



The American College of
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WOMEN'S HEALTH CARE PHYSICIANS

patient education **Fact Sheet**

PFS007: *BRCA1* and *BRCA2* Mutations MARCH 2015

***BRCA1* and *BRCA2* Mutations**

*Cancer is a complex disease thought to be caused by several different factors. A few types of cancer run in families. These types, called “hereditary” or “familial” cancer, have been linked to changes in **genes** that can be passed from parents to children. Changes in genes are called **mutations**.*

Hereditary breast and ovarian cancer syndrome** is a type of familial cancer. It most commonly is linked to mutations in two genes called ***BRCA1* and *BRCA2. Inheriting one of these mutations increases the risk of getting breast cancer, ovarian cancer, and other types of cancer. About 10% of cases of ovarian cancer and 3–5% of cases of breast cancer are due to mutations in *BRCA1* and *BRCA2*.*

***BRCA* Mutations and Cancer**

Cancer is a disease that affects the normal growth of cells in the body. Normal, healthy cells grow, divide, and are replaced on a regular basis. Cancer occurs when cells begin to grow out of control. Cancer cells can quickly multiply and form growths or tumors. In some types of cancer, cells spread to other parts of the body, where they can grow to form new cancerous areas.

BRCA1 and *BRCA2* are known as tumor suppressor genes. They keep cells from growing too rapidly or in an uncontrolled way. Thousands of mutations in *BRCA1* and *BRCA2* have been found. Some have been linked to an increased risk of cancer.

How Cancer Genes Work

All genes come in pairs. One copy of each gene in a pair is inherited from the mother, and the other copy is inherited from the father. Cells need both copies to work normally. Inheriting one copy of a *BRCA1* or *BRCA2* mutation increases the risk of getting cancer, but it does not necessarily mean that you will get cancer. The other copy of the gene without a mutation keeps cells from growing out of control. But if the normal copy of the gene becomes damaged, it can increase the risk that cancer will occur. Genes can be damaged by many factors, including chemicals, radiation, smoking, and sun exposure. Many of the factors that damage genes are unknown.

Who Is Affected?

About 1 in 300 people carry a *BRCA1* mutation, and 1 in 800 carry a *BRCA2* mutation. These mutations are found more frequently in certain ethnic groups, including people of Ashkenazi (Eastern European) Jewish, French Canadian, and Icelandic backgrounds, but they can occur in anyone.

Effect of *BRCA* Mutations on Cancer Risk

All women have a certain risk of getting breast cancer or ovarian cancer at some point in their lives. Having a *BRCA* mutation increases this risk (Table 1). Women who have a *BRCA1* or *BRCA2* mutation also have an increased risk of cancer of the **ovary, fallopian tube, peritoneum**, and pancreas. Men who have a *BRCA1* or *BRCA2* mutation have an increased risk of breast cancer and an increased risk of prostate and pancreatic cancer.

Table 1. Breast Cancer and Ovarian Cancer Risk for Women With *BRCA* Mutations

Type of Cancer	Risk for the General Population	Risk With <i>BRCA1</i> Mutation	Risk With <i>BRCA2</i> Mutation
Breast	12%	55–65%	45%
Ovary	1.4%	39%	11–17%

Tests for *BRCA1* and *BRCA2* Mutations

All women should be asked specific questions about their personal and family history of breast cancer and ovarian cancer (see box). If answers to these questions suggest that you may have inherited one of these mutations, genetic testing may be offered. Genetic testing requires a **DNA** sample from blood or saliva. There are several approaches to testing that can be followed.

If a relative with breast cancer or ovarian cancer is available, the relative's *BRCA* genes can be analyzed to find out if a specific *BRCA* mutation is present. This is called DNA sequencing. Your DNA then can be tested to see if you have the same mutation. This option is the best way to know if you are at risk. If no relative is available, and you and your family belong to an ethnic group with high numbers of people with a specific *BRCA* mutation, you can be tested for this mutation. If you are not part of a high-risk ethnic group, another option is to have DNA sequencing of your *BRCA* genes. This option usually is not the first choice because of the time and expense involved.

Before you have genetic testing, a health care provider with expertise in cancer genetics can help you understand how the test is done, what the results may mean, and what you may do depending on the test results. You also should discuss current laws about genetic discrimination and privacy of genetic information. The Federal Genetic Information Nondiscrimination Act of 2008 protects people against health and employment discrimination based on genetic information. Many states have similar laws.

Understanding Test Results

A positive test result means that you have the *BRCA* mutation for which you have been tested. A negative test result can mean several things, depending on the testing that you have had performed:

- If you were tested for a specific *BRCA* mutation linked to cancer in your family (eg, a family member with cancer has given a DNA sample and a known *BRCA* mutation is found), and you have a negative test result for that *BRCA* mutation, you have not inherited the gene. You have the same risk of breast and ovarian cancer as the general population.
- If you have a family history of cancer but no family member with cancer has given a DNA sample, and you have a negative test result for a *BRCA* mutation, it can mean that your family has a gene that increases cancer risk that is not a *BRCA* mutation. Or, it can mean that your family has a *BRCA* mutation that cannot be found with current tests. With these two possibilities, it remains unclear whether you have an inherited predisposition for cancer. A third possibility is that your family does not have a gene that increases the risk of cancer.

