours were located in the head of the pancreas. Around half (51%) of the patients lived in the top two quintiles for socioeconomic status (least disadvantaged). Analysis of the hospital characteristics showed that the majority (~90%) were diagnosed in a metropolitan area, in public hospitals (89%), and in a hospital with a capacity of at least 200 beds. However, 25% of patients with PDAC were diagnosed in a hospital with fewer than 10 cases annually, and 6% overall (27% of all patients undergoing surgical resection) had surgery for PDAC in a hospital with an annual surgical volume of fewer than five resections per year.

PATIENT CHARACTERISTICS		**n=871**	**(%)**
Age at diagnosis (years)	< 55	86	(9.9)
	55 – 64	140	(16.1)
	65 – 74	267	(30.7)
	75 – 84	253	(29.1)
	> 85	112	(12.9)
	Missing diagnosis date	13	(1.5)
Sex	Male	461	(52.9)
	Female	410	(47.1)
Eastern Cooperative Oncology Group (ECOG)	0	91	(10.5)
	1	123	(14.1)
	2	73	(8.4)
	3	56	(6.4)
	4	11	(1.3)
	Not clearly documented	517	(59.4)
Resectability at Diagnosis	Resectable	162	(18.6)
	Borderline resectable	70	(8.0)
	Locally advanced	132	(15.2)
	Metastatic	406	(46.6)
	Not clearly documented*	66	(7.6)
	Unknown#	35	(4.0)
Site of tumour	Head	422	(48.5)
	Neck	40	(4.6)
	Body	125	(14.4)
	Tail	117	(13.4)
	Uncinate process	70	(8.0)
	Ampulla of vater (Ampullary)	39	(4.5)
	Distal bile duct	25	(2.9)
	Pancreas (not otherwise specified)	33	(3.8)
Socio-economic Status (index for Australia 2016, *rank within state from most disadvantaged to least disadvantaged*)	Quintile 1	174	(19.9)
	Quintile 2	128	(14.7)
	Quintile 3	125	(14.4)
	Quintile 4	206	(23.7)
	Quintile 5	238	(27.3)
HOSPITAL CHARACTERISTICS (diagnosing hospital)		**n=871**	
Location	Metropolitan	795	(91.3)
	Regional	51	(5.9)
	Other**	16	(1.8)
	Unknown	9	(1.0)
Hospital Type	Public	772	(88.6)
	Private	74	(8.5)
	Other**	16	(1.8)
	Unknown	9	(1.0)
Hospital Capacity *(no. of beds)*	100 – 199	42	(4.8)
	200 – 500	188	(21.6)
	>500	616	(70.7)
	Other**	16	(1.8)
	Unknown	9	(1.0)

Annual Diagnosis Case Volume *(based on UGICR diagnosing hospital)*	< 10	215	(24.7)
	10 – 29	260	(29.9)
	> 30	331	(38.0)
	Case Volume Not Known	49	(5.6)
	Other**	16	(1.8)
Annual Surgical Volume *(based on UGICR treating hospital)*	< 5	56	(6.4)
	6 – 10	98	(11.2)
	11 – 15	35	(4.0)
	Surgical Volume Not Known	15	(1.7)
	No attempted surgery	667	(76.6)

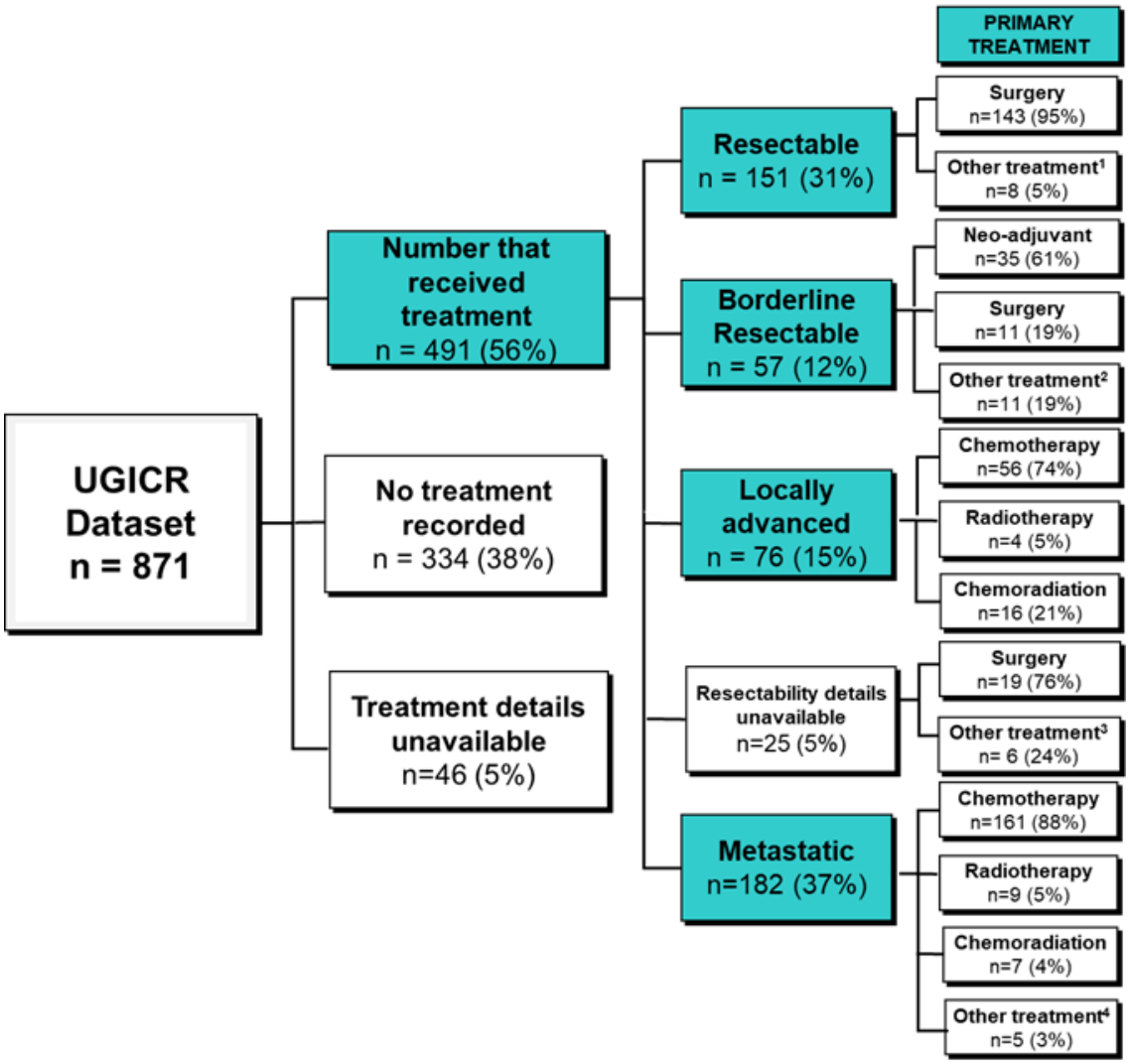
* Not clearly documented = where resectability is unclear in clinical records e.g. "not for surgery", # Unknown = where full diagnosis information is unable to be captured as patient may have records at non-participating sites, interstate or overseas, ** Other = radiation oncology centre only

Table 3.1: *Patient and Hospital Characteristics*

3.3.2 Patterns of treatment

Figure 3.2 outlines the patterns of treatment for patients diagnosed with PDAC. Fifty-six percent of patients received some form of cancer directed treatment (surgery, chemo and/or radiotherapy), 38% had no cancer directed treatment recorded and 5% had their treatment details missing. For those who received treatment, 31% were resectable, 12% were borderline resectable, 15% were locally advanced, 37% had metastatic disease, and in 5% resectability was not able to be determined. In addition, 37% (n=180/491) were less than 65 years, 37% (n=184/491) were between 65-74 years and 25% were over 75 years of age. In comparison, of those who had no treatment recorded, 5% were considered potentially resectable, 14% had locally advanced disease, 60% had metastatic disease at diagnosis (and in 20% stage was not able to be determined). Eleven percent (n=37/334) were less than 65 years, 21% (n=69/334) were between 65-74 years, but the majority (66%, n=221/334) were over the age of 75 years. Of those who underwent surgery, 82% (n=160/196) had a completed surgical resection. In the borderline resectable group, 49% (17/35) of patients who received neoadjuvant therapy went on to have surgery. Overall, 62% (n=98/160) of the cases reported a margin clearance ≥ 1mm (R0 resection) or a clear margin status but with no distance specified, 23% (n=36/160) had a margin clearance ≤ 1mm (R1 resection), 4% (n=7/160) had a R2 margin resection and 12%

(n=19/160) had their margin status missing. Of all patients who had a complete resection, 62% n=99/160) received adjuvant therapy.



Other treatment[1] = 4 diagnostic laparoscopy, 4 chemotherapy, Other treatment[2] = 9 chemotherapy with other intent, 2 radiotherapy, Other treatment[3] = 5 chemotherapy, 1 radiotherapy, Other treatment[4] = 4 exploratory laparotomy, 1 diagnostic laparoscopy

Figure 3.2: *Patterns of treatment*

3.3.3 Compliance with quality indicators

Twenty-two out of the 27 quality indicators were analysed for compliance. Data was never collected on one indicator (management with biliary stent), and for four indicators, data reliability was being assessed at the time of reporting. The full results are displayed in *Table 3.2*. Compliance with individual quality indicators ranged from 9% to 98%. Seven indicators had high compliance (>85%); these included tissue biopsies undertaken before treatment (n=357/364, 98%), baseline CA19-9 taken (n=389/440, 88%), resectability of tumour was clearly defined and documented (n=770/836, 92%), adjuvant chemotherapy after surgery was given or a reason documented for not receiving treatment (n=102/107, 95%), and patients with metastatic disease referred to or seen by a palliative care specialist (n=348/372, 94%).

Seven quality indicators had a compliance between 70-84% and eight with less than 70%. Indicators with less than 70% compliance included documented performance status at diagnosis (n=602/871, 69%), pathology report configured according to a nationally endorsed synoptic system (n=91/140, 65%), disease management discussed at multidisciplinary team (MDT) meetings (n=553/831, 67%), and participation in a clinical trial (n=72/795, 9%).

When assessed by resectability of tumour, 66% (n=212/319) of patients with non-metastatic PDAC complied with the indicator measuring ‘documented pancreatic protocol (PPCT) or MRI for diagnosis and/or staging’. Further, 96% (n=217/226) in the potentially resectable (includes borderline resectable disease), 86 % (n=109/127) in the locally advanced and 46% (176/385) of those diagnosed with metastatic disease had their disease management discussed at a MDT meeting.

Outcomes of care indicators showed that 64/247 (26%) patients died within 30 days of their last dose of chemotherapy and 105/150 (70%) patients were alive 12 months after undergoing surgery. For the latter, 80% (n=119/150) were clearly resectable at diagnosis, 13% (n=19/150) were borderline resectable and 7% (n=10/150) did not have their resectability documented clearly. For pancreas alone (excluding periampullary PDAC), 69% (n=82/119) were alive at 12 months following surgery.

	Consensus-based Quality Indicator *Reasons for exclusion for each indicator*	Number eligible / denominator	Overall Compliance /Numerator n (%)	Confidence Intervals
Diagnosis and staging				
1	Documented PPCT or MRI scan for diagnosis and/or staging in patients with non-metastatic disease *Patients with metastatic disease* *Missing*	**319** *406* *146*	**212** (66)	61 - 72
2	Tissue biopsy attempted prior to chemotherapy or radiotherapy *No chemotherapy or radiotherapy* *Surgical tissue biopsy#* *Missing*	**364** *378* *92* *37*	**357** (98)	96 – 99
3	Documented baseline CA19-9 level before treatment *No treatment administered* *Missing*	**440** *334* *97*	**389** (88)	85 - 91
4	Documented ECOG at presentation and/or ASA at a diagnostic procedure	**871**	**602** (69)	66 – 72
5	Time from referral to all **treatment** within 60 days *No active treatment administered* *Missing*	**424** *334* *113*	**308** (73)	68 – 77
5a	Time from first GP or ED referral to **definitive treatment*** within 60 days *Not for definitive treatment* *Missing*	**207** *646* *18*	**157** (76)	69 – 82
6	MRI, CT or PET completed following neo-adjuvant treatment *No neo-adjuvant treatment administered* *Missing*	**34** *833* *4*	**15** (44)	27 – 62
7	Operability (resectability) of tumour is clearly defined and documented as either operable/ resectable, borderline resectable, locally advanced or metastatic *Missing*	**836** *35*	**770** (92)	90 –94
Surgery				
8	RCPA or equivalent reporting system (synoptic report) used to document findings for patients undergoing surgical resection *Not for surgical treatment* *Attempted surgery with pathology report not cited by data collector* *Missing*	**140** *647* *16* *68*	**91**, (65)	56 – 73
9	Standard lymphadenectomy with the removal of ≥ 10 lymph nodes pathologically examined and documented *As per QI 8*	**140**	**117** (84)	76 – 89
10	R0 resections (≥ 1mm margin) for those that do have a synoptic report *Not for surgical treatment* *Those without a synoptic report* *Attempted surgery with pathology report not cited by data collector* *Missing*	**92** *647* *48* *16* *68*	**62** (67)	57 – 77
11	Number of patients undergoing pancreatic cancer surgery in a level 1-4 hospital**	N/A	N/A	N/A
12	All resectable patients who did not undergo surgery should have a valid reason documented *Unresectable (LA or metastatic) PDAC* *Attempted surgery* *Missing*	**41** *537* *193* *100*	**30** (73)	57 – 86

	Consensus-based Quality Indicator *Reasons for exclusion for each indicator*	Number eligible / denominator	Overall Compliance /Numerator n (%)	Confidence Intervals
Other Treatment				
13	Adjuvant chemotherapy administered following surgery or a reason documented for not undergoing treatment *Not for surgical treatment* *Surgery abandoned intraoperatively* *Diagnostic laparoscopy or Exploratory laparotomy* *Missing*	**107** *647* *37* *9* *71*	**102** (95)	89 – 98
14	Chemotherapy ± chemo-radiation offered to patients with locally advanced disease, or a reason documented for not undergoing treatment *Disease resectability other than locally advanced* *Missing*	**120** *638* *113*	**96** (80)	72 – 87
15	Neo-adjuvant chemotherapy ± chemo-radiation offered to patients with borderline resectable disease, or a valid reason documented for not undergoing treatment *Disease resectability other than borderline disease* *Missing*	**66** *700* *105*	**54** (82)	70 – 90
16	Seen by a medical or radiation oncologist or a reason documented for not doing so *Seen by medical or radiation oncologist missing* *Missing*	**292** *566* *13*	**254** (87)	83 – 91
Patient Management				
17	Disease management discussed at a MDT meeting *Missing*	**831** *41*	**553** (67)	63 - 70
18	Biliary obstruction managed surgically or by stent	N/A	N/A	N/A
19	Patients with metastatic disease referred to (or seen by) a palliative care specialist *Disease resectability other than metastatic disease* *Missing*	**372** *465* *34*	**348** (94)	91 – 96
20	Patients having completed treatment followed up by a specialist every three to six months for up to 2 years	N/A	N/A	N/A
21	Patients included in a clinical trial *Missing*	**795** *76*	**72** (9)	7 – 11
Outcomes				
22	Patients not requiring a re-operation following surgical resection *Not for surgical treatment* *Diagnostic laparoscopy or Exploratory laparotomy* *Missing*	**181** *647* *13* *30*	**160** (88)	7 – 17
23	Patient alive within 30-days of last dose of chemotherapy *No chemotherapy administered* *Missing*	**247** *391* *233*	**183** (74)	21 – 32
24	>2 ED presentations in the last 30-days before death	N/A	N/A	N/A
25a	Patients alive at one year following surgery *Not for surgical treatment* *Surgery abandoned intraoperatively* *Diagnostic laparoscopy or Exploratory laparotomy* *Missing*	**150** *647* *37* *9* *28*	**105** (70)	62 – 77
25b	Patients alive at 2 years following surgery *As above*	**150**	**44** (29)	22 – 37
26	≥14 days in acute hospital	N/A	N/A	N/A
27a	30-day mortality rate following surgical resection *As per QI 25a*	**150**	**6** (4)	2 – 10
27b	90-day mortality rate following surgical resection (includes 30-day mortality) *As per QI 25a*	**150**	**7** (5)	2 – 9

Table 3.2: *Compliance with quality indicators*

Legend for Table 3.2
N/A – not analysed, # surgical tissue biopsy excluded to ensure unresectable patients undergoing treatment other than surgery are appropriately staged, * Definitive treatment (as defined by the UGICR Hepatopancreatobiliary Working Group) = surgery and/or neoadjuvant therapy (does not include other intent), ** Level 1: *primary care only (emergency care for minor musculoskeletal injuries)*, Level 2: *primary and secondary services* , Level 3: *Primary, secondary and limited tertiary services*, Level 4: *Comprehensive primary, secondary and tertiary specialist services*

3.3.4 Association between patient and hospital characteristic, quality indicator adherence and survival

The association between risk of death and patient characteristics, hospital characteristics and the quality indicators are displayed in *Table 3.3*. The univariable analysis showed that patient and hospital characteristics associated with increased risk of death included older age (>75 compared with <55 years), higher ECOG performance status score (ECOG score > 2 compared with ECOG of 1), resectability at diagnosis (compared with borderline, locally advanced, metastatic, and not clearly documented or unknown had higher risk), being diagnosed in a regional area (compared with metropolitan) and a hospital capacity of 200-500 (compared with > 500 beds). There was a decreased risk of death associated with some tumour sites (ampulla of vater and the distal bile duct when compared with tumours of the head of pancreas), and being diagnosed in a hospital with an annual diagnosis case volume of PDAC of 10 or more (compared with < 10 cases).

Seven indicators were statistically significant predictors of improved survival in the univariable model (*Table 3*): having protocol-based imaging in non-metastatic disease (HR, 0.68; 95% CI, 0.51 – 0.90); documented ECOG at presentation and/or ASA at a diagnostic procedure (HR, 0.59; 95% CI, 0.50 – 0.69); those with a R0 margin resection and a synoptic report (HR, 0.51; 95% CI, 0.26 – 0.98); receiving adjuvant chemotherapy following surgery or having a reason documented for not being treated (HR, 0.25; 95% CI, 0.10 – 0.64); patients with locally advanced disease undergoing treatment or a reason documented for not having treatment (HR, 0.61; 95% CI, 0.38 – 0.98); disease management discussed at a MDT meeting (HR, 0.33; 95% CI, 0.28 – 0.39); being included in a clinical trial (HR, 0.65; 95% CI, 0.49 – 0.85).

Characteristics and Overall Survival	Univariable Analysis		
Predictor Variable	Hazard ratio	95% CI	P value
Age Group			
<55 *	Reference		
55 – 64	1.16	0.84 – 1.59	0.371
65 – 74	1.21	0.91 – 1.61	0.201
75 – 84	***1.69***	***1.27 – 2.26***	***<0.001***
> 85	***3.19***	***2.32 – 4.39***	***<0.001***
Sex			
Male *	Reference		
Female	1.12	0.98 – 1.32	0.124
ECOG Performance Status			
0 - fully active*	Reference		
1	1.25	0.91 – 1.74	0.171
2	***2.71***	***1.91 – 3.84***	***<0.001***
3	***3.96***	***2.73 – 5.77***	***<0.001***
4	***6.89***	***3.52 –13.50***	***<0.001***
Not documented	***1.43***	***1.17 – 2.01***	***0.002***
Resectability at Diagnosis			
Resectable*	Reference		
Borderline Resectable	***1.61***	***1.12 – 2.33***	***0.011***
Locally advanced	***2.83***	***2.25 – 4.04***	***<0.001***
Metastatic	***5.63***	***4.37 – 7.25***	***<0.001***
Not clearly documented	***3.20***	***2.26 – 4.54***	***<0.001***
Site of Tumour			
Head *	Reference		
Neck	1.05	0.73 – 1.50	0.810
Body	***1.35***	***1.09 – 1.68***	***0.006***
Tail	***1.25***	***1.00 – 1.57***	***0.048***
Uncinate process	0.94	0.71 – 1.24	0.640
Ampulla of Vater	***0.23***	***0.13 – 0.41***	***<0.001***
Distal Bile Duct	***0.41***	***0.23 – 0.75***	***0.004***
Pancreas (not otherwise specified)	***2.72***	***1.88 – 3.94***	***<0.001***

Characteristics and Overall Survival	**Univariable Analysis**		
Predictor Variable	Hazard ratio	95% CI	P value
SES			
Quintile 1* *(most disadvantaged)*	Reference		
Quintile 2	1.09	0.85 – 1.40	0.502
Quintile 3	0.97	0.75 – 1.26	0.828
Quintile 4	0.93	0.74 – 1.16	0.508
Quintile 5 *(least disadvantaged)*	0.95	0.76 – 1.18	0.645
Hospital Type			
Public*	Reference		
Private	1.04	0.79 – 1.36	0.791
Hospital Area			
Metropolitan*	Reference		
Regional	***1.58***	***1.17 – 2.12***	***0.003***
Hospital Capacity			
> 500*	Reference		
200 – 500	***1.23***	***1.02 – 1.47***	***0.028***
100 – 199	1.29	0.93 – 1.79	0.125
Hospital Case Volume			
<10*	Reference		
10 – 29	***0.77***	***0.63 – 0.94***	***0.010***
>30	***0.78***	***0.65 – 0.94***	***0.010***
Surgical Case Volume			
<5*	Reference		
6 – 10	0.76	0.47 – 1.24	0.274
11 – 15	1.36	0.79 – 2.33	0.270
No known Surgical Volume	0.64	0.25 – 1.66	0.361
No Surgery	***3.87***	***2.66 – 5.63***	***<0.001***

Quality Indicators and Overall Survival	Univariable Analysis		
Predictor Variable	Hazard ratio	95% CI	P value
1.Documented PPCT or MRI scan for diagnosis and/or staging (non-metastatic)	***0.68***	***0.51 – 0.90***	***0.007***
2.Tissue biopsy attempted prior to chemotherapy or radiotherapy biopsy	0.59	0.24 – 1.42	0.236
3.Documented baseline CA19-9 level before treatment	1.13	0.79 – 1.60	0.509
4.Documented ECOG at presentation and/or ASA at a diagnostic procedure	***0.59***	***0.50 – 0.69***	***<0.001***
5.Time from referral to **treatment** within 60 days	1.00	0.77 – 1.30	0.986
5a.Time from referral to **definitive treatment** within 60 days	1.10	0.69 – 1.76	0.68
6.MRI, CT or PET completed following neo-adjuvant treatment	1.88	0.70 – 5.04	0.212
7.Resectability of tumour is clearly defined and documented	0.91	0.69 – 1.21	0.529
8.RCPA or equivalent reporting system used to document findings	1.23	0.69 – 2.18	0.488
9.Standard lymphadenectomy with the removal of ≥ 10 lymph nodes	1.21	0.57 – 2.56	0.622
10.R0 resections (≥ 1mm margin) for those with a synoptic report	***0.51***	***0.26 – 0.98***	***0.042***
12.Patients who did not undergo surgery should have a valid reason documented	1.67	0.73 – 3.83	0.229
13.Adjuvant chemotherapy administered following surgery or a reason documented	***0.25***	***0.10 – 0.64***	***0.004***
14.Chemotherapy ± chemo-radiation offered to patients with locally advanced disease, or a reason documented for not undergoing treatment	***0.61***	***0.38 – 0.98***	***0.039***
15.Neo-adjuvant chemotherapy ± chemo-radiation offered to patients with borderline resectable disease, or a valid reason documented for not undergoing treatment	0.64	0.30 – 1.33	0.228
16.Patients who saw a medical or radiation oncologist or a reason documented for not doing so	0.76	0.53 – 1.07	0.118
17.Disease management discussed at a MDT meeting	***0.33***	***0.28 – 0.39***	***<0.001***
19.Patients with metastatic disease referred to (or seen by) a palliative care specialist	1.37	0.87 – 2.18	0.178
21.Patients included in a clinical trial	***0.65***	***0.49 – 0.85***	***0.002***

Table 3.3: *Univariable analysis*

The relationships between patient and hospital characteristics were tested in a multivariable model and age-group, ECOG performance status, resectability at diagnosis, and tumour site held their significance. After adjusting for these confounders, six indicators remained statistically significant (*Table 3.4)*.

Quality Indicators	Hazard Ratio	p - value	95% CI
1. Documented PPCT or MRI scan for diagnosis and/or staging (in non-metastatic disease)	***0.745***	***0.044***	***0.559 – 0.992***
4. Documented ECOG at presentation and/or ASA	***0.728***	***0.003***	***0.589 – 0.900***
10. R0 resection (≥ 1mm margin) for those with a synoptic report	0.526	0.055	0.272 – 1.014
13. Adjuvant chemotherapy administered following surgery or a reason documented	***0.238***	***0.003***	***0.092 – 0.617***
14. Chemotherapy ± chemo-radiation offered to patients with locally advanced disease, or a reason documented for not undergoing treatment	***0.587***	***0.030***	***0.363 – 0.949***
17. Disease management discussed at a MDT meeting	***0.591***	***<0.001***	***0.490 – 0.713***
21. Patients included in a clinical trial	***0.749***	***0.045***	***0.565 – 0.994***

Table 3.4: *Multivariable analysis*

3.3.5 Sensitivity Analysis

Data were re-analysed after removing periampullary cancers (Ampulla of Vater and distal bile duct) for the indicators assessing documented PPCT or MRI (HR, 0.51; 95% CI, 0.43 – 0.60), adjuvant chemotherapy administered following surgery (HR, 0.32; 95% CI, 0.25 – 0.79) and patients included in a clinical trial (HR, 0.62; 95% CI, 0.11 – 0.90) to assess any impact on the results. The results remained unchanged. Overall survival was tested separately for PDAC compared to periampullary cancers. One-year overall survival was 28% in patients diagnosed with PDAC compared to 57% for patients diagnosed with periampullary cancers.

3.4 Discussion

This study used observational data collected by the UGICR to report on the quality of care provided to patients diagnosed with PDAC from 2016 to 2018 in Victoria, and it fills a significant gap in the literature on the impact of quality care and survival in this population.

A systematic review of observational studies assessing the overall burden of PDAC in Europe showed a median survival of 2 to 8.1 months in those who received chemotherapy, radiotherapy or palliative surgery compared to a median survival of only 1.1 months in those who received no cancer-directed therapy. Fifty-four percent of those treated and 52% of those not treated had stage IV disease. Age was a factor with median survival of 1 to 3.2 months in those with a median age of 70 to 76 years, compared to 5 to 6.1 months in those with a median age 62 to 67 years[34] In our study, 38% of patients had no cancer directed treatment recorded, with the majority being 75 years or over and having advanced disease. There is some evidence that PDAC may be undertreated as a result of poor communication on available treatments options.[73] In addition, a nihilistic attitude to pancreatic cancer based on historically poor outcomes and lack of knowledge of incremental but real improvements in treatment options and their impact on quality of life and overall survival, can also result in undertreatment.[74,75]

Survival in PDAC calculated using registry data are dependent on factors such as patient characteristics, disease specifics and the care received (diagnosis and staging, treatment and patient management).[76] Patient characteristics associated with poor outcomes in our study, and as a result used for adjustment of the QIs, were age, ECOG performance status, resectability and site of tumour. Further, our findings from univariable analyses show an increased risk of poor outcomes if patients were diagnosed in a regional area, or in a hospital with lower capacity or annual diagnosis case volume, albeit the small numbers. Patients

diagnosed in facilities with lower volumes may be less likely to be offered treatment options such as surgery, chemotherapy or palliative care.[4,77,78]

Eighteen process and four outcome QIs were assessed for compliance and the variations in care reported. Of the process QIs, six were associated with improved survival following adjustment with a 25% to 75% decrease in risk of death. Earlier studies conducted by Burmeister and colleagues from Queensland, Australia, developed 18 care statements on a range of management indicators and they found seven indicators were statistically significantly associated with survival.[4] Our study validated two similar indicators, these being adjuvant chemotherapy administered following surgery and patients being discussed at MDT meetings as associated with improved survival. Our findings further show that meeting the following QIs: having a dedicated PPCT or MRI in non-metastatic disease; ECOG performance status documented at presentation and/or ASA recorded at a diagnostic procedure; patients with locally advanced disease having treatment or a reason documented for not undergoing treatment; and being included in a clinical trial were significantly associated with improved survival.

Accurate preoperative imaging and discussions at MDT meetings play a vital role in patient selection for surgery and ongoing disease management. A PPCT is the preferred modality for evaluating the extent of PDAC and its proximity to vascular structures. A consensus statement released by the Society of Abdominal Radiology and the American Pancreatic Association recommended that patients with no obvious metastatic disease or extensive local invasion at initial routine CT examination undergo a PPCT to determine accurate disease staging and to avoid unnecessary surgical exploration. An MRI has also shown equal sensitivity and specificity in staging PDAC [79,80] Assessment of this indicator showed that a third of patients with non-metastatic disease did not have a documented PPCT or MRI. Further, clinical practice guidelines recommend that management decisions across all disease

stages, should be made within the framework of a MDT discussion to ensure that a full range of treatment options are considered.[81,82] Yet in our dataset, overall compliance was 67% with only 46% of patients with metastatic PDAC discussed at MDT meetings. Whether or not it's appropriate for patients with metastatic disease to be routinely discussed at a MDT meeting is somewhat controversial with a commonly held view amongst medical oncologists that such discussions are superfluous despite this being recommended by the Optimal Care Guidelines.[26] These two indicators will be further explored in the upcoming Chapters to further understand the barriers and enablers to their implementation in practice.

Our results show that the reporting of an ECOG performance score or diagnostic ASA improves survival. This finding may be confounded by the fact that performance scores are usually documented when a treatment is considered compared to patients with significant comorbidities or metastatic disease who may not be eligible for treatment, leading to poorer survival.

An important recommendation in clinical practice guidelines is for patients to participate in clinical trials which can include new therapeutics in advanced disease or palliative care as well as clinical research initiatives that include biorepository and observational studies.[81] Our findings showed that only 9% of patients were included in a clinical trial over the three year study period, yet this was associated with a 25% reduction in the risk of death after adjustment for confounders. However, often patients with good performance status are included in clinical trials leading to selection bias and better outcomes. Another consideration is the number of available trials which impacts the number of patients eligible to participate in a trial. Our data provides overall population statistics based on availability and participation in trials over a three-year period.

The treatment pathway for both pancreatic and other periampullary cancers is similar and includes surgery followed by adjuvant chemotherapy in potentially resectable disease or

chemotherapy ± chemoradiation in advanced disease.[83,84] Mortality in periampullary cancers is lower than cancers originating in the head or body of the pancreas due to their earlier presentation.[85] A sensitivity analysis showed that the results for quality of care were not affected by the small number of these tumours in our study.

While this study has used observational data, the survival estimates over time using the adjusted indicators (*Table 3.4*) show that when clinical practice is more compliant with agreed best practice, there is an association with better outcomes.

A strength of our study was the size of the cohort we included, with 871 patients recruited from a range of health services and followed over a three-year period or until death by trained data collectors. The aforementioned systematic review revealed that 88% of studies included less than 500 patients.[34] As patients were identified by the population-based VCR it was possible to compare the demographics of the registry population and the population not captured by the registry. This enabled us to assess recruitment bias. However, our study had some limitations. We found that the included population was biased towards patients diagnosed in the metropolitan area and in public hospitals. Recently, more regional and private sites have been approved for data collection and data collection is ongoing, but data from these sites are not included in the current dataset. It is also plausible that patient characteristics such as co-morbidities, which are not captured by the registry are different across different centres for a range of reasons (age, geography etc) and, as a consequence a more comprehensive adjustment of the QIs to include comorbidities would enhance our understanding of compliance with optimal care. Data collectors reviewed medical records in hospitals and consulting rooms, but some information may not have been captured, particularly if it occurred outside the diagnosing hospital. For example, if an MRI was performed in a private radiology centre and was not available to the participating treating hospitals, it may not have been captured by the registry. For 13% of patients, poor documentation meant that the time from referral to diagnosis could not be assessed. Timing is

an important issue for all patients, but particularly those with unresectable disease needing to be seen by palliative care specialists. For example, referral 3 days before death is unlikely to confer many benefits compared to > 3 months before death.[86]

3.5 Conclusion

Capture of a concise data set by the UGICR has enabled quality of care to be assessed and report on factors associated with improved survival. Over time, the registry will be able to provide further details back to health services, benchmarking their performance based on compliance with current and emerging indicators. It is hoped that ultimately adherence to best practice indicators will lead to system-level improvement in survivorship and, ultimately, survival.

3.6 Chapter Summary

In this research, 22 of the 27 QIs were evaluated for compliance, and 18 QIs further assessed for association with survival. Five indicators were not reported. For one indicator, the UGICR did not capture data to enable it to be constructed. Four indicators were not reported because the reliability of the data was being investigated. For example, it was difficult to report on end-of-life indicators 24 and 26 when the registry had not yet reached maximum population capture, and it was unclear if patients were presenting to emergency departments or being admitted to hospitals that were not currently participating in the registry. This would affect the reliability of these indicators being measured.

A total of 871 patients were eligible for this study with 52% male, 74% over the age of 65, 27% potentially resectable and 47% with metastatic disease at diagnosis. Fifty-six percent of patients received some form of cancer directed treatment. Compliance with the following QIs was associated with improved patient survival in a multivariable analysis after adjusting for confounders: (1) imaging using a pancreatic protocol CT or MRI (*HR=0.75; 95% CI, 0.56-0.99*); (2) documented ECOG at presentation and/or diagnostic ASA (*HR,0.73; 95% CI, 0.59-0.90*); (3) disease management discussed at a multidisciplinary team meeting (*HR,0.59; 95% CI, 0.49-0.71*); (4) being included in a clinical trial (*HR, 0.75; 95% CI, 0.57-0.99*); (5) adjuvant chemotherapy administered following surgery or a reason documented (*HR, 0.24; 95% CI, 0.09 – 0.62*); and (6) chemotherapy ± chemo-radiation offered to patients with locally advanced disease (*HR, 0.59; 95% CI, 0.36-0.95*).

Capture of a concise data set has enabled quality of care to be assessed. Using this observational dataset and not withstanding inherent limitations in interpreting cause and effect relationships, higher compliance with a key set of QIs was associated with improved survival.

The UGICR is developing benchmark reports based on the formatted QIs and the calculations used to analyse compliance in this study. This is an important next step for the registry. By reporting and providing feedback using these quality metrics to participating sites, the results will allow each provider to compare and investigate within their organisation the areas where compliance could be improved.

"The first step is transformation of the individual. This transformation is discontinuous. It comes from understanding of the system of profound knowledge. The individual, transformed, will perceive new meaning to his life, to events, to numbers, to interactions between people. Once the individual understands the system of profound knowledge, he will apply its principles in every kind of relationship with other people. He will have a basis for judgment of his own decisions and for transformation of the organizations that he belongs to."

W. Edwards Deming

Chapter 4: Barriers and Enablers to Protocol Imaging

In the next two Chapters we explore the barriers and enablers to site implementation and stakeholders' view on implementation of two QIs with poor compliance to determine the reasons for their variation. It addresses the last aim for this thesis and objective 5, to explore the barriers and enablers to providing quality care to patients with PC

Preliminary data from the registry showed that of those who had attempted surgery, 18 % had their surgery abandoned intraoperatively *(as per figure below)*. An audit of the abandoned surgeries revealed that on average patients stayed in hospital for close to 12 days. Surgery was often abandoned due to vascular invasion, adherence to blood vessels or due to liver metastasis. Abandonment of surgery can have significant implications for patients including the psychological impact, recovery time, cost and resources. Further, approximately 20% did not achieve a clear margin (R0) resection. For those who have <1 mm (R1) margin resection or those with margin involvement (R2) following surgery, survival outcomes are similar to patients diagnosed with advanced disease.[87]

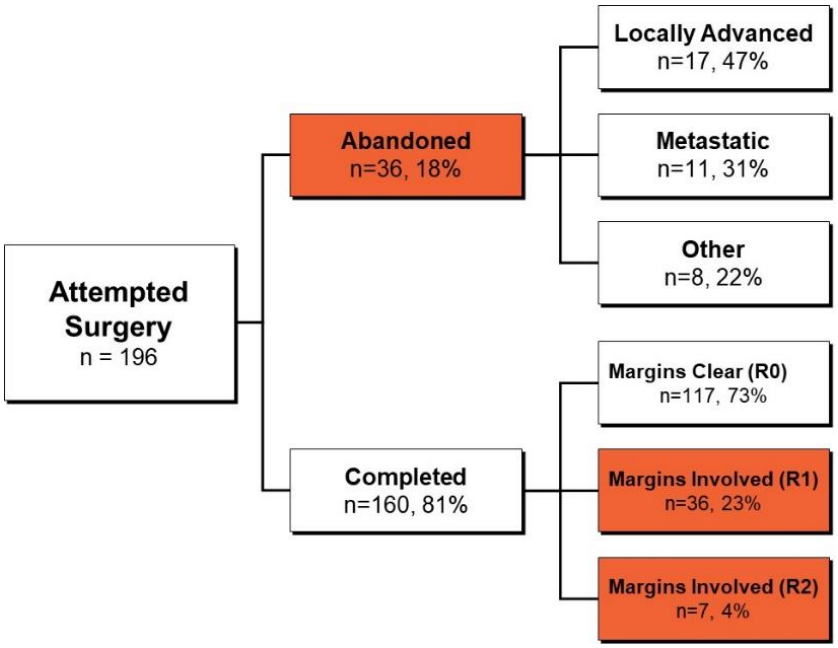


***Figure 4.1**: Outcomes of Surgery*

Accurate pre-operative imaging plays a vital role in patient selection for surgery and in allocating stage-appropriate therapies to patients diagnosed with PC. In this Chapter, this study aims to: (1) understand the current diagnosis and staging practices for PC; and (2) explore the factors (barriers and enablers) that influence the use of pancreatic protocol computed tomography (PPCT) or magnetic resonance imaging (MRI) to confirm diagnosis and/or accurately stage PC.

A focus group was initially convened to address the question 'who needs to do what, differently'? This step is part of a four-step method for developing interventions designed to change clinical practice based on a theoretical framework.[88]

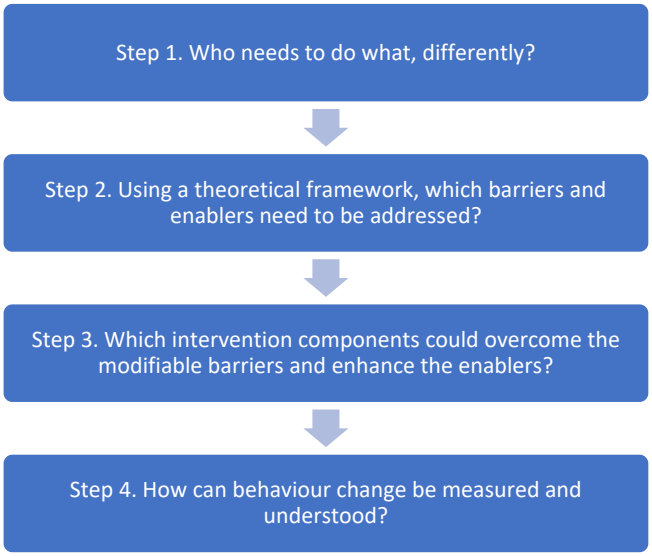


Figure 4.2: *Four steps to behaviour change*

Following the focus group meeting, semi-structured interviews were conducted with radiologists, surgeons, gastroenterologists, medical and radiation oncologists from the states of New South Wales (NSW) and Victoria, Australia. Interviews were conducted either in person or via video conferencing. All interviews were recorded, transcribed verbatim, de-identified and data were thematically coded according to the 12 domains explored within the theoretical domains framework (TDF). Common belief statements were generated to compare the variation between participant responses. The full study exploring the barriers and enablers to protocol imaging is described as follows.

4.1 Background

Accurate pre-operative imaging plays a vital role in patient selection for surgery and in allocating stage-appropriate therapies to patients diagnosed with pancreatic cancer (PC).[89] The recommended method of assessing operability is based on high-quality multi-phase computed tomography (CT) that examines the abdominal area in the arterial and portal venous phase. Such a CT scan can determine the proximity of the tumour to major vascular structures and the presence of locally advanced disease or intra and extra-abdominal metastases.[90,91] In 2012, the Society of Abdominal Radiology and the American Pancreatic Association released a consensus statement describing a standardised reporting template for the accurate staging of PC to improve disease management. This statement was authored by a multi-institutional group of experts comprising radiologists, gastroenterologists, and hepatopancreatobiliary surgeons.[19] For accurate disease staging, it was recommended that all patients with no obvious metastatic disease or local invasion at initial routine CT, undergo a repeat examination with a dedicated pancreas protocol multiphase computed tomography (PPCT) prior to endoscopy, biliary stenting or invasive tissue sampling.[19,92,93]

More recently, evidence-based clinical practice guidelines recommend that PPCT be used to assess the extent of the disease across all stages of PC.[81,94,95] Where there is clinical suspicion of PC, a PPCT is also considered to be the primary imaging modality to diagnose and stage the extent of the disease within one single session.[96,97] The pancreas is anatomically intertwined with critical vascular structures: specifically the celiac artery, hepatic artery, superior mesenteric artery, portal vein and the superior mesenteric vein. A PPCT evaluation of vascular involvement is highly predictive of the extent of vascular involvement which in turn determines operability and overall survival.[93] In addition, a PPCT is also required for accurate planning and delivery of targeted radiotherapy, which requires clear delineation of the tumour in relation to normal pancreatic parenchyma and surrounding normal structures.

Magnetic resonance imaging (MRI) is considered by some to be equivalent to a CT in detecting and staging PC. However, recent evidence recommends the addition of MRI as an adjunct to detect the presence of liver metastases, rather than a replacement for PPCT.[91] The liver is the most common organ affected by metastasis, and establishing the accurate extent of liver disease can help avoid futile attempts at surgical resection.[98] It has been suggested that all patients with PC deemed resectable should undergo liver MRI to complement CT evaluation, but this is not always feasible due to limited resources and access to MRI.[91]

A set of quality indicators for PC was developed by Australian clinicians in 2018 and compliance with these indicators is reported by the Upper Gastrointestinal Cancer Registry (UGICR).[60,61] Preliminary analysis of registry data show 29% (n=64/224) of patients with potentially resectable and 43% (n=54/125) of patients with locally advanced disease (without metastases) did not undergo either a documented PPCT or MRI. In a disease where surgery is complex but remains the best chance for long-term survival in patients with localised disease, incomplete or sub optimal pre-operative staging can result in adverse outcomes such as planned procedures and surgery being abandoned intraoperatively or a margin-positive resection, resulting in poorer survival.[49]

Given the likely benefits of PPCT and MRI, and the evidence for variation in these practices, it is important to understand the reasons why patients with PC may or may not be receiving this care. Here we explore the barriers and enablers to the implementation of a PPCT or MRI for diagnosis and/or staging of PC. In so doing, we will inform tailored knowledge translation and quality improvement interventions which address modifiable barriers and enhance enablers of PPCT and MRI use.

This study aims to: (1) understand the current diagnosis and staging practices for PC; and (2) explore the factors (barriers and enablers) that influence the use of a PPCT or MRI to confirm diagnosis and/or accurately stage PC.

4.2 Methods

This research explored the barriers and enablers to two important clinical behaviours in the management of PC. This Chapter reports on the use of a PPCT or MRI.

This study is underpinned by the theoretical domains framework (TDF). The TDF was developed through international collaboration between behavioral scientists and implementation researchers. The framework consolidates theories relevant to behavioral and psychological processes determining the influences on healthcare practitioners' behavior. Constructs from these theories are grouped into domains (*displayed in Figure 4.3*) and provide a theoretical lens to identify determinants of behavior.[99,100]

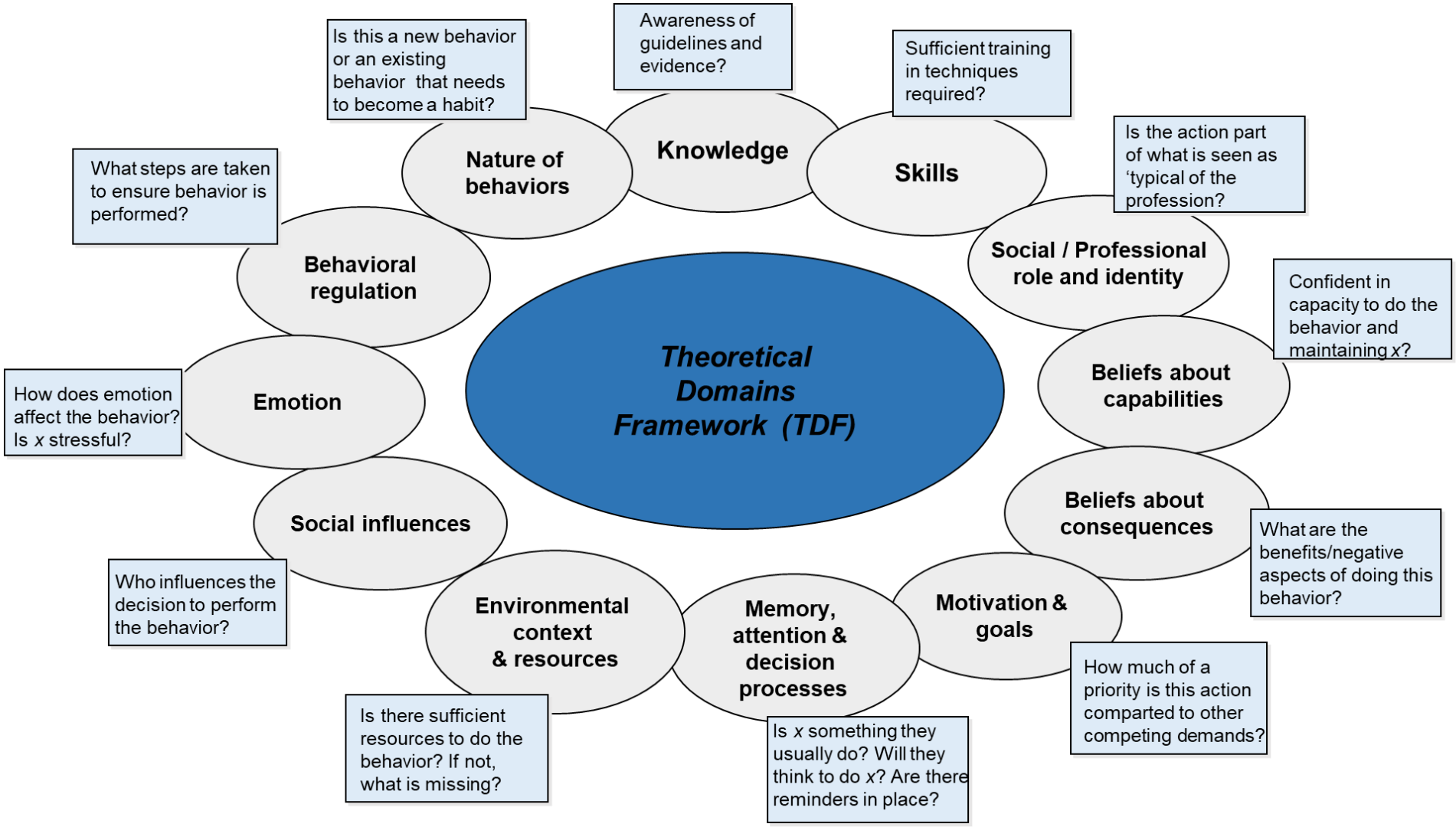


Figure 4.3: *Theoretical Domains Framework* [99,100]

4.2.1 STEP ONE: Describing ideal practice - Focus Group

A focus group was convened comprising clinical experts involved in the treatment and management of PC to understand the steps involved in the use of PPCT and MRI in a clinical setting. Following a systematic approach for using the TDF to implement evidence based interventions into practice,[88] the group considered '*who needs to do what differently'* and developed a decision tree (*Appendix 4.2*) which clearly articulated the clinical decisions and processes involved in appropriate execution of PPCT and MRI. This decision tree formed the reference, or 'ideal practice', of the interview questions, which were grouped into domains according to the TDF.

4.2.2 STEP TWO: Understanding the barriers to and enablers of ideal practice

Medical specialists involved in the treatment of patients with PC (radiologists, surgeons, medical and radiation oncologists and gastroenterologists) from public and private hospitals, within metropolitan and regional areas, across the states of New South Wales (NSW) and Victoria (VIC) were invited to participate in semi-structured interviews underpinned by the TDF. A stratified purposeful sampling strategy was used to recruit participants, followed by snowball sampling.[101] This initially involved inviting by email clinicians contributing to the Upper Gastrointestinal Cancer Registry (UGICR) and clinicians identified as specialising in PC on hospital websites.[60] In addition, those interviewed were asked to nominate other specialists for researchers to contact. Participants who opted-in to the study provided consent through email.

An interview guide was developed to explore factors influencing the implementation of protocol-based imaging (CTs and MRIs) in the management of all patients diagnosed with PC. Open-ended questions were asked to cover each domain of the TDF. The interview schedule was initially piloted with two surgeons (DC and CHCP) and a nurse specialist (TD),

following which it underwent further refinement. The interview schedule is provided as *Appendix 4.3.*

Interviews were conducted either in person or using Zoom video conferencing (https://zoom.us/) by two researchers (ADM - lead interviewer and SEG). With participants' consent, interviews were recorded on video and audio using Zoom conferencing software, transcribed verbatim, de-identified and imported into NVIVO 12.0 Plus qualitative software (QSR International Pty Ltd. Version 12, 2018) for analysis.

4.2.3 Analysis

Interview transcripts were thematically coded according to the 12 domains of the TDF. Overarching themes perceived to influence the implementation of protocol-based imaging and associated belief statements were then generated. A belief statement was defined as "a collection of responses with a similar underlying belief" that determined the relevance and role of the domain in influencing the behaviours around protocol-based imaging.[99,102]

A random sample of transcripts (n=3, 10%) were analysed independently by two researchers, who then met to discuss the generation of themes and coding guidelines. Any discrepancies were discussed with a further researcher for resolution. The full summary of results was independently reviewed and presented to the same focus group as Stage One above over two meetings for feedback and interpretation of findings.

4.2.4 Ethics

Ethics approval was obtained from Monash University Human Research Ethics Committee (MUHREC): Project Number 19446.

4.3 Findings

4.3.1 Focus Group

Twelve clinical experts were invited to the initial focus group and nine participated. The focus group comprised three surgeons, two medical oncologists, a radiation oncologist, a palliative care specialist, a nurse specialist and a nurse care coordinator. The decision tree, presented in *Appendix 4.2*, clearly articulated the clinical pathway leading to a PPCT, and the appropriate precursors and outcomes. This was agreed by the focus group as the evidence- and consensus- based ideal clinical practice.

4.3.2 Interviews

A total of 49 specialists were approached across the two states and 21 (40%) participants were interviewed. Participant characteristics are summarised in *Table 4.1*. Most were male (n=20, 95%); 71% were from metropolitan settings, and 62% were from Victoria. The case volume of surgeons varied by state and rurality. Surgeons in the state of Victoria and in regional areas commonly saw between one and three PC cases per week, compared to five to ten PC cases seen by surgeons working in NSW and metropolitan regions. This difference is likely related to the model of centralised care in NSW. Clinicians working in other disciplines from both states reported seeing from zero to two cases per week.

DISCIPLINE	Invited	Included	NSW	VIC	Metro	Regional	Public	Private
Surgeon	18	10	4	6	7	3	9	1
Radiologist	7	5	1	4	4	1	4	1
Med. Oncologist	13	3	1	2	1	2	2	1
Rad. Oncologist	4	1	1	0	1	-	1	-
Gastroenterologist	7	2	1	1	2	-	2	-
TOTAL	**49**	**21**	8	13	15	6	18	3

Table 4.1: *Participant Characteristics*

4.3.3 Factors influencing the implementation of a PPCT or MRI

Across the relevant domains, 20 themes and 30 specific beliefs were identified. *Table 4.2* summarises the main belief statements generated from the interviews, categorised according to the domains of the TDF. Each belief statement is demonstrated by representative quotes.

All TDF domains, with the exception of *social influences* were identified by participants as relevant to protocol-based imaging using either a PPCT or MRI, with the domains of *knowledge*, *skills* and *environmental context and resources* being offered by most participants as influencing their decisions.

There was variation within the domain of *knowledge* about the differences between a PPCT or MRI and when each modality should be used for diagnosis and/or staging, even between radiologists. Some participants viewed the modalities as equivalent. However, the majority stated that there were clear differences outlining when they would use each. PPCT was viewed as the cornerstone for the staging of PC by the majority of specialists (*beliefs about consequences*) and most believed that if a normal single-phase CT scan or MRI showed clear evidence of metastatic disease there was no need for further protocol-based imaging (*beliefs about consequences*). Many viewed the MRI as a more challenging modality than a CT scan for a number of reasons. Some specialists described that the MRI required patients to cooperate for a longer period of time, generated anxiety in patients which could require sedation (*emotions*) and half the participants deemed that they were less accessible and more costly to the patient as they did not receive a rebate within the Australian context, *(environmental context and resources)*. While there was a general awareness of some evidence-based clinical practice guidelines relevant to protocol-based imaging, not all were familiar with the recommendations within the guidelines and many did not know of any specific research. A further belief that emerged within this domain was the notion that organisational protocols were more relevant to practice than the guidelines itself (*knowledge*).

A number of surgeons and other specialists stated that they were not aware of, nor did they follow, any protocols or referral pathways to facilitate the implementation of protocolised imaging. However, those who did follow clear, well laid-out protocols mentioned uniform management across the board, no delays in imaging and a higher volume of surgery undertaken that was concentrated amongst a limited number of surgeons (*behavioural regulation*). Many specialists believed that their organisation had the capacity to manage PC by providing the necessary resources including surgeons, radiologists, oncologists, intensive care and multidisciplinary team (MDT) services. Yet, a number of specialists mentioned that the volume of PC cases determined the focus within the organisation. For example, some described themselves as a " pancreatic centre of excellence" due to the high volumes and focus on PC cases managed within the organisation whilst a minority alluded to the fact that within their organisations they were the only surgeon managing patients with PC and not having a specific framework to streamline processes for patients (*environmental context and resources*) which may affect the implementation of a PPCT or MRI.

Overwhelmingly, having access to expert radiologists or radiology practices specialising in pancreatic radiology (i.e. "a good quality radiologist whom you trust") was viewed as essential for the diagnostic and staging modalities by all craft groups (*skills*). Related to this was the strong belief that quality and interpretation of imaging provided by specialist radiologists play a large role in providing confidence to clinicians in the diagnosis and staging of PC (*beliefs about capabilities*).

It was acknowledged by around half of the participants that the pathway to the diagnosis and staging of PC is complex and can involve numerous disciplines (*social/professional role and identity*). An identified barrier to a timely PPCT or MRI is that referral from primary care to the most relevant specialist (*beliefs about capabilities*) can be intercepted or delayed by referral to other disciplines such as gastroenterology, specialists that may not necessarily

undertake a PPCT or MRI as the first step. Conversely, in the metropolitan private sector, a potential barrier identified was the disincentive to undertake full imaging if an opportunity arose to take a patient with potentially resectable cancer straight to surgery (*motivation and goals*).

For all participants, the motivation to undertake a PPCT or MRI was to provide good quality care (*motivation and goals*). However, a belief reported by a minority that emerged as a barrier to PPCT or MRI from the domain of *emotions* was the potential for nihilism, especially in terms of management of older patients who were otherwise well enough to undertake surgical resection. A further belief reported by a few was that in some cases patients themselves were a barrier to optimal care and did not wish to know their diagnosis. In this context imaging may not be undertaken, placing value on the patient perspective (*emotions*).

Related to the patient perspective, a few participants mentioned distance to radiology services as a potential barrier for patients in regional or remote areas, while others recognised that often these patients were resigned to the fact that they would have to travel. Whether these decisions were overlayed as a consequence of patients' preference or a result of clinical therapeutic nihilism of course is difficult to estimate (*environmental context and resources*). Related to patients with PC living in regional areas was the belief that "having a succession plan, an age range of clinicians… with a policy of working together", and establishing sound practices, was a driving force that would enable services to remain in the regional vicinity and not be lost to the cities (*nature of behaviours*). It was further highlighted by regional specialists that a quality PPCT would detect the more complex cases such as those needing vascular resections, and these would then need to be referred to surgeons based in the metropolitan areas with expertise in this type of resection.

