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Hereditary Breast and Ovarian Cancer

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 Risk³⁻⁷

Cancer	Risk of Cancer, %		
	With <i>BRCA1</i> Mutation	With <i>BRCA2</i> Mutation	Without <i>BRCA</i> Mutation
Women			
Breast cancer by age 70	55-65	45-47	9
Ovarian cancer by age 70	39	11-17	1
2nd breast cancer in lifetime	83	62	15
Men			
Breast cancer by age 70	1	7	0.06

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}

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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/. 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/.

If the person decides to be tested, you can order the BRCAVantage® Comprehensive test from Quest Diagnostics. This test looks for mutations in the *BRCA1* and *BRCA2* genes. Or you can order the BRCAVantage® 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 Services 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/.

References

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