

Research Ambition

Historical underfunding in research means that pancreatic cancer remains one of the deadliest cancers with a five-year survival rate of just 7%.

Over 80% of people are diagnosed late; 70% of patients receive no treatment with curative intent.

Current treatments are limited and highly toxic, and people with pancreatic cancer are often too unwell to tolerate the challenging side-effects they cause

<u>The scale of the challenge we face may seem almost insurmountable, but</u> <u>through research we will make significant advances in how to detect and treat</u> <u>this disease.</u>

We already see progress building in the field, but it is vital that we maintain this momentum and accelerate the pace of discoveries that we so urgently need. We must also remain focused, committing our efforts as a research community to critical areas of unmet need, that if addressed, represent watershed moments for the detection, treatment and care of people with pancreatic cancer.

Pancreatic Cancer UK aim to double the survival rates of pancreatic cancer over the next 5 years. Although ambitious, it is also reasonable to expect better than 7% survival for people affected by this devastating disease.

Research is absolutely essential to achieve change now but is most important for the long-term sustained survival improvement we need to see. The most significant improvements in detection and advances in treatment options and efficacy will be from research breakthroughs.

We have detailed key areas in early detection and treatment discovery that we believe should form the focus of the research we support. This should be used to frame any applicants' proposals to the charity, helping you to draw the line of sight from even the most discovery focused research through to long term patient benefit.

Accelerate early detection and interception

Detection in the general population (early symptomatic diagnosis)

We know the vast majority of people who get pancreatic cancer will not have any predisposition to the disease. The only time we will know about it is when they start presenting with vague and unspecific symptoms.

However, we also know that even these vague and unspecific symptoms present months and years before someone is actually diagnosed, meaning we could identify people sooner, if we knew when and where to actively look for symptoms.



We will invest in research that tackles these key scientific 'How might we' questions:

- Support the discovery and validation of new biomarkers that would indicate the presence of pancreatic cancer at an early stage?
- Incorporate those biomarkers into better detection tools that can be quickly and effectively integrated into the NHS?
- Use hospital records to identify more people who have early signs of cancer and should be sent for imaging?
- Enable GPs to quickly identify and refer patients for further specific diagnostic tests?
- Differentiate type 3C diabetes, which is associated with pancreatic cancer, from other types of diabetes?

Identify and stratify at-risk groups

We know that obesity, pancreatitis and advancing age increase your risk of pancreatic cancer. We know that a certain genetic makeup and family history increases your risk too.

Even though we know what the risk factors are, a key challenge is understanding the level of risk and when is the right moment to intervene or not, for each person, so we are sure we are truly treating disease and not causing unnecessary harm.

We will invest in research that tackles these key scientific 'How might we' questions:

- Better understand the risk factors to work out when, how and if clinical intervention is appropriate for someone who is at risk?
- Develop better ways to enrich risk groups e.g. family history, chronic pancreatitis?
- Support the development of pragmatic and appropriate surveillance strategies?
- Identify and then stratify the risk of premalignant lesions (pancreas cysts)?

Drive Treatment Discovery & Translation

Discovery of novel therapeutic targets

The more researchers understand about cancer at the molecular and cellular level, the more opportunities there are to exploit its weakness for treatment.

Currently, we don't know enough about the fundamentals of pancreatic cancer initiation nor how it progresses, which has limited our ability to identify potential



targets for therapy and hindered the development of novel therapeutic interventions.

We will invest in research that tackles these key scientific 'How might we' questions:

- Understand how pancreatic cancer evolves in the patient and why it metastasises so quickly around the body?
- Understand the heterogeneity and subtypes of pancreatic cancer and how can we harness that for personalised treatment?
- Better understand the interaction between cancer, host and tumour microenvironment?
- Understand why cachexia is so prevalent in pancreatic cancer patients and how can it be eliminated?

Early translational research

Translational research is key to progressing promising findings towards clinical trials for novel therapies in pancreatic cancer.

It validates discoveries at a cellular level using complex, disease-replicating preclinical models (e.g. animal models, organoid). It allows us to take a step back to better understand and refine current treatments. It enables us to quickly translate treatments effective in other cancer types into use for pancreatic cancer patients.

However, we do not reach this critical step in treatment development frequently or effectively enough, meaning potential breakthroughs languish in the lab, or benefits are only limited to other cancers.

We will invest in research that tackles these key scientific 'How might we' questions:

- Develop new and improve current pre-clinical experimental systems to better replicate the complexity of human disease?
- Fast track the translation of new therapies from other cancer types into pancreatic cancer?
- Utilise translational research to enhance treatment effect and decrease side effects of current pancreatic cancer treatments?
- Increase the capacity, throughput and coordination of the pre-clinical modelling community?