Implementation of a pancreatic protocol CT (PPCT) or magnetic resonance imaging (MRI) for diagnosis and/or staging			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
Knowledge	Clinical Practice Guidelines	I am aware of clinical practice guidelines	*"We're all aware of the NCCN guidelines, I think they're household names, and they're fairly general too, and they're fairly easy to adhere to. They don't influence practice too much, because we have our own department protocols and procedures that we regard as more important than established international guidelines" (Radiation Oncologist)* *"I'm aware of them, I don't refer to them. I know they exist." (HPB Surgeon)*
		I do not know or am not aware of clinical practice guidelines	*"All of the medical oncologists would not necessarily know of them, and all of the GPs definitely wouldn't know of them" (HPB Surgeon)*
	Research	I am aware of research about PPCT or MRI	*"There has been research done on those in terms of diagnosis. We've looked more at the locally advanced and borderline resectable tumours, looking at what are the criteria [on PPCT or MRI] which will be used on those patients who may be suitable for neo-adjuvant therapies" (HPB Surgeon)*
		I am not aware of any research about PPCT or on MRIs	*"I haven't actually read any of that literature in any sort of meaningful form actually since finishing my training which was you know that was quite a long time ago" (HPB Surgeon)*
	Difference between a PPCT and a MRI	A PPCT and MRI are equivalent	*"I think generally speaking they're fairly equivalent" (Radiologist)* *"I prefer CT, but that's because we're are trained to read the CT than an MRI, but I also don't believe that there's much of a difference between the information they give" (Gastroenterologist)* *"Look there are minor strengths and weaknesses of each, but as a rule they're pretty equivalent. It's rare that once you've done one good quality CT or MRI that you need to get the other one done as well" (Gastroenterologist)*
		There are differences between a PPCT and MRI	*"MRI is more challenging as a modality to get good quality imaging. For patients, it takes longer and they have to be more cooperative for that period, so it is a more challenging modality to do well. CT on the other hand is pretty quick, the techs are great, the patients don't have to lie very still for very long" (Radiologist)* *"We believe the CT is better with better resolution and anterior image. Most radiologists elsewhere believe that MRI is better especially when they are not specialists because it is that feeling that in the evolution of technology MRI came after therefore its better. (Radiologist, VIC)* *"For the pancreas the CT is better, but if you've got a suspected liver lesion than the MRI is better" (HPB Surgeon)*
Skills	Radiology	Specialist Radiologists are critical to performing and interpreting findings	*"We need to have a radiologist or radiology practice who is well versed and skilled in these procedures, particularly in terms of the timing of the procedures that they perform. (HPB Surgeon)* *"The only people who have that understanding are either radiologists who regularly have an interest and expertise and experience in assessing CT pancreas and some HPB surgeons. I wouldn't expect a general surgeon or an oncologist or other physician to be able to assess a pancreatic CT for resectability." (Radiologist)*
	Other	Apart from radiology, other skills are necessary for diagnosis and staging of PC	*"ultimately the formal reporting of the study is solely the domain of the radiologist. But in terms of establishing the staging, it would be discussed in the MDM setting and then you would have input from surgeons, gastroenterologists, radiologists, oncologists and also the pathologists where relevant." (Radiologist)* *"I guess broadly speaking there's obviously the radiographers who are an integral part of our team, and they actually do the imaging." (Radiologist)*
Social/Professional Role and Identity	Role for diagnosing and staging	The pathway to diagnosing and staging is complex	*" General surgeons are involved, as opposed to HPB surgeons, particularly in the country. Gastroenterologists are involved because the patients often present with jaundice and potentially oncologists are involved because they may get a referral with a suspicion of pancreatic cancer. Then it would be emergency department doctors, as a large proportion of pancreatic cancer patients present acutely with jaundice and they would first be seen in the emergency department. And then GPs will also get patients who present with weight loss, back pain, and jaundice, and finally endocrinologists sometimes identify these patients, for example if they have new onset diabetes or diabetes that is more difficult to control they might raise their suspicion and diagnose the pancreatic lesion" (HPB Surgeon)*

Implementation of a pancreatic protocol CT (PPCT) or magnetic resonance imaging (MRI) for diagnosis and/or staging			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
Beliefs about Capabilities	Challenges	PPCT or MRI is often not the primary path for diagnosis	*"The problem is patients often have symptoms for quite some time, and at a primary care level, some end up waiting a long time. They often are referred to a gastroenterologist; it is a long waiting time to see a gastroenterologist who then often end up doing an endoscopy and a colonoscopy. Then the penny drops that there is something more in about 10% of cases. That's a bit irritating from our point of view, when the patient's had symptoms there, it would've been easier just to do the decent CT scan." (HPB Surgeon)*
	Imaging	PC can be identified using a PPCT or MRI	*"The obvious ones are obvious, and the difficult ones are difficult. I think we would see most cases, but I can certainly think offhand of a number of cases where there was a known pancreatic cancer that we couldn't identify. So there is certainly cases we don't see" (Radiologist)* *"In 70 or 80% of the cases you're going to get the diagnosis with a good quality CT but you have to remain mindful of the patients who have presented with symptoms of concern such as weight loss, new onset diabetes or abdominal pain. You have to be careful not to rely solely on the CT and so therefore liberal use of EUS may be appropriate." (HPB Surgeon)*
		The quality and interpretation play a large role in my confidence to diagnose PC	*"A good CT is better than a bad MRI. The MRI does sometimes have complementary information on it, like diffusion weighting and that sort of stuff that can that weren't actually visible on the CT. I tend to favour CT's because I find them just easier to look at." (HPB Surgeon).* *"I tell patients don't go to the cheap local bulk billing radiology service because they don't do good quality scans, and the reports are you know next to useless" (HPB Surgeon)* *Virtually all of the major HPB and pancreatic cancer cases need further imaging - ever have somebody who has had all the diagnostic imaging work done, I would say never. The only time that that would ever happen is if it's been referred to me directly (HPB Surgeon)* *I think pancreas cancer is much harder to diagnose in the undefined patient where you're doing a general CT and your index of suspicion is not very high, and it can be a very subtle and an easily missed finding." (Radiologist)*
Beliefs about consequences	Benefits	PPCT or MRI are the best available imaging modalities for diagnosing and staging of PC	*"CT imaging is our cornerstone, and having good quality CT imaging is essential, and MRI can sometimes add important additional information" (Rad Oncologist)* *"If you ever get referred to a radiology department for a CT with query pancreas cancer, to not have a pancreas specific CT protocol is negligent practice" (Radiologist)*
	Cost to the patient	Not having a PPCT or MRI may result in missing out on potential for curative surgery or undergoing unnecessary surgery.	*"Some people will miss out on the potential for a curative operation, and others will be operated on unnecessarily." (HPB Surgeon)* *"In more than half of the patients the disease is worse in life than it is on the scans, and you end up doing more extensive operation, portal vein resections which you weren't expecting, sometimes arterial resections that you weren't expecting to do." (HPB Surgeon)*
	Routinely applied PPCT or MRI	We do not request or use a PPCT or MRI if it is clear the patient is unsuitable for curative treatment	*"Somebody who is elderly, very frail, they've got a metastatic disease and you've done a very poor quality [CT or MRI] but it looks very obvious they've got a metastatic disease or non-metastatic disease, should you put somebody through a CT scan or a MRI scan where that patient it has no bearing on the treatment. If they have metastatic disease, they are never going to go to surgery, they are never going to go through chemotherapy, they are elderly, and in a nursing home, the question would be then why are we doing this? The answer is we shouldn't be doing it in this case." (HPB Surgeon)*
Motivation and Goals	Incentives	There are disincentives for undertaking a PPCT or MRI	*"There's a disincentive to do a scan on someone in the private sector. If you have a patient who is referred to you as pancreas cancer and they are non-metastatic, then there is an opportunity to operate on them. If you then do a proper CT and identify that they are unresectable you cannot justify operating on them. In the private sector there is potential for unscrupulous activity and not doing the scans and just operating on the patients and finding they are not resectable. So it's a bit perverse" (HPB Surgeon)*
		The best incentive is providing good quality care	*"I think the incentive is just patient care, I don't think there's anything more than that. And doing the best job by the patient" (Radiologist)*

Implementation of a pancreatic protocol CT (PPCT) or magnetic resonance imaging (MRI) for diagnosis and/or staging			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
		Rebates should be offered for MRIs	*"I think it would be ideal if the MRIs were rebated so that you could get them done as necessary in an appropriate facility in a timely manner. If a patient's under surveillance who have a planned scan in 6 months or 12 months they can go to the public hospital and get it done, but you still can't do that for pancreas pathology, you can do an MRCP as an outpatient which doesn't incur cost. But the moment you start adding contrast agents into the MRI, it costs the patients money, and it's a significant amount of money for some people who can't afford it. That needs to be addressed as far as incentive is concerned, you need to have it [MRI] accessible so that you can do the appropriate tests at the appropriate time" (HPB Surgeon)*
Memory, Attention and Decision Processes	Reminders	There are no reminders in place to prompt us to order a PPCT or MRI	*"No there's no reminder systems. There's no checklists. We just rely on ourselves getting it right." (HPB Surgeon)*
		Multidisciplinary team meetings work as a prompt or reminder to order PPCT or MRI	*"If you have missed something that can become quite obvious at the MDT" (Gastroenterologist)* *"I mean the MDT process is a safeguard I guess to make sure the patients don't fall through the cracks in terms of appropriate investigations or tests being performed" (HPB Surgeon)*
Environmental Context and Resources	Environmental Stressors	A CT is more accessible than an MRI	*"We have a waiting list for imaging, and we have an enormous waiting list for MRI so many months. If you are lucky you'd get a CT more than likely next week but you'd get an MRI in many months. So we have a huge restraint on our ability to do what we want to do and we have to find ways around that." (Med Oncologist)*
		Travel is a burden for getting a PPCT or MRI	*"There's always the tyranny of distance in regional Australia, so you know some of my patients have to travel two or three hours by car to get to the closest radiology service." (HPB Surgeon)*
	Rebate or Funders	There are rules or regulations from rebates or funders that influence my decision about using a PPCT or MRI	*"We always make sure we put down MRCP, with MRI of the pancreas, to make sure there's a decent rebate for the patient" (HPB Surgeon)*
	Costs	PPCT is more affordable than MRIs	*"From the MRI side of things it's a little bit harder because it's a more costly test, it's a more intensive test, it takes more time, and not every patient is suitable." (Radiologist)* *"Between normal CT and pancreatic CT there's little difference but between no MR and an MR there is a huge cost difference." (Radiologist)*
	Organisational Perspective	The volume of cases is a significant consideration on whether the organisation focuses on PC	*"In the post treatment staging and the pre-operative work up that responsibility largely falls to me. The reason that has occurred is because I'm the only HPB surgeon here so if I was working at a bigger unit with more HPB surgeons then essentially the arrangement would be different that we would probably have an allied health member who would then become the co-ordinator, but we don't really have that system set up" (HPB Surgeon)* *"Our unit here likes to regard itself as a pancreatic centre of excellence, I think we perform almost half of the resections across the state, we've published our outcome results… it's driven a lot by the surgeons, but it's a high volume self-declared pancreatic specialist unit" (Radiation Oncologist)*
Emotions	Feelings	There can be a nihilistic attitude towards PC	*"There's a nihilistic attitude, even in a meeting that we have for example, if the patient's 83 or 84 and they've got pancreas cancer and somebody requests a proper CT, there'll be people who question whether you really want to put them through it, the patient's old and they're not going to get to surgery and you're sort of pushing it. So that's sort of an emotional response rather than a clinical one, you know it's a value judgement on the patient and sort of you know rolling your eyes like what's the value of this, what's the point of this?" (HPB Surgeon)*
		Patients influence decisions on whether to do a PPCT or MRI	*"On occasion patients, especially rural patients, are very pragmatic and will say I don't want to know if I have pancreas cancer, I really don't actually want to do that much about it and so there are on occasions some patient factors that might influence your decision about how aggressively to investigate and treat." (HPB Surgeon)* *"MRI's do generate some anxiety in quite a lot of patients and patients often need sedation to have MRI's. They are quite noisy and quite claustrophobic so patients don't like that. If you're sitting with a patient who needs an MRI and they say "I'll need to have sedation" you think, this means you do generally have to send them to a public hospital because we have less facilities in private centres." (HPB Surgeon)*

Implementation of a pancreatic protocol CT (PPCT) or magnetic resonance imaging (MRI) for diagnosis and/or staging			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
Behavioural Regulation	Protocols or Referral Pathways	I am not aware of any protocols or referral pathways for PPCT or MRI	*"I think that's a problem because we don't follow pathways and we don't follow a pathway that's strongly evidence based that embeds quality within it." (Medical Oncologist)* *"I'm not sure that it's spelled out in writing anywhere in terms of a protocol, you'd have to ask the radiologists that. Certainly from a surgical point of view we don't refer to protocols." (HPB Surgeon)* *"I don't know if it's, there's a unit handbook that's given to all the registrars, and if they don't know that they soon find that out, because you know you order the scan it's the wrong one you just have to order it again." (HPB Surgeon)*
		We have clear protocols for management of patient with PC	*"We've got a pretty coordinated approach to the management of the patients, all the surgeons and oncologists follow the same protocols. There has to be good reasons that people wouldn't have proper treatment, we follow pretty aggressive treatment protocols for patients" (HPB Surgeon)*
Nature of Behaviours	Established practices	We have well established practices to ensure that the work remains in the vicinity	*"We want to keep the work here and not lose it to metro… why, because it's interesting and 2) it serves patients well. Part of the integrated cancer work is to provide best work close to home as is reasonably safe" (HPB Surgeon)*

Table 4.2: *Summary of relevant TDF domains, belief statements and representative quotes*

4.4 Discussion

Appropriate implementation of a PPCT or MRI reduces the risk of an adverse outcome in patients who are diagnosed with non-metastatic PC. Proper staging including PPCT/MRI allied with assessment of co morbidities enables informed personalisation of therapy to a surgery first, neoadjuvant, chemotherapy or supportive pathway, minimising futile interventions. Behavioural research can help identify the factors that influence the implementation of this best practice. To our knowledge this is the first study to explore the barriers and enablers to the use of PPCT or MRI for diagnosis and/or staging in PC using the TDF as a guiding framework. The use of the TDF allowed for a comprehensive evaluation of specialists' behaviour with respect to this practice, using a systematic approach. It provides a basis from which to tailor future interventions aiming to overcome barriers and harness enablers, and so improve uptake of PPCT or MRI and therefore potentially improve outcomes for patients diagnosed with PC. Further, our approach to this study was based on methods implemented by Graco and colleagues which have been important in categorising the opinions of specialists.[103] However, in our study we opted not to include the frequency of belief statements to avoid important beliefs being overlooked.

Current practice shows that diagnosis of PC is often reliant on preliminary imaging such as a single phase CT scan or an endoscopic ultrasound (EUS), followed by referral to the appropriate specialists who may then order a PPCT to stage PC preoperatively if appropriate (*Appendix 4.2*). *Knowledge* and *skills* were revealed as important domains in this study, as it was not widely understood that there is a hierarchy approach to the application of PPCT or MRI. We did not anticipate this gap in knowledge or awareness related to the recommendations within clinical practice guidelines and the differences in perspectives on the information provided by a PPCT compared to MRI. The PPCT has higher accuracy in identifying the extent of PC, locoregional extension, vascular invasion, distant metastases and

resectability, whereas the MRI has some advantages over CT in detecting small tumours, distant metastases especially to the liver and isoattenuating tumours.[104] Therefore, MRI is best reserved for diagnosis rather than staging of PC, particularly as highlighted in our study, it is a more challenging modality both from a clinical and patient perspective.

Pre-operative staging using a PPCT, ideally reported using standardised templates, provides confidence and enhanced decision-making ability to surgeons on patient selection for surgical resection.[105] A practice of concern was the motivation to undertake surgery without the necessary preoperative staging by some surgeons. Without proper staging using a PPCT, the likelihood of achieving complete curative resection is at risk and patients who may have benefited from neo-adjuvant therapy may miss out due to surgery undertaken too early.[89] Organisations, should have systems in place to ensure patients with clinical suspicion of PC undergo proper staging to better select patients likely to benefit from surgery with curative intent. A potential safeguard is the mandatory presentation of patients to MDT meetings prior to management decisions being reached, especially where considerable multidisciplinary expertise is essential for optimal care and all the more so in smaller/low volume centres.[106] The use of protocols and algorithms for the investigation and staging will be more likely to ensure uniformity and equity of access to care.[107]

Although not viewed as an impediment to receiving a PPCT or MRI, several factors resulted in delays to receiving appropriate imaging. Such factors included referrals to other specialists, the distance travelled to reach radiological services, as well as the technical details of the actual scans, accessibility of the reports and finally the quality of the scan and interpretation of the radiological report. A cross-sectional study assessing presentations to a GP before a cancer diagnosis found that patients with PC were at the highest risk of presenting multiple times before being referred to an appropriate specialist.[108] Further research is required to understand the timeliness of referrals, the impact of distance on

protocol-based imaging and the quality of imaging in primary care. Participants in this study believed that radiologists and radiology services that specialise in pancreatic radiology produce imaging and reports of higher quality. An opportunity also exists for radiologists to play a more proactive role in contacting the primary provider to hasten the implementation of a PPCT in a single session if they become suspicious of pancreatic aetiology. Therefore, further research would explore: (1) the GP's understanding of the importance of referring patients to specialist radiology services; and (2) radiology centres taking responsibility for ensuring that patients with a suspicion of PC receive the best available service (requiring the necessary expertise in pancreas radiology).

Within the domain of *environmental context and resources*, it was widely understood that without access to PPCT as well as skilled radiologists, hospitals with a low-volume of cases may be disadvantaged compared to high-volume tertiary metropolitan based centres. A meta-analysis reviewing the relationship between hospital volume and outcome confirmed the association between higher hospital volume and lower post-operative mortality and lower length of stay.[46]

This study provides detailed insights into the perceptions of specialists involved in deciding whether a patient has a PPCT or MRI and whether it is undertaken. The breadth of the specialists involved in the project across two States in Australia provides a novel and broad view of barriers and facilitators.

A limitation of this study was that we had less participation from disciplines other than surgeons in NSW, and this limits our ability to report on a range of perspectives from this state. In a similar respect we may not have captured all perspectives from individual disciplines due to lower participation. For example, only one radiation oncologist agreed to be interviewed in this study, although four were invited and followed-up. Further, a well-known concept in qualitative research is data-saturation. Although we interviewed a

heterogenous population, data was collected until no new information presented on the barriers and enablers within the 12 a priori domains.[109]

4.4.1 Recommendations

Our study highlights the importance of the TDF domains of *knowledge, skills* and *environmental context and resources* in understanding the diagnosis and staging practices for PC.

Clinical practice guidelines that are often systematically developed, based on the most current evidence, and have the potential to improve health outcomes and provide consistency of care.[110] Deviation from guidelines can occur if organisational protocols or procedures do not align with international, peer-reviewed, evidence-based guidelines. Organisational protocols should be revised and kept up-to-date with current evidence.[111] Given that a barrier to the routine implementation of PPCT is the lack of knowledge, we recommend the dissemination of knowledge to clinicians and mechanisms to profile such guidelines through forums that provide educational opportunities.

There is evidence that audit and feedback, and reminders can attain positive behaviour change.[112] Further, an earlier review highlighted a lack of health services research examining the influence of guidelines in PC management.[113] This study adds important literature on the use of clinical pathways to facilitate the implementation of guidelines by identifying practices and beliefs that prevent evidence-based care. An important consideration is the role of MDT meetings as a reminder for undertaking PPCT or MRIs, providing access to a range of relevant disciplines, especially specialist radiologists and a forum for receiving feedback. While MDT meetings are endorsed as best practice in cancer care, they are not mandatory and this can limit the consistency in care received by patients.[114]

4.4.2 Conclusion

It is imperative that diagnosis and staging investigations using the most appropriate imaging modalities are conducted in a timely, efficient and effective manner. This qualitative study used a knowledge translation approach and psychological theories in health to explore factors associated with implementing the appropriate imaging investigations for diagnosis and/or staging in PC. The results provide an understanding of specialists' opinion and behaviour in relation to a PPCT or MRI and should be used to inform the design of future interventions to improve compliance with this practice.

4.5 Chapter Summary

In this Chapter, we explored the barriers and enablers to protocol imaging. This project used a knowledge translation approach, underpinned by the TDF to understand the reasons why evidence-based practice may not occur. The manuscript for this study is currently under review.

In total 21 clinicians (5 radiologists, 10 surgeons, 2 gastroenterologists, 4 medical and radiation oncologists) were interviewed over a four-month-period. Belief statements relevant to the TDF domains were generated. Across the 11 relevant domains, 20 themes and 30 specific beliefs were identified. All TDF domains, with the exception of *social influences* were identified by participants as relevant to protocol-based imaging using either a PPCT or MRI, with the domains of *knowledge*, *skills* and *environmental context and resources* being offered by most participants as being relevant in influencing their decisions.

PC has amongst the lowest survival of any major cancer type. Therefore, to maximise outcomes and personalise therapy it is imperative that diagnosis and staging investigations using the most appropriate imaging modalities are conducted in a timely, efficient and effective manner.

An important consideration highlighted in this study is the role of the MDT meetings as a mechanism for providing individualised treatment plans to optimise care. It is the next QI that is explored in Chapter 5.

"A miracle is just a glimpse of super-conscious laws. It can be empowered in one's being only when there is receptivity and conductivity. The true miracle is the transformation of oneself from negativity to positivity, from scepticism to spirituality, from cynicism to love-experience, and from reasoning to realisation"

Srinivas Arka

Chapter 5: Barriers and Enablers to Multidisciplinary team Meetings

In this Chapter, we take a further step to explore the barriers and enablers to the perceived value and efficiency of MDT meetings. This remains part of the final aim of this thesis and objective 5.

Evidence-based clinical practice guidelines recommend MDT discussions to review and plan management of patients in a variety of cancers. The objective of such collaboration is to enhance interaction between specialities enabling the expertise of different disciplines to inform on the optimal stage-specific care pathway for these complex conditions. The perceived value of the MDT discussion is dependent on attendance, timing, leadership, teamwork and culture. However, not all patients diagnosed with cancer are presented at an MDT meeting.

The objectives of this study were to: (1) identify the factors (barriers and enablers) influencing presentation of all patients to, and the perceived value of, MDT meetings in the management of patients with PC; and (2) identify potential interventions that could overcome modifiable barriers and enhance enablers, using the TDF.

The methods in this chapter are similar to that presented in Chapter 4, with the exception that palliative care specialists and nurse specialists were also approached for participation. The full study is as follows.

5.1 Background

Case discussions at multidisciplinary team (MDTs) meetings play an important role in selecting the optimal management strategy in a variety of cancers.[115] Prior to the era of MDT meetings, cancer treatment and management was often influenced by individual attitudes and beliefs, without formalised communication between specialities.[116] Presentation of patients with newly diagnosed pancreatic cancer (PC) to a MDT meeting is now recommended as the standard of care to plan treatment and for disease management across all tumour stages: potentially curable, locally advanced and metastatic PC.[81,94,95] The objective of such collaboration is to enhance the interaction between specialities enabling the expertise of different disciplines to inform a personalised stage-specific care plan taking into account a patient's functional status and preferences.[117] Specialities that may need to be involved in these MDT meetings (with the extent of input depending on a range of factors including but not limited to disease stage) include surgery, gastroenterology, medical and radiation oncology, radiology, pathology, palliative care, nursing and allied health.[118]

Whilst the impact of MDT meetings on survival outcomes in cancer has not been definitively proven, the benefits to patients whose details are discussed at MDT meetings stem from them being more likely to receive accurate and complete pre-operative staging and neo-adjuvant/adjuvant or palliative treatment compared to those who are not discussed at MDT meetings, as well as engagement of sub-specialists relevant to their specific circumstances.[119,120] In an Australian-based study of patients with PC, 21% of patients were considered to be unsuitable for surgical intervention following the MDT discussion.[121] In a further study in oesophago-gastric cancer, 24 % of patients had their treatment plans modified following an MDT discussion.[122] Therefore, MDT meetings can optimise patient selection for specific treatment. In the case of localised disease, this may avoid adverse surgical outcomes such as planned procedures and surgery being abandoned intraoperatively

or a macroscopic margin-positive resection, thereby avoiding unnecessary surgery and its subsequent morbidity.[49]

In the case of patients with advanced disease, the perceived value of discussing patients with advanced PC at MDT meetings is somewhat controversial, but MDT meetings may contribute to optimal medical management (e.g. appropriate choice of systemic chemotherapy and symptom management), as well as early referral to palliative care services, the benefits of which have been clearly demonstrated in advanced lung and gastrointestinal cancers.[123-125]

A set of quality indicators for PC was developed by Australian clinicians in 2018 and adherence to these indicators was evaluated using data collected by the Upper Gastrointestinal Cancer Registry (UGICR), deemed as a clinical quality registry.[60,61] Case discussion at an MDT is one of these quality indicators. Preliminary data from the UGICR show that 33% (n=278/831) of newly diagnosed patients were not discussed in an MDT setting, with the majority of these (n=209/278, 75%) being patients with metastatic disease.

While MDT meetings provide a useful mechanism to discuss treatment pathways, currently for patients with potentially operable disease, single organ metastatic disease, or for whom the diagnosis is uncertain[92] data from the UGICR show that in 21% (n=41/188) of cases, surgical treatment was undertaken prior to discussion at the meeting. This practice is not aligned with clinical guidelines that recommend diagnostic workup of a suspected mass and that treatment should be performed after discussion at an MDT meeting.[26,126]

In light of these observations that not all patients are currently discussed at MDT meetings, and, in some cases, discussed after treatment, there is apparent variation between evidence-based/agreed optimal practice and observed current practice.

Therefore, the aims of this study were to:

(i) explore the barriers and enablers to case presentation of all patients diagnosed with PC to an MDT meeting;

(ii) identify the factors influencing the perceived value of MDT meetings in the management of PC; and

(iii) determine potential intervention components that could overcome modifiable barriers and/or enhance enablers.

5.2 Methods

Please refer Chapter 4.2

5.3 Findings

5.3.1 Focus Group

Twelve clinical experts were invited to participate in the focus group interview and nine participated. The focus group comprised three surgeons, two medical oncologists, a radiation oncologist, a palliative care specialist, a nurse specialist and a cancer nurse care specialist. The decision tree developed by the focus group to describe the pathway for delivering evidence-based, clinical practice is presented in *Appendix 4.2* and articulates the referral pathway necessary for the case presentation of patients with PC to an MDT meeting for discussion.

5.3.2 Interviews

A total of 59 medical and 3 nursing specialists, 16 (26%) of whom were female, were approached across the two states and 26 medical and three nursing specialists were interviewed, giving a 47% response rate. Participant characteristics are summarised in *Table 5.1*. Most were male (n=22, 76%), worked in metropolitan settings (n=22, 76%), and were from Victoria (n=18, 62%). Interview duration ranged from 12 to 62 minutes, with an average interview time of 25 minutes.

DISCIPLINE	Invited	Included	NSW	VIC	Metro	Regional	Public	Private
Surgeon	18	10	4	6	7	3	9	1
Radiologist	7	5	1	4	4	1	4	1
Med. Oncologist	13	3	1	2	1	2	2	1
Palliative Care	10	5	2	3	4	1	5	-
Nurse Specialist	3	3	1	2	3	-	3	-
Gastroenterologist	7	2	1	1	2	-	2	-
Rad. Oncologist	4	1	1	0	1	-	1	-
TOTAL	**62**	**29**	11	18	22	7	26	3

***Table 5.1**: Participant characteristics*

5.3.3 Factors influencing the conduct and perceived value of an MDT meeting

Across the relevant domains, 22 themes and 40 specific beliefs were identified.

All TDF domains resonated with participants as relevant to the effective implementation of MDT meetings, with the domains of *environmental context and resources*, *skills*, *beliefs about capabilities, motivation and goals* and *social influences* being by most participants as influencing their attendance at, and decisions relating to, case presentations at MDT meetings. *Table 5.2* summarises the main belief statements generated from these interviews, categorised according to the domains of the TDF. Each belief statement is supported by representative quotes.

Implementing knowledge into practice

In the domain of *knowledge*, a small number were not aware (or in the case of metastatic disease, did not agree) that all patients diagnosed with PC should be presented to MDT meetings, reporting a lack of awareness of the guideline recommendations. The participants who did not feel that it was their role to place patients on the list for MDT meetings (*social/professional role and identity)* tended to be less familiar with the guideline recommendations. Further, some reported having a well-established practice with respect to MDT meetings as the standard of care and a training ground for new clinicians (*nature of behaviours*), with a minority reporting that MDT meetings have been held in their organisation for at least two decades. Although MDT practices have been well established in

some organisations, around half the participants reported that there were no clear protocols or established referral pathways facilitating the case presentation of all patients to MDT meetings (*behavioural regulation*). In addition, the majority of participants reported relying on their memory to place patients on an MDT list, with others finding email reminders from MDT coordinators to be significant prompts to placing patients on the list (*memory, attention and decision processes*).

Disciplines not represented at MDT meetings

The majority of participants reported wide representation at MDT meetings from disciplines including surgeons and oncologists, nurse care coordinators and junior staff members (*Skills*). However, more than half the participants interviewed observed a lack of palliative care representation at MDT meetings. The palliative care specialists interviewed reported being aware of the lack of widespread participation by their specialty and believed their attendance at MDT meetings would allow a wider representation of patient values. However, they also reported that clinical commitments often took precedence, limiting their ability to regularly participate in MDT meetings (*environmental context and resources*). A less prevalent belief relevant to palliative care reflected the paradox that patients most likely to significantly benefit from palliative care input were often not presented for discussion because of the lack of palliative care representation (*skills*). In addition to palliative care, a few felt that MDT meetings would benefit from psychologist or psychiatrist attendance (*skills*).

Benefits, roadblocks and incentives

Overwhelmingly, those interviewed agreed that MDT meetings were beneficial and an important aspect of care, resulting in less risk to patients (*beliefs about consequences*). However, many participants reported that there was limited capacity to discuss all patients at the MDT meeting due to time constraints. It was evident that, for a number of clinicians,

patients with advanced or metastatic disease in particular were not discussed as “there were too many of them” (*beliefs about capabilities*).

A small number of interviewees did view MDT meetings as a potential “roadblock to care,” as in some clinical scenarios they viewed it possible to deliver timely treatment without the need for an MDT discussion. A minority of participants believed that a “a good specialist” does not necessarily need to wait for treatment decisions to be made at an MDT meeting as they were responsible for their own actions (*beliefs about capabilities*).

Approximately half the participants reported that providing good-quality care was an important driver for participation and factors such as the opportunity to enhance learning were useful incentives that motivated attendance (*motivation and goals*). So too were practical enablers that facilitated time-management for busy clinicians (such as food and/or coffee for meetings held early in the morning). There was some variation in the responses to the potential benefits of financial incentives, with some participants aware that there was the option of the hospital claiming financial compensation for discussing a patient at an MDT meeting. However, due to reasons such as the required paperwork to realize these payments, these payments were often unclaimed and difficult to implement, and yet did not reduce their drive to attend (*motivation and goals*).

Running on goodwill

Radiologists reported they were often required to spend time prior to the MDT meeting reviewing images for presentation at the MDT meeting and that this was challenging if there were large volumes of cases to review in a short period of time (*beliefs about capabilities*). The burden of this preparatory review of imaging for MDT meetings was high, particularly in institutions running a number of separate MDT meetings. Radiologists reported feeling frustrated and fatigued by the MDT process and the need to review cases for a significant number of MDT meetings over a given week or fortnight. Radiologists also expressed

frustration at having to review cases at short notice which may have influenced the "optimal assessment" of these cases (*emotions*) impacting on the accuracy of interpretation and duty of care to patients.

Interviewees acknowledged that their participation in MDT meetings can vary due to numerous factors and a recurring belief identified was the number of MDT meetings that participants were required to attend. Other factors were competing clinical commitments and the scheduling of the meetings with many reporting that their MDT meetings were often held afterhours (*environmental context and resources)*. A common belief by the majority related to the substantial costs associated with the conduct of MDT meetings, given the number of specialists "sitting" in a meeting and the overall staff time involved which could result in inefficiency (*environmental context and resources*).

Organisational focus and resourcing

The perceived value and efficiency of an MDT meeting depended upon the organisational focus and resources allocated to it. A majority of the participants reported a strong organisational focus on MDT meetings within their settings, with a few believing this focus was excessive. The investment made by some organisations in advanced technological solutions was perceived as an important enabler, albeit that they only worked well with good internet connectivity and the implementation of video conferencing to facilitate the interchange between specialists at different hospitals. A few participants provided their perspectives on the current gaps which included the lack of clerical support or MDT coordination, and in some organisations, MDT meetings being cancelled due to staffing issues. In addition, MDT outcomes were reported to be poorly captured and difficult for specialists to refer to at a later stage (*environmental context and resources*). In the organisations where nurse specialists attended, they viewed their roles as a patient advocate,

with the ability to triage referrals, monitor patient symptoms in the outpatient setting and provide supportive care when required (*professional role and identity).*

The role of social influences on participation

Over half the participants regarded the MDT meetings positively with many stating that they found the discussions enjoyable and collegiate with a supportive environment that fostered development of junior specialists (*social influences & emotions*). However, a minority of participants believed that "dissenting views … can create issues for clinicians" leaving some at a crossroad as to whether to use their own clinical judgement or follow the recommendations of the MDT. A few participants highlighted that the skills of the MDT chair are important in "curtailing unnecessary discussions" or "keeping vocal colleagues in tow". Many reported that the surgeons often lead the discussions as they were the primary clinicians. A minority reported voicing their opinions in an MDT meetings to be challenging and waited until after the MDT meeting to discuss their perspective with fellow specialists (*social influences)*.

The key barriers and enablers from the interviews are summarised in *Table 5.3*.

Disease Management for all patients discussed at a Multidisciplinary Team (MDT) Meeting			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
Knowledge	Clinical Practice Guidelines	I am aware that clinical practice guideline recommends all patients diagnosed with PC are presented at MDT meetings	*"Yes we're familiar with those [recommendations] but it's not something we look at on a week to week basis, but we know they exist, and I think we comply with them largely." (HPB Surgeon)*
		I am not aware that clinical practice guideline recommends all patients diagnosed with PC are presented at MDT meetings	*"I don't even know what you mean by guidelines, most patients as far as I know are presented, I said 99% before, but I don't know if there's guidelines actually" (Nurse Specialist)*
	Research	I am aware of research on the effectiveness of MDT meetings in PC	*I'm aware the research is there, and in fact it was emailed around to the group, but I have to admit I didn't read it." (Pall Care Specialist)*
		I am not aware of any research on the effectiveness of MDT meetings in PC	*"I'm not particularly aware, no not particularly, I don't know that there's any specific research that I've seen that would indicate that they do better or worse." (HPB Surgeon)*
		Quality is an important driver for a successful MDT meeting and is an important area for research	*The primary focus of MDTs is patient care, but in the longer run if you do not maintain the quality, [patient care] will slowly get less important. (Palliative care specialist)* *The areas of research which we do need to consider is the consistency of MDT decisions both between MDTs across in different jurisdictions or states, or even within local health districts or between hospitals, and also consistency within the MDTs over a period of time. (HPB Surgeon)*
Skills	Attendance	There is wide representation from numerous disciplines (craft groups) at our MDT meetings.	*"By craft group we have the hepatobiliary surgeons, gastroenterology, radiology, pathology, oncology, radiation therapy, radiation oncology, and then there are nurse coordinators from various units, but they sit more quietly at the back so I don't know who they are and exactly what their job is" (Radiologist)*
	Gaps	The absence of palliative care representation is a gap in the MDT meetings	*"I think the most important thing at the MDT meetings [is] that someone actually knows the patient and I think that differs from what some of my colleagues think. One of my colleagues says that the most important thing is that they come up with what would be the ideal management from the cancer's point of view and then see whether it applies to the patient. Whereas I'd probably come from the other way around and say someone in the room needs to know the patient and what is likely to be appropriate for them." (Pall Care Specialist)* *"We would be incredibly useful, just for a moment to say hang on a minute how old did you say that patient was again, and just to drop that in and that can change the flow of the decision making in that patient, to perhaps prevent some treatment that might not be in the person's best interests, or to swing in earlier with support services to enable them to tolerate the treatment better or – but because we're not there that doesn't happen" (Pall Care Specialist)* *"You should have a palliative care physician if you're going to treat all patients with pancreas cancer. We don't, and we function without them, but you know you should." (HPB Surgeon)*
		The absence of a psychologist or psychiatrist is a gap in the MDT meeting	*"I would expect a psychiatrist to be involved because you recognise that depression is common with pancreatic cancer. It can occur a year or two even prior to the diagnosis of the pancreatic cancer, and then having cancer in itself obviously has a lot of psychosocial effects on the patient and their family as well" (Pall Care Spec)*
		Being an MDT chair is an important skill to ensure the meeting runs effectively	*"We'll often have 20 patients to discuss which we'll need to get through quite quickly ... We'll get through them, but we have to sometimes curtail our discussions and that's kind of the role of the MDT chair is to cut the nonsense out of a meeting and just get inputs down on paper pretty quickly and move on." (HPB Surgeon)*
Social/Professional Role and Identity	MDT List	It is the role of the primary clinician to place patients on the MDT list	*"I think that that comes down to the unit that first takes the referral, so we get some from hepatobiliary surgeons, or some from the gastroenterology unit, and so the clinician who first makes contact whether that's the person who saw them in clinic or the person who saw them in ED, would, refer them to the MDT managers, the meeting list for that unit, and then they make sure that they're processed" (Radiologist)*
Beliefs about Capabilities	Radiology Input	It can be difficult for the radiologists to review imaging in time for MDT meetings	*"It's the capability of the radiologists to look at all the scans in time, if they're presented with 30 cases to do tomorrow morning, they're capable of doing it, if they stay here until midnight, that's really the limiting factor" (HPB Surgeon)*

Disease Management for all patients discussed at a Multidisciplinary Team (MDT) Meeting			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
	Discussion of all patients	There is no capacity to discuss all patients at a MDT meeting	*"In GI cancer multidisciplinary team meeting, we see maybe 30% of all GI cancers prior to initial management and maybe 50% in total. So if there was a demand for every patient being presented at a multidisciplinary team meeting I think it would require a doubling of resources." (Med Oncologist)* *"Patients who have widespread metastatic disease they don't need to be discussed at a MDT, they're sometimes put in for audit, but we don't talk about them, there's no point-… we have 45 patients that we talk about each MDT, and you can't. There's too many of them" ((HPB Surgeon)*
		Patients are placed on the list for the next meeting if they are not discussed at the present MDT meeting	*"The discussion will then be carried forward for another time. If there's someone who is particularly urgent we can obviously dial in we have the capacity to teleconference and if there's an urgent patient, I'll get my registrar to present the case to the MDT so some can be carried over and obviously some can't and that's on a case by case basis." (HPB Surgeon)*
		MDT meetings are not regarded as a roadblock to treatment	*"Obviously if they're a jaundice patient with pancreas cancer then I'll occasionally be forced to go ahead and put a stent in ERCP before the MDT discussion taking place. I think there are reasonable things you can do which won't breach the MDT protocol and so you have to keep that in mind but there are things that can be done you know before the MDT discussion takes place, within reason." (HPB Surgeon)* *"in terms of decision making in terms of what needs to be done, the MDT is not that important" (Rad Onc)* *"You can't place your responsibility on the MDT, you are still responsible…, the MDT is a tool, it's a guidance rather than a definitive - you are still the provider and you are still responsible for your actions" (HPB Surgeon)*
Beliefs about consequences	Benefits	A regular MDT meeting is an important aspect of a patient's treatment and care	*"I think the benefit is huge, you are getting experts in a room so I think absolutely that is great thing to have and you can see the importance of having it when sometimes the consultants don't necessarily on the decision, the in-depth discussion about why they should be resectable and why they're not. You are actually exploring every avenue and trying to do what is best for the patient. I mean I think they're vital for patient safety, for their outcomes, for what actually is ethically right." (Nurse Specialist)* *"It enables good communication between all the specialists involved, so I think it creates a sense of unity, and it helps with data collection, and it helps ensure everybody is saying the same thing to patients" (Rad Oncologist)*
	Risks	There is a risk of inappropriate care when a patient is not discussed at a MDT meeting prior to treatment	*"If patients aren't discussed then there is a considerable risk that patients will inappropriately go to the operating room, because the radiologist hasn't said, "by the way they've got a small liver metastasis" that nobody's seen. Or because the radiologists would say, "that's wrapped around the artery there" and the surgeon didn't think that it was. The consequences are significant for an individual patient if they get the wrong or unnecessary treatment.*
Motivation and Goals	Incentives	Rebates for regular MDT meetings are inadequate or difficult to implement	*"In all honesty these meetings are very important, but they're certainly not financed and they're under resourced, so there's an extraordinary amount of good will that goes into MDT meetings." (Radiologist)* *"I think there's always talk about setting up for a Medicare rebate for the MDT, but there's always a barrier like the paperwork is too hard or the auditing is too hard or someone just doesn't want to" (Radiologist)*
		Food & coffee or educational incentives are attractive and encourage me to attend the MDT meetings	*"Food is a big incentive, we have lunch, if there's no food I leave because I have to eat, and I don't know some of the guys seem to be able to get through the meeting with no lunch, I can't do that. So that incentivises me to come." (Pall Care Spec)* *"It's actually very beneficial to my education, you know to have this group discussion and I just learn more and more, and that's why I'm probably so much more experienced now because I've been going to these meetings." (Radiologist)*
		Setting time aside is a good incentive to drive participation and quality of MDT meetings	*"One incentive would be to have time set aside to prepare for the MDT, which is not always possible due to staffing shortages but if the person who reviews cases for the MDT were able to set aside two hours the day prior that would be an incentive for sure" (Radiologist)*

Disease Management for all patients discussed at a Multidisciplinary Team (MDT) Meeting			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
		The best incentive is providing good quality care (which in turn protects from potential litigations)	*"I mean the biggest incentive is providing better care to your patients, and as clinicians there is no greater incentive than that. In terms of clinical audits and performance reviews, there should be a clear incentive there because, if you're discussing a patient through MDM and managing them as per the MDM recommendations, then you are also protecting yourselves from any potential litigations or malpractice scenarios." (Med Oncologist)*
Memory, Attention and Decision Processes	Reminders	There are no reminders in place to prompt us to place patients on the MDT list	*"I'm not aware that there are any [reminders] at all. I mean an online submission form is one thing with tick boxes and various other things that you have to fill out on it so that's the provision of data but in terms of actually saying this person needs to be discussed at a multidisciplinary team meeting I don't think there's any prompts that we have particularly." (Med Oncologist)*
		There are emails or prompts mainly from MDT coordinators that act as reminders to place patients on the MDT list	*"Periodic emails that comes out almost 3 times a week before the next MDM is due, so there is constant bombardment of emails from the MDT coordinator saying that the next MDM is coming up so put patients on if you've got any. Three days before the MDM a final reminder comes out … that often prompts people to put patients on" (Med Oncologist)* *"Previously we had a good care coordinator is gold, and she would say this patient's had 4 cycles of neoadjuvant chemotherapy and needs to be considered for radiotherapy, I'll organise a CT and put them on for discussion. The nurse would precipitate all of that. Good quality care coordination - absolute gold" (Rad Oncologist)*
Environmental Context and Resources	Organisational Perspective	There are proper resources allocated to hold regular MDT meetings	*"They're supported by the institution who are paying for the coordinators to do the coordinating, and we have a room that is dedicated for MDTs with a big screen, the pathologist's desk, and the radiologist's desks. Clearly, the organisation has put some time, thought, money into creating it. So institutionally I think the MDTs are supported." (Pall Care Spec)* *"Our department has a very heavy focus to the point that it feels like we spend more time in multidisciplinary meetings than actually reporting studies. Which you know is probably good." (Radiologist)*
		Patient care may be affected if there are gaps in resourcing	*"MDT's can't happen unless an organisation funds clerical support to coordinate the meeting, make sure the standards are there and that there's a focal point of contact to coordinate that in a clerical fashion. There's a huge burden on others and in some organisations if this is missing and that takes away from patient care." (Nurse Specialist)* *"When we're short staffed you either have to cancel the MDT or cancel something else … it's a meeting and it requires preparation and time. Sometimes we just have to cancel a meeting and there are meetings that have a higher priority in our view than others." (Radiologist)*
	Costs	The main cost is the time given by the radiologists and the clinicians	*"There's a huge amount of cost involved in MDT, that main cost factor is staff time because there's half a dozen physicians, surgeons sitting there for an hour in the actual MDT but there's a lot of work involved in preparing the MDT. For example, every pancreatic MDT requires at least two hours preparation of radiologist's time. (Radiologist)* *"There is a need to review the radiology and for 35 people to look at it and listen to the discussion about it there's potentially a lot of wasted time in MDT meetings and frankly that leads to frustration and also to non-attendance by some specialists." (Med Oncologist)*
	MDT Participation	Participation at a MDT meeting is affected by competing MDT meetings	*"That's part of the issue, we have our upper GI meeting, we have the hepatobiliary meeting, we have the neuro endocrine meeting, we have the pancreas meeting, we have the colorectal meeting, so we have a lot of GI meetings... we've got 5, 6 MDTs, it's a huge amount. (Rad Oncologist)*
		The timing of meetings is a barrier to our participation in MDT meetings	*"The other barriers are the timing, so multidisciplinary team meetings are frequently conducted after hours which makes it difficult for people who have work life balance issues. (Med Oncologist)* *"It's usually fairly early in the morning or very late, so it's not really built into the hospital timetable, so people really have to sacrifice their own spare time to get to them." (HPB Surgeon)*
		Other clinical commitments impact on participation in MDT meetings	*"We provide outreach surgery to other smaller places and on days that we've got to get out there after the meeting it's all a bit of a rush. So trying to have quarantine time to commit to the MDT is a challenge for*

Disease Management for all patients discussed at a Multidisciplinary Team (MDT) Meeting			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
			everyone involved and that's always going to be the case especially when you've got VMO's[visiting medical officers] rather than staff. Our surgeons are all VMO's here." (HPB Surgeon) *"Often in the MDT, the surgeon maybe called away to operate and they're not there at the meeting ... and if they've got patients then they get delayed again to the next meeting/week" (Nurse Specialist)*
	Technology	The use of technology increases the perceived value and efficiency of MDT meetings	*"For instance they [another site] have one room with I think three screens all large so they can do three different things at a time, probably about six or seven computers so that they can be changing what's on one screen while people are looking at another one and they actually record the notes in the meeting at the time by ticking boxes in spreadsheet pages or typing notes into spreadsheet or document pages… it is interesting how in the well-resourced hospitals they have capacity to do it much more efficiently " (Med Oncologist)* *"I think one of the biggest things about MDTs … there's certainly much more use of video technology, so that health professionals can sort of dial in by video conference, to be part of that conversation and discussion." (Pall Care Spec)*
		Technical issues are a barrier to an effective MDT meeting	*"Our equipment in the room is outdated and our screens are not a great resolution. Sometimes it is difficult to hear when the pathologist or the radiologist is speaking. There is a microphone in the room but I don't know if they're working" (Nurse Specialist)* *"We've discovered today that the bandwidth on Zoom for whatever reason here is sub-par and there were ten people online in the MDT meeting… we need an electronic system that supports the MDT adequately" (Med Oncologist)* *We get many cases from outside and the imaging is being viewed in ways that is not adequate for diagnostic use. It's time consuming and there's a cost factor because to incorporate the imaging into our system is expensive, the overall volume of external studies it's about storage space which is expensive. A CT is a huge amount of data and a single CT doesn't weigh in heavily, but we have thousands, tens of thousands CT's" (Radiologist)*
	Data Collection	There is poor documentation of outcomes following a MDT meeting	*"We don't have a good way of collecting data and outcomes at the meetings. It would be good to have a projected uniform database that we can all use to discuss cases. At present you might see them [patient] 2 weeks afterwards and say oh what did we recommend for that patient, and there's sometimes emails with the recommendations but they can be written with pretty scant information." [Rad Oncologist)* *"There's very poor documentation of what was discussed and recommendations, very poor communication with the GP, very poor communication with the patient. We don't have the DHS [Department of Health] MDT software, and there would be some merit in that. As we move to our new EMR [electronic medical record system] then it would be nice if we had agreed recording of a number of elements." (Med Oncologist)*
	Time	The length of time for a MDT meeting is a significant limitation for the volume of patients to be discussed	*"I think our MDTs are too short for the volume of patients, I think patients are just put through them just to pretty much dot the I's across the T's so that it's being done." (Nurse Specialist)* *"The meetings which happen every 2 weeks, that is a definite barrier to presenting everybody, because you know there is a time pressure. If the meeting's every fortnight all of a sudden it's 2 full weeks before the patient can be presented, so you have someone sitting with pancreas cancer that nobody's doing anything for. That is a definite barrier because there's a much greater incentive to just make up your own mind and do your own thing for that patient." (HPB Surgeon)* *"It's never sufficient [time] but it just has to do. This is where the chairperson comes in and makes sure that we don't go down rabbit holes … For someone with a CA19-9 of 70 and they are upfront resectable, should we be discussing, the answer is no, it's wasting other people's time, because you're going to get the same answer from everyone." (HPB Surgeon)*
Social Influences	Perception	MDT meetings are perceived positively by my colleagues and I	*"Well they keep coming so they must find them valuable. Valuable for their own education, valuable for raising the profile of their particular discipline, valuable for the social interaction they get with colleagues." (Med Oncologist)*

Disease Management for all patients discussed at a Multidisciplinary Team (MDT) Meeting			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
			"We made the effort about six or seven years ago - an MDT wasn't funded… no-one was forcing us but we felt that we should do it and so a bunch of surgeons invited the oncologists and we set it up and started running it and it's been well attended ever since. With no incentive other than professional satisfaction and diligence we set that up and people continue to support it so I would say that people think they're a good idea." (HPB Surgeon)
		There are dissenting views that can dissuade from a MDT meeting	*"With borderline resectable cases there is often a perceived sense that there could be dissenting view and the person presenting the patient might hold a particular view and others might not necessarily agree. Then you are in a situation whether you go ahead with your own clinical judgement or whether you feel that there is an obligation to follow the MDM recommendation. And often, no consensus can create issues for the clinicians." (Med Oncologist)*
	Communication	Communication in MDT meetings are often collegial	*"It's usually fairly collegial. It's seldom ever acrimonious. I mean occasionally somebody flies off the handle… usually we try and do that [respond] with a degree of emotional intelligence and sensitivity. " (Med Oncologist)*
		It is difficult to participate in the discussion	*"I'm not as confident, so I tend to have discussions with the various players outside of the meeting to make decisions ... certainly the men dominate, there's no doubt about that, and it is a very male MDT, so all the surgeons are male, and the current chair and the current main oncologist is male. So there are some challenges getting a female voice heard in that context, and particularly a female voice with a soft specialty like palliative care" (Pall Care Spec)* *"As a surgeon I would say no-one dominates but I'm sure the surgeons dominate. Many of the referrals come through the surgeon and then the oncologists who are the other major players but the surgeons do tend to dominate" (HPB Surgeon)* *Every meeting I feel I haven't made my own personal voice heard loudly enough or strongly enough. I often feel that I should've spoken up and I didn't. I can't adequately promote the cause of palliative care in that meeting. While I enjoy some of the discussion and I do put my 2 cents worth in, it really takes me to basically stand up physically and make my point to get my message across. (Pall Care Spec)*
Emotions	Feelings	MDT meetings are enjoyable and supportive	*"Professionally they're very enjoyable and it's one of the situations where you get to interact with your colleagues in a larger format, and you often get feedback on some of the cases that you might see and report, so that's always nice. And you get to be part of the decision making around the care of that patient – so that's fulfilling." (Radiologist)* *"We enjoy throwing ideas around and we enjoy the collegiate support that we've got from our colleagues. We can go back to a patient and say 20 people in the room agreed with this especially when you're a young surgeon or a young oncologist that can be daunting so it is good to have that support." (HPB Surgeon)*
		MDT meetingss can cause frustration and fatigue	*"24 hours is short notice [to review a case]…it doesn't enable us to review cases in a meaningful way and I think that's unfair on the patient and everybody else because treatment decisions are being made based on haphazard or not optimal assessment." (Radiologist)* *"There is such a thing as MDT fatigue definitely. We have around 10 meetings a fortnight, in a fortnightly cycle. So that's many meetings to prepare and attend." (Radiologist)* *"So radiologists and the pathologists every few weeks express genuine annoyance, they say this is really difficult for me to give an opinion, I didn't get any notification of this…it's quite understandable annoyance (Pall Care Spec)*
Behavioural Regulation	Protocols or Referral Pathways	I am not aware of any protocols or established referral pathways that facilitate the discussion of all patients with PC at a MDT meeting	*"Referral pathways in the regional centres are very complex…some general surgeons will send the pancreas cancers our way some won't. There is no way actually that we can sort of ensure that all of our residents are put through an MDT and so until the area executive deem that that has to happen and they mandate referral pathways then that's never going to occur." (HPB Surgeon)*

Disease Management for all patients discussed at a Multidisciplinary Team (MDT) Meeting			
Domain	**Themes**	**Belief Statements**	**Representative Quotes**
Nature of Behaviours	Established Behaviour	MDT meetings are well established as the standard of care and as a training ground for new clinicians	*"It's very hard to get a decision out of a trainee sitting an exam without having an MDT …generations of surgeons coming through are naturally going to want to discuss everything in an MDT." (HPB Surgeon)* *"In my mind it's well and truly established as a standard of care and I can't imagine that ever changing so I think everyone would be absolutely united in believing that this is critical, and you know should be appropriately resourced." (HPB Surgeon)*

Table 5.2*: Summary of relevant TDF domains, belief statements and representative quotes*

Summary of key barriers and enablers to the presentation of patients at MDT meetings
Identified Barriers
Awareness of clinical practice guideline recommendations that **all** patients with PC be discussed at an MDT meeting (*knowledge*)
Lack of palliative care representation at MDT meetings can result in fewer patients with advanced disease being presented (*skills*)
Lack of capacity to discuss large volumes of patients, including patients with advanced disease at current MDT meetings within allocated time (*belief about capabilities*)
Higher volumes increase the burden on radiologists for reporting at MDT meetings (*beliefs about capabilities*) and cause frustration or fatigue if cases are added at short notice (*emotions*)
Clinicians may not view MDT meetings as a requirement prior to initiating treatment (*beliefs about capabilities*)
A number of MDT meetings and clinical commitments impact specialist attendance (*environmental context and resources*)
Dissenting views that impact on a specialist's clinical judgement can deter attendance (*social influences*)
Healthcare professionals' confidence to voice their opinions at MDT meetings (*social influences*)
Identified Enablers
A regular MDT is viewed as beneficial to patient care (*beliefs about consequences*) and provides good quality care (*motivations & goals*)
Agreed protocols and referral pathways that can prioritise cases for discussion in a standardised manner for all stages of PC (*behavioural regulation*)
An MDT chair who is skilled at managing diverse views and developing a culture that ensures all participants get to voice their opinions where required (*skills*)
Participation in MDT meetings can be increased by incorporating the discussions into the working day rather than afterhours (*motivation & goals*)
Organisations with focus on MDT meetings provide the necessary resources such as MDT or care coordinators who facilitate the referral and care pathway following an MDT discussion, technical set-up and associated support (*environmental context and resources*)
Documentation and data collection can be improved with the inclusion of developed software systems specific to MDT meetings, provided it is supported with education and training (*environmental context and resources*)
A culture of collegial communication (social influences) can lead to increased participation and make MDTs enjoyable and supportive (*emotions*)

Table 5.3: *Summary of key barriers and enablers*

5.4 Discussion

We identified that the organisational structures central to MDT meetings were dependent on the organisation and chairing of sessions, adequate availability of key personnel, teamwork and culture. These, in turn, can be dependent on the structures external to the meetings, including factors such as the physical environment of the meeting venue, availability of technology and equipment and post-meeting coordination of services.[127] Our study highlighted some of these factors as key barriers and enablers to specialist attendance at MDTs, and the way in which their value is perceived. The most relevant TDF domains in our study were; *environmental context and resources, beliefs about capabilities, skills, motivation and goals and social influences*.

Planning treatment and disease management via MDT meetings is an important clinical and organisational intervention that can reduce the risk of adverse patient outcomes and inappropriate care for patients with PC.[128] In an Australian study, the authors showed a reduction in mortality from 16% to zero secondary to a number of initiatives, one being the inclusion of MDT meetings prior to PC surgery.[129]

Our research involved a theoretical exploration of health practitioner opinions and behaviour in order to identify the factors influencing the participation of key multidisciplinary craft representatives; several factors that may influence the presentation of all patients at MDT meetings; and the perceived value of the MDT discussions for patients with PC. This study provides a foundation to consider future interventions aiming to overcome barriers and/or harness enablers to improve not only the perceived value, but also the efficiency of MDT meetings, allowing more patients to benefit from this systematic approach to health care.

Our approach to this study was based on methods implemented by Graco and colleagues in categorising the opinions of specialists.[103] However, unlike Graco et al, we opted not to include quantitative assessment of the frequency of belief statements to avoid less frequent

but important beliefs being overlooked. This approach will guide the design of surveys to document those beliefs in a wider sample and ultimately the choice of interventions to optimise the benefits of MDTs for improved patient care.

Systematic reviews in oncology have highlighted that up to 45% of patients have changes in their diagnostic reports and up to 42% in patients with gastrointestinal cancers can have their treatment plans altered based on discussion at an MDT meeting.[119,130] Further, although the quality of MDT meetings may not have a direct bearing on whether cases are presented for discussion at a meeting, there is a reciprocal or interdependent relationship. A recent study highlighted that given the considerable resources allocated to MDT meetings, the evaluation of quality is an important factor in patient-care and treatment decision-making.[131]

The vast majority of our participants placed high value on the MDT meeting, agreeing that they are beneficial on many fronts including the education of junior staff and trainees. However, our study highlights the time and resource-intensive nature of the meetings and the burden they place on some specialities, most notably radiology. In addition, presenting patients across all stages of PC to time-limited MDT meetings is clearly not feasible or sustainable in their current form in many organisations, particularly as these same MDT meetings can also require the discussion of other cancers such as primary or secondary liver cancer and biliary cancer, all competing for time and focus such that patients with metastatic PC cannot be discussed. These impediments create a gap between "work-as-done" in the real world and "work-as-imagined" as proposed by guidelines. Organisations are resilient, complex adaptive systems where work gets done despite these challenges but it is important to acknowledge, understand and mitigate such challenges in achieving optimal functioning.[132] Strategies to enhance internal structures, so as to allow more patients to be discussed, are needed and have been proposed in the literature.[133] These strategies include virtual MDT meetings and the use of electronic MDT software packages and checklists to enhance referral pathways, healthcare professionals' participation, available time and data

collection (*Table* 5.2).[134,135] A real-world impact during the preparation of this chapter was the COVID-19 pandemic that facilitated the use of virtual meetings requiring upskilling on a global scale. The benefits of using virtual meetings has drawn positive reviews in a recent study but also have the added benefits of digitally recorded sessions, ease of access to clinical material (radiographs and advance imaging) and the ability to connect across different regions.[136]

Whilst the majority of participants were not aware of any protocols or referral pathways to facilitate the presentation of patients to MDT meetings, there is an opportunity to increase the volume of patients discussed by developing agreed protocols and referral pathways that can prioritise cases for discussion in a standardised manner for all stages of PC.[26,137]

Our findings show that the organisational structures external to MDT meetings that can be enhanced include the role of MDT coordinators, ensuring that competing meetings are booked at different times and notification of cases providing sufficient time for radiology review. The role of a dedicated MDT or PC care coordinator was viewed highly to facilitate attendance at the meeting through scheduling and reminders, to ensure cases were scheduled for discussion, and to support processes such as referral pathways following an MDT meeting. However, funds to implement these facilitatory structures and positions may not be available in some organisations. In the Australian setting, reimbursement is available for MDT meetings, however, participants reported that this was time-consuming or difficult to access. If harnessed, funds generated from the MDT reimbursement could assist in resourcing these potential enabling resources.

The skills of the MDT meeting chairperson can be an important enabler in ensuring that all participants are included in the discussions and divergent views are managed appropriately. An effective chairperson will ensure all attendees can participate to enable better decision-making, and has the clinical expertise to guide discussions.[115] As an example, this study

identified that the lack of palliative care input in MDT meetings was a significant barrier. The majority of patients with PC are diagnosed with advanced disease, have a high symptom burden and reach end-of-life within a short period of time.[34] Palliative care input provides a patient-centred approach with a focus on pain and symptom management and can avoid inappropriately aggressive treatment.[138] Current MDT practices are often focused on early stage disease, which can explain why palliative care specialists are not typically present at MDT meetings; but equally, the lack of representation can deter clinicians from presenting patients with advanced disease. Palliative care specialists acknowledged that their input in MDT meetings would be valuable. However, a minority found it difficult to participate in discussions due to a lack of confidence in voicing their opinion within the existing meeting structures and dynamics. A study conducted by Devitt and colleagues a decade ago, reported similar findings with allied health professionals describing similar inhibitions due to time constraints and lack of respect for their contribution, with some meetings seen as intimidating.[139] Such barriers can result in the psychosocial concerns of patients being neglected. The MDT chair can play an important role in inviting key disciplines to comment and ensuring discussions are holistic.

This study provides insight into the attitudes and beliefs of a diverse sample of clinical disciplines involved in presenting patients suspected or diagnosed with PC to MDT meetings. Our cohort included specialists working in both private and public health systems across two Australian jurisdictions. Participants were invited based on a preliminary focus group discussion. It is possible that key disciplines with potential to contribute to MDT meetings are not be represented. For example, pathologists who contribute to MDT meetings across many cancer streams and clarify areas of diagnostic uncertainty were not included in this study. While it would be interesting to extend this study into other clinical areas and specialties, we cannot assume that the barriers and enablers we identified will be generalisable to other settings. Although we had a heterogenous population, data was

collected until no new information presented on the barriers and enablers within the 12 *a priori* TDF domains.[109] We have also avoided placing weight emphasis on any of the issues identified. Understanding the prevalence of the healthcare professionals' opinions across and within specialities requires further exploration.

5.4.1 Conclusion

Patients with PC have amongst the lowest survival of any major cancer type and their management is complex. Presenting cases at MDT meetings allows for a collective, multidisciplinary approach to treatment and management. Yet our data and those of others show that implementation of best practice remains an issue. This qualitative study used a knowledge translation approach and a behavioural framework to explore the factors that influence the implementation of MDT meetings. The results demonstrate that MDT meetings were thought to be integral to the provision of quality care. The organisational structures internal and external to MDT meetings need to be strengthened with the development of agreed evidence-based protocols and referral pathways, a focus on improved resource allocation and capabilities and a culture that fosters widespread collaboration to benefit patients with all stages of PC.

5.5 Chapter Summary

This chapter provides an insight into the barriers and enablers to evidence-based practice of MDT meetings. The manuscript for this study is currently under review.

In total 29 clinicians (5 radiologists, 10 surgeons, 5 palliative care specialists, 3 medical oncologists and a radiation oncologist, 3 nurse specialists and 2 gastroenterologists) were interviewed over a four-month-period. Twenty-two themes and forty belief statements relevant to all TDF domains were generated. Key enablers influencing MDT practices included a strong organisational focus (*social/professional role and identity*), beliefs about the benefits of an MDT discussion (*beliefs about consequences*), the use of technology, e.g. video conferencing (*environmental context and resources*), the motivation to provide good quality care (*motivation and goals*), the provision of food and coffee (*motivation and goals*) and collegiality (*social influences*). Barriers included: absence of palliative care representation (*skills*), competing MDT meetings (*environmental context and resources*), the accumulative costs of staff time (*beliefs about consequences*), the lack of capacity to discuss all patients within the allotted time (*beliefs about capabilities*) and reduced confidence to participate in discussions (*social influences*).

The results demonstrate that MDT meetings are integral to the provision of quality care. The organisational structures internal and external to MDT meetings need to be strengthened with the development of agreed evidence-based protocols and referral pathways, a focus on resource allocation and capabilities and a culture that fosters widespread collaboration for all stages of PC.

"Quality is never an accident; it is always the result of high intention, sincere effort, intelligent direction and skilful execution; it represents the wise choice of many alternatives"

William A Foster

Chapter 6: Patient-Reported Outcomes in Pancreatic Cancer

This chapter focuses on the measures derived from the patient perspective and addresses the second overall objective of this thesis.

Patient reported outcome measures (PROMs) are increasingly being used to assess the quality of care provided to patients and to add a patient 'voice' within the healthcare system.[140] One such voice who gave deep insights into being diagnosed with PC, the impact of treatment and her experiences within the health system for this thesis was Lynda Williams. She was diagnosed with stage IV PC in October 2015 and died from the disease in July 2017. *Appendix 5.1* contains a three-minute mp3 recording and summary of her insights.

At a population level, CQRs such as UGICR use predefined indicators to assess variation across the structure, process and outcome measures from a clinical perspective. This has been described in detail in Chapter 2 with the development of a core set of QIs. However, clinical measures often do not consider a patient's wellbeing, functional status and health-related QoL. Further, the views on 'what matters' to a patient may differ to that of a clinician. For example, in one study, clinicians placed higher importance on symptoms such as pain, nausea, vomiting, abdominal complaints, itching and jaundice compared to patients in a palliative setting.[141]

Integration of PROMs into clinical practice, health service or health systems level have shown to improve patient-clinician communication, overall patient care and outcomes.[142] However, with the exponential rise in the number of PROMs developed for cancer care, it is especially important that the selected PROM has undergone psychometric evaluation in a PC population and is deemed reliable, valid and sensitive to change, rather than merely extrapolated from other populations. This chapter supplements the QIs discussed in Chapter 2 by adding the patient perspective. It examines the PRO measures, their attributes and their

application in patients with PC. The UGICR intends to integrate PROMs in the registry, using results from the following systematic review to identify the most appropriate tool to be collected.

6.1 Published Journal Article

Maharaj AD, Samoborec S, Evans SM, Zalcberg JR, Neale RE, Goldstein D, Merrett ND, White K, Croagh D, Pilgrim CHC, Evans PM, Knowles BPF, Leong T, Philip J, Smith M, Ioannou LJ. Patient-Reported Outcome Measures (PROMs) in Pancreatic Cancer: A Systematic Review. HPB(Oxford) 2020;22(2); 187-203.
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REVIEW ARTICLE

Patient-reported outcome measures (PROMs) in pancreatic cancer: a systematic review

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Abstract

Background: The aim of this systematic review is to examine patient-reported outcome measures (PROMs), their attributes and application in patients with pancreatic cancer (PC).

Method: A systematic literature search was undertaken of articles published to June 2018 to identify PROMs applied in primary studies in PC. Characteristics of the included studies and PROMs were described with identified scales grouped into five domains. The psychometric properties of the identified PROMs were further assessed for reliability and validity among patients with PC.

Results: From 1688 studies screened, 170 were included. Almost half (48%) were conducted in patients with unresectable PC; the majority of these (68%) were evaluated in randomized controlled trials. Median questionnaire completion rates fell below 10% of the original cohort within 12 months in patients with unresectable PC compared to 75% in patients with resectable PC. Seventy PROMs were identified, 32 measuring unidimensional parameters (e.g. pain) and 35 measuring multidimensional (e.g. quality of life) constructs. Only five (7%) PROMs were disease-specific and 13 (19%) were validated in patients with PC. Fifty scales were grouped into 19 physical, 9 psychological, 6 psychiatric, 9 social and 7 other domains.

Conclusion: Three multidimensional PROMs, the: (i) FACT-HEP in unresectable PC; (ii) QLQ-PAN26 (in conjunction with its core QLQ-C30 PROM) in resectable PC; and (iii) MDASI-GI are recommended as instruments to capture quality of life in patients with PC. Summarised scales and psychometric evaluation provide a framework to choose PROMs for scales not captured by the recommended PROMs.

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Background

Pancreatic cancer (PC) is the fourth leading cause of cancer death in Western society and was recently projected to overtake breast cancer to become the third leading cause of cancer death in the United States.[1] Surgery is the only potentially curative treatment, yet only 10–20% of patients progress to surgery and over 50% of patients have metastatic disease at diagnosis.[1,2] Across the entire population, the median survival following a diagnosis of PC is less than 12 months. Apart from its poor survival,[3] the associated symptom burden and high psychological distress[4] cause altered quality of life (QoL) and significant suffering for patients and their families.

In an Australian study, two-thirds of patients diagnosed with PC report at least one moderate to high-level physical or psychological unmet need, yet 20% did not access psychological support and only 45% accessed palliative care despite recommendations that in

this population, patients benefit from early and intense supportive care management.[5] Patients' perspectives reveal the impact of these unmet needs on health-related outcomes such as functional status, symptoms, wellbeing and quality of life. Patient-reported outcomes (PROs) measured by structured instruments (e.g. standardised questionnaires), also known as patient-reported outcome measures (PROMs) have been considered increasingly important in the last three decades following pioneering work undertaken by the Medical Outcomes Study[6] and the Food and Drug Administration's PRO guidance for industry.[7]

The most widely accepted definition of PROs is, *"any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else"*.[7] The PROs can be applied at the individual (clinician–patient interactions), health service (such as comparisons of treatment effectiveness or understanding variation among providers) or health system level (population surveillance and policy)[8,9] to improve clinical decision making, inform clinical research or gain approval of new therapies.

PROMs include an extensive range of constructs that can be unidimensional (e.g. pain, fatigue and anxiety) or multidimensional, such as QoL. These constructs can be composed of numerous scales and single items, be generic, disease or symptom specific[10] and capture domains of varying importance or relevance to clinicians or patients.[11,12] A rapid expansion in the number of PROMs available has made selection of the most appropriate instrument for a defined purpose somewhat difficult. This has been exacerbated by the prolific development of digital tools and "apps", many of which are well intentioned but lacking in rigorous development methods assessing item selection, validity, reliability, responsiveness and interpretability.[13]

The purpose of this systematic review is to: (i) identify from primary studies the PROMs that have been applied in patients with PC; and (ii) describe and evaluate measures used to assess PROs. This is intended to guide researchers and clinicians in their selection of PROMs at the individual, health service or health system level.

Methods

Protocol and registration

The protocol for this review was registered in PROSPERO (https://www.crd.york.ac.uk/PROSPERO) with the number CRD42018087467.

Search strategy

A systematic literature search of MEDLINE, EMBASE and PSYCHINFO databases was undertaken from inception to 12 June 2018. The search strategy included terms for pancreatic neoplasm, PROMs, QoL, symptom assessment, psychometrics, self-report, surveys and questionnaires (for a comprehensive list of terms refer to Appendix A). Relevant studies were imported into the COVIDENCE online software designed for systematic reviews (www.covidence.org) for study selection.

