

Breast Cancer Risk Factors You Cannot Change

A risk factor is anything that increases your chances of getting a disease, such as breast cancer. But having a risk factor, or even many, does not mean that you are sure to get the disease.

Some risk factors for breast cancer are things you cannot change, such as getting older or inheriting certain gene changes. These make your risk of breast cancer higher.

For information on other known and possible breast cancer risk factors, see:

- Lifestyle-related Breast Cancer Risk Factors
- Factors with Unclear Effects on Breast Cancer Risk
- Disproven or Controversial Breast Cancer Risk Factors
- Being born female
- Getting older
- Inheriting certain gene changes
- Having a family history of breast cancer
- Having a personal history of breast cancer
- Race and ethnicity
- Being taller
- Having dense breast tissue
- Having certain benign breast conditions
- Starting menstrual periods early
- Going through menopause later
- Having radiation to your chest
- Exposure to diethylstilbestrol (DES)

Being born female

This is the main risk factor for breast cancer. Men can get breast cancer, too, but this disease is much more common in women than in men.

Getting older

As you get older, your risk of breast cancer goes up. Most breast cancers are found in women age 55 and older.

Inheriting certain gene changes

About 5% to 10% of breast cancer cases are thought to be hereditary, meaning that they result directly from gene changes (mutations) passed on from a parent.

BRCA1 and BRCA2: The most common cause of hereditary breast cancer is an inherited mutation in the *BRCA1* or *BRCA2* gene. In normal cells, these genes help make proteins that repair damaged DNA. Mutated versions of these genes can lead to abnormal cell growth, which can lead to cancer.

- If you have inherited a mutated copy of either gene from a parent, you have a higher risk of breast cancer.
- On average, a woman with a *BRCA1* or *BRCA2* gene mutation has up to a 7 in 10 chance of getting breast cancer by age 80. This risk is also affected by how many other family members have had breast cancer. (It goes up if more family members are affected.)
- Women with one of these mutations are more likely to be diagnosed with breast cancer at a younger age, as well as to have cancer in both breasts.
- Women with one of these gene changes also have a higher risk of developing ovarian cancer and some other cancers. (Men who inherit one of these gene changes also have a higher risk of breast and some other cancers.)
- In the United States, *BRCA* mutations are more common in Jewish people of Ashkenazi (Eastern Europe) origin than in other racial and ethnic groups, but anyone can have them.

Other genes: Other gene mutations can also lead to inherited breast cancers. These gene mutations are much less common, and most of them do not increase the risk of breast cancer as much as the *BRCA* genes.

- *ATM:* The *ATM* gene normally helps repair damaged DNA (or helps kill the cell if the damaged can't be fixed). Inheriting 2 abnormal copies of this gene causes the disease ataxia-telangiectasia. Inheriting one abnormal copy of this gene has been linked to a high rate of breast cancer in some families.
- **PALB2:** The PALB2 gene makes a protein that interacts with the protein made by the BRCA2 gene. Mutations in this gene can lead to a higher risk of breast cancer.
- TP53: The TP53 gene helps stop the growth of cells with damaged DNA. Inherited

mutations of this gene cause **Li-Fraumeni syndrome**. People with this syndrome have an increased risk of breast cancer, as well as some other cancers such as leukemia, brain tumors, and sarcomas (cancers of bones or connective tissue). This mutation is a rare cause of breast cancer.

- **CHEK2**: The CHEK2 gene is another gene that normally helps with DNA repair. A CHEK2 mutation increases breast cancer risk.
- **PTEN:** The *PTEN* gene normally helps regulate cell growth. Inherited mutations in this gene can cause **Cowdensyndrome**, a rare disorder that puts people at higher risk for both cancer and benign (non-cancer) tumors in the breasts, as well as growths in the digestive tract, thyroid, uterus, and ovaries.
- **CDH1:** Inherited mutations in this gene cause **hereditary diffuse gastric cancer**, a syndrome in which people develop a rare type of stomach cancer. Women with mutations in this gene also have an increased risk of invasive lobular breast cancer.
- *STK11:* Defects in this gene can lead to **Peutz-Jeghers syndrome**. People affected with this disorder have pigmented spots on their lips and in their mouths, polyps (abnormal growths) in the urinary and digestive tracts, and a higher risk of many types of cancer, including breast cancer.

