Pancreatic Cancer UK

Pancreatic Cancer

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Learning objectives

- Learn more about the role of the pancreas in health
- Learn how pancreatic cancer can effect these functions
- Learn more about how pancreatic cancer can present, its signs and symptoms
- Learn more about how it is diagnosed.

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The Pancreas

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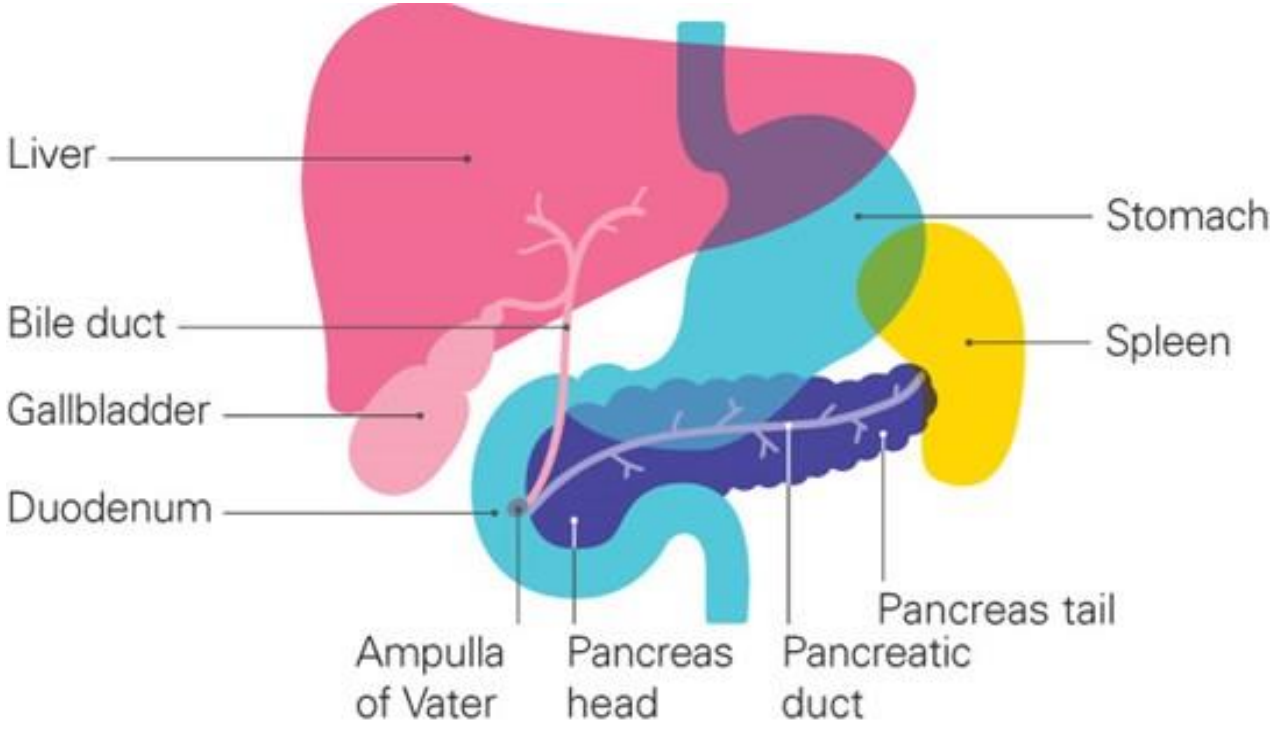

- Large gland situated deep in the abdomen in between the stomach and the spine.
- Plays an important role in digestion.
- Produces enzymes and hormones to help break down food and regulate blood sugar.

