



Genetic Testing for BRCA1 and BRCA2

How common are *BRCA1* and *BRCA2* mutations in the general population?

Inherited mutations in *BRCA1* and *BRCA2* are relatively uncommon in the general population. The carrier frequency is estimated to range from 1 in 300 to 1 in 800. Certain ethnic groups have been shown to have a higher carrier frequency (i.e., individuals of Ashkenazi Jewish descent).

What percentage of breast and ovarian cancer cases are estimated to be caused by *BRCA1* and *BRCA2* mutations?

Five to 10 percent of all breast cancer cases and up to 14 percent of all ovarian cancer cases are thought to be caused by *BRCA1* and *BRCA2* mutations.

Can *BRCA1* and *BRCA2* mutations be inherited from either side of the family?

Yes, either parent can pass along a *BRCA1* or *BRCA2* mutation. Therefore, it is important to obtain a complete family history when assessing genetic risk.

Which patients should I consider referring to a genetic counselor for risk assessment and to discuss the option of genetic testing for *BRCA1* and *BRCA2* mutations?

Most individuals do not have a mutation in the *BRCA1* or *BRCA2* gene. While specific indications for genetic counseling and testing vary among professional organizations, certain aspects of your patient's personal and/or family history may increase his or her likelihood of carrying a *BRCA1* or *BRCA2* mutation. The indications below are to be used as a guide and are not a substitute for clinical judgment. Not all clinical scenarios can be anticipated. For instance, genetic testing guidelines may not take into consideration a situation where the family history is limited.

Indications include:

A personal history of:

- Breast cancer at a young age (younger than age 50) or ovarian cancer at any age
- Bilateral breast cancer or two or more primary tumors of the breast
- Breast and ovarian cancer (in the same individual)
- Breast cancer in a male

AND/OR

A maternal or paternal family history of:

- Two or more individuals in the family (parent, child, sibling, grandparent, aunt/uncle) with breast and/or ovarian cancer
- One or more close male relatives with breast cancer
- Early onset breast or ovarian cancer (before age 50) in a close relative
- Confirmed *BRCA1* or *BRCA2* mutation

Note: Individuals who belong to ethnic groups with increased mutation prevalence, such as those of Ashkenazi Jewish descent, may be appropriate candidates for referral even if they have a less striking personal or family history of breast and/or ovarian cancer.

Ideally, the decision to test should start with the patient's family member affected with either breast or ovarian cancer, since this helps determine if the cancer is associated with one of the mutations and makes test interpretation more straightforward.

You may find it helpful to refer to specific genetic testing guidelines published by professional organizations, some of which are listed on the third page of this document.

Genetic testing for breast cancer risk may be complicated by:

- The possibility of false negative results since other genes and mutations carrying similar cancer risk, but not yet discovered or tested for, may be present;
- The possibility of tests results with mutations noted to have "uncertain clinical significance";
- The cost of full-scale testing. Costs range from \$385 (when a mutation present in an affected family member has already been identified) to \$460 (for the first member of an Ashkenazi Jewish family to be tested) to \$3120 (for full sequencing of both genes);
- The imprecision of what a positive test result means. The results do not provide an individual patient with information regarding if or when or where cancer may develop.

What are the advantages and disadvantages of *BRCA1* and *BRCA2* testing?

Test advantages:

- Testing may clarify risk of specific cancers.
- Testing may lead to an increased sense of control and decreased stress for the patient.
- For families with a known mutation, a negative test result reduces the patient's risk of breast and ovarian cancer to that of the general population.
- Testing may help patients focus on the medical and lifestyle choices available to them (earlier/increased screening, chemoprevention, surgical options).
- Testing may help inform other family members about their potential risk.
- For cancer patients, a positive test result may decrease feelings of self-blame.

Test disadvantages:

- Testing may cause a patient to experience stress.
- Testing positive may result in guilt or fear over possibly passing a mutation to children.
- Although very rare, a patient may face insurance or employment discrimination due to a positive test result.
- Individuals with a negative test result may think they have no chance of getting cancer and thus forgo appropriate screening tests.

What else do I need to know when deciding whether to offer *BRCA1* and *BRCA2* testing?

Patient education and informed consent are critical aspects of the genetic testing process and will help individuals decide if genetic testing is right for them. Pretest counseling, usually done by genetic counselors, addresses testing costs; other options besides testing; psychosocial aspects; the implications of potential test results, and available medical management. If help is needed, a genetic counselor can also provide assistance with dissemination of relevant information to at-risk family members.

What is the risk for breast and ovarian cancer in individuals found to have a *BRCA1* or *BRCA2* mutation?

For women with a mutation in either *BRCA1* or *BRCA2*, studies have shown the lifetime risk of breast cancer to range between 50-87 percent. The lifetime risk of ovarian cancer has been noted to range between 15-44 percent, depending on the specific mutation. Men with a *BRCA* mutation have a 5-10 percent lifetime risk of developing breast cancer. Men without such mutations have a 0.1 percent lifetime risk.

How can I find a genetic counselor in my area for my patients?

Call the NYSDOH Cancer Services Program's toll free number, 1-866-442-CANCER. This number will connect you with an operator who has access to contact information for genetic counselors across New York State. These counselors are aware of the direct-to-consumer campaign and the likely increase in consumer demand. Counselors whose fees are based on a zero-based, sliding scale are available.

For more information:

***BRCA1* and *BRCA2* Testing and Risk Management Guidelines:**

- National Comprehensive Cancer Network (these guidelines also contain information on managing patients found positive for *BRCA1* or *BRCA2*)
http://www.nccn.org/professionals/physician_gls/PDF/genetics_screening.pdf
- U.S. Preventive Services Task Force <http://www.ahrq.gov/clinic/uspstf/uspstrgen.htm>
- National Cancer Institute <http://www.cancer.gov/cancertopics/pdq/genetics/breast-and-ovarian/healthprofessional>

About genetic counselors:

- National Society of Genetic Counselors <http://www.nsgc.org/>
- New York State Genetic Counselors <http://www.nysgeneticcounselors.org/>
- National Cancer Institute's Cancer Information Service 1-800-4-CANCER or www.cancer.gov
- International Society of Nurses in Genetics <http://www.isong.org/>

About medical genetics:

- American College of Medical Genetics
<http://www.acmg.net/>
- CancerNet www.cancernet.nci.nih.gov
- Genetic Alliance www.geneticalliance.org
- Genetic counselor www.cancernet.nci.nih.gov/genesrch.shtml
- GeneTests www.genetests.org

About genetic testing for breast and ovarian cancer risk:

- National Cancer Institute-Fact Sheets <http://www.cancer.gov/cancertopics/Genetic-Testing-for-Breast-and-Ovarian-Cancer-Risk> and <http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA>
- Centers for Disease Control and Prevention
<http://www.cdc.gov/genomics/training/perspectives/factshts/breastcancer.htm>
- National Institute of Health-Genetics Through a Primary Care Lens: A Web-Based Resource for Faculty Development <http://www.genetests.org> then click on "Genetic Tools" in the right hand tool bar