Inherited mutations in several other genes have also been linked to breast cancer, but these account for only a small number of cases.

Genetic counseling and testing: Genetic testing can be done to look for inherited mutations in the *BRCA1* and *BRCA2* genes (or less commonly in genes such as *PTEN*, *TP53*, or others mentioned above). This might be an option for some women who have been diagnosed with breast cancer, as well as for certain women with factors that put them at higher risk for breast cancer, such as a strong family history. While genetic testing can be helpful in some cases, not every woman needs to be tested, and the pros and cons need to be considered carefully. To learn more, see <u>Genetic Counseling and Testing for Breast Cancer Risk</u>.

Having a family history of breast cancer

It's important to note that most women who get breast cancer do **not** have a family history of the disease. But women who have close blood relatives with breast cancer have a higher risk:

• Having a first-degree relative (mother, sister, or daughter) with breast cancer almost doubles a woman's risk. Having 2 first-degree relatives increases her risk by about 3-fold.

• Women with a father or brother who has had breast cancer also have a higher risk of breast cancer.

A number of factors can affect breast density, such as age, menopausal status, the use of certain drugs (including menopausal hormone therapy), pregnancy, and genetics.

To learn more, see our information on breast density and mammograms¹.

Having certain benign breast conditions

Women diagnosed with certain types of benign (non-cancer) breast conditions may have a higher risk of breast cancer. Some of these conditions are more closely linked to breast cancer risk than others. Doctors often divide benign breast conditions into different groups, depending on how they affect this risk.

Non-proliferative lesions: These conditions don't seem to affect breast cancer risk, or if they do, the increase in risk is very small. They include:

- Fibrosis and/or simple cysts (sometimes called fibrocystic changes)
- Mild hyperplasia
- Adenosis (non-sclerosing)
- Phyllodes tumor (benign)
- A single papilloma
- Fat necrosis
- Duct ectasia
- Periductal fibrosis
- Squamous and apocrine metaplasia
- Epithelial-related calcifications
- Other tumors (lipoma, hamartoma, hemangioma, neurofibroma, adenomyoepithelioma)

Mastitis (infection of the breast) is not a tumor and does not increase the risk of breast cancer.

Proliferative lesions without atypia (cell abnormalities): In these conditions there's excessive growth of cells in the ducts or lobules of the breast, but the cells don't look very abnormal. These conditions seem to raise a woman's risk of breast cancer slightly. They include:

- Usual ductal hyperplasia (without atypia)
- Fibroadenoma
- Sclerosing adenosis

- Several papillomas (called **papillomatosis**)
- Radial scar

Proliferative lesions with atypia: In these conditions, the cells in the ducts or lobules of the breast tissue grow excessively, and some of them no longer look normal. These types of lesions include:

- <u>Atypical ductal hyperplasia (ADH)</u>²
- Atypical lobular hyperplasia (ALH)³

Breast cancer risk is about 4 to 5 times higher than normal in women with these changes. If a woman also has a family history of breast cancer and either hyperplasia or atypical hyperplasia, she has an even higher risk of breast cancer.

Lobular carcinoma in situ (LCIS)

In <u>LCIS</u>⁴, cells that look like cancer cells are growing in the lobules of the milk-producing glands of the breast, but they are not growing through the wall of the lobules. LCIS is not considered to be cancer, and it typically does not spread beyond the lobule (that is, it doesn't become invasive breast cancer) if it isn't treated. But women with LCIS have a 7 to 12 times higher risk of developing breast cancer (which can be in either breast).

For more on these conditions, see <u>Non-cancerous Breast Conditions</u>⁵.

Starting menstrual periods early

Women who have had more menstrual cycles because they started menstruating early (especially before age 12) have a slightly higher risk of breast cancer. The increase in risk may be due to a longer lifetime exposure to the hormones estrogen and progesterone.