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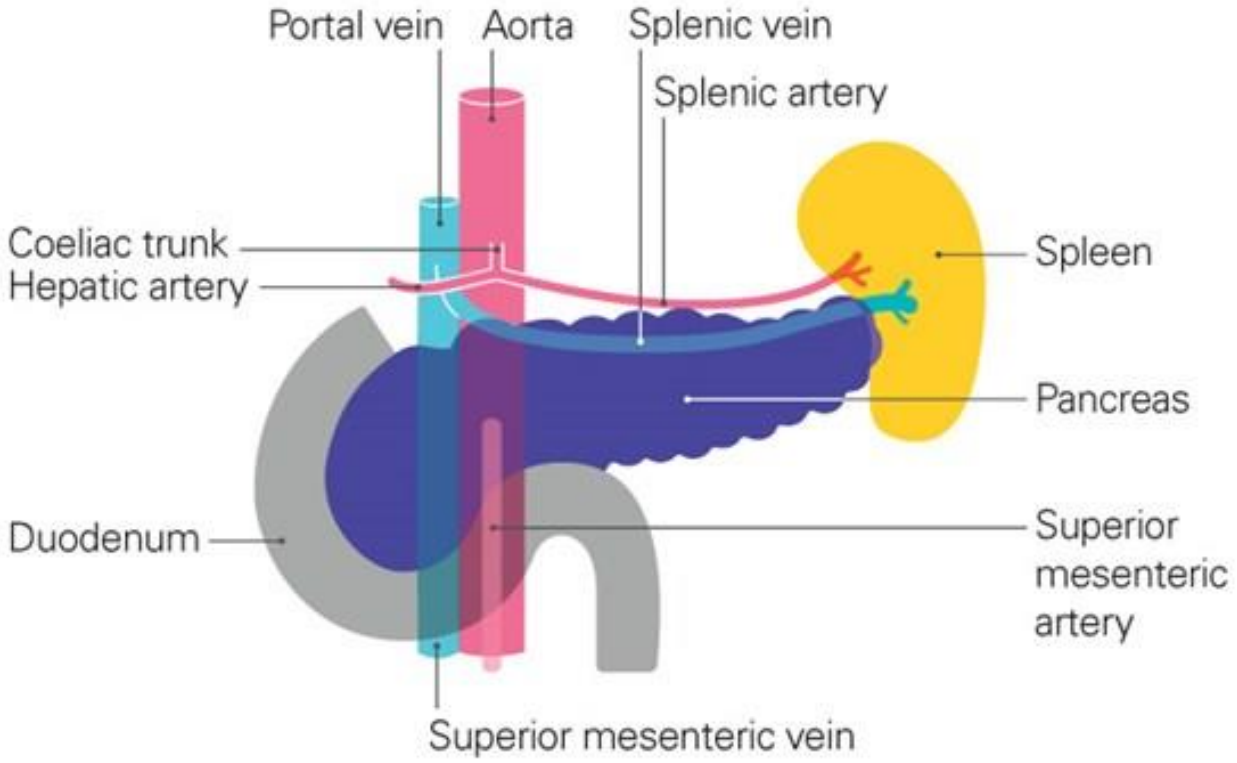

- The pancreas is positioned close to a number of major blood vessels.
- The close proximity to these vessels poses challenges to offering surgery even for those with localised disease

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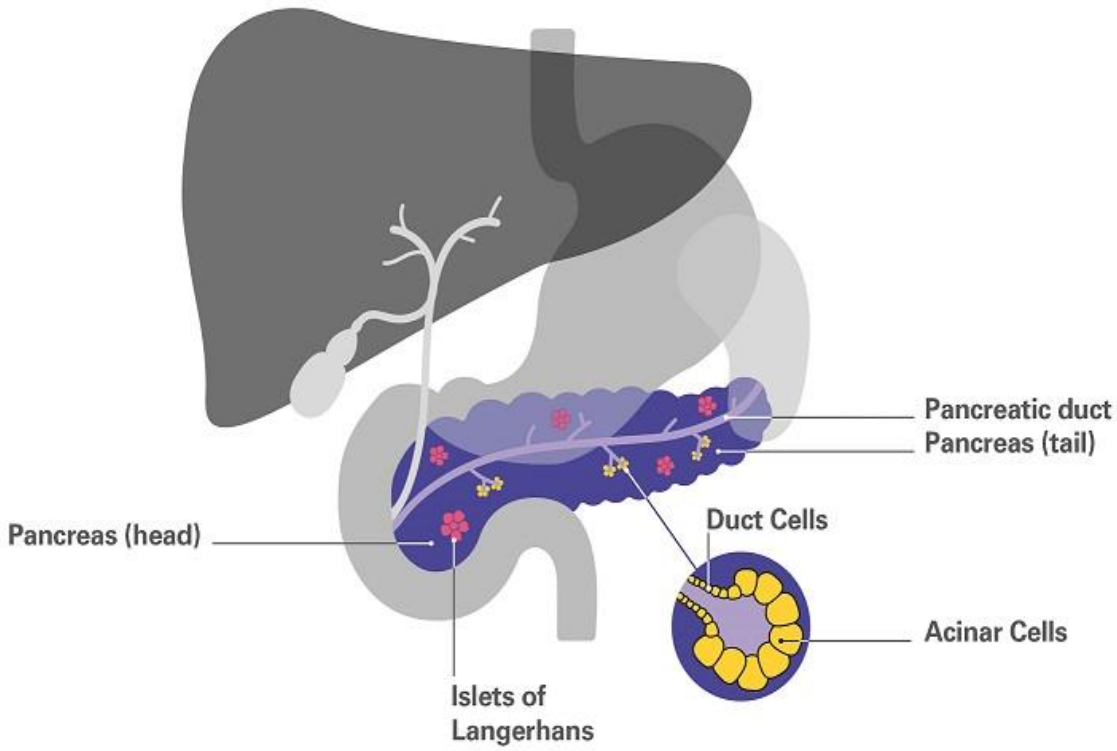
Exocrine Pancreas



The exocrine function describes the role of the pancreas in breaking down and absorbing nutrients in the small intestine.

Acinar (asina) cells are contained mostly in the head of the pancreas and secrete pancreatic enzymes when stimulated.

The pancreatic juices contain enzymes:

- Protease to break down protein
- Lipase to break down fat
- Amylase to break down carbohydrate

The pancreatic enzymes travel along the pancreatic duct and become activated when they reach the duodenum.