Eligibility criteria

Randomised controlled trials (RCTs) and prospective cohort or cross-sectional (CS) studies were included, regardless of their sample size. The overall inclusion criteria were studies that included participants diagnosed with PC that were part of a pancreatic, gastrointestinal (GI) or other cancer study and that used at least one PROM to evaluate general QoL, health-related QoL, survival, time until definitive deterioration and morbidity. We excluded qualitative studies, review articles, and protocol papers and studies that investigated only neuroendocrine tumours, pancreatic cysts, biliary obstruction or disorders unrelated to PC. Studies purely focussing on patient-reported experience measures (PREMs) such as satisfaction with care or health utilities were also excluded.

Study selection

Two authors (AM, SE) independently assessed titles and abstracts for inclusion and full-text articles for eligibility. Abstracts that reported on the use of PROMs and contained sufficient information to be able to complete required data fields were also retained. Any conflicts were resolved with an independent third reviewer (LI).

Data items and extraction

Data were extracted using a standardised, pre-defined collection form in Microsoft Excel 2016. Study details, publication date, country, setting, design, population, intervention, baseline sample characteristics (sample size, mean or median age, sex, disease stage and performance status (PS)), PROMs applied, PROMs scales or single items, method (e.g. paper based, technological device), mode (patient-reported or other), language, when applied (baseline, follow-up), questionnaire completion rate and study endpoints were collected. Disease stage was grouped into three categories: (i) resectable; (ii) unresectable (locally advanced and metastatic disease); and (iii) all (which included both resectable and unresectable disease). One author extracted data (AM) and this was independently verified by a second author (SS).

Risk of bias and quality assessment of individual studies

Risk of bias was not assessed or articles scored on methodological quality as the aim of this part of the study was to identify PROMs rather than examine the quality of the data, methods or treatment effects.

Evaluation and categorisation of identified PROMs

A detailed content analysis was undertaken to explore the dimensionality of each instrument. Identified scales and single items of each instrument were collated and grouped into a framework of *physical*, *psychological*, *psychiatric*, *social* and *other* domains.

Involvement of patients with PC in the development of the instrument as well as psychometric properties including reliability, validity, and responsiveness/sensitivity of instruments was assessed. Reliability is a measure of the homogeneity of items within a scale (internal consistency) and the extent to which the same results are drawn on repeated administration of the PROMs.[14] Reliability coefficients range from 0 to 1.0 where the latter indicates prediction without error. The Cronbach's alpha score is reported as an assessment of internal consistency with a score of >0.7 regarded as acceptable reliability.[15]

Validity refers to "the degree to which a test is capable of measuring what it is intended to measure.[16]" It considers the dimensions of logic/face validity and content (determined by expert opinion), construct (determined by factorial analysis) and criterion validity (established through diagnostic tests).[17] Instruments assessing any of content, criterion (concurrent), or construct (convergent, divergent, discriminant) validity were listed. Responsiveness or sensitivity is defined as the "ability of an instrument to detect change over time in the construct to be measured'.[18]

Results

Study selection

A total of 1688 titles and abstracts were screened for eligibility and 277 articles were assessed for inclusion (Fig. 1). Of these, 170 (References: Appendix B) studies (145 full-text and 25 abstracts) met the inclusion criteria. Reasons for ineligibility included: studies with duplicate datasets; studies not having sufficient PROMs-related information to complete all fields; ineligible study design such as review articles or protocol papers; and studies in an ineligible population.

Descriptive analysis of included studies

Table 1 summarises the characteristics of the primary studies. The median sample size across the 170 included studies was 76 (Range 10–16,095) with a total of 38,930 participants. A total of 109 studies solely focused on a PC cohort and, of the 143 studies that reported sex, there was an approximately equal proportion of men and women. Eighty-two studies reported mean age (63

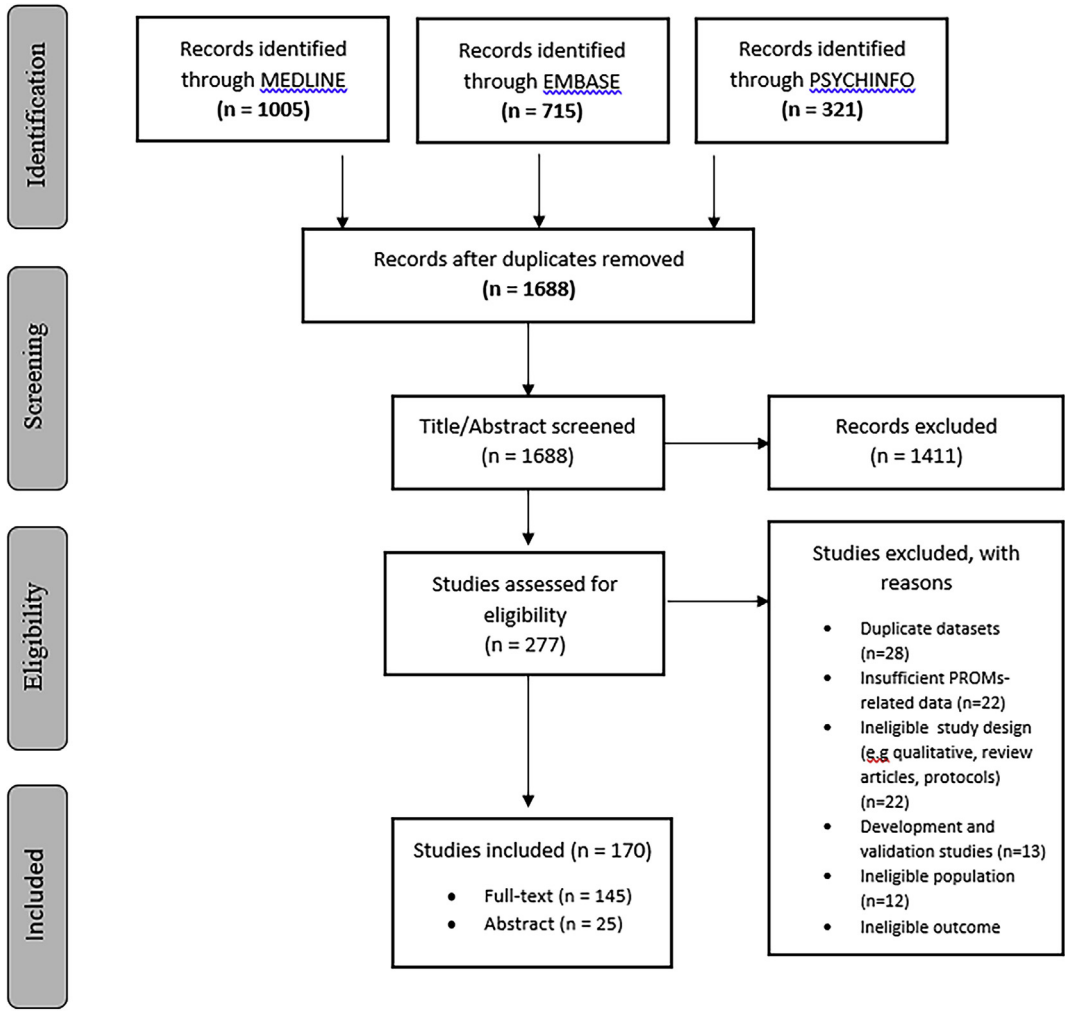


Figure 1 Prisma flow diagram of systematic review

Table 1 Descriptive analysis of Identified Studies (n = 170)

		n = 170 (%)	
Study Sample (Total = 38,930)	Median	76 *(Range:10 – 16,095)*	
Population	Gastrointestinal	20	(12)
	Pancreatic Cancer	109	(64)
	Pancreatic Disease	13	(8)
	Pancreatic and Periampullary Cancer	10	(6)
	Other	18	(11)
Sex (n = 143)	Male	18,233	(50)
	Female	18,056	(50)
Age Groups (Mean/Median)	<60	27	(16)
	60–70	113	(66)
	>70	9	(5)
	NS	22	(13)
Study Design	RCT	70	(44)
	RCTs with cross-sectional (CS) analysis of PROs	4	
	Prospective	58	(36)
	Prospective with CS analysis of PROs	4	
	Cross-sectional	32	(19)
	Other	2	(1)
Publication Year	<1995	3	(2)
	1995–1999	6	(4)
	2000–2004	15	(9)
	2005–2009	28	(16)
	2010–2014	58	(34)
	>2015–Jun 2018	60	(35)
Outcomes[a]	Quality of Life (QoL)	129	(76)
	Health-related QoL (HRQoL)	24	(14)
	Clinical Endpoints *(Survival*, *Mortality, Morbidity, TUDD)*	59	(35)
	Psychological *(Anxiety, Depression*, *Psychological distress)*	25	(15)
	Pain	23	(14)
	Other	10	(6)
Operability	Resectable	40	(24)
	Unresectable	81	(48)
	All Stages	25	(15)
	NS	24	(14)
Method[a]	Paper-based ± Mail	41	(24)
	Phone ± Other	11	(6)
	Technology *(online*, *computer*, *tablet*, *smartphone*, *email)*	7	(4)
	NS	113	(66)
Mode	Patient Reported	108	(64)
	Patient Reported and other	8	(5)
	Data Collector or other	8	(5)
	NS	46	(27)
Language	English ± presumed	67	(40)
	Other stated languages	28	(16)
	NS	75	(44)

NS – Not Stated/Specified, WHO – World Health Organisation.
[a] Some studies reported more than one functional outcome/method.

years) and 66 reported median age (64 years). Forty-four percent of PROMs were applied in a randomised control trial (RCT) setting followed by 36% in prospective cohort studies. There has been a rise in the application of PROMs, with only 9 studies identified prior to year 2000, 58 from 2010 to 2014 and 60 studies from 2015 to June 2018.

Outcomes and application of PROMs

The outcome investigated in the majority of studies (153/170; 90%) was the multidimensional construct, QoL. Psychological or psychosocial distress and unidimensional outcomes of pain, anxiety or depression were other PROs measured (Table 1). Almost half (48%) of the studies were conducted in patients with unresectable PC, with the majority of these designed as RCTs (68%). Only a third of studies (34%, n = 58) reported the method of questionnaire delivery. Of these, paper-based was the most common form and only seven studies reported using technological devices (e.g. computer, tablet, mobile phone) as a means of collecting PROMs. Approximately 70% of studies confirmed that patients were the direct source of information, with only 5% using data collectors to interpret a patient's response to questionnaires. The language in which the questionnaire was administered was identified in 95 studies, including 40 studies where the language was not reported but presumed to be English (studies from the United States, United Kingdom, Canada, Australia, New Zealand). Of the 55 studies that reported language, half applied the questionnaires in English. Median questionnaire completion rates fell to below 10% of the original cohort within 12 months in patients with unresectable PC compared to 75% in those with resectable PC at the same time point (Fig. 2).

Evaluation and categorisation of PROMs

From the 170 studies included, we identified 73 instruments, three of which were excluded from further analysis as questionnaire details were not found. Table 2 summarises the attributes of these 70 instruments, including items within each instrument, when the instrument was developed, the frequency of use of each instrument in studies, whether patients were involved in the instrument's development and the population in which it has been validated. The number of items per instrument ranged from one (GRoC, NRS, VAS) to 136 (SIP). The 70 PROMs were applied 314 times. The most commonly used instrument was the EORTC QLQ-C30, applied in 89 studies, with its disease-specific EORTC instrument, the QLQ-PAN26 used in 44 studies.

Table 3a, b details the domains and scales captured by the 35 multidimensional instruments. These instruments capture 19 scales within the physical domain, 9 scales within the psychological domain. 6 scales within the psychiatric domain, 9 scales within the social domain and 5 scales within the other domain. Pain and activities of daily living (ADL) in the physical domain, anxiety and depression in the psychological domain and social support or their limitations within the social domain were the most commonly collected scales.

Table 4a,b outlines domains and scales captured by the 32 unidimensional instruments. These captured five scales within the physical domain, 4 scales within the psychological domain, 2 scales within the psychiatric domain, 3 scales within social domain and 5 scales within the other domain. The dimensionality of three instruments could not be determined. Five instruments (QLQ-PAN26, FACT-Hep, MDASI-GI, GIQLI, DDQ-15) were considered disease-specific. No single instrument

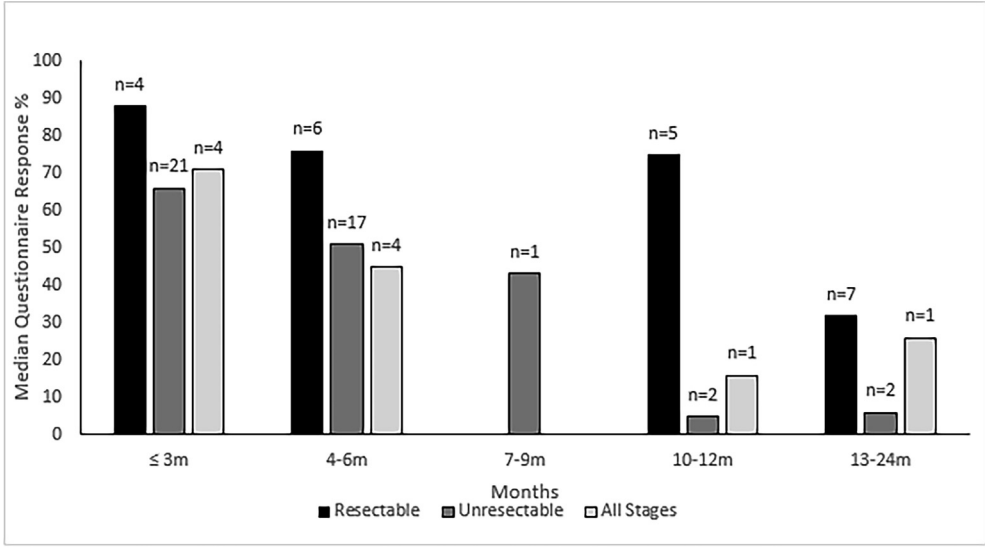


Figure 2 Final time-points for questionnaire completion

Table 2 Identified PROMs

PROMs Full Name	PROMs Abbreviated	No. of Items	Year Developed /Published	Frequency of use in PC studies	Developed with patients/consumers?	Population Validated
European Organization for the Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire - Core[19]	QLQ-C30	30	1984	89	Lung cancer n = 305	NA
EORTC Quality of life Questionnaire -Pancreatic Cancer[20,21]	QLQ-PAN26 (*Disease-specific (DS)*)	26	1997	44	PC – all stages (phase 1) n = 34	Resectable PC *(n = 300)*
Visual Analogue Scale[22]	VAS	1	1985	16	NE	NA
Short Form Health Survey-36[23]	SF-36	36	1988	14	NE	NA
Functional Assessment of Cancer Therapy – Hepatobiliary[24,25]	FACT-HEP *(DS)*	45	2002	11	Hepatobiliary cancers (phase 1) n = 81	Unresectable PC *(n = 96)*
EuroQoL – 5D Questionnaire[26]	EQ-5D	5	1987–1991	10	NE	NA
Hospital Anxiety Depression Scale[27,28]	HADS	14	1983	14	NE	GI cancer *(PC - NE)*
Brief Pain Inventory[29,30]	BPI	15	1982	8	NE	Mixed cancers *(PC - Yes)*
Functional Assessment of Cancer Therapy-General[31]	FACT-G	27	1993	8	Mixed cancers n = 45	Unresectable PC
Edmonton Symptom Assessment System[32–34]	ESAS	10	1991	7	NE	Content *(Unresectable PC –Yes, n = 22)*, Cognitive *(GI Cancer)*
Numeric Rating Scale[35]	NRS	1	NE	7	NE	NA
Gastrointestinal Quality of Life Index[36]	GIQLI *(DS)*	36	1993	5	*Questionnaire constructed by study team*	GI cancer *(PC – Yes, n = NE, stage = NE)*
M.D. Anderson Symptom Inventory[37]	MDASI	19	2000	3	*Generated by working group*	GI cancer *(PC - Yes)*
M.D. Anderson Symptom Inventory –Gastrointestinal[38]	MDASI – GI *(DS)*	24	2010	1	GI cancer *(PC – Yes)* n = 25	GI cancer *(PC – Yes All stages, n = 46)*
Audit of Diabetes Dependent Quality of Life[39]	ADDQoL	19	1994	3	Adults with diabetes n = 12	NA
Beck Depression Inventory[40]	BDI	21	1961	3	*Developed from clinical observations of depressed psychiatric patients*	NA
Functional Assessment of Chronic Illness Therapy-Spiritual[41]	FACIT-Sp	39	1990	3	Input of cancer patients *(PC – NE)* n = 200 +	NA
Linear-Analogue Self-Assessment[42]	LASA	10	1976	3	NE	NA
Rotterdam Symptom Checklist[43]	RSCL	34	1983	3	NE	NA
Beck Anxiety Inventory[44]	BAI	21	1990	2	*Archival data from the ACL, the PDR, and the SAC were used to generate an initial pool of 86 items*	NA

Table 2 (*continued*)

PROMs Full Name	PROMs Abbreviated	No. of Items	Year Developed /Published	Frequency of use in PC studies	Developed with patients/consumers?	Population Validated
Beck Hopelessness Scale[45]	BHS	20	1987	2	NE	NA
Functional Assessment of Chronic Illness Therapy-Fatigue[46]	FACIT-F	40	2005	2	Anaemic cancer patients *(PC – NE)* n = 14	NA
Functional Assessment of Cancer Therapy – Pancreas[a]	FACT-PA	–	NE	2	NA	NA
Memorial Symptom Assessment Scale[33,47]	MSAS	32	1990	2	*Developed following a review of the literature*	Mixed Cancers *(Unresectable PC – Yes, n = 22)*
Profile of Mood states[48]	POMS	65	1964	1	NE	NA
Profile of Mood states – SF[49]	POMS – SF	37	1981	1	*Original POMs shortened with cancer patients (PC – NE)*	NA
European Organization for the Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire - Palliative Care[50]	QLQ-C15-PAL	15	2005	2	Palliative care with advanced cancers *(PC – NE)* n = 41	NA
Short Form Health Survey-12[51]	SF-12	12	1996	2	*Derived from SF-36*	NA
Spitzer QoL Index[52]	SQI	15	1981	2	Involved cancer patients (n = 4) and their relatives	NA
Brief Fatigue Inventory[53]	BFI	9	1999	1	NE	GI Cancer *(PC - NE)*
Body Image Scale[54]	BIS	10	2001	1	Mixed cancers *(PC – NE)* n = 276	NA
Brief Symptom Inventory[55]	BSI	53	1993	1	NE *(derived from parent instrument SCL-90-R)*	NA
Brief Symptom Inventory – Shortened[56]	BSI -18	18	2001	1	NE	NA
Cantril Ladder Scale[57]	CLS	2	1963	1	NE	NA
Cancer Rehabilitation Evaluation System - Short Form[58]	CARE-SF	59	1991	1	NE *(derived from parent instrument CARES)*	NA
Center for Epidemiologic Studies – Depression[59]	CES-D	20	1977	1	NE	GI Cancer *(PC - NE)*
Digestive Disease Questionnaire-15[60]	DDQ-15 *(DS)*	15	2001	1	Yes *n = unclear*	UGI Cancers *(PC – Yes, n = NE, stage = NE)*
Duke-UNC Functional Social Support[61]	DUFSS	14	1988	1	NE	NA
Functional Assessment of Anorexia/Cachexia Therapy[62]	FAACT	39	1993	2	NE	NA
Functional Assessment of Cancer Therapy–Anaemia[63]	FACT-AN	47	1997	1	NE	NA
Fear of Cancer Recurrence Inventory[64]	FCRI	42	2009	1	NE	NA
Functional Living Index-Cancer[65]	FLIC	22	1984	1	Yes - *panel consisted of a male patient, a*	NA

(*continued on next page*)

Table 2 (*continued*)

PROMs Full Name	PROMs Abbreviated	No. of Items	Year Developed /Published	Frequency of use in PC studies	Developed with patients/consumers?	Population Validated
					female patient, and two patient spouses	
Functional Living Index – Emesis[66]	FLIE	18	1992	1	NE	NA
Fatigue Symptom Inventory[67]	FSI	14	1998	1	Breast cancer n = 15	NA
Geriatric Depression Scale[68]	GDS	30	1982	1	NE	NA
Global Rating of Change[69]	GRoC	1	1989	1	NE	NA
Hamilton Rating Scale for Depression[70,71]	HAM-D	21	1967	1	NE	Mixed cancers *(PC - Yes)*
Kurihara Questionnaire[72]	Kurihara	22	1992	1	*Initial 62 items devised by 30 investigators*	NA
Linear analogue Multiscale/ Uniscale Questionnaire[a]		–	NE	1	NA	NA
Life Orientation Test –Revised[73]	LOT-R	10	1985	1	NE *(items generated by authors)*	NA
Medicare Current Beneficiary Survey[a]	MCBS	–	NE	1	NA	NA
Medical Outcomes Study[74]	MOS-24	20	1988	1	NE	NA
Memorial Pain Assessment Card[75]	MPAC	4	1985	1	*Developed by the Analgesic Studies Section of Memorial Sloan-Kettering Cancer Center (MSKCC)*	NA
McGill Quality of Life[33,76,77]	MQOL	17	1995	1	NE	Mixed cancers *(All stages PC – Yes, n = 1)*
Problem Checklist[78]	PCL	20	2002	1	*Developed by the staff at Johns Hopkins*	NA
Patient-Generated Subjective Global Assessment[79]	PG-SGA	23	1994	1	NE *-Adapted from the parent SGA*	NA
Personal (Patient) Health Questionnaire[80]	PHQ9	9	2000	1	NE	NA
Problems and Needs for Palliative care[81]	PNPC	90	2004	1	Mixed cancers *(PC – NE)*	Mixed cancers *(Unresectable PC – Yes, n = 1)*
Pittsburgh Sleep Quality Index[82]	PSQI	19	1988	1	NE	NA
Penn State Worry Questionnaire[83]	PSWQ	16	1988	1	NE	NA
Prognosis and Treatment Perceptions Questionnaire[84]	PTPQ	*DNF*	2014	1	NE *-originally adapted based on a questionnaire developed for parents of children with cancer and additional validated items from previous studies.*	UGI Cancer *(Unresectable PC – Yes, n = 39)*
Rolls-Royce Quality of Life[85]	RRQoL	*DNF*	1995	1	NA	NA
	STAI	20	1966	2	NE	NA

Table 2 (*continued*)

PROMs Full Name	PROMs Abbreviated	No. of Items	Year Developed /Published	Frequency of use in PC studies	Developed with patients/consumers?	Population Validated
State Trait Anxiety Inventory[86]						
Sleep Assessment Questionnaire[87]	SAQ	17	1996	1	NE	NA
Self-administered Comorbidity Questionnaire[88]	SCQ	12	2003	1	NE – *a panel of 5 physicians selected 12 medical conditions which were simplified in language*	NA
Supportive Care Needs Survey-Short Form[89]	SCNS-SF	34	2009	1	*Supportive Care Needs Survey was adapted from an existing care needs questionnaire. Consumer reps included in review of content*	NA
Short Form Health Survey-8[90]	SF-8	8	2001	1	NE	NA
Sickness Impact Profile[91]	SIP	136	1976	1	Yes – *included patients, patient carers, apparently healthy and healthcare professionals*	NA
Sexual QoL Questionnaire[92,93]	SQoL	11 (Male) 18 (Female	2005 & 2008	1	Yes – *semi-structured interviews for item generation*	NA
Subjective Significance Questionnaire[94]	SSQ	4	1998	1	NE	NA
Vulnerable Elders Survey[95]	VES	13	2001	1	NE	NA
Visick Scale[96]	Visick	*DNF*	1948	1	NA	NA
World Health Organization Quality of Life – 26[97]	WHOQoL	26	1993	1	Yes – *involved focus groups*	NA

[a] Instruments excluded from further analysis as questionnaire details were not found, DNF = dimensionality not found, FREQ = frequency (number of times instrument was applied in included studies), GI = gastrointestinal, UGI = upper gastrointestinal, NE = not evident, NA = not applicable, PC = pancreatic cancer.

captured the entirety of the five domains or 50 scales. However, the 'Problems and Needs for Palliative Care' (PNPC) instrument with 90 items captured 37 (74%) of the 50 scales. In unresectable PC, 83% of studies asked patients to complete one or two instruments, 10% three and 7% four to five instruments. In contrast, in studies in patients with resectable PC, 73% of studies asked patients to complete one or two instruments, 25% three and 2% more than three instruments.

Psychometric evaluation of PROMs applied in PC

Table 5 summarises the psychometric properties of PROMS applied in PC. The majority (93%) of the instruments were evaluated for reliability and validity in diverse settings, with only 13 (19%) of these having undergone some form of validation in a PC population. The multidimensional PROMs, QLQ-PAN26 in patients with resectable PC (n = 300), FACT-HEP in those with unresectable PC (n = 96) and MDASI-GI across all stages (n = 46), met all psychometric evaluation criteria, with the exception of the hepatic scale (Cronbach's alpha 0.69) within QLQ-PAN26. Only two unidimensional instruments had been validated in a PC cohort; one assessed pain (BPI) and the other depression (HAM-D).

Discussion

This systematic review identified 170 studies that met the inclusion criteria and comprehensively evaluated and described the range of PROMs completed by patients with PC. The items from the 70 multidimensional and unidimensional instruments were grouped into 50 categories, allowing a detailed understanding of

Table 3a Framework summarising physical and other scales for multidimensional PC instruments

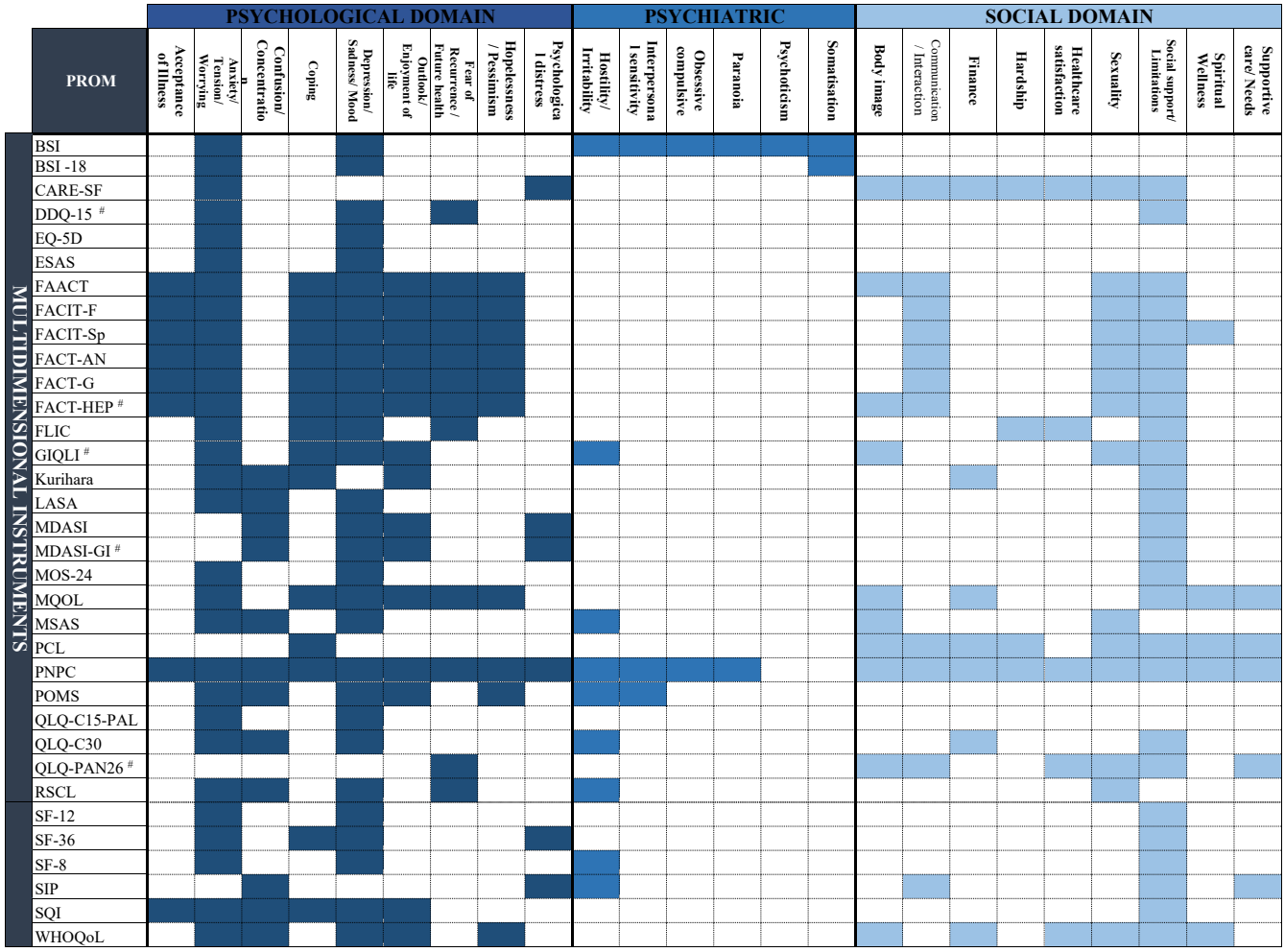
	PROM	PHYSICAL DOMAIN																			OTHER DOMAIN						
		Activities of daily living	Appetite/ Food intake	Constipation	Frequent Bowel Motions	Drowsiness	Dry mouth/ Mouth sores	Dyspnoea	Fatigue	Flatulence / Bloating	Digestion	Sleep	Itchiness	Jaundice	Nausea / Vomiting	Numbness / Tingling	Pain / Pain interference	Swallowing	Taste changes	Energy/ Vitality/ Endurance	Anaemia	Anorexia/ Cachexia/ Malnutrition	Comorbidities	Diabetes	Health status/ Wellbeing	General/ Change in QoL	Side-effects/ Complications
MULTIDIMENSIONAL INSTRUMENTS	CARE-SF	■	■		■							■					■					■					■
	DDQ-15 #	■	■									■								■					■		
	EQ-5D	■															■										
	ESAS		■			■		■	■						■		■								■		
	FAACT	■	■									■			■		■		■	■		■			■	■	■
	FACIT-F	■							■			■			■		■			■						■	■
	FACIT-Sp	■										■			■		■			■						■	■
	FACT-AN	■						■	■			■			■		■			■	■					■	■
	FACT-G	■										■			■		■			■						■	■
	FACT-HEP #	■	■	■	■		■		■	■	■	■	■	■	■		■		■	■		■				■	■
	FLIC	■													■		■								■		
	GIQLI #	■	■	■	■				■	■	■	■			■		■	■		■							■
	Kurihara	■	■									■			■							■					
	LASA	■	■									■			■		■								■	■	
	MDASI	■	■			■	■	■	■			■			■	■	■										
	MDASI-GI #	■	■	■	■	■	■	■	■	■		■			■		■	■	■								
	MOS-24	■															■			■					■		
	MQOL		■	■	■			■	■			■			■		■								■	■	
	MSAS		■	■	■	■	■	■		■		■	■		■	■	■	■	■	■		■					
	PCL								■								■										
	PNPC	■	■	■	■		■	■	■	■		■	■		■	■	■	■	■								
	POMS					■			■																		
	QLQ-C15-PAL	■	■	■				■	■			■			■		■									■	
	QLQ-C30	■	■		■			■	■						■		■								■	■	
	QLQ-PAN26#		■				■		■	■	■		■	■			■		■			■					■
	RSCL	■	■	■	■		■	■	■	■	■	■			■	■	■	■		■							
	SF-12	■															■			■					■		
	SF-36	■							■								■			■					■		
	SF-8	■															■			■					■		
	SIP	■	■									■															
	SQI	■							■											■					■	■	
	WHOQoL	■							■			■					■			■					■	■	

■	*Scales related to physical domain*
■	*Scales related to other domain*
■	*Scales related to psychological domain*
■	*Scales related to psychiatric domain*
■	*Scales related to social domain*

the gaps and overlaps between instruments. We further highlight the prominent application of the generic EORTC QLQ-C30, followed by the disease-specific QLQ-PAN26 instrument in PC across both RCTs and prospective cohort studies, and that the poor prognosis associated with a diagnosis of PC draws continued focus on QoL. To our knowledge, this is the first systematic review in which the application, reliability and validity of PROMs in PC has been evaluated.

Recent research has demonstrated that the collection and integration of PROs in clinical practice has been associated with reduced emergency department visits, as well as improved: communication between patient and clinician; quality of care; patient experience; QOL; and provider experience.[98] Basch and colleagues found that the integration of PROs into the routine care of patients with metastatic cancer receiving chemotherapy was associated with improved survival compared with usual care.[99] There is an impetus to use PROMs data to benchmark provider performance and assess appropriateness of care, and to measure results against 'what matters to patients'.[98] Recently introduced treatment regimens are associated with improved survival, albeit incremental. However, this has been counteracted by increased adverse effects in both the neo-adjuvant and adjuvant settings.[100,101] In this environment, survival improvements must be balanced against decrements in QoL. The challenge remains how to best measure PROs and use these to guide clinical care.[102]

Table 3b Framework summarising Psychological, Psychiatric and Social Scales for Multidimensional PC Instruments



Psychometric evaluation of a questionnaire is characterised by its viability, validity and sensitivity to change. Even though the majority of questionnaires in this review were validated, only 13% were validated in patients with PC. The five validated disease-specific instruments (QLQ-PAN26, FACT-Hep, MDASI-GI, GIQLI, DDQ-15) used good sample sizes to establish validity, whilst other instruments evaluated questionnaires in patients with a range of different cancers or in patients with GI cancer, with the number of patients with PC not always evident in the study or the sample size being as low as one. Considering the unique challenges faced by patients with PC, the considerable burden of disease, and the poor prognosis, the use of a PC-specific validated instrument is especially important to ensure that the instruments used are "fit for purpose" and not merely extrapolated from other populations. When selecting a PROM, consideration should be given to the questionnaire's appropriateness, acceptability, feasibility, interpretability, precision, reliability and responsiveness.[103]

The QLQ-PAN26 is recommended for use with its core PROM, QLQ-C30. When used in conjunction, they capture 35 of

Table 4a Framework summarising physical and other scales for unidimensional PC instruments

	PROM	PHYSICAL DOMAIN																			OTHER DOMAIN						
		Activities of daily living	Appetite / Food intake	Constipation	Frequent Bowel Motions	Drowsiness	Dry mouth/ Mouth sores	Dyspnoea	Fatigue	Flatulence / Bloating	Digestion	Sleep	Itchiness	Jaundice	Nausea / Vomiting	Numbness / Tingling	Pain / Pain interference	Swallowing	Taste changes	Energy/ Vitality/ Endurance	Anaemia	Anorexia/ Cachexia/ Malnutrition	Comorbidities	Diabetes	Health status/ Wellbeing	General/ Change in QoL	Side-effects/ Complications
UNIDIMENSIONAL INSTRUMENTS	ADDQoL																							■			
	BFI								■																		
	BPI																■										
	CLS																									■	
	FLIE														■												
	FSI								■																		
	GRoC																									■	
	MPAC																■										
	NRS																■										
	PG-SGA																					■					
	PSQI											■															
	SAQ											■															
	SCQ																						■				
	SSQ																									■	
	VAS																■										
	VES	■																							■		

■	*Scales related to physical domain*
■	*Scales related to other domain*
■	*Scales related to psychological domain*
■	*Scales related to psychiatric domain*
■	*Scales related to social domain*

the 50 scales, compared to FACT-HEP and MDASI-GI which capture 29 and 20 scales respectively. The MDASI-GI measures one (social support/limitation) of 9 scales in the social domain and no scales in the other. It did not measure the hepatic scales of itchiness and jaundice in the physical domain and anxiety/tension/worry in the psychological. Both the MDASI-GI and the QLQ PROMs did not capture some of the functional scales within the psychological domain. These include coping, acceptance of illness and feelings of hopelessness/pessimism which maybe a reflection of its application mainly in patients with resectable disease.

Methods, modes of questionnaire administration, and language are important acceptability factors in PROM response data that should accommodate the needs of patients with diverse linguistic, cultural, educational, and functional skills.[104] Our review highlights the poor reporting of the method of administration and language delivery in studies. One study[105] noted that when given a choice between electronic capture and paper forms, 90% of participants preferred paper-based methods. This finding may be because patients with pancreatic cancer tend to be of an age (mean age, 66 years) where they may be less comfortable with technological devices and social media than a younger population. In comparison, two other studies,[106,107] reported online capture of 46% (mean age, 59 years) and 54% (mean age not stated) respectively which may represent improved technological literacy in the population in the six years between these studies and the study by Boyd and colleagues.[105] Over half the studies did not disclose the language(s) in which the instruments were applied. However, the most frequently applied tool in PC, the EORTC QLQ-C30 instrument, has been translated into and validated in more than 100 languages, while the disease-specific QLQ-PAN26 has been translated into 30 languages.[21]

It is important when selecting a PROM to consider the feasibility of data collection and the length of time taken to complete the questionnaire from a patient's perspective. Both are dependent upon the number of items included. These ranged from one to 136, but the ideal number of items that balances participant burden with adequate capture of relevant PROs requires further research. Further, feasibility is affected by the high rate of attrition due to disease-related morbidity, disease progression and death within 12 months, especially in patients with unresectable PC. Based on this review, the recommended follow-up time point for PROMs collection in patients with unresectable PC is 3–6 months to evaluate the impact of disease progression.

Table 4b Framework summarising Psychological, Psychiatric and Social Scales for Unidimensional PC Instruments

	PROM	PSYCHOLOGICAL										PSYCHIATRIC						SOCIAL									
		Acceptance of Illness	Anxiety/ Tension/ Worrying	Confusion/ Concentration	Coping	Depression/ Sadness/ Mood	Enjoyment of life	Outlook/ Future health	Fear of Recurrence / Pessimism	Hopelessness / Pessimism	Psychological distress	Hostility/ Irritability	Interpersonal sensitivity	Obsessive compulsive	Paranoia	Psychoticism	Somatisation	Body image	Communication / Interaction	Finance	Hardship	Healthcare satisfaction	Sexuality	Social support/ Limitations	Spiritual Wellness	Supportive care/ Needs
UNIDIMENSIONAL INSTRUMENTS	BAI		■																								
	BDI					■																					
	BHS									■		■															
	BIS																	■									
	CES-D					■											■										
	DUFSS																							■			
	FCRI							■																			
	GDS					■																					
	HADS		■			■																					
	HAM-D					■																					
	LOT-R									■																	
	MPAC					■																					
	PHQ9					■																					
	PSWQ		■																								
	SCNS-SF																										■
	SQoL - F																						■				
	SQoL - M																						■				
	STAI		■																								

	Scales related to physical domain
	Scales related to other domain
	Scales related to psychological domain
	Scales related to psychiatric domain
	Scales related to social domain

Table 5 PROMs psychometrically evaluated in PC

Multidimensional PROM	No. of Items	Developed with PC patients	Reliability (≥0.70 Cronbach's alpha or equivalent)	Extent of validation	Responsiveness /sensitivity	Scales covered
QLQ-C30	30	No	NE	NE	NE	17
QLQ-PAN26	26	**Yes**	0.69–0.97	Construct	**Yes**	18
FACT-HEP	45	**Yes**	0.74–0.94	Construct	**Yes**	29
ESAS	10	NE	0.79	Content	NE	9
GIQLI	36	No	0.9–0.93	Content, Concurrent, Construct	**Yes**	21
MDASI-GI	24	**Yes**	0.8–0.87	Concurrent, construct	**Yes**	20
MSAS	32	NE	NE	Content	NE	22
DDQ-15	15	**Yes**	0.92	Content, Concurrent	NE	9
#MQOL	17	NE	0.89	Content, Concurrent, Construct	NE	21
PNPC	90	NE	0.67–0.92	Concurrent, Construct	NE	37
PTPQ	13	NE	NE	Content	NE	–
Unidimensional PROM	**No. of Items**	**Developed with PC patients**	**Reliable (≥0.70 Cronbach's alpha or equivalent)**	**Extent of validation**		**Scales covered**
BPI	15	NE	0.87–0.92	Criterion, Construct	N/A	1
HAM-D	21	NE	0.77	Concurrent, Construct	N/A	1

NE – not evident, N/A-not assessed, Content Validity = relevance and representativeness of data elements. Concurrent Validity = a type of criterion validity which compares scores of a new instrument against an already established instrument. Construct Validity = degree to which instrument is measuring what it intends. Convergent, divergent and discriminant validity are subtypes of construct validity. #MQOL measures 21 scales from 17 items due to the nature of the questions (http://www.npcrc.org/files/news/mcgill_quality_of_life.pdf).

We used a detailed systematic search to identify PROMs in patients with PC using rigorous guidelines and methods. One possible limitation is the somewhat arbitrary classification of questionnaire items into different scales and constructs, although we minimised error by having the initial categorisation checked by other members of the research team. In addition, a small number of items (dizziness, incontinence, loss of hair, impaired vision, hearing, sweats, swelling, dependence on medicinal substances and medical aids) were not categorised as separate scales due to their infrequency and limited space in the table. Where possible, these were mapped to the most relevant scales (e.g. side effects). Furthermore, as no time limits were placed in the search strategy, some of the PROMs instruments may no longer be in use. However, instruments such as the Visick scale, developed in 1948, were still applied in the year 2000.[108]

This systematic review provides an insight into the range of unidimensional and multidimensional instruments used to capture particular domains of interest. No single instrument captured the entirety of the five domains or 50 scales. Few of the PROMs have been developed, validated and tested for reliability specifically in patients with PC. Taking responsiveness or sensitivity into consideration, we recommend three multidimensional PROMs: FACT-HEP in patients with unresectable PC; QLQ-PAN26 (in conjunction with its core QLQ-C30 PROM) in those with resectable PC; and MDASI-GI irrespective of stage. The MDASI-GI predominantly measures scales within two of the five domains. In comparison, the existing FACT-Hep and QLQ-PAN26 measure a more comprehensive set of scales across four of the five domains but need further validation in all stages of PC. The summarised scales and psychometric evaluation table provide the necessary framework to choose the most appropriate PROMs for any unmet scales not captured by the recommended PROMs.

Contributors

AM, LI, JZ and SME designed the study. AM and SS extracted and collated the data. AM provided the initial analysis and all authors interpreted the data. AM prepared the manuscript. All authors edited and reviewed the manuscript and gave final approval for submission of the final manuscript.

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Conflicts of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hpb.2019.09.002.

6.2 Chapter Summary

The purpose of undertaking this systematic review was to identify the most appropriate PROMs that can be collected by the UGICR.

A systematic literature search was undertaken of articles published to June 2018 to identify PROMs applied in primary studies in PC. Characteristics of the included studies and PROMs were described with identified scales grouped into five domains. The psychometric properties of the identified PROMs were further assessed for reliability and validity among patients with PC.

From 1688 studies screened, 170 were included *(Appendix 6.2).* Almost half (48%) were conducted in patients with unresectable PC; the majority of these (68%) were evaluated in randomized controlled trials. Median questionnaire completion rates fell below 10% of the original cohort within 12 months in patients with unresectable PC compared to 75% in patients with resectable PC. Seventy PROMs were identified, 32 measuring unidimensional parameters (e.g. pain) and 35 measuring multidimensional (e.g. quality of life) constructs. Only five (7%) PROMs were disease-specific and 13 (19%) were validated in patients with PC. Fifty scales were grouped into 19 physical, 9 psychological, 6 psychiatric, 9 social and 7 other domains.

Three multidimensional PROMs, the: (1) FACT-HEP in unresectable PC; (2) QLQ-PAN26 (in conjunction with its core QLQ-C30 PROM) in resectable PC; and (3) MDASI-GI are recommended as instruments to capture quality of life in patients with PC. Summarised scales and psychometric evaluation provide a framework to choose PROMs for scales not captured by the recommended PROMs.

The figure below summarises the frequency of the measured scales for all domains from the scales identified. Depression and anxiety were the most measured scales in PC overall.

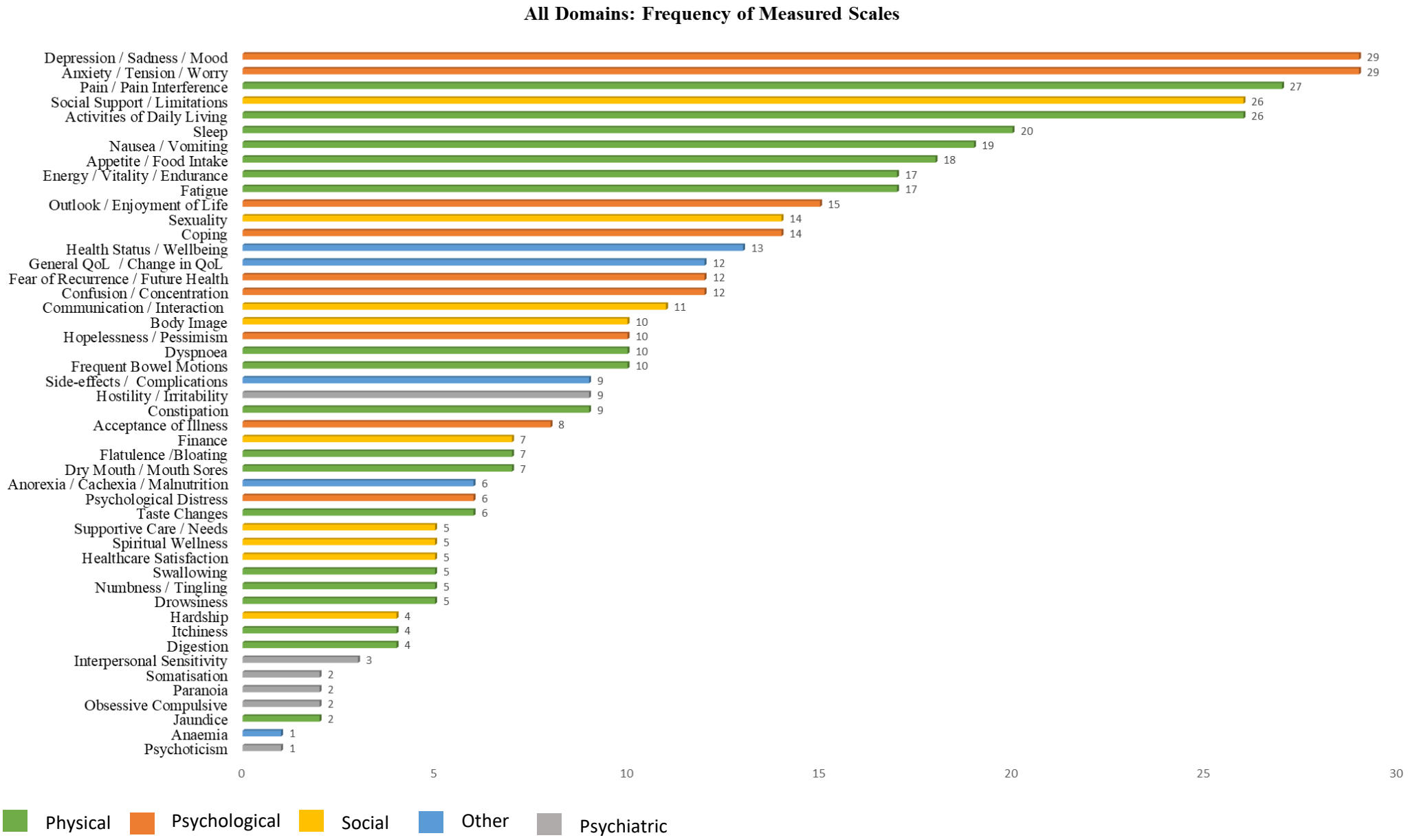

Figure 6. 1: *Frequency of measured scales (all domains) summarised*

Om Bhur Bhuvaḥ Swaḥ

The primeval sound that traverses the realms of this earth, the skies and heavens

Tat-savitur Vareñyaṃ

And that divine effulgence that we adore

Bhargo Devasya Dheemahi

We contemplate on your divine glory

Dhiyo Yonaḥ Prachodayāt

Please enlighten our intellect

Gayatri Mantra (Universal Sanskrit Prayer)

Chapter 7: Conclusion and Future Directions

PC is a cancer with a poor prognosis and with high symptom and significant psychological burden. The current landscape for good quality care in PC involves early diagnosis and staging, appropriate and timely stage-specific treatment, and optimised patient management.

This thesis set out to explore measures that can be used to monitor quality of care at a population level. It evaluated whether compliance with evidence-based QIs was associated with improved outcomes for patients with PC using the UGICR as a tool for change. The existing literature and a consensus-based approach was used to identify the QIs that measured quality from a clinical perspective across the trajectory of the disease. These QIs were then incorporated into the UGICR and three years of data were collected and assessed for compliance and association with survival. The findings from this analysis supported the hypothesis that compliance with agreed best practice improved patient outcomes. In addition, the attitudes and opinions of specialists who manage patients with PC were explored in relation to two QIs with low compliance. The two QIs, 'having a documented PPCT or MRI scan in non-metastatic disease', and 'disease management discussed at an MDT meeting', have the potential to avoid unnecessary surgery or margin positive resection. With this new information on barriers and enablers, we have a strong foundation on which to develop and test interventions to improve practice. A systematic review identified three multidimensional PROMs as appropriate measures for use in PC; the QLQ-PAN26 in conjunction with its core QLQ-C30 PROM is currently being tested for feasibility to collect at a population level in the UGICR.

The IOM updated its earlier 1999 report on delivering high-quality cancer care in 2013 and conceptualised the domains of the cancer care continuum: prevention and risk reduction; screening; diagnosis; treatment; survivorship; and end-of-life care. It further defined six

components of a high-quality cancer care delivery system integral to the transformation of the existing models of cancer care. These six components were: (1) the engaged patient; (2) an adequately-staffed, trained and coordinated workforce; (3) evidence-based cancer care; (4) a learning health care information technology (IT) system for cancer; (5) translation of evidence into clinical practice, quality measurement, and performance improvement; (6) and accessible, affordable cancer care.[143]

Chapter 2 of this thesis addressed four of the six areas of the cancer continuum, with the identification of QIs that measure best-practice in PC and in accordance with the Optimal Care Pathway.[26] Prevention and risk reduction, and screening to facilitate early diagnosis were two areas in PC that were not addressed with the QIs and are yet to be reliably measured. These are areas where future efforts can be directed. There is evidence that a malignant cell in the pancreas can take more than 10 years to become metastatic, providing a significant window of opportunity for early detection. Novel biomarkers such as the study of circulating tumour DNA, plasma microRNA signatures and biological exosomes may become useful diagnostic biomarkers in the future.[144,145]

In Australia, the UGICR has an important role to play in optimising the quality of care for patients diagnosed with PC and addressing IOM's six components by routinely collecting data, analysing and providing regular feedback through benchmark reports to enable quality improvement across health services within highlighted areas of concern.[146] Clinical practice can only be improved through the uptake of knowledge from these reports by decision makers within healthcare systems who can work to identify strategies to implement change. However, there is a lack of health services research in PC. Gagliardi and colleagues emphasised that no studies investigated the influence of guideline availability, interventions used to implement guidelines or promote-guideline compliant care.[113] This growing field of research groups quality improvement, implementation research, knowledge translation, and

knowledge transfer under the banner of *implementation science*s. This is defined as the "scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, and, hence, to improve the quality and effectiveness of health services and care".[147] As highlighted in Chapters 4 and 5, implementing evidence-based guidelines into clinical practice is a complex process. An important future consideration is the role of facilitation within and across health service levels, defined as "the process of enabling the implementation of evidence into practice" or "a deliberate and valued process of interactive problem solving and support that occurs in the context of a recognized need for improvement and a supportive interpersonal relationship".[148,149] Facilitators include opinion leaders, coaches, champions, research facilitators, clinical/practice facilitators, outreach facilitators, linking agents, knowledge brokers and external-internal facilitators.[150] This is an important consideration. The UGICR does have high clinician engagement and has principal investigators at each participating site. However, principal investigators are working clinicians and are often time-poor, a barrier highlighted in Chapter 5, and may not have the time and resources to disseminate the information received from the UGICR in a systematic manner.

In Chapter 1, the aetiological risk factors for PC were introduced and in Chapter 3, when studying the impact of QI adherence on survival, a number of other hospital and patient factors were considered in the univariable and multivariable analyses. Prognostic factors included in the analyses included age, ECOG performance status, operability of tumour and tumour site. Risk adjustment is an important consideration for the registry in future quality reports that benchmark outcomes of care among providers. Risk (or severity) adjustment accounts for differences in patient case mix that can influence objective health outcomes, such as survival, symptoms, functioning and QoL.[151] Risk can be categorised by demographic characteristics (age, sex, ethnicity and origin), clinical factors (performance

status and comorbidities), socio-economic characteristics (education, income or marital status), health behaviours (smoking, alcohol consumption and diet), and preferences that concern QoL and expectations on the healthcare system (centralised vs decentralised models of care).[152] These factors collected over time can be used to determine statistical prognostic models that generate the probability of a clinical event.[153] This can be further used to develop risk scores to stratify all patients to a particular risk status to address specific population management challenges, match risk with the levels of care and individualise treatment plans to outweigh any potential harm and improve function.[154] A limitation of the study presented in Chapter 3 was that when assessing the outcome of interest (QI adherence) we were not able to adjust for all factors which may have also have accounted for variation in survival.

In order to gather a comprehensive list of risk (prognostic) factors known to impact survival after PC diagnosis, a systematic review was undertaken (please see *Appendix 7.1*). This research formed a minor component of the work undertaken in this thesis and was led by Dr Liane Ioannou. In total 1738 articles were screened for eligibility, 187 full-text articles were assessed for inclusion and 54 articles of 49 unique models were included in this study. Prognostic models were defined as various types, such as nomograms, prognostic indexes, predictive models and risk prediction models. Results showed that the majority of the models (n= 28, 57.1%) were developed in patients with unresectable (locally advanced and metastatic) disease, 17 models in resectable disease (34.7%) and four in all stages (8.2%), regardless of resectability. Of the 49 models, 34 (69.4%) were validated, either internally and/or externally, with only four models reporting modest-good discriminative ability (concordance (c) statistic or area under the receiver operating characteristic curve (AUROC) greater than 0.70) in both the derivation and validation cohorts. The prognostic factors that were most frequently *evaluated* for inclusion were: age (98.0%), sex (89.8%), tumour site/location (61.2%), performance status (51.0%) and CA 19-9 (51.0%). From a total of 35

models that reported hazard ratios, and 95% confidence intervals, the key factors predicting improved survival were resection of primary tumour (mean HR, 0.23; 95% CI, 1.50-2.87), high performance status (mean HR, 0.57; 95% CI, 1.36-8.15) and a lower T stage (mean HR, 0.59; 95% CI, 1.15-1.83). The factors predictive of poorer survival were: poor performance status (mean HR, 2.91; 95% CI, 1.36-8.15), high lymph node ratio (mean HR, 2.87; 95% CI, 1.34-6.79), and no resection of primary tumour (mean HR, 2.22; 95% CI, 1.50-2.87).

Future research is required to develop and validate a risk adjustment model to be used by the registry. This model will provide a weighting to various prognostic factors, such that the relative impact of quality of care (assessed through adherence to each QI) can be considered in relation to other factors over which the treating hospital and clinicians have no control. The systematic review provides an important first step in this process.

PC will continue to be a challenge into the near future in the absence of novel treatments. The exploration of immunotherapy and advanced drug delivery systems based on nano-formulations provides hope for a better future.[155,156] Research into advancing clinical trials in such areas will provide opportunities for patients diagnosed with PC that may result in improved outcomes and a new standard of care, requiring the development of new QIs. Periodically, the current set of QIs will need to be reviewed for ceiling effect and retirement as outlined in the book chapter (*Appendix 1.1*).

Future research may involve developing and testing interventions to address barriers to uptake of pancreatic protocol imaging and presentation of patients at MDMs. Such interventions should target enablers to optimise the likelihood of success. An intervention to improve uptake of pancreatic protocol imaging should address gaps in knowledge, using data from the registry to demonstrate its importance in reducing abandoned surgery and positive margins. The intervention should also include a referral pathway for patients with suspected

PC to a specialist radiologist prior to surgery and an alert to ensure that patients are presented at MDT meetings and that pancreatic protocol imaging is flagged for discussion.

An intervention aimed at improving case presentation of patients at MDT meetings should consider strategies to encourage representation by palliative care specialists and psychology/psychiatry, improve efficiency of meetings and processes to ensure patients are included on the list for discussion and foster inclusiveness by all members of the team. Investment in technology may facilitate the meeting but time constraints may require new ways of thinking about the meeting itself. Perhaps two meetings may be required; one focusing on optimising palliative care and the other on presenting patients with potentially curable disease. Outcome measures could include the impact of increased case presentations to MDT meetings on PROMs such as psychological wellbeing, especially if referral pathways are formalised within the meeting; and survival.

Both these proposed interventions could be conducted as a registry-based randomised clinical trial (RCT), using the UGICR as the point of recruitment to the study. In comparison to conventional RCTs, registry-based trials exhibit high external validity due to the inclusion of 'real-world' patients who can be rapidly recruited due to broad eligibility criterion, contributions from centres that would not normally participate, the ability to investigate standard of care in their usual setting and collect data as part of routine care.[157] The registry has potential to deliver a program for enhanced implementation of best practices similar to the PACAP-1 multicentre stepped-wedge cluster RCT.[158] The intervention is the translation of optimal care into daily clinical practice and the implementation process involves monitoring, return visits, and provider feedback combined with education and reminders.

Finally, vital to the sustained improvement of quality of care is the engaged patient, the providers and researchers that are integrated into a learning healthcare system that can

contribute to the current knowledge base on PC, the design of more effective strategies that continuously improve and adjust cancer care. This vision was outlined by the National Cancer Institute highlighting their three priorities: (1) enabling a seamless data environment for patients, providers and researchers through the application of data science and computational health analytics; (2) process, visualise and analyse data using an open application programming interface and collaborative platforms; and developing a data science aware workforce capable of using a digital ecosystem.[159] Although the focus for the Institute is genomic data involving clinical trials, there are opportunities to learn from this vision for application to observational data presented by clinical quality registries. The concept of a learning healthcare system using observational data embarks on the notion that data derived during the course of clinical care can be transformed into practical evidence achieved under normal clinical conditions, which can produce new evidence faster and more efficiently than the pragmatic clinical trial where knowledge production can be slow and the expense is relatively high.[160] The risk for using observed data is that inferences of association for causation and the incomplete control of confounding, can lead to adverse health care decisions. Therefore, comparative effectiveness research investigating empirical comparisons of observational studies and clinical trials may establish the trustworthiness of the learning healthcare system using observed registry data.[161,162]

The UGICR is a tool which may improve quality of care provided to patients diagnosed with PC, through ongoing monitoring of care using clinical QIs and PROMs; evaluation and provision of risk-adjusted data in regular reports and feedback to the wider stakeholders that include patients, providers and collaborators; development of new research; and contribution to the learning healthcare system, through a process of continuous improvement. Ultimately though, the provision of high-quality care depends on the triad of the patient, clinician and health system working together.

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APPENDICES

Appendix 1.1 Book Chapter: Quality of care indicators in PC

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Abstract

Quality of care is defined by a range of dimensions (safe, effective, efficient, timely, patient-centred and equitable care) and components (structure, process, outcome). From a clinical perspective, quality of care is measured through the development of core-sets of quality indicators that is based on current evidence and best practice. In addition, Patient-Reported Outcome Measures (PROMs) are equally important in understanding a patient's perspective on their wellbeing, functional status and health-related quality of life. The latter is an important consideration in values-based healthcare. To achieve optimal care in pancreatic cancer which is characterised by poor survival, high symptom and psychological burden, care needs to be monitored using the above described measures, then evaluated to identify variations that exist and reported back to relevant stakeholders within a framework of a continuous quality improvement cycle.

Keywords

Quality of care, Quality indicators, Pancreatic Cancer, PROMs, Value-based health

Take home messages

- Establishing rigorous and disciplined measures of quality are a critical step in evaluating quality of care for patients diagnosed with pancreatic cancer.
- The measures or quality indicators should evaluate all facets of the disease trajectory, namely diagnosis and staging, surgery, other treatment, patient management and outcomes, within the framework of a continuous improvement cycle.
- Clinical measures often do not take into account a patient's wellbeing, functional status and health-related quality of life. These are best evaluated using patient-reported outcome measures.

Pearls and pitfalls

- The measurement of quality is hampered by inadequate data sources, a lack of systematic outcome assessment, suboptimal documentation of care delivery and a lack of formal monitoring systems.
- Escalating costs of health care coupled with increased burden on financial and human resources is a barrier to quality improvement.
- The current model of healthcare delivery has led to a siloed speciality-driven approach with the potential to game the system, slow progress in performance improvement and is projected to be unsustainable in the near future.

Future perspectives

- Quality of Care indicators will play a pivotal role in establishing a value-based healthcare delivery system that measures and manages patient level costs over complete cycles of care.

Introduction

There has been a shift in our understanding and evaluation of quality of care in the past few decades, driven by maestros who dedicated their lives to improvement sciences. The conversation has moved from achieving not only improved clinical outcomes but also to understanding 'what matters to patients'. In pancreatic cancer, which is often classified as a low survival cancer, optimised care can improve survival and quality of life. Measurement from a clinical and patient perspective using well developed quality indicators is critical in evaluating variations in care and identifying areas for improvement.

Defining Quality of Care

The measurement of quality to improve health care is complex with no single, precise or ideal definition of quality. The definition of quality as it is best known is captured in Box 1.

Box 1: Defining Quality

In 1990, the Institute of Medicine (IOM) Committee compiled, analysed and debated on the many available definitions. The committee's final definition is outlined as follows:

> *"Quality of care is the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge."*[1]

Quality of care is best viewed in terms of performance on a range of dimensions as further defined by the Institute of Medicine (safe, effective, efficient, timely, patient-centred and equitable care) and the components of health care (structure, process, outcome) described by Donabedian. [2,3]

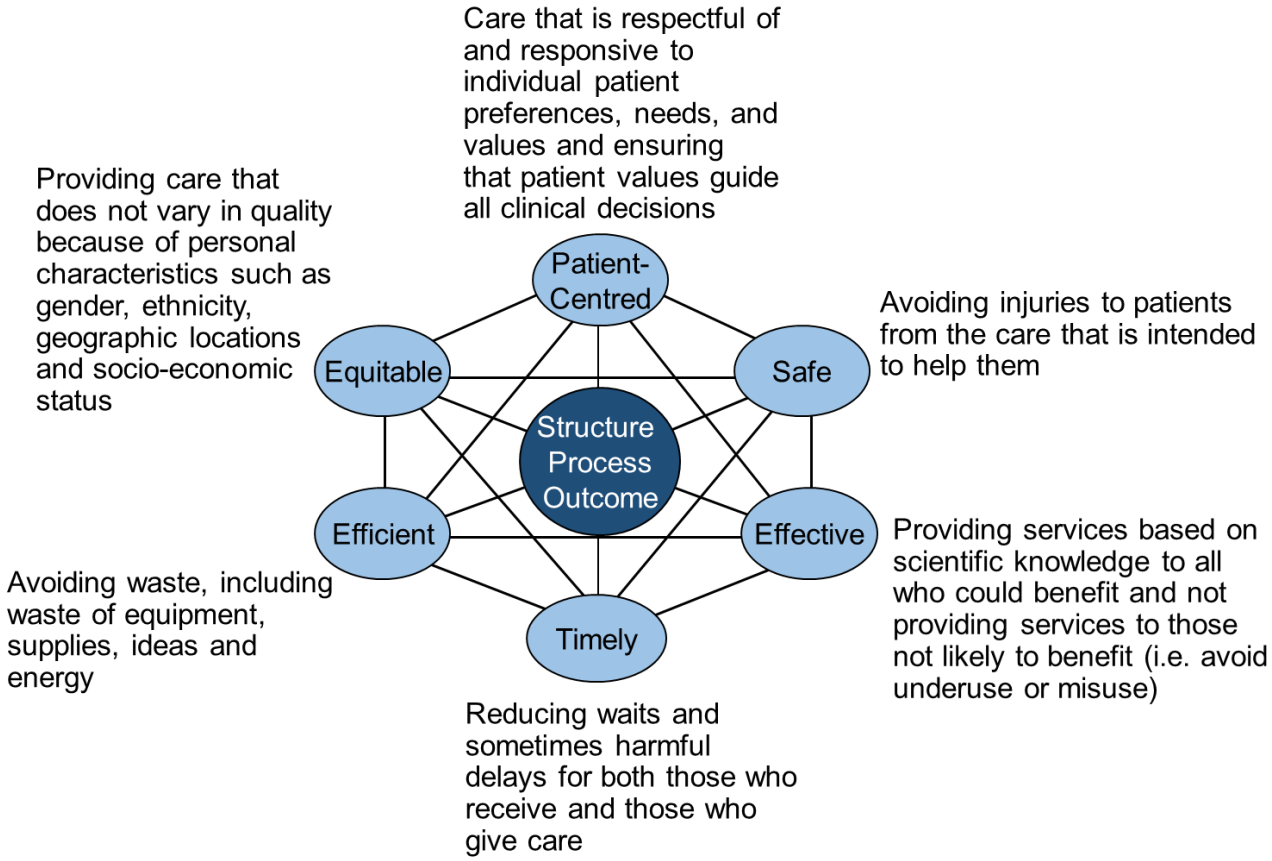
Structures measure the foundation on which a service is built. For example, the services it provides and the governance structure in place. Without strong foundations health systems are unable to safely, and effectively deliver care which is equitable, timely and patient-centred.

