

NCRI Pancreatic Study Group Priorities 2023 - 2026



NCRI Partners

NCRI is a UK-wide partnership between research funders working together to maximise the value and benefits of cancer research for the benefit of patients and the public. A key strength of NCRI is our broad membership with representation across both charity and government funders as well as across all four nations in the United Kingdom.



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Introduction

The NCRI Groups bring the cancer research community together to develop practice-changing research, from basic to clinical research and across all cancer types, supporting NCRI's strategy. The NCRI Pancreatic Study Group is a multi-disciplinary community of researchers and consumers focused on developing research to improve outcomes for cancer patients and identify areas of unmet need.

Each NCRI Group engages in a prioritisation process to identify the priority areas in its area of research (Appendix A). This process dictates the work of the group as well as providing an assessment of the state of research for the wider research community.

The NCRI Pancreatic Study Group of the NCRI Upper Gastrointestinal Group has identified its research priorities based on strategy setting session held in June 2022, review by the Group's Chair, and discussion in the Pancreatic Study Group meeting held in January 2023.

There are multiple areas the NCRI Pancreatic Study Group has identified as priorities, an overview of which can be seen below with full details on the following pages of this document. The Group will initially focus on 4 key priorities, forming time-limited working groups to address these priorities. When one working group finishes, capacity will be transferred to address the next priority. An overview of the NCRI Pancreatic Study Group structure can be found on page 6.

The strategies of NCRI Groups will be refreshed every three years. In addition, the research landscape will continue to be routinely assessed by NCRI to ensure the most pressing questions in the pancreatic cancer research landscape are addressed over the course of this three-year strategy.

NCRI Pancreatic Study Group strategic areas at a glance

1. Improving survival outcomes
2. Supporting patients and carers
3. Better detection; early intervention
4. Doing research differently – accessing already available data

