# CANCER FACTS

National Cancer Institute • National Institutes of Health
Department of Health and Human Services


## Genetic Testing for BRCA1 and BRCA2: It's Your Choice

### 1. What are BRCA1 and BRCA2?

Each year, more than 192,000 American women learn they have breast cancer. Approximately 5 to 10 percent of these women have a hereditary form of the disease. Changes, called alterations or mutations, in certain genes make some women more susceptible to developing breast and other types of cancer. Inherited alterations in the genes called BRCA1 and BRCA2 (short for breast cancer 1 and breast cancer 2) are involved in many cases of hereditary breast and ovarian cancer. Researchers are searching for other genes that may also increase a woman's cancer risk.

The likelihood that breast and/or ovarian cancer is associated with BRCA1 or BRCA2 is highest in families with a history of multiple cases of breast cancer, cases of both breast and ovarian cancer, one or more family members with two primary cancers (original tumors at different sites), or an Ashkenazi (Eastern European) Jewish background. However, **not every** woman in such families carries an alteration in BRCA1 or BRCA2, and not every cancer in such families is linked to alterations in these genes.

### 2. How do alterations in BRCA1 and BRCA2 affect a person's risk of cancer?

A woman's lifetime chance of developing breast and/or ovarian cancer is greatly increased if she inherits an altered BRCA1 or BRCA2 gene. Women with an inherited alteration in one of these genes have an increased risk of developing these cancers at a young age (before menopause), and often have multiple close family members with the disease. These women may also have an increased chance of developing colon cancer.

Men with an altered BRCA1 or BRCA2 gene also have an increased risk of breast cancer (primarily if the alteration is in BRCA2), and possibly prostate cancer. Alterations in the BRCA2 gene have also been associated with an increased risk of lymphoma, melanoma, and cancers of the pancreas, gallbladder, bile duct, and stomach in some men and women.

According to estimates of lifetime risk, about 13.2 percent (132 out of 1,000 individuals) of women in the general population will develop breast cancer, compared with estimates of 36 to 85 percent (360–850 out of 1,000) of women with an altered BRCA1 or BRCA2 gene. In other words, women with an altered BRCA1 or BRCA2 gene are 3 to 7 times more likely to develop breast cancer than women without alterations in those genes. Lifetime risk estimates of ovarian cancer for women in the general population indicate that 1.7 percent (17 out of 1,000) will get ovarian cancer, compared with 16 to 60 percent (160–600 out of 1,000) of women with altered BRCA1 or BRCA2 genes. No data are available from long-term studies of the general population comparing the cancer risk in women who have a BRCA1 or BRCA2 alteration with women who do not have an alteration in these genes. Therefore, these figures are estimated ranges that may change as more research data are added.

Some evidence suggests that there are slight differences in patterns of cancer between people with BRCA1 alterations and people with BRCA2 alterations, and even between people with different alterations in the same gene. For example, one study found that alterations in a certain part of the BRCA2 gene were associated with a higher risk for ovarian cancer in women, and a lower risk for prostate cancer in men, than alterations in other areas of BRCA2.

Most research related to BRCA1 and BRCA2 has been done on large families with many affected individuals. Estimates of breast and ovarian cancer risk associated with BRCA1 and BRCA2 alterations have been calculated from studies of these families. Because family members share a proportion of their genes and, often, their environment, it is possible that the large number of cancer cases seen in these families may be partly due to other genetic or environmental factors. Therefore, risk estimates that are based on families with many affected members may not accurately reflect the levels of risk in the general population.