Processes of care are those interventions which are highly correlated with better health outcomes for patients. For example, there is strong evidence that surgical antibiotic prophylaxis administered within two hours prior to incision, according to the type of operation will reduce risk of post-operative infection.[4] Processes of care can often be extracted from administrative datasets or collected through audit with relative ease.

Outcomes of care are arguably the most important means of measuring the quality of care provided by health services. However, there are complexities in measuring outcomes which are not as clear cut as when assessing either structures or processes of care. For example, choosing the time point to measure an outcome is important; too early after the care may not have provided sufficient time for the effect to be realised. Outcomes measured some time after an episode of care may be impacted by other factors aside from the treatment which was delivered.[5] For this reason, outcomes require careful deliberations. Risk adjustment is also essential in order to be certain that patients outcomes are being adjusted for variables that are not related to the delivery of health care, e.g. age or comorbidities.[6]

The conceptual framework that underpins the evaluation of quality care is presented in *Figure 1*.

Figure 1: Conceptual framework that underpins the quality of care



Variations in Quality of Care

To understand quality in pancreatic cancer and the variations that exist to achieve optimal care, we have to first ask the question, 'what is good quality of care'? This is explored using examples relating to care of patients with pancreatic cancer and applying the aforementioned dimensions of quality in Box 2.

Box 2: Exemplars of variations in care in pancreatic cancer

Is care safe? There is accumulating evidence that patients undergoing pancreaticoduodenectomy in hospitals managing low volumes of patients have higher mortality rates than those treating high volumes of patients with pancreatic cancer.[7,8] This is likely the result of increased ability to deliver safe care in hospitals resourced to manage these complex patients. As a result of this evidence, a call has recently been made in a number of United States (US) health services to limit pancreatic surgery privileges to surgeons performing at least five cases per year and facilities with at least 20 cases per year.[9] In addition to using mortality to assess safety of care, other markers of unsafe care include iatrogenic injuries and complications such as infection, haemorrhage, pressure ulcers, drug errors, and wound dehiscence.

Is care effective? There are cases where planned procedures (e.g. diagnostic laparoscopy) or a planned surgery for potentially resectable disease is abandoned intraoperatively. An abandoned surgery may indicate that the patient has not been effectively staged. In addition, surgery should ideally result in clear margins (margin-negative or R0). Unfortunately, around 20% of cases have microscopically positive (R1) or macroscopically positive (R2) margins resulting in poorer clinical outcomes.[10] R1 margins may be a marker of ineffective pre-operative staging before undertaking surgery.

Is care timely? Pancreatic cancer is an aggressive disease with majority of patients diagnosed at an advanced stage. The pathway to early diagnosis is complicated by the onset of generalised gastrointestinal symptoms, comorbidities and delays in referral. Patients can experience significant delays from referral to diagnosis when undergoing investigations for generalised gastrointestinal symptoms with a median delay of 64.5 days.[11]

Is care equitable? Differences in complications and mortality may be due to disparity in quality of care provided by individual providers or institutions. We know that people

living in regional or rural locations can be less likely than their city counterparts to receive anti-cancer therapy.[12] Patients living in areas with higher socio-economic status are also more likely to receive access to more advanced medical care that is associated with improved survival and improved quality of life.[13]

Is care efficient? Structured reporting of surgical pathology increases the accuracy, accessibility, completeness and uniformity of surgical pathology diagnosis. However, there is variable quality of pathological reporting with some evidence that up to 44% of free text reports do not contain sufficient information for disease stage to be inferred. In one study margin status was recorded in only 11% of reports.[14]

Is care patient-centred? Current expert opinion and international recommendations state that management decisions, certainly for early pancreatic cancer should be made within the framework of a multidisciplinary team (MDT) meeting to ensure that the full range of available and appropriate treatment options are considered.[15] Yet, only a third of patients diagnosed with pancreatic cancer are presented to MDT meetings.[13]

To understand the reasons behind variations in care, evaluating the quality of care delivered to patients diagnosed with pancreatic cancer is an essential step.

Monitoring Quality of Care

The measurement of quality of care for patients diagnosed with pancreatic cancer across the trajectory of the disease requires an understanding of scientific principles to underpin our measurement tools to obtain reliable and comparable data. Sources of data for quality assessment can include direct observation of a health care encounter, medical records, administrative databases, incident reports, clinical registries, patient satisfaction and patient experience surveys. Currently, the measurement of quality is hampered by inadequate data sources, a lack of systematic outcome assessment, suboptimal documentation of care delivery and a lack of formal monitoring systems.[16] A persisting challenge in measuring quality is ensuring that metrics used are reliable and reproducible. A high level of scientific credibility from measurement tools and data sources is demanded.

Clinical Indicators

Clinical indicators provide the basis for evaluation of care in pancreatic cancer. They quantitatively measure aspects of the structure, process and outcomes of patient care to act as a ‘flag’ that indicate areas for further investigation.[16]

Clinical indicators can be used as a basis for self-improvement to inform policy and strategy making, to monitor performance of services and of funding bodies, to empower consumers to help make decisions about their choice of health services and to identify poor performance. Increasingly they are providing the basis for financial incentives related to select health service parameters. [17]

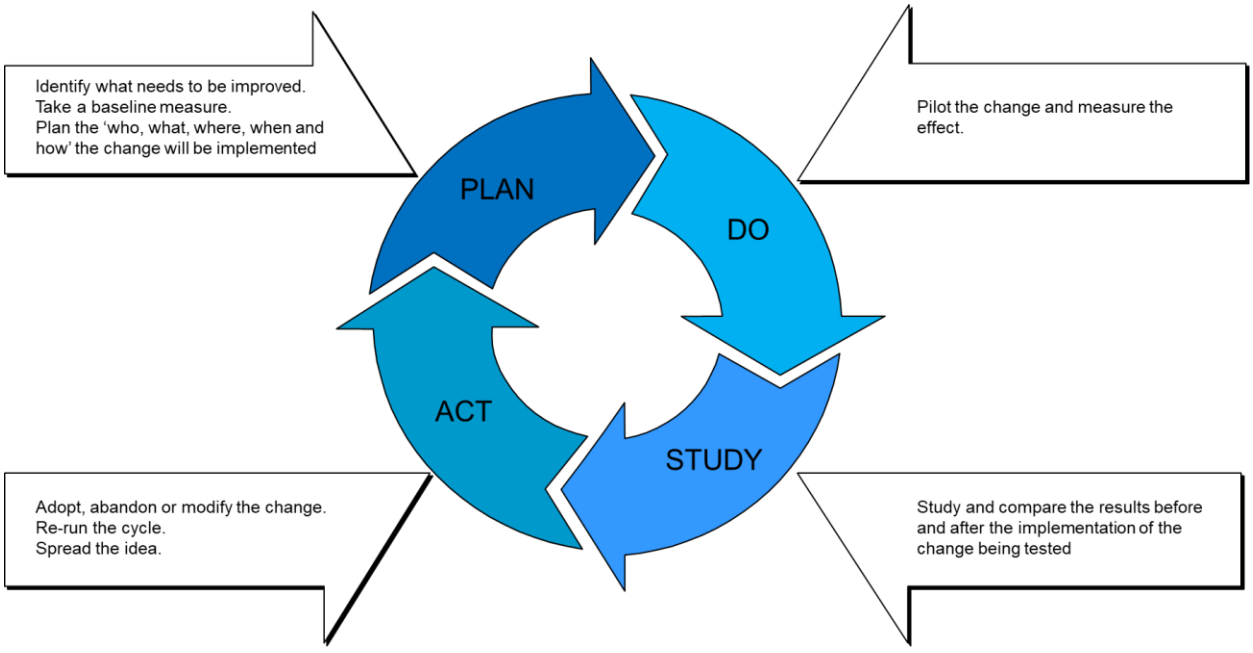
Clinical indicators, in and of themselves, are ineffective unless incorporated into a quality improvement cycle.

Box 3: The Father of Quality

Edward Deming developed such an approach into the manufacturing industry post the second World War in Japan, and it has since been widely implemented in health service delivery.[18] Considered the Father of Quality, Deming introduced the Total Quality Management paradigm, which promoted systematic analysis and measurement of processes linked to producing quality outputs.

The Deming continuous quality improvement cycle ensured that on an ongoing basis opportunities to improve were harnessed. The Deming Cycle, also referred to as the Plan-Do-Study-Act cycle, or the Plan-Do-Check-Act (*Figure 2)*.

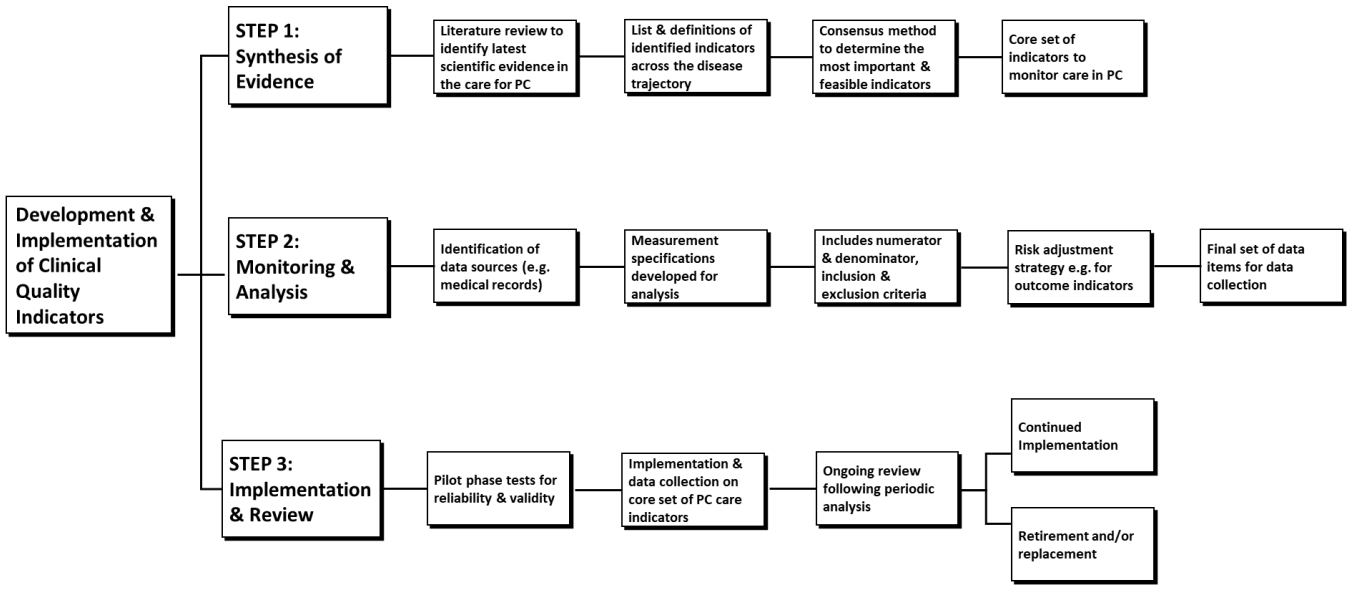
Figure 2: Plan-Do-Study-Act cycle and Model for Improvement[19]



Development and Implementation of Clinical Quality Indicators in Pancreatic Cancer

Clinical indicators for pancreatic cancer care should include all facets of the disease trajectory, namely *diagnosis and staging, surgery, other treatment, patient management* and *outcomes.* They can be derived from academic literature or, where scientific evidence is lacking, determined by an expert panel of health professionals in a consensus process.[16] The most widely used consensus method is the Delphi technique initially developed in 1969. The Delphi method includes questionnaires or surveys to determine the most appropriate indicators from a panel of experts.[20] More recently, a modified Delphi method was introduced which includes an initial survey followed by the panel meeting face to face to discuss the results of the first survey round, focussing on areas of disagreement and the opportunity to modify the original list of proposed indicators. Other consensus methods include the Nominal Group Technique which is a structured process and requires participants to brainstorm ideas followed by a discussion and ranking of an item's importance.[21] *Figure 3 provides a schematic outlining the processes in the development of clinical indicators. Step 1* summarises the development of a core set of quality indicators; *Step 2* discusses how to monitor and analyse the data, and *Step 3* describes the processes for implementation and review (Figure 3).

Figure 3: Steps to developing clinical quality of care indicators for pancreatic cancer.



Legend: Adapted from Fitch et al & Prosser-Snelling E, Morris E. [17,21]

Step 1: Synthesis of Evidence

In 2009, Bilimoria and colleagues identified a set of surgical quality indicators for pancreatic cancer. This was subsequently built upon by Burmeister and colleagues in 2016, who identified a set of care statements that included patient management indicators.[22,23] Further to this work, the authors of this chapter developed, through a modified Delphi approach, a core set of 27 clinical quality indicators to monitor care across all areas of the disease trajectory (*seven* diagnosis and staging, *five* surgical, *four* other treatment, *five* patient management and *six* outcome measures) as listed in *Table 1*. [24]

Table 1: Core set of pancreatic cancer indicators developed through a modified Delphi approach[24]

INDICATORS
Diagnosis & Staging
Documented pancreatic protocol CT or MRI scan for diagnosis and/or staging
Tissue biopsy attempted prior to chemotherapy or radiotherapy
Documented baseline CA19-9 level before treatment
Documented ECOG and/or ASA at presentation
Time from referral to definitive treatment within 60 days (relief of biliary obstruction is not definitive treatment)
MRI, CT or PET completed following neoadjuvant treatment
Operability of tumour is clearly defined and documented as either operable/resectable, borderline resectable, locally advanced (unresectable) or metastatic (unresectable)
Surgery
Royal College of Pathologists of Australasia or equivalent reporting system used to document findings for patients undergoing surgical resection
Standard lymphadenectomy with the removal of ≥ 10 lymph nodes pathologically examined and documented
"Number of R1 resections (positive ≤ 1mm margin) for those that have a synoptic report (refer to 2.1.7) Number of R1 resections (positive ≤ 1mm margin) for those that do not have a synoptic report"
Number of patients undergoing pancreatic cancer surgery in a level 1-4 hospital (check private hospital)

INDICATORS
All patients who did not undergo surgery should have a valid reason documented
Other Treatment
Adjuvant chemotherapy administered following surgery or a reason documented for not undergoing treatment
Chemotherapy ± chemo-radiation offered to patients with locally advanced disease, or a reason documented for not undergoing treatment
Neo-adjuvant chemotherapy ± chemo-radiation offered to patients with borderline resectable disease, or a valid reason documented for not undergoing treatment
Number of patients who saw a medical or radiation oncologist or a reason documented for not doing so
Patient Management
Disease management for all patients discussed at a MDT meeting
Number of patients with biliary obstruction managed surgically or by stent
All patients with metastatic disease referred to (or seen by) palliative care specialist
All patients having completed treatment followed up specialist every three to six months for up to 2 years
Number of patients included in a clinical trial
Outcome
Patients requiring a re-operation following surgical resection
Patient died within 30-days of last dose of chemotherapy
>2 ED presentations in the last 30-days before death
2 year and 5 year survival rates for patients who underwent a surgical resection
≥14 days in acute hospital
30-day and 90-day mortality rate following surgical resection (level of risk adjustment to be determined)

Step 2: Monitoring and Analysis

Once a core set of clinical quality indicators to monitor care in pancreatic cancer has been established via a consensus method, the next phase *(Figure 3, step 2)* is to determine the data sources from which data will be collected such as administrative data or medical record review. Measurement specifications include determining the numerator, denominator, inclusion and exclusion criteria for each clinical quality indicator. A risk adjustment and risk stratification approach may be required, particularly if the indicator is assessing a health outcome which may be impacted by factors other than those within the capacity of the health service to control. Risk adjustment may be used to introduce a weighted approach to consider the impact of major confounders impacting the outcome. These are commonly the patient's age and stage of disease at the time when the indicator is being measured. Risk stratification may involve measuring the indicator in a particular subset of the population of patients with pancreatic cancer; for example only those with stage I disease undergoing surgery.

It is also important to consider how data will collected and by whom. Data can be collected by clinicians or trained data collectors. Ideally, the person collecting the data for quality indicators should be impartial and independent to avoid any potential biases in recruitment or data collection. An important consideration is where the data will be stored. Electronic databases such as REDCap (Research Electronic Data Capture) provide a secure, web-based software platform designed to support data capture and storage.[25]

Step 3: Implementation and Review

Following the development of key data items for collection of relevant information, implementation should begin with a pilot phase to test the reliability and validity of the data items. This can be dependent on the accuracy of the coding and recording of data if using an administrative data source, and data completeness for other sources such as medical chart review.[26] *Figure 3, step 3* outlines the lifecycle of a clinical quality indicator. Following implementation of the core set, periodic analysis and evaluation is necessary not only for feedback and reporting but also for quality assurance that each indicator is continually measuring 'what it is meant to measure'. With time some clinical quality indicators may become obsolete due to the changing landscape of evidence and others may become appropriate if sufficient evidence has accumulated to deem it quality care. For example, the administration of neo-adjuvant therapy in *resectable* pancreatic cancer is yet to be established as best practice, although it has gained momentum as standard of care for other gastrointestinal cancers.[27]

Value-based Health Care

The escalating costs of health care, due in part to expensive new technology and drugs, coupled with increased burden on financial and human resources is a barrier to quality improvement. Health care expenditure continues to increase across many countries at a rate above that of inflation. The current model of health care delivery in many countries provides care in a fee-for-service approach often focusing solely on service volume. Costing systems are organised by spending category such as employee costs, equipment, devices, imaging, laboratory tests, and pharmaceuticals. This model has led to a siloed speciality-driven approach with the potential to game the system, slow progress in performance improvement and is projected to be unsustainable in the near future. The alternative proposal is an overhaul of the current system to introduce value-based health care delivery, a model that measures and manages patient level costs over complete cycles of care for a variety of medical conditions. [28]

Michael Porter first introduced the concept of value-based health care in an article published in the New England Journal of Medicine in 2009.[29] In this article, Porter espouses that to achieve a value-based delivery system the following steps are required:

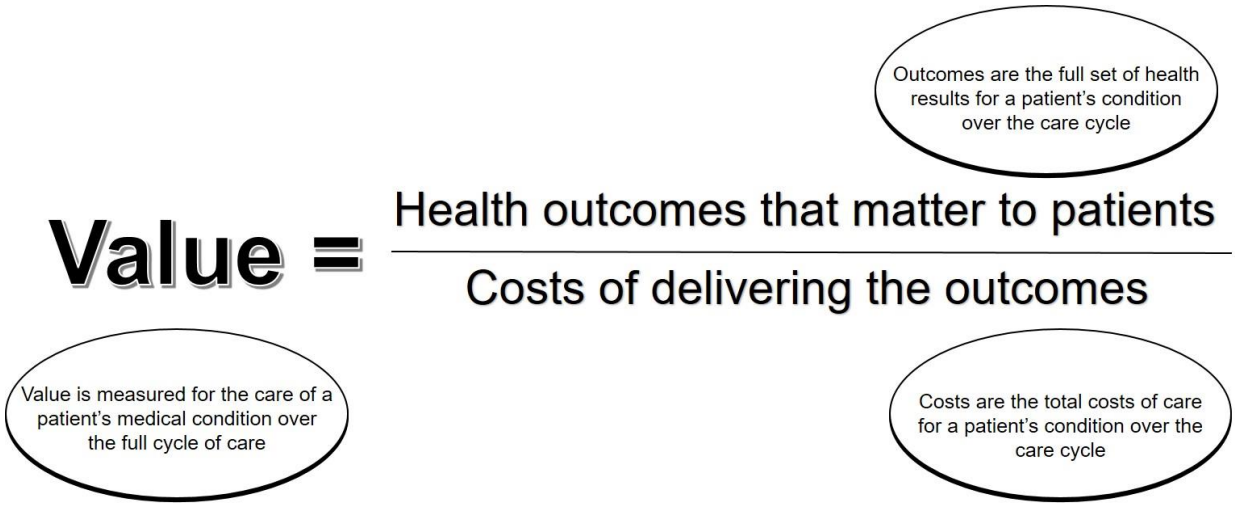
1. Measure and disseminate health outcomes for every provider and every medical condition. Outcomes must be measured over the full cycle of care from diagnosis through to treatment and recovery or end-of-life. The degree of health prior to treatment should be considered when assessing outcomes following diagnosis and treatment. Outcomes should assess the quality of health and recovery achieved, time required for recovery, patient discomfort and sustainability of recovery.
2. Re-examine how prevention, wellness, screening and routine health services are delivered. There is a need to invest where required to defined patient populations with unified reimbursement.
3. Reorganise care around medical conditions or sets of closely related conditions
4. Reimbursement should align everyone's interests around improving value for patients. Bundled payments to cover the entire cycle of care for a medical condition will shift the focus towards restoring function and maintaining health.
5. Providers should compete for patients, based on value at the medical-condition level. This will foster excellent providers.
6. Electronic medical records will enable value improvement if they support integrated care and outcome measurement.

7. Consumers must engage in their health and in health care. They must take responsibility for their health.

Of a particular note, is the importance of assessing clinical measures such as complications and survival as well as patient-reported outcomes (PROs).

Value-based care can be conceptualised by the following formula in Figure 4:[29]

Figure 4: Value-based health care delivery



Patient-Reported Outcome Measures (PROMs) in pancreatic cancer

When discussing clinical indicators earlier in this chapter, the objective was to determine from clinicians or experts in the field of pancreatic cancer, the most important and feasible measures to monitor clinical outcomes. However, clinical measures often do not take into account a patient's wellbeing, functional status and health-related quality of life. Further, the views on 'what matters' to a patient may differ to that of a clinician. For example, in one study, clinicians placed higher importance on symptoms such as pain, nausea, vomiting, abdominal complaints, itching and jaundice compared to patients in a palliative setting.[30] Which leads us to the question, how do we determine the health outcomes that matter most to patients diagnosed with pancreatic cancer?

Pancreatic cancer is characterised by poor survival, high symptom and psychological burden and as described by one study, 'a tsunami of unmet needs'.[31,32] Integration of PROs into

clinical practice, health service or health systems level using structured instruments (e.g. standardised questionnaires) known as Patient-Reported Outcome Measures (PROMs) have shown to improve patient-clinician communication, overall patient care and outcomes.[33]

There has been an exponential rise in the number of PROMs developed for cancer care over the past three decades. Given the considerable burden of this disease and poor survival, it is especially important that the selected PROM has undergone psychometric evaluation in a pancreatic cancer population and is deemed reliable, valid and sensitive to change, rather than merely extrapolated from other populations. Following an extensive and detailed systematic review, we recommend one of three multidimensional PROMs be used depending on the intent: FACT-HEP in patients with unresectable pancreatic cancer; QLQ-PAN26 (in conjunction with its core QLQ-C30 PROM) in those with resectable pancreatic cancer; and MDASI-GI, a tool that may be useful irrespective of disease stage.[34]

Evaluating Quality of Care

Establishing and evaluating rigorous and disciplined measures of quality are a critical step in evaluating quality of care. We have demonstrated that the comprehensive evaluation of quality of care in pancreatic cancer requires a two-fold approach based on clinical quality indicators and PROMs. In addition, the evaluation of outcome measures at the patient-level can estimate value in health care delivery that is patient-centric.

Several authors have now used this approach to evaluate quality of care in defined populations of patients with pancreatic cancer. Bilimoria and colleagues demonstrated variability in the surgical quality of care in pancreatic cancer. Adherence to individual level indicators ranged from 49.6% to 97.2 % and hospital-level indicators ranged from 6.8% to 99.9%.[22] Burmeister and colleagues were able to demonstrate significant disparities based on socio-economic status. Further, not all patients were presented to MDTs (31%), received psychosocial support (19%), participated in clinical trials (7%), or were first seen by a hepatobiliary surgeon (19%).[13]

There has been continued efforts to develop and standardise core clinical and patient-reported indicators but a significant gap remains in the literature on the evaluation of quality of care for patients diagnosed with pancreatic cancer.

Feedback and Reporting

The development and implementation of quality indicators requires detailed synthesis and evaluation, with good access to population health and statistical resources.[17] Increasing attention is being paid to the importance of using state-wide or national clinical quality registries to monitor, benchmark, and report risk-adjusted data on quality of care. Clinical quality registries have shown to drive continuous improvement by using a feedback mechanism to report on the appropriateness of care (process) and the effectiveness of care (outcomes). They also generate more reliable and credible information compared to administrative databases.[35] Examples of clinical quality registries that exist for pancreatic cancer are the Pancreatic Cancer Collaborative Registry,[36] Danish Pancreatic Cancer Database,[37] and the Upper Gastrointestinal Registry (UGICR) which has a module dedicated to pancreatic cancer.[38]

Regardless of whether data for clinical indicators or PROMs are supported by a clinical registry, feedback provided through timely reporting, quality indicators can be effective in improving professional practice. [39]

Examining Variation

Inevitably, when examining quality of care using quality indicators, sub-optimal performance will be identified. We have discussed the need to incorporate quality indicators in a continuous improvement cycle, but how do we identify what needs to be done in order to improve? Often this requires a deep understanding of the variation identified. There are many factors which impact best practice hasn't been identified. Understanding this is pivotal when developing the improvement cycle.

One patient management indicator developed as part of the core set *(Table 1)* is *'disease management for all patients discussed in a MDT meeting'*. Data from the UGICR show that approximately 30 % of patients are not discussed at MDT meetings, the majority (67%) of which are those with metastatic disease. Although 90% of patients undergoing a surgical resection are discussed at MDT meetings, 27% are discussed following their surgery rather than prior to treatment. A qualitative approach such as interviews or focus groups may be necessary to identify the barriers and enablers impacting on health professionals involved in patient care, in order to facilitate quality improvement and optimise performance measured through this indicator.

Conclusions

In this chapter, we have introduced a conceptual framework to consider when introducing a system to monitor quality of care in patients with pancreatic cancer. We have outlined clinical indicators selected by an expert panel to measure quality of care and discussed the need to incorporate measurement within a continuous quality improvement cycle, in which data are constantly being examined and improvement sought. We have discussed value-based health care and describe why it is an important societal consideration when examining quality of care. Finally, we provide some models to help understand variation in quality of care.

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Appendix 2.1: Ethics Approval

Monash University Human Research Ethics Committee

Approval Certificate

This is to certify that the project below was considered by the Monash University Human Research Ethics Committee. The Committee was satisfied that the proposal meets the requirements of the *National Statement on Ethical Conduct in Human Research* and has granted approval.

Project Number: 9943
Project Title: Delphi Process - Monitoring Quality of Care for Patients with Pancreatic Cancer
Chief Investigator: Assoc Professor Susan Evans
Expiry Date: 24/07/2022

Terms of approval - failure to comply with the terms below is in breach of your approval and the *Australian Code for the Responsible Conduct of Research*.

1. The Chief Investigator is responsible for ensuring that permission letters are obtained, if relevant, before any data collection can occur at the specified organisation.
2. Approval is only valid whilst you hold a position at Monash University.
3. It is responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval and to ensure the project is conducted as approved by MUHREC.
4. You should notify MUHREC immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.
5. The Explanatory Statement must be on Monash letterhead and the Monash University complaints clause must include your project number.
6. Amendments to approved projects including changes to personnel must not commence without written approval from MHUREC.
7. Annual Report - continued approval of this project is dependent on the submission of an Annual Report.
8. Final Report - should be provided at the conclusion of the project. MUHREC should be notified if the project is discontinued before the expected completion date.
9. Monitoring - project may be subject to an audit or any other form of monitoring by MUHREC at any time.
10. Retention and storage of data - The Chief Investigator is responsible for the storage and retention of the original data pertaining to the project for a minimum period of five years.

Thank you for your assistance.

Professor Nip Thomson

Chair, MUHREC

CC: Professor John Zalcberg, Miss Liane Ioannou, Mrs Ashika Maharaj, Ms Jennifer Holland

List of approved documents:

Document Type	File Name	Date	Version
Explanatory Statement	ExplanatoryStatement	28/06/2017	3.0
Consent Form	ConsentForm	28/06/2017	1.0
Supporting Documentation	PancreasProtocol v3(FINAL)	28/06/2017	3.0
Questionnaires / Surveys	ExampleQuestionnaire&Supplementary	28/06/2017	3.0
Explanatory Statement	EXPLANATORY STATEMENT_2	19/07/2017	4.0
Consent Form	DelphiConsentForm_2	19/07/2017	2.0

Appendix 2.2: Supplementary Document (incl explanatory statement)

PANCREATIC CANCER QUALITY INDICATORS
DELPHI PROCESS ROUND ONE – ONLINE SURVEY

SUPPLEMENTARY DOCUMENT

This document contains useful information that may assist you in completing the online survey for the Delphi Process. Please keep it open as you undertake the survey and refer to it when required.

Version 4.0

23 August 2017

TABLE OF CONTENTS

IMPORTANT CONTACT INFORMATION

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EXPLANATORY STATEMENT

Thank you for your participation in this modified Delphi panel to develop a set of quality indicators, based on evidence, patient experience and clinician perspective to judge and assess quality performance in pancreatic cancer.

YOUR ROLE

We have developed 107 proposed indicators after reviewing domestic and international guidelines, as well as multimodality studies of factors measuring quality of care in patients with pancreatic cancer. In this survey, you are asked to use the Likert scale (from 1 to 9) to rank the importance of including the proposed indicator in the Pancreatic Cancer Registry for Quality Improvement (P-CR4QI) database. A rating of 1 suggests that the indicator is 'not important' while 9 suggests that the indicator is 'very important'. When making this decision, consider the guideline from where it was taken and its grade of evidence/recommendation.

These details will be elaborated in the indicator index. Similar indicators have been grouped under the same indicator reference number but are differentiated by letters (e.g. 1.1.1**a** and 1.1.1**b**); please compare the indicators and take their differences into consideration when rating them individually. *We will only be selecting one indicator from those that are similar, so choose the one you would prefer and score it significantly higher than the next best one in that category*. In this way we hope we will see a clear preference.

If you believe that you do not have the knowledge or experience to make an informed decision, there is an 'unable to comment' option.

The online survey should take approximately 1 – 2 hours. ***** To save and continue the survey later:** You can save your survey and return to it later by simply closing the survey. Qualtrics automatically saves your progress using cookies. However, please note that this will only work as long as you return to the survey on the same internet browser on the same computer. *The completion of the first online survey is due Monday **18th September 2017***.

A full day face-to-face meeting will be held in Sydney on 14th October 2017 where the scores from the online survey will be made available. Individual scores will be confidential.

You have been sent an email containing a link to the survey which is conducted in Qualtrics and a unique identifier (number). Please record this number on the survey as you begin. You can save the survey and return to it for completion.

STRUCTURE OF THE SURVEY

What are indicators?

"A clinical (or quality) indicator is simply a measure of the clinical management and/or outcome of care. A well designed indicator should screen, flag or draw attention to a specific clinical issue. Indicators are designed to indicate potential problems that might need addressing, by identifying variations with data results. They are used to assess, compare and determine the potential to improve care and are therefore tools to assist in assessing whether or not a standard in patient care is met."[1]

This survey has been structured to reflect the chronological process of pancreatic cancer management. Each indicator has been given its own reference number. The first number corresponds with the process (1 = Diagnosis & Staging, 2 = Surgery, 3 = Treatment, 4 = Management and 5 = Outcomes). The second number corresponds with the sub-category if further categorisation has been necessary. Statements associated with each indicator have been sourced **verbatim** from accompanying references

1. Diagnosis and Staging
2. Surgery
3. Treatment
4. Management
5. Outcomes

Please rate the indicators according to importance. **We suggest that you rate the indicators you wish to see in the final set with highest importance.** Numbers with a, b, c or d, denotes a group of similar indicators (please assign a much higher value to your preferred choice)

[1] Australian Council on Healthcare Standards. Clinical Indicator Program Report 2016. 18th Edition. New South Wales: ACHS; 2016

ABBREVIATIONS

Table 1: Full list of abbreviations that have been used in this document

AGITG	Australasian Gastro-Intestinal Trials Group
CA 19-9	Carbohydrate Antigen 19-9
CAP	College of American Pathologists
CE	Content Experts
CRT	Chemo-radiation Therapy
CT	Computed Tomography
EUS	Endoscopic Ultrasound
EUS ± FNA	Endoscopic Ultrasound ± Fine Need Aspirate
HPB	Hepatopancreatobiliary
HREC	Human Research Ethics Committee
LAPC	Locally Advanced Pancreatic Cancer
LFT	Liver Function Test
MDT	Multidisciplinary Team
MRI	Magnetic Resonance Imaging
NHMRC	National Health and Medical Research Council
NSW	New South Wales
PC	Pancreatic Cancer
P-CR4QI	Pancreatic Cancer Registry for Quality Improvement
PET	Positron Emission Tomography
RAM	Rand/Ucla Appropriateness Method
RCT	Randomised Control Trial
SBRT	Stereotactic Body Radiation Therapy
SEMS	Self-Expanding Metal Stent
UGI	Upper Gastro-Intestinal

UGICR	Upper Gastro-Intestinal Cancer Registry
US	Ultrasound
VCR	Victorian Cancer Registry
VIC	Victoria

FULL REFERENCES

Throughout the survey, guidelines and articles have been referred to using abbreviated terms. The subsequent tables state the full references and the links from which you can access the literature.

Guidelines

Table 2: The full references and links of the guidelines used

ABBREVIATED REFERENCE	FULL REFERENCE
ASCO 2016a	Potentially Curable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guidelines (United States)
	http://www.asco.org/practice-guidelines/quality-guidelines/guidelines/gastrointestinal-cancer#/12146
ASCO 2016b	Locally Advanced, Unresectable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guidelines (United States)
	http://www.asco.org/practice-guidelines/quality-guidelines/guidelines/gastrointestinal-cancer#/12151
ASCO 2016c	Metastatic Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guidelines (United States)
	http://www.asco.org/practice-guidelines/quality-guidelines/guidelines/gastrointestinal-cancer#/12156
BMJ Best Practice 2016	Pancreatic Cancer: British Medical Journal Best Practice Online (United Kingdom)
	http://bestpractice.bmj.com/best-practice/monograph-pdf/265.pdf
CCO 2016	Pancreatic Cancer: Expert Insights for Optimal Treatment. Clinical Care Options (United States)
	https://www.clinicaloptions.com/Oncology/Treatment%20Updates/Pancreatic%20Insights/Downloadable%20PDF%20Resource/Summary_Resource.aspx
ESMO 2015	European Society for Medical Oncology - Cancer of the Pancreas: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up (Switzerland)
	http://*www.esmo.org/Guidelines/Gastrointestinal-Cancers/Cancer-of-the-Pancreas*

NCCN Version 2. 2017	National Comprehensive Cancer Network - Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma (United States of America)
	This document can be provided on request
VIC OCP 2015	Optimal Care Pathway for People with Pancreatic Cancer (Australia)
	http://www.cancervic.org.au/downloads/health-professionals/optimal-care-pathways/Optimal_care_pathway_for_people_with_pancreatic_cancer.pdf

Articles

In the indicators that measure outcome, there were insufficient guidelines. In these cases, articles that investigated certain quality of life measures or complications of different treatments have been used as a justification. The full references and links where you can access these articles have been provided below in *Table 3*.

Table 3: The full references and links of the articles used

ABBREVIATED REFERENCE	APPENDIX REF	FULL REFERENCE
Arnachellum et al., 2016	**2**	Arnachellum R.P et al. Pancreatic Adenocarcinoma in the Finistere Area, France, between 2002 & 2011 (1002 Cases). Pancreas. 2016 Aug;45(7):953-60
		https://www.ncbi.nlm.nih.gov/pubmed/26765965
Burmeister et al., 2016a	**3**	Burmeister, E. A. et al. Using a Delphi process to determine optimal care for patients with pancreatic cancer. Asia-Pac J Clin Oncol 2016;12: 105–114
		https://www.ncbi.nlm.nih.gov/pubmed/26800012
Burmeister et al., 2016b	**4**	Burmeister E.A et al. Factors associated with Quality of Care for patients with pancreatic cancer in Australia. Med J Aust 2016; 205 (10): 459-465. || doi: 10.5694/mja16.00567
		https://www.mja.com.au/journal/2016/205/10/factors-associated-quality-care-patients-pancreatic-cancer-australia
Bilimoria et al., 2009	**5**	Bilimoria KY et al; Pancreatic Cancer Quality Indicator Development Expert Panel, American College of Surgeons. Assessment of pancreatic cancer care in US based on formally developed quality indicators. J Natl Cancer Inst. 2009 Jun 16;101(12):848-59

		https://www.ncbi.nlm.nih.gov/pubmed/19509366
De Leede et al., 2016		Common variables in European pancreatic cancer registries: The introduction of the EURECCA pancreatic cancer project. European Journal of Surgical Oncology 2016 Mar; **42**(9): 1414-1419.
		https://www.ncbi.nlm.nih.gov/pubmed/27061790
Gagliardi et al., 2016	**6**	Gagliardi AR et al. Identifying Factors Influencing Pancreatic Cancer Management to Inform Quality Improvement Efforts and Future Research: A Scoping Systematic Review. Pancreas. 2016 Feb;45(2):161-6
		https://www.ncbi.nlm.nih.gov/pubmed/26752254
Gandy et al., 2016 (AGITG Consensus)	**7**	Gandy et al. Refining the care of patients with pancreatic cancer: the AGITG Pancreatic Cancer Workshop consensus. Med J Aust 2016; 204 (11): 419-422.
		https://www.mja.com.au/journal/2016/204/11/refining-care-patients-pancreatic-cancer-agitg-pancreatic-cancer-workshop
Nordby et al., 2013	**8**	Nordby, Tom et al. "Opportunities of Improvement in the Management of Pancreatic and Periampullary Tumors: Prospective Evaluation of Outcome from a Multidisciplinary Research Program." Scandinavian Journal of Gastroenterology 48.5 (2013): 617–625. PMC. Web. 16 June 2017.
		https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3665210/pdf/GAS-48-617.pdf
Visser et al., 2012	**9**	Visser BC et al. Failure to comply with NCCN guidelines for the management of pancreatic cancer compromises outcomes. HPB (Oxford). 2012 Aug;14(8):539-47
		https://www.ncbi.nlm.nih.gov/pubmed/22762402
Van Rijssen et al., 2016	**10**	Van Rijssen, L. B., et al. National compliance to an evidence-based multidisciplinary guideline on pancreatic and periampullary carcinoma. Pancreatology 2016; 16(1): 133-137
		https://www.ncbi.nlm.nih.gov/pubmed/26560441

STAGING

In the online survey, indicators may refer to a particular stage of pancreatic cancer. Where this is the case, the indicators are referring to the stages designated below in *Table 4.*[2]

Table 4: Definitions of Primary Tumour (T), Regional Lymph Node (N) and Distant Metastasis (M)

T Category	T Criteria
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma *in situ* This includes high-grade pancreatic intraepithelial neoplasia (PanIn-3), intraductal papillary mucinous neoplasm with high-grade dysplasia, intraductal tubulopapillary neoplasm with high-grade dysplasia, and mucinous cystic neoplasm with high-grade dysplasia
T1	Tumour ≤ 2 cm in greatest dimension
T1a	Tumour ≤ 0.5 cm in greatest dimension
T1b	Tumour > 0.5 cm and < 1cm in greatest dimension
T1c	Tumour 1 – 2 cm in greatest dimension
T2	Tumour > 2 cm and ≤ 4 cm in greatest dimension
T3	Tumour > 4cm in greatest dimension
T4	Tumour involves celiac axis, superior mesenteric artery, and/or common hepatic artery, regardless of size
N Category	**N Criteria**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastasis in 1 to 3 regional lymph nodes
N2	Metastasis in 4 or more regional lymph nodes
M Category	**M Criteria**
M0	No distant metastasis
M1	Distant metastasis

Table 5: AJCC Prognostic Stage Groups

When T is …	And N is …	And M is …	Then stage is …
Tis	N0	M0	0
T1	N0	M0	IA
T1	N1	M0	IIB
T1	N2	M0	III
T2	N0	M0	IB
T2	N1	M0	IIB
T2	N2	M0	III
T3	N0	M0	IIA
T3	N1	M0	IIB
T3	N2	M0	III
T4	Any N	M0	III
Any T	Any N	M1	IV

[2] American Joint Committee on Cancer. The AJCC TNM Cancer Staging Manual. 8th Edition ed. Chicago 2016

SUMMARY LIST OF INDICATORS

Table 6: Summarised list of potential indicators to monitor the quality of care in PC

1. DIAGNOSIS AND STAGING		
1.1		History and Physical
1.1.1	a	Documented history and physical examination
	b	Documented history and physical examination with preoperative risk assessment
	c	Documented preoperative risk assessment
1.1.2	a	Documented physical status, geriatric assessment if elderly, comorbidities and performance status prior to surgery or treatment
	b	Documented comorbidity profile prior to surgery or treatment
	c	Documented performance status prior to surgery or treatment
	d	Documented geriatric assessment prior to surgery or treatment
1.1.3	a	Documented referral to genetic counsellor for young patients
	b	Documented referral to genetic counsellor for patients with a family history of cancer
	c	Documented referral to genetic counsellor for patients with Ashkenazi Jewish ancestry
1.2		Presence of Jaundice
1.2.1	a	In patients with jaundice, documented results of LFTs, abdominal US ± CT is present
	b	In patients with jaundice, documented results of LFTs and abdominal US is present
1.3		Imaging Modalities
1.3.1	a	Documented pancreatic protocol CT for diagnosis or staging
	b	Documented multiphase CT of chest, abdomen and pelvis
1.3.2		Documented pancreatic protocol CT or MRI scan for diagnosis and/or staging
1.3.3		Documented CT of chest, abdomen and pelvis; or PET scan
1.4		EUS and Biopsy
1.4.1	a	Tissue biopsy confirming diagnosis
	b	Tissue biopsy confirming advanced, unresectable disease prior to palliative therapy
1.4.2		EUS confirming PC
1.4.3	a	EUS ± biopsy of the tumour confirming diagnosis and/or staging of PC
	b	EUS ± FNA confirming disease in patients with clinical suspicion of PC
1.4.4		EUS ± biopsy or contrast enhanced MRI confirming PC
1.4.5		EUS ± biopsy or MRCP confirming PC
1.4.6		EUS services available on site where PC surgery performed
1.5		CA 19-9
1.5.1	a	Documented baseline CA19-9 level before treatment
	b	Documented baseline CA19-9 level assessing treatment response
	c	Documented baseline CA19-9 level in patients presenting with ongoing epigastric or back pain
1.6		Staging
1.6.1	a	Staging completed and documented within one week of presentation
	b	Staging investigations completed and documented within four weeks of presentation
	c	Staging completed and documented following high quality dedicated imaging at presentation
1.6.2		Staging completed and documented within four weeks of surgery
1.6.3		Staging and assessment completed and documented following neoadjuvant treatment
1.6.4	a	Documented TNM clinical stage in patients who do not undergo surgical resection
	b	Operability of tumour is clearly defined and documented
1.6.5		In patients with resectable disease, stage, patent SMV, portal vein and definable tissue plane between the tumour and regional structures documented

2. SURGERY		
2.1		Resectability
2.1.1	a	All patients defined operable offered surgery or a valid reason documented for not undergoing surgery
	b	All patients defined operable with adequate performance status offered surgery or a valid reason documented for not undergoing surgery
2.1.2		Patients with stage IV disease who underwent surgical resection
2.1.3		Patients potentially resectable do not have a tissue biopsy prior to surgery
2.1.4		Suspicious adenopathy evaluated by frozen section
2.1.5		Time from diagnosis to surgery or first treatment less than 2 months
2.1.6		Time from final MDT to surgery is 3 weeks
2.1.7		College of American Pathologists (CAP) or equivalent reporting system used to document findings for patients undergoing surgical resection
2.2		Lymph Node Examination
2.2.1	a	Standard lymphadenectomy with the removal of ≥ 10 lymph nodes pathologically examined and documented
	b	Standard lymphadenectomy with the removal of ≥ 15 lymph nodes pathologically staged and documented
2.3		Margins
2.3.1		Tumour clearance for all seven margins identified and documented to identify an R0 resection
2.4		Surgical Institutions
2.4.1	a	Surgery performed at a high volume institution with an annual case load of ≥ 12 resections per year
	b	Surgery performed at a high volume institution with an annual case load of ≥ 15 resections per year
2.4.2		Institution is equipped with appropriately certified staff and 24 hour access to radiology and ICU units
2.5		Surgeon
2.5.1		Surgery is undertaken by surgeons who perform ≥ 5 resections per year
2.6		Other
2.6.1		Coeliac plexus block discussed and documented prior to surgical procedure
3. TREATMENT		
3.1		Neo-Adjuvant Therapy
3.1.1		Neo-adjuvant chemotherapy ± chemo-radiation offered to patients with borderline resectable disease, or a valid reason documented for not undergoing treatment
3.2		Adjuvant Therapy
3.2.1	a	Adjuvant chemotherapy administered following surgery or a valid reason documented for not undergoing treatment
	b	Adjuvant chemotherapy administered following surgery with minimum Gemcitabine or 5-Flurouracil, or a valid reason documented for not undergoing treatment
3.2.2		Chemo-radiation offered to patients with microscopically positive (R1) resection, or a valid reason documented for not receiving CRT
3.2.3	a	Surgery and chemotherapy or chemo-radiation (neo-adjuvant or adjuvant) provided to all patients with Stage I – III disease
	b	Surgery and chemotherapy or chemo-radiation (neo-adjuvant or adjuvant) provided to all patients with Stage I disease
	c	Surgery and chemotherapy or chemo-radiation (neo-adjuvant or adjuvant) provided to all patients with Stage II disease
	d	Surgery and chemotherapy or chemo-radiation (neo-adjuvant or adjuvant) provided to all patients with Stage III disease

3.3		Supportive Therapy
3.3.1	a	All patients who do not undergo surgical resection offered chemotherapy ± chemo-radiation, or a valid reason documented for not doing so
	b	All patients with metastatic disease and good performance status offered chemotherapy with Folfirinox or Gemcitabine ± Nab-paclitaxel, or a valid reason documented for not doing so
	c	All patients with LAPC and poor performance status offered chemotherapy with Gemcitabine as a minimum, or a valid reason documented for not doing so
	d	All patients with metastatic disease and poor performance status offered chemotherapy with Gemcitabine as a minimum, or a valid reason documented for not doing so
3.3.2	a	All patients with LAPC offered CRT or SBRT, or a valid reason documented for not doing so
	b	All patients with LAPC offered CRT or SBRT following initial chemotherapy, or a valid reason documented for not doing so
4. MANAGEMENT		
4.1		Hepatopancreatobiliary Surgeon
4.1.1	a	Patients with potentially resectable disease referred to a HPB surgeon
	b	All patients with a HPB surgeon as the primary specialist in non-metastatic PC
4.2		Participation in Clinical Trials
4.2.1	a	All patients included in a clinical trial, or a valid reason documented for not being included
	b	Patients with borderline resectable disease included in a clinical trial, or a valid reason documented for not being included
	c	Patients with LAPC included in a clinical trial, or a valid reason documented for not being included
4.3		Diet and Nutrition
4.3.1		All patients referred to a dietician after diagnosis
4.3.2		All patients treated with pancreatic enzyme replacement therapy
4.3.3		Cachexia, anorexia and weight loss managed with nutritional supplements and appetite stimulants
4.4		Patient Management
4.4.1		All patients assigned a care coordinator
4.4.2	a	All patients with a documented treatment or clinical plan
	b	All patients with a documented treatment or clinical plan outlining interventions and limitations, goals of care, patient preferences and support systems
	c	Treatment or clinical plan outlining interventions and limitations, goals of care, patient preferences and support systems documented and discussed with patients and caregivers
4.4.3	a	Baseline performance status, symptom burden and comorbidity profile evaluated and documented for all patients
	b	Baseline symptom burden evaluated and documented for all patients
4.5		Multidisciplinary Environment
4.5.1	a	Disease management for all patients discussed at a MDT meeting
	b	Resectability discussed at a MDT meeting
4.6		Symptom Management
4.6.1	a	Biliary or duodenal obstruction managed by endoscopic placement of SEMs
	b	Biliary or duodenal/gastric obstruction managed surgically or by endoscopic placement of SEMs
	c	Biliary or gastric outlet obstruction managed surgically in patients with good performance status
4.6.2		Patients with resectable disease not stented prior to surgery or reason for stenting documented
4.6.3		SEM stent used for biliary drainage prior to surgery
4.6.4		Pain managed with opioid analgesics, palliative radiation or nerve blocks or reason for not treating pain documented

4.7		Psychosocial Support
4.7.1		All patients offered psychosocial support following diagnosis
4.8		Palliative Care
4.8.1	a	All patients referred to palliative care services following diagnosis
	b	Patients with LAPC referred to palliative care services following diagnosis
	c	Patients with metastatic disease referred to palliative care services following diagnosis
4.9		Follow-up and Surveillance
4.9.1	a	All patients having completed treatment followed up every three to six months
	b	Patients with LAPC having completed treatment followed up every three to four months
	c	Patients with metastatic disease on active cancer-directed therapy followed up every two to three months
5. OUTCOME		
5.1		Perioperative Measures
5.1.1	a	Institution monitors their risk-adjusted perioperative mortality following surgical resection
	b	Risk-adjusted perioperative mortality following surgical resection is less than 5%
5.1.2		Institution monitors their stage-specific 2 year and 5 year survival rates for patients who underwent a surgical resection
5.1.3		Institution monitors their margin-negative resection rate
5.1.4		Institution monitors their median estimated blood loss
5.1.5		Institution monitors their median operative time for surgical resections
5.1.6		Institution monitors their 30 day readmission rate following a surgical resection
5.2		Surgical Complications
5.2.1		Patients who developed pancreatic fistula following surgical resection
5.2.2		Patients who developed biliary fistula following surgical resection
5.2.3		Patients who developed delayed gastric emptying following surgical resection
5.2.4		Patients who developed a pulmonary embolism following surgical resection
5.2.5		Patients who developed a portal vein thrombosis following surgical resection
5.2.6		Patients requiring a re-operation following surgical resection

GRADE OF RECOMMENDATION

When conducting the literature review to extract relevant guidelines, each source had their own method of grading recommendations. Each guidelines' classification systems have been summarised here for your reference.

Table 7: The grade of recommendation system of each guideline used

	LEVELS OF EVIDENCE AND RECOMMENDATION GRADE			
GUIDELINE	A	B	C	D
ASCO	**HIGH:** High confidence that the available evidence reflects the true magnitude and direction of the net effect.	**INTERMEDIATE:** Intermediate confidence that the available evidence reflects the true magnitude and direction of the net effect.	**LOW:** Low confidence that the available evidence reflects the true magnitude and direction of the net effect.	**INSUFFICIENT:** Evidence is insufficient to discern the true magnitude and direction of the net effect.
	STRONG: There is high confidence that the recommendation reflects best practice	**MODERATE:** There is moderate confidence that the recommendation reflects best practice.	**WEAK:** There is some confidence that the recommendation offers the best current guidance for practice.	
BMJ Best Practice	**Evidence Level A:** Systematic Reviews (SRs) or Randomised Control Trials (RCTs) of > 200 participants	**Evidence Level B:** Randomised Control Trials (RCTs) of < 200 participants, methodologically flawed RCTs of > 200 participants, methodologically flawed SRs or good quality observational (Cohort) studies	**Evidence Level C:** Poor quality observational (Cohort) studies or methodologically flawed RCTs of < 200 participants	**Evidence Level D:**
CCO	No grade system used			
NCCN	**CATEGORY 1:** Based upon high level evidence, there is uniform NCCN consensus that the intervention is appropriate	**CATEGORY 2A:** Based upon lower-level evidence, there is uniform consensus that the intervention is appropriate	**CATEGORY 2B:** Based upon lower-level evidence, there is uniform consensus that the intervention is appropriate	**CATEGORY 3:** Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

	LEVELS OF EVIDENCE AND RECOMMENDATION GRADE			
GUIDELINE	A	B	C	D
ESMO	**Level 1:** Evidence from at least on large randomised controlled trial of good methodological quality or meta-analyses of well conducted RCT without heterogeneity	**Level II**: Small or large RCTs with a suspicion of bias or meta-analyses with demonstrated heterogeneity.	**Level III:** Prospective cohort studies; or **Level IV:** Retrospective cohort studies/case-control studies	**Level V:** or studies without control group, case reports or expert opinions
	A: Strong evidence for efficacy with a substantial clinical benefit	**B:** Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended	**C:** Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages, optional	**D:** Moderate evidence against or for adverse outcome, generally not recommended **E:** Strong evidence against efficacy or for adverse event, never recommended
VIC OCP	No grade system used			

* Based on the number system from the NCCP guidelines

INDICATOR INDEX

This indicator index includes details of the sources from which each indicator was derived, the full guidelines from the source, the proposed numerator and denominator for measurement. To find the same indicator in the index and on the online survey, please use the reference number.

EXAMPLE:

Ref. no.	This is the indicator that has been proposed to be measured by the UGIC registry. It is based on the guidelines and articles that are listed in 'reference source details'.	The highest grade
Reference(s)	Numerator	Denominator
The source(s) on which the indicator was based on. All sources that recommended the same guideline are listed. The individual grade of recommendation is listed next to the reference. For further information on what this grade means, please consult page 17.	The proposed numerator that will be used when measuring this indicator	The proposed denominator that will be used when measuring this indicator
Reference source details		
Each number corresponds to the reference stated in the reference box. The statements and/or recommendations are **verbatim** to the original sources.		

1. DIAGNOSIS and STAGING

1.1 History and Physical

1.1.1a	Documented history and physical examination	No grade listed
Reference(s)	Numerator	Denominator
1) BMJ Best Practice, 2016 2) Burmeister et al. 2016a	Number of patients with documented history and physical examination pre-diagnosis	All patients with pancreatic cancer
Reference source details		
1) *Step by Step diagnostic approach. History and physical examination:* All patients with suspected pancreatic cancer should be investigated and managed without delay. Physicians should consider pancreatic cancer in any patients who present with unexplained upper abdominal pain, painless obstructive jaundice, weight loss and back pain. 2) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to treatment		

1.1.1b	Documented history and physical examination with preoperative risk assessment	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al, 2009	Number of patients with documented history, physical examination and pre-operative risk assessment	Number of patients who underwent a surgical resection
Reference source details		
1) *Table 2: High-validity pancreatic cancer quality indicator no.7:* If a patient undergoes resection, then a history and physical with thorough preoperative risk assessment should be performed		

1.1.1c Documented pre-operative risk assessment		No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al, 2009	Number of patients with documented pre-operative risk assessment	Number of patients who underwent a surgical resection
Reference source details		
1) *Table 2: High-validity pancreatic cancer quality indicator no.7:* If a patient undergoes resection, then a history and physical with thorough preoperative risk assessment should be performed		

1.1.2a Documented physical status, geriatric assessment if elderly, comorbidities and performance status prior to surgery or treatment		No grade listed
Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with all of the following documented: physical status; geriatric assessment; comorbidity profile; and performance status	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to any treatment		

1.1.2b Documented comorbidity profile prior to surgery or treatment		No grade listed
Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with documented comorbidity profile	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to any treatment		

1.1.2c	Documented performance status prior to surgery or treatment	No grade listed
Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with documented performance status	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to any treatment		

1.1.2d	Documented geriatric assessment prior to surgery or treatment	No grade listed
Reference(s)	Numerator	Denominator
2) Burmeister et al. 2016a	Number of patients with documented geriatric assessment	All patients diagnosed with pancreatic cancer above the age of……
Reference source details		
2) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to any treatment		

1.1.3a	Documented referral to genetic counsellor for young patients	B
Reference(s)	Numerator	Denominator
1) NCCN 2017	Number of young patients referred to a genetic counsellor	Number of patients diagnosed with pancreatic cancer below the age of ….
Reference source details		
1) *PANC-1 footnote:* If pancreatic cancer is diagnosed, consider referral for genetic counselling for patients who are young, those with a family history of Cancer or those of Ashkenazi Jewish ancestry [2A]		

1.1.3b	Documented referral to genetic counsellor for patients with a family history of cancer	B
Reference(s)	Numerator	Denominator
2) NCCN 2017	Number of patients with a family history of cancer referred to a genetic counsellor	Number of patients with a family history diagnosed with pancreatic cancer
Reference source details		
2) *PANC-1 footnote:* If pancreatic cancer is diagnosed, consider referral for genetic counselling for patients who are young, those with a family history of Cancer or those of Ashkenazi Jewish ancestry [2A]		

1.1.3c	Documented referral to genetic counsellor for patients with Ashkenazi Jewish ancestry	B
Reference(s)	Numerator	Denominator
3) NCCN 2017	Number of patients with Ashkenazi Jewish ancestry referred to a genetic counsellor	Number of patients with Ashkenazi Jewish ancestry diagnosed with pancreatic cancer
Reference source details		
3) *PANC-1 footnote:* If pancreatic cancer is diagnosed, consider referral for genetic counselling for patients who are young, those with a family history of Cancer or those of Ashkenazi Jewish ancestry [2A]		

1.2 Presence of Jaundice

1.2.1a	In patients with jaundice, documented results of LFTs, abdominal US ± CT is present	No grade listed
Reference(s)	Numerator	Denominator
1) Vic OCP 2015	Number of patients with documented results of LFTs, abdominal US ± CT	Number of patients presenting with jaundice
Reference source details		
1) *Step 2: Presentation, initial investigations and referral.* 'Where jaundice is present, the following should be ordered within 48 hours and followed up as rapidly as possible: • Liver Function Tests (LFTs) • Abdominal ultrasound • CT where appropriate		

1.2.1b	In patients with jaundice, documented results of LFTs and abdominal US is present	No grade listed
Reference(s)	Numerator	Denominator
1) Vic OCP 2015	Number of patients with documented results of LFTs and abdominal US	Number of patients presenting with jaundice
Reference source details		
1) *Step 2: Presentation, initial investigations and referral.* 'Where jaundice is present, the following should be ordered within 48 hours and followed up as rapidly as possible: • Liver Function Tests (LFTs) • Abdominal ultrasound • CT where appropriate		

1.3 Imaging Modalities

1.3.1a Documented pancreatic protocol CT for diagnosis or staging		No Grade Listed
Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) Burmeister et al. 2016b 3) VIC OCP 2015	Number of patients with pancreatic protocol CT confirming diagnosis or staging	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Diagnostic Tests:* All patients with suspected disease on ultrasound should undergo pancreas-specific CT. This has been shown to achieve 97% diagnostic rates of pancreatic cancer with accurate prediction of resectability in 80-90% of patients. 2) *Care statement:* All patients should have a triple phase/pancreas protocol CT scan for staging 3) *Step 3. Diagnostic Workup:* Contrast-enhanced multidector CT according to suggested pancreatic protocol		

1.3.1b Documented multiphase CT of chest, abdomen and pelvis		B
Reference(s)	Numerator	Denominator
1) ASCO 2016b and 2016c	Number of patients who had a multiphase CT of chest, abdomen and pelvis	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Key Recommendations 1.1:* A multiphase CT scan of the chest, abdomen and pelvis should be performed to assess extent of disease. Other staging studies should only be performed as dictated by symptoms (Locally advanced & Metastatic) [Intermediate, Strong]		

1.3.2	Documented pancreatic protocol CT or MRI scan for diagnosis and/or staging	A

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) Bilimoria et al. 2009 3) NCCN 2017	Number of patients with pancreatic protocol CT or MRI scan for diagnosis and/or staging	All patients diagnosed with pancreatic cancer

Reference source details

1) *Recommendation 1.1:* A multiphase CT of abdomen and pelvis using a pancreatic protocol or MRI should be performed for all patients to assess the anatomic relationships of the primary tumour and presence of intra-abdominal metastases [High, Strong]
2) *Derived from Table 2. High validity pancreatic cancer QI:* Triple phase, multi slice CT or MRI scan should be obtained
3) *Principles of diagnosis, imaging and staging #3:* Imaging should include dedicated pancreatic CT (preferred) or MRI with contrast [2A]

1.3.3	Documented CT of chest, abdomen and pelvis; or PET scan	No grade listed

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a 2) VIC OCP 2015	Number of patients with diagnosis and staging confirmed by a CT or PET scan	All patients diagnosed with pancreatic cancer

Reference source details

1) *Derived from Table 1. Statements with highest importance or for which consensus not reached:* If disease appears to be localised a PET scan should be performed (unable to reach consensus
2) *Step 3.2. Diagnosis, staging and treatment planning:* Comprehensive staging of pancreatic cancer should be done simultaneously using the imaging modalities for diagnosis and include CT, chest/abdominal/Pelvis & PET.