Foreword

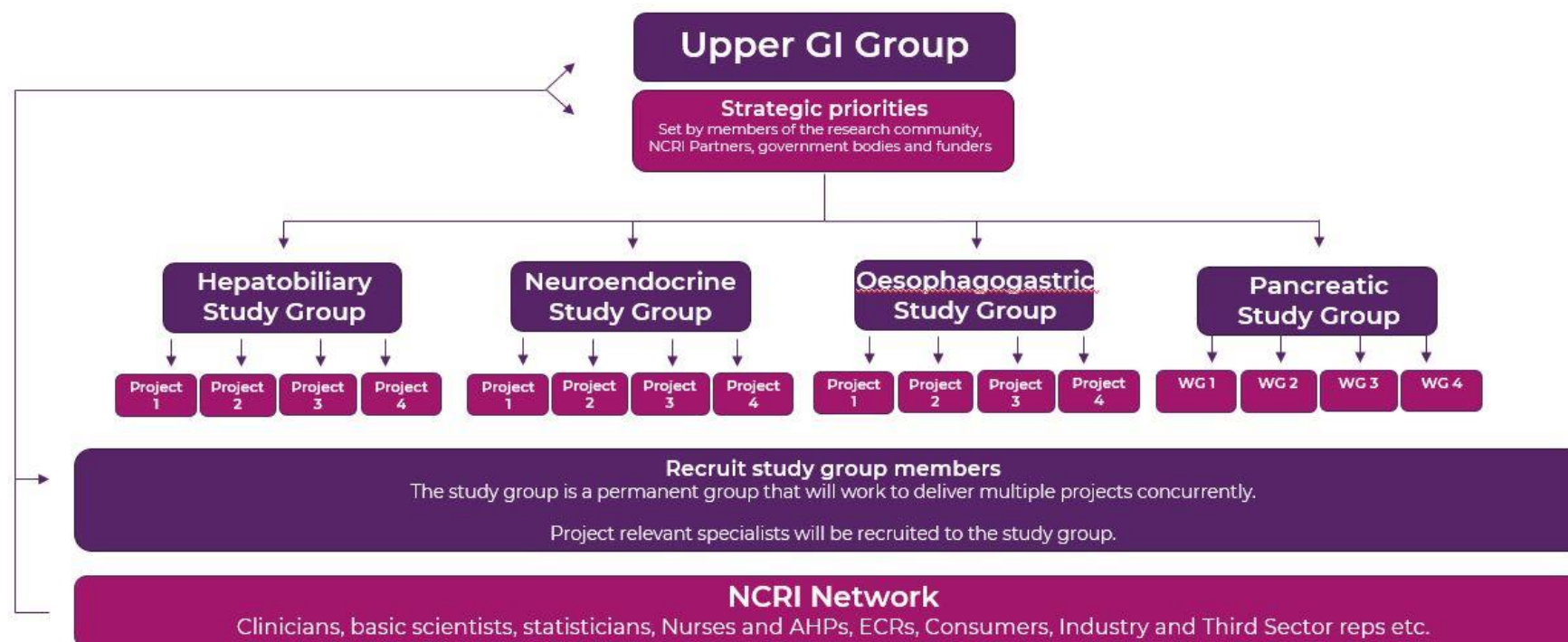


“Pancreatic cancer is one of the most challenging diseases – it is difficult to diagnose and to treat. Despite considerable progress particularly over the last decade in very many aspects of cancer research, outcomes for patients with pancreatic cancer have changed little. Our national expertise during this time has focussed on recognising that not all pancreatic cancers are the same at the molecular level, developing biomarker-stratified treatment approaches, as well as exploring new ways to detect disease early. Our next phase is to capitalise on these strengths, integrating our research into the national genomics landscape and the public health cancer prevention programmes. We must also widen our agenda and work with our patients and advocacy groups, to

address support and well-being needs that are so frequently overlooked. There is much work to do.”

Dr Pippa Corrie, Chair of NCRI Pancreatic Study Group

NCRI Upper Gastrointestinal Group and Pancreatic Study Group structure at a glance



NCRI Pancreatic Working Groups

Initial working groups in set up

The NCRI Pancreatic Study Group has identified eight strategic priorities, full details of which can be found on the following pages of this document. Time-limited working groups will be set up to address four key priorities for the NCRI Pancreatic Study Group, each of which are outlined below. Once one working group reaches completion, capacity will be transferred to the next priority.

Working Group 1: Identification and testing of novel therapeutics

Working closely with the PrecisionPanc team, we will establish a new Novel Therapeutics working group to promote, design and implement signal-seeking trials testing novel therapeutics, which are essential to secure success of larger scale phase III trials aimed at establishing new standards of care.

Working Group 2: Exploration of novel perioperative therapies

Building on our early pancreatic cancer framework, the Perioperative Umbrella Working Group will develop a multi-arm platform study to test different neoadjuvant and adjuvant regimens and generate signals which might justify larger scale randomised trials. The group will also seek to write a position statement on what are the key outcome measures associated with neoadjuvant therapy.

Working Group 3: Evaluate precision radiotherapy

The Radiotherapy working group will initially focus on the role of SABR in locally advanced disease and oligometastases, as part of a framework study. The aim is to understand where Stereotactic ablative radiotherapy (SABR) sits by looking at outcomes including quality of life, cost effectiveness as well as predictive biomarkers/personalisation to differentiate patients with oligorecurrence and oligoprogression versus distant metastatic disease.

Working Group 4: Improve psychosocial and supportive care for pancreatic cancer patients

We propose to bring together a multidisciplinary working group with interest and expertise to scope what is needed to improve psychosocial and supportive care needs for pancreatic cancer patients and their families, potentially generating disease-specific tools for use in routine clinics.

NCRI Pancreatic Study Group strategic priorities 2023

Below are the full priorities identified by the NCRI Pancreatic Study Group.