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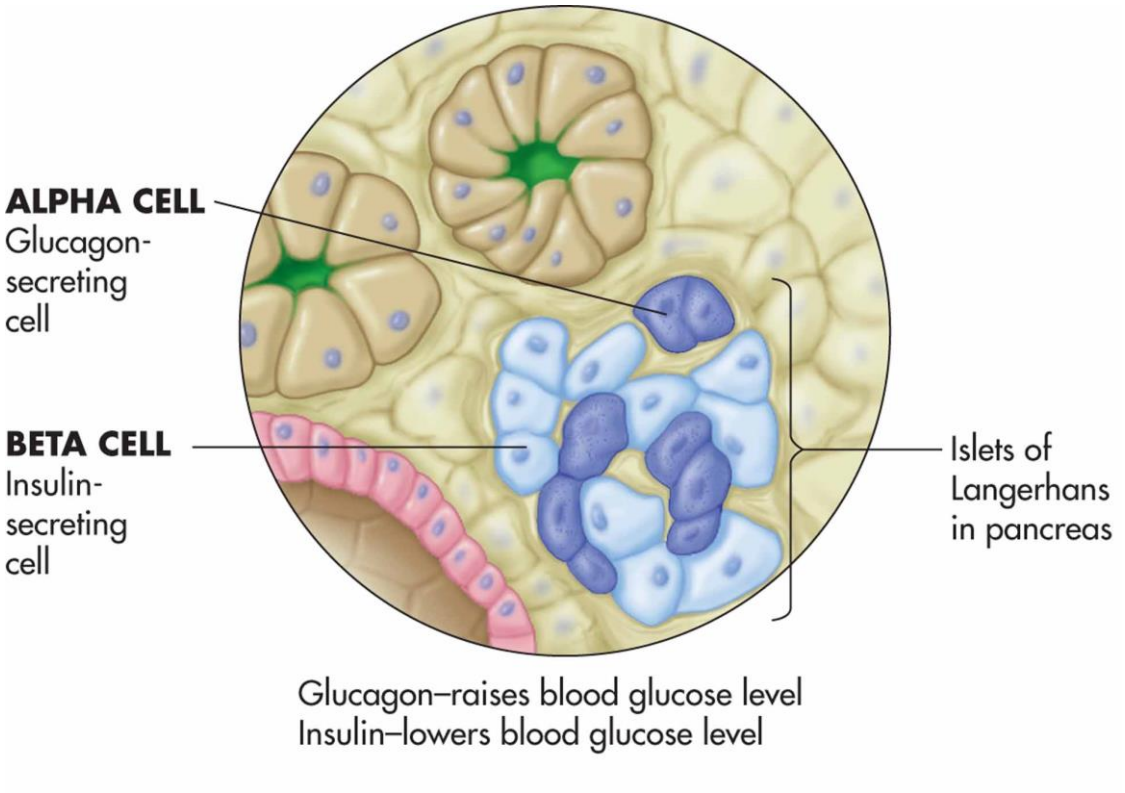
Endocrine Pancreas



- Produces hormones from the **Islets of Langerhans** cells to regulate blood glucose levels.
  - **Insulin**, produced by beta cells, reduces the amount of glucose in the blood.
  - **Glucagon**, produced by alpha cells, helps to increase the amount of glucose in the blood if it becomes too low.

- **Somatostatin**, produced in delta cells, plays many roles in digestion, including inhibiting the amount of glucagon and insulin, to prevent excessive secretion.

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Pancreatic Cancer can affect both of these functions

Digestion – PEI present in vast majority of cases, enzyme insufficiency in 66-94% of people at presentation. Function deteriorates by approx.10% every month.

(M. Philips PERT breakfast meeting June 2021)

Diabetes – Diabetes and PDAC demonstrate "dual causality,"

- long-standing type 2 diabetes (T2DM) is a risk factor for the development of PDAC
- PDAC is a presumed cause of diabetes in a large number of cases.

It is estimated 65% of patients have diabetes mellitus at diagnosis. Whereas the prevalence of diabetes ranged from 15 to 21% in the other age-matched cancer cohorts.
New-onset diabetes can be an early warning sign of the presence of pancreatic cancer, and individuals with new-onset diabetes are a high-risk group for pancreatic cancer.

https://www.lctc.org.uk/research/uk-edi/

(Diabetes Volume 66, May 2017)

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Pancreatic Adenocarcinoma & Pancreatic Neuroendocrine Tumours; is there a difference?

