



# Early Detection in Pancreatic Cancer

## Environment Report

September 2023

Prepared by Moira Clay Consulting Pty Ltd for  
PanKind The Australian Pancreatic Cancer Foundation



**The Australian Pancreatic  
Cancer Foundation**

## Table of Contents

Executive Summary.....	4
Introduction.....	5
Part 1: Publication analysis.....	7
Global publications (2019 – present) .....	7
Australian publications (2019 – present) .....	10
Part 2: Funding Analysis .....	13
Part 3: Translational Research.....	16
Global.....	16
GRAIL LLC.....	16
Biological Dynamics Inc. ....	17
Immunovia .....	17
Australia .....	17
AdvanCell Isotopes.....	17
Clinical trials .....	18
Part 4: Stakeholder Consultation .....	20
Conclusions .....	22
References .....	23
Appendix 1: Australian competitive grants for pancreatic cancer (2019-present) .....	26
Appendix 2: External stakeholders that participated in online consultation .....	28



## Tables and Figures

Table 1: Metrics for global publications on early detection in pancreatic cancer .....	8
Table 2: Metrics for Australian publications on early detection in pancreatic cancer .....	10
Table 3: Top three Australian researchers with corresponding authorships (2019-present) .....	10
Table 4: NHMRC research funding for pancreatic cancer research (2019-present).....	13
Table 5: NHMRC pancreatic cancer research funding by research areas (2019-present) .....	14
Table 6: Researchers awarded NHMRC pancreatic cancer research funding (2019-present) .....	14
Table 7: Researchers awarded PanKind early detection research funding (2019-present).....	15
Table 8: Australian clinical trials in the early detection of pancreatic cancer .....	19
Figure 1: Author network for global publications on early detection in pancreatic cancer.....	9
Figure 2: Keyword network in global publications on early detection in pancreatic cancer .....	9
Figure 3: Author network for Australian publications on early detection of pancreatic cancer.....	11
Figure 4: Keyword network in Australian publications on early detection of pancreatic cancer .....	12



## Executive Summary

This report presents an analysis of research on early detection of pancreatic cancer.

A comprehensive analysis of global research publications focused on the early detection of pancreatic cancer indicated this field is a relatively active research space consisting of publications of high quality and with global impact. Network analysis demonstrates that global researchers are highly collaborative and connected, with their research focused across 5 major themes - early detection and screening, clinical studies and staging of patients, biomarkers and experimental research, cancer chemotherapy and diabetes and other incidence factors. Australian research publications have a lower impact, with all research publications below global average. Research appears to be largely focused across two main themes - early detection and clinical studies and biomarkers. Dr Alina Stoita and Professor Marco Falasca were the leading corresponding authors with respect to the number of research publications in the early detection of pancreatic cancer within Australia. However, it is important to note that the total number of research publications with the corresponding author in Australia is very low, indicating that this is still a developing research area as compared to internationally. Network analysis indicates a fragmented, siloed nature of research in this field within Australia,

The total amount of research funding allocated to Australian institutions for pancreatic cancer research between 2019 and present is \$38.5M. Just over 23.9% of the funding was directed towards building capacity through funding people and teams (including fellowships, scholarships and investigator grants) and the balance towards funding specific research projects and programs. The NHMRC (45.2%) was the largest funder of Australian early detection of pancreatic cancer research, followed by PanKind (28.8%) and the MRFF (26.0%). Research focused on the early detection of pancreatic cancer received 23.1% and 29.6% of total funding from the NHMRC and MRFF respectively. No funding has been awarded to pancreatic cancer from Cancer Australia or its funding partners between 2019 – present.

An analysis of translational research activities across the clinical and commercial sectors was also performed. Of all the clinical trials available for patients with pancreatic cancer, 14.3% of clinical trials are focused specifically on early detection or diagnosis at various locations across Australia. A number of international companies have now developed blood-based diagnostic tests marketed for the early detection of pancreatic cancer. These are at various stages of clinical trial development at sites throughout Europe and the US, with some of these tests available for order by a healthcare professional. At present, none of these blood-based diagnostic tests are currently available in Australia. AdvanCell isotopes is an Australian company with the capability to develop a highly sensitive and specific imaging agent for the early detection of pancreatic cancer. AdvanCell are currently focused on developing novel targeted alpha therapies for a range of cancers, with a clinical trial in pancreatic cancer due to commence in 2026.

Consultations with stakeholders indicated that early detection of pancreatic cancer is an urgent priority to improve survival rates. Several challenges for achieving this were raised, all pointing to the need for a strategic approach for developing a comprehensive interdisciplinary research program incorporating multiple scientific teams, technologies together with clinical and industry partners. The fragmented nature of research in Australia with reduced collaboration was echoed in consultations and highlighted as a significant factor limiting opportunity for breakthroughs in this space.

The analysis of early detection of pancreatic cancer research has demonstrated there is the base foundation and strong interest to develop further research capacity and capability in the early detection of pancreatic cancer within Australia and internationally. A strategic approach, in addition to both increased and sustained research funding, was highlighted as crucial to develop capacity and capability within Australia and address the unmet needs in this area.



## Introduction

Pancreatic cancer is a highly invasive digestive system tumour with an extremely poor prognosis. It is currently the third most common cause of cancer-related death in Australia and is projected to become the second leading cause of cancer-related death by 2030<sup>a1</sup>. Five-year survival rates for individuals diagnosed with pancreatic cancer is approximately 12%<sup>2</sup>, due to the overwhelming majority of patients diagnosed with locally advanced or distant metastatic disease<sup>3</sup>. Pancreatic cancer is typically diagnosed using multiple imaging modalities, preferably dynamic contrast-enhanced computed tomography (CT), but can also include transabdominal ultrasound and/or abdominal magnetic resonance imaging (MRI)<sup>4</sup>. Endoscopic ultrasonography (EUS) is increasingly used for high-resolution spatial imaging of the pancreas and to obtain a cytologic or histologic specimen via EUS-guided fine needle aspiration for a definitive histological diagnosis<sup>5</sup>. Due to a lack of specific symptoms, only about 10% of patients are diagnosed with early stage disease and can therefore benefit from potentially curative surgical resection, chemotherapy and radiotherapy<sup>6</sup>. Clearly, there is an urgent need to better detect early-stage disease to improve both patient quality of life and reduce overall mortality.

The importance of early diagnosis of pancreatic cancer is acknowledged worldwide<sup>7</sup>, and several health-care organisations have advised a transition to early detection<sup>b</sup>. Early detection and diagnosis of pancreatic cancer requires effective surveillance programs, to identify asymptomatic patients at elevated risk of developing pancreatic cancer, in combination with highly specific biomarkers and imaging modalities to facilitate early diagnosis. Currently, there are no reliable screening tests for pancreatic cancer for individuals with average risk, and several obstacles exist in addressing this issue. First, pancreatic cancer remains a relatively uncommon disease, with an estimated diagnosis risk of 1.5% for every Australian<sup>a</sup>. This low prevalence renders population-based screening using the existing invasive and expensive clinical diagnostic modalities unfeasible<sup>8</sup>. Second, there is no validated reliable tumour biomarker approved with sufficient diagnostic accuracy for the early detection and diagnosis of pancreatic cancer. Carbohydrate antigen 19-9 (CA19-9) is the most extensively studied serum biomarker<sup>9</sup>, however it lacks both sensitivity and specificity as a screening tool for the early detection of pancreatic cancer<sup>10</sup>.

An effective surveillance program for pancreatic cancer requires a comprehensive understanding of the risk factors predisposing individuals to elevated risk of developing pancreatic cancer. The accurate identification of high-risk individuals and their prioritisation for further screening programs is a much more rational approach to screening the entire, general population. This approach is likely to increase the rate of detection and reduce the consequences of false-positive results<sup>11</sup>. However, few high-penetrance risk factors are currently known for pancreatic cancer. Several groups at high risk of pancreatic cancer have been identified, including individuals in families with an inherited or genetic risk including hereditary cancer syndromes<sup>12</sup>, those with cystic lesions of the pancreas<sup>13</sup>, individuals with chronic or hereditary pancreatitis<sup>14</sup> or older than 50 years of age with newly diagnosed type 2 diabetes<sup>15</sup>. Multiple international programs for individuals with elevated risk of developing pancreatic cancer are available in a research setting<sup>16,17</sup>. The Australian Pancreatic Cancer Genome Initiative launched a EUS-based screening test for high-risk individuals called The Australian Pancreatic Cancer Screening Program (APCSP) at various clinical sites throughout Australia<sup>18-22</sup>. While the early signs from these trials are promising with increased survival for some patients<sup>16,23,24</sup>, patients who meet recommended surveillance criteria account for a only small proportion of those who go on to develop pancreatic cancer. Additionally, the timely identification of resectable lesions still proved challenging using multiple imaging methods, indicating a clear need for more sensitive, reliable biomarkers.

