

# Hereditary Breast and Ovarian Cancer

## How common are breast and ovarian cancer?

Breast cancer is common among American women, affecting about 1 in 8 (13 percent) women. More than 200,000 women are diagnosed with breast cancer each year in the United States (U.S.). Breast cancer rarely occurs in men; fewer than 2,000 cases are diagnosed each year in the U.S.

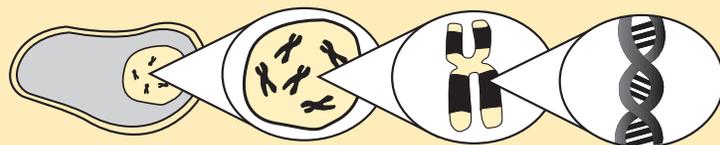
Ovarian cancer is not as common as breast cancer, with around 22,000 cases diagnosed per year in the U.S. Only 1 in 70 (1.4 percent) women will develop ovarian cancer.

## What is Hereditary Breast and Ovarian Cancer Syndrome?

It has been estimated that about 5-10 percent of all breast and ovarian cancer cases are hereditary. This means the individual has inherited an increased likelihood for developing breast and ovarian cancer. In most families with an inherited predisposition, several people will have cancer. The most common hereditary breast and ovarian cancer condition is called the Hereditary Breast and Ovarian Cancer syndrome. It is important to remember, however, that most breast and ovarian cancer is not hereditary.

## How is Hereditary Breast and Ovarian Cancer syndrome inherited?

Inherited information is contained in every cell in our body on structures called chromosomes. Each cell has 46 chromosomes that come in pairs - 23 from our mother and 23 from our father. Each chromosome is made up of thousands of genes. Genes, like chromosomes, come in pairs. They are packages of genetic information (DNA) that act as instructions for making the substances that help our bodies function properly. A change in this genetic information can interfere with proper body functions by causing the gene to no longer work. These gene changes are called mutations.



*BRCA1* and *BRCA2* are genes that control cell growth and division. If there is a mutation within either a *BRCA1* or a *BRCA2* gene, it can no longer control cell growth and division. Cancer occurs when cells grow in an uncontrolled way. Therefore, a *BRCA1* or *BRCA2* gene mutation increases the likelihood that cancer will develop. For this reason, people with a mutation in either of these genes tend to be diagnosed with cancer at an earlier age and are more likely to develop breast cancer in both breasts (bilateral cancer). *BRCA1* appears to be responsible for 45 percent of families with multiple cases of breast cancer only, and in up to 90 percent of families with both breast and ovarian cancer.

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Mutations in *BRCA2* are thought to account for approximately 35 percent of families with multiple cases of breast cancer. *BRCA2* mutations are also associated with male breast cancer, ovarian cancer, prostate cancer and pancreatic cancer.

## What are the chances of inheriting an altered *BRCA1* or *BRCA2* gene?

*BRCA1* and *BRCA2* are both inherited in an autosomal dominant fashion. Autosomal means that both men and women can inherit a *BRCA* mutation. Dominant means that it takes only one *BRCA* gene mutation to cause an increased likelihood for developing cancer. All people have two copies of each *BRCA* gene, one from each parent. A person who has a parent with a *BRCA1* or *BRCA2* mutation, may inherit either that parent's *BRCA* gene with the mutation or that parent's working *BRCA* gene. Therefore, that individual has a 50 percent chance of inheriting the *BRCA* gene mutation and an increased likelihood for developing certain cancers. That person also has a 50 percent chance of not inheriting the *BRCA* gene mutation and would then have the same risk for developing cancer as the general population. It would be very unlikely for one family to have both a *BRCA1* and a *BRCA2* mutation being passed along.

## Are certain people more likely to have a particular gene mutation?

Two specific mutations in the *BRCA1* gene (187delAG and 5385insC) and one mutation in the *BRCA2* gene (6174delT) are more common in Jewish people of Eastern European ancestry (Ashkenazi Jews). About 1 out of 40 (2.5 percent) Ashkenazi Jewish people have one of these three mutations. The chance of having one of these mutations is much higher for people with a personal or family history of breast or ovarian cancer.

## How are *BRCA1* and *BRCA2* mutations detected?

It is possible to test for *BRCA1* and *BRCA2* mutations. By taking a blood sample from someone who has had breast or ovarian cancer, the laboratory may be able to detect a mutation in one of these genes. Once a mutation has been found, the laboratory can look for that same mutation in other family members (whether or not they have had cancer) to see if they have Hereditary Breast and Ovarian Cancer syndrome.

## Is it possible to receive an unclear *BRCA* test result?

About 10-15 percent of people who have complete gene testing for both the *BRCA1* and *BRCA2* genes, are found to have an unclear result. This means that the person is found to have a gene alteration, but it is not clear if it causes an increased risk for cancer. In some cases, it may be possible with additional testing to determine whether or not the gene change is associated with an increased risk for cancer. In other cases, it may take years before we know the meaning of the result.

## What if testing does not detect an altered *BRCA1* or *BRCA2* gene?

Negative results (meaning a *BRCA1* or *BRCA2* mutation is not found) can mean several things. First, it might mean that there is a *BRCA1* or *BRCA2* gene mutation that cannot be detected by current testing methods. This is a limitation of many genetic tests. It could also mean that a different gene is responsible for the cancers in the family. For this reason, families who test negative for the *BRCA* genes may be interested in pursuing testing for other breast cancer genes as they are discovered in the future. It is also possible that the cancers in the family are not hereditary. Since breast cancer is a common disease, more than one woman in a family may have it by chance alone.