Pancreatic Adenocarcinoma (PDAC)

- Exocrine pancreatic cancer (including Pancreatic Ductal Adenocarcinoma (PDAC)) is the most common and aggressive subtype of pancreatic cancer
- **Accounts for 95% of pancreatic malignancies**
- Originates in the ductal cells
- **8% receive surgery**
- **1 year survival 18.9%**
- Ongoing symptoms management,
  - Diet, think pancreatic enzyme insufficiency (PEI) and pancreatic enzyme replacement therapy (PERT) https://www.pancreaticcancer.org.uk/information/managing-symptoms-and-side-effects/diet-and-pancreatic-cancer/pancreatic-enzyme-replacement-therapy-pert
  - Diabetic monitoring and treatment
  - Exercise
  - Psychological support

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Pancreatic Neuroendocrine Tumour (pNET)

- Endocrine pancreatic cancer is a rare cancer and largely less aggressive (although higher grade pNETs are more aggressive)
- Accounts for 5% of pancreatic malignancies
- Originates in the neuroendocrine cells within the pancreas – known as Islet of Langerhans
- **40% receive surgery**
- **1 year survival 79.8%**
- Affect in the pancreas can be similar to PDAC in regards to
  - Diet, think pancreatic enzyme insufficiency (PEI) and treatment with pancreatic enzyme replacement therapy (PERT)
    https://www.neuroendocrinecancer.org.uk/neuroendocrine-cancer/diet-nutrition/
    https://www.pancreaticcancer.org.uk/information/managing-symptoms-and-side-effects/diet-and-pancreatic-cancer/pancreatic-enzyme-replacement-therapy-pert
  - Diabetic monitoring and treatment
  - Psychological Support

- **For pNET (and all NET) patient support and information**
  https://www.neuroendocrinecancer.org.uk/

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Presentation, Diagnosis & Staging

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Early diagnosis is essential to increase survival

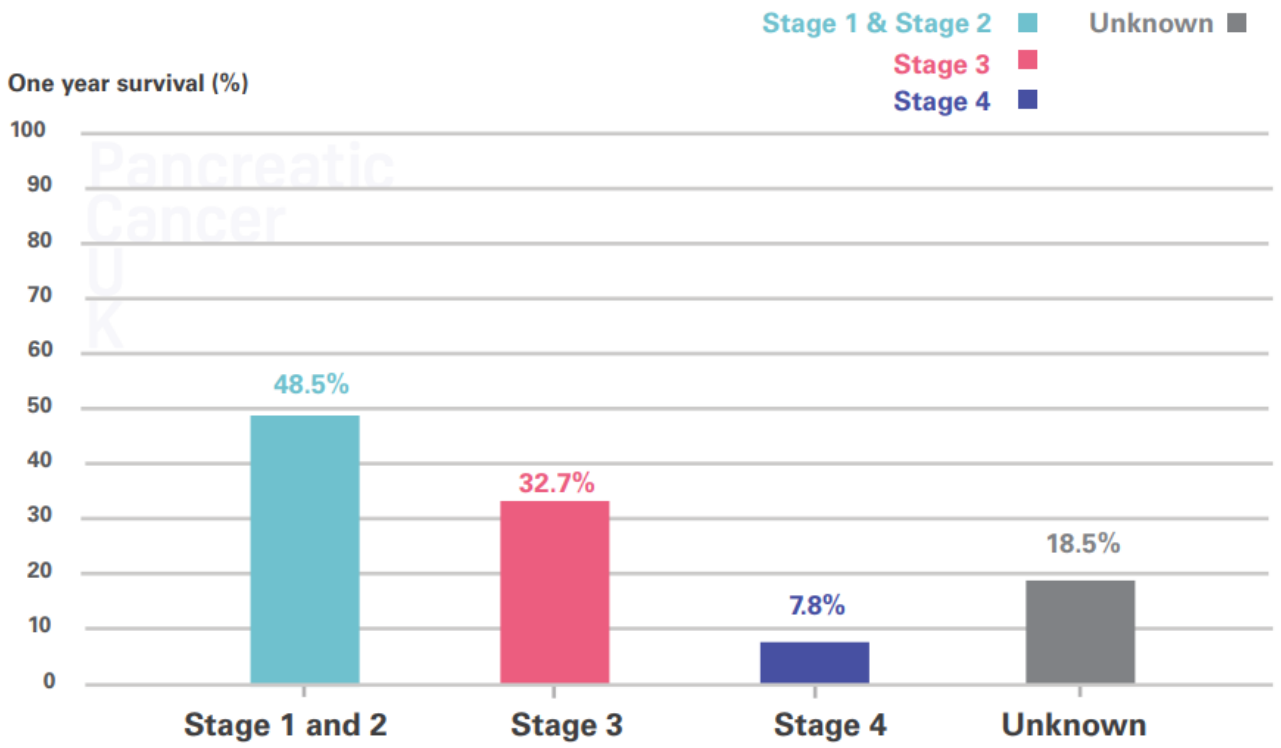

Figure 1: One year survival for people with exocrine pancreatic cancer diagnosed at each stage

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What are the known risk factors?

There is **good** evidence that, age, smoking, being overweight, family history of cancer, pancreatitis and diabetes **may** increase your risk of pancreatic cancer.

Some evidence has suggested that there are other things **may** also increase risk, such as alcohol, red and processed meat and hx of cancer – more research is needed.

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Hereditary/Familial/Gene Link

Familial pancreatic cancer

Familial pancreatic cancer is pancreatic cancer that runs in families. This includes:

- families with two or more first-degree relatives (parent, brother, sister or child) with pancreatic cancer
- families with three or more relatives with pancreatic cancer on the same side of the family
- families with a known family cancer syndrome and at least one family member with pancreatic cancer.