---

<sup>a</sup> <https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia>

<sup>b</sup> [https://apps.who.int/gb/ebwha/pdf\\_files/EB140/B140\\_31-en.pdf](https://apps.who.int/gb/ebwha/pdf_files/EB140/B140_31-en.pdf)



Reliable and effective biomarkers represents an important unmet clinical need to identify individuals at risk of developing pancreatic cancer. Several novel blood-based biomarkers have been investigated for the management of pancreatic cancer, but their role is still limited. Combinations of CA19-9 with various novel biomarkers, such as Carcinoembryonic antigen, Carbohydrate antigen 125, Carbohydrate antigen 242, Interleukin 25 and Death receptor 6, into panels or signatures<sup>25,26</sup> increased the accuracy of diagnosis, however these are yet to be implemented into routine clinical practice. Liquid biopsy represents a promising approach for the comprehensive identification of novel biomarkers and can be used in a complementary manner to existing imaging and biopsy methods to improve overall diagnostic accuracy. This non-invasive technique can analyse a range of candidate circulating tumour biomarkers such as circulating tumour cells, cell-free DNA and non-coding RNA, exosomes and inflammatory and growth factors, in a variety of bodily fluids such as blood, urine, fine needle aspirates at biopsy and saliva<sup>27</sup>. Significant progress has been made with the development of devices from a variety of companies that are contributing to the clinical application of liquid biopsy, including GRAIL LLC, Biological Dynamics Inc and Immunovia (see Part 3: Translational research). While this technique has received a great deal of attention for by the cancer research community, most studies that explored novel biomarkers using this technique, including the widely publicised CancerSEEK test, were identified in the context of symptomatic disease<sup>25,26,28-31</sup>. To date, very little data has been obtained on the performance criteria of these biomarkers in the surveillance of asymptomatic individuals. Therefore, the clinical application of these technologies as a surveillance tool for early stage pancreatic cancer remains limited by the identification of robust and reliable diagnostic biomarkers for early stage pancreatic cancer.

Emerging artificial intelligence (AI) and associated machine learning algorithms have the potential to rapidly alter the landscape of early pancreatic cancer detection and diagnosis. AI-based approaches have been used to analyse and integrate complex multi-omics data to identify various biomarkers correlated to patients clinical outcomes<sup>32-34</sup>. They are also being applied to various types of imaging data (CT, MRI and EUS) to identify subtle imaging features beyond human perceptible range<sup>35,36</sup>. AI-based approaches are also increasingly being used in the development of various risk prediction models on the basis of either electronic health records<sup>37,38</sup> or data collected for research purposes<sup>39,40</sup>. One recent study developed an AI tool with the potential to identify individuals at greatest risk for pancreatic cancer up to three years prior to diagnosis<sup>41</sup>. Using medical records from over 27,000 pancreatic cancer cases from two independent healthcare systems (Denmark and the US), researchers identified that incorporating the disease trajectories as input to the model, rather than only presence or absence of a pancreatic cancer diagnoses, vastly improved the ability of AI to predict pancreatic cancer occurrence. While this study provided the best model to date for predicting risk of pancreatic cancer in the general population, model improvements are required to increase its predictive performance across different healthcare systems<sup>41</sup>. Increased real-world availability of data beyond disease status, such as medication, clinical observations, health records from primary care providers, is expected to further increase prediction accuracy<sup>41</sup>. Once established, AI-based real-world high-risk prediction surveillance methods show significant potential as a cost-effective, scalable method for early detection and diagnosis of pancreatic cancer. Further advances require a concerted collaborative effort among researchers from a variety of backgrounds to validate findings from these approaches and test these more broadly in clinical trials prior to their wider application.

Early detection and diagnosis is a priority of several international consortia, including Pancreatic Cancer Detection Consortia (PCDC), the Chronic Pancreatitis, Diabetes and Pancreatic Cancer consortia (CPDPC) and the Pancreatic Cancer Initial Detection via liquid biopsy (PANCAID) consortium. PanKind (Australian Pancreatic Cancer Foundation) is the only foundation in Australia exclusively dedicated to improving survival rates and quality of life for people impacted by pancreatic cancer. Investing in research to accelerate treatments and improve early diagnosis of pancreatic cancer is a strategic focus for PanKind.

The 2021 National Pancreatic Cancer Roadmap developed by Cancer Australia has early detection as a priority for improving outcomes for people diagnosed with pancreatic cancer. The PanKind Early



Detection Initiative has been established to take a strategic approach to improving early detection of pancreatic cancer. The Initiative has an ambitious goal of tripling survival by 2030.

In October this year, PanKind is bringing together funded researchers and other stakeholders to chart a strategic and systematic path to accelerating early detection of pancreatic cancer. Professor Moira Clay (Moira Clay Consulting Pty Ltd) will be facilitating this workshop.

This report will set the scene for the October workshop by providing an overview of the state of play for technology and techniques for early detection in pancreatic cancer. The report comprises the following sections:

1. Publication analysis
2. Funding analysis
3. Translational research
4. Stakeholder consultation
5. Conclusions

## Part 1: Publication analysis

An analysis of pancreatic cancer publications between 2019 – present was conducted. Publication searches were performed in Scopus using the keywords “pancreatic cancer” and “early detection”. Network clusters were constructed from Scopus data using VOSviewer. Bibliometric analyses were conducted using SciVal.

### Global publications (2019 – present)

There were 700 peer-reviewed research publications identified worldwide using the keywords “pancreatic cancer” and “early detection” between 2019- present. The average Field Weight Citation Impact (FWCI)<sup>c</sup> of these was 1.73, with a significant proportion of publications in the top 10% most cited publications (15.9%) and highest quality journals (32.6%). Keywords<sup>d</sup> were added to search terms “pancreatic cancer” and “early detection” to further identify peer-reviewed research publications within the domains of imaging, biomarkers, liquid biopsy or artificial intelligence (Table 1). The FWCI of publications within each of these sub-fields remained above the global average, with an equivalent number of publications in the top 10% most cited publications and in highest quality journals. Overall, these data indicate that international pancreatic cancer research within the early detection space is an active area with high quality, global impact.

---

<sup>a</sup> Field weighted citation impact (FWCI) is a measure of actual citation count, relative to the expected world citation count of a similar publication. A figure of 1.00 indicates that the publication is performing exactly as expected, while a value more than 1.00 indicates that the output is more cited than expected according to the global average in the field.

<sup>d</sup> Keyword filters (title, abstract and keywords) “pancreatic cancer” AND “early detection” AND “imaging” or “biomarker” or “liquid biopsy” or “artificial intelligence”



**Table 1: Metrics for global publications on early detection in pancreatic cancer**

Keywords	Publications (n)	FWCI	Pubs in top 10% most cited (n)	Pubs in top 10% journals (n)
"Early detection" and "Pancreatic cancer"	700	1.73	111 (15.9%)	228 (32.6%)
"Early detection" and "Pancreatic cancer" and "Imaging"	229	1.87	41 (17.9%)	85 (37.1%)
"Early detection" and "Pancreatic cancer" and "Biomarker"	301	1.59	42 (14.0%)	94 (31.2%)
"Early detection" and "Pancreatic cancer" and "Liquid Biopsy"	67	1.41	8 (11.9%)	22 (32.8%)
"Early detection" and "Pancreatic cancer" and "Artificial Intelligence"	36	1.35	5 (13.9%)	12 (33.3%)

Network analysis examines and visualises the relationships between publications based on authorship or keywords. We constructed a co-authorship map for all globally led early detection pancreatic cancer research publications. Figure 1<sup>e</sup> shows a well-connected, highly collaborative research network, consisting of eight main co-authorship clusters as shown in different colours. The most connected authors (determined by overall connectivity score) were Dr Fay Kastrinos (dark blue), Prof Marcia Canto (yellow), Prof Ralph Hruban (yellow) and Dr Salvatore Paiella (dark blue).