1.4 EUS and Biopsy

1.4.1a	Tissue biopsy confirming diagnosis	No grade listed

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016b 2) Arnachellum et al. 2016 3) De Leede et al. 2016	Number of patients with tissue biopsy confirming pancreatic cancer	All patients diagnosed with pancreatic cancer

Reference source details

1) *Care statement deemed to be most important in Delphi process:* Tissue diagnosis should be obtained where possible
2) *Derived from Table 2*. Comparison of Tumour characteristics and Therapeutic Modalities: Histological proof as a data item
3) *Derived from Table 2*. Shared items in eleven participating registries of the EURECCA pancreas consortium: Diagnosis cytology or histology

1.4.1b	Tissue biopsy confirming advanced, unresectable disease prior to palliative therapy	No grade listed

Reference(s)	Numerator	Denominator
1) BMJ Best Practice, 2016	Number of patients with advanced, unresectable disease and a tissue biopsy	Number of patients with unresectable disease selected for palliative therapy

Reference source details

1) *Step by Step diagnostic approach. Tissue diagnosis*: Diagnosis by histology is not required before surgical resection. By contrast, in patients with advanced, unresectable disease selected for palliative therapy, biopsy confirmation is required

1.4.2 Endoscopic Ultrasound (EUS) confirming PC		No grade listed
Reference(s)	Numerator	Denominator
1) Burmeister et al, 2016a	Number of patients with confirmed pancreatic cancer who underwent an EUS	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Derived from Table 1. Statements with highest importance or for which consensus was not reached:* All patients should have an EUS (unable to reach consensus)		

1.4.3a EUS ± biopsy of the tumour confirming diagnosis and/or staging of PC		A
Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) ESMO 2015	Number of patients with an EUS± biopsy confirming pancreatic cancer and stage	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Recommendation 1.1:* EUS and/or diagnostic laparoscopy maybe used as supplemental studies to facilitate acquisition of a biopsy specimen. (High,strong) 2) *Derived from Table 4. Summary of key points and recommendations:* EUS provides some complementary information and allows biopsy of the tumour. (II, A)		

1.4.3b EUS ± FNA confirming disease in patients with clinical suspicion of PC		B
Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) NCCN 2017	Number of patients with clinical suspicion of pancreatic cancer and an EUS ± FNA	Number of patients with clinical suspicion of pancreatic cancer
Reference source details		
1) *Step 3. Diagnosis and Staging:* EUS±FNA should be considered if there is no mass on CT but a clinical suspicion of pancreatic cancer is present. 2) *Principles of diagnosis, imaging and staging:* EUS is not recommended as a routine staging tool. EUS maybe complementary to CT for staging. EUS-FNA is preferable to CT guided FNA [2A]		

1.4.4 EUS ± biopsy or contrast enhanced MRI confirming PC		No grade listed
Reference(s)	Numerator	Denominator
1) VIC OCP 2015	Number of patients with clinical suspicion of pancreatic cancer and EUS ± FNA or contrast enhanced MRI	Number of patients with clinical suspicion of pancreatic cancer
Reference source details		
1) *Step 3. Diagnosis, staging and treatment planning:* If there is uncertainty; EUS ± biopsy, contrast enhanced MRI or MRCP in patients who cannot tolerate contrast or diagnostic lap with or without lap US.		

1.4.5 EUS ± biopsy or MRCP confirming PC		No grade listed
Reference(s)	Numerator	Denominator
1) VIC OCP 2015	Number of patients with clinical suspicion of pancreatic cancer unable to tolerate contrast and EUS ± FNA or MRCP	Number of patients with clinical suspicion of pancreatic cancer who cannot tolerate contrast
Reference source details		
1) *Step 3. Diagnosis, staging and treatment planning:* If there is uncertainty; EUS ± biopsy, contrast enhanced MRI or MRCP in patients who cannot tolerate contrast or diagnostic lap with or without lap US.		

1.4.6 EUS services available on site where PC surgery performed		No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Number of institutions where PC surgery performed with EUS services on site	N/A
Reference source details		
1) *Derived from Table 3. Moderate validity pancreatic cancer quality indicators No.32:* Hospital where pancreatic surgery is performed, should have EUS services on site		

1.5 CA 19-9 levels

1.5.1a	Documented baseline CA19-9 level before treatment	A

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) CCO 2016 3) ESMO 2015	Number of patients with documented CA 19-9 level prior to any treatment	All patients diagnosed with pancreatic cancer

Reference source details

1) *Recommendation 1.1:* A serum level of CA 19-9 and baseline standard laboratory studies should be assayed [High, Strong]
2) CA19-9 may be useful for diagnosis, staging, determining resectability, assessing treatment response
3) *Staging and risk assessment. Key point:* CA 19-9 is the most useful tumour marker in pancreatic cancer [IV, B]

1.5.1b	Documented CA19-9 level assessing treatment response	No Grade Listed

Reference(s)	Numerator	Denominator
1) CCO 2016	Number of patients with documented CA 19-9 levels assessing treatment response	Number of patients undergoing treatment for pancreatic cancer

Reference source details

1) CA19-9 may be useful for diagnosis, staging, determining resectability, assessing treatment response

1.5.1c	Documented CA19-9 level in patients presenting with ongoing epigastric or back pain	No Grade Listed

Reference(s)	Numerator	Denominator
2) Burmeister et al. 2016a	Number of patients with documented CA 19-9 levels	Number of patients presenting with ongoing epigastric or back pain

Reference source details

2) *Derived from Table 1*. Presentation and staging: All patients presenting with ongoing epigastric or back pain should have a CA19-9 blood test

1.6 Staging

1.6.1a	Staging completed and documented within one week of presentation	No grade listed

Reference(s)	Numerator	Denominator
1) VIC OCP 2015	Number of patients with staging assessed and completed within one week of presentation	All patients diagnosed with pancreatic cancer

Reference source details

1) *Step 3. Diagnosis, staging and treatment planning:* Diagnostic and staging should be completed within one week

1.6.1b	Staging investigations completed and documented within four weeks of presentation	No grade listed

Reference(s)	Numerator	Denominator
1) Gandy et al. 2016 (AGITG Consensus)	Number of patients with staging completed within four weeks of presentation	All patients diagnosed with pancreatic cancer

Reference source details

1) *Summary:* Staging investigations to be completed within 4 weeks of presentation by pancreatic protocol computed tomography, endoscopic US and when possible biopsy

1.6.1c	Staging completed and documented following high quality dedicated imaging at presentation	B

Reference(s)	Numerator	Denominator
1) NCCN 2017	Number of patients with staging & assessment completed at presentation following high quality imaging	All patients diagnosed with pancreatic cancer

Reference source details

1) *Principles of diagnosis, imaging and staging #2:* To provide adequate staging and assessment, high quality dedicated imaging of the pancreas should be performed at presentation, preferably within 4 weeks of surgery and following neoadjuvant treatment [2A]

1.6.2	Staging completed and documented within four weeks of surgery	B
Reference(s)	Numerator	Denominator
2) NCCN 2017	Number of patients with staging & assessment completed within four weeks of surgery	Number of patients undergoing a surgical resection
Reference source details		
2) *Principles of diagnosis, imaging and staging #2:* To provide adequate staging and assessment, high quality dedicated imaging of the pancreas should be performed at presentation, preferably within 4 weeks of surgery and following neoadjuvant treatment [2A]		

1.6.3	Staging and assessment completed and documented following neoadjuvant treatment	B
Reference(s)	Numerator	Denominator
3) NCCN 2017	Number of patients with staging & assessment completed following neoadjuvant therapy	Number of patients receiving neoadjuvant therapy
Reference source details		
3) *Principles of diagnosis, imaging and staging #2:* To provide adequate staging and assessment, high quality dedicated imaging of the pancreas should be performed at presentation, preferably within 4 weeks of surgery and following neoadjuvant treatment [2A]		

1.6.4a	Documented TNM clinical stage in patients who do not undergo surgical resection	No grade listed
Reference(s)	Numerator	Denominator
4) Bilimoria et al. 2009	Number of patients with unresectable disease and documented TNM clinical stage	Number of patients with unresectable pancreatic cancer
Reference source details		
4) *Derived from Table 2. High validity QI No.21:* If a patient does not undergo resection, then a TNM clinical stage should be done		

1.6.4b Operability of tumour is clearly defined and documented		No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Gandy et al. 2016 (AGITG Consensus)	Number of patients with tumour operability defined and documented	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Derived from Table 2. High validity QI No.21:* If a patient does not undergo resection, then a TNM clinical stage should be done 2) *Pre-operative classification of resectability:* Operability of tumours should be clearly defined. • 1a - those clearly resectable by standard pancreatectomy; • 1b - clearly resectable tumours that may require portal venous resection; • 2a - borderline resectable tumours that require venous resection; • 2b - borderline resectable tumours that require arterial resection; • 3 - locally advanced or metastatic disease		

1.6.5	In patients with resectable disease, stage, patent SMV, portal vein and definable tissue plane between the tumour and regional structures documented	No grade listed

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) CCO 2016	Number of patients with documented SMV, PV and definable tissue plane between the tumor and regional structures prior to resection	Number of patients with resectable disease

Reference source details

1) *Table 3. Moderate-validity pancreatic cancer QI no.35:* If a patient is to undergo resection, then on the basis of the CT or MRI, surgeon should document 1) no metastatic disease, 2) patent SMV and portal vein and 3) a definable tissue plane between the tumor and regional arterial structures
2) *Staging Criteria for Non-metastatic Pancreatic Cancer:*

Staging Criteria for Nonmetastatic Pancreatic Cancer[2,4]

Criteria	Resectable	Borderline Resectable	Localized Unresectable
Evidence of extrapancreatic disease	No evidence	No evidence	Lymph nodes beyond field of resection
SMA encasement	No evidence	≤ 180°	> 180°
SMV/portal vein	Patent SMPV	Impingement or short segment occulsion	Unreconstructable occlusion
Celiac encasement	No evidence	≤ 180°	> 180° (body/tail)
Hepatic artery	No arterial tumor contact	Abutment or encasement	Invasion or encasement

SMA, superior mesenteric artery; SMPV, superior mesenteric-portal vein confluence; SMV, superior mesenteric vein.

2. SURGERY

2.1 Resectability

2.1.1a	All patients defined operable offered surgery or a valid reason documented for not undergoing surgery	B

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) Bilimoria et al. 2009 3) Burmeister et al. 2016a and 2016b 4) VIC OCP 2015 5) Visser et al. 2012	Number of patients with operable disease who underwent a resection or have a documented reason for resection not attempted	Number of patients with operable disease

Reference source details

1) *Recommendation 2.1:* Primary surgical resection of tumour and regional lymph nodes recommended for patients who meet stated criteria [Intermediate, Strong]
2) *Derived from Table 2. High validity QI No.22:* If a patient has clinical I or II disease, then the patient should undergo resection or have a valid reason for not undergoing resection
3) *Derived from Table 1 (very important) and Care Statements:* All patients with a small lesion and technically resectable disease plus adequate performance status should be offered a resection
4) *Step 4. Treatment:* Curative surgery should be undertaken with or without chemotherapy in resectable disease by Whipples procedure (pancreaticoduodenal), distal pancreatectomy or total pancreatectomy
5) *NCCN-based definition of compliant treatment:* Surgery recommended for stages 0 to III.

2.1.1b	All patients defined operable with adequate performance status offered surgery or a valid reason documented for not undergoing surgical	No grade listed

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a and 2016b	Number of patients with operable disease and adequate performance status who underwent a resection or a valid reason documented for resection not attempted	Number of patients with operable disease and adequate performance status

Reference source details

6) *Derived from Table 1 (very important) and Care Statements:* All patients with a small lesion and technically resectable disease plus adequate performance status should be offered a resection

2.1.2	Patients with stage IV disease who underwent surgical resection	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Number of patients with clinical stage IV disease who underwent a resection	Number of patients with clinical stage IV disease
Reference source details		
1) *Table 2. High-validity pancreatic cancer QI no.24:* If a patient has clinical stage IV disease then a cancer-directed resection should not be done		

2.1.3	Patients potentially resectable do not have a tissue biopsy prior to surgery	No grade listed
Reference(s)	Numerator	Denominator
2) Burmeister et al. 2016a	Number of patients who underwent surgery with no tissue biopsy prior to surgery	Number of patients with potentially resectable disease
Reference source details		
2) *Table 1. Statements with highest importance or unable to reach consensus:* Potential resectable patients should not have a tissue biopsy prior to surgery (unable to reach consensus)		

2.1.4	Suspicious adenopathy evaluated by frozen section	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Number of patients with suspicious adenopathy that is evaluated by frozen section	Number of patients who underwent surgical resection with suspicious adenopathy
Reference source details		
1) *Table 2. High-validity pancreatic cancer QI no.18:* If a patient undergoes resection, then suspicious adenopathy outside the scope of planned resection should be evaluated by frozen section		

2.1.5 Time from diagnosis to surgery or first treatment less than 2 months		No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Number of patients who underwent surgical resection or treatment within 2 months from diagnosis	Number of patients who underwent surgical resection or treatment
Reference source details		
1) Table 2. High-validity pancreatic cancer QI no. 26: If patient is to receive treatment, then the time from diagnosis to surgery or first treatment should be less than 2 months		

2.1.6 Time from final MDT meeting to surgery is 3 weeks		No grade listed
Reference(s)	Numerator	Denominator
1) Van Rijssen et al. 2016	Number of patients who underwent surgical resection or treatment within 3 weeks from final MDT meeting	Number of patients who underwent surgical resection or treatment
Reference source details		
1) Results. Third Indicator: Time interval between final MDT meeting and start of treatment (surgery)		

2.1.7	College of American Pathologists or equivalent reporting system used to document findings for patients undergoing surgical resection	B

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Bilimoria et al. 2009 3) Bilimoria et al. 2009 4) NCCN 2017	Number of patients who underwent a surgical resection with a documented CAP or equivalent reporting system	Number of patients who underwent a surgical resection

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.11 – no.17*
2) *Table 2. High-validity pancreatic cancer QI no.20:* College of American Pathologists checklists or equivalent reporting system should be followed and documented
3) *Table 3. Moderate-validity pancreatic cancer QI no.37:* Surgeon should document intraoperative findings including absence of arterial involvement, metastatic disease (liver, peritoneal, omental), and distant adenopathy
4) *Pathologic Analysis:* NCCN supports pathology synoptic reports from the College of American Pathologists (CAP) [2A]

2.2 Lymph Nodes Examination

2.2.1a	Standard lymphadenectomy with the removal of ≥ 10 lymph nodes pathologically examined and documented	No grade listed

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Bilimoria et al. 2009	Number of patients who underwent a surgical resection and had ≥ 10 lymph nodes removed and examined	Number of patients who underwent a surgical resection

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.15 and no.16:* Number of lymph nodes examined and number of positive lymph nodes should be recorded
2) *Table 3. Moderate-validity pancreatic cancer QI no.38:* If a patient undergoes cancer-directed resection, then ≥ 10 regional lymph nodes should be resected and pathologically examined

2.2.1b	Standard lymphadenectomy with the removal of ≥ 15 lymph nodes pathologically staged and documented	C

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) ESMO 2015	Number of patients who underwent a surgical resection and had ≥ 15 lymph nodes removed and examined	Number of patients who underwent a surgical resection

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.15 and no.16:* Number of lymph nodes examined and number of positive lymph nodes should be recorded
2) *Lymphadenectomy:* Standard lymphadenectomy should involve the removal of ≥ 15 lymph nodes to allow adequate pathological staging of the disease [IV,A]

2.3 Margins

2.3.1	Tumour clearance for all seven margins identified and documented to identify an R0 resection	B

Reference(s)	Numerator	Denominator
1) Arnachellum et al. 2016 2) Bilimoria et al. 2009 3) Bilimoria et al. 2009 4) De Leede et al. 5) ESMO 2015 6) Gandy et al. 2016 (AGITG Consensus) 7) NCCN 2017 8) NCCN 2017	Number of patients with all seven margins identified and documented following resection	Number of patients who underwent a surgical resection

Reference source details

1) *Table 2. Comparison of tumor characteristics and therapeutic modalities:* Potentially curative surgery (R0 + R1, c/f with other surgeries) & Curative surgery (negative margin)
2) *Table 2. High validity pancreatic cancer QI no.14:* Margin status should be recorded
3) *Table 3. Moderate-validity pancreatic cancer QI no.36:* Margins should be macroscopically clear
4) *EURECCA registry data item:* Resection Margin (R0 – R2 & unknown)
5) *Table 4. Summary of key points and recommendations – Treatment of localised disease*: Tumour Clearance should be given for all seven margins identified by the surgeon. [IV,B] These seven margins are; anterior, posterior, medial or super mesenteric groove, SMA, pancreatic transection, bile duct and enteric.
6) *AGITG Summary:* Standardised reporting of all seven surgical margins, which identifies an R0 (no tumour cells within a defined distance of the margin) if all surgical margins are clear from 1mm
7) *Principles of surgical technique:* The goals of pancreatoduodenectomy (Whipples) and distal pancreatectomy is an R0 resection, as a margin positive specimen is associated with poor long-term survival [2A]
8) *Pathologic Analysis. Margins:* Definitions of margins and uniformity of nomenclature are critical to accurate reporting. This includes SMA (retroperitoneal/uncinate), Posterior, Portal vein(PV)groove, portal vein, pancreatic neck (transection) and bile duct + other margins specific for Whipples (proximal and distal + anterior surface) (Whipples specimen) and Proximal, anterior (cephalad) peripancreatic surface, + posterior (caudad) peripancreatic in distal pancreatectomy [2A]

2.4 Surgical Institutions

2.4.1a	Surgery performed at a high volume institution with an annual case load of ≥ 12 resections per year	No grade listed

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Bilimoria et al. 2009 3) Gagliardi et al. 2016b 4) VIC OCP 2015	Comparison of number of surgical resections undertaken per year by each institution	N/A

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.1:* If an institution performs PC surgery, then the institution should monitor average annual case volume
2) *Table 3. Moderate Validity QI no. 31*: Institution should perform ≥ 12 cases/year
3) *Factors influencing PC management and outcomes:* Higher hospital case volume had decreased in hospital mortality, and increased rates of survival.
4) *Treatment Options 4.2.1:* There is strong evidence to suggest that high-volume hospitals have better clinical outcomes for complex cancer surgery such as PC resections

2.4.1b	Surgery performed at a high volume institution with an annual case load of ≥ 15 resections per year	B

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Burmeister et al. 2016b 3) Gagliardi et al. 2016b 4) NCCN 2017 5) VIC OCP 2015	Comparison of number of surgical resections undertaken per year by each institution	N/A

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.1*: If an institution performs PC surgery, then the institution should monitor average annual case volume
2) *Care Statement:* Surgery should take place in a tertiary institution where more than 15 resections are performed annually (amended to 11 resections/per year)
3) *Factors influencing PC management and outcomes*: Higher hospital case volume had decreased in hospital mortality, and increased rates of survival.
4) *Priniciples of diagnosis, imaging and staging #1:* Resections should be done at institutions that perform a large number (at least 15-20) of pancreatic resections annually [2A]
5) *Treatment Options 4.2.1:* There is strong evidence to suggest that high-volume hospitals have better clinical outcomes for complex cancer surgery such as PC resections

2.4.2	Institutions is equipped with appropriately certified staff and 24 hour access to radiology and ICU units	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) VIC OCP 2015	Number of institutions where pancreatic cancer surgery is performed with appropriately certified staff and 24 hour access to radiology & ICU units	N/A
Reference source details		
1) *Table 2. High-validity pancreatic cancer QI no.4 – no.6:* Hospital must ensure that the surgeon is certified by the American Board of surgery or equivalent international organisation; Hospital should have interventional radiology services on site; Hospital should have ICU staffed by critical care specialists 2) *Treatment 4.2.1:*Hospital or treatment unit characteristics: ICU; appropriate ward staff, nursing and theatre resources; 24 hour medical staff availability; 24 hour operating room access; pathology; ERCP; 24 hour access to interventional radiology; fully supported by other surgical specialities have better clinical outcomes		

2.5 Surgeon

2.5.1	Surgery is undertaken by surgeons who perform ≥ 5 resections per year	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Burmeister et al. 2016a and 2016b 3) VIC OCP 2015	Comparison of number of surgical resections per surgeon per year	N/A
Reference source details		
1) *Table 2. High-validity pancreatic cancer QI no.2:* If an institution performs PC surgery, then the institution should monitor surgeons annual case volume 2) Resectability should be assessed and surgery performed by surgeons who perform more than 5 pancreatic surgeries per year (very important); Surgery should be performed by surgeons who perform ≥ 5 pancreatic resections per year 3) *Treatment 4.2.1*: Strong evidence to suggest that surgeons who undertake high volume of resections have better clinical outcomes		

2.6 Other

2.6.1 Coeliac plexus block discussed and documented prior to surgical procedure		No grade listed
Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with documented discussion of coeliac plexus block	Number of patients who underwent a surgical procedure
Reference source details		
1) *Table 1:* Potential for coeliac plexus block should be discussed before any surgical procedure (unable to reach consensus)		

3. TREATMENT

3.1 Neo-adjuvant Therapy

3.1.1	Neo-adjuvant chemotherapy ± chemoradiation offered to patients with borderline resectable disease, or a valid reason documented for not undergoing treatment	B

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) ESMO 2015 3) Gandy et al. 2016 (AGITG Consensus) 4) NCCN 2017	Number of patients with borderline resectable disease that received chemotherapy ± chemoradiation or a valid reason documented for not undergoing treatment	Number of patients with borderline resectable disease

1) *Resectable disease. Neoadjuvant therapy:* Neo-adjuvant therapy in resectable disease remains under investigation. Combination chemotherapy or fluorouracil-based chemoradiotherapy can be offered (however no significant improvement in survival reported)
2) *Table 4. Summary of key points.* Treatment of borderline-resecatable lesions: In routine practice, if the patient is not included in a trial, a period of chemotherapy (gemcitabine or Folfirinox) followed by chemoradiation then surgery appears to be the best option [IV,B]
3) *Neo-adjuvant and borderline resectable disease:* Neo-adjuvant increasingly recommended for borderline operable disease while chemotherapy is recommended as initial therapy for patients with loco-regional PC. A small number of patients may be down staged by chemoradiation.
4) *Principles of Chemotherapy:* Limited evidence to recommend neo-adjuvant regimens in resectable/borderline resectable disease off-study; however consultation at a high-volume center is recommended. Options include Folfirinox ± chemoradiation, Gemcitabine + nab-paclitaxel ± chemoradiation [2A]

3.2 Adjuvant Therapy

3.2.1a	Adjuvant chemotherapy administered following surgery or a valid reason documented for not undergoing treatment	No grade listed

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Burmeister et al. 2016b 3) Van Rijssen et al. 2016	Number of patients who received adjuvant chemotherapy or have a valid reason documented for not undergoing adjuvant therapy	Number of patients who underwent a surgical resection

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.23:* Adjuvant chemotherapy with or without radiation should be considered and administered, or a valid reason should be documented for not receiving
2) *Care Statement:* All patients should be offered adjuvant therapy after surgery, assuming performance status is adequate
3) *Results. First indicator:* Use of adjuvant chemotherapy

3.2.1b	Adjuvant chemotherapy administered following surgery with minimum Gemcitabine or 5-Flurouracil, or a valid reason documented for not undergoing treatment	A

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) BMJ Best Practice 2016 3) CCO 2016 4) ESMO 2015 5) NCCN 2017	Number of patients who received adjuvant chemotherapy with Gemcitabine or 5-Flurouracil; or have a valid reason documented for not undergoing adjuvant therapy	Number of patients who underwent a surgical resection

Reference source details

1) *Key Recommendation 4.1: Postoperative resection:* 6 months of adjuvant chemotherapy with either gemcitabine or flurouracil plus folinic acid in the absence of medical or surgical contraindications. No current data to support combination chemotherapy regimens.[High, Strong]
2) *Adjuvant Therapy:* Adjuvant Fluorouracil or Gemcitabine based chemotherapy for 6 months increases median and 5 year survival in people with completely resected pancreatic cancer compared with surgery alone. [C]
3) *Therapeutic Options for Resectable Disease:* Adjuvant chemotherapy is associated with prolonged survival. Gemcitabine & 5 Fluorouracil are equivalent in efficacy. Combination adjuvant chemotherapy with Gemcitabine plus capecitabine significant improvement in OS vs Gem monotherapy
4) *Table 4. Summary of Key Points.* Treatment of localised disease: Adjuvant treatment should be done with either Gemcitabine or 5-FU folinic acid [I,A]
5) *Principles of Chemotherapy*: In an adjuvant setting treatment with chemotherapy is recommended (role of radiation is being evaluated in clinical studies). Options include Gemcitabine or 5-FU/Leucovarin or Gemcitabine + capecitabine [Category 1]

3.2.2	Chemo-radiation offered to patients with microscopically positive (R1) resection, or valid reason documented for not receiving CRT	B

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) BMJ Best Practice 2016 3) ESMO 2015	Number of patients with R1 resection who received adjuvant chemo-radiation or have a valid reason documented for not receiving therapy	Number of patients with R1 resection

Reference source details

1) *Key Recommendation 4.2:* Adjuvant chemo-radiation may be offered to patients who did not receive preoperative therapy and present after resection with microscopically positive (R1) and or node positive disease after completion of 4-6 months systemic adjuvant chemotherapy [intermediate, moderate]
2) *Treatment. Incompletely Resected:* In patients with incomplete resection, adjuvant chemo-radiotherapy is an option (in patients who have not received neoadjuvant treatment) with primary options fluorouracil and gemcitabine plus radiation [C]
3) *Table 4. Treatment of localised disease:* No chemo-radiation should be given to patients with surgery except in clinical trials [I,E]

3.2.3a	Surgery and chemotherapy or chemo-radiation (neo-adjuvant or adjuvant) provided to all patients with Stage I – III disease	No grade listed

Reference(s)	Numerator	Denominator
1) Visser et al. 2012	Number of patients with stage I-III disease who received surgery and chemotherapy or chemo-radiation as neo-adjuvant or adjuvant therapy	Number of patients with stage I to III disease

Reference source details

1) Measures of Quality Care: For patients with Stage I – III disease, surgery and chemotherapy or chemo-radiation (adjuvant or neo-adjuvant) used as measures of quality (NCCN-based definitions of compliant treatment)

3.2.3b	Surgery and chemotherapy or chemo-radiation (neo-adjuvant or adjuvant) provided to all patients with Stage I disease	No grade listed
Reference(s)	Numerator	Denominator
2) Visser et al. 2012	Number of patients with stage I disease who received surgery and chemotherapy or chemo-radiation as neo-adjuvant or adjuvant therapy	Number of patients with stage I disease
Reference source details		
2) Measures of Quality Care: For patients with Stage I – III disease, surgery and chemotherapy or chemo-radiation (adjuvant or neo-adjuvant) used as measures of quality (NCCN-based definitions of compliant treatment)		

3.2.3c	Surgery and chemotherapy or chemo-radiation (neo-adjuvant or adjuvant) provided to all patients with Stage II disease	No grade listed
Reference(s)	Numerator	Denominator
3) Visser et al. 2012	Number of patients with stage II disease who received surgery and chemotherapy or chemo-radiation as neo-adjuvant or adjuvant therapy	Number of patients with stage II disease
Reference source details		
3) Measures of Quality Care: For patients with Stage I – III disease, surgery and chemotherapy or chemo-radiation (adjuvant or neo-adjuvant) used as measures of quality (NCCN-based definitions of compliant treatment)		

3.2.3d	Surgery and chemotherapy or chemo-radiation (neo-adjuvant or adjuvant) provided to all patients with Stage III disease	No grade listed
Reference(s)	Numerator	Denominator
4) Visser et al. 2012	Number of patients with stage III disease who received surgery and chemotherapy or chemo-radiation as neo-adjuvant or adjuvant therapy	Number of patients with stage III disease
Reference source details		
4) Measures of Quality Care: For patients with Stage I – III disease, surgery and chemotherapy or chemo-radiation (adjuvant or neo-adjuvant) used as measures of quality (NCCN-based definitions of compliant treatment)		

3.3 Palliative Therapy

3.3.1a	All patients who do not undergo surgical resection offered chemotherapy ± chemo-radiation, or a valid reason documented for not doing so	B

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) BMJ Best Practice 2016 3) NCCN 2017 4) Visser et al. 2012	Number of patients who do not undergo surgical resection who received chemotherapy ± chemo-radiation or have a valid reason documented for not receiving therapy	Number of patients who do not undergo surgical resection

Reference source details

1) *Table 2: High-validity pancreatic cancer QI no. 25:* If a patient does not undergo resection, chemotherapy with or without radiation should be considered and administered, or a valid reason should be documented for not receiving non-surgical therapy.
2) In patients with locally advanced, chemotherapy or chemo-radiotherapy is recommended to control the tumour and increase QOL
3) *Principles of Chemotherapy*: In locally advanced or unresectable disease, chemotherapy or induction chemotherapy recommended. Depending on performance status, monotherapy or combination chemotherapy maybe considered as initial therapy prior to radiation. [2A]
4) *Measures of Quality Care:* Chemotherapy ± palliative procedures ± palliative radiotherapy

3.3.1b	All patients with metastatic disease and good performance status offered chemotherapy with Folfirinox or Gemcitabine ± Nab-paclitaxel, or a valid reason documented for not doing so	A

Reference(s)	Numerator	Denominator
1) ASCO 2016c 2) BMJ Best Practice 2016 3) CCO 2016 4) ESMO 2015 5) NCCN 2017	Number of patients with metastatic disease and good performance status who received chemotherapy with Folfirinox or Gem± Nab-paclitaxel, or a valid reason documented for not receiving therapy	Number of patients with metastatic disease and good performance status

Reference source details

1) *Key Recommendations 2.1 & 2.2:* Folfirinox or Gemcitabine plus nab-paclitaxel is recommended for patients who meet the following; ECOG PS 0 or 1, favourable or relatively favourable comorbidity profile, patient preference and support system for aggressive medical therapy and access to chemotherapy port & infusion pump management. [Intermediate, Strong]
2) Treatment Options. Metastatic: Chemotherapy with Folfirinox or nab-paclitaxel is recommended in patients with good performance status [Category 1]
3) *Treatment of Metastatic Pancreatic Cancer:* Gemcitabine plus albumin-bound paclitaxel results in improved response and survival vs Gemcitabine alone. Folfirinox is recommended as frontline - associated with improved survival and objective response rates however, also has higher grade 3/4 adverse events. [Category 1]
4) *Table 4. Treatment of Metastatic Disease:* ECOG = 0 or 1 & bilirubin is below 1.5 x ULN - Folfirinox or combination gemcitabine/nab-paclitaxel should be considered. [I,A]
5) *Principles of Chemotherapy:* In metastatic disease – Folfirinox or Gemcitabine + nab-paclitaxel preferred as first-line therapy in patients with good performance status.

3.3.1c	All patients with LAPC and poor performance status offered chemotherapy with Gemcitabine as a minimum, or a valid reason documented for not doing so	A

Reference(s)	Numerator	Denominator
1) ASCO 2016c 2) ESMO 2015	Number of patients with locally advanced disease and poor performance status who received chemotherapy with Gemcitabine, or a valid reason documented for not receiving therapy	Number of patients with locally advanced disease and poor performance status

Reference source details

1) *Key recommendations 2.3:* Gemcitabine alone is recommended for patients with ECOG PS 2 or a comorbidity profile that precludes more aggressive regimens and who wish to pursue cancer directed therapy. [Intermediate, moderate]
2) *Table 4. Treatment of locally advanced disease:* The standard of care is six months of Gemcitabine. [I, A]

3.3.1d	All patients with metastatic disease and poor performance status offered chemotherapy with Gemcitabine as a minimum, or a valid reason documented for not doing so	A

Reference(s)	Numerator	Denominator
1) ASCO 2016c 2) BMJ Best Practice 2016 3) ESMO 2015	Number of patients with metastatic disease and poor performance status who received chemotherapy with Gemcitabine, or a valid reason documented for not receiving therapy	Number of patients with metastatic disease and poor performance status

Reference source details

1) *Key recommendations 2.3:* Gemcitabine alone is recommended for patients with ECOG PS 2 or a comorbidity profile that precludes more aggressive regimens and who wish to pursue cancer directed therapy. [Intermediate, moderate]
2) *Treatment:* In patients with metastatic disease, monotherapy with gemcitabine given weekly in 3 out of 4 weeks, remains the palliative treatment of choice for patients with poor performance status [A&C level evidence]
3) *Table 4. Treatment of Metastatic disease:* For patients with performance status 2 and/or bilirubin level > 1.5x ULN: monotherapy with Gemcitabine can be considered [I, A]

3.3.2a	All patients with LAPC offered chemo-radiation therapy (CRT) or stereotactic body radiation therapy (SBRT), or a valid reason documented for not doing so.	A

Reference(s)	Numerator	Denominator
1) ASCO 2016b 2) BMJ Best Practice 2016 3) CCO 2016 4) ESMO 2015 5) Gandy et al. 2016 (AGITG Consensus)	Number of patients with LAPC treated with CRT or SBRT, or a valid reason documented for not receiving treatment	Number of patients with locally advanced pancreatic cancer

Reference source details

1) *Key Recommendation 2.1:* There is no clear evidence supporting one regimen over another - physician to decide. For some patients chemo-radiotherapy (CRT) or stereotactic body radiation therapy (SBRT) can be offered upfront in locally advanced pancreatic cancer [Intermediate, strong]
2) *Treatment. Locally Advanced Unresectable*: In LAPC, chemo-radiotherapy or short course of stereotactic body radiotherapy (SBRT) can be offered to patients with good performance status
3) *Treatment of Locally Advanced Pancreatic Cancer*: Role of chemo-radiation remains controversial for patients with LAPC. Stereotactic body radiotherapy may hold promise in treating LAPC and maybe considered
4) *Table 4. Summary of Key Points. Treatment of Locally Advanced:* A minor role of chemo-radiation in LAPC has been observed [I, A] with capecitabine and radiotherapy as the only recommended option [IV, C]
5) *Summary:* Value of adding radiation after chemotherapy remains uncertain however, a small number of patients may be downstaged by chemo-radiation

3.3.2b	Patients with LAPC offered CRT or SBRT following initial chemotherapy, or a valid reason documented for not doing so	No grade listed

Reference(s)	Numerator	Denominator
1) ASCO 2016b 2) ASCO 2016b	Number of patients with LAPC treated with CRT or SBRT following initial chemotherapy or a valid reason documented for not continuing treatment	Number of patients with LAPC treated with chemotherapy

Reference source details

1) *Recommendation 3.1:* If there is local disease progression after induction chemo, but without evidence of systemic spread, CRT or SBRT may be offered to those who have completed or terminated first line chemotherapy, ECOG PS ≤ 2, with adequate comorbidity profile - including hepatic and renal function, hematologic status & patient preference [Intermediate, strong]
2) *Recommendation 3.2:* CRT/SBRT may be offered to those who have not responded to an initial 6 months chemo, or have stable disease but have developed unacceptable toxicity or show a decline in performance status as a consequence to chemo-toxicity [Intermediate, strong]

4. MANAGEMENT

4.1 Hepatopancreatobiliary Surgeon

4.1.1a	Patients with potentially resectable disease referred to a HPB surgeon	No grade listed

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a & 2016b	Number of patients with potentially resectable disease referred to a HPB surgeon	Number of patients with potentially resectable disease

Reference source details
1) *Care Statements:* All patients with potentially resectable disease should be referred to a hepatobiliary surgeon (Very-important)

4.1.1b	All patients with a HPB surgeon as the primary specialist in non-metastatic pancreatic cancer	No grade listed

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016b	Number of patients with potentially resectable or locally advanced disease with a HPB surgeon as their primary specialist	Number of patients with potentially resectable or locally advanced disease

Reference source details
1) *Care Statement*: A specialist hepatobiliary surgeon should be the initial/primary specialist unless the patient has obvious metastases

4.2 Participation in Clinical Trials

4.2.1a	All patients included in a clinical trial, or a valid reason documented for not being included	B

Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b & 2016c 2) Bilimoria et al. 2009 3) Burmeister et al. 2016b 4) NCCN 2017 5) VIC OCP 2015	Number of patients participating in a clinical trial, or a valid reason documented for not participating	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendation 1.5 in all stages:* Every person should be given info about clinical trials, including therapeutic trials in all lines of treatment as well as palliative care, biorepository/biomarker, and observational studies [Intermediate, strong]
2) *Table 3: Moderate-validity pancreatic cancer QI no.30:* If an institution treats PC - then institution should participate in clinical trials
3) *Care Statement*: Entry into a clinical trial should be considered for all patients
4) *Boxed statement in footnote Panc A-G*: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged [2A]
5) *Step 3 – 7. Research and Clinical Trials*: Consider research clinical trials where available and appropriate

4.2.1b	Patients with borderline resectable disease included in a clinical trial, or a valid reason documented for not being included	No grade listed

Reference(s)	Numerator	Denominator
1) ESMO 2015	Number of patients with borderline resectable disease participating in a clinical trial or a valid reason documented for not participating	Number of patients with borderline resectable disease

Reference source details

1) *Table 4. Summary of Key Points and Recommendations. Treatment of non-resectable: Borderline resectable*: Patients with borderline resectable lesions should be included in clinical trials wherever possible

4.2.1c	Patients with LAPC included in a clinical trial, or a valid reason documented for not being included	B

Reference(s)	Numerator	Denominator
1) ASCO 2016b	Number of patients with locally advanced disease participating in a clinical trial or a valid reason documented for not participating	Number of patients with locally advanced disease

Reference source details

1) *Key Recommendation 5.2:* Refer people with LAPC who have not benefited from treatment and have disease progression for a clinical trial [Intermediate, strong]

4.3 Diet and Nutrition

4.3.1	All patients referred to a dietician after diagnosis	No grade listed

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016b 2) VIC OCP 2015	Number of patients referred to a dietician	All patients diagnosed with pancreatic cancer

Reference source details

1) Care Statement: All patients should be referred to a dietician soon after diagnosis
2) *Appendix. Supportive Care-Physical Needs*: Weight loss and decrease in appetite may require referrals to a dietician before, during and after treatment.

4.3.2	All patients treated with pancreatic enzyme replacement therapy	B

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) Burmeister et al. 2016b 3) NCCN 2017	Number of patients prescribed pancreatic enzyme replacement	All patients diagnosed with pancreatic cancer

Reference source details

1) *Treatment. Resectable, Locally Advanced and Metastatic:* Pancreatic enzyme supplements should be used to maintain weight and increase quality of life, together with attention to dietary intake and additional nutritional supplements
2) *Care statement:* Pancreatic enzyme replacement therapy should be considered for all patients
3) *Principles of Palliation and Supportive Care:* Prevent and ameliorate suffering while ensuring optimal quality of life – pancreatic exocrine insufficiency treated with enzyme replacement [2A]

4.3.3	Cachexia, anorexia and weight loss managed with nutritional supplements and appetite stimulants	No grade listed

Reference(s)	Numerator	Denominator
1) CCO 2016	Number of patients prescribed nutritional supplements and appetite stimulants	All patients diagnosed with pancreatic cancer

Reference source details

1) *Patient Management and Supportive Care:* Cachexia, anorexia, weight loss managed with nutritional supplements and pharmacologic appetite stimulants

4.4 Patient Management

4.4.1 All patients assigned a care coordinator		No grade listed
Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016b 2) VIC OCP 2015	Number of patients assigned a care coordinator	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Care Statement:* Each patient should be assigned a care coordinator and an individualised treatment/clinical plan 2) *Care Coordination (page 7):* There should be coordination of care between all providers to ensure the patients' needs are met		

4.4.2a All patients with a documented treatment or clinical plan		No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Burmeister et al. 2016b 3) Burmeister et al. 2016a 4) VIC OCP 2015	Number of patients with a documented treatment or clinical plan	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Table 2. High-validity pancreatic cancer QI no.8:* Stage specific treatment plan should be documented 2) *Care Statement:* Each patient should be assigned a care coordinator and an individualised treatment/clinical plan 3) *Table 1. Oncology and other:* Patients should be fully aware of the risks and benefits of interventions prior to any treatment (very important) & patients should be advised of the limitations of chemotherapy (very important) 4) Interventions should be in place to deal with the consequences of cancer and cancer treatment (including managing symptoms, distress and practical issues)		

4.4.2b	All patients with a documented treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems	No grade listed

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Burmeister et al. 2016b 3) Burmeister et al. 2016a 4) VIC OCP 2015	Number of patients with a documented treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems	All patients diagnosed with pancreatic cancer

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.8:* Stage specific treatment plan should be documented
2) *Care Statement:* Each patient should be assigned a care coordinator and an individualised treatment/clinical plan
3) *Table 1. Oncology and other:* Patients should be fully aware of the risks and benefits of interventions prior to any treatment (very important) & patients should be advised of the limitations of chemotherapy (very important)
4) Interventions should be in place to deal with the consequences of cancer and cancer treatment (including managing symptoms, distress and practical issues)

4.4.2c	Treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems documented and discussed with patients & caregivers	B

Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b, 2016c	Number of patients documented to have had a discussion about their treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendations 1.3 for all stages:* Goals of care, patient preferences and support systems should be discussed with every patient and his/her caregiver [Intermediate, Strong]

4.4.3a	Baseline performance status, symptom burden and comorbidity profile evaluated and documented for all patients	A
Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b & 2016c 2) Burmeister et al. 2016a	Number of patients with documented baseline performance status, symptom burden and comorbidity profile	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Key Recommendation 1.2 in all stages:* Baseline performance status, symptom burden and comorbidity profile should be carefully evaluated [High, strong] 2) *Table 1. Presentation and Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to treatment (very important)		

4.4.3b	Baseline symptom burden evaluated and documented for all patients	A
Reference(s)	Numerator	Denominator
3) ASCO 2016a, 2016b & 2016c 4) Burmeister et al. 2016a	Number of patients with symptom burden evaluated and documented	All patients diagnosed with pancreatic cancer
Reference source details		
3) *Key Recommendation 1.2 in all stages:* Baseline performance status, symptom burden and comorbidity profile should be carefully evaluated [High, strong] 4) *Table 1. Presentation and Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to treatment (very important)		

4.5 Multidisciplinary Environment

4.5.1a	Disease management for all patients discussed at a MDT meeting	B

Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b & 2016c 2) Burmeister et al. 2016b 3) Van Rijssen et al. 2016 4) VIC OCP 2015	Number of patients discussed at a multidisciplinary team meeting	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendation 1.4 for all stages:* Multidisciplinary collaboration to formulate treatment and care plans, disease management should be standard of care (Intermediate, Strong)
2) *Care Statement:* All patients should be presented to a MDT
3) *Results. Second Indicator:* Discussion of a patient within a MDT meeting
4) *Referral, Treatment and Palliative Care MDT*: Patients should be referred to a specialist linked to a MDT. Patients should be managed following discussion at a MDT clinic in consultation with palliative care specialists

4.5.1b	Resectability discussed at a MDT	B

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) ESMO 2015 3) Gagliardi et al. 2016 4) NCCN 2017	Number of patients with potentially resectable disease and resectability discussed at a MDT meeting	Number of patients with potentially resectable disease

Reference source details

1) *Step-by-step Treatment Approach:* There is no universally accepted criteria for resection, therefore decisions about resectability should be made by a MDT
2) *Table 4. Summary of key points:* In localised, resectable disease, a multidisciplinary team is necessary
3) *Supplemental table. Multidisciplinary Approach:* Consistency in biochemical, imaging and pathological findings before treatment initiation and during follow-up, is improved with a multidisciplinary approach.
4) *Principles of Diagnosis, Imaging and Staging #1 & #4:* Decisions about diagnostic management and resectability should involve multidisciplinary consultation at a high-volume centre with reference to appropriate high quality imaging studies; & The decision regarding resectability status should be made by consensus at multidisciplinary meetings/discussions [2A]

4.6 Symptom Management

4.6.1a	Biliary or duodenal obstruction managed by endoscopic placement of self-expanding metal stents (SEMs)	B

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) Burmeister et al. 2016b 3) ESMO 2015 4) NCCN 2017	Number of patients with biliary or duodenal obstruction managed with endoscopic placement of SEMs	Number of patients with biliary or duodenal obstruction

Reference source details

1) *Locally Advanced and Metastatic Disease*: Endoscopic palliation is preferred over surgical approaches in LAPC or metastatic
2) *Care Statement:* Biliary obstruction should routinely be managed endoscopically in non-resectable patients
3) *Table 4. Summary of Key Points. Treatment of Metastatic Disease:* Duodenal obstruction is preferably managed by endoscopic placement of an expandable metal stent when possible - favoured over surgery. [IV,B] For biliary stenting: endoscopic method is safer than percutaneous insertion and is as successful as surgical hepatojejunostomy [II,B]
4) *Principles of Palliation and Supportive Care:* Prevent and ameliorate suffering while ensuring optimal quality of life – endoscopic biliary metal stent is the preferred method [2A]

4.6.1b	Biliary or duodenal/gastric obstruction managed surgically or by endoscopic placement of SEMs	No grade listed

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) CCO 2016 3) NCCN 2017	Number of patients with biliary or duodenal/gastric obstruction managed surgically or with endoscopic placement of SEMs	Number of patients with biliary or duodenal/gastric obstruction

Reference source details

1) *Locally Advanced and Metastatic Disease*: Duodenal obstuction (5% of patients) can be managed operatively with gastrojejunostomy or endoscopic stents
2) *Patient Management and Supportive Care:* Biliary and gastric outlet obstruction should be managed with surgical intervention for palliative bypass or placement of biliary and/or duodenal stents
3) *Principles of Palliation and Supportive Care:* For optimal QOL, biliary obstruction (endoscopic biliary metal stent preferred) [2A], and gastric outlet obstruction (gastrojejunostomy ± J tube with good ECOG [2B], enteral stent in poor PS) should be managed

4.6.1c	Biliary or gastric outlet obstruction managed surgically in patients with good performance status	C

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a 2) NCCN 2017	Number of patients with biliary or gastric obstruction and good performance status managed surgically	Number of patients with biliary or gastric obstruction and good performance status

Reference source details

1) *Table 1. Surgery and Biliary Obstruction:* Biliary obstruction should be managed surgically if performance status and prognosis is satisfactory in non-resecatable patients (unable to reach consensus)
2) *Principles of Palliation and Supportive Care*: For optimal QOL, gastric outlet obstruction should be managed with gastrojejunostomy ± J tube in patients with good ECOG [2B]

4.6.2	Patients with resectable disease not stented prior to surgery or reason for stenting documented	No grade listed

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with resectable disease and biliary obstruction not stented or reason for stenting documented	Number of patients with resectable disease and biliary obstruction

Reference source details

1) *Table 1. Surgery and Biliary Obstruction:* Patients with resectable disease should not be stented prior to surgery unless surgery is delayed (unable to reach consensus)

4.6.3	SEM stent used for biliary drainage prior to surgery	No grade listed

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with biliary obstruction managed with a SEM stent prior to surgery; or Number of patients with a plastic stent	Number of patients with biliary obstruction prior to surgery

Reference source details

1) *Table 1. Surgery and Biliary Obstruction:* A SEMs should be used instead of plastic stent if biliary drainage is indicated prior to surgery (unable to reach consensus)

4.6.4 Pain managed with opioid analgesics, palliative radiation or nerve blocks or reason for not treating pain documented		B
Reference(s)	Numerator	Denominator
1) ASCO 2016b and 2016c 2) BMJ Best Practice 2016 3) Burmeister et al. 2016a 4) CCO 2016 5) ESMO 2015	Number of patients prescribed opioids, treated with palliative radiation or administered nerve blocks or reason for not treating pain documented	All patients with pancreatic cancer
Reference source details		
1) *Key Recommendation 7.1 (LAPC) and 5.1 (Metastatic):* Aggressive treatment of pain and other symptoms of cancer and/or cancer directed therapy [Intermediate, Strong] 2) *Treatment. Locally advanced and Metastatic. Pain Management*: Pain control should be commenced along the analgesic ladder with additional options of coeliac block or splanchnicectomy 3) *Table 1. Oncology and Other:* Careful attention to pain control is important using nerve blocks if required (very important) 4) *Patient Management and Supportive Care:* Pain to be managed with narcotic analgesics, radiation or celiac plexus neurolysis 5) *Table 4. Treatment of Metastatic Disease:* Pain control is mandatory and frequently needs the help of a pain specialist		

4.7 Psychosocial Support

4.7.1 All patients offered psychosocial support following diagnosis		B
Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b and 2016c 2) Burmeister et al. 2016b 3) CCO 2016 4) VIC OCP 2015	Number of patients with documented referral to psychologist or social worker or psychosocial support services	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Key Recommendation 5.1(Potentially Curable), 6.1(LAPC), 4.1(Metastatic):* Full assessment of symptom burden, psychological status, and social supports should be offered as early as possible, preferably at the first visit [Intermediate, strong] 2) *Care Statement:* All patients should be offered psychosocial support 3) *Patient Management and Supportive Care:* Depression will require psychiatric consultation 4) *Appendix. Supportive Care*: For psychological wellbeing consider referring patient to psychologist, social worker, or psychiatrist. For social wellbeing consider referring patient to peer support, social worker, psychologist, psychiatrist or occupational therapist		

4.8 Palliative Care

4.8.1a All patients referred to palliative care services following diagnosis		No grade listed
Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) Burmeister et al. 2016a 3) VIC OCP 2015	Number of patients with documented referral to palliative care services	All patients diagnosed with pancreatic cancer
Reference source details		
1) *Key Recommendation 5.1:* Patients with potentially curable disease should have full assessment of symptom burden, psychological status, and social supports as early as possible. In some instances, this may indicate a need for formal palliative care consult and services. 2) *Table 1. MDT and Referrals:* On diagnosis all patients should be referred to palliative care (unable to reach consensus) 3) *Summary. Step 6:* Specialist palliative care is recommended for majority of patients based on need. Early referral can improve quality of life		

4.8.1b Patients with locally advanced disease referred to palliative care services following diagnosis		B
Reference(s)	Numerator	Denominator
1) ASCO 2016b and 2016c 2) Burmeister et al. 2016b	Number of patients with locally advanced disease and documented referral to palliative care services	Number of patients with locally advanced disease
Reference source details		
1) *Key Recommendation 6.1 and 4.1:* Patients with LAPC or metastatic disease should have full assessment of symptom burden, psychological status, and social supports as early as possible, preferably at the first visit. In most cases, this will indicate a need for formal palliative care consult and services. [Intermediate, strong] 2) *Care Statement:* Patients with confirmed metastatic disease should be referred to palliative care		

4.8.1c	Patients with metastatic disease referred to palliative care services following diagnosis	B

Reference(s)	Numerator	Denominator
3) ASCO 2016b and 2016c 4) Burmeister et al. 2016b	Number of patients with metastatic disease and documented referral to palliative care services	Number of patients with metastatic disease

Reference source details

3) *Key Recommendation 6.1 and 4.1:* Patients with LAPC or metastatic disease should have full assessment of symptom burden, psychological status, and social supports as early as possible, preferably at the first visit. In most cases, this will indicate a need for formal palliative care consult and services. [Intermediate, strong]
4) *Care Statement:* Patients with confirmed metastatic disease should be referred to palliative care

4.9 Follow-up and Surveillance

4.9.1a	All patients having completed treatment followed-up every three to six months	B

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) NCCN 2017 3) VIC OCP 2015	Number of patients who completed treatment with documented follow up every 3 – 6 months	Number of patients who completed treatment

Reference source details

1) *Key Recommendation 6.1:* In the absence of RCT evidence, it is recommended that patients who have completed treatment be monitored for recovery of treatment related toxicities and recurrence. Visits maybe offered at 3 - 6 month intervals, the role of serial cross-sectional imaging, the extent to which surveillance intervals should be prolonged overtime and the duration of recommended surveillance are all undefined [Low, moderate]
2) *Panc-5. Postoperative Adjuvant Treatment:* Surveillance every 3-6 months for 2 years then 6-12 months thereafter [2A]
3) *Summary. Step 5:* Surveillance for cancer spread, recurrence or second cancers and screening/ assessment for medical and psychosocial late effects should be monitored. Cancer survivors should be provided with a treatment summary outlining: diagnostic tests; tumour characteristics; type and date of treatment, interventions; support services; and contact information of key providers

4.9.1b	Patients with LAPC having completed treatment followed up every three to four months	C

Reference(s)	Numerator	Denominator
2) ASCO 2016b	Number of patients with LAPC who completed treatment and documented follow up every 3 – 4 months	Number of patients with LAPC who completed treatment

Reference source details

2) *Key Recommendations 8.1 & 8.2:* In the absence of RCT evidence, panel recommends follow-up visits every 3 – 4 months that include physical examination, liver and renal function tests. CA19 -9 and CT should be performed 3 - 4 months during the first 2 years, with imaging intervals increased to 6 months thereafter. Routine use of positron emission tomography is not recommended. Tumour markers should not replace imaging as an assessment. [Low, strong]

4.9.1c	Patients with metastatic disease on active cancer-directed therapy followed up every 2 – 3 months	C

Reference(s)	Numerator	Denominator
1) ASCO 2016c	Number of patients with metastatic disease on active cancer-directed therapy and documented follow up every 2 – 3 months	Number of patients with metastatic disease on active cancer-directed therapy

Reference source details

1) *Key Recommendation 6.1 & 6.2:* For patients on active cancer-directed therapy outside clinical trial, imaging to assess first response should be offered at 2 - 3 months, from the initiation of therapy. CT scans with contrast are the preferred modality. Thereafter clinical assessment, conducted frequently during visits should supplant imaging assessment. The routine use of positron emission tomography scans is not recommended. CA19-9 is not considered an optimal substitute for imaging of assessment of treatment response. [Low, strong]

5. OUTCOME

5.1 Perioperative Measures

5.1.1a	Institution monitors their risk-adjusted perioperative mortality following surgical resection	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Number of patients who died following surgical resection	N/A
Reference source details		
1) *Table 2. High-validity pancreatic cancer QI no.28 & 29:* Hospital should monitor their PC resection risk-adjusted perioperative mortality Hospital risk-adjusted perioperative mortality should be less than 5%		

5.1.1b	Risk-adjusted perioperative mortality following surgical resection is less than 5%	No grade listed
Reference(s)	Numerator	Denominator
2) Bilimoria et al. 2009	Percentage of patients who died following resection	N/A
Reference source details		
2) *Table 2. High-validity pancreatic cancer QI no.28 & 29:* Hospital should monitor their PC resection risk-adjusted perioperative mortality Hospital risk-adjusted perioperative mortality should be less than 5%		

5.1.2	Institution monitors their stage-specific 2 year and 5 year survival rates for patients who underwent a surgical resection	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Stage specific 2 year and 5 year survival rate	N/A
Reference source details		
1) *Table 3. Moderate-validity pancreatic cancer QI no.43:*Hospital should monitor the stage-specific 2 year and 5 year survival rates for their patients who underwent pancreatectomy		

5.1.3	Institution monitors their margin-negative resection rate	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Margin-negative resection rate	N/A
Reference source details		
1) *Table 2. High-validity pancreatic cancer QI no.27:* If an institution performs PC surgery, then they should monitor their margin-negative resection rate		

5.1.4	Institution monitors their median estimated blood loss	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Estimated volume of blood loss per resection	N/A
Reference source details		
1) *Table 3. Moderate-validity pancreatic cancer QI no.39.*		

5.1.5	Institution monitors their median operative time for surgical resections	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Median operative time	N/A
Reference source details		
1) *Table 3. Moderate-validity pancreatic cancer QI no.40 & no.42:* The institution should monitor the median operative time for resections Operative time should be less than 10 hours		

5.1.6	Institution monitors their 30 day readmission rate following a surgical resection	No grade listed
Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	30 day readmission rate	N/A
Reference source details		
1) *Table 3. Moderate-validity pancreatic cancer QI no.41:* Hospital should monitor their readmission rate within 30 days rate		

5.2 Surgical Complications

5.2.1	Patients who developed pancreatic fistula following surgical resection	No grade listed
Reference(s)	Numerator	Denominator
1) Nordby et al. 2013	Number of patients who developed a postoperative pancreatic fistula	Number of patients who underwent a surgical resection
Reference source details		
1) Table II. Postoperative Complications in 135 patients undergoing pancreatic surgery		

5.2.2	Patients who developed biliary fistula following surgical resection	No grade listed
Reference(s)	Numerator	Denominator
1) Nordby et al. 2013	Number of patients who developed a postoperative biliary fistula	Number of patients who underwent a surgical resection
Reference source details		
1) Table II. Postoperative Complications in 135 patients undergoing pancreatic surgery		

5.2.3	Patients who developed delayed gastric emptying following surgical resection	No grade listed
Reference(s)	Numerator	Denominator
2) Nordby et al. 2013	Number of patients who developed delayed gastric emptying following resection	Number of patients who underwent a surgical resection
Reference source details		
2) Table II. Postoperative Complications in 135 patients undergoing pancreatic surgery		

5.2.4	Patients who developed a pulmonary embolism following surgical resection	No grade listed
Reference(s)	Numerator	Denominator
1) Nordby et al. 2013	Number of patients who developed a postoperative pulmonary embolism	Number of patients who underwent a surgical resection
Reference source details		
1) Table II. Postoperative Complications in 135 patients undergoing pancreatic surgery		

5.2.5	Patients who developed a portal vein thrombosis following surgical resection	No grade listed
Reference(s)	Numerator	Denominator
1) Nordby et al. 2013	Number of patients who developed a postoperative portal vein thrombosis	Number of patients who underwent a surgical resection
Reference source details		
1) Table II. Postoperative Complications in 135 patients undergoing pancreatic surgery		

5.2.6 Patients requiring a re-operation following surgical resection		No grade listed
Reference(s)	Numerator	Denominator
1) Nordby et al. 2013	Number of patients who had a re-operation following a surgical resection	Number of patients who underwent a surgical resection
Reference source details		
1) Table II. Postoperative Complications in 135 patients undergoing pancreatic surgery		

APPENDIX 1: Dimensions and Components of Healthcare

Dimensions of Healthcare[3]

- Safe - Avoiding injuries to patients from the care that is intended to help them.
- Effective - Providing services based on scientific knowledge to all who could benefit and refraining from providing services to those not likely to benefit (avoiding overuse, respectively).
- Patient-Centred - Providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions.
- Timely - Reducing waits and sometimes harmful delays for both those who receive and those who give care.
- Efficient - Avoiding waste, including waste of equipment, supplies, ideas and energy.
- Equitable - Providing care that does not vary in quality because of personal characteristics such as gender, ethnicity, geographic locations and socio-economic status.

Components of Healthcare[4]

- Structure - Indicators specify the presence of absence of attributes of the environment where care is provided, including organisation culture, information systems, services and supply, policies and procedures and workforce.
- Process - Indicators reflect the effectiveness of processes and systems of care and the implementation of policies and procedures and guidelines.
- Outcomes - The 'consequences of care'; may be influenced directly or indirectly by the structure and processes. Measurement of quality cannot be allowed to focus routinely on process without an equal or greater focus on assessment of health outcomes. At a national/state level, it is essential that well-defined and carefully measured outcomes are collated over time.

	Dimensions of Healthcare					
Components of Healthcare	Safe	Effective	Patient-Centred	Timely	Efficient	Equitable
Structure	Safe Structure	Effective Structure	Patient-Centred Structure	Timely Structure	Efficient Structure	Equitable Structure
Process	Safe Process	Effective Process	Patient-Centred Process	Timely Process	Efficient Process	Equitable Process
Outcome	Safe Outcome	Effective Outcome	Patient-Centred Outcome	Timely Outcome	Efficient Outcome	Equitable Outcome

[3] Committee on Quality of Health Care in America. Institute of Medicine. Crossing the Quality Chasm: A New Health System for the 21st Century: The National Academies Press; 2001.

[4] Donabedian A. The Quality of Care. JAMA: The Journal of the American Medical Association. 1988; 260(12):1743-8.

Appendix 2.3: Executive Summary Round 1 (Excerpt)

This document contains all indicators that were part of the Round One Online Survey. It includes all indicators selected, rejected and for discussion

EXECUTIVE SUMMARY

Pancreatic Cancer Quality Indicators

Version 1.0
02 October 2017

TABLE OF CONTENTS

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ABBREVIATIONS

Table 1: Full list of abbreviations that have been used in this document

AGITG	Australasian Gastro-Intestinal Trials Group
CA 19-9	Carbohydrate Antigen 19-9
CAP	College of American Pathologists
CE	Content Experts
CRT	Chemo-radiation Therapy
CT	Computed Tomography
EUS	Endoscopic Ultrasound
EUS ± FNA	Endoscopic Ultrasound ± Fine Need Aspirate
HPB	Hepatopancreatobiliary
HREC	Human Research Ethics Committee
LAPC	Locally Advanced Pancreatic Cancer
LFT	Liver Function Test
MDT	Multidisciplinary Team
MRI	Magnetic Resonance Imaging
NHMRC	National Health and Medical Research Council
NSW	New South Wales
PC	Pancreatic Cancer
P-CR4QI	Pancreatic Cancer Registry for Quality Improvement
PET	Positron Emission Tomography
RAM	Rand/Ucla Appropriateness Method
RCT	Randomised Control Trial
SBRT	Stereotactic Body Radiation Therapy
SEMS	Self-Expanding Metal Stent
UGI	Upper Gastro-Intestinal

UGICR	Upper Gastro-Intestinal Cancer Registry
US	Ultrasound
VCR	Victorian Cancer Registry
VIC	Victoria

ABOUT THE RESEARCH

Pancreatic cancer (PC) is the tenth most common cancer diagnosis, the fifth leading cause of cancer-related death (following breast cancer in females) and the leading cause of death from a digestive organ neoplasm in Australia. Despite a significant decline in mortality across almost all neoplasms over the past 15 years, the age-adjusted mortality rate from pancreatic cancer has virtually remained unchanged. Our purpose is to develop a set of quality indicators that are based on evidence, patient experience and clinician perspective to judge and assess quality performance in pancreatic cancer

RESULTS

We expect that the findings of this study will be published in peer-reviewed journals and presented at conferences. Individual participants will not be identifiable.

STORAGE OF DATA

Data collected will be stored in accordance with Monash University regulations, kept on University premises, in a locked filing cabinet for 7 years.

POTENTIAL BENEFIT

The development of a core set of quality indicators to monitor the quality of care in patients with pancreatic cancer will play an essential role in improving their health outcomes and promote analysis of quality outcomes and risk adjustment specific to pancreatic cancer.

INCONVENIENCE/DISCOMFORT

We do not anticipate that you should experience any risks, inconvenience or discomfort as a result of participating in this study.

INFORMED CONSENT AND WITHDRAWAL

Participation in any research project is voluntary. If you do not wish to be involved on the Delphi panel please email the Chief Investigator sue.evans@monash.edu. We will send you a link to the online survey in the email. We will assume that, by completing the survey, you are consenting to participate in the study. You are able to withdraw from the study at any stage of the research.

CONFIDENTIALITY

If you choose to participate, all the information obtained from the discussion will be confidential. No information that could lead to the identification of any individuals will be disclosed in any medical articles or to any party.

COMPLAINTS

Should you have any concerns or complaints about the conduct of the project, you are welcome to contact the Executive Officer, Monash University Human Research Ethics (MUHREC): TEL: +61 3 9905 2052 EMAIL: muhrec@monash.edu

MEETING DETAILS AND AGENDA

MEETING DETAILS

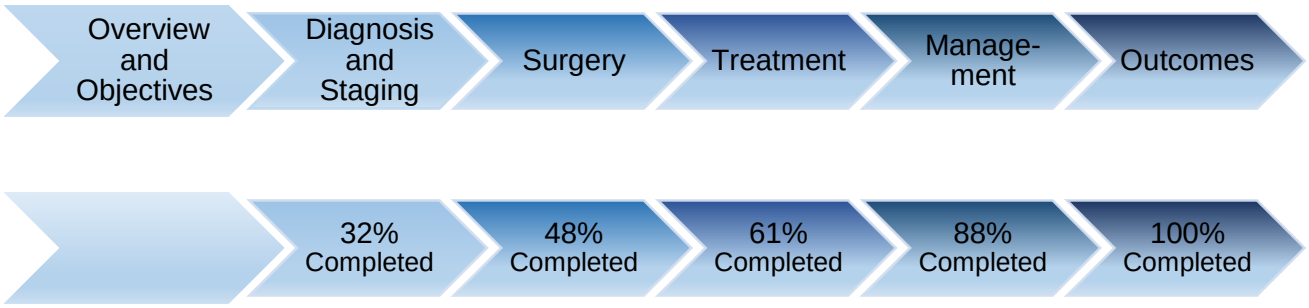
Date	Saturday 14th October 2017
Time	10.00 – 18.00
Location	UNSW Lowy Cancer Research Centre, Corner High and Botany St, Kensington NSW Google Maps
Provisions For The Day	Documents • Hard copy of this executive summary • Panellist rating form Other • Morning Tea, Lunch and Afternoon Tea
What To Bring	Yourselves ☺ Your Laptop Panellists Summary Document (sent via email earlier)
Contact	Please contact Ashika Maharaj + 61 416 879 458 or Dr Liane Ionnou +61 422 118 614 for any further clarifications

MEETING AGENDA

10.00	Welcome, Overview and Project Objectives (Rolling Morning Tea)
10.30	➢ Diagnosis and Staging
12.30	Lunch
13.15	➢ Surgery
	➢ Treatment
15.30	Afternoon Tea
15.45	➢ Management
	➢ Outcomes
17.45	Wrap-up and Conclusion

Please note: The above schedule maybe subject to change however, we will endeavour to keep to schedule as close as possible

TIME POINT VISUAL FOR AGENDA



MEETING OBJECTIVE

Refine and reduce the number of quality-of-care indicators that were derived from the literature review.