The risk of familial pancreatic cancer increases if:

- relatives were diagnosed under the age of 60
- there are more than two people under 60 with pancreatic cancer in the family
- there are people with pancreatic cancer in more than one generation on the same side of the family.

We still don't know what genetic faults cause most familial pancreatic cancers. We only know about the genetic faults that cause about one in five (20%) familial pancreatic cancers.

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These rare genetic conditions can increase the risk of pancreatic cancer.

Peutz-Jeghers syndrome

Faults in the BRCA2 and BRCA1 genes

Both men and women can have faults in the BRCA2 and BRCA1 genes.

Faults in the PALB2 gene

Familial atypical multiple mole and melanoma syndrome (FAMMM)

Lynch syndrome

Li-Fraumeni syndrome

Hereditary pancreatitis

Pancreatitis is inflammation of the pancreas. Hereditary pancreatitis is a rare condition that runs in families. It starts in early childhood, and can keep coming back. It is linked to a fault in the PRSS1 gene. People who carry this faulty gene have a very high chance of developing pancreatitis.

People with hereditary pancreatitis **may** be more likely to get pancreatic cancer. About two fifths (40%) of people with hereditary pancreatitis **may** develop pancreatic cancer at some point in their lives. The **risk may be higher** for people who smoke and people who have diabetes.

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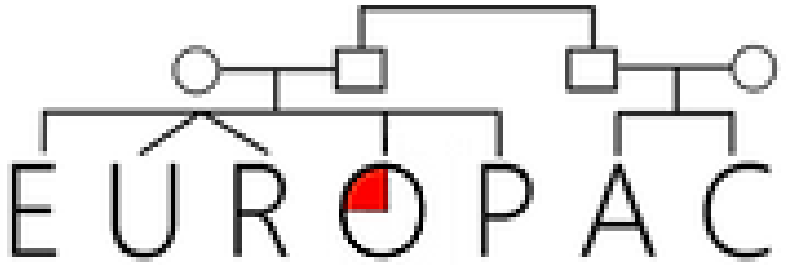

THE EUROPEAN REGISTRY OF FAMILIAL PANCREATIC CANCER AND HEREDITARY PANCREATITIS

- EUROPAC started to recruit families in 1997
- currently have over 1800 families registered.
- study aiming to understand inherited conditions of the pancreas.
- recruit people with a family history of pancreatic cancer and people who have been diagnosed with hereditary pancreatitis.
- offer secondary pancreatic cancer screening to those who are considered to be at a higher risk of developing pancreatic cancer.

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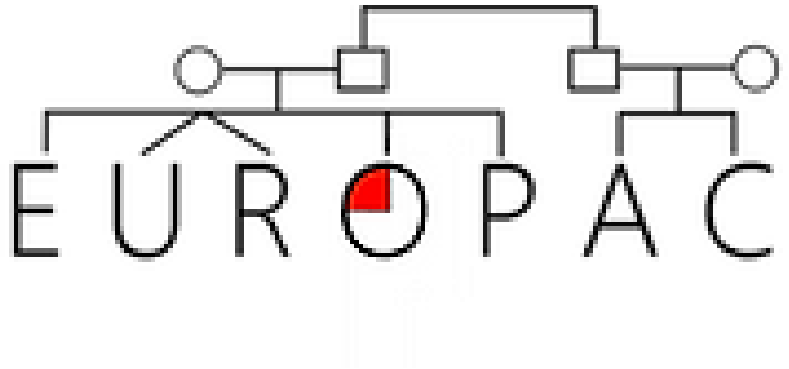

The trial is **based at The Royal Liverpool University Hospital**, where all recruitment takes place. Once recruited, we have 8 screening centres around Britain. These are:

- Glasgow Royal Infirmary
- Freeman Hospital, Newcastle
- St James' Hospital, Leeds
- Queen's Medical Centre, Nottingham
- Morriston Hospital, Swansea
- Bristol Royal Infirmary
- University College London Hospital
- University Hospital, Southampton

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Signs and Symptoms

- Abdominal pain +/- back pain
- Dyspepsia/reflux/bloating
- Fatigue
- Change in bowel habits
- Unintentional weight loss
- New onset diabetes
- Jaundice
- Clots

Nobody knows your body better than you.

If you have any of these symptoms it might suggest a problem with your pancreas, such as pancreatic cancer.

Abdominal (tummy) pain which can spread to the back	Unexplained weight loss and loss of appetite	Jaundice (yellow skin or eyes)	Oily floating poo	Indigestion

If you have jaundice you should go to your GP without delay.
If you have any of the other symptoms and they are unexplained or persistent (lasting 4 weeks or more), visit your GP. Remember, these symptoms can be signs of other conditions and may not be pancreatic cancer.