A network analysis of keywords in globally led early detection pancreatic cancer research publications indicated five main themes or clusters of keywords (Figure 2<sup>f</sup>). These include:

1. Early detection and screening (early detection of cancer, risk factor, germline mutation, magnetic resonance imaging, high risk population, gene mutation, endoscopic ultrasonography);
2. Clinical studies and staging of patients (major clinical study, cancer staging, controlled study, diagnostic accuracy, ca-19-9 antigen, cohort analysis);
3. Biomarkers and experimental research (biomarkers, circulating tumor cell, exosomes, animal model, tumour cell line, gene expression, cell proliferation, unclassified drug);
4. Cancer chemotherapy (gemcitabine, paclitaxel, oxaliplatin, irinotecan, antineoplastic agent);
5. Diabetes and other incidence factors (diabetes mellitus, smoking).

The five most common keywords in globally led early detection pancreatic cancer research publications are (in order) are "pancreas tumor", "early detection of cancer", "controlled study", "genetics" and "major clinical study".

<sup>e</sup> 168 authors appeared after filtering for those that published at least four articles.

<sup>f</sup> 263 keywords occurred at least 15 times. Data cleaning (for duplication, e.g collapsing "pancreas tumor" and "pancreatic cancer" into one field) resulted in 187 keywords reaching the threshold. Each cluster is defined by the occurrence and strength of links between keywords. The symbol size is proportional to the occurrence of keywords, while the thickness of the lines connecting keywords relates to the total number of links between keywords.





### Australian publications (2019 – present)

There were only 15 peer-reviewed research publications led by Australian research groups identified using the keywords “pancreatic cancer” and “early detection” between 2019- present. The average FWCI of these was 0.74, indicating that publications have less global impact than would have been expected. Further, none of these publications featured in the top 10% most cited publications, however a proportion did feature in the highest quality journals (40%). Keywords<sup>2</sup> were added to search terms “pancreatic cancer” and “early detection” to further identify peer-reviewed research publications within the domains of imaging, biomarkers, liquid biopsy or artificial intelligence (Table 2). The FWCI of publications within each of these sub-fields remained below the global average, despite some of these featuring in the highest quality journals. These data depict a vastly distinct situation to that of global publications in this area, with minimal research activity and of somewhat lower than expected global impact.

**Table 2: Metrics for Australian publications on early detection in pancreatic cancer**

Keywords	Publications (n)	FWCI	Pubs in top 10% most cited (n)	Pubs in top 10% journals (n)
“Early detection” and “Pancreatic cancer”	15	0.74	0	6 (40%)
“Early detection” and “Pancreatic cancer” and “Imaging”	4	0.67	0	1 (25.0%)
“Early detection” and “Pancreatic cancer” and “Biomarker”	8	0.89	0	4 (50.0%)
“Early detection” and “Pancreatic cancer” and “Liquid Biopsy”	2	0.80	0	1 (50%)
“Early detection” and “Pancreatic cancer” and “Artificial Intelligence”	1	0.65	0	0

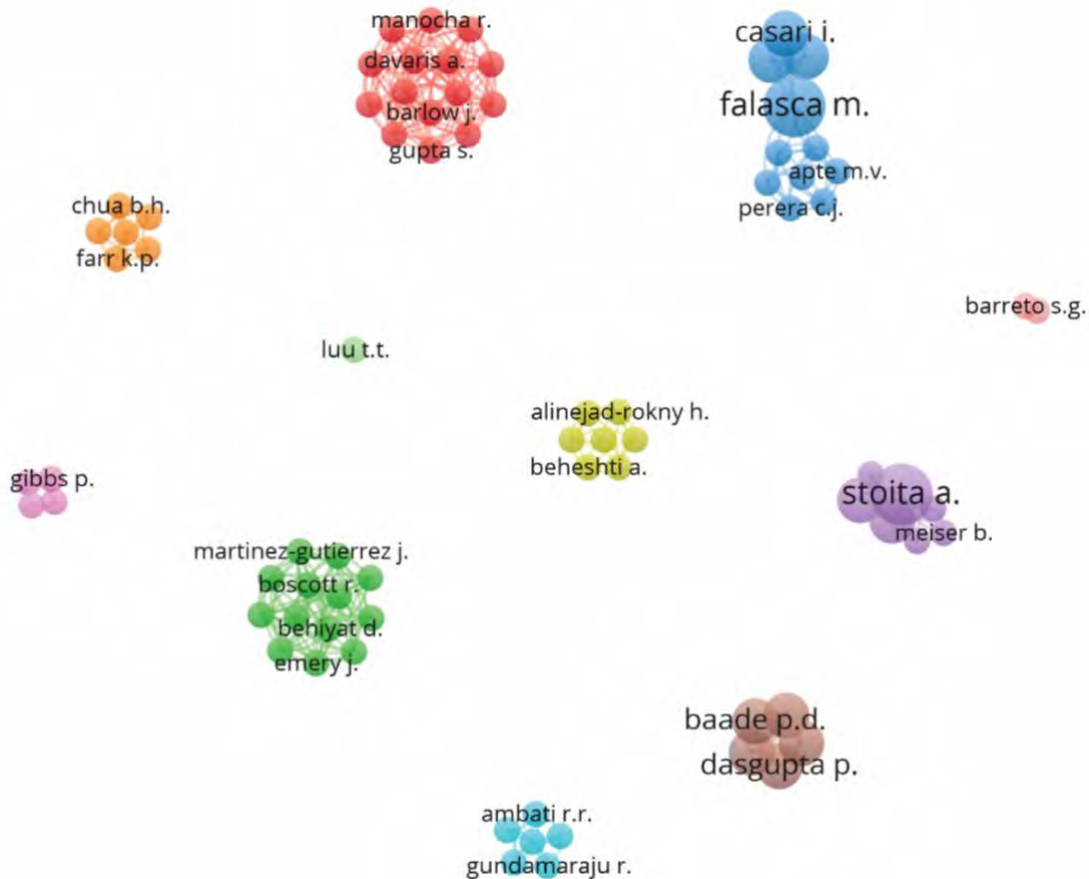
The most prominent Australian corresponding authors in early detection pancreatic cancer publications were Dr Alina Stoita and Prof Marco Falasca (Table 3). Prof Peter Baade was the third most prominent Australian corresponding author followed by a broad spread of researchers from multiple institutions with one publication in the area.

**Table 3: Top three Australian researchers with corresponding authorships (2019-present)**

Researcher	Affiliation	Corresponding authorships	Research field
Alina Stoita	UNSW	3	Biomarkers and Surveillance for high risk patients
Marco Falasca	Curtin	3	Biomarkers and Exosomes
Peter Baade	QUT	2	Disease surveillance and Public health

A network of Australian-led early detection pancreatic cancer research publications showed a very distinct pattern of co-authorship compared to globally led publications, with 11 unconnected, discrete sub-networks of activity as shown in different colours (Figure 3<sup>9</sup>). While the largest sub-network with respect to co-authorship was the team led by corresponding author Dr Bridie Thompson (red), this co-authorship represented one publication only. The most connected authors as calculated over a greater than two publications are Prof Marco Falasca (blue) and Dr Alina Stoita (purple).