### 3. Are specific alterations in BRCA1 and BRCA2 more common in certain populations?

Specific gene alterations have been identified in different ethnic groups. For example, among individuals of Ashkenazi Jewish descent, researchers have found that about 2.3 percent (23 out of 1,000 persons) have an altered BRCA1 or BRCA2 gene. This frequency is about 5 times higher than that of the general population. Among people with alterations in BRCA1 or BRCA2, three particular alterations have been found to be most common in the Ashkenazi Jewish population—two in the BRCA1 gene and one in the BRCA2 gene. It is not known whether the increased frequency of these alterations is responsible for the increased risk of breast cancer in Jewish populations compared with non-Jewish populations. Other ethnic and geographic populations, such as the Norwegian, Dutch, and Icelandic people, also have a higher rate of **certain** genetic alterations in BRCA1 and BRCA2. This information about genetic differences between ethnic groups may help health care providers determine the most appropriate genetic test to select.

## 4. What does a positive BRCA1 or BRCA2 test result mean?

In a family with a history of breast and/or ovarian cancer, it may be most informative to first test a family member who has the disease. If that person is found to have an altered BRCA1 or BRCA2 gene, the specific change is referred to as a "known mutation." Other family members can then be tested to see if they also carry that specific alteration. In this scenario, a positive test result indicates that a person has inherited a known mutation in BRCA1 or BRCA2 and has an increased risk of developing certain cancers, as described above. However, a positive result provides information only about a person's **risk** of developing cancer. It cannot tell whether cancer will actually develop—or when. It is also impossible to predict the effectiveness of special screening or preventive medical procedures for people with alterations in BRCA1 or BRCA2. **Not all** women who inherit an altered gene will develop breast or ovarian cancer.

A positive test result may have important health and social implications for family members, including future generations. Unlike most other medical tests, genetic tests can reveal information not only about the person being tested, but also about that person's relatives. Both men and women who inherit an altered BRCA1 or BRCA2 gene, whether or not they get cancer themselves, may pass the alteration on to their sons and daughters. However, **not all** children of people who have an altered gene will inherit the alteration.

## 5. What does a negative BRCA1 or BRCA2 test result mean?

A negative test result will be interpreted differently, depending upon whether there is a known mutation in the family. If someone in a family has a known mutation in BRCA1 or BRCA2, testing other family members for that specific gene alteration can provide information about their cancer risk. In this case, if a family member tests negative for the known mutation in that family, it is highly unlikely that they have an inherited susceptibility to cancer. This test result is called a "true negative." Having a true negative test result does not mean that a person will not get cancer; it means that the person's risk of cancer is the same as that of the general population.

In cases where no known mutation in BRCA1 or BRCA2 has previously been identified in a family with a history of breast and/or ovarian cancer, a negative test is not informative. It is not possible to tell whether a person has an alteration in BRCA1 or BRCA2 that was not identified by the test (a false negative), or whether the result is a true negative. In addition, it is possible for people to have an alteration in a gene other than BRCA1 or BRCA2 that increases their cancer risk, but is not detectable by this test.

## 6. What does an ambiguous BRCA1 or BRCA2 test result mean?

If the test shows a change in BRCA1 or BRCA2 that has not been associated with cancer in other people, that person's test result may be interpreted as ambiguous or uncertain. One study found that 10 percent of women who underwent BRCA1 and BRCA2 testing had this type of ambiguous genetic change. Because everyone has genetic alterations that

do not increase the risk of disease, it is sometimes not known whether a specific change affects a person's risk of developing cancer. As more research is conducted and more people are tested for BRCA1 or BRCA2 alterations, scientists will learn more about these genetic alterations and cancer risk.

**7. What are the options for a person who tests positive?**

Several approaches are available for managing cancer risk in individuals with alterations in their BRCA1 or BRCA2 genes. However, limited data exist on the effectiveness of these approaches.

- **Surveillance**—If cancer develops, it is important to detect it as soon as possible. Careful monitoring for symptoms of cancer may be able to catch the disease at an earlier stage. Surveillance methods for breast cancer may include mammography and a clinical breast exam. Some health professionals also recommend breast self-exams, but this surveillance method should not be used in place of clinical exams. Studies are currently being conducted to test the effectiveness of other breast cancer screening methods in women with an altered BRCA1 or BRCA2 gene. With careful surveillance, many cancers will be diagnosed early enough to be successfully treated.