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Concerned about these symptoms?
Contact the Pancreatic Cancer UK Support Line
0808 801 0707 freephone weekdays 10am-4pm
support@pancreaticcancer.org.uk
Find out more
pancreaticcancer.org.uk/symptoms

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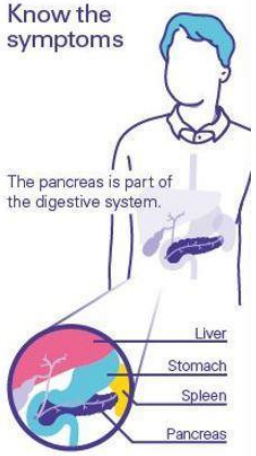
What are the symptoms of pancreatic cancer?

- **Tummy pain which can spread to the back**
- **Unexplained weight loss and loss of appetite**
- **Change in bowel habits**
- **Indigestion**
- **Jaundice (yellow skin or eyes and itchy skin)**

If you have jaundice, go to your GP or A&E straight away.

If you have any of the other symptoms for 4 weeks or more, go to your GP.

Know the symptoms



The pancreas is part of the digestive system.

It produces enzymes which help break down food and hormones which control the sugar levels in our blood.

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The symptoms of pancreatic cancer

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How is pancreatic cancer diagnosed?

This fact sheet is for anyone having tests for pancreatic cancer. Families may also find it helpful. It explains the different tests that you might have, what they involve, and what your test results mean. There is also information about the support available to you.

Every hospital will do things slightly differently, so speak to your GP, consultant or specialist nurse if you have any questions.

You can also speak to our specialist nurses on our confidential Support Line. Call free on **0808 801 0707** or email **nurse@pancreaticcancer.org.uk**

Contents

Why is pancreatic cancer difficult to diagnose? 2
Seeing your GP 3
Tests for pancreatic cancer 5
How long will I have to wait for my test results? 12
What do my test results mean? 13
Coping with your diagnosis 18
What happens next? 19
More information and support 21

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Challenges in early diagnosis

- Vague and non specific symptoms
- No simple diagnostic test
- Symptoms often don’t present until a late stage

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- 48% of patients are diagnosed via A&E emergency route
  - **V's 22% in other cancer cohorts**
  - **One year survival of pancreatic cancer patients presenting via A&E is just 12%**
  - **Survival is 3x higher is diagnosed through GP referral**
- 55% diagnosed with metastatic disease
- 30% diagnosed with locally advanced pancreatic cancer
- 15% operable disease at diagnosis

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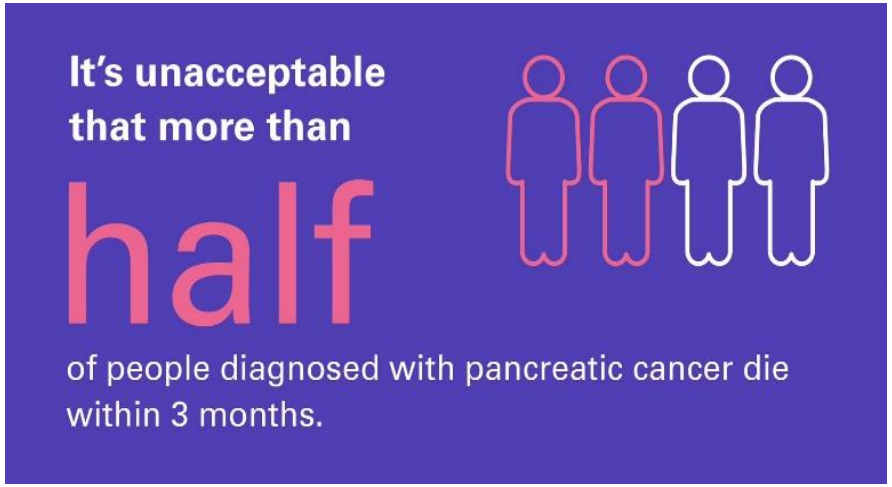
Pancreatic cancer has the lowest survival of all common cancers, with five-year survival just over 7%.

- 1 in 4 people diagnosed with pancreatic cancer will die within one month.
- 1 in 2 people diagnosed die within 3 months.
- 3 in 4 people will die within a year.



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NICE National Institute for Health and Care Excellence

NICE guideline

NICE Guidelines recommend, if a patient is aged 40 and over and has jaundice, they should be referred on a suspected cancer pathway for an appointment within two weeks.

An urgent direct access CT scan should be considered, to be performed within two weeks, or an urgent ultrasound scan if CT is not available, to assess for pancreatic cancer in people aged 60 and over with weight loss and any of the following:

- diarrhoea
- back pain
- abdominal pain
- nausea
- vomiting
- constipation
- new-onset diabetes.


Pancreatic cancer in adults: diagnosis and management

NICE guideline
Published: 7 February 2018
www.nice.org.uk/guidance/ng85

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Diagnostics

Blood tests CA 19-9 and CEA specific pancreatic tumour markers, however if raised does not necessarily mean 'cancer'.

Abdominal Ultrasound inexpensive, non invasive. Around 10% of pancreatic cancers will be missed on abdominal ultrasound making CT scan more reliable for diagnosis.

CT (computed tomography) often given IV injection of contrast to highlight blood supply to certain organs.

