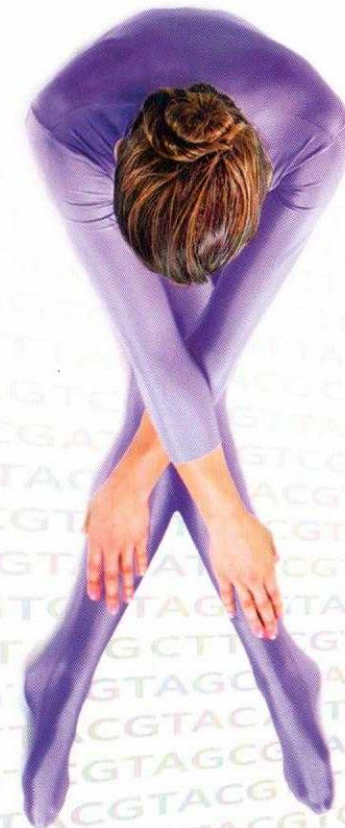


ambrygen.com

PancNext

Genetic testing for hereditary pancreatic cancer

PATIENT GUIDE

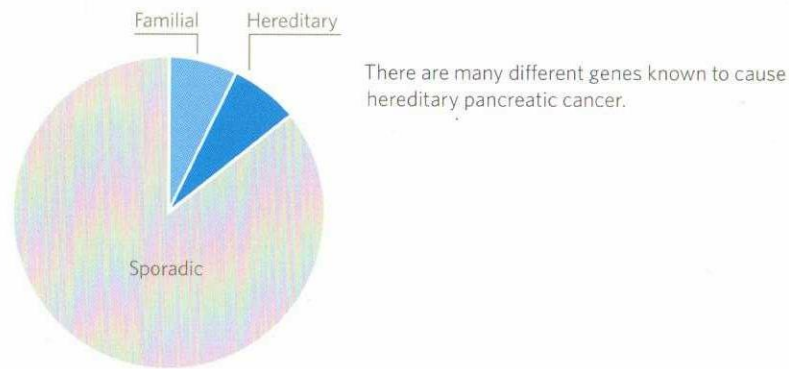


What is Hereditary Pancreatic Cancer?

Pancreatic cancer is a relatively uncommon cancer (it affects about 1 in 65 people in the U.S.). Risk factors for developing pancreatic cancer include cigarette smoking, type 2 diabetes, chronic pancreatitis, obesity, cirrhosis of the liver, and a family history of pancreatic cancer. The majority of pancreatic cancers occur at older ages in people with little or no family history of the disease and no genetic risk. These occurrences are called "sporadic" cancers and happen by chance.

Although many people have a family history of cancer, the majority of cancers are not due to inherited causes. Only about 10% of people who develop pancreatic cancer have a family history of the disease. Some of these families have "*hereditary*" (due to inherited genetic changes called mutations) pancreatic cancer. People who carry these genetic changes are born with them - they do not develop over time. Understanding if a history of pancreatic cancer is due to an inherited mutation can help clarify future risks to develop cancer and help determine options for cancer screening and prevention.

PANCREATIC CANCER BREAKDOWN



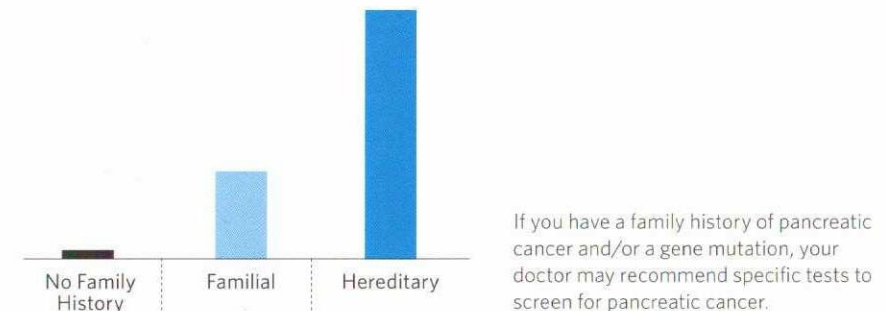
Many families with a history of pancreatic cancer do not have an identifiable genetic cause. These "*familial*" cases may be due to other genes, shared factors such as environment and lifestyle, or a combination of all of these.

What is Your Risk for Pancreatic Cancer?

A healthcare provider can help you learn about your chance of developing pancreatic cancer.