Strategic theme 1: Improving survival outcomes

Priority 1: Identification and testing of novel therapeutics

Survival outcomes for patients with pancreatic cancer are some of the worst associated with any form of cancer. Over 80% of patients present with unresectable disease and life expectancy for many is under 1 year, despite optimal interventions. Pancreatic cancer is resistant to most standard anti-cancer modalities, and the role of immunotherapy has proven disappointing to date. There is a growing understanding that pancreatic cancer is not a single entity and molecular segmentation of the population may be a route to finding more effective treatments in the future.

The PrecisionPanc programme has provided us with a molecular profiling platform which acts as a springboard for a series of PRIMUS interventional studies, several of which now focus on identifying rare biomarker-specific subgroups of patients who might benefit from a targeted intervention. The PrecisionPanc team works closely with the NCRI group and PRIMUS studies are either endorsed or conceived by the NCRI group. PrecisionPanc includes biomarker discovery, with potential for developing novel therapeutics approaches warranting testing in clinical trials.

As the NHSE genomics laboratory hubs start to function, it is essential that there is smooth transition from the PrecisionPanc research programme to service-based molecular testing in order to ensure continuity of the PRIMUS trials and our group must play a part in overseeing this transition.

Working closely with the PrecisionPanc team, we will establish a new Novel Therapeutics working group to promote, design and implement signal-seeking trials testing novel therapeutics, which are essential to secure success of larger scale phase III trials aimed at establishing new standards of care.

Priority 2: Exploration of novel perioperative therapies

Around 20% of pancreatic cancer patients undergo surgery with curative intent, but in as many as 80% of cases, patients will experience recurrence and die from their disease despite surgical intervention. These statistics indicate that, in general, pancreatic cancer spreads fast. While adjuvant chemotherapy is offered routinely, there is increasing interest to intervene earlier in the pathway, prior to surgery. However, few randomised controlled trials have been undertaken in this setting and optimal treatment for resectable and borderline resectable pancreatic cancer has yet to be defined. From a drug development perspective, neoadjuvant therapy is attractive, since access to surgical specimens after treatment can be studied for biological correlates.

Building on our early pancreatic cancer framework, the **Perioperative Umbrella Working Group** will develop a multi-arm platform study to test different neoadjuvant and adjuvant regimens and generate signals which might justify larger scale randomised trials. The group will also seek to write a position statement on what are the key outcome measures associated with neoadjuvant therapy.

Surveillance after pancreatic cancer surgery is not well defined and is not standardised. Implementing regular surveillance tests such as blood biomarkers and imaging when treatment options at recurrence have limited benefits is also questionable, but beg the questions, what is/are the right surveillance test/s to use and what difference can they make to overall outcomes? Within the Perioperative Umbrella, we will explore opportunity to establish a standard of care arm through which these questions can be addressed.

Priority 3: Evaluate precision radiotherapy

To date, prospective randomised trials have failed to demonstrate a benefit of radiotherapy in patients with pancreatic cancer. Even so, standard radiotherapy is being used to consolidate treatment of locally advanced pancreatic cancer. Modern precision radiotherapy techniques have not so far been formally evaluated and the UK is at the cutting edge of developing these new technologies, including proton beam therapy.

The NCRI pancreatic group has a strong track record in undertaking randomised radiotherapy trials. We therefore have a unique opportunity to evaluate precision radiotherapy for example, combined with systemic therapy backbones in locally advanced disease, identify subgroups of patients who may benefit from this intervention.

The **Radiotherapy working group** will initially focus on the role of SABR in locally advanced disease and oligometastases, as part of a framework study. The aim is to understand where SABR sits by looking at outcomes including quality of life, cost effectiveness as well as predictive biomarkers/personalisation to differentiate patients with oligorecurrence and oligoproggression versus distant metastatic disease.