NICE guidelines recommend that patients with suspected pancreatic cancer should be sent for an urgent CT scan.

EUS – (Endoscopic Ultrasound) \| Endoscope & ultrasound combined. Very accurate, good for visualizing Lymph nodes and taking biopsies in particular.

MRI/MRCP (magnetic resonance imaging/cholangiopancreatography) useful addition to imaging, can be more specific for liver metastases and highlighting abnormalities with in the bile ducts

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Diagnostics

ERCP – (endoscopic retrograde cholangiopancreatography) usually for those who are jaundiced, an endoscope is passed through mouth, down the into stomach and then the duodenum. A smaller tube is then inserted through the center of endoscope and dye is injected to highlight any obstruction to its flow through the biliary system.

PET – (Positron Emission Tomography) very specialized nuclear medicine scan that utilizes radioactive substances. Use more often with those cases with locally advanced disease.

NICE guidelines recommend that if a diagnosis isn't clear following a CT scan, patients should be offered an FDG-PET/CT and/or EUS with tissue sampling. NICE also recommend offering FDG-PET/CT to people with localised disease who will behaving cancer treatment (surgery, radiotherapy or systemic therapy)

Good tissue diagnosis is imperative for chemotherapy, clinical trials and/or genetic profiling

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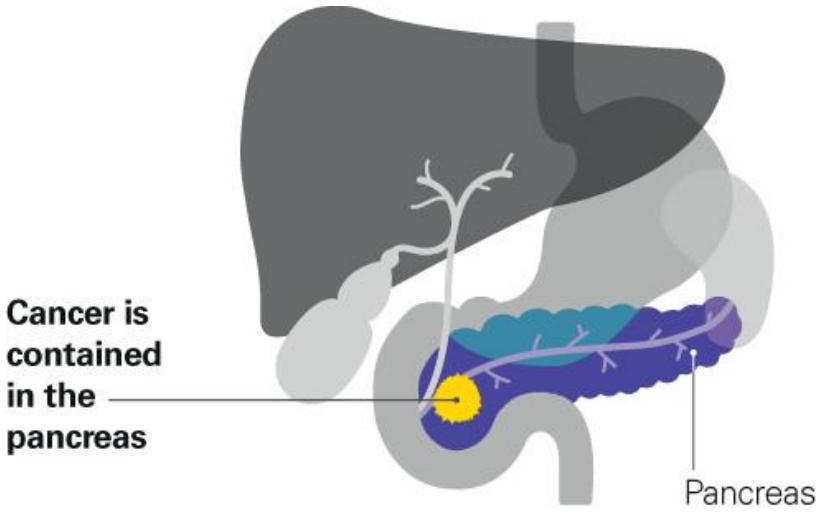
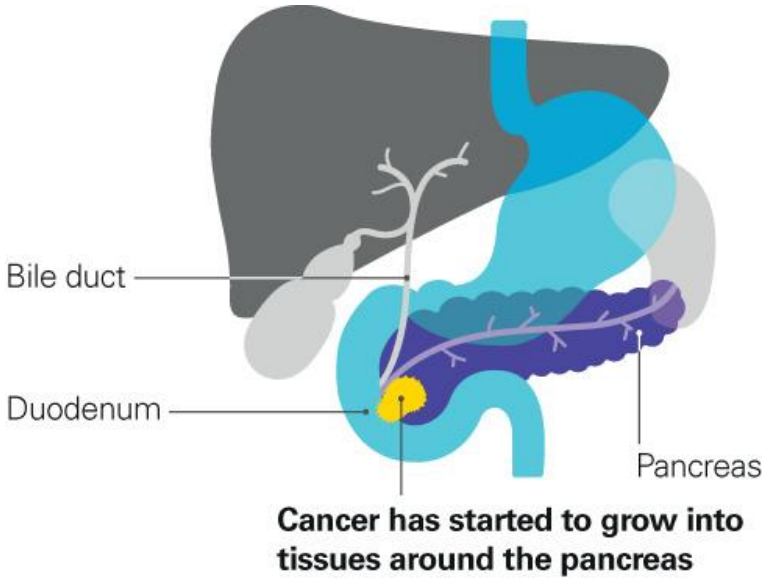
Stage 1