- A person with no family history of pancreatic cancer is most likely at average risk, which is about 1% over a lifetime. People with risk factors for pancreatic cancer (described on page 1) may have a higher risk.
- For the person with a family history of pancreatic cancer, genetic testing may help determine his/her risk of developing cancer.
- If a person has had pancreatic cancer, genetic testing may help determine if he/she has an increased risk for additional cancers.
- Defining a person's pancreatic cancer risk helps his/her healthcare providers make personalized recommendations for cancer screening and prevention.

LIFETIME PANCREATIC CANCER RISKS



NOTES

Is Hereditary Pancreatic Cancer Testing Appropriate for You?

Genetic testing may be appropriate if you have a personal history and/or family history of any of the following:

- | | |
|--|---|
| ☐ Pancreatic cancer diagnosed younger than age 60 | ☐ 3 or more family members with pancreatic, breast, colorectal, uterine, ovarian, and/or melanoma* |
| ☐ More than one cancer in the same person (like pancreatic and colorectal or breast cancer) | ☐ Multiple close family members with pancreatic and other cancers* |
| ☐ 2 or more family members with pancreatic cancer* | |

* On the same side of the family

NOTES

PancNext Genes and Associated Cancer(s)

GENE	ASSOCIATED CANCER(S)	SYNDROME NAMES
<i>APC</i>	Colorectal, duodenal pancreatic, thyroid liver, CNS	Familial adenomatous polyposis (FAP) Attenuated FAP
<i>ATM</i>	Breast, pancreatic	
<i>BRCA1, BRCA2</i>	Breast, prostate, ovarian, pancreatic, male breast	Hereditary breast ovarian cancer (HBOC)
<i>CDKN2A</i>	Melanoma, pancreatic	Cutaneous malignant melanoma syndrome Familial atypical mole-malignant melanoma (FAMMM) syndrome
<i>MLH1, MSH2, MSH6, PMS2, EPCAM</i>	Colorectal, uterine, stomach, ovarian, small bowel, and others	Lynch syndrome
<i>PALB2</i>	Breast, pancreatic	
<i>STK11</i>	Colorectal, breast, small bowel, pancreatic, ovarian	Peutz-Jeghers syndrome (PJS)
<i>TP53</i>	Breast, sarcoma, brain, adrenocortical, and others	Li-Fraumeni syndrome (LFS)

NOTES

Genetic Test Results Explained

If you have genetic testing, you will receive one of three possible results: positive, negative, or inconclusive (variant of unknown significance or VUS).

RESULTS	EXPLANATION
Positive	▪ A mutation was found in one of the genes tested ▪ Increased risk for cancer specific to the gene that has a mutation ▪ Gene-specific cancer screening and prevention recommendations ▪ Offering genetic testing to adult at-risk relatives for the specific mutation is recommended
Negative	▪ No changes, or mutations, were found in any of the genes tested ▪ Cancer risk(s) are based on personal and family history ▪ Cancer screening and prevention recommendations based on family history ▪ Genetic testing most likely will not be appropriate for family members
Inconclusive	▪ A genetic change was found but it is unclear if this change causes an increased risk for cancer or not ▪ Cancer risk(s) are specific to the family history of cancer ▪ Cancer screening and prevention recommendations based on family history ▪ Family studies may be helpful

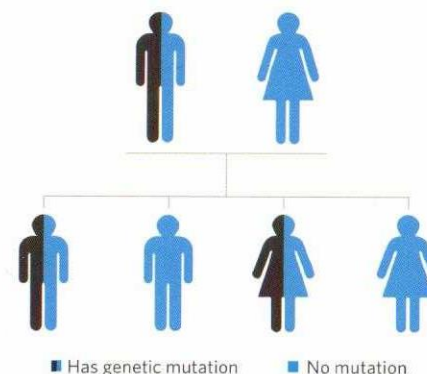
NOTES

If You Are Found to Have a Gene Mutation

- Cancer screening will most likely begin in young adulthood
- Screening will be recommended for cancers specific to the gene in which the mutation was found
- Cancer prevention options will be discussed
- Family members may be offered testing to find out if they carry the same mutation

What This Means for a Family

There is a 50/50 random chance to pass on a genetic mutation in a PancNext gene to your sons and daughters. The image below shows that both men and women can carry and pass on these mutations.



NOTES

Common Questions About Genetic Testing

Q1. HOW DOES PANCNEXT GENETIC TESTING WORK?

The genetic test is done using a blood or saliva sample. Your sample is sent overnight in a special kit to Ambry (all coordinated by your healthcare provider). Once your sample arrives at Ambry, 13 pancreatic cancer genes are studied. Everyone has these genes – they each have a specific role in your body. The genetic test looks for any mutations that cause an increased risk of cancer.