Going through menopause later

Women who have had more menstrual cycles because they went through menopause later (typically after age 55) have a slightly higher risk of breast cancer. The increase in risk may be because they have a longer lifetime exposure to the hormones estrogen and progesterone.

Having radiation to your chest

Women who were treated with <u>radiation therapy</u>⁶ to the chest for another cancer (such as Hodgkin or non-Hodgkin lymphoma) when they were younger have a significantly higher risk for breast cancer. This risk depends on their age when they got radiation. The risk is highest for women who had radiation as a teen or young adult, when the

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Lifestyle-related Breast Cancer Risk Factors

A risk factor is anything that increases your chances of getting a disease, such as breast cancer. But having a risk factor, or even many, does not mean that you are sure to get the disease.

Certain breast cancer risk factors are related to personal behaviors, such as diet and physical activity. Other lifestyle-related risk factors include decisions about having children and taking medicines that contain hormones.

For information on other known and possible breast cancer risk factors, see:

- Breast Cancer Risk Factors You Cannot Change
- Factors with Unclear Effects on Breast Cancer Risk
- Disproven or Controversial Breast Cancer Risk Factors
- Drinking alcohol
- Being overweight or obese
- Not being physically active

- Menopausal hormone therapy
- Breast implants

Drinking alcohol

<u>Drinking alcohol</u>¹ is clearly linked to an increased risk of breast cancer. The risk increases with the amount of alcohol consumed. Women who have 1 alcoholic drink a day have a small (about 7% to 10%) increase in risk compared with those who don't drink, while women who have 2 to 3 drinks a day have about a 20% higher risk. Alcohol is linked to an increased risk of other types of cancer, too.

It is best not to drink alcohol. Women who do drink should have no more than 1 a day².

Being overweight or obese

Being overweight or obese³ after menopause increases breast cancer risk.

Before menopause, a woman's ovaries make most of her estrogen, and fat tissue makes only a small part of the total amount. After menopause (when the ovaries stop making estrogen), most estrogen comes from fat tissue. Having more fat tissue after menopause can raise estrogen levels and increase the chances of getting breast cancer.

Women who are overweight also tend to have higher blood insulin levels. Higher insulin levels have been linked to some cancers, including breast cancer.

Still, the link between weight and breast cancer risk is complex. For example:

- The risk of breast cancer **after** menopause is higher for women who gained weight as an adult.
- For women who are overweight or obese **before** menopause, the risk is actually lower.

The reasons for this aren't exactly clear.

Weight might also have different effects on different types of breast cancer. For example:

• Being overweight after menopause is more strongly linked with an increased risk of

hormone receptor-positive breast cancer⁴.

• Some research suggests that being overweight before menopause might increase your risk of the less common <u>triple-negative breast cancer</u>⁵.

<u>The American Cancer Society recommends</u>⁶ you stay at a healthy weight throughout your life and avoid excess weight gain by balancing your food and drink intake with physical activity.

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number of lifetime menstrual cycles (the same as starting menstrual periods at a later age or going through early menopause).

Birth control

Some birth control methods use hormones, which might increase breast cancer risk.

Oral contraceptives: Most studies have found that women using oral contraceptives (birth control pills) have a slightly higher risk of breast cancer than women who have never used them. Once the pills are stopped, this risk seems to go back to normal within about 10 years.

Birth control shots:Some studies have suggested that getting long-acting progesterone shots (such as Depo-Provera) every 3 months for birth control might increase breast cancer risk, but not all studies have found this.

Birth control implants, intrauterine devices (IUDs), skin patches, vaginal rings: These forms of birth control also use hormones, which in theory could fuel breast cancer growth. Some studies have suggested a link between use of hormone-releasing IUDs and breast cancer risk, but few studies have looked at the use of birth control implants, patches, and rings and breast cancer risk.

