Familial risk of pancreatic cancer fact sheet

This fact sheet is for anyone with concerns that they may be at increased risk of developing pancreatic cancer because a family member(s) has been diagnosed with the disease. It provides information on familial risk of pancreatic cancer, hereditary pancreatic cancers, the screening available for people at higher risk and how to find out if you may be at increased risk of developing pancreatic cancer.

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Introduction

Sometimes cancers are said to ‘run in the family’. This means there is a faulty gene somewhere that gets passed down the generations. People in a family who carry the faulty gene are at increased risk of developing cancer, although it doesn’t mean they will always develop cancer. This is known as inherited, hereditary or familial cancer, or family cancer syndrome.

What are genes?

Each person has exactly the same number of genes – about 30,000. Genes come in pairs, with one set coming from the mother and one set from the father. There are tiny variations in each gene, which make each person an individual. Occasionally, one of these tiny variations can give rise to a disease or to an increased risk of a disease. Such an alteration in a gene is often referred to as a mutation or fault.
Does pancreatic cancer run in families?

In most cases pancreatic cancer doesn’t run in families. However, there are a small number of family cancer syndromes and rare genetic conditions that are linked to a higher risk and incidence of pancreatic cancer. These account for only up to 10 in every 100 cases or 10% of all pancreatic cancers. They are such rare conditions that if there is one in your family you will probably already know about it.

Hereditary pancreatic cancers

Most family cancer syndromes and genetic conditions are linked to exocrine pancreatic cancer. Exocrine cancers make up 95% of all pancreatic cancers and include pancreatic adenocarcinoma, the most common type. These different conditions are described below. There is separate information about inherited endocrine cancers below.

Family cancer syndromes

- **Peutz-Jeghers syndrome** causes multiple growths (polyps) in the digestive tract and dark spots on the skin of the hands and face. It is associated with a faulty gene called STK11 and increases the risk of pancreatic cancer and other cancers including bowel and breast.

- **Breast and ovarian cancer syndromes** are associated with faulty copies of the BRCA1 and BRCA2 genes and may result in increased pancreatic cancer risk.

- **Familial atypical multiple mole and melanoma syndrome (FAMMM)** is caused by a faulty p16 gene. People affected have large numbers of unusual moles which results in an increased risk of both melanoma (skin cancer) and pancreatic cancer.

- **Familial adenomatous polyposis (FAP)** is a bowel condition caused by a faulty APC gene that increases pancreatic cancer risk.

- **Lynch syndrome** (formerly known as hereditary non-polyposis colorectal cancer or HNPCC) is another bowel condition caused by the faulty genes MLH1, MSH2 and MSH6 that can increase someone’s risk of pancreatic cancer. Some people have Lynch syndrome without a faulty gene having yet been defined.
• **Li-Fraumeni syndrome** is due to a faulty p53 gene that increases cancer risk in most organs including the pancreas.

For more information on the different types of pancreatic cancer visit - [www.pancreaticcancer.org.uk/types](http://www.pancreaticcancer.org.uk/types)

**Hereditary pancreatitis (HP)**

This is characterised by recurrent/chronic pancreatitis (inflammation of the pancreas) starting in early childhood. It is mainly associated with a faulty PRSS1 gene. About 40% of people with hereditary pancreatitis will develop pancreatic cancer by age 80, with smoking and diabetes thought to increase the risk.

**Familial pancreatic cancer (FPC)**

People with at least one first-degree relative (parent, brother, sister or child) diagnosed with pancreatic cancer have a slightly higher risk of developing pancreatic cancer than the general population. Two or more cases on the same side of the family, with no recognised gene faults, may indicate ‘familial pancreatic cancer syndrome’. The chance of FPC increases if:

- relatives were diagnosed under 60
- there are more than two cases in the family
- there are cases in more than one generation.

The main gene for FPC isn’t yet known, although 10-20% of FPC families have a BRCA2 gene mutation. As well as being referred for secondary screening (see below) and genetic counselling and/or genetic testing (see below), people with familial pancreatic cancer may also be interested in joining the EUROPAC study ([www.europac-org.eu](http://www.europac-org.eu)) that is searching for the main familial pancreatic cancer gene.