  For ovarian cancer, surveillance methods may include transvaginal ultrasound, CA–125 blood testing, and clinical exams. Surveillance can sometimes find cancer at an early stage, but it is uncertain whether these methods can reduce a person's chance of dying from ovarian cancer.

- **Prophylactic Surgery**—This type of surgery involves removing as much of the at-risk tissue as possible in order to reduce the chance of developing cancer. Preventive mastectomy (removal of healthy breasts) and preventive salpingo-oophorectomy (removal of healthy fallopian tubes and ovaries) do not, however, offer a guarantee against developing these cancers. Because not all at-risk tissue can be removed by these procedures, some women have developed breast cancer, ovarian cancer, or primary peritoneal carcinomatosis (a type of cancer similar to ovarian cancer) even after prophylactic surgery.

- **Risk Avoidance**—Behaviors that may decrease breast cancer risk include exercising regularly and limiting alcohol consumption. Research results on the benefits of these behaviors are based on studies in the general population; the effects of these actions in people with BRCA1 or BRCA2 alterations are not yet known.

- **Chemoprevention**—This approach involves the use of natural or synthetic substances to reduce the risk of developing cancer, or to reduce the chance that cancer will come back. For example, the NCI-supported Breast Cancer Prevention Trial found that the drug tamoxifen reduced the risk of invasive breast cancer by 49 percent in women at increased risk for developing the disease. Few studies have been performed to test the effectiveness of tamoxifen in women with a BRCA1 or BRCA2

alteration. One study found that tamoxifen reduced the incidence of breast cancer by 62 percent in women with alterations in BRCA2. However, the results showed no reduction in breast cancer incidence with tamoxifen use among women with BRCA1 alterations. Additional chemoprevention studies with tamoxifen and other substances in women with an altered BRCA1 or BRCA2 gene are anticipated.

- **Gene Therapy**—At present, altered BRCA1 and BRCA2 genes cannot be repaired. Some day it may be possible to fix or manipulate the genes or sets of genes that increase one's risk of cancer.

**8. What are some of the benefits of genetic testing for breast and ovarian cancer risk?**

There can be benefits to genetic testing, whether a person receives a positive or a negative result. The potential benefits of a negative result include a sense of relief and elimination of the need for special preventive checkups, tests, or surgeries. A positive test result can bring relief from uncertainty and allow people to make informed decisions about their future, including taking steps to reduce cancer risk. In addition, many people are able to participate in medical research that may, in the long run, decrease the risk of death from breast cancer.

**9. What are some of the risks of genetic testing for breast and ovarian cancer risk?**

The direct medical risks of genetic testing are very small, but test results may have an impact on a person's emotions, social relationships, finances, and medical choices. People who receive a positive test result may feel anxious, depressed, or angry. They may choose to undergo preventive measures that have serious long-term implications and whose effectiveness is uncertain. People who receive a negative test result may experience "survivor guilt" caused by avoiding a disease that affects a loved one. They may also be falsely reassured that they have no chance of developing cancer, even though people with a negative test result have the same cancer risk as the general population. Because genetic testing can reveal information about more than one family member, the emotions caused by test results can create tension within families. Test results can also affect personal choices, such as marriage and childbearing. Issues surrounding the privacy and confidentiality of genetic test results are additional potential risks (see below).

**10. What can happen when genetic test results are placed in medical records?**

Clinical test results are normally included in a person's medical records, and the inclusion of genetic test results in a patient's records may have serious implications. For example, when applying for medical, life, or disability insurance, people may be asked to sign forms that give the insurance company permission to access their medical records. The insurance company may take genetic test results into account when making decisions about coverage. An employer may also have the right to look at an employee's medical

records. Individuals considering genetic testing must understand that when test results are placed in their medical records, the results might not be kept private.