Menopausal hormone therapy

Menopausal hormone therapy (MHT) with estrogen (often combined with progesterone) has been used for many years to help relieve symptoms of menopause and help prevent osteoporosis (thinning of the bones). This treatment also goes by other names, such as post-menopausal hormone therapy (PHT) and hormone replacement therapy (HRT).

There are 2 main types of hormone therapy:

For women who still have a uterus (womb), doctors generally prescribe estrogen and progesterone (known as **combined hormone therapy**, or just **HT**). Progesterone is needed because estrogen alone can increase the risk of cancer of the uterus. American Cancer Society

Breast implants

Breast implants have not been linked with an increased risk of the most common types of breast cancer.

However, in rare cases they have been linked with some other types of cancer, including <u>breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)</u>¹¹ and other lymphomas, as well as squamous cell carcinoma. These cancers can form in the scar tissue (capsule) around the implant, and they might show up as a lump, a collection of fluid, swelling, or pain, or skin changes near the implant, or as a change in breast size or shape.

Hyperlinks

- 1. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/alcohol-use-and-</u> <u>cancer.html</u>
- 2. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/acs-guidelines-</u> nutrition-physical-activity-cancer-prevention.html
- 3. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/body-weight-and-</u> <u>cancer-risk.html</u>
- 4. <u>www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-hormone-receptor-status.html</u>
- 5. <u>www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/triple-negative.html</u>
- 6. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/acs-guidelines-</u> <u>nutrition-physical-activity-cancer-prevention.html</u>
- 7. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/acs-guidelines-</u> <u>nutrition-physical-activity-cancer-prevention.html</u>
- 8. <u>www.cancer.org/cancer/types/colon-rectal-cancer/causes-risks-prevention/prevention.html</u>
- 9. <u>www.cancer.org/cancer/types/colon-rectal-cancer/detection-diagnosis-staging/acs-recommendations.html</u>
- 10. <u>www.cancer.org/cancer/risk-prevention/medical-treatments/menopausal-hormone-replacement-therapy-and-cancer-risk.html</u>
- 11. <u>www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery/breast-reconstruction-options/breast-reconstruction-using-implants.html</u>

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Factors with Unclear Effects on Breast Cancer Risk

cancer. And eating certain types of fat is clearly linked to a higher risk of heart disease.

Some studies have also suggested that **diets high in fruits and vegetables and calcium-rich dairy products, but low in red and processed meats** might lower the risk of breast cancer. This remains an active area of research.

Several studies looking at women in Asian countries have found that **diets high in soy products** might lower breast cancer risk. But this link has not been as clear in studies looking at women in Western countries. This might be because Asian women generally eat more soy products (and start at an earlier age) than Western women.

Studies looking at **vitamin levels** in the body have had inconsistent results. So far, there's no strong evidence that taking vitamins (or any other type of dietary supplement) reduces the risk of breast cancer.

The lack of a strong link between diet and breast cancer in studies so far doesn't mean that there's no point in eating a healthy diet. A diet low in fat, red meat, and processed meat and high in fruits and vegetables can have many health benefits, including lowering the risk of some other types of cancer.

Chemicals in the environment

A great deal of research has been reported and more is being done to understand possible environmental influences on breast cancer risk.

Chemicals in the environment that have estrogen-like properties are of special interest. For example, substances found in some plastics, certain cosmetics and personal care products, pesticides, and PCBs (polychlorinated biphenyls) seem to have such properties. In theory, these could affect breast cancer risk.

At this time research does not show a clear link between breast cancer risk and exposure to these substances, but it is hard to study such effects in humans. More studies are needed in this area.

Tobacco smoke

Some studies have found that heavy smoking over a long time might be linked to a slightly higher risk of breast cancer. In some studies, the risk has been highest in certain groups, such as women who started smoking before they had their first child. The 2014 US Surgeon General's report on smoking concluded that there is "suggestive but not sufficient" evidence that smoking increases the risk of breast cancer.