You also can have an unclear test result. This means there is a change in a *BRCA* gene, but it is not known whether the change increases the risk of cancer. Researchers are continuing to study many more *BRCA* mutations to determine how they may or may not influence cancer risk. If you have a negative result or an unclear result, a **genetic counselor** may be able to determine which scenario is most likely for you and what risk-reduction strategies may be appropriate.

What a Positive Test Result Means for You and Your Family

A positive test result for a *BRCA* mutation associated with cancer means that you have an increased risk of getting cancer. It does not mean that you will get cancer. There is no test currently available that can tell which women with a *BRCA* mutation will develop cancer or at what age. It is important to discuss your results with your health care provider and learn about preventive strategies that may be available to you to decrease your risk of cancer (see "Cancer Prevention if You Have a *BRCA* Mutation").

Having a *BRCA* mutation means that you can pass the gene to your children. Each child has a 50% chance of getting the gene. Your siblings also may be at risk of having the gene. Each of your siblings has a 50% chance of having inherited the gene. Whether to tell family members that you have a *BRCA1* or *BRCA2* mutation is your choice. Your health care provider cannot disclose this information to them. You are not obligated to tell your family members, but it often is a good idea to do so. Sharing this information allows your family members to decide whether they want to be tested and to get appropriate preventive care if they also have a mutation.

Should You Be Tested?

If you answer “yes” to any of the following questions, genetic risk assessment is recommended:

- Do you have a personal history of breast cancer and ovarian cancer?*
- Do you have a personal history of ovarian cancer* and a close relative† with ovarian cancer or premenopausal breast cancer or both?
- Do you have a personal history of ovarian cancer* and are you of Ashkenazi Jewish ancestry?
- Have you had a breast cancer diagnosis at age 50 years or younger and do you have a close relative† with ovarian cancer* or male breast cancer at any age?
- Are you of Ashkenazi Jewish ancestry and have you had a breast cancer diagnosis at age 40 years or younger?
- Do you have a close relative† with a known *BRCA1* or *BRCA2* mutation?

If you answer “yes” to any of the following questions, genetic risk assessment may be helpful:

- Have you had a breast cancer diagnosis at age 40 years or younger?
- Do you have a personal history of ovarian cancer, primary peritoneal cancer, or fallopian tube cancer of high-grade, serous histology that was diagnosed at any age?
- Do you have a personal history of bilateral breast cancer (particularly if the first case of breast cancer was diagnosed at age 50 years or younger)?
- Have you had a breast cancer diagnosis at age 50 years or younger and do you also have a close relative† with breast cancer diagnosed at age 50 years or younger?
- Are you of Ashkenazi Jewish ancestry and have you had a breast cancer diagnosis at age 50 years or younger?
- Do you have a personal history of breast cancer diagnosed at any age and two or more close relatives† with breast cancer at any age (particularly if at least one case of breast cancer was diagnosed at age 50 years or younger)?
- Have you never had breast or ovarian cancer but have a close relative† that meets one of the previous criteria?

*Cancer of the peritoneum and fallopian tubes should be considered a part of the spectrum of the hereditary breast and ovarian cancer syndrome.

†Close relative is defined as a first-degree relative (parent or sibling) or second-degree relative (grandparent, grandchild, aunt, uncle, niece, nephew).

Cancer Prevention if You Have a *BRCA* Mutation

If you test positive for a *BRCA* mutation, you may want to discuss preventive strategies with your health care provider. Prevention includes screening tests, medications, and surgery.

Screening Tests

Enhanced breast cancer screening for women with *BRCA* mutations is recommended. Enhanced breast cancer screening may include the following tests:

- Clinical breast exam by a health care provider twice a year
- Annual **mammography** and annual breast **magnetic resonance imaging (MRI)** starting at age 25 years or younger based on the earliest age at which breast cancer was diagnosed in the family

It is also helpful to be aware of how your breasts normally look and feel and report any changes to your health care provider. This is called breast self-awareness.

Screening for ovarian cancer in women with *BRCA* mutations also may be recommended. Current screening tests include periodic blood tests for **CA 125** (a substance that is made by ovarian cancer cells) and an **ultrasound exam** of the ovaries. Testing can begin between the ages of 30 years and 35 years or 5–10 years earlier than the age at which ovarian cancer was diagnosed in the youngest affected relative. These screening tests have a limited ability to find ovarian cancer at an earlier, more treatable stage. Test results may be normal even when cancer is present. There also is a high rate of false-positive results (a positive test result in someone who does not have ovarian cancer).

Medications

The use of drugs to help reduce the risk of or delay the occurrence of cancer is called chemoprevention. Taking a medication called tamoxifen has been shown to reduce the risk of breast cancer in women with *BRCA2* mutations. Tamoxifen is a drug that is used to treat and prevent “**estrogen-positive**” breast cancer. Estrogen-positive means that the cancer cells respond to the hormone estrogen. Estrogen in the bloodstream can cause the cancer cells to grow. Tamoxifen blocks the effects of estrogen on these cancer cells. Tamoxifen works well in women with *BRCA2* mutations because about 70% of breast cancer tumors in this group are estrogen-positive. Less than 25% of tumors in women with *BRCA1* mutations are estrogen-positive. Tamoxifen does not appear to reduce breast cancer risk in women with *BRCA1* mutations.