Q2. CAN GENETIC TEST RESULTS BE USED AGAINST ME?

The Genetic Information Nondiscrimination Act (2008) prohibits discrimination by health insurance companies and employers based on genetic information. Your state may have additional, more comprehensive laws in this area.

Q3. IF I HAVE ALREADY HAD PANCREATIC CANCER, DO I NEED GENETIC TESTING?

Genetic testing is most informative when first performed in a family member who has already had pancreatic cancer. Results can provide an explanation for why the cancer occurred, and, more importantly, can provide information about future cancer risks. Genetic test results can change your ongoing medical management and can help your family members understand their risk of developing cancer.

Q4. WHAT IF I PREVIOUSLY HAD PANCREATIC CANCER GENETIC TESTING AND NO MUTATION WAS IDENTIFIED?

PancNext may be ideal because additional pancreatic cancer genes will be studied that could potentially provide the answer for you and your family. Your healthcare provider can tell us on the order form if you have had genetic testing before.

Q5. HOW SHOULD I TELL MY RELATIVES ABOUT MY GENETIC TEST RESULTS?

Genetic test results may be shared in a number of ways including by telephone call, visiting in person, letter, or email. It can sometimes be challenging because genetic testing is a very personal process, and everyone reacts to this type of news differently. Your healthcare provider may be able to help you come up with a plan to tell your family members, in a way that works best for all of you.

Test Result and Recommendations

To be completed by you and your healthcare provider when you receive your genetic test results and medical management recommendations

TEST RESULT

- ☐ No mutation detected
- ☐ Positive for a mutation in _____ gene
- ☐ Variant of unknown significance in _____ gene

RECOMMENDATIONS FOR YOU

RECOMMENDATIONS FOR FAMILY MEMBERS

- ☐ Genetic testing not appropriate for family members
- ☐ Genetic testing recommended for family members

Billing Questions: Ambry's Patient Protection Plan

Q1. WHAT IS AMBRY'S BILLING POLICY?

Ambry Genetics preverifies insurance coverage and will contact you once your sample is received at Ambry if your out-of-pocket amount for testing is estimated to exceed \$100. This does not, however, limit your out-of-pocket responsibility to \$100. We are committed to working with you and your clinician to make the genetic testing process as simple and cost-effective as possible, and our Billing Department is available to answer any questions you may have. Our Billing Department can be reached by phone at +1-949-900-5795 or billing@ambrygen.com.

Q2. WHAT IS AN EXPLANATION OF BENEFITS (EOB)?

Your insurance company sends you an EOB to explain any treatments/services paid on your behalf. It is not a bill and does not require payment. You can contact us directly to speak with a Billing specialist with any questions/concerns about your EOB.

Q3. HOW MUCH DO AMBRY'S TESTS COST?

We are committed to making the genetic testing process as simple and cost-effective as possible. Prices depend on if your insurance plan is contracted with Ambry, and if they are a private or public plan. We also offer prices when someone pays by cash, or when an institution pays. This not necessarily what is reflected on an EOB, so please contact us directly to speak with a Billing specialist with any questions/concerns.

Q4. WHY DID I RECEIVE A BILL MORE THAN A MONTH AFTER MY TEST?

Some genetic tests take weeks to process to receive the best results. In addition, insurance companies can take over two months to process claims, and longer if we need to send information again. All of this could delay your bill, but we try our best to prevent this from happening.

Resources for Patients

These and other resources can help build a sense of community and aid in answering some common questions.

BRIGHT PINK
brightpink.org

FACING OUR RISK OF CANCER EMPOWERED (FORCE)
facingourrisk.org

HEREDITARY COLON CANCER FOUNDATION
hcctakesguts.org

LI-FRAUMENI SYNDROME ASSOCIATION
lfsassociation.org

PANCREATIC CANCER ACTION NETWORK
pancan.org

GENETIC INFORMATION NONDISCRIMINATION ACT INFORMATION
ginahelp.org

Find a Genetic Counselor

NATIONAL SOCIETY OF GENETIC COUNSELORS
nsgc.org

About Ambry

INNOVATION

Ambry is a leading provider of diagnostic genetic testing, with years of experience using next generation sequencing technologies.

EXPERTISE

Since 2001, Ambry has performed hundreds of thousands of genetic tests and identified more than 45,000 mutations in greater than 500 different genes.

AMBRY GENETICS

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