**Figure 3: Author network for Australian publications on early detection of pancreatic cancer**



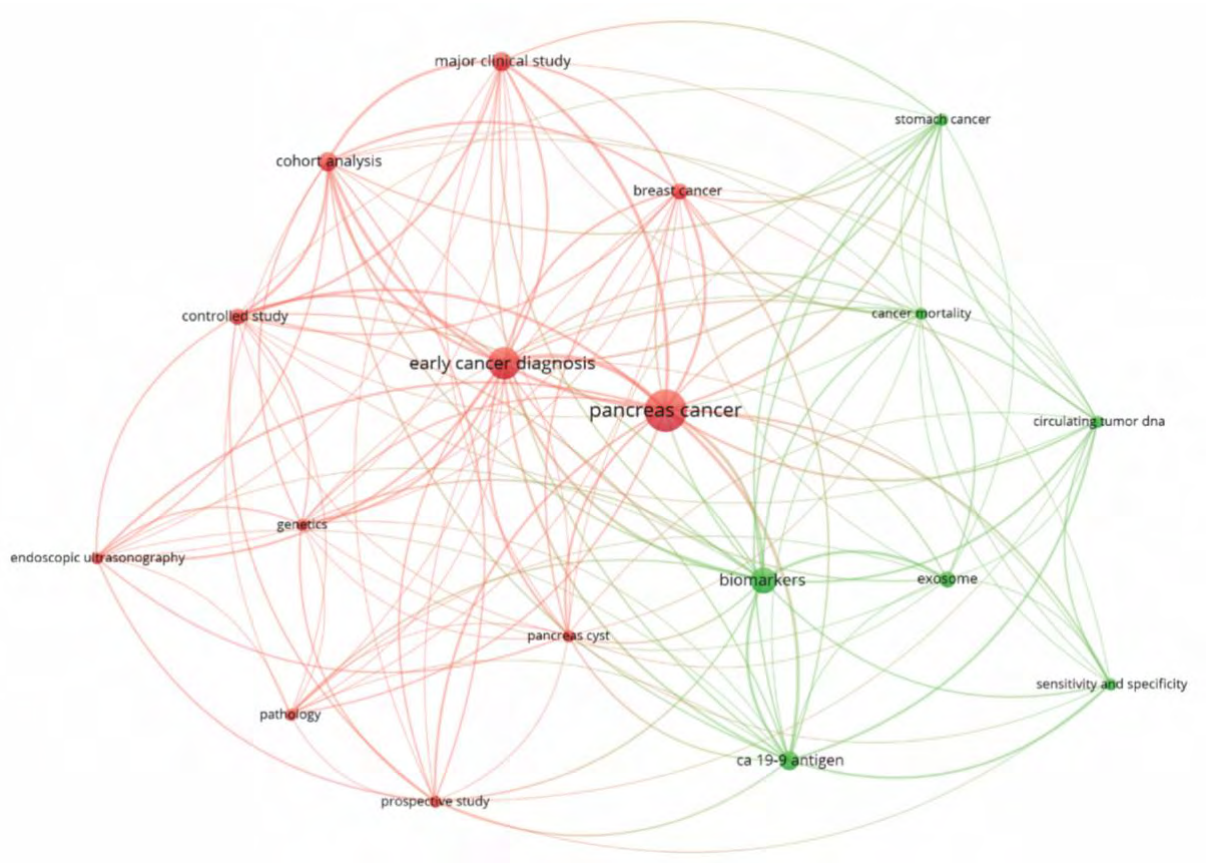
A network analysis of keywords<sup>h</sup> in Australian-led early detection pancreatic cancer research publications indicated two main themes or clusters of keywords (Figure 4). These include:

1. Early detection and clinical studies (early cancer diagnosis, genetics, endoscopic ultrasonography, cohort analysis, major clinical study and controlled study)
2. Biomarkers (biomarkers, exosome, ca 19-9 antigen, circulating tumor dna). The five most common keywords in Australian-led early detection pancreatic cancer research publications are (in order) are almost identical to those identified in global research publications, namely “pancreas cancer”, “early cancer diagnosis”, “biomarkers”, “cohort analysis” and “major clinical study”.

<sup>9</sup> 77 authors appeared in this network. No filtering due to low numbers of publications and authors.

<sup>h</sup> 42 keywords occurred at least 3 times. Data cleaning (for duplication, e.g collapsing “pancreas tumor” and “pancreatic cancer” into one field resulted in only 18 keywords reaching the threshold. Each cluster is defined by the occurrence and strength of links between keywords. The symbol size is proportional to the occurrence of keywords, while the thickness of the lines connecting keywords relates to the total number of links between keywords.

Figure 4: Keyword network in Australian publications on early detection of pancreatic cancer



## Part 2: Funding Analysis

Pancreatic cancer research performed overseas is supported by various country-specific government and non-government sources, some focused on specifically on pancreatic cancer. Major not-for-profit funders of pancreatic cancer research include the Pancreatic Cancer Action Network (PCAN) and the Lustgarten Foundation, with smaller amounts provided by the Hirshberg Foundation, Seena Magowitz Foundation, Prevent Cancer Foundation, American Cancer Society, National Pancreatic Cancer Foundation, National Pancreas Foundation, Pancreatic Cancer UK, Cancer Research UK and Action Against Cancer. It is worth noting that while based overseas, some organisations or departments will fund pancreatic cancer research based in Australia, including the U.S Department of Defence, the Hirshberg Foundation, the National Pancreas Foundation and PCAN.

A high-level analysis was conducted of pancreatic cancer research funding in Australia from major funding bodies, including the National Health and Medical Research Council (NHMRC), the Medical Research Future Fund (MRFF) and Cancer Australia. Publicly available funding announcements/databases were searched for any grant with “pancreatic” or “pancreas” that was awarded between 2019 to present. The two major sources of government funding were the NHMRC and the MRFF, with 22 funded projects amounting to total research funding of \$27.42M identified in this search. Of the 84 projects funded by Cancer Australia and its partners through the Priority-driven Collaborative Cancer Research Schemes during this period, pancreatic cancer did not feature in any funded projects. A full list of funded grants is in Appendix 1.

The MRFF provided a total of \$10.03M research funding for translational pancreatic cancer research across a variety of schemes, including Rare Cancers, Rare Diseases and Unmet Need (2019, 2021) and the Pancreatic Cancer Research Grant scheme (2022). Around 56% of all MRFF funding awarded to pancreatic cancer research was provided from the Pancreatic Cancer Research Grant scheme (2022), with only 1/7 funded projects or 29.59% of funding to pancreatic cancer was focused on the early detection of pancreatic cancer.

The NHMRC funded \$17.39M in pancreatic research between 2019 to present. Between 2019 and 2021, NHMRC pancreatic cancer research funding was less than 0.5% of all NHMRC funding awarded (Table 4). This sharply increased to 1.33% in 2022, with 67% of the total NHMRC funds into pancreatic cancer awarded in 2022.

**Table 4: NHMRC research funding for pancreatic cancer research (2019-present)**

	Total research funding (\$M)			
	2019	2020	2021	2022
All NHMRC funding	887.5	722.62*	957.33	871.25
Pancreatic cancer research funding	3.25	0.74	1.75	11.66
% total	0.37	0.10	0.18	1.33

\*Note: Publicly available data of NHMRC funding from 2020 was incomplete. Funding data for this year was compiled from additional sources including GrantConnect and Outcomes factsheets.

Pancreatic cancer research funded by the NHMRC covered various areas of research. Research projects in the area of biology received the greatest proportion of total funding (47.66%) followed by treatment (28.91%) (Table 5). Early detection, diagnosis and prevention received 23.05% of total funding awarded, however most of this funding (88%) was from one of two funded applications.



**Table 5: NHMRC pancreatic cancer research funding by research areas (2019-present)**

Research area	Total funding (\$M)	% Total funding	Total grants awarded	% total grants
Biology	8.27	47.66	6	40
Treatment	5.03	28.91	6	40
Early detection, diagnosis and prevention	4.01	23.05	2	13.33
Cancer control, survivorship and outcomes	0.067	0.39	1	6.67

NHMRC pancreatic cancer research funding was awarded to 15 researchers either as Chief Investigator A (research project funding) or fellowship/scholarship recipient (people capacity funding) (Table 6). Just over 53% of the NHMRC funding was directed towards building capacity through funding people and teams (including investigator grants and scholarships) and the balance towards funding specific research projects. Recipients are listed in Table 6 by the amount of research funding awarded. Only two funded recipients, Prof. Peter Gibbs and Prof. Minoti Apte, had projects funded in the early detection area. Prof. Minoti Apte's grant was focused on the identification of novel biomarkers for early diagnosis, through developing a better mechanistic understanding of how pancreatic cancer-related diabetes progresses to early stage pancreatic cancer. The grant awarded to Prof. Peter Gibbs was focused on the role of circulating tumour DNA in informing the management of patients with early stage pancreatic cancer.