Combined hormonal birth control pills (those that contain estrogen and another hormone called **progestin**) may reduce the risk of ovarian cancer and fallopian tube cancer in women with *BRCA* mutations, but they also may increase the risk of breast cancer. If you are thinking about using combined hormonal birth control pills, you should carefully weigh the risks and benefits for chemoprevention and birth control.

Surgery

Surgery is another preventive option for women with *BRCA1* and *BRCA2* mutations. This type of surgery is called “risk-reducing surgery.” Risk-reducing bilateral **salpingo-oophorectomy** is the removal of both ovaries and both fallopian tubes. It can significantly reduce the risk of ovarian cancer, fallopian tube cancer, and peritoneal cancer in women with a *BRCA* mutation. If it is done before **menopause**, having this surgery also can reduce the risk of breast cancer. Women with these mutations should consider having this surgery before age 40 years or after they have completed their families.

Bilateral **mastectomy** (surgical removal of both breasts) reduces the risk of breast cancer by more than 90–95%. The type of mastectomy is important in reducing risk. Total mastectomy, in which the entire breast tissue is removed, including the nipple and **areola**, is the most effective risk-reducing surgery for breast cancer. Mastectomy that removes the breast tissue and leaves the nipple and areola also can be considered.

If you are thinking about having preventive surgery, you and your health care provider will consider the risks and benefits. You should discuss the psychological effects as well as short- and long-term complications. Timing of surgery should be based on your needs, your desire to have children, and the effect that surgery will have on your well-being. An important consideration to think about is that salpingo-oophorectomy performed before menopause will cause you to experience menopause immediately, rather than over several years. Signs and symptoms of menopause often can be managed with hormone therapy and other treatments. You can discuss these treatment options with your health care provider before your surgery.

Finding More Information

If you have a personal or family history of breast cancer or ovarian cancer, getting tested for *BRCA* mutations may be something that you want to consider. Talk to your health care provider about screening and testing options. The following organizations offer additional information about *BRCA* and cancer risk:

American Cancer Society
Genetics and Cancer

www.cancer.org/cancer/cancercauses/geneticsandcancer/genetics-and-cancer-landing

Centers for Disease Control and Prevention
KNOW: BRCA

www.cdc.gov/cancer/breast/young_women/knowbrca.htm

National Cancer Institute

BRCA1 and BRCA2: Cancer Risk and Genetic Testing
www.cancer.gov/cancertopics/factsheet/Risk/BRCA

Glossary

Areola: The darker skin around the nipple.

BRCA1 and BRCA2: Genes that function in the control of cell growth. Changes in these genes have been linked to an increased risk of breast cancer and ovarian cancer.

CA 125: A substance in the blood that may increase in the presence of some cancerous tumors.

DNA: The genetic material that is passed down from parents to offspring. DNA is packaged in structures called chromosomes.

Estrogen: A female hormone produced by the ovaries.

Fallopian Tube: A tube through which an egg travels from the ovary to the uterus.

Genes: Segments of DNA that contain instructions for the development of a person's physical traits and control of the processes in the body. They are the basic units of heredity and can be passed down from parent to offspring.

Genetic Counselor: A health care professional with special training in genetics and counseling who can provide expert advice about genetic disorders and prenatal testing.

Hereditary Breast and Ovarian Cancer Syndrome: An inherited susceptibility to breast cancer, ovarian cancer, and other types of cancer. Its characteristics are multiple family members with breast cancer, or ovarian cancer, or both; the presence of breast cancer and ovarian cancer in a single individual; and early age of breast cancer onset.

Magnetic Resonance Imaging (MRI): A method of viewing internal organs and structures by using a strong magnetic field and sound waves.

Mammography: A procedure in which X-rays of the breast are used to detect breast cancer.

Mastectomy: Surgical removal of part or all of the breast.

Menopause: The time in a woman's life when menstruation stops; defined as the absence of menstrual periods for 1 year.

Mutations: Permanent changes in genes that can be passed on from parent to child.

Ovary: One of a pair of organs that contain the eggs released at ovulation and produce hormones.

Peritoneum: The membrane that lines the abdominal cavity and surrounds the internal organs.

Progestin: A synthetic form of progesterone that is similar to the hormone produced naturally by the body.

Salpingo-Oophorectomy: Removal of the ovary and fallopian tube; a bilateral salpingo-oophorectomy is removal of both ovaries and fallopian tubes.

Ultrasound Exam: A test in which sound waves are used to examine internal structures.

PFS007: Designed as an aid to patients, this document sets forth current information and opinions related to women's health. The information does not dictate an exclusive course of treatment or procedure to be followed and should not be construed as excluding other acceptable methods of practice. Variations, taking into account the needs of the individual patient, resources, and limitations unique to the institution or type of practice, may be appropriate.

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