The principal goal is to have a PC quality indicator set which can be utilised by the Upper Gastrointestinal Cancer Registry (UGICR) in each jurisdiction to enable providers of pancreatic cancer treatment to benchmark performance against indicators with other centres in their jurisdiction.

The goal of this face-to-face meeting is to discuss the results, refine and reduce the number of quality indicators voted upon by Delphi members prior to attending this meeting. Reports must be succinct, informative and easy to understand and for this to occur we must have:

1. **A reasonable number of indicators**
2. **A holistic approach to monitoring quality of care**: All aspects of pancreatic cancer management are important and within the indicator set an appropriate range of indicators that monitors the patients journey should be achieved
3. **Measurable Indicators**

STATISTICAL ANALYSIS

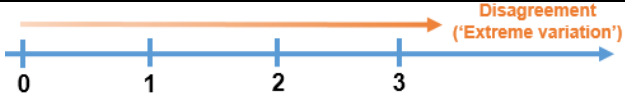
CALCULATION OF STATISTICS

This example has been provided because the statistics on how the panel rated as a whole is important in informing your appraisal of each indicator. If a person selected 'unable to comment', their response was excluded when calculating the statistics. Table 1 provides an example of the raw score which each of the 12 panellists. Table 2 outlines the scoring system used in the Delphi panel. We chose to use the IPRAS value to describe the level of disagreement between panellists for each of the recommendations they were asked to score (from 1-9).

Table 1: Example of how each panellist rated the proposed indicator

Panellist assigned number	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20	#21	#22
Rating given (from 1-9)	9	9	X	9	9	9	9	7	9	7	9	8

Table 2: How the statistics, which have been used to classify indicators are calculated

Measure	Definition	How to calculate	Results
Median	An observation at the 50th percentile	50th percentile	9
Lower IPR	An observation at the 10th percentile	10th percentile	7
Upper IPR	An observation at the 90th percentile	90th percentile	9
IPR	The inter-percentile range. It is a measure of dispersion of a distribution.	Upper IPR – Lower IPR	2
IPRCP	The central point of IPR	(Lower IPR + Upper IPR)/2	8
Asymmetry index	The distance between the central point of the IPR and the central point of the 1-9 scale, i.e. 5	Absolute value (5-IRCP)	3
IPRAS	The inter-percentile range adjusted for symmetry. It is a measure of the degree of asymmetry across the 9-point scale. Using the numbers supplied by the RAND document[1] : **IPRAS = 2.35 + (1.5 x Asymmetry Index)**	= IPRr + (CFA x Asymmetry Index)	**6.85**
		IPRr is the interpercentile range required for disagreement when there is perfect symmetry. CFA is the correction factor for asymmetry, which is a constant set at 1.5	
Disagreement Index (DI)	It is a measure which shows if there was wide or limited dispersion of panellist ratings	IPR/IPRAS	0.29 **0.29 < 1 Therefore, there is agreement**
	 **Disagreement Index (DI)** If the DI is ≥ 1, then it indicates 'extreme variation' in ratings. The lower the DI, the lower the level of disagreement (i.e. the higher the level of agreement/ better consensus).		

[1] Fitch K, Bernstein SJ, Aguilar M, et al. (eds) The RAND/UCLA Appropriateness Method User's Manual. Santa Monica, The RAND Corporation, 2001

SELECTING INDICATORS

Table 3: The criteria for indicator classification

Median		1-3	4-5	6	7-9
Agreement	<1				
Disagreement	>1				

*****There are two components that make up the decision rules, the median value and the disagreement index (DI)*****

- All indicators with DI > 1 are highlighted in **amber**. These indicators are the most important point of discussion during the face-to-face panel discussion. At the conclusion of the meeting, each of these indicators will either become a red or green indicator.

- **Red** if the median value is between 1 – 5 whether or not there is agreement or disagreement. These indicators will be briefly reviewed during the meeting to ensure there are no strong objections to their removal.

- If an indicator has a DI <1.00, which indicates agreement amongst panellists, are highlighted in **green.**

- All indicators that have DI <1 and a median ≥ 7 are **green** for both scores, and will progress to set of candidate indicators. These indicators will be further discussed during the meeting:
  - If the number of indicators needs to be reduced;
  - If a particular aspect of pancreatic cancer management is heavily over-represented;
  - If two of the 'accepted' indicators are too similar.

Table 4: Summary of the distribution of the indicators based on median and agreement

Indicator Sections			
1. Diagnosis and Staging	1 0.94%	15 14.01%	19 17.76%
2. Surgery	0	11 10.28%	5 4.67%
3. Treatment	0	5 4.67%	9 8.41%
4. Management	0	22 20.56%	7 6.54%
5. Outcomes	0	11 10.28%	2 1.87%
TOTAL	1 0.94%	64 59.81%	42 39.25%

STRUCTURE OF THE INDICATOR INDEX

1. DIAGNOSIS AND STAGING

1.1. History and Physical
1.2. Presence of Jaundice
1.3. Imaging Modalities
1.4. EUS and Biopsy
1.5. CA19-9 Levels
1.6. Staging

2. SURGERY

2.1. Resectability
2.2. Lymph Nodes Examination
2.3. Margins
2.4. Surgical Institutions
2.5. Surgeon
2.6. Other

3. TREATMENT

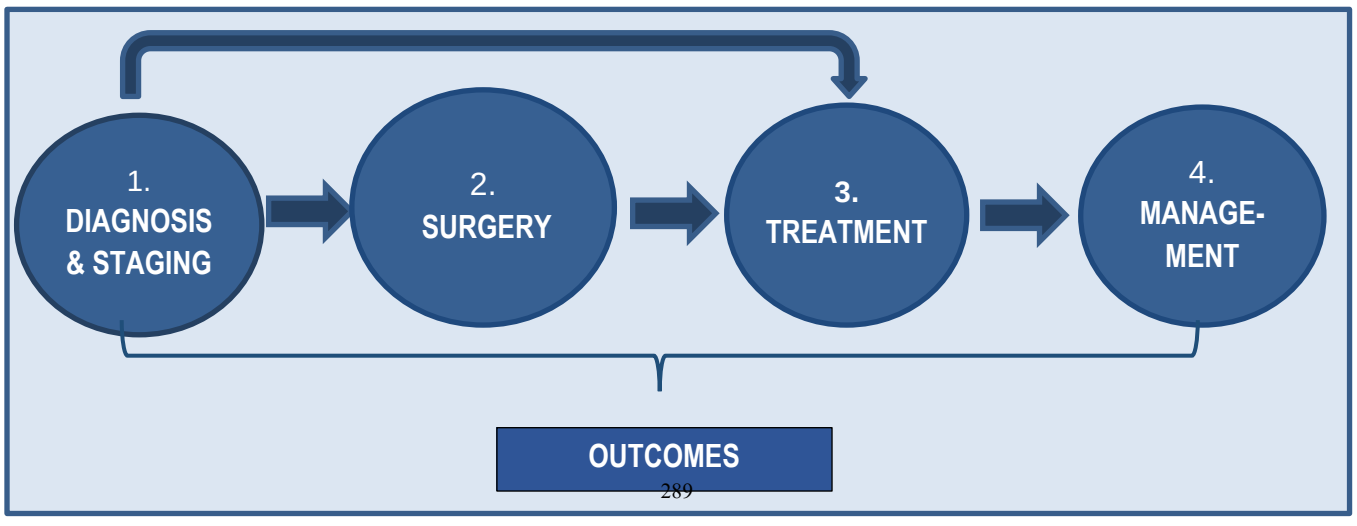
3.1. Adjuvant Therapy
3.2. Neo-Adjuvant Therapy
3.3. Palliative Therapy

4. MANAGEMENT

4.1. HPB Surgeon
4.2. Participation in Clinical Trials
4.3. Diet and Nutrition
4.4. Patient Management
4.5. Multidisciplinary Environment
4.6. Symptom Management & Complications
4.7. Psychosocial Support
4.8. Palliative Care
4.9. Follow-up and Surveillance

5. OUTCOME

5.1 Perioperative Measures
5.2 Surgical Complications



HOW TO USE THE INDICATOR INDEX

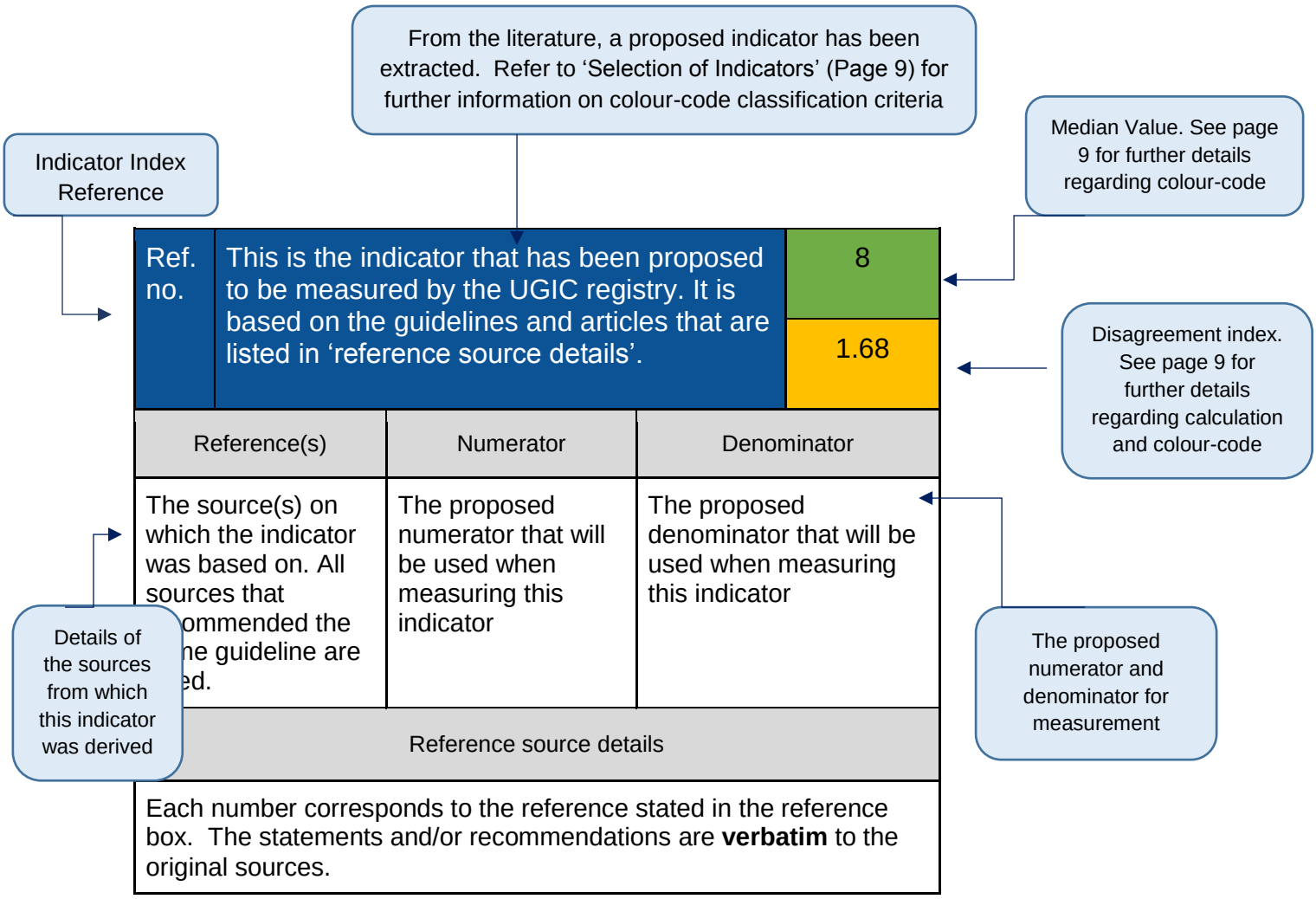
Indicators are presented in chronological order in terms of management of Pancreatic Cancer (Diagnosis and Staging → Surgery → Treatment → Management → Outcomes)

Each indicator also has:

1. Colour-code classification for the indicators:
   a. **RED** – agreement that the indicator is not important
   b. **GREEN** – agreement that the indicator is very important
   c. **AMBER** – disagreement on the importance of the indicator

2. Median value – RED (≤ 5), AMBER (5-6), GREEN (7-9)

3. Disagreement Index – AMBER (≥1), GREEN (<1)



FULL INDICATOR INDEX

1. DIAGNOSIS and STAGING

1.1 History and Physical

1.1.1a	Documented history and physical examination	No Grade Listed	6 1.68

Reference(s)	Numerator	Denominator
1) BMJ Best Practice, 2016 2) Burmeister et al. 2016a	Number of patients with documented history and physical examination pre-diagnosis	All patients with pancreatic cancer

Reference source details

1) *Step by Step diagnostic approach. History and physical examination:* All patients with suspected pancreatic cancer should be investigated and managed without delay. Physicians should consider pancreatic cancer in any patients who present with unexplained upper abdominal pain, painless obstructive jaundice, weight loss and back pain.
2) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to treatment

1.1.1b	Documented history and physical examination with preoperative risk assessment	No Grade Listed	7 1.74

Reference(s)	Numerator	Denominator
1) Bilimoria et al, 2009	Number of patients with documented history, physical examination and pre-operative risk assessment	Number of patients who underwent a surgical resection

Reference source details

1) *Table 2: High-validity pancreatic cancer quality indicator no.7:* If a patient undergoes resection, then a history and physical with thorough preoperative risk assessment should be performed

1.1.1c	Documented pre-operative risk assessment	No Grade Listed	6
			0.88

Reference(s)	Numerator	Denominator
1) Bilimoria et al, 2009	Number of patients with documented pre-operative risk assessment	Number of patients who underwent a surgical resection

Reference source details

1) *Table 2: High-validity pancreatic cancer quality indicator no.7:* If a patient undergoes resection, then a history and physical with thorough preoperative risk assessment should be performed

1.1.2a	Documented physical status, geriatric assessment if elderly, comorbidities and performance status prior to surgery or treatment	No Grade Listed	8
			0.75

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with all of the following documented: physical status; geriatric assessment; comorbidity profile; and performance status	All patients diagnosed with pancreatic cancer

Reference source details

1) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to any treatment

1.1.2b	Documented comorbidity profile prior to surgery or treatment	No Grade Listed	6
			0.67

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with documented comorbidity profile	All patients diagnosed with pancreatic cancer

Reference source details

1) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to any treatment

1.1.2c	Documented performance status prior to surgery or treatment	No grade listed	7
			0.45

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with documented performance status	All patients diagnosed with pancreatic cancer

Reference source details
1) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to any treatment

1.1.2d	Documented geriatric assessment prior to surgery or treatment	No grade listed	5
			1.68

Reference(s)	Numerator	Denominator
2) Burmeister et al. 2016a	Number of patients with documented geriatric assessment	All patients diagnosed with pancreatic cancer above the age of……

Reference source details
2) *Table 1. Statements with highest importance. Presentation & Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to any treatment

1.1.3a	Documented referral to genetic counsellor for young patients	B	5
			0.98

Reference(s)	Numerator	Denominator
1) NCCN 2017	Number of young patients referred to a genetic counsellor	Number of patients diagnosed with pancreatic cancer below the age of ….

Reference source details
1) *PANC-1 footnote:* If pancreatic cancer is diagnosed, consider referral for genetic counselling for patients who are young, those with a family history of Cancer or those of Ashkenazi Jewish ancestry [2A]

1.1.3b	Documented referral to genetic counsellor for patients with a family history of cancer	B	6 1.04

Reference(s)	Numerator	Denominator
2) NCCN 2017	Number of patients with a family history of cancer referred to a genetic counsellor	Number of patients with a family history diagnosed with pancreatic cancer

Reference source details
2) *PANC-1 footnote:* If pancreatic cancer is diagnosed, consider referral for genetic counselling for patients who are young, those with a family history of Cancer or those of Ashkenazi Jewish ancestry [2A]

1.1.3c	Documented referral to genetic counsellor for patients with Ashkenazi Jewish ancestry	B	6 2.55

Reference(s)	Numerator	Denominator
3) NCCN 2017	Number of patients with Ashkenazi Jewish ancestry referred to a genetic counsellor	Number of patients with Ashkenazi Jewish ancestry diagnosed with pancreatic cancer

Reference source details
3) *PANC-1 footnote:* If pancreatic cancer is diagnosed, consider referral for genetic counselling for patients who are young, those with a family history of Cancer or those of Ashkenazi Jewish ancestry [2A]

1.3 Imaging Modalities

1.3.1a	Documented pancreatic protocol CT for diagnosis or staging	No Grade Listed	8
			0.29

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) Burmeister et al. 2016b 3) VIC OCP 2015	Number of patients with pancreatic protocol CT confirming diagnosis or staging	All patients diagnosed with pancreatic cancer

Reference source details

1) *Diagnostic Tests:* All patients with suspected disease on ultrasound should undergo pancreas-specific CT. This has been shown to achieve 97% diagnostic rates of pancreatic cancer with accurate prediction of resectability in 80-90% of patients.
2) *Care statement:* All patients should have a triple phase/pancreas protocol CT scan for staging
3) *Step 3. Diagnostic Workup:* Contrast-enhanced multidector CT according to suggested pancreatic protocol

1.3.1b	Documented multiphase CT of chest, abdomen and pelvis	B	7
			0.75

Reference(s)	Numerator	Denominator
1) ASCO 2016b and 2016c	Number of patients who had a multiphase CT of chest, abdomen and pelvis	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendations 1.1:* A multiphase CT scan of the chest, abdomen and pelvis should be performed to assess extent of disease. Other staging studies should only be performed as dictated by symptoms (Locally advanced & Metastatic) [Intermediate, Strong]

1.3.2	Documented pancreatic protocol CT or MRI scan for diagnosis and/or staging	A	8
			0.37

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) Bilimoria et al. 2009 3) NCCN 2017	Number of patients with pancreatic protocol CT or MRI scan for diagnosis and/or staging	All patients diagnosed with pancreatic cancer

Reference source details

1) *Recommendation 1.1:* A multiphase CT of abdomen and pelvis using a pancreatic protocol or MRI should be performed for all patients to assess the anatomic relationships of the primary tumour and presence of intra-abdominal metastases [High, Strong]
2) *Derived from Table 2. High validity pancreatic cancer QI:* Triple phase, multi slice CT or MRI scan should be obtained
3) *Principles of diagnosis, imaging and staging #3:* Imaging should include dedicated pancreatic CT (preferred) or MRI with contrast [2A]

1.3.3	Documented CT of chest, abdomen and pelvis; or PET scan	No grade listed	6
			1.24

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a 2) VIC OCP 2015	Number of patients with diagnosis and staging confirmed by a CT or PET scan	All patients diagnosed with pancreatic cancer

Reference source details

1) *Derived from Table 1. Statements with highest importance or for which consensus not reached:* If disease appears to be localised a PET scan should be performed (unable to reach consensus
2) *Step 3.2. Diagnosis, staging and treatment planning:* Comprehensive staging of pancreatic cancer should be done simultaneously using the imaging modalities for diagnosis and include CT, chest/abdominal/Pelvis & PET.

1.6 Staging

1.6.1a	Staging completed and documented within one week of presentation	No grade listed	7
			0.96

Reference(s)	Numerator	Denominator
1) VIC OCP 2015	Number of patients with staging assessed and completed within one week of presentation	All patients diagnosed with pancreatic cancer

Reference source details

1) *Step 3. Diagnosis, staging and treatment planning:* Diagnostic and staging should be completed within one week

1.6.1b	Staging investigations completed and documented within four weeks of presentation	No grade listed	9
			0.75

Reference(s)	Numerator	Denominator
1) Gandy et al. 2016 (AGITG Consensus)	Number of patients with staging completed within four weeks of presentation	All patients diagnosed with pancreatic cancer

Reference source details

1) *Summary:* Staging investigations to be completed within 4 weeks of presentation by pancreatic protocol computed tomography, endoscopic US and when possible biopsy

1.6.1c	Staging completed and documented following high quality dedicated imaging at presentation	B	6
			1.09

Reference(s)	Numerator	Denominator
1) NCCN 2017	Number of patients with staging & assessment completed at presentation following high quality imaging	All patients diagnosed with pancreatic cancer

Reference source details

1) *Principles of diagnosis, imaging and staging #2:* To provide adequate staging and assessment, high quality dedicated imaging of the pancreas should be performed at presentation, preferably within 4 weeks of surgery and following neoadjuvant treatment [2A]

1.6.2	Staging completed and documented within four weeks of surgery	B	6
			1.56

Reference(s)	Numerator	Denominator
2) NCCN 2017	Number of patients with staging & assessment completed within four weeks of surgery	Number of patients undergoing a surgical resection

Reference source details

2) *Principles of diagnosis, imaging and staging #2:* To provide adequate staging and assessment, high quality dedicated imaging of the pancreas should be performed at presentation, preferably within 4 weeks of surgery and following neoadjuvant treatment [2A]

1.6.3	Staging and assessment completed and documented following neoadjuvant treatment	B	8
			0.54

Reference(s)	Numerator	Denominator
3) NCCN 2017	Number of patients with staging & assessment completed following neoadjuvant therapy	Number of patients receiving neoadjuvant therapy

Reference source details

3) *Principles of diagnosis, imaging and staging #2:* To provide adequate staging and assessment, high quality dedicated imaging of the pancreas should be performed at presentation, preferably within 4 weeks of surgery and following neoadjuvant treatment [2A]

1.6.4a	Documented TNM clinical stage in patients who do not undergo surgical resection	No grade listed	7
			1.14

Reference(s)	Numerator	Denominator
4) Bilimoria et al. 2009	Number of patients with unresectable disease and documented TNM clinical stage	Number of patients with unresectable pancreatic cancer

Reference source details

4) *Derived from Table 2. High validity QI No.21:* If a patient does not undergo resection, then a TNM clinical stage should be done

2. SURGERY

2.1 Resectability

2.1.1a	All patients defined operable offered surgery or a valid reason documented for not undergoing surgery	B	8
			0.59

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) Bilimoria et al. 2009 3) Burmeister et al. 2016a and 2016b 4) VIC OCP 2015 5) Visser et al. 2012	Number of patients with operable disease who underwent a resection or have a documented reason for resection not attempted	Number of patients with operable disease

Reference source details

1) *Recommendation 2.1:* Primary surgical resection of tumour and regional lymph nodes recommended for patients who meet stated criteria [Intermediate, Strong]
2) *Derived from Table 2. High validity QI No.22:* If a patient has clinical I or II disease, then the patient should undergo resection or have a valid reason for not undergoing resection
3) *Derived from Table 1 (very important) and Care Statements:* All patients with a small lesion and technically resectable disease plus adequate performance status should be offered a resection
4) *Step 4. Treatment:* Curative surgery should be undertaken with or without chemotherapy in resectable disease by Whipples procedure (pancreaticoduodenal), distal pancreatectomy or total pancreatectomy
5) *NCCN-based definition of compliant treatment:* Surgery recommended for stages 0 to III.

2.1.1b	All patients defined operable with adequate performance status offered surgery or a valid reason documented for not undergoing surgical	No grade listed	9
			0.29

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a and 2016b	Number of patients with operable disease and adequate performance status who underwent a resection or a valid reason documented for resection not attempted	Number of patients with operable disease and adequate performance status

Reference source details

6) *Derived from Table 1 (very important) and Care Statements:* All patients with a small lesion and technically resectable disease plus adequate performance status should be offered a resection

2.1.2	Patients with stage IV disease who underwent surgical resection	No grade listed	7
			0.66

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Number of patients with clinical stage IV disease who underwent a resection	Number of patients with clinical stage IV disease

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.24:* If a patient has clinical stage IV disease then a cancer-directed resection should not be done

2.1.3	Patients potentially resectable do not have a tissue biopsy prior to surgery	No grade listed	5.5
			2.55

Reference(s)	Numerator	Denominator
2) Burmeister et al. 2016a	Number of patients who underwent surgery with no tissue biopsy prior to surgery	Number of patients with potentially resectable disease

Reference source details

2) *Table 1. Statements with highest importance or unable to reach consensus:* Potential resectable patients should not have a tissue biopsy prior to surgery (unable to reach consensus)

2.1.4	Suspicious adenopathy evaluated by frozen section	No grade listed	5
			2.32

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Number of patients with suspicious adenopathy that is evaluated by frozen section	Number of patients who underwent surgical resection with suspicious adenopathy

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.18:* If a patient undergoes resection, then suspicious adenopathy outside the scope of planned resection should be evaluated by frozen section

2.3 Margins

2.3.1	Tumour clearance for all seven margins identified and documented to identify an R0 resection	B	9
			0.29

Reference(s)	Numerator	Denominator
1) Arnachellum et al. 2016 2) Bilimoria et al. 2009 3) Bilimoria et al. 2009 4) De Leede et al. 5) ESMO 2015 6) Gandy et al. 2016 (AGITG Consensus) 7) NCCN 2017 8) NCCN 2017	Number of patients with all seven margins identified and documented following resection	Number of patients who underwent a surgical resection

Reference source details

1) *Table 2. Comparison of tumor characteristics and therapeutic modalities:* Potentially curative surgery (R0 + R1, c/f with other surgeries) & Curative surgery (negative margin)
2) *Table 2. High validity pancreatic cancer QI no.14:* Margin status should be recorded
3) *Table 3. Moderate-validity pancreatic cancer QI no.36:* Margins should be macroscopically clear
4) *EURECCA registry data item:* Resection Margin (R0 – R2 & unknown)
5) *Table 4. Summary of key points and recommendations – Treatment of localised disease*: Tumour Clearance should be given for all seven margins identified by the surgeon. [IV,B] These seven margins are; anterior, posterior, medial or super mesenteric groove, SMA, pancreatic transection, bile duct and enteric.
6) *AGITG Summary:* Standardised reporting of all seven surgical margins, which identifies an R0 (no tumour cells within a defined distance of the margin) if all surgical margins are clear from 1mm
7) *Principles of surgical technique:* The goals of pancreatoduodenectomy (Whipples) and distal pancreatectomy is an R0 resection, as a margin positive specimen is associated with poor long-term survival [2A]
8) *Pathologic Analysis. Margins:* Definitions of margins and uniformity of nomenclature are critical to accurate reporting. This includes SMA (retroperitoneal/uncinate), Posterior, Portal vein(PV)groove, portal vein, pancreatic neck (transection) and bile duct + other margins specific for Whipples (proximal and distal + anterior surface) (Whipples specimen) and Proximal, anterior (cephalad) peripancreatic surface, + posterior (caudad) peripancreatic in distal pancreatectomy [2A]

3. TREATMENT

3.1 Neo-adjuvant Therapy

3.1.1	Neo-adjuvant chemotherapy ± chemoradiation offered to patients with borderline resectable disease, or a valid reason documented for not undergoing treatment	B	8 0.29

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) ESMO 2015 3) Gandy et al. 2016 (AGITG Consensus) 4) NCCN 2017	Number of patients with borderline resectable disease that received chemotherapy ± chemoradiation or a valid reason documented for not undergoing treatment	Number of patients with borderline resectable disease

1) *Resectable disease. Neoadjuvant therapy:* Neo-adjuvant therapy in resectable disease remains under investigation. Combination chemotherapy or fluorouracil-based chemoradiotherapy can be offered (however no significant improvement in survival reported)
2) *Table 4. Summary of key points.* Treatment of borderline-resecatable lesions: In routine practice, if the patient is not included in a trial, a period of chemotherapy (gemcitabine or Folfirinox) followed by chemoradiation then surgery appears to be the best option [IV,B]
3) *Neo-adjuvant and borderline resectable disease:* Neo-adjuvant increasingly recommended for borderline operable disease while chemotherapy is recommended as initial therapy for patients with loco-regional PC. A small number of patients may be down staged by chemoradiation.
4) *Principles of Chemotherapy:* Limited evidence to recommend neo-adjuvant regimens in resectable/borderline resectable disease off-study; however consultation at a high-volume center is recommended. Options include Folfirinox ± chemoradiation, Gemcitabine + nab-paclitaxel ± chemoradiation [2A]

3.2 Adjuvant Therapy

3.2.1a	Adjuvant chemotherapy administered following surgery or a valid reason documented for not undergoing treatment	No grade listed	9
			0.49

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Burmeister et al. 2016b 3) Van Rijssen et al. 2016	Number of patients who received adjuvant chemotherapy or have a valid reason documented for not undergoing adjuvant therapy	Number of patients who underwent a surgical resection

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.23:* Adjuvant chemotherapy with or without radiation should be considered and administered, or a valid reason should be documented for not receiving
2) *Care Statement:* All patients should be offered adjuvant therapy after surgery, assuming performance status is adequate
3) *Results. First indicator:* Use of adjuvant chemotherapy

3.2.1b	Adjuvant chemotherapy administered following surgery with minimum Gemcitabine or 5-Flurouracil, or a valid reason documented for not undergoing treatment	A	7.5 0.61

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) BMJ Best Practice 2016 3) CCO 2016 4) ESMO 2015 5) NCCN 2017	Number of patients who received adjuvant chemotherapy with Gemcitabine or 5-Flurouracil; or have a valid reason documented for not undergoing adjuvant therapy	Number of patients who underwent a surgical resection

Reference source details

1) *Key Recommendation 4.1: Postoperative resection:* 6 months of adjuvant chemotherapy with either gemcitabine or flurouracil plus folinic acid in the absence of medical or surgical contraindications. No current data to support combination chemotherapy regimens.[High, Strong]
2) *Adjuvant Therapy:* Adjuvant Fluorouracil or Gemcitabine based chemotherapy for 6 months increases median and 5 year survival in people with completely resected pancreatic cancer compared with surgery alone. [C]
3) *Therapeutic Options for Resectable Disease:* Adjuvant chemotherapy is associated with prolonged survival. Gemcitabine & 5 Fluorouracil are equivalent in efficacy. Combination adjuvant chemotherapy with Gemcitabine plus capecitabine significant improvement in OS vs Gem monotherapy
4) *Table 4. Summary of Key Points.* Treatment of localised disease: Adjuvant treatment should be done with either Gemcitabine or 5-FU folinic acid [I,A]
5) *Principles of Chemotherapy*: In an adjuvant setting treatment with chemotherapy is recommended (role of radiation is being evaluated in clinical studies). Options include Gemcitabine or 5-FU/Leucovarin or Gemcitabine + capecitabine [Category 1]

3.2.2	Chemo-radiation offered to patients with microscopically positive (R1) resection, or valid reason documented for not receiving CRT	B	6 1.06

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) BMJ Best Practice 2016 3) ESMO 2015	Number of patients with R1 resection who received adjuvant chemo-radiation or have a valid reason documented for not receiving therapy	Number of patients with R1 resection

Reference source details

1) *Key Recommendation 4.2:* Adjuvant chemo-radiation may be offered to patients who did not receive preoperative therapy and present after resection with microscopically positive (R1) and or node positive disease after completion of 4-6 months systemic adjuvant chemotherapy [intermediate, moderate]
2) *Treatment. Incompletely Resected:* In patients with incomplete resection, adjuvant chemo-radiotherapy is an option (in patients who have not received neoadjuvant treatment) with primary options fluorouracil and gemcitabine plus radiation [C]
3) *Table 4. Treatment of localised disease:* No chemo-radiation should be given to patients with surgery except in clinical trials [I,E]

3.2.3a	Surgery and chemotherapy or chemo-radiation (neo-adjuvant or adjuvant) provided to all patients with Stage I – III disease	No grade listed	6 2.55

Reference(s)	Numerator	Denominator
1) Visser et al. 2012	Number of patients with stage I-III disease who received surgery and chemotherapy or chemo-radiation as neo-adjuvant or adjuvant therapy	Number of patients with stage I to III disease

Reference source details

1) *Measures of Quality Care:* For patients with Stage I – III disease, surgery and chemotherapy or chemo-radiation (adjuvant or neo-adjuvant) used as measures of quality (NCCN-based definitions of compliant treatment)

4.2 Participation in Clinical Trials

4.2.1a	All patients included in a clinical trial, or a valid reason documented for not being included	B	8
			0.75

Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b & 2016c 2) Bilimoria et al. 2009 3) Burmeister et al. 2016b 4) NCCN 2017 5) VIC OCP 2015	Number of patients participating in a clinical trial, or a valid reason documented for not participating	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendation 1.5 in all stages:* Every person should be given info about clinical trials, including therapeutic trials in all lines of treatment as well as palliative care, biorepository/biomarker, and observational studies [Intermediate, strong]
2) *Table 3: Moderate-validity pancreatic cancer QI no.30:* If an institution treats PC - then institution should participate in clinical trials
3) *Care Statement*: Entry into a clinical trial should be considered for all patients
4) *Boxed statement in footnote Panc A-G*: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged [2A]
5) *Step 3 – 7. Research and Clinical Trials*: Consider research clinical trials where available and appropriate

4.2.1b	Patients with borderline resectable disease included in a clinical trial, or a valid reason documented for not being included	No grade listed	8
			0.81

Reference(s)	Numerator	Denominator
1) ESMO 2015	Number of patients with borderline resectable disease participating in a clinical trial or a valid reason documented for not participating	Number of patients with borderline resectable disease

Reference source details

1) *Table 4. Summary of Key Points and Recommendations. Treatment of non-resectable: Borderline resectable*: Patients with borderline resectable lesions should be included in clinical trials wherever possible

4.2.1c	Patients with LAPC included in a clinical trial, or a valid reason documented for not being included	B	7
			0.54

Reference(s)	Numerator	Denominator
1) ASCO 2016b	Number of patients with locally advanced disease participating in a clinical trial or a valid reason documented for not participating	Number of patients with locally advanced disease

Reference source details
1) *Key Recommendation 5.2:* Refer people with LAPC who have not benefited from treatment and have disease progression for a clinical trial [Intermediate, strong]

4.3 Diet and Nutrition

4.3.1	All patients referred to a dietician after diagnosis	No grade listed	6
			0.75

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016b 2) VIC OCP 2015	Number of patients referred to a dietician	All patients diagnosed with pancreatic cancer

Reference source details
1) Care Statement: All patients should be referred to a dietician soon after diagnosis 2) *Appendix. Supportive Care-Physical Needs*: Weight loss and decrease in appetite may require referrals to a dietician before, during and after treatment.

4.4.2b	All patients with a documented treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems	No grade listed	7
			0.54

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009 2) Burmeister et al. 2016b 3) Burmeister et al. 2016a 4) VIC OCP 2015	Number of patients with a documented treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems	All patients diagnosed with pancreatic cancer

Reference source details

1) *Table 2. High-validity pancreatic cancer QI no.8:* Stage specific treatment plan should be documented
2) *Care Statement:* Each patient should be assigned a care coordinator and an individualised treatment/clinical plan
3) *Table 1. Oncology and other:* Patients should be fully aware of the risks and benefits of interventions prior to any treatment (very important) & patients should be advised of the limitations of chemotherapy (very important)
4) Interventions should be in place to deal with the consequences of cancer and cancer treatment (including managing symptoms, distress and practical issues)

4.4.2c	Treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems documented and discussed with patients & caregivers	B	8
			0.54

Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b, 2016c	Number of patients documented to have had a discussion about their treatment or clinical plan outlining interventions & limitations, goals of care, patient preferences and support systems	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendations 1.3 for all stages:* Goals of care, patient preferences and support systems should be discussed with every patient and his/her caregiver [Intermediate, Strong]

4.4.3a	Baseline performance status, symptom burden and comorbidity profile evaluated and documented for all patients	A	8
			0.49

Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b & 2016c 2) Burmeister et al. 2016a	Number of patients with documented baseline performance status, symptom burden and comorbidity profile	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendation 1.2 in all stages:* Baseline performance status, symptom burden and comorbidity profile should be carefully evaluated [High, strong]
2) *Table 1. Presentation and Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to treatment (very important)

4.4.3b	Baseline symptom burden evaluated and documented for all patients	A	6
			1.09

Reference(s)	Numerator	Denominator
3) ASCO 2016a, 2016b & 2016c 4) Burmeister et al. 2016a	Number of patients with symptom burden evaluated and documented	All patients diagnosed with pancreatic cancer

Reference source details

3) *Key Recommendation 1.2 in all stages:* Baseline performance status, symptom burden and comorbidity profile should be carefully evaluated [High, strong]
4) *Table 1. Presentation and Staging:* All patients should have a full physical examination, geriatric assessment if elderly, assessment of comorbidities and performance status prior to treatment (very important)

4.5 Multidisciplinary Environment

4.5.1a	Disease management for all patients discussed at a MDT meeting	B	9
			0.54

Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b & 2016c 2) Burmeister et al. 2016b 3) Van Rijssen et al. 2016 4) VIC OCP 2015	Number of patients discussed at a multidisciplinary team meeting	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendation 1.4 for all stages:* Multidisciplinary collaboration to formulate treatment and care plans, disease management should be standard of care (Intermediate, Strong)
2) *Care Statement:* All patients should be presented to a MDT
3) *Results. Second Indicator:* Discussion of a patient within a MDT meeting
4) *Referral, Treatment and Palliative Care MDT*: Patients should be referred to a specialist linked to a MDT. Patients should be managed following discussion at a MDT clinic in consultation with palliative care specialists

4.5.1b	Resectability discussed at a MDT	B	9
			0.16

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) ESMO 2015 3) Gagliardi et al. 2016 4) NCCN 2017	Number of patients with potentially resectable disease and resectability discussed at a MDT meeting	Number of patients with potentially resectable disease

Reference source details

1) *Step-by-step Treatment Approach:* There is no universally accepted criteria for resection, therefore decisions about resectability should be made by a MDT
2) *Table 4. Summary of key points:* In localised, resectable disease, a multidisciplinary team is necessary
3) *Supplemental table. Multidisciplinary Approach:* Consistency in biochemical, imaging and pathological findings before treatment initiation and during follow-up, is improved with a multidisciplinary approach.
4) *Principles of Diagnosis, Imaging and Staging #1 & #4:* Decisions about diagnostic management and resectability should involve multidisciplinary consultation at a high-volume centre with reference to appropriate high quality imaging studies; & The decision regarding resectability status should be made by consensus at multidisciplinary meetings/discussions [2A]

4.6 Symptom Management

4.6.1a	Biliary or duodenal obstruction managed by endoscopic placement of self-expanding metal stents (SEMs)	B	7
			0.75

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) Burmeister et al. 2016b 3) ESMO 2015 4) NCCN 2017	Number of patients with biliary or duodenal obstruction managed with endoscopic placement of SEMs	Number of patients with biliary or duodenal obstruction

Reference source details

1) *Locally Advanced and Metastatic Disease*: Endoscopic palliation is preferred over surgical approaches in LAPC or metastatic
2) *Care Statement:* Biliary obstruction should routinely be managed endoscopically in non-resectable patients
3) *Table 4. Summary of Key Points. Treatment of Metastatic Disease:* Duodenal obstruction is preferably managed by endoscopic placement of an expandable metal stent when possible - favoured over surgery. [IV,B] For biliary stenting: endoscopic method is safer than percutaneous insertion and is as successful as surgical hepatojejunostomy [II,B]
4) *Principles of Palliation and Supportive Care:* Prevent and ameliorate suffering while ensuring optimal quality of life – endoscopic biliary metal stent is the preferred method [2A]

4.6.1b	Biliary or duodenal/gastric obstruction managed surgically or by endoscopic placement of SEMs	No grade listed	8
			0.41

Reference(s)	Numerator	Denominator
1) BMJ Best Practice 2016 2) CCO 2016 3) NCCN 2017	Number of patients with biliary or duodenal/gastric obstruction managed surgically or with endoscopic placement of SEMs	Number of patients with biliary or duodenal/gastric obstruction

Reference source details

1) *Locally Advanced and Metastatic Disease*: Duodenal obstuction (5% of patients) can be managed operatively with gastrojejunostomy or endoscopic stents
2) *Patient Management and Supportive Care:* Biliary and gastric outlet obstruction should be managed with surgical intervention for palliative bypass or placement of biliary and/or duodenal stents
3) *Principles of Palliation and Supportive Care:* For optimal QOL, biliary obstruction (endoscopic biliary metal stent preferred) [2A], and gastric outlet obstruction (gastrojejunostomy ± J tube with good ECOG [2B], enteral stent in poor PS) should be managed

4.6.1c	Biliary or gastric outlet obstruction managed surgically in patients with good performance status	C	6
			1.93

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a 2) NCCN 2017	Number of patients with biliary or gastric obstruction and good performance status managed surgically	Number of patients with biliary or gastric obstruction and good performance status

Reference source details

1) *Table 1. Surgery and Biliary Obstruction:* Biliary obstruction should be managed surgically if performance status and prognosis is satisfactory in non-resecatable patients (unable to reach consensus)
2) *Principles of Palliation and Supportive Care*: For optimal QOL, gastric outlet obstruction should be managed with gastrojejunostomy ± J tube in patients with good ECOG [2B]

4.6.2	Patients with resectable disease not stented prior to surgery or reason for stenting documented	No grade listed	7
			0.75

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with resectable disease and biliary obstruction not stented or reason for stenting documented	Number of patients with resectable disease and biliary obstruction

Reference source details

1) *Table 1. Surgery and Biliary Obstruction:* Patients with resectable disease should not be stented prior to surgery unless surgery is delayed (unable to reach consensus)

4.6.3	SEM stent used for biliary drainage prior to surgery	No grade listed	6
			1.35

Reference(s)	Numerator	Denominator
1) Burmeister et al. 2016a	Number of patients with biliary obstruction managed with a SEM stent prior to surgery; or Number of patients with a plastic stent	Number of patients with biliary obstruction prior to surgery

Reference source details

1) *Table 1. Surgery and Biliary Obstruction:* A SEMs should be used instead of plastic stent if biliary drainage is indicated prior to surgery (unable to reach consensus)

4.6.4	Pain managed with opioid analgesics, palliative radiation or nerve blocks or reason for not treating pain documented	B	8.5 0.56

Reference(s)	Numerator	Denominator
1) ASCO 2016b and 2016c 2) BMJ Best Practice 2016 3) Burmeister et al. 2016a 4) CCO 2016 5) ESMO 2015	Number of patients prescribed opioids, treated with palliative radiation or administered nerve blocks or reason for not treating pain documented	All patients with pancreatic cancer

Reference source details

1) *Key Recommendation 7.1 (LAPC) and 5.1 (Metastatic):* Aggressive treatment of pain and other symptoms of cancer and/or cancer directed therapy [Intermediate, Strong]
2) *Treatment. Locally advanced and Metastatic. Pain Management*: Pain control should be commenced along the analgesic ladder with additional options of coeliac block or splanchnicectomy
3) *Table 1. Oncology and Other:* Careful attention to pain control is important using nerve blocks if required (very important)
4) *Patient Management and Supportive Care:* Pain to be managed with narcotic analgesics, radiation or celiac plexus neurolysis
5) *Table 4. Treatment of Metastatic Disease:* Pain control is mandatory and frequently needs the help of a pain specialist

4.7 Psychosocial Support

4.7.1	All patients offered psychosocial support following diagnosis	B	8 0.54

Reference(s)	Numerator	Denominator
1) ASCO 2016a, 2016b and 2016c 2) Burmeister et al. 2016b 3) CCO 2016 4) VIC OCP 2015	Number of patients with documented referral to psychologist or social worker or psychosocial support services	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendation 5.1(Potentially Curable), 6.1(LAPC), 4.1(Metastatic):* Full assessment of symptom burden, psychological status, and social supports should be offered as early as possible, preferably at the first visit [Intermediate, strong]
2) *Care Statement:* All patients should be offered psychosocial support
3) *Patient Management and Supportive Care:* Depression will require psychiatric consultation
4) *Appendix. Supportive Care*: For psychological wellbeing consider referring patient to psychologist, social worker, or psychiatrist. For social wellbeing consider referring patient to peer support, social worker, psychologist, psychiatrist or occupational therapist

4.8 Palliative Care

4.8.1a	All patients referred to palliative care services following diagnosis	No grade listed	5
			2.48

Reference(s)	Numerator	Denominator
1) ASCO 2016a 2) Burmeister et al. 2016a 3) VIC OCP 2015	Number of patients with documented referral to palliative care services	All patients diagnosed with pancreatic cancer

Reference source details

1) *Key Recommendation 5.1:* Patients with potentially curable disease should have full assessment of symptom burden, psychological status, and social supports as early as possible. In some instances, this may indicate a need for formal palliative care consult and services.
2) *Table 1. MDT and Referrals:* On diagnosis all patients should be referred to palliative care (unable to reach consensus)
3) *Summary. Step 6:* Specialist palliative care is recommended for majority of patients based on need. Early referral can improve quality of life

4.8.1b	Patients with locally advanced disease referred to palliative care services following diagnosis	B	8
			1.26

Reference(s)	Numerator	Denominator
1) ASCO 2016b and 2016c 2) Burmeister et al. 2016b	Number of patients with locally advanced disease and documented referral to palliative care services	Number of patients with locally advanced disease

Reference source details

1) *Key Recommendation 6.1 and 4.1:* Patients with LAPC or metastatic disease should have full assessment of symptom burden, psychological status, and social supports as early as possible, preferably at the first visit. In most cases, this will indicate a need for formal palliative care consult and services. [Intermediate, strong]
2) *Care Statement:* Patients with confirmed metastatic disease should be referred to palliative care

4.9.1b	Patients with LAPC having completed treatment followed up every three to four months	C	7
			0.49

Reference(s)	Numerator	Denominator
2) ASCO 2016b	Number of patients with LAPC who completed treatment and documented follow up every 3 – 4 months	Number of patients with LAPC who completed treatment

Reference source details
2) *Key Recommendations 8.1 & 8.2:* In the absence of RCT evidence, panel recommends follow-up visits every 3 – 4 months that include physical examination, liver and renal function tests. CA19 -9 and CT should be performed 3 - 4 months during the first 2 years, with imaging intervals increased to 6 months thereafter. Routine use of positron emission tomography is not recommended. Tumour markers should not replace imaging as an assessment. [Low, strong]

4.9.1c	Patients with metastatic disease on active cancer-directed therapy followed up every 2 – 3 months	C	8
			1.09

Reference(s)	Numerator	Denominator
1) ASCO 2016c	Number of patients with metastatic disease on active cancer-directed therapy and documented follow up every 2 – 3 months	Number of patients with metastatic disease on active cancer-directed therapy

Reference source details
1) *Key Recommendation 6.1 & 6.2:* For patients on active cancer-directed therapy outside clinical trial, imaging to assess first response should be offered at 2 - 3 months, from the initiation of therapy. CT scans with contrast are the preferred modality. Thereafter clinical assessment, conducted frequently during visits should supplant imaging assessment. The routine use of positron emission tomography scans is not recommended. CA19-9 is not considered an optimal substitute for imaging of assessment of treatment response. [Low, strong]

5. OUTCOME

5.1 Perioperative Measures

5.1.1a	Institution monitors their risk-adjusted perioperative mortality following surgical resection	No grade listed	8
			0.75

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Number of patients who died following surgical resection	N/A

Reference source details
1) *Table 2. High-validity pancreatic cancer QI no.28 & 29:* Hospital should monitor their PC resection risk-adjusted perioperative mortality Hospital risk-adjusted perioperative mortality should be less than 5%

5.1.1b	Risk-adjusted perioperative mortality following surgical resection is less than 5%	No grade listed	8
			0.19

Reference(s)	Numerator	Denominator
2) Bilimoria et al. 2009	Percentage of patients who died following resection	N/A

Reference source details
2) *Table 2. High-validity pancreatic cancer QI no.28 & 29:* Hospital should monitor their PC resection risk-adjusted perioperative mortality Hospital risk-adjusted perioperative mortality should be less than 5%

5.1.2	Institution monitors their stage-specific 2 year and 5 year survival rates for patients who underwent a surgical resection	No grade listed	8
			0.75

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Stage specific 2 year and 5 year survival rate	N/A

Reference source details
1) *Table 3. Moderate-validity pancreatic cancer QI no.43:*Hospital should monitor the stage-specific 2 year and 5 year survival rates for their patients who underwent pancreatectomy

5.1.3	Institution monitors their margin-negative resection rate	No grade listed	7.5
			0.56

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Margin-negative resection rate	N/A

Reference source details
1) *Table 2. High-validity pancreatic cancer QI no.27:* If an institution performs PC surgery, then they should monitor their margin-negative resection rate

5.1.4	Institution monitors their median estimated blood loss	No grade listed	6
			0.52

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Estimated volume of blood loss per resection	N/A

Reference source details
1) *Table 3. Moderate-validity pancreatic cancer QI no.39.*

5.1.5	Institution monitors their median operative time for surgical resections	No grade listed	6
			1.09

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	Median operative time	N/A

Reference source details
1) *Table 3. Moderate-validity pancreatic cancer QI no.40 & no.42:* The institution should monitor the median operative time for resections Operative time should be less than 10 hours

5.1.6	Institution monitors their 30 day readmission rate following a surgical resection	No grade listed	7
			0.56

Reference(s)	Numerator	Denominator
1) Bilimoria et al. 2009	30 day readmission rate	N/A

Reference source details
1) *Table 3. Moderate-validity pancreatic cancer QI no.41:* Hospital should monitor their readmission rate within 30 days rate

5.2 Surgical Complications

5.2.1	Patients who developed pancreatic fistula following surgical resection	No grade listed	8
			0.59

Reference(s)	Numerator	Denominator
1) Nordby et al. 2013	Number of patients who developed a postoperative pancreatic fistula	Number of patients who underwent a surgical resection

Reference source details
1) Table II. Postoperative Complications in 135 patients undergoing pancreatic surgery

5.2.2	Patients who developed biliary fistula following surgical resection	No grade listed	6
			0.48

Reference(s)	Numerator	Denominator
1) Nordby et al. 2013	Number of patients who developed a postoperative biliary fistula	Number of patients who underwent a surgical resection

Reference source details
1) Table II. Postoperative Complications in 135 patients undergoing pancreatic surgery

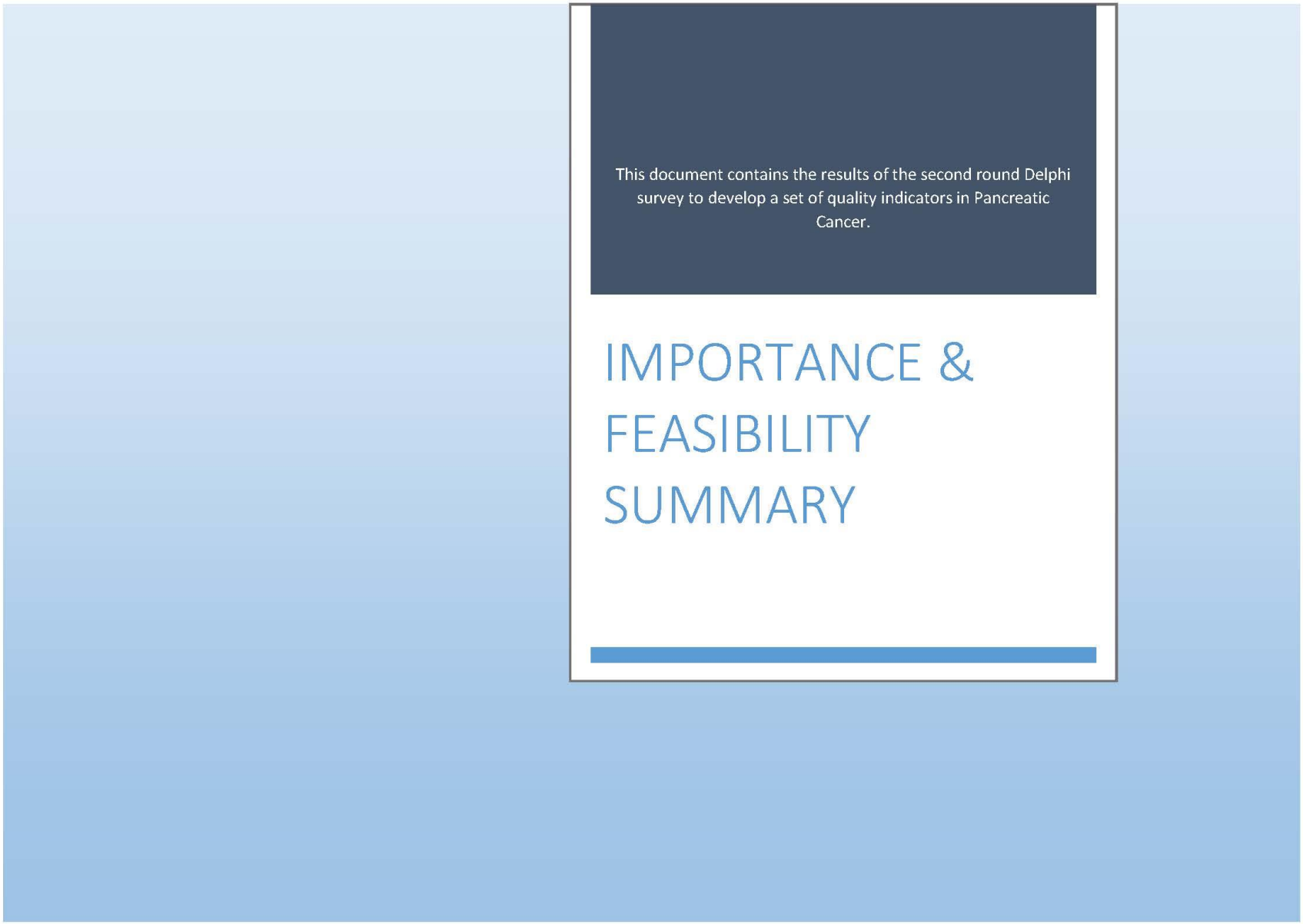
Appendix 2.4: Delphi Round 1 Summary Document (Excerpt)

1. Diagnosis & Staging

INDICATOR NUMBER		INDICATOR	MEDIAN	DI	1	2	3	4	5	6	7	8	9
1.1		History and Physical											
1.1.1	a	Documented history and physical examination	6	1.68	1	1	1	**1**	2	4	1	4	4
	b	Documented history and physical examination with preoperative risk assessment	7	1.74	0	2	1	0	2	**2**	5	5	2
	c	Documented preoperative risk assessment	6	0.88	0	**2**	0	0	1	7	2	5	2
1.1.2	a	Documented physical status, geriatric assessment if elderly, comorbidities and performance status prior to surgery or treatment	8	0.75	0	0	1	0	**2**	2	4	1	9
	b	Documented comorbidity profile prior to surgery or treatment	6	0.67	0	**1**	0	0	4	5	2	5	2
	c	Documented performance status prior to surgery or treatment	7	0.45	0	**1**	0	0	1	7	4	4	2
	d	Documented geriatric assessment prior to surgery or treatment	5	1.68	0	**2**	1	3	5	3	4	1	0
1.1.3	a	Documented referral to genetic counsellor for young patients	5	0.98	0	**2**	1	4	6	5	0	1	0
	b	Documented referral to genetic counsellor for patients with a family history of cancer	6	1.04	0	**1**	0	2	4	5	4	2	1
	c	Documented referral to genetic counsellor for patients with Ashkenazi Jewish ancestry	6	2.55	0	**3**	1	2	2	3	4	4	0
1.14		Your Comments											

INDICATOR NUMBER		INDICATOR	MEDIAN	DI	1	2	3	4	5	6	7	8	9
1.2		**Presence of Jaundice**											
1.2.1	a	In patients with jaundice, documented results of LFTs, abdominal US ± CT is present	8	0.81	0	0	0	2	1	2	2	**4**	8
	b	In patients with jaundice, documented results of LFTs and abdominal US is present	7	1.17	0	1	1	3	3	1	**3**	4	3
1.2.2		**Your Comments**											
1.3		**Imaging Modalities**											
1.3.1	a	Documented pancreatic protocol CT for diagnosis or staging	8	0.29	0	0	1	0	0	0	6	**2**	8
	b	Documented multiphase CT of chest, abdomen and pelvis	7	0.75	0	0	0	0	3	3	**5**	1	5
1.3.2		Documented pancreatic protocol CT or MRI scan for diagnosis and/or staging	8	0.37	0	0	0	1	0	1	2	5	**8**
1.3.3		Documented CT of chest, abdomen and pelvis; or PET scan	6	1.24	0	1	1	**2**	2	7	1	2	1
1.3.4		**Your Comments**											

Appendix 2.5: Delphi Round 2 Importance and Feasibility Summary (Excerpt)



1. Diagnosis & Staging

INDICATORS			IMPORTANCE		FEASIBILITY	
			Median	DI	Median	DI
1.1 History and Physical						
1.1.1	a	Documented history and physical examination	2	0.94	7	3.23
	b	Documented history and physical examination with preoperative risk assessment	2	1.45	4	3.23
	c	Documented preoperative risk assessment	5	1.57	6.5	3.26
1.1.2	a	Documented physical status, geriatric assessment if elderly, comorbidities and performance status prior to surgery or treatment	2	1.45	2	0.69
	b	Documented comorbidity profile prior to surgery or treatment	3	2.32	4	2.13
	c	Documented ECOG and/or ASA at presentation (Previously: Documented performance status prior to surgery or treatment)	9	0.13	8	0.45
	d	Documented geriatric assessment prior to surgery or treatment	1	0.26	3	0.49
1.1.3	a	Documented referral to genetic counsellor for young patients	2	0.87	4	0.75
	b	Documented referral to genetic counsellor for patients with a family history of cancer	2	0.74	3	1.45
	c	Documented Family history taken (Previously: Documented referral to genetic counsellor for patients with Ashkenazi Jewish ancestry)	6	1.56	6	2.17
1.2 Presence of Jaundice						
1.2.1	a	In patients with jaundice, documented results of LFTs, abdominal US ± CT is present	2	1.87	8	1.35

INDICATORS			IMPORTANCE		FEASIBILITY	
			Median	DI	Median	DI
	b	In patients with jaundice, documented results of LFTs and abdominal US is present	2	0.7	8	1.01
1.3 Imaging Modalities						
1.3.1	a	Documented pancreatic protocol CT for diagnosis or staging	3.5	2.25	9	0.26
	b	Documented multiphase CT of chest, abdomen and pelvis	2	1.56	9	0.26
1.3.2		Documented pancreatic protocol CT or MRI scan for diagnosis and/or staging	9	0.13	9	0.26
1.3.3		Documented CT of chest, abdomen and pelvis; or PET scan	3	1.5	9	0.13
1.4 EUS and Biopsy						
1.4.1	a	Tissue biopsy attempted prior to chemotherapy or radiotherapy (Previously: Tissue biopsy confirming diagnosis)	9	0.13	9	0.13
	b	Tissue biopsy confirming advanced, unresectable disease prior to palliative therapy	3	1.01	8	0.69
1.4.2		EUS confirming PC	2	1.01	8	1.04
1.4.3	a	EUS ± biopsy of the tumour confirming diagnosis and/or staging of PC	2	0.71	8	0.74
	b	EUS ± FNA confirming disease in patients with clinical suspicion of PC	2	1.4	7.5	1.01
1.4.4		EUS ± biopsy or contrast enhanced MRI confirming PC	1	0.49	8	1.08
1.4.5		EUS ± biopsy or MRCP confirming PC	1.5	0.46	8	1.08

2. Surgery

INDICATORS			IMPORTANCE		FEASIBILITY	
			Median	DI	Median	DI
2.1 Resectability						
2.1.1	a	All patients who did not undergo surgery should have a valid reason documented (Previously: All patients defined operable offered surgery or a valid reason documented for not undergoing surgery)	9	0.10	8	0.64
	b	All patients defined operable with adequate performance status offered surgery or a valid reason documented for not undergoing surgery	2	0.45	7	2.35
2.1.2		Patients with stage IV disease who underwent surgical resection	1	0.81	7	2.35
2.1.3		Patients potentially resectable do not have a tissue biopsy prior to surgery	1	0.59	5	3.4
2.1.4		Suspicious adenopathy evaluated by frozen section	1	0.13	6	3.12
2.1.5		Time from diagnosis to surgery or first treatment less than 2 months	1	1.45	7	2.26
2.1.6		Time from final MDT to surgery is 3 weeks	2	1.25	8	1.01
2.1.7		RCPA or equivalent reporting system used to document findings for patients undergoing surgical resection (Previously: College of American Pathologists (CAP) or equivalent reporting system used to document findings for patients undergoing surgical resection)	9	0	9	0.13
2.2 Lymph Node Examination						
2.2.1	a	Standard lymphadenectomy with the removal of ≥ 10 lymph nodes pathologically examined and documented	9	0.10	9	0.13
	b	Standard lymphadenectomy with the removal of ≥ 15 lymph nodes pathologically staged and documented	2	1.34	8	3.4

Appendix 2.6: UGICR list of Data Items

Data item	Definition
Primary site of tumour	The site of the primary tumour within the area of the pancreas based on the highest level of imaging
Diagnosis Complete	All fields on the diagnosis form have been completed
MRI of Pancreas	The patient had a contrast enhanced MRI of the pancreas prior to any treatment
Pancreatic Protocol CT	The patient had a pancreatic protocol CT prior to treatment. Pancreatic protocol CT scan included any CT scan of the abdomen that had both arterial and portal venous phases documented in the technique section of the report.
Tissue specimen obtained pre-treatment	If a sample of tissue was taken from the primary tumour or metastasis prior to treatment
Biopsy attempted but not successful	A biopsy of the tissue was attempted however no tissue was obtained prior to treatment
Pathological diagnosis	The pathological diagnosis assigned from the result of diagnostic investigations.
Chemotherapy (any intent)	If the person received oral or intravenous chemotherapy with the intent of targeting the pancreatic cancer.
Radiotherapy (any intent)	If the person received radiotherapy targeting their pancreatic cancer primary tumour or metastasis.
Treatment Summary Complete	All data fields in the treatment summary form have been completed.
Surgery Type	The type of surgery that was intended to be performed on the patient. Eg. Resection surgery
Surgery Details Complete	All fields from the surgery form have been completed
CA 19-9 Measured	If the Ca 19-9 level was recorded prior to the patient receiving any anti-tumour treatment.
ECOG	If the performance status of the patient prior to receiving any anti-tumour treatment was documented in the medical record
ASA (diagnostic)	The ASA score of the patient was documented in the medical record for any diagnostic procedures (not including ASA score documented for curative surgery)
ASA (surgical)	The ASA score of the patient was documented in the medical record for an attempt at curative surgery
Neoadjuvant Intent	If the patient received chemotherapy or radiotherapy with the intent of stabilising or shrinking the primary tumour prior to surgery
Surgery date	The date surgical procedure took place
Date chemotherapy commenced	The date the patient received their first chemotherapy with neoadjuvant intent
Chemotherapy Details Complete	All fields on the chemotherapy form have been completed
Date Neoadjuvant radiotherapy commenced	The date the patient received their first radiotherapy with neoadjuvant intent
Radiotherapy Details Complete	All fields on the radiotherapy form have been completed
Referral date	The date the patient was first referred to a HPB surgeon, a medical oncologist or a radiation oncologist in relation to pancreatic cancer
Resectability of tumour at diagnosis	The resectability of the tumour is documented in the medical record prior to treatment
MRI	If the patient received a restaging MRI scan after neoadjuvant therapy
Pancreatic Protocol CT	If the patient received a restaging Pancreatic protocol CT scan after neoadjuvant therapy
CT Pancreas	If the patient received a restaging Pancreatic CT scan after neoadjuvant therapy
PET Scan	If the patient received a restaging PET scan after neoadjuvant therapy
Restaging Details Complete	All data items on the Restaging details form are complete
Pathology Report viewed by data collector	The data collector was able to visualise the resection pathology report when collecting data on the patient

Overall, can the report be classified as synoptic	If the pathology report was structured in a way that is considered synoptic according to RCPA reporting checklists. The definition of synoptic used: The report must clearly include *all* the following headings, Tumour type, Tumour size, Tumour grade, Lymph node status, Margin Status, Lymphovascular invasion, Perineural invasion
Number of lymph nodes examined	The number of lymph nodes examined on the resection specimen by the pathologist
Closest Margin	The smallest width of tissue (mm) free of cancer cells in the resected specimen.
Neoadjuvant chemotherapy and/or neoadjuvant radiotherapy	If the patient received either chemotherapy or radiotherapy documented as neoadjuvant intent, with the intent of shrinking or stabilising the tumour prior to surgery.
Reason/s for no surgery (select all that apply)	The reason why the patient did not proceed to curative surgery.
Reviewed by Medical Oncologist	If the patient was reviewed by a medical oncologist as an inpatient or an outpatient
Reviewed by Radiation Oncologist	If the patient was reviewed by a radiation oncologist as an inpatient or an outpatient
Reason/s for no chemo-therapy	The reason/s documented in the medical record why the patient did not receive chemotherapy
Reason/s for radiotherapy	The reason/s documented in the medical record why the patient did not receive radiotherapy
Reason/s for no neo-adjuvant (select all that apply)	The reason documented in the medical record why the patient did not receive neoadjuvant treatment
Type of pancreatic resection	The type of surgical resection the patient received as listed on the operation report eg. Whipples, Distal pancreatectomy etc.
Adjuvant Intent	If the patient received chemotherapy documented as adjuvant intent, with the intent of eliminating any remaining tumour cells
Reason/s for no adjuvant chemotherapy	The reason/s documented in the medical record why the patient did not receive adjuvant chemotherapy
Other Intent	If the patient received chemotherapy with an intent that was not neoadjuvant or adjuvant intent. Includes palliative intent.
Reason/s for no chemo-therapy	The reason/s documented in the medical record why the patient did not receive chemotherapy of other intent.
Discussion at a multi-disciplinary team meeting	If the patient was discussed at an UGI or HPB speciality Multi-disciplinary team meeting prior to receiving anti-tumour treatment
Date earliest multi-disciplinary team meeting discussion	The date the patient was first discussed at the multi-disciplinary team meeting in relation to their pancreatic cancer diagnosis.
Date of earliest treatment	The date the patient received their first anti-tumour treatment (curative surgery, chemotherapy, radiotherapy)
Referral to or Contact with Palliative Care	If the patient was referred to an external palliative care facility, or if they were managed by a palliative care team as an inpatient.
Enrolled in a Clinical Trial	If the patient was enrolled in a clinical trial involving an anti-tumour intervention such as a drug or device.
Health status check complete	All data items on the Health status check page are complete
Deceased	If the patient is deceased
Date of Death	The date of the patients death according to the most accurate source
Date of last chemotherapy	The date the patient received their last dose of oral or intravenous chemotherapy
End of life details complete	All data items on the End of Life details page are complete
2 or more ED presentations in the last 30 days prior to death	If the patient presented to ED at least twice in the last 30 days prior to death.
14 or more days in acute hospital during the last 30 days of life	If the patient spent 14 or more days as an inpatient in an acute hospital in the last 30 days of their life.