Researchers are also looking at whether <u>secondhand smoke</u>¹ increases the risk of breast cancer. Both mainstream and secondhand smoke contain chemicals that, in high concentrations, cause breast cancer in rodents. Studies in rodents have shown that chemicals in tobacco smoke reach breast tissue and are found in breast milk. In human studies, the evidence on secondhand smoke and breast cancer risk is not clear. Most studies have not found a link, but some studies have suggested it might increase risk, particularly in premenopausal women. The 2014 US Surgeon General's report concluded that there is "suggestive but not sufficient" evidence of a link at this point. In any case, this possible link to breast cancer is yet another reason to avoid secondhand smoke.

Night shift work

Women who work at night, such as nurses on a night shift, might have an increased risk of breast cancer. This is an active area of research. This effect may be due to changes in levels of melatonin, a hormone that's affected by the body's exposure to light, but other hormones are also being studied.

Hyperlinks

1. <u>www.cancer.org/cancer/risk-prevention/tobacco/health-risks-of-tobacco/secondhand-smoke.html</u>

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Disproven or Controversial Breast Cancer Risk Factors

There are some factors that research has shown are not linked to breast cancer. You may see information online or hear about these disproven or controversial risk factors, but it's important to learn the facts.

For information on known and possible breast cancer risk factors, see:

- Lifestyle-related Breast Cancer Risk Factors
- Breast Cancer Risk Factors You Cannot Change
- Factors with Unclear Effects on Breast Cancer Risk

- Antiperspirants
- Bras
- Induced abortion

Antiperspirants

Online and social media rumors have suggested that chemicals in underarm antiperspirants are absorbed through the skin, interfere with lymph circulation, and cause toxins to build up in the breast, eventually leading to breast cancer.

Based on the available evidence (including what we know about how the body works), there is little if any reason to believe that antiperspirants increase the risk of breast cancer. For more information, see <u>Antiperspirants and Breast Cancer Risk</u>¹.

Bras

Online and social media rumors and at least one book have suggested that bras cause breast cancer by obstructing lymph flow. There is no scientific or clinical basis for this claim, and a 2014 study of more than 1,500 women found no association between wearing a bra and breast cancer risk.

Induced abortion

Several studies have provided very strong data that neither induced abortions nor spontaneous abortions (miscarriages) have an overall effect on the risk of breast cancer. For more detailed information, see <u>Abortion and Breast Cancer Risk</u>².

Hyperlinks

- 1. <u>www.cancer.org/cancer/risk-prevention/chemicals/antiperspirants-and-breast-cancer-risk.html</u>
- 2. <u>www.cancer.org/cancer/risk-prevention/medical-treatments/abortion-and-breast-cancer-risk.html</u>

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Can I Lower My Risk of Breast Cancer?

There is no sure way to prevent breast cancer. But there are steps you can take that might lower your risk.

- Lowering your risk
- Steps all women can take
- · What to consider for women at increased risk of breast cancer
- Is there a link between diet/vitamins and breast cancer risk?

Lowering your risk

A **risk factor** is anything that increases your chances of getting a disease, like breast cancer.

Many risk factors for breast cancer are beyond your control, like being born female and getting older. But other risk factors can be changed. This includes lifestyle changes like being physically active and staying at a healthy weight. Making these changes may lower your chance of getting breast cancer.

If you are at increased risk for breast cancer, there are a few additional steps you can take that might reduce your risk.

avoid this, talk to your health care provider about non-hormonal options to treat menopausal symptoms.

What to consider for women at increased risk of breast cancer

If you are at increased risk for breast cancer (for instance, because you have a strong family history of breast cancer, a known inherited gene mutation that increases breast cancer risk, such as in the *BRCA1* or *BRCA2* gene, or you have had <u>DCIS</u>³ or <u>LCIS</u>⁴), there are some things you can consider that might help lower your chances of developing breast cancer (or help find it early):

- Genetic counseling and testing for breast cancer risk (if it hasn't been done already)
- Medicines to lower breast cancer risk
- Preventive (prophylactic) surgery
- Close observation to look for early signs of breast cancer

Your health care provider can help you determine your risk of breast cancer, as well as which, if any, of these options might be right for you.