Stage 2



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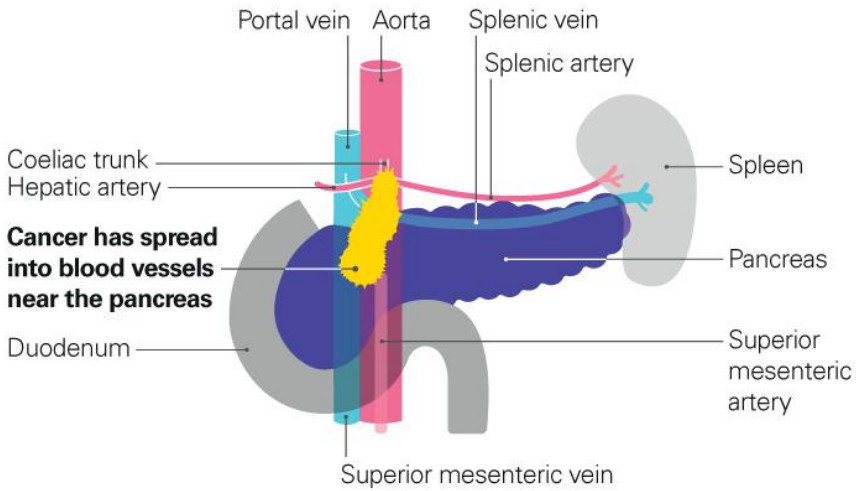
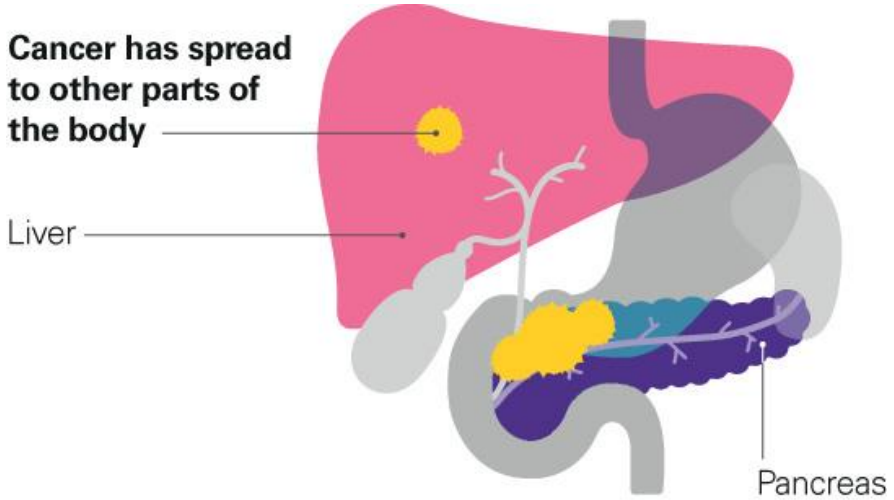
Stage 3



Stage 4



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NICE National Institute for Health and Care Excellence

NICE guideline

Staging

- For people with newly diagnosed pancreatic cancer who have not had a pancreatic protocol **CT scan**, offer a pancreatic protocol CT scan that includes the chest, abdomen and pelvis.

- Offer fluorodeoxyglucose-positron emission tomography/CT (**FDG-PET/CT**) to people with localised disease on CT who will be having cancer treatment (surgery, radiotherapy or systemic therapy).

- If more information is needed to decide the person's clinical management, consider one or more of the following

    - MRI, for suspected liver metastases
    - endoscopic ultrasound, if more information is needed for tumour and node staging
    - laparoscopy with laparoscopic ultrasound, for suspected small-volume peritoneal and/or liver metastases if resectional surgery is a possibility.

Pancreatic cancer in adults: diagnosis and management

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Table 2. TNM classification 7th edition[a]

Primary tumour (T)	
T0 = No evidence of primary tumour	
Tis = Carcinoma *in situ*	
T1 = Tumour limited to the pancreas, ≤2 cm in greatest dimension	
T2 = Tumour limited to the pancreas, >2 cm in greatest dimension	
T3 = Tumour extends beyond the pancreas but without involvement of the coeliac axis or the superior mesenteric artery	
T4 = Tumour involves the coeliac axis or the superior mesenteric artery (unresectable primary tumour)	
Regional lymph nodes (N)	
NX = Regional lymph nodes cannot be assessed	
N0 = No regional lymph node metastasis	
N1 = Regional lymph node metastasis	
(A minimum number of 10 lymph nodes analysed is recommended.)	
The regional lymph nodes are the peripancreatic nodes which may be subdivided as follows:	
Superior	Superior to head and body
Inferior	Inferior to head and body
Anterior	Anterior pancreaticoduodenal, pyloric (for tumours of head only), and proximal mesenteric
Posterior	Posterior pancreaticoduodenal, common bile duct, and proximal mesenteric
Splenic	Hilum of spleen and tail of pancreas (for tumours of body and tail only)
Coeliac	For tumours of head only
Distant metastasis (M)	
M1	Distant metastasis

[a]By permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Handbook, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springer.com.

ANNALS OF ONCOLOGY
driving innovation in oncology

Cancer of the pancreas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

Annals of Oncology 26 (Supplement 5): v56–v68, 2015
doi:10.1093/annonc/mdv295

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Summary

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There is good evidence that older age, family history of pancreatic cancer, pancreatitis, diabetes, smoking and being overweight increases the risk of pancreatic cancer.

Diagnosis is complex
Early diagnosis is crucial in improving survival outcomes for people with pancreatic cancer.

The most common symptoms of pancreatic cancer are:

- abdominal and back pain
- unexplained weight loss
- indigestion

Other symptoms include: change in bowel habit, loss of appetite, jaundice, new-onset diabetes, fatigue, blood clots, bloating/burping/flatulence, and nausea and vomiting.

To consider for all,

- Diet and digestion
- Diabetes
- Emotional Support
- Pro-active symptom management
- Information

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