Appendix 3.1: Ethics Approval

Monash University Human Research Ethics Committee

Approval Certificate

This is to certify that the project below was considered by the Monash University Human Research Ethics Committee. The Committee was satisfied that the proposal meets the requirements of the *National Statement on Ethical Conduct in Human Research* and has granted approval.

Project ID: 15325
Project Title: Patterns of Care and Adherence to Developed Quality Indicators in Pancreatic Cancer, Victoria (Australia)
Chief Investigator: Assoc Professor Susan Evans
Approval Date: 08/08/2018
Expiry Date: 08/08/2023

Terms of approval - failure to comply with the terms below is in breach of your approval and the *Australian Code for the Responsible Conduct of Research*.

1. The Chief Investigator is responsible for ensuring that permission letters are obtained, if relevant, before any data collection can occur at the specified organisation.
2. Approval is only valid whilst you hold a position at Monash University.
3. It is responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval and to ensure the project is conducted as approved by MUHREC.
4. You should notify MUHREC immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.
5. The Explanatory Statement must be on Monash letterhead and the Monash University complaints clause must include your project number.
6. Amendments to approved projects including changes to personnel must not commence without written approval from MHUREC.
7. Annual Report - continued approval of this project is dependent on the submission of an Annual Report.
8. Final Report - should be provided at the conclusion of the project. MUHREC should be notified if the project is discontinued before the expected completion date.
9. Monitoring - project may be subject to an audit or any other form of monitoring by MUHREC at any time.
10. Retention and storage of data - The Chief Investigator is responsible for the storage and retention of the original data pertaining to the project for a minimum period of five years.

Kind Regards,

Professor Nip Thomson

Chair, MUHREC

CC: Professor John Zalcberg, Dr Liane Ioannou, Mrs Ashika Maharaj, Ms Jennifer Holland

List of approved documents:

Document Type	File Name	Date	Version
Consent Form	UGICR_Letter_of_explanation	26/03/2018	1.0
Supporting Documentation	200718Patterns_Care_Adherence_Protocol_v2	20/07/2018	2.0

Appendix 3.2: Formatted Quality Indicators and Calculations for Evaluation of Quality of Care (Examples)

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
1	**Documented pancreatic protocol CT (PPCT) or MRI scan for diagnosis and/or staging**	Proportion of patients with non-metastatic pancreatic cancer who underwent a pancreatic protocol CT or MRI scan to confirm diagnosis and/or staging	A multiphase CT of abdomen and pelvis using a dedicated pancreatic protocol or MRI should be performed for all patients to assess the anatomic relationships of the primary tumour and presence of intra-abdominal metastases. A pancreas CT protocol involves dual/triphasic (i.e., arterial, late arterial, and venous phases) cross-sectional imaging with thin slices using multidetector CT.	1.Potentially Curable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guidelines (United States). Published online April 11, 2017, DOI: 10.1200/JCO.2017.72.4948 2.Bilimoria KY et al; Pancreatic Cancer Quality Indicator Development Expert Panel, American College of Surgeons. Assessment of pancreatic cancer care in US based on formally developed quality indicators. J Natl Cancer Inst. 2009 Jun 16;101(12):848-59 3.National Comprehensive Cancer Network - Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma (United States of America). 2017. Available from www.nccn.org	Numerator: Number of patients with a PPCT or MRI Denominator: All patients with non-metastatic pancreatic cancer. Exclusions: Patients with metatstatic disease	• Primary site of tumour	• dx_tum_site	1, Head 2, Neck 3, Body 4, Tail 5, Uncinate process 6, Ampulla of Vater (Ampullary) 7, Periampullary area 8, Distal bile duct 9, Pancreas -99, Not stated	Numerator: (dx_resectability<=2 & dx_tum_site!=. & dx_mri!=. & dx_ct_pancreas!=. & dx_ct_pancreas!=-99 & dx_mri!=-99) dx_mri==1|dx_ct_panc_prot ==1 Denominator: dx_resectability<=2 & dx_tum_site!=. & dx_mri!=. & dx_ct_pancreas!=. & dx_ct_pancreas!=-99 & dx_mri!=-99
						• Resectability of tumour at diagnosis	• dx_resectability	0, Resectable 1, Borderline resectable 2, Unresectable (Locally advanced) 3, Unresectable (Metastatic disease) 4, Unresectable (unclear if locally advanced or metastatic) 5, Not clearly documented -99, Unknown	
						• Diagnosis Complete	• diagnosis_complete	0=No 1=Unverified/Not entered 2=Complete	
						• MRI of Pancreas	• dx_mri	1, Yes 0, No -99, Unknown	
						• Panreatic Protocol CT	• dx_ct_panc_prot	1 = Yes 0 = No -99, Unknown	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
2	**Tissue biopsy attempted prior to chemotherapy or radiotherapy**	Proportion of all patients who underwent any treatment with chemotherapy or radiotherapy (this includes neo-adjuvant therapy) with attempted tissue biopsy to treatment	A pre-treatment (chemotherapy or radiotherapy) tissue biopsy should be obtained where possible to confirm diagnosis and/or stage of disease. Tissue samples will be derived first hand in the case of surgical resections. However, in the majority of cases where patients do not undergo resections a tissue biopsy via Endoscopic Ultrasound Fine Needle Aspirate (EUS-FNA), percutaneous FNA or exfoliative and brush cytology can be obtained. No patient should undergo treatment with chemotherapy or radiotherapy without attempted tissue biopsy.	1.Burmeister E.A et al. Factors associated with Quality of Care for patients with pancreatic cancer in Australia. Med J Aust 2016; 205 (10): 459-465. || doi: 10.5694/mja16.00567 2.Clarke D, Clarke B, Thomson S, Garden O, Lazarus N. The role of preoperative biopsy in pancreatic cancer. HPB : The Official Journal of the International Hepato Pancreato Biliary Association. 2004;6(3):144-153.	Numerator: Number of patients with an attempted tissue biopsy before treatment with chemotherapy or radiotherapy Denominator: All patients who have been treated with chemotherapy or radiotherapy Exclusions: Exclude where date is not known	• Primary site of tumour	• dx_tum_site	**1, Head** **2, Neck** **3, Body** **4, Tail** **5, Uncinate process** **6, Ampulla of Vater (Ampullary)** 7, Periampullary area **8, Distal bile duct** **9, Pancreas** -99, Not stated	**(denominator) Numerator** (dx_tum_site >0 & path_synoptic_yn!=1 & (chemo_yn==1 | radio_yn==1)& dx_tum_site !=.) & dx_tissue_yn==1| dx_tissue_fail==1| path_morph!=.
						• Diagnosis Complete	• diagnosis_complete	0=No 1=Unverified/Not entered **2=Complete**	
						• Tissue specimen obtained pre-treatment	• dx_tissue_yn	**1, Yes** 0, No	
						• Biopsy attempted but not successful	• dx_tissue_fail	**1, Yes** 0, No	
						• Pathological diagnosis	• path_morph	1 = (Ductal) adenocarcinoma 2 = Colloid carcinoma (mucinous noncystic carcinoma) 3 = Signet-ring cell carcinoma 4 = Adenosquamous carcinoma 5 = Mucinous cystic neoplasm with an associated invasive carcinoma 6 = Intraductal papillary-mucinous neoplam with an associated invasive carcinoma 7 = Intraductal tubulopapillary neoplasm with an associated invasive carcinoma 8 = Undifferentiated (anaplastic) carcinoma 9 = Undifferentiated carcinoma with osteoclast-like giant cells 10 = Acinar cell carcinoma 11 = Acinar cell cystadenocarcinoma 12 = Serous cystadenocarcinoma 13 = Mixed acinar-ductal carcinoma 14 = Mixed ductal-neuroendocrine carcinoma 15 = Mixed acinar-neuroendocrine carcinoma 16 = Mixed acinar-neuroendocrine-ductal carcinoma 17 = Solid-pseudopapillary	
						• Chemotherapy (any intent)	• chemo_yn	**1, Yes** 0, No -99, Unknown	
						• Radiotherapy (any intent)	• radio_yn	**1, Yes** 0, No -99, Unknown	
						• Overall, can the report be classified as synoptic	• path_synoptic_yn	**1, Yes** 0, No	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
3	**Documented baseline CA19-9 level before treatment**	Proportion of all patients who underwent surgery or other treatment with a documented CA19-9 level before treatment	Currently, CA19-9 is the most clinically studied and useful biomarker for PC. Pre-operative CA 19-9 serum levels provide important prognostic information in pancreatic cancer patients, correlate with tumor stage and independently predict overall survival. An increasing postoperative CA 19-9 serum level or failure of the CA 19-9 serum levels to normalize post-operatively is associated with a poor prognosis and suggests residual disease or the presence of occult metastases, while a decline or normalization of the post-operative CA 19-9 serum level, is associated with improved survival. CA 19-9 serum levels assessment can be used as a surrogate marker of response to chemotherapy with a ≥20–50% decrease in CA 19-9 serum levels following chemotherapy associated with a positive tumor response and increased survival.	1.Potentially Curable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guidelines (United States). Published online April 11, 2017, DOI: 10.1200/JCO.2017.72.4948 2.Ballehaninna UK, Chamberlain RS. Serum CA 19-9 as a Biomarker for Pancreatic Cancer—A Comprehensive Review. Indian journal of surgical oncology. 2011;2(2):88-100. doi:10.1007/s13193-011-0042-1.	Numerator: Number of patients with documented CA19-9 level prior to treatment (surgery and/or other treatment) Denominator: All patients with pancreatic cancer who had treatment (surgery, chemotherapy or radiotherapy) Exclusions: Those who did not undergo treatment	• Primary site of tumour	• dx_tum_site	1, Head 2, Neck 3, Body 4, Tail 5, Uncinate process 6, Ampulla of Vater (Ampullary) 7, Periampullary area 8, Distal bile duct 9, Pancreas -99, Not stated	(denominator) Numerator (dx_tum_site >0 & diagnosis_complete==2 & (surg_yn==1 | chemo_yn==1 | radio_yn==1) & surgery_details_complete==2 & treatment_summary_complete==2 & dx_ca19_9!=-99 & dx_ca19_9!=.) & dx_ca19_9==1
						• Diagnosis Complete	• diagnosis_complete	0=No 1=Unverified/Not entered 2=Complete	
						• Surgery Type	• surg_type	1 = Exploratory laparotomy 2 = Diagnostic laparoscopy 3 = (Attempted) Pancreatic resection surgery	
						• Surgery Details Complete	• surgery_details_complete	0=No 1=Unverified/Not entered 2=Complete	
						• Chemotherapy (any intent)	• chemo_yn	1, Yes 0, No -99, Unknown	
						• Radiotherapy (any intent)	• radio_yn	1, Yes 0, No -99, Unknown	
						• Treatment Summary Complete	• tx_summary_complete	0=No 1=Unverified/Not entered 2=Complete	
						• CA 19-9 Measured	• dx_CA19-9	1 = Yes 0 = Not documented -99, Unknown	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
4	**Documented ECOG and/or ASA at presentation**	Proportion of patients with performance status documented as measured by ECOG or ASA prior to any treatment/at diagnosis	Performance status is the classification of a patient's physical wellbeing based on their level of function and can be measured with classification systems such as ECOG (Eastern Cooperative Oncology Group) or ASA (American Society of Anthesiologists) scales. Performance status has been consistently identified as a prognostic factor for patients with PC and is an important measure to predict chemotherapy toxicity and surgical risk. Performance status should not be used to simply rule in or out patients for surgery.	1.Burmeister, E. A. et al. Using a Delphi process to determine optimal care for patients with pancreatic cancer. Asia-Pac J Clin Oncol 2016;12: 105–114 2.Potentially Curable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guidelines (United States). Published online April 11, 2017, DOI: 10.1200/JCO.2017.72.4948	Numerator: Number of patients with documented ECOG or ASA prior to treatment (surgery and/or other treatment) Denominator: All patients diagnosed with pancreatic cancer Exclusions: No exclusions.	• Primary site of tumour	• dx_tum_site	1, Head 2, Neck 3, Body 4, Tail 5, Uncinate process 6, Ampulla of Vater (Ampullary) 7, Periampullary area 8, Distal bile duct 9, Pancreas -99, Not stated	(denominator) Numerator (dx_tum_site >0 & diagnosis_complete==2 & dx_tum_site !=. & diagnosis_complete !=.) dx_ecog >= 0 | pt_asa_dx >= 0
						• Diagnosis Complete	• diagnosis_complete	0=No 1=Unverified/Not entered 2=Complete	
						• ECOG	• dx_ecog	0, Fully active 1, Restricted in physically strenuous activity 2, Unable to carry out any work activities 3, Capable of only limited self-care 4, Completely disabled 5, Dead -99, Not documented	
						• ASA	• pt_asa_dx	1, ASA 1 2, ASA 2 3, ASA 3 4, ASA 4 5, ASA 5 -99, Unknown/not documented	
						• ASA	• surg_asa_score	1, ASA 1 2, ASA 2 3, ASA 3 4, ASA 4 5, ASA 5 -99, Unknown/not documented	
						• Surgery Details Complete	• surgery_details_complete	0=No 1=Unverified/Not entered 2=Complete	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
5	**Time from referral to definitive treatment within 60 days (relief of billiary obstruction is not definitive treatment)**	Proportion of patients with documented definitive treatment (surgical and/or other treatment) within 60 days from referral by GP or ED presentation	Current evidence suggests that timeliness of care may not be a factor in survival outcomes for pancreatic cancer. However, it is an important measure of patient-centered care. The timeliness of care is considered a proxy quality measure of a health care system, as it reflects the efficiency of the system or the availability of resources.	1.Jooste, V., Dejardin, O., Bouvier, V., Arveux, P., Maynadie, M., Launoy, G. and Bouvier, A.-M. (2016), Pancreatic cancer: Wait times from presentation to treatment and survival in a population-based study. Int. J. Cancer, 139: 1073–1080. doi:10.1002/ijc.30166	Numerator: Number of patients who underwent surgery, chemotherapy and/or radiotherapy within 60 days of referral Denominator: All patients with pancreatic cancer who had definitive treatment Exclusions: Patients who received no treatment. Patients treated for symptom management e.g relief of biliary obstruction	• Primary site of tumour	• dx_tum_site	1, Head 2, Neck 3, Body 4, Tail 5, Uncinate process 6, Ampulla of Vater (Ampullary) 7, Periampullary area 8, Distal bile duct 9, Pancreas -99, Not stated	gen indicator5 = 0 if dx_tum_site >0 & (surg_yn==1 |chemoneo_yn==1 | radioneo_yn ==1) & dx_referral_date!=14610 & surg_date!=14610 egen earliestdate_tx = rowmin(surg_date chemoneo_start radioneo_start) format earliestdate_tx %td gen ref_tx_60 = (earliestdate_tx - dx_referral_date) <=60 replace ref_tx_60 =. if dx_referral_date ==. | earliestdate_tx ==. tab ref_tx_60 recode indicator5 0 = 1 if ref_tx_60 ==1 tab indicator5
						• Diagnosis Complete	• diagnosis_complete	0=No 1=Unverified/Not entered 2=Complete	
						• Surgery Type	• surg_type	1 = Exploratory laparotomy 2 = Diagnostic laparoscopy 3 = (Attempted) Pancreatic resection surgery	
						• Surgery Details Complete	• surgery_details_ complete	0=No 1=Unverified/Not entered 2=Complete	
						• Neoadjuvant Intent	• chemoneo_yn	1, Yes 0, No -99, Unknown	
						• Neoadjuvant Intent	• radioneo_yn	1, Yes 0, No -99, Unknown	
						• Surgery	• surg_date	DATE	
						• Date chemotherapy commenced	• chemoneo_start	DATE	
						• Chemotherapy Details Complete	• chemotherapy_details_ complete	0=No 1=Unverified/Not entered 2=Complete	
						• Date Neoadjuvant radiotherapy commenced	• radioneo_start	DATE	
						• Radiotherapy Details Complete	• radiotherapy_details_ complete	0=No 1=Unverified/Not entered 2=Complete	
						• Referral	• dx_referral_date	DATE	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
6	**MRI, CT or PET completed following neoadjuvant treatment**	Proportion of patients who underwent neo-adjuvant treatment restaged with the following imaging: MRI, PPCT or PET	A borderline resectable lesion can be defined as one that has a higher likelihood of an incomplete resection. Neo-adjuvant therapy is an option for patients with borderline resectable disease. Neo-Adjuvant therapy may increase the proportion of patients receiving systemic therapy; identify early disease progression before a potentially debilitating surgical procedure without associated benefit; and possible down-staging. Imaging is necessary following neo-adjuvant to determine whether the tumour mass has shrunk, increasing the likelihood of an R0 resection or surgery.	1.National Comprehensive Cancer Network. (2017). NCCN Clinical Practice Guidelines in Oncology. Pancreatic Adenocarcinoma (Version 2). United States of America 2.Gandy et al. Refining the care of patients with pancreatic cancer: the AGITG Pancreatic Cancer Workshop consensus. Med J Aust 2016; 204 (11): 419-422.	Numerator: Number of patients with imaging (MRI, PPCT or PET) following neo-adjuvant treatment Denominator: All patients with borderline resectable disease who underwent neo-adjuvant treatment Exclusions: Localised, Locally Advanced or Metastatic	• Primary site of tumour	• dx_tum_site	1, Head 2, Neck 3, Body 4, Tail 5, Uncinate process 6, Ampulla of Vater (Ampullary) 7, Periampullary area 8, Distal bile duct 9, Pancreas -99, Not stated	(denominator) Numerator (dx_tum_site >0 & diagnosis_complete==2 & dx_resectability<=1 & restaging_after_neoa_v_1==2 & (neo_yn==1 | chemoneo_yn==1)) neo_restage_mri==1| dx_ct_panc_prot_2==1 |neo_restage_pet==1
						• Resectability of tumour at diagnosis	• dx_resectability	0, Resectable 1, Borderline resectable 2, Unresectable (Locally advanced) 3, Unresectable (Metastatic disease) 4, Unresectable (unclear if locally advanced or metastatic) 5, Not clearly documented -99, Unknown	
						• Diagnosis Complete	• diagnosis_complete	0=No 1=Unverified/Not entered 2=Complete	
						• Neoadjuvant Intent	• chemoneo_yn	1, Yes 0, No -99, Unknown	
						• Neoadjuvant Intent	• radioneo_yn	1, Yes 0, No -99, Unknown	
						• MRI	• neo_restage_mri	1, Yes 0, No -99, Unknown	
						• Pancreatic Protocol CT	• dx_ct_panc_prot_2	1, Yes 0, No -99, Unknown	
						• CT Pancreas	• neo_restage_ctpanc	1, Yes 0, No -99, Unknown	
						• PET Scan	• neo_restage_pet	1, Yes 0, No -99, Unknown	
						• Restaging Details Complete	• Restaging_details_complete	0=No 1=Unverified/Not entered 2=Complete	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
7	**Operability of tumour is clearly defined and documented as either operable/resectable, borderline resectable, locally advanced (unresectable) or metastatic (unresectable)**	Proportion of patients with documented operability of tumour as defined operable/resectable, borderline resectable, locally advanced (unresectable) or metastatic (unresectable)	The goal of initial diagnostic & staging tests are to affirm whether a tumour is operable or advanced in stage. This in turn determines the care that is provided. At a minimum, there should be clear documentation of operability of tumour and corresponding stage to enable the care pathway needed, without reason to second guess.	1.Bilimoria KY et al; Pancreatic Cancer Quality Indicator Development Expert Panel, American College of Surgeons. Assessment of pancreatic cancer care in US based on formally developed quality indicators. J Natl Cancer Inst. 2009 Jun 16;101(12):848-59 2.Gandy et al. Refining the care of patients with pancreatic cancer: the AGITG Pancreatic Cancer Workshop consensus. Med J Aust 2016; 204 (11): 419-422.	Numerator: Number of patients clearly defined as operable/resectable, borderline resectable, locally advanced or metastatic Denominator: All patients diagnosed with pancreatic cancer Exclusions:	• Diagnosis Complete	• diagnosis_complete	0=No 1=Unverified/Not entered 2=Complete	(denominator) Numerator (diagnosis_complete==2 & dx_resectability!=-99) dx_resectability>=0 & dx_resectability<=3
						• Resectability of tumour at diagnosis	• dx_resectability	0, Resectable 1, Borderline resectable 2, Unresectable (Locally advanced) 3, Unresectable (Metastatic disease) 4, Unresectable (unclear if locally advanced or metastatic) 5, Not clearly documented -99, Unknown	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			UPDATED STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
8	**RCPA or equivalent reporting system used to document findings for patients undergoing surgical resection**	Proportion of patients with a RCPA or equivalent synoptic reporting used to document findings for patients undergoing surgical resection	The Royal College of Pathologists of Australasia (RCPA) have developed a suite of National Structured Pathology Reporting of Cancer that when implemented improve the completeness of pathology reporting of cancer. A structured pathology reporting protocol is available for pancreatic cancer that includes standardised elements, terminology and definitions for cancer reporting. Compared with traditional narrative reporting, structured reporting provides more complete information and improves the utility of histopathological reports. Pathology reporting for PC should involve synoptic reports that include accurate and complete information addressed by pathological data set checklists. Gill et al, conducted a study which examined whether introduction of a standardised pancreatic cancer minimum data set improved the reporting of key pathological features across multiple institutions. They concluded that synoptic reporting of pancreatic resections without any other intervention increases the information contained within histopathology reports. Therefore, the introduction of minimal data set synoptic reports is a simple and feasible mechanism to immediately improve reporting for pancreatectomy specimens. Examples of equivalent systems to RCPA would be College of American Pathologist (CAP) reports/checklists	1.National Comprehensive Cancer Network. (2017). NCCN Clinical Practice Guidelines in Oncology. Pancreatic Adenocarcinoma (Version 2). United States of America 2.The Royal College of Pathologists of Australasia (RCPA). Available from https://www.rcpa.edu.au/Home 3.AGITG. Definition of surgical standards for pancreatic cancer: A consensus statement by the Australasian Gastro-Intestinal Trials Group. Available from https://gicancer.org.au/wp-content/uploads/2017/09/AGITG-Pancreatic-Cancer-Surgical-Guidelines-Report-2015.pdf 4.Gills A, John A, Eckstein R. Synoptic reporting improves histopathological assessment of pancreatic resection specimens. Path. 2009 Feb. 41(2): 161–167	Numerator: Number of patients who have a RCPA or equivalent reporting checklist (e.g. CAP) Denominator: All resectable patients with pancreatic cancer undergoing surgery Exclusions:	• Primary site of tumour	• dx_tum_site	1, Head 2, Neck 3, Body 4, Tail 5, Uncinate process 6, Ampulla of Vater (Ampullary) 7, Periampullary area 8, Distal bile duct 9, Pancreas -99, Not stated	(denominator) numerator (dx_tum_site >0 & diagnosis_complete==2 & path_report_yn==1 & surgery_details_complete==2 & dx_tum_site !=. & diagnosis_complete !=. & surgery_details_complete !=. & path_report_yn!=.) path_synoptic_yn==1
						• Diagnosis Complete	• diagnosis_complete	0=No 1=Unverified/Not entered 2=Complete	
						• Pathology Report viewed by data collector	• path_report_yn	1, Yes 0, No	
						• Overall, can the report be classified as synoptic	• path_synoptic_yn	1, Yes 0, No	
						• Surgery Details Complete	• surgery_details_complete	0=No 1=Unverified/Not entered 2=Complete	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			UPDATED STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
9	**Standard lymphadenectomy with the removal of ≥ 10 lymph nodes pathologically examined and documented**	Proportion of patients with ≥ 10 lymph nodes pathologically examined (or measure proportion who have less than 10 lymph nodes examined)	Lymph node status of patient with resectable pancreatic cancer is an important predictor of survival. The lymphatic vasculature offers the most direct route from the primary tumor to the frequently invaded draining lymph nodes during PDAC metastasis. Evidence suggests that metastasis to lymph nodes is an early event in pancreatic cancer progression, and presence of tumor cells in lymph nodes represents one of the most negative prognostic factors with respect to patient outcomes	1.Bilimoria KY et al; Pancreatic Cancer Quality Indicator Development Expert Panel, American College of Surgeons. Assessment of pancreatic cancer care in US based on formally developed quality indicators. J Natl Cancer Inst. 2009 Jun 16;101(12):848-59 2.Fink D et al; The lymphatic System and Pancreatic Cancer. Cancer Lett. 2016 Oct 10;381(1):217-36 3.European Society for Medical Oncology - Cancer of the Pancreas: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up (Switzerland)	Numerator: Number of patients with ≥ 10 lymph nodes pathologically examined Denominator: All with pancreatic cancer who have undergone surgery Exclusions:	• Pathology Report viewed by data collector	• path_report_yn	1, Yes 0, No	(denominator) numerator (path_report_yn==1 & path_nodes_exam !=. & surgery_details_complete==2) path_nodes_exam > 9
						• Number of lymph nodes examined	• path_nodes_exam	NUMBER	
						• Surgery Details Complete	• surgery_details_complete	0=No 1=Unverified/Not entered 2=Complete	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			UPDATED STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
10B	**Number of R0 resections (≥ 1mm margin) for those that do have a synoptic report**	Proportion of patients with R0 resections (≥ 1mm margin) for those that have a synoptic report	The goal of surgery is to achieve macroscopically clear margins, i.e. negative margin or R0 resection. Tumour clearance should be given for all seven margins identified by the surgeon. These seven margins are; pancreatic transection (neck), SMV/PV, SMA, posterior, proximal (gastric/duodenal), distal (distal duodenal/jejunal), bile duct and +/- portal vein (applicable only if PV resection performed). Assessment and reporting of margin status should be standardised on pathological reporting to allow comparison between groups of patients. The SMA, PV and posterior margins are most frequently involved in R1 resections. A resection specimen is considered R0 if all surgical margins are clear by ≥ 1mm. Regardless of the R status, the microscopic clearance of critical margins must be recorded in pathology report.	1.AGITG. Definition of surgical standards for pancreatic cancer: A consensus statement by the Australasian Gastro-Intestinal Trials Group. Available from https://gicancer.org.au/wp-content/uploads/2017/09/AGITG-Pancreatic-Cancer-Surgical-Guidelines-Report-2015.pdf 2.European Society for Medical Oncology - Cancer of the Pancreas: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up (Switzerland)	Numerator: Number of patients with R0 resections that have synoptic reporting Denominator: All patients with pancreatic cancer who have undergone surgery	• Pathology Report viewed by data collector	• path_report_yn	1, Yes 0, No	(denominator) numerator (path_report_yn==1 & path_synoptic_yn==1 & surgery_details_complete==2 & surgery_details_complete !=. & path_report_yn!=.& path_synoptic_yn!=.) path_overall_marg_status==1 | path_overall_marg_status==2
						• Synoptic Report	• path_synoptic_yn	1, Yes 0, No -99, Unknown	
						• Closest Margin	• path_synoptic_yn	1, Clearance ≥ 1mm (R0) 2, Reported as clear with no distance stated 3, < 1mm clearance or margin involved microscopically (R1) 4, Margin involved macroscopically (R2) 5, Margin status not documented	
						• Surgery Details Complete	• surgery_details_complete	0=No 1=Unverified/Not entered 2=Complete	

	INDICATOR	DESCRIPTION	RATIONALE & EVIDENCE	REFERENCES	SPECIFICATIONS	DATA ITEMS			UPDATED STATA / R CALCULATION
						LABEL	VARIABLE / FIELD NAME	CALCULATION OR SLIDER LABELS	
12	**Patients who are potentially resectable and who did not undergo surgery have a valid reason documented**	Proportion of patients deemed potentially resectable who do not undergo surgery have a valid reason documented	Surgery is the only potentially curative treatment currently for PC. Bilimoria et al found that for patients with Stage I disease, a minority underwent resection (26.8%). After accounting for those who did not undergo resection due to advanced age, severe comorbidities, or patient refusal, 51.7% of patients with Stage I disease did not receive resection. Most alarmingly, 38.2% of patients were never offered surgery. This highlights a concern that many patients are not receiving surgical evaluation and potentially beneficial resection.	1. Bilimoria KY, Bentrem DJ, Ko CY, et al.: Validation of the 6th edition AJCC Pancreatic Cancer Staging System: Report from the National Cancer Database. Cancer 2007;110:738–744. 2. Witkowski ER, Smith JK, Tseng JF. Outcomes following resection of pancreatic cancer. Journal of Surgical Oncology. 2013;107(1):97-103	Numerator: Number of patients with pancreatic cancer who did not undergo a surgical resection with a valid reason documented Denominator: All resectable patients with pancreatic cancer who did not undergo surgery Exclusions: Unresectable PC	• Diagnosis Complete	• diagnosis_complete	0=No 1=Unverified/Not entered 2=Complete	(denominator) numerator ((dx_resectability==0 | dx_resectability==1) & neo_yn!=1 & surg_type !=3 & surgery_details_complete==2 & treatment_summary_complete==2) surg_none_reason___1==1 | surg_none_reason___2==1 | surg_none_reason___3==1 | surg_none_reason___4==1 | surg_none_reason___5==1 | surg_none_reason___6==1 | surg_none_reason___0==1 & surg_none_reason____99 ~=.
						• Resectability of tumour at diagnosis	• dx_resectability	0, Resectable 1, Borderline resectable 2, Unresectable (Locally advanced) 3, Unresectable (Metastatic disease) 4, Unresectable (unclear if locally advanced or metastatic) 5, Not clearly documented -99, Unknown	
						• Surgery Type	• surg_type	1 = Exploratory laparotomy 2 = Diagnostic laparoscopy 3 = (Attempted) Pancreatic resection surgery	
						• Neoadjuvant chemotherapy and/or neoadjuvant radiotherapy	• neo_yn	1, Yes 0, No -99, Unknown	
						• Reason/s for no surgery (select all that apply)	• surg_none_reason	1=Metastatic or locally advanced disease 2=Advanced age 3=Comorbidities 4=Patient too unwell/ Performance status 5=Patient declined surgery 6=Patient died prior to planned surgery 0=Other (please specify) -99=Reason not documented	
						• Treatment Summary Complete	• tx_summary_complete	0=No 1=Unverified/Not entered 2=Complete	

Appendix 4.1: Ethics Approval

Monash University Human Research Ethics Committee

Approval Certificate

This is to certify that the project below was considered by the Monash University Human Research Ethics Committee. The Committee was satisfied that the proposal meets the requirements of the *National Statement on Ethical Conduct in Human Research* and has granted approval.

Project ID:	19446
Project Title:	Barriers and Enablers to Quality Indicator Implementation in Pancreatic Cancer: A Qualitative Study Using the Theoretical Domains Framework (TDF)
Chief Investigator:	Professor Susan Evans
Approval Date:	06/05/2019
Expiry Date:	06/05/2024

Terms of approval - failure to comply with the terms below is in breach of your approval and the *Australian Code for the Responsible Conduct of Research*.

1. The Chief Investigator is responsible for ensuring that permission letters are obtained, if relevant, before any data collection can occur at the specified organisation.
2. Approval is only valid whilst you hold a position at Monash University.
3. It is responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval and to ensure the project is conducted as approved by MUHREC.
4. You should notify MUHREC immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.
5. The Explanatory Statement must be on Monash letterhead and the Monash University complaints clause must include your project number.
6. Amendments to approved projects including changes to personnel must not commence without written approval from MUHREC.
7. Annual Report - continued approval of this project is dependent on the submission of an Annual Report.
8. Final Report - should be provided at the conclusion of the project. MUHREC should be notified if the project is discontinued before the expected completion date.
9. Monitoring - project may be subject to an audit or any other form of monitoring by MUHREC at any time.
10. Retention and storage of data - The Chief Investigator is responsible for the storage and retention of the original data pertaining to the project for a minimum period of five years.

Kind Regards,

Professor Nip Thomson

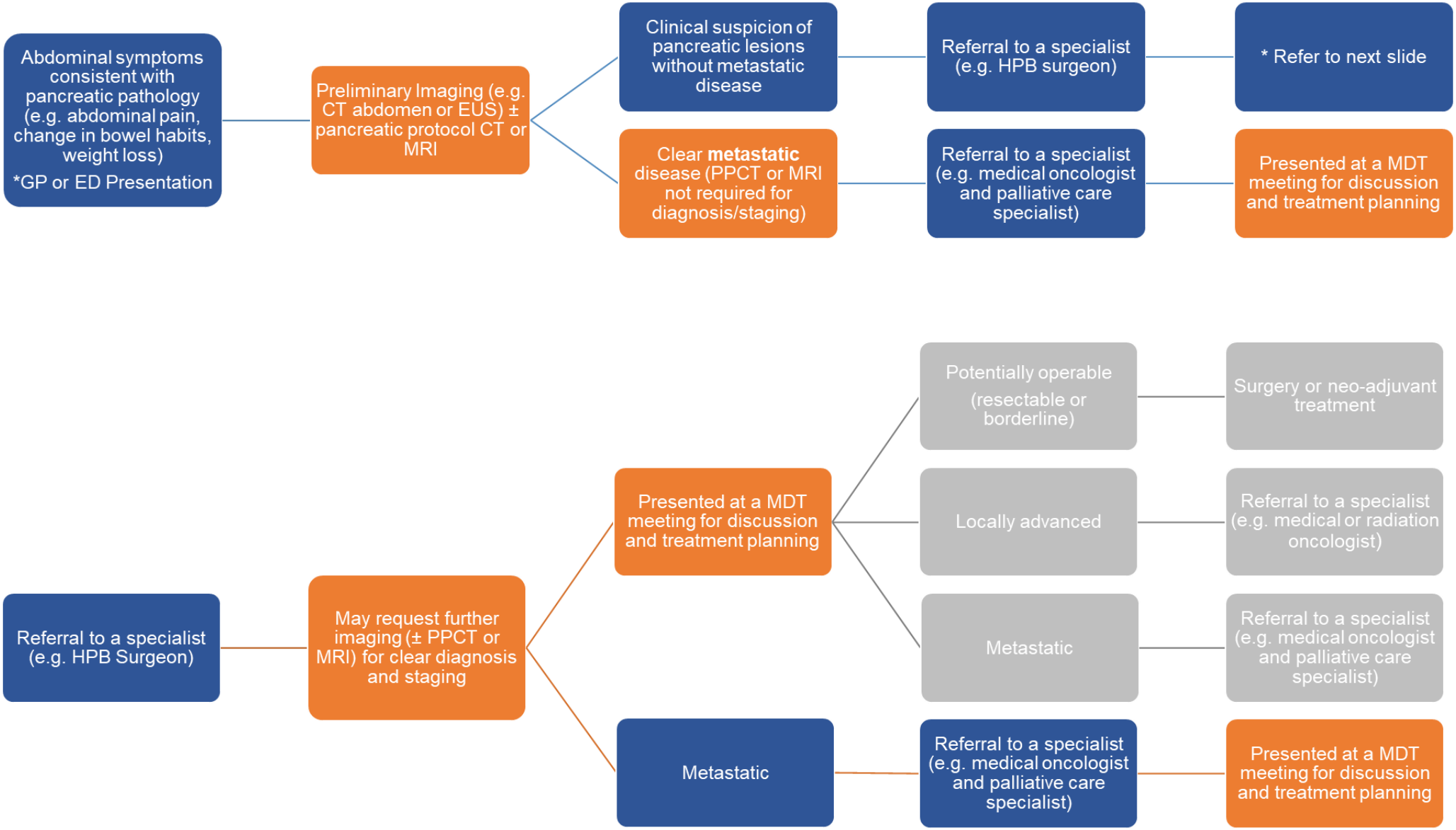
Chair, MUHREC

CC: Mrs Ashika Maharaj, Professor Susan Evans, Professor Sally Green, Professor John Zalcberg, Dr Liane Ioannou

List of approved documents:

Document Type	File Name	Date	Version
Supporting Documentation	Interview_Schedule_AM	01/04/2019	2
Supporting Documentation	EMAIL INVITE_barriers&enablers	01/04/2019	1
Supporting Documentation	01042019_BarriersEnablersProtocol_v2	01/04/2019	2
Explanatory Statement	EXPLANATORY STATEMENT_barriers&enablers	01/04/2019	2

Appendix 4.2 A Decision Tree for Protocol Imaging and MDT Meetings for Patients Diagnosed with Pancreatic Cancer



Appendix 4.3: Interview Schedule (PPCT/MRI)

TITLE: Barriers and Enablers to Selected Indicator Implementation in Pancreatic Cancer: a qualitative study using the theoretical domains framework.

Introduction

As outlined in the explanatory statement, this study aims to identify and explore the barriers and enablers to two practices:

1. Implementation of a PPCT or MRI scan for diagnosis and/or staging, and
2. Disease management for all patients discussed at a MDT

- We are interviewing a range of specialists across Victoria and NSW, who manage patients with pancreatic cancer, particularly in relation to the two practices we are exploring
- Interviews will be recorded
- You can stop the interview at any time
- We are using a framework known as the theoretical domains framework that include 12 domains. Some questions may appear repetitive but the approach is to follow a structure so that we don't miss any important concepts and we understand from your perspective how these practices work in the real world.
- This study will be published and data will be aggregated. We can assure you that no identifiable data will be published.

Before we start do you have any questions?

Background information

Can you describe your role and area of care?

Prompt questions

- How many years of experience do you have working as a surgeon/ oncologist/ radiologist/ chair of a MDT / care coordinator?
- How many cases of PC would you see in a week?
- Do you work in the private or public sector or both?
- Do you work mainly in metropolitan areas, regional or both?
- What is the mix of resectable vs non-resectable PC cases you see?
- To understand some of the systems in place within your organization: What type of medical record system is in use? Paper based / electronic? Use of reminders/prompts/pathways in system?
- Is there access to a radiology department in your hospital? What radiology services do they offer? If not, where are the nearest radiology services? Is there a waiting list for services? (can potentially be under the domain environmental context?)
- Is there access to a MDT for PC in your hospital? How often do you hold MDTs for PC in your hospital? If not, where is the nearest MDT meeting that takes place? (can potentially be under the domain environmental context?)

Earlier a decision tree that outlined the potential process incorporating the two practices was circulated. Are there any comments regarding the decision tree?

Now I am going to ask you questions on the factors that influence the two clinical practices we are studying.

First, I will ask if and how a PPCT or MRI scan is used for the diagnosis/staging of PC in your hospital or clinic, and then I will ask about disease management at multidisciplinary team meetings for patients diagnosed with PC.

Implementation of a PPCT or MRI scan for diagnosis and/or staging (Surgeons/Oncologists /Radiologists)

Understanding clinical practice

Prompt questions:

- Are you involved in the ordering or interpreting of the results of the diagnostic tests PPCT or MRI for suspected PC?
    - If so, what tests do you order? How would you decide which test between the two?
    - Do you believe the tests are equivalent?
    - Which patients do you test for PC?
    - Roughly what proportion of your HPB patients do you refer for testing for PC?
    - Where are the results of the assessments/tests recorded? (and by who?)
    - Do you know roughly how long your patients wait for a diagnostic test?

Factors influencing practice

In the Theoretical Domains Framework, there is a set of 12 domains that are known to influence clinical behaviors.

Firstly, before I prompt with specific questions about potential factors that are known to influence clinical practice, can I first ask you what you think are the biggest influences on your decision to order or use a PPCT or MRI for patients with a clinical suspicion of PC in your hospital?

Prompt questions to explore factors influencing practice (grouped by TDF domains).

TDF Domains	TDF Definitions [Constructs] [1]	Prompt questions
Thinking about Knowledge	An awareness of the existence of something. [Knowledge including knowledge of condition/scientific rationale. Procedural knowledge. Knowledge of task environment.]	**Are you aware of any clinical practice guidelines on the management of patients with clinical suspicion/diagnosis of PC?** Do you feel your colleagues are aware of these guidelines? How credible are the sources or developers of these guidelines? **Are you familiar with the recommendations in these guidelines for referral for imaging?** Are you aware of any protocols within your organization for CT scans or MRIs in the diagnosing/staging pancreatic cancer? Were they externally / internally developed? What do you think is best practice in the diagnosis and staging of PC? **Are you aware of any research about the prevalence and impact of PPCT or MRI on the diagnosis and staging of PC?** **When you order a PPCT what do you expect a radiologist to do?**
Next we want to understand the Skills that maybe required	An ability or proficiency acquired through practice. [Skills Skills development Competence Ability Interpersonal skills Practice Skill assessment]	**Apart from radiology, What skill sets are needed use of a PPCT or MRI?** How would you go about ordering the test? Are these scans difficult to interpret?
Now thinking about Social professional role and identity	A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting. [Professional identity Professional role Social identity	**In addition to your role in diagnosing or staging PC, who else maybe involved in diagnosing and staging?**

TDF Domains	TDF Definitions [Constructs] [1]	Prompt questions
	Identity Professional boundaries Professional confidence Group identity Leadership Organizational commitment]	**Thinking about this from an organizational perspective, could you describe the focus within your organization to manage PC?** Or is the management of PC referred to other centres (e.g. metropolitan hospitals)
Moving onto the domain Beliefs about capabilities	Acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use. [Self-confidence Perceived competence Self-efficacy Perceived behavioral control Beliefs Self-esteem Empowerment Professional confidence]	Any difficulties in assessing the results from a PPCT or MRI? **What are the challenges in determining/ diagnosing the presence of PC in general and using/ordering different tests/tools in particular?** What would help you to identify your patients with PC? **How confident would you and your peers be that you can identify PC in your patients through the implementation of a PPCT or MRI?**
Now thinking about the Beliefs about consequences	Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation. [Beliefs Outcome expectancies Characteristics of outcome expectancies Anticipated regret Consequences]	**What do you think your peers or colleagues believe are the benefits and costs of implementing a PPCT or MRI? (for your patients, you, your colleagues and the organization)** What are the benefits and costs of not implementing a PPCT or MRI? (for your patients, you, your colleagues and the organization) **Do you or your peers believe there are any consequences for not routinely applying a PPCT or MRI where there is suspicion of a pancreatic lesion?** Do you think the benefits of these tests outweigh the costs? Does the evidence suggest that implementing a PPCT or MRI is worthwhile?
Coming now to Motivation and goals	A conscious decision to perform a behavior or resolve to act in a certain way. Mental representations of	**Should there be incentives to implementing a PPCT or MRI for all suspected cases of PC?** What could these be?

TDF Domains	TDF Definitions [Constructs] [1]	Prompt questions
	outcomes or end states that an individual wants to achieve. [Stability of intentions Stages of change model Transtheoretical model and stages of change Goals (distal/proximal) Goal priority Goal/target setting Goals (autonomous/controlled) Action planning Implementation intention]	What would be the implications of not having adequate imaging? **Are there occasions where your peers and colleagues feel there is no need to order a PPCT or MRI before any treatment** Are there other aspects of your role that interfere with the implementation of a PPCT or MRI for all suspected cases of PC?
We are now going to discuss Memory, attention and decision processes	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives. [Memory Attention Attention control Decision making Cognitive overload/tiredness]	**Are there any reminders in place to prompt you and your colleagues to do any of the relevant tests? If not, do you think these would be helpful?'** Is ordering a PPCT or MRI something you do routinely for clinical suspicion of PC?
Thinking now in terms of the Environmental context and resources	Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior. [Environmental stressors Resources/material resources Organizational culture/climate Salient events/critical incidents Person x environment interaction Barriers and facilitators]	**Are there any resources that influence whether you or your peers order a PPCT or MRI?** Are there sufficient human resources? Are there sufficient physical resources? Do you have enough time/do you have competing demands? Does the working environment have an effect? **Are there environmental stressors that impact on the ability for you and your peers to implement a PPCT or MRI?** **Are there rules/regulations from rebate or funders that influence the decisions about using a PPCT or MRI for diagnosis or staging?**

TDF Domains	TDF Definitions [Constructs] [1]	Prompt questions
Thinking about Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviors. [Social pressure Social norms Group conformity Social comparisons Group norms Social support Power Intergroup conflict Alienation Group identity Modeling]	Do you seek opinions of colleagues in whether to use a PPCT or MRI in suspected cases of PC? **What are the views of your colleagues regarding the use of a PPCT or MRI routinely?**
The next domain in the framework is centred on any Emotions attached to this practice	A complex reaction pattern, involving experiential, behavioral, and psychological elements, by which an individual attempts to deal with a personally significant matter or event. [Fear Anxiety Affect Stress Depression Positive/negative effect Burn-out]	**How do you and your colleagues feel about ordering a PPCT or MRI for all patients with suspicion of PC?** Does this alter your clinical management decisions?
Finally, on Behavioral regulation	Anything aimed at managing or changing objectively observed or measured actions. [Self-monitoring Breaking habit Action planning]	**Are there any protocols or referral pathways that facilitate the implementation of a PPCT or MRI scan for patients with suspicion of PC?**

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Appendix 5.1: Interview Schedule (MDT meetings)

TITLE: Barriers and enablers to the discussion of all patients at multidisciplinary team meetings: a qualitative study using the theoretical domains framework.

Introduction as per *Appendix 4.3*

<u>Disease management for all patients discussed at a MDT</u> (Care Coordinators/ MDT Chair/ Surgeons/ Oncologists/ Radiologists

Understanding clinical practice

We will now discuss the second practice in a similar fashion to the first.

Prompt questions (current practice)

- Are all patients diagnosed with PC discussed at a MDT meeting?
    - If not, under what circumstances would they not be referred for a MDT meeting?
- Who attends the MDT meeting?
- Where is the referral to a MDT recorded?
- Is a referral to a MDT meeting mandatory in your hospital?
- Would you/others involve the patient in a MDT? If so, how?
- Where is the MDT meeting held?
- How often are they held?

Factors influencing practice

Now I want to ask you about what influences your attendance or referral of a patient to a MDT meeting. Firstly, before I prompt with specific questions about potential factors that are known to influence clinical practice, can I first ask you tell me what you think are the biggest influences on your decisions to refer your patients with PC to a MDT meeting?

Prompt questions to explore factors influencing practice (grouped by TDF domains).

TDF Domains	TDF Definitions [Constructs]	Prompt questions (if required)
Thinking about Knowledge	An awareness of the existence of something. [Knowledge including knowledge of condition/scientific rationale. Procedural knowledge. Knowledge of task environment.]	We discussed some guidelines before: **Are you and your peers familiar with the recommendations in these guidelines for presentation of all patients diagnosed with PC to a MDT meeting?** **Are you aware of any research about the effectiveness of MDT meetings in PC?**

TDF Domains	TDF Definitions [Constructs]	Prompt questions (if required)
Thinking about the Skills required	An ability or proficiency acquired through practice. [Skills Skills development Competence Ability Interpersonal skills Practice Skill assessment]	**Who should be present at a MDT meeting for the management of PC?**
In the context of Social professional role and identity	A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting. [Professional identity Professional role Social identity Identity Professional boundaries Professional confidence Group identity Leadership Organizational commitment]	Do you think organizing a MDT meeting is part of your role? If not, whose role is it? **Whose role is it to ensure that patients are placed on the list for a MDT meeting?** Do you think participating in a MDT meeting is part of your role? If not, whose role is it? Do you think that the organization and coordination of a MDT meeting should be the role of another professional group? **Going beyond you role and thinking at an organizational level are you able to describe the focus within your organization to hold regular MDT meetings for all patients diagnosed with PC?**
In our next framework, on Beliefs about capabilities	Acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use. [Self-confidence Perceived competence Self-efficacy Perceived behavioral control Beliefs Self-esteem Empowerment Professional confidence]	**What difficulties do you and your colleagues see in making sure that all patients with PC are discussed at an MDT meeting?** What would help you or your hospital to effectively organise a MDT meeting What would help you to attend or participate in a MDT meeting? How confident are you that you can effectively take part in a MDT meeting?
Now following on to Beliefs	Acceptance of the truth, reality, or validity about outcomes of a behaviour in	**What do you think your peers or colleagues believe are the benefits and costs of regular**

TDF Domains	TDF Definitions [Constructs]	Prompt questions (if required)
about consequences	a given situation. [Beliefs Outcome expectancies Characteristics of outcome expectancies Anticipated regret Consequences]	**MDT meetings? (for all your patients, you, your colleagues and the organization)** What are the benefits and costs of not having regular MDT meetings? (for **all** your patients, you, your colleagues and the organization) What will happen if there are no MDT meetings within your organization? Does the evidence suggest having regular MDT meetings to discuss the treatment planning for all patients with PC is worthwhile?
Coming to the Motivation and goals that drive behaviour	A conscious decision to perform a behavior or resolve to act in a certain way. Mental representations of outcomes or end states that an individual wants to achieve. [Stability of intentions Stages of change model Transtheoretical model and stages of change Goals (distal/proximal) Goal priority Goal/target setting Goals (autonomous/controlled) Action planning Implementation intention]	**Are there incentives to be involved in a MDT meeting?** **If no then: Should there be?** Do you feel you have to be involved in a MDT meeting? **Are there other aspects of your role that interfere with the participation/organization of a MDT meeting on a regular basis?**
Thinking about Memory, attention and decision processes	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives. [Memory Attention Attention control Decision making Cognitive overload/tiredness]	**What reminders are there to ensure that you and your colleagues place patients on the list for discussion at an MDT?** Are there any reminders in place to prompt you to attend a MDT meeting? If no, do you think these would be helpful?' Is it something you do routinely?

TDF Domains	TDF Definitions [Constructs]	Prompt questions (if required)
In the Environmental context and available resources	Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior. [Environmental stressors Resources/material resources Organizational culture/climate Salient events/critical incidents Person x environment interaction Barriers and facilitators]	Do resources influence whether you participate or organize a MDT meeting bearing in mind this is for all patients? Are there sufficient human resources? Are there clear communication channels? Are there sufficient physical resources? Do you have enough time/do you have competing demands? Does the working environment in your hospital have an effect? **Are there environmental stressors that impact on the ability for you and your colleagues to participate in a MDT meeting?**
Considering Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviors. [Social pressure Social norms Group conformity Social comparisons Group norms Social support Power Intergroup conflict Alienation Group identity Modeling]	Do you seek opinions of colleagues in whether/how to treat PC at the MDT meeting? **What are the views of your colleagues regarding MDT meetings in general?** Do you observe others or learn from others at a MDT meeting? **How do team members communicate within a MDT meeting?** Do you feel the roles are clear in a MDT meeting?
Thinking of any Emotions generated with this practice	A complex reaction pattern, involving experiential, behavioral, and psychological elements, by which an individual attempts to deal with a personally significant matter or event. [Fear	**How do you or your colleagues feel about regular MDT meetings?** Does this alter your clinical management decisions?

TDF Domains	TDF Definitions [Constructs]	Prompt questions (if required)
	Anxiety Affect Stress Depression Positive/negative effect Burn-out]	
And finally on Behavioral regulation	Anything aimed at managing or changing objectively observed or measured actions. [Self-monitoring Breaking habit Action planning]	**Are there any protocols or referral pathways that facilitate the discussion of all PC patients at a MDT meeting?**

If time permits and only if these items have not yet been covered:

- What do you think are the key actions/decisions when managing a patient with PC that maximize the beneficial outcomes for the patient in relation to these two practices?
- Is there an aspect of the patient pathway we should pay more attention to in future interviews?
- If there was one thing you could change in your hospital to improve the management of patients with PC, what would you change?

Final questions:

- Is there anything else about the management of patients with PC that you would like to mention that is not already covered?
- Do you have any additional comments on the content of the interview or feedback on how the interview went?

THANK YOU VERY MUCH FOR YOUR TIME

Appendix 6.1: Lynda Williams (March 11, 1950 - July 6, 2017)

Eulogy
Lynda was born in 1950, in New Zealand, and was a mother of five children. She was a childbirth educator and was awarded the NZ Order of Merit for 35 years of service to women's health. Sadly, she passed away in 2017 from stage IV pancreatic cancer, five months after giving the following interview:

MP3 recording
(Please double click the icon below)

Lynda_Williams_File - 4_1_19, 23.37.mp3

Transcript of recording

On being the engaged patient: My oncologist is a 38 year old guy who is totally freaked out at my having access to my patient portal. I have given him a book called the patient will see you now. I've already got a bit of a heads up and that I know that my last blood test for the pancreatic cancer biomarker CA19-9 has shown a further drop and so I'm predicting that the cancer hasn't spread.

On patient characteristics: Yes. I've got an iPhone but I've got an antique phone that I use for emails because I'm not up with the technology. I don't do Apps, any Apps at all. I have no clue about Apps.

On side-effects of treatment and impact on quality of life: I've quit my second round of chemo session. Being on a weekly session with Paclitaxel, even after I had the dose reduced, and I leapt up and down to get that reduced. It's still too much. So for me lying here, not able to read, not interested in watching TV, feeling terrible, not able to get out in my garden. You know it's not worth it. I mean I'm not having no quality of life.

On supportive care: Comparing where we were the Christmas before last, when we had Christmas at my son's new house. You know we are in a much healthier place and working through stuff and making decisions together. I think that is a gift.

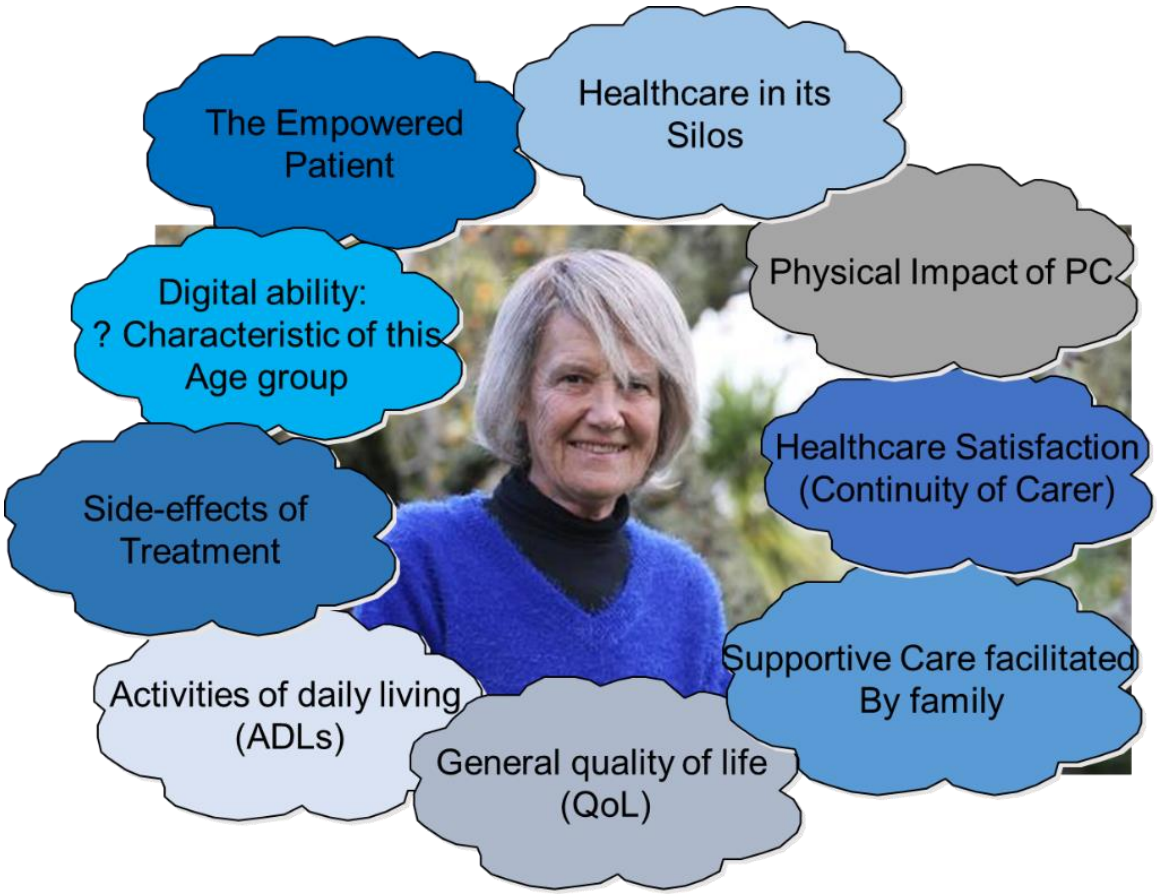
Has that been facilitated in anyway by the system? No

On continuity of care: I believe on continuity of care for beginning of life when you're giving birth and I've discovered that it is just as important at your end-of-life when you're making major decisions. And its not available! We have to see the same person each time... they're just totally and utterly freaked out! They've got holidays, rosters and they want education time, conferences etc. I mean, I don't mind that it is one or two people working as part of the team, and have read your notes. It is absolutely devastating to the patient sitting on the other side of the desk to realise the person you're talking to knows absolutely nothing about their case.

On being a cancer patient and healthcare satisfaction: It is basically a full-on part-time job being a cancer patient. And I only had chemo. I didn't have radiotherapy or anything else. You fall through the cracks when something happens that may or may not be related to your cancer or cancer-treatment. I went back into the system for that. They treat you as a body part. The person did not know that I had pancreatic cancer, being referred in for an appointment that they judged was not urgent, so they said that it would be four to five months before I got an appointment. I said, "How do you know that I'm still going to be alive then"? The person who's looking at referrals isn't seeing what else is going on. And when we are focused on pancreatic cancer, we haven't got time to 'muck' about as I say on my blog quite frequently. I mean there's that sense of urgency to everything – 75-80 % of us die within a year. We haven't got time to 'muck' about. Don't go giving us appointments for other things six months down the track.

With pancreatic cancer, you've got so few options. That's been my experience of my journey.

Visual Summary of interview



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Appendix 7.1: Prognostic models to predict survival in patients with PC: A systematic review

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Conflicts of Interest

All authors declare that they have no conflict of interest.

Author Statement

LJI and SME wrote the first draft of the manuscript and developed the systematic review protocol. ADM and JTL screened studies for inclusion and risk of bias. JTL assisted with data extraction for the updated search. AE provided guidance and oversight of the data synthesis. The remaining authors, JRZ, DG, JGK, NDM, CC, EAB, KW, REN, SEG, reviewed and provided feedback on various drafts of the manuscript and approved the final manuscript.

Abstract

Background: Pancreatic ductal adenocarcinoma (PDAC) has a poor survival rate with few current treatments offering cure or long-term survival. Reliable prognostic models are necessary to select who should undergo different treatments, to avoid futile, morbid treatments, and to provide adequate information to patients. The aim of this review was to systematically evaluate prognostic models developed to predict overall survival in patients diagnosed with PDAC.

Methods: We conducted a comprehensive search of eight electronic databases from their date of inception through to December 2019. Studies that published models predicting survival in patients with PDAC were identified. Inclusion and risk of bias were evaluated independently by two researchers according to specific criteria. Data were extracted on study population, setting, sample size, study period, study design, validation, prognostic factors and model discrimination.

Data Synthesis: We identified 3297 studies; 187 full-text articles were retrieved and 54 studies of 49 unique prognostic models were included in the qualitative synthesis. Of the 49 prognostic models, 28 (57.1%) were conducted in patients with advanced disease (incorporating unresectable (not further defined), locally advanced or metastatic disease), 17 (34.7%) in patients with resectable disease, and four (8.2%) in all patients with PDAC, regardless of stage/treatment. A total of 34 (69.4%) models were validated, either externally or internally, and 35 (71.4%) reported model discrimination, with c statistic and area under the receiver-operating-characteristic curve (AUROC) values in derivation cohorts ranging from 0.60 to 0.88. Only four models reported values >0.70 in both derivation and validation cohorts. Of the prognostic factors evaluated in the models, those most frequently included were lymph node ratio (83%), tumour volume/size (71%), performance status (68%), tumour grade (68%), serum CRP (63%), metastatic stage (62%) and liver metastasis (60%). According to hazard ratio (HR) values, the prognostic factors shown to predict poorer survival were performance status (mean HR=2.91), lymph node ratio (mean HR=2.87), serum albumin (2.58) and resection of primary tumour (mean HR=2.22).