Strategic theme 2: Supporting patients and carers

Priority 1: Improve psychosocial and supportive care for pancreatic cancer patients

Patient advocates report that exercise and nutrition support help pancreatic cancer patients to better cope with arduous treatment and can improve the mental stress of coping with the diagnosis and prognosis. There are several pilot studies either underway, in set-up, or being developed, which explore the role of exercise and diet in pancreatic cancer patients. We would like to formally collate information regarding these studies, coordinate their conduct to ensure they are completed and consider next steps based on their outcomes, in order to create a national framework for pancreatic cancer support throughout the patient pathway.

Patients and carers, as well as healthcare professionals (HCPs), all agree that holistic care is critical for cancer patient well-being. For pancreatic patients, who frequently struggle with multiple complex symptoms, as well as high levels of anxiety linked to such poor prognosis, high quality, disease-orientated support is lacking and needs to be improved. The Macmillan-led holistic needs assessment tool is available in most trusts but appears not to deliver meaningful benefits for pancreatic cancer patients. Experts are developing a new online platform (in association with the Oncology-TRC), to build a databank of patients' holistic needs at different stages of cancer, with the view of predicting who will need supportive and palliative care interventions sooner. This type of approach could be tailored towards pancreatic cancer.

We propose to bring together a **multidisciplinary working group** with interest and expertise to scope what is needed to improve psychosocial and supportive care needs for pancreatic cancer patients and their families, potentially generating disease-specific tools for use in routine clinics.

Strategic theme 3: Better Detection; earlier intervention

Priority 1: Improve the early detection of pancreatic cancer

Early detection of pancreatic cancer is critical to changing outcomes from this disease which carries such poor prognosis. In December 2020, a virtual innovation sandpit was held and funds were awarded to 5 projects aimed at developing novel ways of detecting pancreatic cancer early. Our national pancreatic cancer charities (Pancreatic Cancer UK and Pancreatic Cancer Research Fund) are active in this space. We will seek to engage with charities, scientists and clinicians to facilitate translating key findings into interventional studies.

Priority 2: Identification of prognostic and predictive biomarkers to better personalise and expedite care

Biomarkers throughout the course of the pancreatic cancer patient pathway are sadly lacking. We need biomarkers to help identify disease early, to determine outcomes following diagnosis and to predict for response to different treatments. Genetic variants might exist that would help to predict those patients more likely to develop particularly challenging symptoms associated with pancreatic cancer, such as pain or cachexia. Our group will work with scientists to identify key putative biomarkers that warrant evaluating prospectively and test appropriate interventions.

We will seek to identify suitable sources of biosamples (blood and tissue) linked to well-annotated patient data, in order to clearly define their role in clinical practice. In particular, we will seek to determine how best to promote, enhance and access the 2 major pancreatic cancer sample repositories in the UK – PrecisionPanc (already alluded to) and the Pancreatic Cancer Research Fund Tissue Bank (<https://www.thepancreastissuebank.org>).

We will also work with national teams developing innovative platform approaches to rapid testing of novel interventions across multiple cancer types (e.g., the Grail/Galeri programme), some of which will be driven through the national genomics laboratory hubs e.g., novel cancer vaccines.

Strategic theme 4: Doing research differently – accessing real world data

Pancreatic Cancer UK is currently working with a multidisciplinary group of healthcare professionals to undertake a landscaping exercise, aimed at developing clear pathways from first symptoms and presentation through to treatment of early and advanced cancer. The aim is to publish standardised pathways which will be available to both patients/carers and to HCPs as a reference to what should be offered routinely to patients. This will be a particularly valuable base from which to build research proposals.

Priority 1: Health service data access

Prospective controlled trials are expensive. In contrast with many international health systems, the NHS is a single public service. As our health service has become digitalised, so the potential to access national datasets has grown, but currently the mechanisms for accessing even fully anonymised data is extremely challenging.

We propose a future working group to consider what practice-changing outcomes we could generate from analysis of real-world data held within NHS health records. Once defined, the group will approach NHS Digital/DataCan to seek access to the data and address the questions raised. The group will undertake a health economic exercise to compare and contrast addressing the question via a prospective trial versus real world data.