## What if testing reveals that a person has inherited an altered *BRCA1* gene?

Women who inherit a *BRCA1* mutation have an increased chance for developing breast and ovarian cancers. Research is taking place to determine the exact risks of developing these cancers. These risks may vary from family to family and from one individual to another. Women who have an altered *BRCA1* gene have a 50-85 percent risk of developing breast cancer by age 70. Their risk for ovarian cancer is 40-60 percent by age 70. A woman who has already had breast cancer and is found to have an altered *BRCA1* gene has an increased risk for breast cancer in her other breast.

Men also have an increased risk for developing prostate cancer, estimated to be 16 percent by age 70. People who have inherited a *BRCA1* mutation may develop one or more cancers or none at all

## What if testing reveals that a person has inherited an altered *BRCA2* mutation?

Both men and women who inherit a *BRCA2* mutation have an increased chance for developing breast cancer. Women have a similar risk of developing breast cancer as found with *BRCA1*. The chance for a male with a *BRCA2* mutation to develop breast cancer is approximately 5-10 percent. Women with a *BRCA2* mutation have a 10-20 percent risk for developing ovarian cancer by age 70. Men with a mutation in the *BRCA2* gene have a 16 percent lifetime risk for developing prostate cancer. Men and women with a *BRCA2* mutation also have slightly increased risks for developing pancreatic cancer, throat cancer, stomach cancer, and melanoma skin cancer.

## If a woman has an altered *BRCA* gene, what are the options for cancer screening and prevention?

Women with a *BRCA* gene mutation have several choices. At a minimum, they should have careful screening to help find cancers at the earliest possible stage, when they are most easily treated. This means having yearly breast imaging (by mammography and MRI), having breast examinations by a physician every six months, and

performing monthly breast self-examinations. Screening for ovarian cancer is not very effective. However, women may choose to receive ultrasounds, together with pelvic examinations and certain blood tests, in an attempt to help find ovarian cancer early.

Another option is to take medication (called chemo-prevention) to reduce the risk of cancer. Both Tamoxifen and Raloxifene (Evista) have been shown to decrease the risk for breast cancer in high-risk postmenopausal women. Birth control pills have been shown in some studies to decrease the risk for ovarian cancer; however, some studies have shown no benefit.

A third option is to have surgery to remove at-risk body parts before cancer develops. An example of this would be having risk-reducing mastectomy to remove the breasts to try to prevent breast cancer. Women can also have their ovaries and fallopian tubes removed to try to prevent ovarian cancer. If this surgery is performed before age 50, it also decreases the risk for breast cancer in women with a *BRCA* mutation. Since ovarian cancer screening has not been proven to be effective, it is strongly recommended that women with a *BRCA* mutation have their ovaries and fallopian tubes removed when they have completed childbearing (ideally between the ages of 35 and 40). It is important to understand that while both of these surgeries greatly reduce the risk of developing cancer, they do not eliminate the risk completely.

## If a man has an altered *BRCA* gene, what are the options for cancer screening and prevention?

Men with a *BRCA* mutation should have annual screening for prostate cancer starting at age 50. Prostate screening includes a rectal exam and a special prostate blood test, known as PSA. Men with an altered *BRCA2* gene should perform monthly breast self-examinations to detect any changes within their breasts. They should also have annual breast examinations by their doctor and can discuss the option of mammography with their physicians, although there are no standard recommendations for this.

## What are the possible risks of *BRCA1* and *BRCA2* testing?

The only physical risk of testing is that of a routine blood draw. However, other risks and benefits should be considered before undergoing testing. The process of genetic testing may be emotionally difficult whether or not a *BRCA* gene mutation is found. Finding a mutation may indirectly provide information about other family members, who may have chosen not to be tested. In addition, costs for the cancer screening and prevention options may or may not be covered by health insurance. Another issue of genetic testing is the possibility that the results could be used by an employer or insurance company to discriminate against a person. The Genetic Information Nondiscrimination Act (GINA) was signed into law in May 2008. GINA makes it illegal for health insurers to deny insurance coverage or charge a higher rate or premium to an otherwise healthy individual found to have a potential genetic condition or genetic predisposition towards a disease or disorder. Protections in health insurance will take effect in May 2009 or when a large group policy first renews after that date. GINA also makes it illegal for employers to use an employee's genetic information when making hiring, firing, placement, or promotion decisions. Employment protections will be implemented in November 2009. In the meantime, there is a national law already in place which specifies that pre-symptomatic genetic conditions cannot be considered a "pre-existing" condition by group health insurers (this law does not apply to self-insurers). While a single individual in a group plan cannot have their premiums raised, the federal law does not prohibit group insurers from raising the premiums of an entire group. There is also a state law that offers protection. Under Ohio law, insurers are not permitted to request genetic test results or use this information in determining whether to provide coverage, cancel a policy, or limit benefits. However, the law does not prohibit insurers from raising premiums for the entire group on the basis of genetic test results. Currently, the ability to obtain life and disability insurance are not protected by any laws.

## What are the possible benefits of *BRCA1* and *BRCA2* testing?

One of the major advantages of learning *BRCA* gene test results is reduced uncertainty about the risks of cancer for people and their families. In addition, the testing may allow doctors to modify medical care to decrease the risk of breast and ovarian cancers. Likewise, if the *BRCA* gene testing is negative, it may allow doctors to decrease the frequency of cancer screening.

The decision to participate in *BRCA1* or *BRCA2* testing is a complicated one. People and families must not only weigh the risks and benefits of testing, but they must also consider their unique situations. Ultimately, people must make their own decisions.