**Table 6: Researchers awarded NHMRC pancreatic cancer research funding (2019-present)**

	Affiliation	Funding awarded (\$M)
Peter Gibbs	WEHI	3.53
Paul Timpson	UNSW	2.88
Sean Grimmond	UoM	2.70
Frederic Hollande	UoM	1.23
Claudine Bonder	UniSA	1.16
Shane Grey	UNSW	0.95
Thomas Cox	UNSW	0.83
Daniella Loessner	Monash	0.81
David Croucher	UNSW	0.77
Phoebe Phillips	UNSW	0.74
Zaklina Kovacevic	USyd	0.64
Brooke Pereira	UNSW	0.53
Minoti Apte	UNSW	0.48
Omali Pityarachichi	UNSW	0.098
Nadia Khan	Monash	0.067

The not-for-profit sector is an important funder of pancreatic cancer research including PanKind and Pancare. Pancare funds research into pancreatic cancer through fellowship/scholarships (people capacity funding) and research project funding as a partner of Cancer Australia through the PdCCRs scheme. Of the total funding awarded (~\$2M since 2011), only one project was funded in early detection of pancreatic cancer to Dr Alina Stoita, however this was awarded prior to 2019.

PanKind has funded a total of \$11.10M in pancreatic cancer between 2019 to present across a variety of streams, with a scheme “Early Detection Innovation Grant” (2020, 2021, 2022) targeted to the early detection of pancreatic cancer. Around 14.97% of all funding from PanKind has focused on early detection, with award recipients within this stream listed in Table 7 by the amount of research funding awarded to them. Two recipients of the 2021 Early Detection innovation scheme from PanKind, Prof. Claudine Bonder and Dr Zaklina Kovacevic, went on to successfully obtain CIA 2022 NHMRC Ideas Grants.

**Table 7: Researchers awarded PanKind early detection research funding (2019-present)**

	<b>Affiliation</b>	<b>Funding awarded (\$K)</b>
Rachel Neale	QIMR	300
Phoebe Phillips	UNSW	299
Andrew Metz	Epworth Medical Foundation	164
Anubhav Mittal	USyd	100
John Rasko	USyd	100
Marco Falasca	Curtin	100
Jason Lee	QIMR	100
Chamini Perera	UNSW	99.89
Ying Zhu	UTS	99.70
Claudine Bonder	UniSA	99.54
David Cavallucci	Royal Brisbane and Women’s Hospital	99.44
Zaklina Kovacevic	USyd	99.07

## Part 3: Translational Research

Research translation is an important component of maximising research impact on the community. A desktop analysis of the commercialisation activity on early detection of pancreatic cancer was conducted, with a focus on technologies in clinical trial and/or close to being available for patients. A snapshot of these is listed below:

### Global

#### GRAIL LLC

GRAIL LLC, is a healthcare company based in the US, focused on the early detection of several fatal cancer types by combining the power of next-generation sequencing and machine learning approaches<sup>i</sup>. GRAIL has developed a Galleri® multi-cancer early detection (MCED) test, a diagnostic tool which detects a distinct DNA methylation pattern predictive of over 50 cancer types from circulating cell-free DNA isolated from blood samples of patients. In addition to detecting a wide range of cancer types, some of which have lack screening tools, this test uses artificial intelligence to then predict the tissue of origin of the cancer. Individuals with a positive cancer signal can then be fast tracked for further diagnostic evaluation for that specific cancer type. Several companies are actively working to develop MCED tests, however the GRAIL Galleri® MCED test is the most clinically advanced. Several large scale clinical studies (NCT02889978, NCT04241796, ISRCTN91431511) have assessed the sensitivity and accuracy of the Galleri® MCED test<sup>42,43</sup>. The accuracy of the tissue origin of the cancer has been reported for wide variety of cancer types, including pancreatic cancer<sup>i</sup>. Relatively high sensitivity has been reported for the detection of a range of late-stage cancers with high disease burden<sup>42</sup>. However, the detection of early, stage I, and II cancers with high enough sensitivity for population level screening has proven more challenging. The majority of clinical studies to date have reported on the performance of the Galleri® MCED test in symptomatic patients. Recent data was published from an large-scale observational GRAIL funded study (SYMPLIFY) run at National Health Service (NHS) sites throughout England and Wales, which included symptomatic patients referred from primary care for urgent cancer investigation<sup>44</sup>. The overall sensitivity of the Galleri® MCED test in identifying the presence or absence of cancer across all types was 66.3%. Like previous studies, increased sensitivity was observed with increasing cancer stage (24.2% stage I vs 95.3% stage IV) with high (85.2%) accuracy identifying the tissue origin of the cancer in symptomatic patients. Sensitivity was highest for patients with symptoms of upper gastrointestinal cancer, with most patients (91.7%) who went on to be diagnosed with pancreatic cancer initially testing positive with the Galleri® MCED test albeit at late stage disease.

These results supported the feasibility of the Galleri® MCED test on a wider scale to complement existing single-cancer screening tests. A clinical surveillance program of the Galleri® MCED test has since been initiated in the United States. While it is not currently approved by the US Food and Drug Administration, it can be purchased with a prescription for people with an elevated cancer risk at a cost of around \$US1000. The initial findings from the clinical surveillance program indicate that the real-world performance of the Galleri® MCED test is consistent with previous clinical studies, with the program ongoing in the US. Results from the ongoing clinical trial in England (ISRCTN91431511) run in partnership with GRAIL and the NHS are anticipated to be reported in 2023. From this, the NHS will decide as to whether to introduce this screening test alongside the current standard of care. This test is not yet available in Australia. The true clinical validity of the Galleri® MCED test for the early pancreatic cancer diagnosis remains to be determined, as clinical sensitivity needs to be established in asymptomatic individuals with pancreatic cancer. The data reported by GRAIL on the sensitivities for detecting breast cancer in asymptomatic individuals<sup>45</sup> suggests that current levels

<sup>i</sup> <https://grail.com>

<sup>j</sup> [https://grail.com/wp-content/uploads/2023/06/Klein\\_ASCO-2023\\_PATHFINDER-Dx-Workup\\_Poster\\_FINAL.pdf](https://grail.com/wp-content/uploads/2023/06/Klein_ASCO-2023_PATHFINDER-Dx-Workup_Poster_FINAL.pdf)



are problematic and that circulating tumour DNA as an early diagnostic is still far from clinical implementation.

### Biological Dynamics Inc.

Another blood based MCED test focused on detecting circulating extracellular vesicles or exosomes released by tumours has been produced by *Biological Dynamics Inc*, a biotechnology company based in the US<sup>k</sup>. Biological Dynamics Inc have produced an early diagnostic detection platform called the ExoVerita™ assay, which utilises alternating current electrokinetics to create an electric field to isolate and purify tumour exosomes containing protein biomarkers from patients' blood sample. These protein biomarkers can be used as a classifier to detect the early stages of pancreatic cancer<sup>46</sup>. The classified protein biomarkers indicative of early stage pancreatic cancer were previously identified by measuring all the proteins contained within extracellular vesicles isolated from diagnosed pancreatic cancer patients (stages I-IV). These were then used to train a machine learning algorithm to discriminate cancer from healthy controls. A pilot study of this system in a small cohort of cancer patients indicated a high sensitivity (95.5%) of detecting stage I pancreatic cancer<sup>46</sup>, highlighting the clinical utility of extracellular vesicles for early pancreatic cancer detection. A clinical study (NCT05625529) was recently launched to investigate the performance of the ExoVerita™ assay in the early detection of pancreatic cancer in those patients at elevated risk (familial history of pancreatic cancer, germline mutations, history of pancreatitis) comparing to current standard of care methods of surveillance. This study is actively recruiting at select clinical and academic centres throughout the US. Results are expected to be announced from 2025.