**Is screening available for people at higher risk of pancreatic cancer?**

Screening for people at higher risk of developing cancer is known as secondary cancer screening. For pancreatic cancer, this includes people:

- from families with family cancer syndromes (with at least one case of pancreatic cancer)
- with hereditary pancreatitis (HP)
- from families with familial pancreatic cancer (FPC).
Unless advised differently by a specialist, screening should start at age 40, or ten years earlier than the youngest affected family member.

Screening can’t stop someone getting pancreatic cancer but diagnosing the disease at an earlier stage may result in more successful treatment.

**What does screening involve?**

Screening should be tailored to each individual’s risk and circumstances and is best discussed in a specialist research centre. If you are screened you could be offered:

- an EUS (Endoscopic Ultrasound)
- a CT (Computerised Tomography) scan (or alternatively, an MRI scan)
- a blood test to check for tumour markers such as CA19-9.

If you have hereditary pancreatitis, damage to the pancreas may make the EUS less sensitive, in which case you may be offered an annual MRI scan.

People with hereditary pancreatitis or familial pancreatic cancer syndrome may also be interested in taking part in the EUROPAC screening study (see below).

For more information on the different tests used to detect pancreatic cancer visit - [www.pancreaticcancer.org.uk/tests](http://www.pancreaticcancer.org.uk/tests)

**Is genetic counselling/genetic testing available for people at higher risk of pancreatic cancer?**

People with familial pancreatic cancer or another genetic condition linked to increased risk of pancreatic cancer should be offered genetic counselling and genetic testing if appropriate.

- Genetic counselling is used to advise people at risk of an inherited condition about the specific condition, the chance of them developing it or passing it on, and their options to manage it.

- Genetic testing is used to confirm or rule out a suspected inherited condition or to assess someone’s chance of developing or passing on a specific inherited condition.

If a fault in a specific gene is suspected, genetic counselling will always be offered before genetic testing. This is so people are prepared for what it
means if they find out they have a faulty gene that greatly increases their risk of developing pancreatic cancer.

If you are referred for a consultation at a genetic clinic it's helpful if you can gather information beforehand including:

- how everyone in the family is related to you and to each other
- how old each affected relative is and their age when they were diagnosed
- what other cancers have been diagnosed in the family.

The doctors can then work out how likely it is that there is a faulty gene in the family. Depending on this risk assessment you may be:

- offered genetic counselling/testing and/or screening if you do have an increased risk
- told that you aren’t at any more risk than the general population.

If you are at increased risk of pancreatic cancer, after discussion with a specialist it's up to you to decide what screening or testing you wish to have. You can take as much time as you need to decide.

**How do I find out if I am at increased familial risk of pancreatic cancer?**

If you've read the information on these pages about increased familial risk and are worried about pancreatic cancer you should start by talking to your doctor, especially if you have any worrying symptoms. Give them as much information as possible about pancreatic cancer or known family cancer syndromes in your family. Once you have discussed your particular circumstances, ask if you should be referred to a specialist in pancreatic disease or for genetic counselling or be put in touch with the EUROPAC research team.

**EUROPAC**

The European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer (EUROPAC) ([www.europac-org.eu](http://www.europac-org.eu)) is looking at two types of families – those with inherited pancreatitis and those with an inherited predisposition to pancreatic cancer (familial pancreatic cancer). Researchers hope not only to learn more about the genetic causes of pancreatic cancer but
also to assist in the development of new treatments. In addition, the ability to identify people at high risk will allow researchers to develop new screening systems to detect early pancreatic cancer.

**Hereditary pancreatitis registry**

People with hereditary pancreatitis can join the study by completing questionnaires and giving a blood sample. The blood is taken after speaking to an expert in pancreatic diseases and sometimes a geneticist (specialist in diseases associated with genes) for genetic counselling. The blood is tested for altered genes known to cause pancreatic disease. Participants can choose whether or not to be told about any findings relevant to their family: if a gene mutation was identified, family members who don’t have pancreatitis could have genetic counselling and genetic tests if appropriate.

**Familial pancreatic cancer registry**

People with familial pancreatic cancer and their unaffected family members can join the study by completing questionnaires and giving a blood sample. The blood is tested to try to identify which gene(s) may be responsible for familial pancreatic cancer. If a link is identified between a family history and pancreatic cancer unaffected family members may be offered secondary screening. If the faulty gene(s) is identified individuals on the registry will be offered testing if appropriate.