Some physicians keep test results out of medical records. However, even if genetic test results are not included in a person's medical records, there may still be some risk of discrimination. Information about a person's genetic profile can sometimes be gathered from that person's family medical history.

**11. What is genetic discrimination, and what laws protect people from this type of discrimination?**

Genetic discrimination occurs when people are treated differently by their insurance company or employer because they have a gene alteration that increases their risk of a disease, such as cancer. People who undergo genetic testing to find out whether they have an alteration in their BRCA1 or BRCA2 gene may be at risk for genetic discrimination.

A positive genetic test result may affect a person's insurance coverage, particularly their health insurance. A person with a positive result may be denied coverage for medical expenses related to their genetic condition, dropped from their current health plan, or unable to qualify for new insurance. Some insurers view the affected individual as a potential cancer patient whose medical treatment would be costly to the insurance company.

The Health Insurance Portability and Accountability Act (HIPAA) of 1996 provides some protection for people who have employer-based health insurance. The Act prohibits group health plans from using genetic information as a basis for denying coverage if a person does not currently have a disease. However, the Act does not prohibit employers from refusing to offer health coverage as part of their benefits, or prevent insurance companies from requesting genetic information.

In 2000, the Department of Health and Human Services released the HIPAA National Standards to Protect Patients' Personal Medical Records. This regulation covers medical records maintained by health care providers, health plans, and health care clearinghouses. Although the standards are not specific to genetic information, they provide the first comprehensive Federal protection for the privacy of health information.

A person who tests positive for a BRCA1 or BRCA2 alteration may also experience genetic discrimination in the workplace if an employer learns about the test result. Although there are currently no Federal laws specific to genetic nondiscrimination, some protection from discrimination by employers is offered through the Americans with Disabilities Act of 1990 (ADA). In 1995, the Equal Employment Opportunity Commission (EEOC) expanded the definition of "disabled" to include individuals who carry genes that put them at higher risk for genetic disorders. The extent of this protection, however, has not yet been tested in the courts.

Several states also have laws that address genetic discrimination by employers and health insurance companies. The degree of discrimination protection varies from state to state. Therefore, the decisions that people make about genetic testing while living in one state may have repercussions in the future if they move to another area.

**12. How are the tests for BRCA1 or BRCA2 performed?**

Testing for alterations in a person's BRCA1 or BRCA2 gene is done on a blood sample. The person's blood is drawn in a laboratory, doctor's office, hospital, or clinic, and the blood sample is sent to a laboratory to check for alterations in the BRCA1 and/or BRCA2 genes.

**13. How much does testing cost and how long does it take to get the results?**

The cost for genetic testing can range from several hundred to several thousand dollars. Insurance policies vary with regard to whether the cost of genetic testing is covered.

As addressed above, because the results of genetic tests can affect a person's health insurance coverage, some individuals may not want to use their insurance to pay for testing. Some people may choose to pay out-of-pocket for the test, even when their insurer would be willing to cover the cost. To protect their privacy, some may not even want their insurer to know they are thinking about genetic testing. Others may decide to ask their insurance company to cover these costs. People who are considering genetic testing may want to find out more about their particular insurance company's policies and the privacy protection laws in their state before submitting the charge for the test.

From the date that blood is drawn, it can take several weeks or months for test results to become available. The length of time depends on the tests performed and other factors. Individuals who decide to get tested should check with their doctor or genetic counselor to find out when test results might be available.

**14. What factors increase the chance of developing breast and/or ovarian cancer?**

The following factors have been associated with increased breast and/or ovarian cancer risk. It is not yet known exactly how these factors influence risk in people with BRCA1 or BRCA2 alterations.

- **Age**—The risk of breast and ovarian cancers increases with age. Most breast and ovarian cancers occur in women over the age of 50. Women with an altered BRCA1 or BRCA2 gene often develop breast or ovarian cancer **before** age 50.