### Immunovia

Immunovia is a Swedish biotechnology company who have developed a blood-based test, called the IMMray PanCan-d test, for the early detection and diagnosis of pancreatic cancer<sup>l</sup>. This test is an antibody-based microarray technology combined with machine learning algorithms to measure nine serum biomarkers, including CA19-9, associated with pancreatic cancer. An individual's measurements of each biomarker are entered into machine learning algorithms to predict the risk-profile of the patient of either having or developing pancreatic cancer. The biomarker signature was identified from previously diagnosed patients following multiple rounds of microarrays combined with bioinformatics analysis, creating a unique "disease fingerprint" for pancreatic cancer. As distinct from MCED tests, the IMMray PanCan-d test is designed to be used in patients previously identified at risk of developing pancreatic cancer (family history or known predisposing mutations) rather than a general screening tool. A multi-centre clinical trial (NCT03693378) in the US and Europe was launched to assess the performance and accuracy of the IMMray PanCan-d test in the early detection of pancreatic cancer in patients at high risk for hereditary or familial pancreatic cancer. Results from this study demonstrated that the IMMray PanCan-d test could detect pancreatic cancer with a high specificity and sensitivity reported<sup>47</sup>. At present, the IMMray PanCan-d test is still a laboratory-based test available to be ordered by a healthcare professional for individuals in most states of the US. It is not currently approved by the US Food and Drug Administration.

### Australia

#### AdvanCell Isotopes

AdvanCell Isotopes is a radiopharmaceutical company founded in Australia focused on the development of a novel type of radiation therapy called targeted alpha therapy<sup>m</sup>. Targeted alpha therapy is a type of radionuclide therapy, where a radioactive atom called alpha particle-emitting radionuclides is linked to tumour specific cell-targeting molecules such as a monoclonal antibody

<sup>k</sup> <https://biologicaldynamics.com>

<sup>l</sup> <https://immunovia.com>

<sup>m</sup> <https://advancell.com.au>



or peptides<sup>48</sup>. Following systemic delivery to the body via injection, the cell targeting molecule binds to its specific target on cancer cells and the attached radioactive atom irradiates the cell. These alpha particle-emitting radionuclides are highly cytotoxic due to the very high energy that they deposit in a cell producing complex double stranded DNA damage<sup>49</sup> resulting in the potent, selective killing of malignant cells. The short-range emissions of alpha particles confine their cytotoxic effect to cancer cells and the surrounding tumour microenvironment, limiting toxic effects to healthy, noncancerous tissue<sup>49</sup>. For every novel alpha targeted therapy developed, production of a companion diagnostic imaging agent in parallel is required to enable accurate patient stratification and to assess the biodistribution and dosimetry of the alpha targeted therapy. This imaging agent has the potential to be a superior diagnostic with respect to sensitivity and specificity for pancreatic cancer than existing imaging modalities, like that observed clinically in prostate cancer (ANZCTR1261700005358)<sup>50</sup>. Combined with improved methods of surveillance to identify patients at elevated risk, this technology could facilitate a powerful approach for the early detection of pancreatic cancer via more sensitive imaging and consequently more accurate surgical planning. The major challenge with targeted alpha therapies is the large scale production of the isotopes required to make the therapy. AdvanCell has developed a manufacturing platform capable of delivering a clinical scale of alpha radioligand therapies, specifically <sup>212</sup>Pb targeted alpha therapy. AdvanCell has recently launched the first clinical trial investigating the efficacy and toxicity of <sup>212</sup>Pb targeted alpha therapy, <sup>212</sup>Pb-ADV001, for patients with metastatic prostate cancer in Brisbane (NCT05720130). AdvanCell is now in the process of progressing clinical trials and expanding the manufacturing platform technology to several sites across Australia and into the US. Additionally, the manufacturing platform is being repurposed to expand the portfolio of alpha radioligand therapies to other hard to treat cancers such as pancreatic cancer (<sup>212</sup>Pb-ADV003). This first-in-human clinical trial for pancreatic cancer is anticipated to start in 2026.

### Clinical trials

In addition to commercial activity, we reviewed all Australian clinical trials in pancreatic cancer on the Australian Clinical Trials Registry<sup>n</sup>. The trial registry was filtered by the keywords of pancreatic cancer and the recruitment status of “not yet recruiting”, “recruiting” or “active, not recruiting”. 63 clinical trials were identified, with nine focused on early detection or diagnosis. These are listed in Table 8.

---

<sup>n</sup> <https://anzctr.org.au/default.aspx>



**Table 8: Australian clinical trials in the early detection of pancreatic cancer**

<b>Trial ID</b>	<b>Study title</b>	<b>Recruitment sites</b>	<b>Field</b>	<b>Primary sponsor</b>
ACTRN12623000518662	The clinical utility of [68Ga]-labelled fibroblast activation protein inhibitor (FAPI) positron emission tomography and computed tomography (PET/CT) in patients with resectable or borderline resectable pancreatic ductal adenocarcinoma (PDAC) undergoing neoadjuvant chemotherapy.	QLD	Imaging	Metro South Health
ACTRN12623000508673	SCANPatient: Synoptic reporting of computerised tomography (CT) scans assessing cancer of the pancreas. A stepped wedge randomised controlled trial	All except NT	Imaging	Monash University
ACTRN12622000695707	Gallium-68 fibroblast activation protein inhibitor (68Ga-FAPI) positron emission tomography/computed tomography (PET/CT) versus 18F-fluorodeoxyglucose (18F-FDG) PET/CT for pancreatic cancer: A feasibility study	QLD	Imaging	I-MED Radiology Network
ACTRN12621000935831	A pilot study to evaluate the diagnostic and therapeutic applications of FAPI-PET in pancreatic cancer.	QLD	Imaging	Royal Brisbane and Women's Hospital
ACTRN12619001033134	Bio-distribution evaluations of MUC-1 specific targeted immune-radiotherapy for advanced pancreatic adenocarcinoma: a first pilot human study.	SA	Imaging	Royal Adelaide Hospital
ACTRN12617001242314	Endoscopic Ultrasound Guided portal vein sampling as an ultimate staging procedure in patients with pancreatic cancer: a feasibility study.	SA	Liquid Biopsy	Royal Adelaide Hospital
ACTRN12616001138471	Developing novel blood-based DNA and RNA biomarkers to detect adenocarcinoma by assessing the blood from people aged 25 years and older, who have recently been diagnosed with prostate, breast, lung, pancreas, gallbladder, biliary tract, duodenal, periampullary, oesophageal or stomach cancer.	SA	Liquid Biopsy	Flinders Medical Centre
ACTRN12616000787482	Safety and tolerability of MIL-38/ Gallium67 (MILGa) in patients with advanced prostate, bladder and pancreatic cancer.	NSW	Imaging	Minomic International
ACTRN12607000604404	A prospective study investigating the impact of the addition of FDG-PET/CT on treatment decisions compared to standard pre-operative work up for patients with suspected pancreatic, peri-ampullary or bile duct malignancies	QLD	Imaging	Royal Brisbane and Women's Hospital



## Part 4: Stakeholder Consultation

Consultations (online) were held with external stakeholders within the early detection of pancreatic cancer space. A list of all stakeholder consultations is in Appendix 2. Stakeholders addressed five questions:

### 1. What is the current evidence for early detection of pancreatic cancer?

*Three themes emerged from responses to this question:*

- All stakeholders were unanimous in their views on the importance for the early detection of pancreatic cancer and the positive impact this has on patient prognosis.
- We can now accurately predict predisposition to pancreatic cancer, however the majority of cases are sporadic which means this does not capture the true disease burden.
- Patients diagnosed at stage 1A have an 80% five year survival rate, yet only 1-2% of patients are diagnosed at stage 1A. Diagnosis at stage 1A currently is based on luck.

### 2. What are the biggest challenges / gaps/ unanswered questions in early detection?

*Six themes emerged from responses to this question:*

- Pancreatic cancer is a less common cancer (<15 per 100,000) and represents a significant barrier for engaging industry and pharma.
- Symptoms of pancreatic cancer are so generalised and vague, resulting in practical challenges for clinicians to know who to progress for screening.
- The current approaches for accurate diagnosis are labour intensive and not cost effective for population-based screening.
- There are inadequate funding sources for the extensive preclinical research required to address many of the current challenges in early detection.
- A comprehensive, interdisciplinary approach to research on early detection is urgently required. This is slow, expensive and of little incentive for researchers struggling in the current funding landscape.
- Precarious workforce security is a major issue. This particularly applies to early to mid-career researchers who have the innovation ideas and career time frames required to address the significant challenges.