Nb: Access to real world data has been highlighted by several NCRI Groups and we will need to work with other colleagues with the intention of ensuring that access to such data is made easier and more straightforward in the future across all cancers, setting out a clear and simple process for future users.

Priority 2: Data capture and patient reported outcomes

There is a strong case for ensuring that prospective trials recruiting pancreatic cancer patients include outcome measures beyond standard efficacy outputs of survival and response, but must also address key challenging symptoms, including cachexia, pain etc. We need to collect data on phenotype and genotype of recruited patients, to prognosticate and predict their incidence of cachexia, pain and other symptoms further down the line.

There is potential for a project on standardisation and linkage of trial databases and datasets, which could add value to information already available and avoid duplication of effort.

NCRI Cross-cutting priority

Identify barriers resulting in a lack of diversity in clinical trials and propose solutions to improve equality, diversity, and inclusion.

Barriers resulting in a lack of diversity in clinical trials across cancer types has been raised as an issue in many of NCRI's discussions with researchers. For this reason, this priority will be addressed collaboratively in a working group comprising experts from across NCRI Groups. This priority aims to establish the reasons behind a lack of diversity in clinical trials and provide solutions to increase participation of a diverse cohort of patients in future studies. A working group will address the common issues across the board, as well as identifying cancer-type specific barriers, and produce guidelines on the steps to take to improve the inclusion of patients from a range of backgrounds into clinical trials from their inception. More details on this working group will be decided in due course.

General themes of the NCRI Pancreatic Study Group

- **Prioritising bio sample collection:**

- Within all clinical studies, there should be opportunities taken to collect relevant bio samples. The patient consenting process needs to promote access as widely as possible for specific as well as related research.
- Biobanks are difficult to establish and fund, but should be invested in where possible, as a means of promoting national and international research into pancreatic cancer. The NCRI network of investigators and patients should actively contribute samples and data to them, once established.

- **Communication with patients and carers:**

- Patients and carers need high quality information to help them understand the pancreatic cancer patient pathway and how research fits with their care.
- There is a need to improve and provide timely access to information at the outset of pancreatic cancer diagnosis, demystifying treatment options and raising awareness regarding research opportunities that might be accessed as their first line of treatment.
- Healthcare professionals should consider working with their local community to create local “pancreatic cancer champions” who can support patients and carers and promote their access to research and treatment.

