Hereditary breast cancer accounts for 5% to 10% of female breast cancer and 5% to 20% of male breast cancer.¹ The most common cause of these cancers is a mutation in the BRCA1 or BRCA2 gene. People with a mutation in one of these genes have hereditary breast and ovarian cancer (HBOC) syndrome. They are at increased risk for breast, ovarian, and certain other types of cancer. Like other hereditary cancers, cancer associated with HBOC often occurs at an earlier age.

**BRCA1 and BRCA2**

BRCA1 and BRCA2 are tumor suppressor genes. Certain mutations in these genes increase the risk of breast cancer in both women and men (Table 1). They account for 3% to 5% of all breast cancers and 15% to 20% of hereditary breast cancer.² Mutations in these genes also increase the risk of ovarian cancer in women. In addition, BRCA mutations increase the risk of people having more than 1 primary cancer in their lifetime. This could be a second breast cancer or another type of cancer.

Table 1. BRCA1 and BRCA2 and Breast Cancer Risk³⁷

<table>
<thead>
<tr>
<th>Cancer</th>
<th>With BRCA1 Mutation</th>
<th>With BRCA2 Mutation</th>
<th>Without BRCA Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer by age 70</td>
<td>55–65</td>
<td>45–47</td>
<td>9</td>
</tr>
<tr>
<td>Ovarian cancer by age 70</td>
<td>39</td>
<td>11–17</td>
<td>1</td>
</tr>
<tr>
<td>2nd breast cancer in lifetime</td>
<td>83</td>
<td>62</td>
<td>15</td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer by age 70</td>
<td>1</td>
<td>7</td>
<td>0.06</td>
</tr>
</tbody>
</table>

BRCA mutations also increase the risk of certain other types of cancer. These include prostate, pancreas and melanoma.

**Inheritance of BRCA Mutations**

Mutations in BRCA1 and BRCA2 are autosomal dominant. This is also true of the other cancer susceptibility genes listed in the sidebar on page 1. So if a person has one of these mutations, other members of their family might have it too.

**Other Breast Cancer Susceptibility Genes**

Other breast cancer susceptibility genes have been identified. Mutations in these genes are rare and they are linked to other syndromes or conditions. But they are also known to increase the risk of developing breast and some other cancers. These genes and some of the cancers their mutations predispose people to include:

- TP53: breast cancer, soft tissue sarcoma, osteosarcoma, brain tumors, adrenocortical carcinoma, and leukemia
- PTEN: cancer of the breast, uterus (including endometrium), and thyroid
- CDH1: lobular breast cancer, diffuse gastric cancer, and possibly colorectal cancer
- STK11: cancer of the breast, gastrointestinal tract, pancreas, cervix, and ovary
- PALB2: breast cancer and pancreatic cancer

Together, these 5 genes account for another 3% to 4.5% of hereditary breast cancers.⁸,⁹
### Relative | Risk (%) of Having the Same Mutation
--- | ---
Identical twin | 100
Fraternal twin | 50
Parent, sibling, child | 50
Grandparent, uncle, aunt, niece, nephew | 25
First cousin | 12.5

### How to Test for Hereditary Breast and Ovarian Cancer

The first step is to decide if the person meets the criteria for BRCA mutation testing. Quest Diagnostics has created a quiz to help with this. It's available at [BRCAvantage.com/take-the-quiz/](BRCAvantage.com/take-the-quiz/). There is a quiz for women and one for men. People who answer “yes” to any of the questions might be at risk for these hereditary cancers and may meet the criteria for testing. Quest Diagnostics’ genetic counselors can also help you decide if a person meets the criteria and who in the family is the best person to test. You can call Quest Genomics Client Services at 866-GENE-INFO (866-436-3463) to speak to a genetic counselor.

The next step is to help the person decide whether to be tested. Quest Diagnostics has written a Patient Support Guide that can help. It includes facts about HBOC syndrome and mutation testing. You can order copies at [BRCAvantage.com/order-guide/](BRCAvantage.com/order-guide/).

If the person decides to be tested, you can order the BRCAvantag® Comprehensive test from Quest Diagnostics. This test looks for mutations in the BRCA1 and BRCA2 genes. Or you can order the BRCAvantag® with Reflex to Breast Plus Panel. This test first looks for mutations in the BRCA1 and BRCA2 genes. If none are found, it reflexes to a test for mutations in the other breast cancer susceptibility genes listed in the sidebar on page 1. Information about additional testing options, including for people of Ashkenazi Jewish ancestry, is available here.

### Quest Diagnostics’ Concierge Service

Quest Diagnostics’ Concierge Service team provides assistance to your patient when undergoing screening for hereditary breast cancer. When a completed order and patient blood sample are received, they will:
- Verify coverage of your patient’s plan
- Determine their likely out-of-pocket cost

If the out-of-pocket cost is estimated to be over $350, they will notify you and/or your patient before beginning the test. You and your patient can then decide whether to proceed with the test.

Quest Diagnostics also offers financial help for people who meet the requirements. This depends on household income. Patients who qualify won’t have to pay more than $200 for the test. For more information go to [BRCAvantage.com/provider-resources/reimbursement-support-financial-assistance/](BRCAvantage.com/provider-resources/reimbursement-support-financial-assistance/)

### References