### 3. Where are the opportunities to advance early detection in the next 5 to 10 years?

*Two themes emerged from responses to this question:*

- Development of an accurate diagnostic test by combining the rapid developments in:
  - Liquid biopsy tests to screen panel of biomarkers from multiple body fluids, including blood, urine and faeces together with,
  - Artificial intelligence and machine learning approaches to identify biomarkers defining risk profiles of patients from retrospective analysis of patient genetic data, and improve the sensitivity of imaging.
- Important to monitor the implementation of recently developed diagnostic tests in Europe and the US. While these tests are not perfect, the field will learn a great deal from positive and negative data and their implementation will ultimately lower the costs of this technology.

### 4. What is needed to realise these opportunities?

*Five themes emerged from responses to this question:*

- Multi-disciplinary, collaborative approaches and teams to perform the required research.
- Sustained funding to support the long term, multidisciplinary studies required to transition a scientific discovery to a diagnostic test that can be used in clinic.
- Strategic approach to identify important and realistic research directions.



- Strategic approach to develop a shared venture, by identifying the laboratories capable of contributing to a multi-disciplinary program and foster true collaboration across sector.
- Collaboration with international consortia to improve access to patient samples and increase scientific collaboration. These include the World Pancreatic Cancer Coalition, US-based PCDC, the Early Detection Research Network, and the CPDPC all funded through the National Cancer Institute or the European Union funded PANCAID consortium.

#### **5. Who are the key translational partners in early detection?**

*Five themes emerged from responses to this question:*

- Scientists, particularly early-mid career researchers with innovative ideas and time.
- Clinicians across the spectrum (gastroenterologists, surgeons, oncologists) for patient data, ideas on how to translate research to clinic and also the patient population to follow up novel interventions.
- Industry and pharma for small seed based funding to develop ideas in first stage.
- Philanthropy and private wealth, most likely the partner that will change outcomes due to personal interest.



## Conclusions

The aim of this project was to analyse the state of play of research with technology and techniques in the early detection in pancreatic cancer on a national and international level. It has highlighted several themes:

- There is extensive international research across a variety of technologies and techniques in the early detection of pancreatic cancer, with researchers highly collaborative and having impact above world average.
- The early detection of pancreatic cancer remains an emerging field of research within Australia, and of somewhat lower than expected global impact as measured by FWCI.
- Research in the early detection of pancreatic cancer in Australia, at present, appears fragmented and siloed.
- Dr Alina Stoita and Prof Marco Falasca are the most active researchers, based on articles as corresponding author, and the most collaborative.
- Pancreatic cancer research has received very low (<0.5% total budget) levels of funding from the NHMRC in recent years, with this increasing in 2022 (1.3%). Cancer Australia has not funded a project via the PdCCRs in pancreatic cancer since 2019.
- Blood-based tests for the early detection and diagnosis of pancreatic cancer are in clinical development and available for patients overseas, but not yet in Australia.
- There are several clinical trials underway for the early detection and diagnosis of pancreatic cancer around Australia.
- There is widespread recognition that the early detection of pancreatic cancer is an urgent priority to improve survival rates for patients from external stakeholders including researchers, clinicians and a national government funding agency.
- External stakeholders raised various challenges for the early detection of pancreatic cancer, all highlighting the importance of a strategic approach towards establishing collaborative, interdisciplinary research teams and developing sustainable funding.

These findings are important for the future planning of early detection in pancreatic cancer research in Australia. There is no doubt that with a strategic approach to developing comprehensive and collaborative research teams, increased advocacy for sustainable funding and leveraging from international research activities, better outcomes would be achieved for all Australians diagnosed with pancreatic cancer.



## References

- 1 Rahib, L *et al.* Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. **Cancer Res**, (2014).
- 2 Siegel, RL *et al.* Cancer statistics, 2023. **CA Cancer J Clin**, (2023).
- 3 Pereira, SP *et al.* Early detection of pancreatic cancer. **Lancet Gastroenterol Hepatol**, (2020).
- 4 Loveday, BPT *et al.* Pancreatic cancer: An update on diagnosis and management. **Aust J Gen Pract**, (2019).
- 5 Yousaf, MN *et al.* Endoscopic ultrasound (EUS) and the management of pancreatic cancer. **BMJ Open Gastroenterol**, (2020).
- 6 Nevala-Plagemann, C *et al.* From state-of-the-art treatments to novel therapies for advanced-stage pancreatic cancer. **Nat Rev Clin Oncol**, (2020).
- 7 Canto, MI *et al.* International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. **Gut**, (2013).
- 8 Lucas, AL & Kastrinos, F. Screening for Pancreatic Cancer. **JAMA**, (2019).
- 9 Yang, J *et al.* Early screening and diagnosis strategies of pancreatic cancer: a comprehensive review. **Cancer Commun (Lond)**, (2021).
- 10 Zhang, L *et al.* Challenges in diagnosis of pancreatic cancer. **World J Gastroenterol**, (2018).
- 11 Poruk, KE *et al.* Screening for pancreatic cancer: why, how, and who? **Ann Surg**, (2013).
- 12 Stoita, A *et al.* Review of screening for pancreatic cancer in high risk individuals. **World J Gastroenterol**, (2011).
- 13 Vege, SS *et al.* American gastroenterological association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. **Gastroenterology**, (2015).
- 14 Umans, DS *et al.* Pancreatitis and pancreatic cancer: A case of the chicken or the egg. **World J Gastroenterol**, (2021).
- 15 Sharma, A *et al.* Fasting Blood Glucose Levels Provide Estimate of Duration and Progression of Pancreatic Cancer Before Diagnosis. **Gastroenterology**, (2018).
- 16 Dbouk, M *et al.* The Multicenter Cancer of Pancreas Screening Study: Impact on Stage and Survival. **J Clin Oncol**, (2022).
- 17 Overbeek, KA *et al.* Long-term yield of pancreatic cancer surveillance in high-risk individuals. **Gut**, (2022).
- 18 Dwarte, T *et al.* Genetic counselling and personalised risk assessment in the Australian pancreatic cancer screening program. **Hered Cancer Clin Pract**, (2019).
- 19 O'Neill, RS *et al.* Long-term positive psychological outcomes in an Australian pancreatic cancer screening program. **Fam Cancer**, (2020).
- 20 Efthymiou, M *et al.* Outcomes of endoscopic ultrasound as a one-off pancreatic cancer screening tool for 122 high- and moderate-risk patients. **JGH Open**, (2020).
- 21 O'Neill, RS *et al.* Macrophage inhibitory cytokine-1/growth differentiation factor-15 in premalignant and neoplastic tumours in a high-risk pancreatic cancer cohort. **World J Gastroenterol**, (2020).
- 22 Murali, K *et al.* Significant detection of new germline pathogenic variants in Australian Pancreatic Cancer Screening Program participants. **Hered Cancer Clin Pract**, (2021).
- 23 Canto, MI *et al.* Risk of Neoplastic Progression in Individuals at High Risk for Pancreatic Cancer Undergoing Long-term Surveillance. **Gastroenterology**, (2018).