Genetic counseling and testing

If there are reasons to think you might have inherited a gene change that increases your risk of breast cancer (such having as a strong family history of breast cancer, or a family member with a known gene mutation), you might want to talk to your doctor about genetic counseling to see if you should be tested. To learn more, see Genetic Counseling and Testing for Breast Cancer Risk.

If you decide to be tested and a gene change is found, this might affect your decision about using the options below to help lower your risk for breast cancer (or find it early)

Medicines to lower breast cancer risk

Prescription medicines can be used to help lower breast cancer risk in certain women at increased risk of breast cancer.

Medicines such as **tamoxifen** and **raloxifene** block the action of estrogen in breast tissue. Tamoxifen might be an option even if you haven't gone through menopause, while raloxifene is only used for women who have gone through menopause.

Other drugs, called

Is there a link between diet/vitamins and breast cancer risk?

The possible link between diet and breast cancer risk is not clear, but this is an active area of study. Some (but not all) studies have suggested that a diet that is high in vegetables, fruit, and calcium-rich dairy products, but low in red and processed meats might help lower the risk of breast cancer.

It's also not clear if specific vegetables, fruits, or other foods can lower risk. And most studies have not found that lowering fat intake has much of an effect on breast cancer risk (although some have suggested it might help lower the risk of *dying* from breast cancer).

But just because the science isn't clear on this doesn't mean that there's no point in eating a healthy diet. A diet low in fat, processed and red meat, and sugary drinks, but high in fruits and vegetables can have many health benefits, including lowering the risk of some other types of cancer.

So far, there's no strong evidence that taking vitamins or any other type of dietary supplement reduces the risk of breast cancer.

Learn more: For more on the links between body weight, physical activity, diet, alcohol, and the risk of breast cancer (as well as other cancers), see the <u>American Cancer</u> <u>Society Guidelines for Diet and Physical Activity for Cancer Prevention</u>⁷.

Hyperlinks

- 1. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/alcohol-use-and-</u> <u>cancer.html</u>
- 2. <u>www.cancer.org/cancer/risk-prevention/medical-treatments/menopausal-hormone-replacement-therapy-and-cancer-risk.html</u>
- 3. <u>www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/dcis.html</u>
- 4. <u>www.cancer.org/cancer/types/breast-cancer/non-cancerous-breast-conditions/lobular-carcinoma-in-situ.html</u>
- 5. <u>www.cancer.org/cancer/types/breast-cancer/screening-tests-and-early-detection/mammograms.html</u>
- 6. www.cancer.org/cancer/types/breast-cancer/screening-tests-and-early-

prostate cancer. The risk of having an inherited syndrome is also affected by:

- Which family members are affected (Cancer in close relatives such as a mother or sister is more concerning than cancer in more distant relatives.)
- The number of family members affected
- The age when your relatives were diagnosed (Cancer occurring at a younger age is more of a concern.)

Other inherited gene mutations

Inherited changes in some other genes can also increase breast cancer risk, including these es cadInheritf0 01218 affected by:

(or might be covered only partially) by some of them.

If you do decide to get tested, the genetic counselor (or other health professional) can also help explain what the results mean, both for you and possibly other family members. To learn more about genetic testing in general, see <u>Genetics and Cancer</u>³.

Testing for BRCA and other gene mutations

Some expert groups have developed guidelines for which women (and men) should consider genetic counseling and possibly testing for *BRCA* and other gene mutations. These guidelines can be complex, and not all doctors agree with them, but in general they include two main groups of people:

Women who have already been diagnosed with breast cancer: Most doctors agree that not all women with breast cancer need genetic counseling and testing. But counseling and testing is more likely to be helpful if:

- You were diagnosed with breast cancer at a younger age
- You have triple-negative breast cancer
- You have been diagnosed with a second breast cancer (not a recurrence of the first cancer)
- You are of Ashkenazi Jewish descent
- You have a family history of breast cancer (especially at a younger age or in men), ovarian cancer, pancreatic cancer, or prostate cancer