- **Family History**—Women who have a first-degree relative (mother, sister, or daughter) or other close relative with breast and/or ovarian cancer may be at increased risk for developing these cancers. In addition, women with relatives who have had colon cancer are at increased risk of developing ovarian cancer.

- **Medical History**—Women who have already had breast cancer are at increased risk of developing breast cancer again, or of developing ovarian cancer. Women who have had colon cancer also have an increased risk of developing ovarian cancer.

- **Hormonal Influences**—Estrogen is naturally produced by the body and stimulates the normal growth of breast tissue. It is suspected that excess estrogen may contribute to breast cancer risk because of its natural role in stimulating breast cell growth. Women who had their first menstrual period before the age of 12 or experienced menopause after age 55 have a slightly increased risk of breast cancer, as do women who had their first child after age 30. Each of these factors increases the amount of time a woman's body is exposed to estrogen. Removal of a woman's ovaries, which produce estrogen, reduces the risk of breast cancer.

- **Birth Control Pills (Oral Contraceptives)**—Most studies show a slight increase or no change in breast cancer risk in women taking birth control pills. Some studies suggest that a woman who has taken birth control pills for a long period of time, and began taking them at an early age or before her first pregnancy, has a small increase in her risk for developing breast cancer. In contrast, taking birth control pills may decrease a woman's risk of ovarian cancer.

- **Hormone Replacement Therapy**—A woman's risk for developing breast cancer may be increased by hormone replacement therapy (HRT), especially when it is used for a long period of time. Doctors may prescribe HRT to reduce the discomfort from symptoms of menopause, such as hot flashes. Some evidence suggests that women who use HRT after menopause may also have a slightly increased risk of developing ovarian cancer. HRT may have positive health effects as well, such as lowering a woman's risk of heart disease and osteoporosis. These protective effects diminish after a woman discontinues therapy. The risks and benefits of HRT should be carefully considered by a woman and her health care provider.

- **Dietary Fat**—Although early studies suggested a possible association between a high-fat diet and increased breast cancer risk, more recent studies have been inconclusive. It is not yet known whether a diet low in fat will lower breast cancer risk.

- **Physical Activity**—Studies of the relationship between physical activity and breast cancer have had mixed results. However, some studies suggest that regular exercise, particularly in women age 40 and younger, may decrease breast cancer risk.

- **Alcohol**—Alcohol use may increase breast cancer risk, but no biological mechanism for the relationship between alcohol and breast cancer risk has been established.

- **Environmental Factors**—Exposure of the breast to ionizing radiation, such as radiation therapy for Hodgkin's disease or other disorders, is associated with an

increased risk of breast cancer, especially when the exposure occurred at a young age. Evidence for the effect of occupational, environmental, or chemical exposures on breast cancer risk is limited. For example, there is some evidence to suggest that organochlorine residues in the environment, such as those from insecticides, might be associated with an increase in breast cancer risk. However, the significance of this evidence has been debated. Scientific research is currently in progress to study the effects of various environmental factors on breast cancer risk.

**15. Where can people get more information about genetic testing for cancer risk?**

A person who is considering genetic testing should speak with a professional trained in genetics before deciding whether to be tested. These professionals may include doctors, genetic counselors, and other health care workers trained in genetics (such as nurses, psychologists, or social workers). For more information on genetic testing or for help finding a health care professional trained in genetics, contact the National Cancer Institute's Cancer Information Service (CIS) at 1–800–4–CANCER (1–800–422–6237) (see below). The CIS can also provide information about clinical trials (research studies with people) and answer questions about cancer.

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## National Cancer Institute (NCI) Resources

**Cancer Information Service (toll-free)**

Telephone: 1–800–4–CANCER (1–800–422–6237)
TTY: 1–800–332–8615

**Online**

NCI's Web site: http://www.cancer.gov
*LiveHelp*, NCI's live online assistance:
https://cissecure.nci.nih.gov/livehelp/welcome.asp

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