- 24 Vasen, H *et al.* Benefit of Surveillance for Pancreatic Cancer in High-Risk Individuals: Outcome of Long-Term Prospective Follow-Up Studies From Three European Expert Centers. **J Clin Oncol**, (2016).
- 25 Gu, YL *et al.* Applicative Value of Serum CA19-9, CEA, CA125 and CA242 in Diagnosis and Prognosis for Patients with Pancreatic Cancer Treated by Concurrent Chemoradiotherapy. **Asian Pac J Cancer Prev**, (2015).
- 26 Aronsson, L *et al.* High-density and targeted glycoproteomic profiling of serum proteins in pancreatic cancer and intraductal papillary mucinous neoplasm. **Scand J Gastroenterol**, (2018).
- 27 Zhang, X *et al.* Circulating biomarkers for early diagnosis of pancreatic cancer: facts and hopes. **Am J Cancer Res**, (2018).
- 28 Schultz, NA *et al.* MicroRNA biomarkers in whole blood for detection of pancreatic cancer. **JAMA**, (2014).
- 29 Capello, M *et al.* Sequential Validation of Blood-Based Protein Biomarker Candidates for Early-Stage Pancreatic Cancer. **J Natl Cancer Inst**, (2017).
- 30 Cohen, JD *et al.* Detection and localization of surgically resectable cancers with a multi-analyte blood test. **Science**, (2018).
- 31 Melo, SA *et al.* Glypican-1 identifies cancer exosomes and detects early pancreatic cancer. **Nature**, (2015).
- 32 Ko, J *et al.* Combining Machine Learning and Nanofluidic Technology To Diagnose Pancreatic Cancer Using Exosomes. **ACS Nano**, (2017).
- 33 Yu, S *et al.* Plasma extracellular vesicle long RNA profiling identifies a diagnostic signature for the detection of pancreatic ductal adenocarcinoma. **Gut**, (2020).
- 34 Kehl, KL *et al.* Artificial intelligence-aided clinical annotation of a large multi-cancer genomic dataset. **Nat Commun**, (2021).
- 35 Singh, DP *et al.* Computerized tomography scan in pre-diagnostic pancreatic ductal adenocarcinoma: Stages of progression and potential benefits of early intervention: A retrospective study. **Pancreatology**, (2020).
- 36 Qureshi, TA *et al.* Predicting pancreatic ductal adenocarcinoma using artificial intelligence analysis of pre-diagnostic computed tomography images. **Cancer Biomark**, (2022).
- 37 Stapley, S *et al.* The risk of pancreatic cancer in symptomatic patients in primary care: a large case-control study using electronic records. **Br J Cancer**, (2012).
- 38 Sharma, A *et al.* Model to Determine Risk of Pancreatic Cancer in Patients With New-Onset Diabetes. **Gastroenterology**, (2018).
- 39 Klein, AP *et al.* An absolute risk model to identify individuals at elevated risk for pancreatic cancer in the general population. **PLoS One**, (2013).
- 40 Muhammad, W *et al.* Pancreatic Cancer Prediction Through an Artificial Neural Network. **Front Artif Intell**, (2019).
- 41 Placido, D *et al.* A deep learning algorithm to predict risk of pancreatic cancer from disease trajectories. **Nat Med**, (2023).
- 42 Klein, EA *et al.* Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. **Ann Oncol**, (2021).
- 43 Liu, MC *et al.* Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA. **Ann Oncol**, (2020).
- 44 Nicholson, BD *et al.* Multi-cancer early detection test in symptomatic patients referred for cancer investigation in England and Wales (SYMPLIFY): a large-scale, observational cohort study. **Lancet Oncol**, (2023).



- 25
- 45 Fiala, C & Diamandis, EP. Can Grail find the trail to early cancer detection? ***Clin Chem Lab Med***, (2019).
- 46 Hinestrosa, JP *et al.* Early-stage multi-cancer detection using an extracellular vesicle protein-based blood test. ***Commun Med (Lond)***, (2022).
- 47 Brand, RE *et al.* Detection of Early-Stage Pancreatic Ductal Adenocarcinoma From Blood Samples: Results of a Multiplex Biomarker Signature Validation Study. ***Clin Transl Gastroenterol***, (2022).
- 48 Pallares, RM & Abergel, RJ. Development of radiopharmaceuticals for targeted alpha therapy: Where do we stand? ***Front Med (Lausanne)***, (2022).
- 49 Targeted Alpha Therapy Working, G *et al.* Targeted Alpha Therapy, an Emerging Class of Cancer Agents: A Review. ***JAMA Oncol***, (2018).
- 50 Hofman, MS *et al.* Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. ***Lancet***, (2020).



### Appendix 1: Australian competitive grants for pancreatic cancer (2019-present)

CIA	Year	Funding Body	Title of project	Funding (\$)
A/Prof Vanessa Beesley	2020	MRFF	PRoCESS: Pancreatic cancer Relatives Counselling and Education Support Service trial. Assessing the effect of nurse-led counselling, compared with information alone, on participant-reported outcomes and use of medical services	801,229
A/Prof Charles Pilgrim	2021	MRFF	SCANPatient: Synoptic reporting of CT scans assessing cancer of the pancreas	2,970,301
Prof Meinir Krishnasamy	2022	MRFF	Overcoming inequity of opportunity for optimal pain and symptom management for Australians affected by pancreatic cancer	1,239,777
Prof Guy Maddern	2022	MRFF	Faecal Microbiota Transplantation to improve pain, symptom management and treatment efficacy in patients with pancreatic cancer	1,521,832
Dr Daniel Croagh	2022	MRFF	Supplemental Jejunal feeding to Improve Quality of Life (SuperQoL)	1,668,079
Prof Benjamin Theiry	2022	MRFF	First-in-Human feasibility and safety trial of a theranostic agent for image-guided treatment and radiosensitisation of advanced pancreatic cancer	1,273,047
Prof Dennis Taaffe	2021	MRFF	A Multicomponent Exercise Medicine Programme in Patients with Pancreatic Cancer Undergoing Neoadjuvant Therapy (the EXPAN trial): A Two-armed Phase I Randomised Controlled Trial	561,910
Prof Sean Grimmond	2019	NHMRC Investigator	Dissecting the mutational landscapes, cellular ecosystems and therapeutic vulnerabilities of pancreatic cancer	2,700,000
Prof Minoti Apte	2019	NHMRC Ideas	Pancreatic Cancer-Related Diabetes: Novel Role of Pancreatic Stellate Cells	486,210
Ms Nadia Khan	2019	NHMRC scholarship	Utilisation of health services in pancreatic and oesophagogastric cancers	67,660



A/Prof Phoebe Phillips	2020	NHMRC Ideas	Hijacking a death switch in pancreatic and lung cancer cells to develop a novel therapy	738,947
Prof Shane Grey	2021	NHMRC Ideas	Harnessing a novel immune check point for cancer killing	924,922.
A/Prof Thomas Cox	2021	NHMRC Development	A First-In-Class Tumour Matrix Targeting Approach to Enhance Chemotherapy in Pancreatic Cancer	827,500
Prof Peter Gibbs	2022	NHMRC Investigator	Circulating tumour DNA informed management of early-stage colorectal cancer and pancreas cancer	3,529,302
Prof Paul Timpson	2022	NHMRC Investigator	Anti-fibrotic targeting and biosensor imaging in pancreatic cancer (PC): taking cancer targeting to new dimensions	2,882,170
Dr Omali Pitiyarachchi	2022	NHMRC Scholarship	Moving Towards Personalising Treatment for Patients with Pancreatic Cancer Using a Patient-Derived Tumour Explant Model	98,470
Dr Brooke Pereira	2022	NHMRC Ideas	Repurposing the in-clinic PCSK9 inhibitor evolocumab to enhance Gemcitabine/Abiraterone chemotherapy in pancreatic cancer guided by single-cell intravital imaging	532,570
A/Prof David Croucher	2022	NHMRC Ideas	Targeting metastatic pancreatic cancer via selective inhibition of oncogenic JNK	775,663
Prof Frederic Hollande	2022	NHMRC Ideas	Developing novel therapeutic strategies and predictive biomarkers in Pancreatic Cancer	1,230,897
A/Prof Daniela Loessner	2022	NHMRC Ideas	Targeting the 4Ms in cancer treatment – matrix, mechanics, microenvironment, metabolism	814,559
Prof Claudine Bonder	2022	NHMRC Ideas	Targeting desmoglein-2 to reinvigorate anti-tumour immunity	1,159,847
Dr Zaklina Kovacevic	2022	NHMRC Ideas	Unlocking the potential of cancer associated fibroblasts to defeat pancreatic cancer.	636,920



## Appendix 2: External stakeholders that participated in online consultation

<b>Name</b>	<b>Organisation</b>
Katrina Anderson	Cancer Australia
Cindy Toms	Cancer Australia
Professor Jaswinder Samra	North Shore Private Hospital/ USyd
Professor Marco Falasca	Curtin
Professor Minoti Apte	UNSW
Doctor Simon Puttick	AdvanCell Isotopes Pty Limited

