What is Hereditary Breast Cancer?

Breast cancer is the most common cancer in women in the U.S. (affects about 1 in 8). The majority of breast cancer is diagnosed 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 breast cancers are not due to inherited causes. Only about 5-10% of breast cancer is “hereditary” (due to inherited genetic changes called mutations). People who carry these mutations are born with them - they do not develop over time. Understanding if cancer is due to an inherited mutation can help clarify future risks to develop cancer and help determine options for cancer screening and prevention.

BREAST CANCER TYPE BREAKDOWN

About 20% of women who develop breast cancer have a family history of breast cancer but do not have an identifiable gene mutation. These “familial” cases of breast cancer may be due to genes, shared factors such as environment or lifestyle, or a combination of all of these.

NOTES
What is Your Risk for Breast Cancer?

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

• A woman with no family history of breast cancer is most likely at average risk. The average risk of developing breast cancer is about 12% over a woman’s lifetime.

• For the person who has a family history of breast cancer, genetic testing may be appropriate to help determine his/her risk of developing breast cancer.

• If someone has had breast cancer, genetic testing may be appropriate to help determine if she/he has an increased risk for additional cancers.

• Defining a person’s breast cancer risk helps his/her healthcare providers make personalized recommendations for cancer screening and prevention.

NOTES

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Is Breast Cancer Genetic Testing Appropriate for You?

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

- Breast cancer diagnosed at age 45 or younger
- More than one cancer in the same person (like two separate breast cancers, or breast and ovarian cancer)
- Ovarian, Fallopian tube, or primary peritoneal cancer at any age
- Male breast cancer at any age
- 3 or more family members with breast, ovarian, pancreatic, and/or prostate cancer*
- Breast, uterine, and thyroid cancer*
- Multiple family members with breast and other cancers*

* On the same side of the family

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## BreastNext Genes and Associated Cancer(s)

<table>
<thead>
<tr>
<th>GENE</th>
<th>ASSOCIATED CANCER(S)</th>
<th>SYNDROME NAMES</th>
</tr>
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<tbody>
<tr>
<td>ATM</td>
<td>Breast, pancreatic</td>
<td></td>
</tr>
<tr>
<td>BARD1</td>
<td>Breast, possibly ovarian</td>
<td></td>
</tr>
<tr>
<td>BRCA1, BRCA2</td>
<td>Breast, ovarian, pancreatic, prostate, male breast</td>
<td>Hereditary breast ovarian cancer (HBOC)</td>
</tr>
<tr>
<td>BRIP1</td>
<td>Breast, ovarian</td>
<td></td>
</tr>
<tr>
<td>CDH1</td>
<td>Breast (lobular type), gastric (diffuse type)</td>
<td>Hereditary diffuse gastric cancer (HDGC)</td>
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<tr>
<td>CHEK2</td>
<td>Breast, colorectal</td>
<td></td>
</tr>
<tr>
<td>MRE11A</td>
<td>Breast, possibly ovarian</td>
<td></td>
</tr>
<tr>
<td>MUTYH</td>
<td>Breast, colorectal, colon polyps</td>
<td>MUTYH-associated polyposis (MAP)</td>
</tr>
<tr>
<td>NBN</td>
<td>Breast, possibly ovarian</td>
<td></td>
</tr>
<tr>
<td>NF1</td>
<td>Breast, optic glioma, CNS, GIST, PGL/PCC</td>
<td>Neurofibromatosis type 1 (NF1)</td>
</tr>
<tr>
<td>PALB2</td>
<td>Breast, ovarian, pancreatic, male breast</td>
<td></td>
</tr>
<tr>
<td>PTEN</td>
<td>Breast, thyroid, uterine, colorectal, kidney, non-cancer findings</td>
<td>PTEN hamartoma tumor syndrome (PHTS) Cowden syndrome (CS)</td>
</tr>
<tr>
<td>RAD50</td>
<td>Breast, possibly ovarian</td>
<td></td>
</tr>
<tr>
<td>RAD51C</td>
<td>Breast, ovarian</td>
<td></td>
</tr>
<tr>
<td>RAD51D</td>
<td>Breast, ovarian</td>
<td></td>
</tr>
<tr>
<td>TPS3</td>
<td>Breast, sarcoma, brain, adrenocortical, leukemia, and others</td>
<td>Li-Fraumeni syndrome (LFS)</td>
</tr>
</tbody>
</table>

CNS: central nervous system  
GIST: gastrointestinal stromal tumor  
PGL/PCC: paragangliomas/pheochromocytomas
## 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).

<table>
<thead>
<tr>
<th>RESULTS</th>
<th>EXPLANATION</th>
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</table>
| **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

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If You Test Positive for a Gene Mutation

- Breast screening will most likely begin in young adulthood, and may include breast MRI in addition to mammogram
- Screening for other cancer(s) will be recommended specific to the gene in which the mutation was found
- Cancer prevention options will be discussed, including possible preventive surgeries
- Family members may be tested 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 BreastNext gene to your sons and daughters. The image below shows that both men and women can carry and pass on these mutations. Most inherited cancer syndromes occur when a gene mutation is inherited from one parent.*

*Typically, MUTYH-associated polyposis occurs when a mutation in MUTYH is inherited from both parents.
Common Questions About Genetic Testing

Q1. HOW DOES BREASTNEXT GENETIC TESTING WORK?
The genetic test is done using a blood or saliva sample. Your sample is collected using a special kit that is shipped overnight to Ambry (all coordinated by your healthcare provider). Once your sample arrives at Ambry, 17 genes are studied for mutations. Everyone has these genes - they each have a specific role in your body. The genetic test looks for mutations that cause an increased risk for cancer.

Q2. CAN GENETIC TEST RESULTS BE USED AGAINST ME?
In the U.S., the Genetic Information Nondiscrimination Act (2008) prohibits discrimination by health insurance companies and employers based on genetic information. Depending on where you live in the world, you may have different (or fewer) laws in this area.

Q3. IF I HAVE ALREADY HAD BREAST CANCER, DO I NEED GENETIC TESTING?
Genetic testing is most useful when first performed in a family member who has already had breast cancer. Results can provide an explanation for why the breast 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 BRCA1 AND BRCA2 GENETIC TESTING AND NO MUTATION WAS IDENTIFIED?
BreastNext may be ideal because 15 additional breast cancer genes will be analyzed that could potentially provide an answer for you and your family. Your healthcare provider can indicate on the order form that BRCA1 and BRCA2 were previously analyzed.

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

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RECOMMENDATIONS FOR FAMILY MEMBERS

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

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Q1. WHAT IS AMBRY’S BILLING POLICY?
Ambry’s billing policy is to preverify insurance coverage (with or without your sample) for genetic testing. We will contact you after your sample is received, if your out-of-pocket cost is estimated to exceed $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 is 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.

AMBRY’S HEREDITARY CANCER SITE FOR FAMILIES
patients.ambrygen.com/cancer

BRIGHT PINK
brightpink.org

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

SUSAN G. KOMEN BREAST CANCER FOUNDATION
komen.org

YOUNG SURVIVAL COALITION
younsgsurvival.org

GENETIC INFORMATION NONDISCRIMINATION ACT INFORMATION
ginahelp.org

Find a Genetic Counselor

NATIONAL SOCIETY OF GENETIC COUNSELORS
nsgc.org

CANADIAN ASSOCIATION OF GENETIC COUNSELLORS
cagc-accg.ca

About Ambry

Ambry is a genetics-based healthcare company that is dedicated to open scientific exchange so we can work together to understand and treat all human disease faster.

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info@ambrygen.com

For more details about these tests, visit ambrygen.com