Conclusion Most prognostic models were developed using retrospective data and performed poorly (<0.70). Research is required to develop and validate prognostic models in prospective cohorts aiming to improve model performance. This will provide a valuable tool for clinicians, enabling them to identify patients at diagnosis with a high risk of poor survival to

inform decision making and provide targeted interventions, and researchers, allowing for the design of intervention trials and ability to provide risk-adjusted comparison data.

Keywords: pancreatic cancer, risk prediction, prognostic factors, survival

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is the 12th most common cancer diagnosis in men and the 11th in women, the seventh leading cause of cancer-related death and the fourth leading cause of death from a digestive organ neoplasm, worldwide.[1, 2] The mortality rate is higher in developed countries; for example PDAC is the third-leading cause of cancer-related death in the United States and is predicted to be the second by 2020.[69] Despite a significant decline in mortality across almost all neoplasms over the past 15 years, the age-adjusted mortality rate from PDAC has remained largely unchanged.[3] There were an estimated 458,918 new cases of PDAC worldwide in 2018, which is equivalent to more than 1,200 people diagnosed each day, with a median survival of less than 12 months and an overall 5-year survival rate of approximately 6%.[1, 2]

Surgery currently is the only potentially curative treatment for patients with PDAC. Unfortunately, only 10-20% of patients present with potentially resectable disease, with around 53% metastatic at diagnosis.[1] Adjuvant chemotherapy has been shown to significantly improve survival in patients who have had resection, although until recently these gains using single agents have been relatively modest, increasing 5-year survival from around 10% (ESPAC-1 and CONKO-001) to 15-20% (ESPAC-1, ESPAC-3, CONKO-001). More recently combination chemotherapy in the adjuvant setting has provided further improvements with 5-year survival of 28.4% (ESPAC-4) and median survival of 54 months.[70] Nevertheless, the majority of patients who undergo resection eventually succumb to recurrent disease and distant metastasis.[4] Furthermore, many patients are unable to receive adjuvant chemotherapy due to complications arising from resection.

Palliative chemotherapy with or without radiotherapy remains the mainstay of treatment for the vast majority of patients who have locally advanced and metastatic disease. Once again, combination chemotherapies have been shown to provide superior outcomes compared to single agent regimens at the cost of greater toxicity. For example, modified combination therapy with Folfirinox provides a median survival of 11 months in metastatic pancreatic compared to 7 months with gemcitabine monotherapy. However, while recently developed regimens of chemotherapy have improved the prognosis for patients with advanced disease, there is a lack of effective agents, with resistance occurring in approximately 20% of patients and only a select few patients receiving the benefit.[5, 6] With the advent of these more effective but also more toxic treatments,[71] there has been increased interest in prognostic models that can guide treatment selection in patients with PDAC.

Prognostic models are statistical models that estimate, objectively and reproducibly, the probability that an individual with given risk factors will achieve a specific outcome (example survival) over a defined period of time. Prognostic models can be used in a clinical setting, allowing clinicians and patients to objectively assess the risk benefit analytics of targeted interventions and treatments, informing clinical decision making and patient counselling. In a research setting prognostic models are often used to assist in the design of intervention trials, identification of patients for randomised control trials and provision of risk-adjusted comparison data for quality assessment.[5, 7] With increasing ability to understand clinical, epidemiological and biological predictors of health outcomes, prognostic models provide a means of informing clinical care and assessing its quality. Quality assessment emphasizes measuring health outcomes rather than processes of care, as outcomes are of greater interest to patients and funders. However, compared to processes, outcomes are less directly controlled by clinicians or health systems, emphasising the importance of controlling for factors that are beyond the reach of clinicians or health systems by using rigorous risk-adjustment methods.[8]

Traditionally, anatomical-based models to predict survival following a diagnosis of PDAC have used the American Joint Committee on Cancer (AJCC) staging system, based on pathological tumour, node and clinicopathological metastases (TNM) status.[9] However, due to the fact that only a small percentage of PDAC patients undergo resection, pathological staging is not a suitable prognosticator for most patients. Clinical staging according to resectability (resectable, borderline resectable, locally advanced or metastatic) is more widely used to predict survival and aid clinical decision making. However, survival cannot be precisely predicted for individual patients based on these staging systems alone. Due to the ongoing discovery and development of prognostic factors, including biological factors, which predict patient outcomes with better accuracy than purely anatomical-based staging, other reliable prognostic tools have been developed.

The aim of this review was to systematically examine prognostic models developed to predict overall survival in patients diagnosed with PDAC and undergoing surgical treatment, to identify (1) which prognostic factors are consistently reported as independent predictors of overall survival and (2) whether a reliable prognostic model exists.

Methods

Data Sources & Search Strategy

A systematic search of eight electronic database engines, Medline (1950-present), CINAHL, The Cochrane Library, EBM Reviews, ProQuest Central, PubMed, Scopus and Web of Science, was conducted from database inception to December 2019. Search terms were developed in consultation with a medical librarian. The search strategy included keywords and medical subject headings (MeSH) for PDAC, prognostic model and mortality. For example, the search terms for PDAC included the MeSH term 'Pancreatic Neoplasm' as well as the following keywords: 'pancreatic cancer, pancreatic tumour, pancreatic carcinoma and pancreatic neoplasm'. Search results related to prognostic model were combined with those for mortality, with the end search combined with the search results for PDAC (see Supplementary Material for Medline Search). Reference lists were examined for additional relevant studies. All citations from search outputs were imported and managed with Endnote X8.

Study Selection

All citations were screened for eligibility by two independent reviewers (LI and AM or JL), based on title and abstract (if available), and were assigned an eligibility code (yes, no, or unsure). Reviewers were blind to the other reviewer's decisions. Full-text articles for potentially relevant citations (assigned yes or unsure by either reviewer) were assessed for inclusion by two reviewers. We included articles if they were published in English language and reported on the development and/or validation of a prognostic model to predict overall survival in patients with PDAC. The outcome, overall survival, was defined as survival from diagnosis, including survival in pre-defined months, disease-free or disease-specific survival, and/or long-term survival. Studies were excluded if the study population was patients with neuroendocrine tumours or included non-PDAC patients (i.e. patients undergoing a specific procedure, for example pancreatoduodenectomy). Studies reporting on postoperative mortality, or mortality following non-surgical treatment, were also excluded.

Data Extraction

Data was extracted, including: first author name, year, country, population characteristics, setting, study design, study period, stage, sample size, validation, prognostic factors and model discrimination. In order to facilitate high-level comparison, prognostic factors were grouped into seven categories: patient demographics, comorbidities, biomarkers (serum

chemistry and haematology), primary tumour details, staging (clinical or pathological), radiological features, surgical and non-surgical treatment. To determine the practical utility of each model, two reviewers (LI and AM or JL) independently assessed study design, with a focus on the type of data used, and model discrimination. Disagreement between reviewers was resolved during consultation.

Model discrimination was determined by using the concordance (c) statistic or, the equivalent, area under the receiver operating characteristic curve (AUROC) (where reported). The c statistic is defined as the proportion of times the model correctly discriminates between individuals (i.e. a patient with high-risk and a patient with low-risk of poor overall survival).[10] A c statistic or AUROC of 0.50 indicates that the model performs no better than chance, with 0.70 to 0.80 indicating modest discriminative ability, and greater than 0.80 indicating good discriminative ability.[10] If the c statistic or AUROC was not reported other operational statistics were extracted, where available.

Risk of Bias Assessment

A quality appraisal was undertaken by two of the authors (LI and AM or JL) with each article assessed for risk of bias on the domains of study participation, study attrition, prognostic factor measurement, outcome measurement and statistical analysis according to the Quality in Prognostic Studies (QUIPS) tool.[11] Confounder measurement was not assessed, as it was deemed not relevant for the development of prognostic models. However, emphasis was placed on the measurement of prognostic factors given their importance in the models and statistical analysis, in particular assessment of model discrimination. Disagreement between reviewers was resolved during consultation. Studies were rated low-to-moderate risk of bias if they adequately handled most or all sources of bias across the five quality criteria.

Data Synthesis

Quantitative synthesis (meta-analysis) was not conducted due to the heterogeneity of included studies with regard to population (stage and treatment), outcome measures (different definitions of survival), study design (prospective and retrospective) and statistical analyses (model discrimination). Therefore, we qualitatively synthesised the results, focusing on the populations in which the model had been developed and tested, study design, model discrimination, and the types of prognostic variables evaluated and included in each model.

Registration

Key features of this protocol were registered in PROSPERO (CRD42018095370).

Results

The search yielded a total of 3297 publications; after duplicates were removed 1738 remained which were screened for eligibility (see Figure 1). Full-text articles were obtained for 187 publications and assessed for inclusion, with an additional 29 publications sourced from reference lists. A total of 54 publications (51 full-text, two abstracts and one PhD thesis) of 49 unique prognostic models met the inclusion criteria for data extraction.

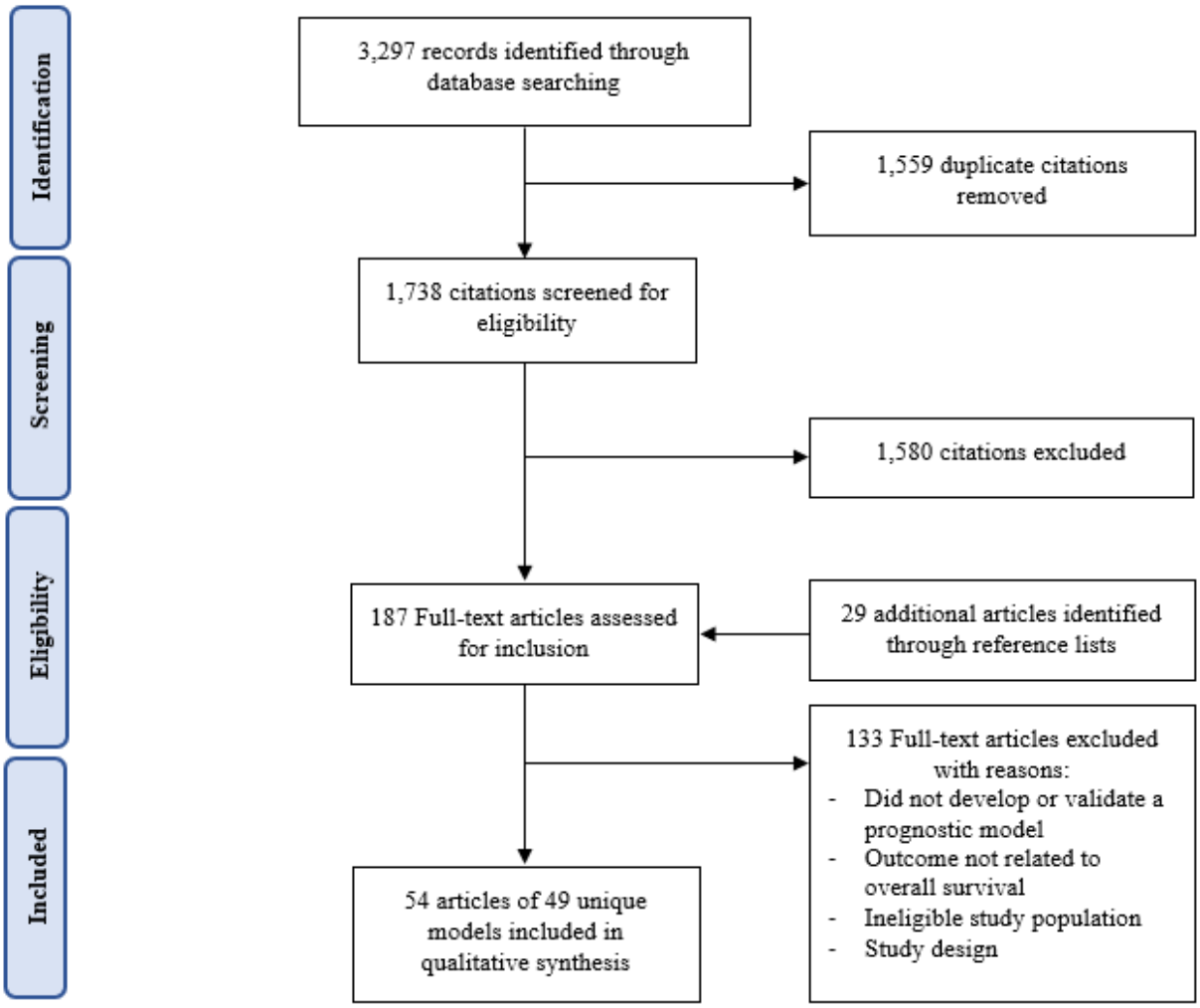

Figure 1. PRISMA Flow Diagram

Description of Prognostic Models

The earliest prognostic model was published in 1996, with 32 (65.3%) published between 2015 and 2019 (Table 1). Most studies were undertaken with patients from Asia (n=20, 40.8%) and Europe (n=15, 30.6%) with the remainder from US and Canada (n=10, 20.4%) and one from Australia (2.0%). Three were international studies in which patients were recruited from multiple countries (6.1%). Most models were developed in patients with advanced PDAC (n= 28, 57.1%). Of those with advanced disease, the majority (n=17, 60.7%) were developed in unresectable patients (not further defined), while only four models (14.3%) developed in patients with locally advanced disease and seven (25.0%) in metastatic patients. Seventeen models (34.7%) were developed in patients with resectable disease and four (8.2%) were in all PDAC patients regardless of stage or treatment. Most models (n=37, 75.5%) were developed using data collected retrospectively, and the median sample size for all the models was 403 patients. Prognostic models were most commonly constructed to predict overall survival (n=34, 69.4%), followed by survival within a specified timeframe (i.e. 9, 12, 24 months etc.) (n=11, 22.4%), and less frequently long-term survival (LTS) (n=1, 2.0%) and disease-specific survival (DSS) (n=3, 6.1%).

Table 1. Descriptive statistics of prognostic models (n=49)

Prognostic Models	Categories	N (%)
Year of Publication	≤1999	2 (4.1)
	2000-2004	3 (6.1)
	2005-2009	2 (4.1)
	2010-2014	10 (20.4)
	2015-Present	32 (65.3)
Country#	Asia	20 (40.8)
	US & Canada	10 (20.4)
	Europe	15 (30.6)
	Australia	1 (2.0)
	International	3 (6.1)
Stage	All*	4 (8.2)
	Resectable	17 (34.7)
	Advanced Disease	28 (57.1)
	Unresectable	17 (60.7)
	Locally Advanced	4 (14.3)
	Metastatic	7 (25.0)
Study Design	Retrospective	37 (75.5)
	Prospective	12 (24.5)
Sample Size	*Minimum; Maximum*	14; 37,135
	Median (SD)	403 (6654.46)
Model Type	Nomogram	25 (51.0)
	Prognostic Index	12 (24.5)
	Prognostic Model	4 (8.2)
	Predictive Model	1 (2.0)
	Risk Score	6 (12.2)
	Symptom Score	1 (2.0)
Outcome	Overall Survival (OS)	34 (69.4)
	Survival (in months)	11 (22.4)
	Long-term Survival (LTS)	1 (2.0)
	Disease-specific Survival (DSS)	3 (6.1)

Validation	Internally validated (only)	16 (32.7)
	External validated (only)	6 (12.2)
	Both internal and external validation	12 (24.5)
	None	15 (30.6)

*Footnote: *One study excluded patients with metastatic disease. [#]Country where patients were recruited.*

The sample sizes of included studies ranged from 14 to 37,135 patients, with median survival ranging from 10.7 to 23.0 months in resectable patients, 3.1 to 12.6 months in unresectable patients (not further classified), 9.9 to 15.4 months in locally advanced patients, and 3.2 to 8.2 months in metastatic patients (see Table 2).

Model Validation & Discrimination

Of the 49 prognostic models, 34 (69.4%) were validated, 18 (36.7%) using an external cohort of patients, 16 (32.7%) were internally validated only and 15 (30.6%) did not report internal or external validation. Thirty-five models (71.4%) reported model discrimination, with 27 (77.1%) reporting c statistics and three (6.1%) reporting AUROC. The other five models reported risk score Cox coefficient (n=1), Gehan's Wilcoxon Test (n=1) and coefficient of multiple determination (R^2) (n=3). The c statistic and AUROC values for the derivation cohorts ranged from 0.60 to 0.88 (mean=0.70), with 10 models reporting a value above 0.70, indicating modest discriminative ability. Of those 10 models, only four showed similar (>0.7) model discrimination upon validation, one using an internal validation method, one in an external validation cohort only and two in both internal and external validation.

Model performance differed marginally across patient subgroups, with values ranging from 0.60 to 0.88 (mean=0.70) in resectable patients compared to 0.60 to 0.75 (mean=0.68) in patients with advanced disease (unresectable, locally advanced and metastatic). In patients with PDAC regardless of stage/treatment the c statistic ranged from 0.68 to 0.86 (mean=0.76).

Table 2. Detailed summary of prognostic models [12-58]

Source	Country[#]	Population & Setting	Model	Study Design	Recruitment Period	No. of Patients by Cohort DC	No. of Patients by Cohort VC	Outcome	Median Survival (in months) DC	Median Survival (in months) VC	Model discrimination
All											
Fontana 2016 [12]	Italy	Patients diagnosed with PDAC at a single institution.	Risk Score	Prospective	2012	27	NA	OS	NR	NA	C statistic = 0.855
Katz 2012 [13]	US	Patients with PDAC in the SEER cancer registry.	Prognostic Nomogram *(Resectable and Unresectable)*	Retrospective	1988-2005	37,135	NA	Survival (12, 18, 24, 30, 36m)	NR	NA	NR
Pu 2018 [14] (*excludes patients with metastatic disease*)	US (DC) China (VC)	Patients with confirmed PDAC and no distant metastasis were recruited from the SEER database (DC). Patients with PDAC undergoing radical resection at a single institution were recruited for the validation cohort (VC).	Prognostic Nomogram	Retrospective	2010-2014 (DC) 2012-2015 (VC)	12,343	127	OS	11.0	17.0	C statistic = 0.677 (DC) C statistic = 0.631 (VC)
Song 2018 [15]	US	Patients diagnosed with PC in the SEER database.	Prognostic Nomogram	Retrospective	2004-2014	26,583	26,445	DSS (1, 3, 5 years)	NR	NR	C statistic = 0.741 (DC) C statistic = 0.734 (VC)
Resectable											
Balzano 2017 [16]	Italy	Patients who underwent resection for PDAC were recruited at a single centre in Italy. The validation cohort was recruited from two other tertiary centres in Italy.	Risk Score	Prospective (cohort study)	2008-2012 (DC) 2009-2014 (VC)	296	182	Survival (12m)	NR	NR	C statistic = 0.72 (DC)
Brennan 2004 [17] Ferrone 2005 [18]a Clark 2008 [19]b de Castro 2009 [20]c	US (DC) US[a] (VC) UK[b] (VC) The Netherlands[c] (VC)	Patients who underwent resection for histologically confirmed PDAC at a single institution in the US and UK[b], as well as a database at a single institution in US[a] and The Netherlands[c].	Prognostic Nomogram	Prospective (cross-sectional analysis) Retrospective[a,b,c]	1983-2000 1985-2003[a] 1995-2005[b] 1985-2004[c]	555	424[a] 63[b] 263[c]	Survival (12, 24, 36m)	NR	NR[a] 10.7[b] NR[c]	C statistic = 0.64 C statistic = 0.62[a] Not Replicated[b] C statistic = 0·61[c]
Dasari 2016 [21]	UK	Patients with a diagnosis of PDAC, distal cholangiocarcinoma, ampullary carcinoma or duocenal carcinoma who went on to have a PD were recruited at a single institution in the UK. The validation cohort was then recruited from another institution's database.	Prognostic Index	Retrospective	2004-2013 (DC) 2008-2013 (VC)	567	194	Survival (12, 36m)	NR	NR	C statistic = 0.77 (DC) C statistic = 0.74 (VC)
Dreyer 2018 [22]	Australia (DC) UK[a] (VC) Germany[b] (VC)	Patients with resected primary PDAC recruited through the Australian Pancreatic Cancer Genome Initiative (APGI). Validation cohorts consisted of patients who underwent resection for PDAC at a single institution in the UK[a] and Germany[b].	Prognostic Nomogram *(Preoperative and Postoperative)*	Retrospective	NR	518	198[a] 468[b]	DSS OS[b]	19.9	19.1[a] 16.3[b]	NR Cox coefficient = 0.59a[a] Cox coefficient = 0.66[b]
Hartwig 2011 [23]	Germany	Patients who underwent resection for PDAC from an electronic database at a single institution.	Risk Score	Prospective (cross-sectional analysis)	2001-2009	1071	NA	OS	NR	NA	NR

Hsu 2013 [24] Joliat 2015 [25]a	US (DC) Switzerland[a] (VC)	Patients who underwent elective PD or total pancreatectomy for PDAC at a single institution. Patients who underwent PD with curative intent for PDAC of the pancreatic head at single institution.[a]	Risk Score	Retrospective Retrospective[a]	1993-2005 2000-2012[a]	740	120[a]	Survival (12m)	18.2	19[a]	NR
Huang 2019 [72]	US (DC) Belgium[a] (VC) The Netherlands[b] (VC) Slovenia[c] (VC) Norway[d] (VC)	Patients with PDAC TNM stage I-II, who underwent surgical resection from five national cancer registries.	Prognostic Nomogram	Retrospective	2003-2014	9,519	1,105[a] 982[b] 118[c] 113[d]	Survival (1-, 2-, 3- and 5-year)	18-23	NR	C statistic = 0.60 C statistic = 0.58[a] C statistic = 0.62[b] C statistic = 0.58[c] C statistic = 0.63[d]
Li 2018 [73]	US	Patients with PDAC of the pancreatic head who underwent Pancreaticoduodenectomy from 11 Registries Research Data and seven Registries Research Data[a] of the SEER database.	Prognostic Nomogram	Retrospective	2004-2013	4,383	1,743[a]	DSS	17.0	18.0	C statistic = 0.64 (DC) C statistic = 0.65 (VC)
Lu 2017 [26]	China	Patients with PDAC who went on to have surgical resection at a single institution.	Prognostic Nomogram	Retrospective	2004-2012	79	NA	Survival (12, 36m)	NR	NA	C statistic = 0.61
Mattiucci 2010 [27] (Abstract)	Italy	Patients with PC in a large pooled National database treated with preoperative radiotherapy and optionally concurrent and adjuvant chemotherapy.	Prognostic Nomogram	Prospective (cross-sectional analysis)	1985-2008	798	NA	OS	NR	NA	AUROC = 0.59+/-0.04.
Onoe 2017 [28]	Japan	Patients with PDAC of the pancreatic head who were evaluated for the degree of vessel invasion before they underwent PD at a single institution.	Prognostic Model	Retrospective	2005-2012	103	NA	OS	NR	NA	NR
Paniccia 2015 [29]	US	Patients with histologically proven invasive PDAC who underwent pancreatic surgical resection identified via a national database.	Prognostic Nomogram	Retrospective	1998-2002	431	NA	LTS (10y)	NR	NA	C statistic = 0.770 (DC) C statistic = 0.748 (VC)
Pu 2018 [30]	US	Patients identified on the National cancer institute's SEER database as having one of the following diagnoses or procedures; pancreatic carcinoma, adenocarcinoma or infiltrating ductal carcinoma, or having had a PPPD, Whipple procedure, total pancreatectomy or extended PD.	Prognostic Nomogram	Retrospective	2010-2013	3458	NA	OS	20	NA	C statistic = 0.633
Shen 2018 [31]	China	Patients with PDAC of the head with suspected peripancreatic venous invasion preoperatively and who underwent attempted curative pancreatic resectional surgery with venous reconstruction at four institutions.	Prognostic Nomogram	Retrospective	2012-2016	178	61	OS	12.4	11.7	C statistic = 0.814 (DC) C statistic = 0.824 (VC)
Tol 2015 [32]	The Netherlands	Patients with PDAC who underwent PD at a single institution.	Prognostic Nomogram	Retrospective	1992-2012	760	NA	Survival (3y)	19	NA	C statistic = 0.658

Xu 2017 [33]	China	Patients with histologically proven PDAC who underwent PD at a single institute.	Prognostic Nomogram	Retrospective	2006-2015	265	NA	OS	NR	NA	C statistic = 0.884
Yang 2016 [34]	China	Patients with PC who underwent a surgical resection (without preoperative treatment) at a single institution.	Prognostic Nomogram	Retrospective	2004-2008	96	NA	OS	NR	NA	C statistic = 0.659
Unresectable (Not further defined)											
Cubiella 1999 [43]	Spain	Patients with PDAC not suitable for surgical resection, due to either locally advanced tumours or metastatic spread, at a single institution.	Prognostic Index	Retrospective	1990-1995	134	NA	Survival (12m)	3.11	NA	NR
Deng 2017 [44]	China	Patients with stage III or IV, pathologically proven PDAC receiving gemcitabine-based chemotherapy from three Chinese hospitals.	Prognostic Nomogram	Prospective	2004-2013	1017	509	Survival (12m)	7.2	7.1	C statistic = 0.696
Gao 2018 [74]	China	Patients with unresectable PC who received interventional therapy from a single institution.	Prognostic Nomogram	Retrospective	2010-2016	139	NA	OS	5.0	NA	C statistic = 0.701
Hamada 2014 [45]	Japan	Patients with unresectable PC receiving gemcitabine-based chemotherapy as the first-line anticancer treatment at five Japanese hospitals.	Prognostic Nomogram	Prospective	2001-2013	531	NA	Survival (12, 18m)	11.3	NA	C statistic = 0.686
Hamamoto 2015 [46] (Abstract)	*International:* Japan Taiwan	Patients with advanced PDAC enrolled in an international multicentre randomized phase III trial.	Prognostic Index	Prospective (cross-sectional analysis)	NR	834	NA	OS	NR	NR	C statistic = 0.689
Ishii 1996 [47]	Japan	Patients with unresectable or metastatic PDAC received no other treatment prior to systemic chemotherapy in phase 2 trials at a single institution.	Prognostic Index	Retrospective	1984-1993	65	NA	OS	3.9	NA	NR
Jamal 2010 [48] *Jamal 2014* [49]*a**	Canada	Patients diagnosed with unresectable PC at single institution. *Validated in patients with PDAC of the pancreatic head undergoing PD at a single institution (resectable).*[a]	Symptom Score	Retrospective *Retrospective*[a]	2001-2006 *2001-2010*[a]	94	32 *83*[a]	OS	9.0	*23*[a]	P<0.0001 Gehan's Wilcoxon Test (DC) *P=0.02 Gehan's Wilcoxon Test (VC)* *NR*[a]
Kou 2016 [50]	Japan	Patients with advanced PDAC receiving palliative chemotherapy at two institutions.	Prognostic Model	Retrospective	2006-2013	306	NA	OS	11.3	NA	C statistic = 0.658
Marechal 2007 [51]	Belgium	Patients with pathologically proven unresectable or metastatic adenocarcinoma of the pancreas at two institutions.	Prognostic Index	Retrospective	2001-2004	99	NA	OS	8.5	NA	NR
Matsubara 2010 [52]	Japan	Patients with locally advanced or metastatic PDAC that received at least two cycles of gemcitabine monotherapy at a single institution.	Prognostic Nomogram	Prospective	2002-2007	304	NA	OS	7.8	NA	C statistic = 0.672
Stocken 2008 [53]	*International:* North America	Patients with pathologically proven unresectable PC treated with	Prognostic Index	Prospective	1997-1998	653	NA	OS	4.7	NA	$R^2 = 0.26$

	Europe	marimstat, gemcitabine or a combination of the two, who were part of two international phase III British Biotech studies.									
Tingle 2018 [75]	UK	Patients with unresectable PDAC referred for palliative Chemotherapy at a single institution.	Prognostic Scoring System	Retrospective	2010-2015 2016-2017[a]	115	30[a]	OS	NR	NR	NR
Torres 2015 [54]	Spain	Patients diagnosed with Stage III and Stage IV PDAC treated with Gemcitabine and Erlotinib combined therapy at a single institution.	Prognostic Index	Retrospective	2008-2011	14	NA	OS	12.6	NA	$R^2 = 0.926$
Vienot 2017 [55]	France	Patients with histologically proven PDAC treated at a single institution.	Prognostic Nomogram	Retrospective	2003-2016	462	163	OS	NR	NR	C statistic = 0.75 (DC) C statistic = 0.63 (VC)
Xue 2015 [56]	China	Patients with pathologically proven invasive ductal carcinoma of the pancreas who were deemed unresectable due to locally advanced disease or metastases found on CT and receiving palliative chemotherapy. All patients were recruited at a single institution.	Prognostic Index	Retrospective	2006-2013	118	NA	OS	8.8	NA	NR
Yi 2011 [57]	Korea	Patients with advanced PC who received gemcitabine-based chemotherapy at a single institution.	Prognostic Model	Retrospective	1999-2008	298	NA	OS	7.0	NA	AUROC = 0.685
Zhang 2019 [76]	China	Patients with advanced (AJCC stage III and IV) PDAC receiving primary treatment at a single institution.	Prognostic Scoring System	Retrospective	2011-2015	320	NA	OS	7.7	NA	NR
Locally Advanced											
Bjerregaard 2012 [35]	Denmark	Patients with LAPC treated with CRT at a single institution.	Prognostic Model	Retrospective	2001-2010	176	NA	OS	11.5	NA	$R^2 = 0.34$
Choi 2018 [36]	South Korea	Patients with LAPC treated with concurrent CRT at a single institution.	Prognostic Nomogram	Retrospective	2004-2015	426	NA	Progression-free survival and OS	15.4	NA	C statistic = 0.656
Ikeda 2001 [37]	Japan	Patients with LAPC receiving concurrent radiotherapy and chemotherapy at a single institution.	Prognostic Index	Retrospective	1993-1998	55	NA	OS	9.9	NA	NR
Vernerey 2016 [38]	France	Patients with LAPC enrolled in an international, multicentre RCT. Validation cohort consisted of patients with LAPC treated at a single institution.	Prognostic Nomogram	Prospective	2008-2011 (DC) 2003-2013 (VC)	442	106	OS	NR	NR	C statistic = 0.60
Metastatic											
Fernandez 2018 [77]	Spain	Patients with metastatic PC receiving first-line treatment with nab-paclitaxel plus gemcitabine at 20 hospitals.	Prognostic Nomogram	Retrospective	2013-2015	210	NA	OS	7.2	NA	NR

Goldstein 2019 [78]	*International:* US Australia Austria Belgium Canada France Germany Italy Russia Spain Ukraine	Patients with metastatic PDAC, undergoing first-line therapy from a large, international, randomised phase 3 clinical trial.	Prognostic Nomogram	Retrospective	2009-2012	861	NA	OS	NR	NA	C statistic = 0.67
Hang 2018 [5]	China	Patients with metastatic PC receiving gemcitabine chemotherapy as part of one of three different clinical trials or recruited as a patient from a single institution.	Prognostic Nomogram	Retrospective	NR	445	273[a] 133[b]	OS	6.7 6.0	7.8[a] 6.1[b]	C statistic = 0.658
Morizane 2011 [39]	Japan	Patients with metastatic PDAC who had been treated with a gemcitabine-containing regimen at a single institution.	Prognostic Index	Prospective	2001-2007	409	145	OS	6.6	4.8	NR
Park 2016 [40]	South Korea	Patients with pathologically proven metastatic PDAC at a single institution	Prognostic Index	Retrospective	2006-2014	403	NA	OS	8.2	NA	C statistic = 0.731
Ueno 2000 [41]	Japan	Patients with metastatic PDAC receiving systemic chemotherapy at a single institution.	Prognostic Index	Retrospective	1984-1999	103	NA	OS	3.2	NR	NR
Wendling 2016 [42]	UK	Patients with metastatic PC in the control arm of a Phase III RCT.	Prognostic Model	Retrospective	2001-2013	271	398	OS	7.6	8.0	*Parametric Models*: AUROC = 0.68 AUROC = 0.60 *Cox Models*: AUROC = 0.65 AUROC = 0.64

Abbreviations: AUROC, Area under ROC (Receiver Operating Characteristic) Curve; CRT, chemoradiotherapy; CT, computed tomography ; DC, derivation cohort; DSS, Disease-specific survival; LAPC, locally advanced pancreatic cancer; LTS, Long-term survival; NA, Not Applicable; NR, Not reported; OS, Overall Survival; PC, pancreatic cancer; PD, pancreatoduodenectomy; PDAC, Pancreatic ductal adenocarcinoma; PPPD, pylorus-preserving pancreatoduodenectomy; RCT, Randomised Control Trial; SEER, Surveillance, Epidemiology and End Results; VC, validation cohort.

*This study was conducted to determine the ability of the model to predict survival in resectable patients.

[#]Country where patients were recruited from.

Use of Variables in Models

The number of prognostic factors evaluated ranged from 6 to 54 with a median of 16. Following evaluation, the number of prognostic factors selected for inclusion in the models ranged from 2 to 14 with an average a median of 5 (see Table 3). There were no variables which were unanimously found to be predictive of survival, when included in more than one study. The prognostic factors that were most frequently *evaluated* (in univariate analysis) for inclusion were: age (98.0%), sex (89.8%), tumour site/location (61.2%), performance status (51.0%) and CA 19-9 (51.0%). Of the variables evaluated, the prognostic factors most frequently *included* in the final models were: lymph node ratio (83%), tumour volume/size (71%), performance status (68%), tumour grade (68%), serum CRP (63%), metastatic stage (62%) and liver metastasis (60%).

Of the models developed in patients with resectable disease, tumour grade, T stage and resection margin status were the most prevalent prognostic factors included in survival models. They were included in 12/14 (85.7%), 7/11 (63.6%) and 5/10 (50.0%) of models where they were examined, respectively. Lymph node ratio was examined in fewer studies but found to be predictive of survival in five of the six studies where it was examined. Of the models developed in patients with advanced disease, performance status (included in 16 out of 20 models (80.0%)), liver metastasis (6/9 (66.7%)) and serum CA 19-9 (13/23 (56.5)), were the most prevalent prognostic factors included in survival models. Of the models developed in all patients with PDAC, regardless of stage or treatment, the most prevalent prognostic factors included in survival models were age, tumour grade and AJCC TNM staging and primary tumour resection.

Table 3a. Variables considered by studies for inclusion in prognostic models

	Evaluated (Univariate)	Evaluated (Multivariate)	Significant (Multivariate)	Included in Final Model	Patient Demographics								Comorbidities									Biomarkers (Serum Chemistry & Haematology)								Primary Tumour Details			
					Age	*Sex*	*Race*	*Marital Status*	*Education Level*	*Insurance Status*	*Income*	*Other*	*Performance Status*	*Diabetes*	*Weight*	*BMI*	*Pain*	*Jaundice*	*Smoking*	*Comorbidity (General)*	*Alcohol*	*Other*	*Serum CA 19-9*	*Serum CEA*	*Serum CRP*	*Albumin*	*NLR*	*Haemoglobin*	*WBC/Leukocytes*	*Other*	*Site/Location*	*Size*	*Differentiation/Grade*	*Type/Histology*
All Stages																																
Fontana 2016 [12]	17•	NR	4	5																												
Pu 2017 [14]	8	6	5	5	■																										■	
Song 2018 [15]	9	8	7	7	■		■	■																						■	■	
Resectable																																
Balzano 2017 [16]	54	13	4	4									■				■					■										
Brennan 2004 [17]	NR	NR	NR	14	■	■									■		■													■		■
Dasari 2016 [21]	16	6	3	3																												
Dreyer 2018 [22]*	15	11	6[b]; 7[b]	5[a]; 9[b]	a,b																									a	a,b		b	
Hartwig 2011 [23]	21	8	8	8	■									■								■										
Hsu 2013 [24]	15	NA•	NA	4	■															■												■	■
Huang 2019 [72]	18	7	6	5	■	■																										
Katz 2012 [13]#	NR	7	7	7	■	■	■																								■	■
Li 2018 [73]	11	8	8	8	■	■																									■	■
Lu 2017 [26]	11	11	2	2										■					■		■											
Mattiucci 2010 [27]	14•	NR	NR	NR																												
Onge 2017 [28]	14	11	2	2																												
Panniccia 2015 [29]	23•	10	10	10	■				■	■																					■	■
Pu 2018 [30]	12	9	4	4	■																											■
Shen 2018 [31]	8	6	4	4	■																											
Tol 2015 [32]	22•	6	4	4												■																■
Xu 2017 [33]	11	6	6	6																						■			■			■
Yang 2016 [34]	10	3	1	2																									■			
Unresectable (Not further defined)																																
Cubiella 1999 [43]	34	8	2	2									■																				
Deng 2017 [44]	13	7	7	7	■																	■				■						
Gao 2018 [74]	22	11	3	3																			■						■			
Hamada 2014 [45]	6	6	4	6	*	*							■																		■	
Hamamoto 2015 [46]	27^	NR	NR	10	■																			■			■		■			
Ishii 1996 [47]	14	5	3	3									■																			
Jamal 2010 [48]	9•	NR	2	4											■		■	*	*													
Katz 2012 [13]#	NR	7	7	7	■	■	■																								■	

Kou 2016 [50]	12	10	6	6																														
Marechal 2007 [51]	25	10	5	5																														
Matsubara 2010 [52]	15	4	4	4																														
Stocken 2008 [53]	18	9	9	8																														
Tingle 2018 [75]	10	10	2	2																														
Torres 2015 [54]	9	5	3	5																														
Vienot 2017 [55]	51	9	9	9																														
Xue 2015 [56]	14	6	3	3																														
Yi 2011 [57]	26	4	4	4																														
Zhang 2019 [76]	12	7	5	3																														
Locally Advanced																																		
Bierregaard 2012 [35]	17	9	3	9																														
Choi 2018 [36]	14	6	4	4																														
Ikeda 2001 [37]	19	4	3	3																														
Vernerey 2016 [38]	30	8	5	5																														
Metastatic																																		
Fernandez 2018 [77]	19•	3	3	3																														
Goldstein 2019 [78]	32	18	5	6																														
Hang 2018 [5]	24	15	7	5																														
Morizane 2011 [39]	24	14	4	4																														
Park 2016 [40]	23	17	5	5																														
Ueno 2000 [41]	20	6	3	3																														
Wendling 2016 [42]	31	11	2	12																														
Evaluated					48	44	8	2	1	2	1	NA	25	12	9	9	11	7	10	3	4	NA	25	13	8	20	10	15	10	NA	30	21	22	2
Included					18	6	2	1	1	1	0	NA	17	2	3	0	6	2	2	1	0	NA	14	4	5	8	5	2	4	NA	6	8	15	1
%					38	14	25	50	100	50	0	NA	68	17	33	0	55	29	20	33	0	NA	56	31	63	40	50	13	40	NA	20	38	68	50

Footnote: Uncoloured cells represent that the factor was not considered for inclusion. Abbreviations: NA – Not Applicable; NR – Not reported.

Katz 2012 was in all patients (regardless of stage) but Individual models were developed for resectable and unresectable patients, therefore it is reported in this table under both resectable and unresectable.

+Dreyer 2018 developed two prognostic models a) preoperative and b) postoperative.

^The variables evaluated were not listed in the publication.

•No univariate and/or multivariate analysis was undertaken.

*Variable was included in final model but was not statistically significant in multivariate analysis.

Table 3b. Variables considered by studies for inclusion in prognostic models

	Evaluated (Univariate)	Evaluated (Multivariate)	Significant (Multivariate)	Included in Final Model	Staging				Radiological Features								Surgical									Non-Surgical Treatment			
					T Stage	*N Stage*	*M Stage*	*AJCC TNM Stage*	*Volume/Size*	*Perineural invasion*	*Vascular invasion*	*Invasion/Extension Other*	*Liver Metastases*	*Peritoneum Metastases*	*Distant Mets/Mets Other*	*Other*	*Resection*	*Resection Margin Status*	*Procedure Type*	*Surgical Complications*	*Lymph Node Dissection*	*No. of nodes Examined*	*No. of positive nodes*	*LNR*	*Other*	*Chemo - Adjuvant*	*Chemo - Neoadjuvant*	*Radiotherapy*	*Other*
All Stages																													
Fontana 2016 [12]	17•	NR	4	5																									
Pu 2017 [14]	8	6	5	5																									
Song 2018 [15]	9	8	7	7																									
Resectable																													
Balzano 2017 [16]	54	13	4	4																									
Brennan 2004 [17]	NR	NR	NR	14																									
Dasari 2016 [21]	16	6	3	3																									
Dreyer 2018 [22]+	15	11	6a; 7b	5a; 9b	b	*b			a,b	b	b																		
Hartwig 2011 [23]	21	8	8	8																									
Hsu 2013 [24]	15	NA•	NA	4																									
Huang 2019 [72]	18	7	6	5																									
Katz 2012 [13]#	NR	7	7	7																									
Li 2018 [73]	11	8	8	8																									
Lu 2017 [26]	11	11	2	2																									
Mattiucci 2010 [27]	14•	NR	NR	NR																									
Onoe 2017 [28]	14	11	2	2																									
Paniccia 2015 [29]	23•	10	10	10																									
Pu 2018 [30]	12	9	4	4																									
Shen 2018 [31]	8	6	4	4																									
Tol 2015 [32]	22•	6	4	4																									
Xu 2017 [33]	11	6	6	6																									
Yang 2016 [34]	10	3	1	2				*																					
Unresectable (Not further defined)																													
Cubiella 1999 [43]	34	8	2	2																									
Deng 2017 [44]	13	7	7	7																									
Gao 2018 [74]	22	11	3	3																									
Hamada 2014 [45]	6	6	4	6																									
Hamamoto 2015 [46]	27^	NR	NR	10																									
Ishii 1996 [47]	14	5	3	3																									
Jamal 2010 [48]	9•	NR	2	4																									

Katz 2012 [13]#	NR	7	7	7																											
Kou 2016 [50]	12	10	6	6																											
Marechal 2007 [51]	25	10	5	5																											
Matsubara 2010 [52]	15	4	4	4																											
Stocken 2008 [53]	18	9	9	8																											
Tingle 2018 [75]	10	10	2	2																											
Torres 2015 [54]	9	5	3	5																											
Vienot 2017 [55]	51	9	9	9																											
Xue 2015 [56]	14	6	3	3																											
Yi 2011 [57]	26	4	4	4																											
Zhang 2019 [76]	12	7	5	3																											
Locally Advanced																															
Bjerregaard 2012 [35]	17	9	3	9				*																							
Choi 2018 [36]	14	6	4	4																											
Ikeda 2001 [37]	19	4	3	3																											
Vernerey 2016 [38]	30	8	5	5																											
Metastatic																															
Fernandez 2018 [77]	19•	3	3	3																											
Goldstein 2019 [78]	32	18	5	6																											
Hang 2018 [5]	24	15	7	5																											
Morizane 2011 [39]	24	14	4	4																											
Park 2016 [40]	23	17	5	5																											
Ueno 2000 [41]	20	6	3	3																											
Wendling 2016 [42]	31	11	2	12																											
				Evaluated	14	21	13	22	7	5	4	9	10	7	10	NA	12	10	9	5	1	8	8	6	NA	12	5	6	NA
				Included	7	4	8	9	5	1	2	3	6	2	0	NA	7	5	0	0	0	2	2	5	NA	2	1	2	NA
				%	50	19	62	41	71	20	50	33	60	29	0	NA	58	50	0	0	0	25	25	83	NA	17	20	33	NA

Footnote: Uncoloured cells represent that the factor was not considered for inclusion. Abbreviations: NA – Not Applicable; NR – Not reported.

Katz 2012 was in all patients (regardless of stage) but Individual models were developed for resectable and unresectable patients, therefore it is reported in this table under both resectable and unresectable.

+Dreyer 2018 developed two prognostic models a) preoperative and b) postoperative.

^The variables evaluated were not listed in the publication.

•No univariate and/or multivariate analysis was undertaken.

*Variable was included in final model but was not statistically significant in multivariate analysis.

Key Prognostic Factors

A total of 35 models reported hazard ratios with 95% confidence intervals for key prognostic factors (see Table 4). The prognostic factors that most strongly predicted improved survival were resection of primary tumour (mean HR=0.23), high performance status (mean HR= 0.57) and lower T stage (mean HR=0.59). Normal CA 19-9 (mean HR=0.48), normal serum CRP (mean HR=0.49) and receiving neoadjuvant chemotherapy were found to be significant prognostic factors in only one model. The prognostic factors that were shown to predict poorer survival were: poor performance status (mean HR=2.91), high lymph node ratio (mean HR=2.87), low serum albumin (2.58) and no resection of primary tumour (mean HR=2.22). Decreased weight (mean HR=3.01) was found to be a significant prognostic factors in only one model.

Table 4. Summary of Hazard Ratio for prognostic factors included in prognostic models

Variables *(Reduced Risk/Increased Risk)*	**All Studies (n=35)**					**Resectable (n=13)**					**Unresectable (n=21)**				
		Reduced Risk (<1)		*Increased Risk (>1)*			*Reduced Risk (<1)*		*Increased Risk (>1)*			*Reduced Risk (<1)*		*Increased Risk (>1)*	
	Studies (n)	Range	Mean	Range	Mean	Studies (n)	Range	Mean	Range	Median	Studies (n)	Range	Median	Range	Median
Patient Demographics															
Age *(Decreasing/Increasing)*	13	NA	NA	1.01-1.78	1.23	7	NA	NA	1.01-1.78	1.20	4	NA	NA	1.01-1.53	1.24
Sex (Female/*Male*)	4	0.91-0.96	0.94	1.1	1.1	3	0.91-0.96	0.94	1.1	1.1	1	0.95	0.95	NA	NA
Comorbidities															
Performance Status *(Good/Poor)*	10	0.27-0.98	0.57	1.36-8.15	2.91	0	NA	NA	NA	NA	10	0.27-0.98	0.57	1.36-8.15	2.91
Diabetes *(Yes)*	1	NA	NA	1.53	1.53	0	NA	NA	NA	NA	1	NA	NA	1.53	1.53
Weight *(Increasing/Decreasing)*	1	NA	NA	3.01	3.01	0	NA	NA	NA	NA	1	NA	NA	3.01	3.01
Pain *(No/Yes)*	3	NA	NA	1.29-1.69	1.46	0	NA	NA	NA	NA	3	NA	NA	1.29-1.69	1.46
Jaundice *(No/Yes)*	1	NA	NA	1.96	1.96	0	NA	NA	NA	NA	1	NA	NA	1.96	1.96
Smoking *(No/Yes)*	1	NA	NA	1.5	1.5	0	NA	NA	NA	NA	1	NA	NA	1.5	1.5
Biomarkers															
CA 19-9 *(Normal/Elevated)*	12	0.48	0.48	1.02-2.70	1.64	1	NA	NA	1.48	1.48	11	0.48	0.48	1.02-2.70	1.65
CEA *(Normal/Elevated)*	3	NA	NA	1.46-2.43	1.51	0	NA	NA	NA	NA	3	NA	NA	1.46-2.43	1.51
CRP *(Normal/Elevated)*	3	0.49	0.49	1.54-1.57	1.56	0	NA	NA	NA	NA	3	0.49	0.49	1.54-1.57	1.56
Albumin *(Normal/Low)*	7	0.94-0.96	0.95	1.70-4.06	2.58	0	NA	NA	NA	NA	7	0.94-0.96	0.95	1.70-4.06	2.58
NLR *(Normal/Elevated)*	4	NA	NA	1.05-2.54	1.61	1	NA	NA	1.06	1.06	3	NA	NA	1.05-2.54	1.79
Haemoglobin *(Normal/Low)*	1	NA	NA	1.36	1.36	0	NA	NA	NA	NA	1	NA	NA	1.36	1.36
WBC *(Normal/Low)*	3	NA	NA	1.04-1.77	1.28	0	NA	NA	NA	NA	3	NA	NA	1.04-1.77	1.28
Primary Tumour Details															
Site/Location *(Head/Body or Tail)*	4	0.83-0.89	0.86	1.10-2.67	1.63	2	NA	NA	1.11-2.67	1.89	1	NA	NA	1.10	1.10
Size *(Decreasing/Increasing)*	7	NA	NA	1.01-1.60	1.26	3	NA	NA	1.20-1.60	1.39	3	NA	NA	1.01-1.07	1.03
Differentiation/Grade *(Good/Poor)*	12	0.48-0.81	0.66	1.07-3.88	1.91	9	0.48-0.81	0.66	1.31-3.88	1.96	1	NA	NA	1.31	1.31
Staging															
T Stage *(Decreasing/Increasing)*	5	0.17-0.86	0.59	1.15-1.83	1.51	5	0.17-0.86	0.59	1.15-1.83	1.51	0	NA	NA	NA	NA
N Stage *(Decreasing/Increasing)*	5	0.51-0.78	0.68	1.28-2.43	1.78	4	0.51-0.78	0.68	1.42-2.43	1.88	1	NA	NA	1.28	1.28
M Stage *(M0/M1)*	5	NA	NA	1.29-1.88	1.68	2	NA	NA	1.66-1.88	1.77	3	NA	NA	1.29-1.87	1.61
AJCC TNM Stage *(Decreasing/Increasing)*	8	NA	NA	1.05-2.68	1.71	2	NA	NA	1.74-2.68	2.21	4	NA	NA	1.11-2.22	1.49
Radiological Features															
Volume/Size *(Decreasing/Increasing)*	4	NA	NA	1.02-1.44	1.22	2	NA	NA	1.14-1.44	1.32	2	NA	NA	1.02-1.14	1.08
Invasion/Extension *(No/Yes)*	5	NA	NA	1.26-3.21	1.94	5	NA	NA	1.26-3.21	1.94	0	NA	NA	NA	NA
Liver Mets *(No/Yes)*	5	NA	NA	1.42-2.63	1.83	0	NA	NA	NA	NA	5	NA	NA	1.42-2.63	1.83
Peritoneum Mets *(No/Yes)*	1	NA	NA	1.76	1.76	0	NA	NA	NA	NA	1	NA	NA	1.76	1.76
Surgery															
Resection *(Yes/No)*	6	0.12-0.33	0.23	1.50-2.87	2.22	0	NA	NA	NA	NA	4	0.12	0.12	1.50-2.87	2.03
Resection Margin Status *(R0/R1 or R2)*	4	0.64	0.64	1.62-1.36	1.80	4	0.64	0.64	1.62-1.36	1.80	0	NA	NA	NA	NA

No. of Nodes Examined *(Increasing/Decreasing)*	3	0.66-0.99	0.86	NA	NA	2	0.66-0.99	0.83	NA	NA	0	NA	NA	NA	NA
No. of Positive nodes *(Decreasing/Increasing)*	2	NA	NA	1.05-2.17	1.49	2	NA	NA	1.05-2.17	1.49	0	NA	NA	NA	NA
Lymph Node Ratio *(Decreasing/Increasing)*	5	NA	NA	1.34-6.79	2.87	5	NA	NA	1.34-6.79	2.87	0	NA	NA	NA	NA
Non-Surgical Treatment															
Chemo - Adjuvant *(Yes/No)*	1	NA	NA	1.54	1.54	1	NA	NA	1.54	1.54	0	NA	NA	NA	NA
Chemo - Neoadjuvant *(Yes/No)*	1	0.57	0.57	NA	NA	0	NA	NA	NA	NA	1	0.57	0.57	NA	NA
Radiotherapy *(Yes/No)*	2	0.71	0.71	NA	NA	1	0.71	0.71	NA	NA	1	0.71	0.71	NA	NA

Footnote: Only hazard ratios (HR) that are significant (95% confidence interval does not include 1) are reported in this table. A total of 14/49 studies were excluded from this analysis. Fontana 2016 and Torres 2015 included biomarkers not reported by other studies so were not included. Balzano 2017, Paniccia 2015, Cubiella 1999, Jamal 2010 and Ueno 2000 reported Odds Ratio or Risk Ratio instead of HR so were excluded. Brennan 2004, Hsu 2013, Mattiucci 2010, Fernandez 2018, Wendling 2016, Hamamoto 2015 and Ishii 1996 were also excluded as HR were not reported. Katz 2012 was in all patients (regardless of stage) but Individual models were developed for resectable and unresectable patients, therefore it is reported in this table under both resectable and unresectable.

Risk of Bias Assessment

We assessed 47 of the 49 studies reporting on the development of unique prognostic models for risk of bias. Two of the studies were reported in abstracts only and did not provide sufficient data to conduct a risk of bias assessment. Of the 47 studies assessed, 20 (42.6%) were rated as having an overall low risk of bias, 21 (44.7%) with a moderate overall risk of bias and six (12.8%) with a high overall risk of bias (see Table 5). The domains with the highest risk of bias was study attrition (prospective studies only), measurement of prognostic factors, and reporting of the statistical analysis.

Table 5. Risk of Bias Assessment

Study	Overall Bias	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Statistical Analysis & Reporting
All PC						
Fontana 2016 [12]	High	Moderate	High	Moderate	Low	Low
Katz 2012 [13]	Low	Low	NA	Low	Low	Moderate
Pu 2017 [14]	Low	Low	NA	Low	Low	Low
Song 2018 [15]	Low	Low	NA	Low	Low	Low
Resectable PC						
Balzano 2017 [16]	Moderate	Low	High	Moderate	Low	Low
Brennan 2004 [17]	Moderate	Moderate	NA	Low	Low	Moderate
Dasari 2016 [21]	High	Moderate	NA	Moderate	Moderate	Low
Dreyer 2018 [22]	Moderate	Moderate	NA	Low	Low	Moderate
Hartwig 2011 [23]	High	Low	NA	Moderate	Moderate	Moderate
Hsu 2013 [24]	Moderate	Low	NA	Moderate	Low	Moderate
Huang 2019 [72]	Low	Low	NA	Low	Moderate	Low
Li 2018 [73]	Low	Low	NA	Low	Moderate	Low
Lu 2017 [26]	High	High	NA	Moderate	Moderate	Low
Mattiucci 2010 [27]*	-	-	-	-	-	-
Onoe 2017 [28]	Low	Low	NA	Low	Low	Moderate
Paniccia 2015 [29]	Low	Low	NA	Moderate	Low	Low
Pu 2018 [30]	Low	Low	NA	Low	Low	Low
Shen 2018 [31]	Moderate	Low	NA	Low	High	Low
Tol 2015 [32]	Low	Low	NA	Low	Low	Low
Xu 2017 [33]	Low	Low	NA	Low	Low	Low
Yang 2016 [34]	Low	Moderate	NA	Low	Low	Low
Unresectable (Not further defined)						
Cubiella 1999 [43]	Moderate	Low	NA	Moderate	Low	Moderate
Deng 2017 [44]	High	Low	Moderate	Moderate	Low	Moderate
Gao 2018 [74]	Moderate	Moderate	NA	Low	Moderate	Moderate
Hamada 2014 [45]	High	Low	High	High	Low	Low
Hamamoto 2015 [46]*	-	-	-	-	-	-
Ishii 1996 [47]	Moderate	Moderate	NA	Low	Low	Moderate
Jamal 2010 [48]	Low	Low	NA	Low	Low	Moderate
Kou 2016 [50]	Low	Low	NA	Low	Low	Low
Marechal 2007 [51]	Low	Low	NA	Low	Low	Moderate
Matsubara 2010 [52]	Moderate	Low	High	Low	Low	Low
Stocken 2008 [53]	Moderate	Moderate	High	Low	Low	Low
Tingle 2018 [75]	Moderate	Moderate	NA	Moderate	Moderate	Low
Torres 2015 [54]	Moderate	Moderate	NA	Moderate	Low	Low
Vienot 2017 [55]	Low	Low	NA	Moderate	Low	Low
Xue 2015 [56]	Moderate	Low	NA	Moderate	Low	Moderate
Yi 2011 [57]	Low	Low	NA	Moderate	Low	Low
Zhang 2019 [76]	Moderate	Low	NA	Moderate	Low	Moderate
Locally Advanced						
Bjerregaard 2012 [35]	Low	Low	NA	Low	Low	Low
Choi 2018 [36]	Moderate	Moderate	NA	Moderate	Low	Low
Ikeda 2001 [37]	Moderate	Moderate	NA	Low	Low	Moderate
Vernerey 2016 [38]	Low	Low	Low	Moderate	Low	Low
Metastatic						

Study	Overall Bias	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Statistical Analysis & Reporting
Fernandez 2018 [77]	Moderate	Moderate	NA	Moderate	Low	Moderate
Goldstein 2019 [78]	Moderate	Moderate	NA	Low	High	Low
Hang 2018 [5]	Moderate	Moderate	NA	Moderate	Low	Low
Morizane 2011 [39]	Moderate	Low	High	Low	Low	Moderate
Park 2016 [40]	Low	Low	NA	Low	Low	Low
Ueno 2000 [41]	Moderate	Low	NA	Moderate	Low	Moderate
Wendling 2016 [42]	Low	Low	NA	Low	Low	Low

Footnote: Study quality and bias assessed using Quality in Prognostic Studies (QUIPS) tool. Overall bias was calculated based on summary ratings for each of the five domains. Abbreviations: NA – Not Applicable.
*Studies published as abstracts only, not sufficient data to conduct risk of bias assessment. Risk of bias due to confounding not assessed, as deemed not relevant.

Discussion

In this systematic review, we identified 49 unique prognostic models predicting survival of patients with PDAC. Only four of the models were developed to predict survival from diagnosis, regardless of whether the patient was classified as having resectable, unresectable, local advanced or metastatic disease. Furthermore, most models were developed based on retrospective data, many had a moderate to high risk of bias and performed poorly, with only four models reporting moderate discrimination in both the derivation and validation cohorts.[15, 16, 21, 29, 31]

Study Design

A prospective study design is preferable for developing prognostic models as it enables optimal measurement of prognostic factors and outcome/s. However, studies using retrospective data have the benefit of longer-term follow-up and high generalisability, albeit usually at the expense of data quality.[59] Very few models in this review were developed using prospective data. While prospective models might be less generalizable, they are more adept for use in a clinical setting or for the identification of patients for therapeutic research such as randomised control trials (RCTs).[5, 7] Models developed and validated using retrospective data are more useful in a research setting, in particular to provide risk-adjusted comparison data; for example, to compare differences in performance between hospitals.[5, 7]

The ideal sample size for prognostic model generation has been widely discussed, with sample size and power calculations requiring justification.[60] A recent review noted that studies used for developing prognostic models often have relatively small sample sizes for the complex challenges posed by identifying factors and effect, and a large sample size is required to reduce the number of potential biases arising from conducting these analyses.[60] Only 15 out of the 43 models (36%) used a sample size greater than 500 for their derivation

cohort [ref these two studies]. Of the four models showing moderate discriminative ability, all were developed using retrospective data; yet only two had a derivation sample size greater than 500 and the other two had derivation sample sizes of 178 and 431, respectively.[29, 31]

There are numerous types of prognostic models such as nomograms, prognostic indexes, predictive models and risk prediction models.[61] Nomograms are graphical tools that generate a valid numerical probability of a clinical outcome for each patient; they are increasingly being developed and used across numerous cancer types.[5, 62] Furthermore, nomograms have been shown to be equivalent, and in some cases superior, to the AJCC TNM staging system in various tumour types, leading to advocacy of their use in standard practice, instead of or as an expansion of the standard staging system.[62] Three of the four moderately performing models were nomograms, with one developing a prognostic index.[21]

Model Validation and Discrimination

Validation is a critical step in developing a prognostic model, yet only 34 (69.2%) models were validated, 18 (52.9%) using an external cohort of patients. The remaining were internally validated using either split-sample, cross-validation or bootstrapping techniques. Lack of external validation limits generalisability and transportability of the model.[63] In addition to external validation with an independent data set from a different location, it is also strongly suggested that external validation should be performed by different authors to those who developed the model.[64] Of the 18 models that were externally validated, 12 (66.7%) were validated using an independent data set,[14-17,21,22, 24, 31,38,55,72,73] while only two (11.1%) were validated by different authors than those who developed the model.[17,24]

Model discrimination is an important component of determining model performance, as it evaluates the ability of the model to differentiate between low- and high-risk patients. Only 35 (71.4%) of the reviewed models reported model discrimination, with four reporting a c-statistic above 0.7 in both the derivation and validation cohorts indicating moderate model performance. Furthermore, all but one of these models were externally validated; the fourth was internally validated using a split-sample approach.[15, 21, 29, 31] In all cases, external validation was undertaken within the same country on a similar patient cohort by the same authors who developed the model using data from another institution[21, 31] or a validation cohort from a national database[15].

Prognostic Factors

For model development, identifying prognostic factors should be based on prior research or sound clinical reasoning in order to minimise the risk of failing to consider or evaluate factors that might have a significant impact on outcome.[60, 62] However, data availability appears to be a major issue in the development of these models, resulting in decreased prognostic accuracy.[62] This is especially the case in models derived from multicentre or population-based cohorts, with many potentially prognostic factors being less likely to be routinely and consistently recorded, leading to a large number of published models selecting prognostic factors based on data availability.[65]

In order for models to be useful in a clinical and/or research setting the factors need to be readily available in the patient medical record for all patients, as well as recorded accurately and consistently. Furthermore, for models that are used to provide risk-adjusted comparison data, the factors need to outside the control of the clinicians and health services.[66] Two key prognostic factors that were identified in this review to be significant predictors of both improved survival and poorer survival from PDAC were performance status and whether the patient underwent resection of primary tumour. However, while a patient's surgical status is recorded routinely and accurately, performance status is not routinely recorded nor is it consistently measured, with different clinicians and health services using different performance scales (i.e. Eastern Cooperative Oncology Group (ECOG), Karnofsky Performance Status (KPS), American Society of Anaesthesiologists (ASA) score, World Health Organisation performance status classification etc.). Of the 25 models that evaluated performance status, 16 measured performance using the ECOG (64.0%), three the ASA score (12.0%), two the WHO (8.0%) and two the KPS (8.0%), while two models did not report the tool used to measure performance (8.0%). Therefore, while performance status is an important prognostic factor for survival in patients with PDAC, the use of this factor in prognostic models in a clinical setting is problematic. Further efforts to include performance status in risk prediction models need to consider the multitude of instruments used to measure this risk factor. Crosswalk studies may be required to substitute one instrument for another.

Of the four models in this review reporting moderate discriminative ability, only one was developed in all patients with PDAC, regardless of operability or stage, with an appropriate sample size, rigorous validation and low overall risk of bias.[15] The prognostic factors used in this model included age, tumour location, tumour grade, AJCC TNM staging, surgery status, tumour size, marital status and race. According to the AJCC TNM Staging system, clinical

staging of PDAC may be obtained from physical examination and three-dimensional radiographic imaging studies and that, if appropriate clinical and radiographic findings are present, preoperative biopsy is not necessary before resection. Clear documentation of stage based on either radiology or pathology remains a major challenge in health services and in particular in patients with unresectable disease.[9] While a model which includes only eight variables such as this model offers promise in providing risk-adjusted comparison data, the lack of clear documentation of TNM stage makes it challenging to use in clinical settings.

Limitations

This review was limited to papers published in English language and referenced in the databases searched. Given the heterogeneity of factors assessed in each study, the tools used to capture these risk factors and cut points used, it was not possible to undertake pooled analysis of studies.

Conclusions & Future Directions

Prognostic models have the potential to provide a more accurate estimate of survival, given known patient-related factors, than clinical judgment alone. They enable assessment and comparison of health outcomes after known patient risk factors are taken into account. With the increase in number and sophistication of cancer prognostic models it is necessary to ensure they are developed, evaluated and applied appropriately.[67] Future activity should focus on developing standardised nomograms to enable international comparisons of health outcomes to be undertaken. This will require not just the standardization of risk factors but also standardizing of data definitions and time points for data collection. The International Consortium for Health Outcomes Measurement (ICHOM) have developed standardized datasets for 26 health conditions, but, as yet, a set for pancreatic cancer has not been developed.[68]

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