- **Trial design:**

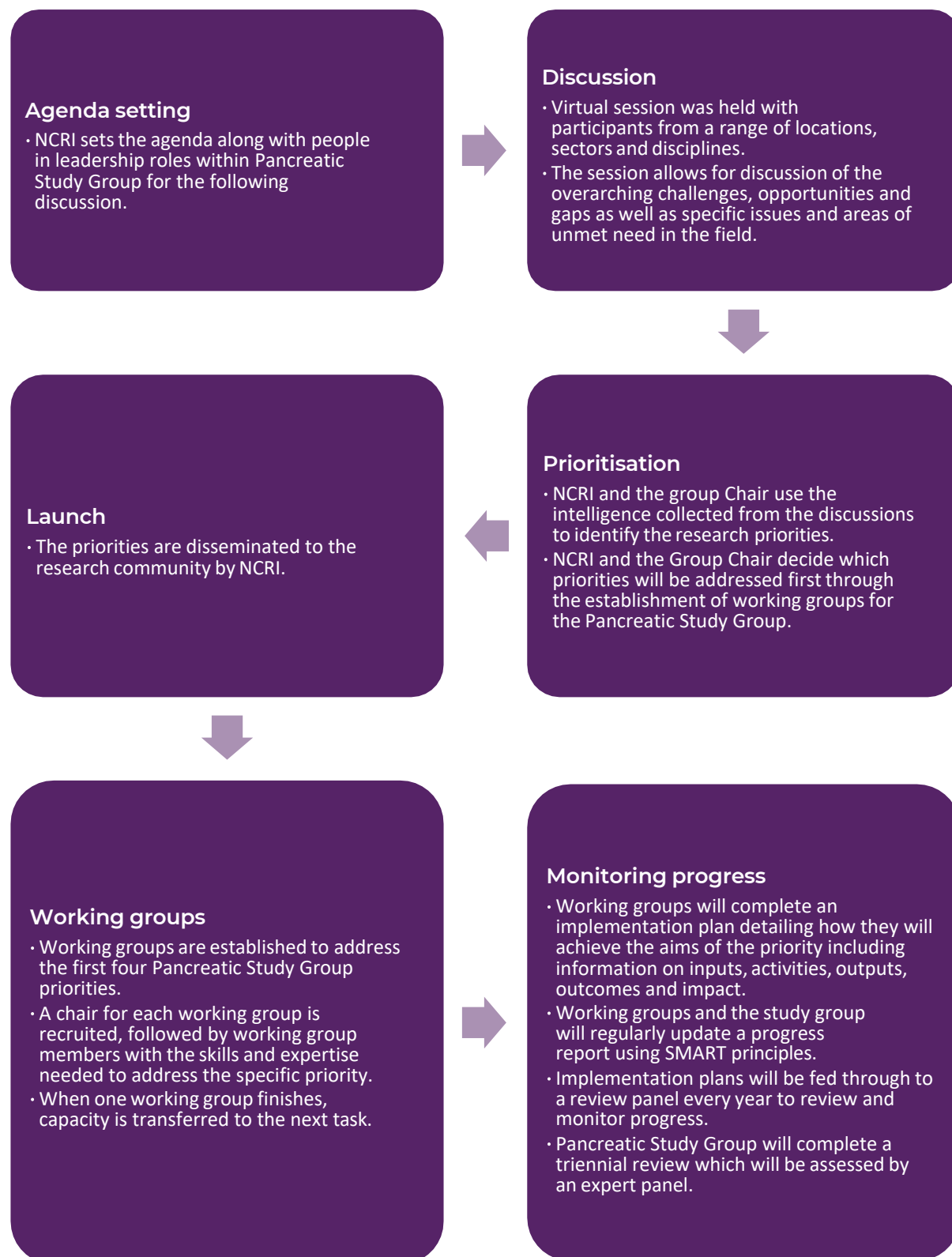
- All trials developed by the study group must be well-designed, with clear, clinically meaningful, endpoints and suitable control groups, co-developed with patient representation. In particular, given that pancreatic cancer patients are highly symptomatic, including patient experience outcome measures is a high priority.

Next steps

Working groups addressing the highlighted tasks are currently being formed. These groups will be made up of the experts needed to address each research question. To be the first to hear about opportunities to join these working groups please sign up to the [NCRI Upper Gastrointestinal Network](#). The progress of these working groups will be published in the annual reports and triennial review of NCRI Upper Gastrointestinal Group. These can be found on the [NCRI website](#). Members of the NCRI Upper Gastrointestinal Network will also be updated periodically on the progress of the group.

Please [get in touch](#) if you have any questions or comments regarding this report or if you are interested in joining one of the [NCRI Networks](#), the [NCRI Consumer Forum](#) or our [NCRI Early Career Researcher Forum](#).

Appendix A - NCRI Pancreatic Study Group priority setting process



Appendix B - NCRI Pancreatic Study Group priority discussion contributors

The NCRI Pancreatic Study Group developed their strategic priorities through discussions with professionals from a range of sectors and disciplines, including NCRI Consumer Forum members, early career researchers and NCRI Partners, as well as members of the NCRI Strategy Advisory Group (SAG). We thank all contributors for their invaluable input into these discussions and the subsequent priorities addressing the most pressing needs in pancreatic research today.

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