**Secondary screening study**

EUROPAC has developed a separate secondary screening study for people on either register who are at high risk of developing pancreatic cancer. Screening combines imaging (EUS and/or CT) and blood tests with the option of molecular analysis of pancreatic juice sampled through an ERCP. The juice is examined for changes in genes called K-Ras, p53 and p16. If there are any changes in these genes, the case is referred to the Liverpool Professorial Pancreas Research Unit for further testing. The aim is to identify the best screening regime to detect the early changes of pancreatic cancer. Screening usually starts at age 40 and is accessed via the EUROPAC registry, which allows a full risk assessment.

**How do I get in touch with EUROPAC?**

Anyone interested in taking part in the study can contact the team directly by email ([europac@liv.ac.uk](mailto:europac@liv.ac.uk)) or phone (+44 (0)151 706 4168 – answering
Hereditary pancreatic endocrine tumours

Less than 5% of all pancreatic cancers start in the hormone producing cells of the pancreas. These are called endocrine or neuroendocrine tumours. Of these, an even smaller number are related to inherited syndromes. If your family is affected by one of these inherited syndromes ask your doctor what screening and support is available.

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**Multiple endocrine neoplasia type 1 (MEN1)**

MEN1 is an autosomal dominant (passed on by either parent) familial cancer syndrome caused by mutations in the MEN1 gene. Multiple endocrine tumours can develop in different endocrine glands, including the parathyroid gland, the pituitary gland and the pancreas. About 75% of people with MEN1 will develop tumours in the pancreas.

Screening for MEN1 gene carriers should begin in early childhood with blood tests every year and scans every three years. Agreed guidelines recommend screening from age five for pituitary tumours and insulinomas, from eight for parathyroid tumours and from 20 for other neuroendocrine tumours, including in the pancreas. EUS should be used to screen for pancreatic tumours.

AMEND ([www.amend.org.uk](http://www.amend.org.uk)) offers information and support for people with MEN disorders.

**von Hippel-Lindau (VHL) Syndrome**

This is another type of autosomal dominant familial cancer syndrome and is linked to the VHL gene. It causes a multiplication of small blood vessels in the brain, spinal cord and back of the eyes and also cancers of the kidney and the adrenal gland. About two thirds of people with VHL have harmless cysts in the pancreas. However, about 10% of people with VHL also have one or more pancreatic neuroendocrine tumours (usually non-functioning).

Screening for VHL gene carriers should begin at age 10 with annual abdominal ultrasound to look for tumours in the kidneys, adrenal glands,
pancreas and pelvis. From age 20 there should be 1-2 yearly abdominal CT or MRI scans, with EUS for the pancreas.

**Neurofibromatosis type 1**

This condition is caused by mutations in the NF1 gene and generally presents in childhood or adolescence. As well as other problems, it leads to an increased risk of many tumours, including somatostatinomas. The Neuro Foundation ([www.nfauk.org](http://www.nfauk.org)) offers information and support for people with the condition.

**Tuberous sclerosis**

This is an autosomal dominant genetic condition arising from faulty TSC1 and TSC2 genes. It causes extra tissue growth in different organs, including the pancreas, which may become cancerous. The Tuberous Sclerosis Association ([www.tuberous-sclerosis.org](http://www.tuberous-sclerosis.org)) offers information and support for people with the condition.

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**Glossary**

You can find an A to Z of some of the common medical words that you may hear when you are finding out about pancreatic cancer on our website – [www.pancreaticcancer.org.uk/glossary](http://www.pancreaticcancer.org.uk/glossary)

**This fact sheet has been produced by the Support and Information Team at Pancreatic Cancer UK. It has been reviewed by healthcare professionals and people affected by pancreatic cancer.**

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**Pancreatic Cancer UK** makes every effort to make sure that its services provide up-to-date, unbiased and accurate information about pancreatic cancer. We hope that this information will add to the medical advice you have received and help you to take part in decisions related to your treatment and care. Please do continue to talk to your doctor, specialist nurse or other members of your care team if you are worried about any medical issues.
Give us your feedback We hope you have found this information helpful. If you have any comments or suggestions about this fact sheet or any of our other publications please complete our Information Feedback Form at www.pancreaticcancer.org.uk/informationfeedback or write to the Information and Development Manager at the address below.

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