Other groups of people: Genetic counseling and testing might also be recommended for other people who are at higher risk for inherited gene mutations, including:

- People with a known family history of a BRCA (or other) gene mutation
- Women diagnosed with ovarian cancer or pancreatic cancer, or men diagnosed with breast cancer, pancreatic cancer, or high-grade or metastatic prostate cancer
- People with a family history of breast cancer at a younger age, more than one family member with breast cancer, or breast cancer in a male family member
- People with a close family member with a history of ovarian cancer, pancreatic cancer, or metastatic prostate cancer

How genetic testing is done

The results of genetic testing can sometimes be complex or confusing, which is why it's important to go over them with a genetic counselor or cancer genetics professional. They can explain what they might mean for you (and possibly other family members).

Direct-to-consumer genetic tests

Some genetic tests are now available directly to the public, but there are some concerns with these types of tests. For example, a test that looks for a small number of *BRCA1* and *BRCA2* gene mutations has been approved by the FDA. However, there are more than 1,000 known *BRCA* mutations. This means there are many *BRCA* mutations that would not be detected by this test. People with a negative test result might assume they don't have to be concerned about their risk, when in fact they might still have a different *BRCA* mutation.

Our section on <u>genetics and cancer</u>⁵ has more information about genetic mutations and testing for them.

Hyperlinks

- 1. www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes.html
- 2. www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes.html
- 3. www.cancer.org/cancer/risk-prevention/genetics.html
- 4. <u>www.cancer.org/cancer/risk-prevention/genetics/genetic-testing-for-cancer-risk/what-happens-during-genetic-testing-for-cancer.html</u>
- 5. <u>www.cancer.org/cancer/risk-prevention/genetics.html</u>

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Deciding Whether to Use Medicine to Reduce Breast Cancer Risk

For women with a higher-than-average risk of breast cancer, some medicines can help reduce this risk. But these drugs can also have side effects, so it's important to weigh their pros and cons before deciding to take one.

- Chemoprevention
- Should I take a drug to help reduce my breast cancer risk?
- Am I at higher risk for breast cancer?
- Are there reasons not to take one of these drugs to help reduce breast cancer risk?

Chemoprevention

Taking medicines to help lower the risk of getting a disease is called **chemoprevention**.

The most commonly used medicines to lower breast cancer risk are tamoxifen and raloxifene. Other medicines called aromatase inhibitors (such as anastrozole and exemestane) might also be options.

Should I take a drug to help reduce my breast cancer risk?

The first step in deciding if you should take a drug to help lower your chances of getting breast cancer is to have a health care provider assess your breast cancer risk.

Most experts say that your breast cancer risk should be higher than average for you to consider taking one of these drugs. If you do have a higher-than-average risk, you need to compare the benefit of possibly reducing your chance of getting breast cancer with the risk of side effects and other problems from taking one of these drugs.

Am I at higher risk for breast cancer?

A risk factor is anything that raises your risk of getting a disease. Your risk factors will need to be assessed to find out if you are at higher-than-average risk for breast cancer. But keep in mind that having risk factors does not mean that you will definitely develop breast cancer. In fact, most women who have one or more risk factors never develop breast cancer.

Some important risk factors for breast cancer include:

- Getting older
- · Having close relatives who have had breast cancer
- Having a longer menstrual history (more total menstrual cycles)
- Having had invasive breast cancer or <u>ductal carcinoma in situ (DCIS)</u>¹ before
- Being diagnosed with lobular carcinoma in situ (LCIS)²
- Being diagnosed with <u>atypical ductal hyperplasia (ADH) or atypical lobular</u> <u>hyperplasia (ALH)</u>³
- Having a gene mutation linked to a <u>family cancer syndrome</u>⁴ (such as a *BRCA* mutation)

Some of these factors can increase your risk more than others.

How is breast cancer risk assessed?

Researchers have built some statistical models to help predict a woman's risk of getting breast cancer.

For example, the <u>Breast Cancer Risk Assessment Tool</u>⁵ (based on the modified **Gail Model**) is commonly used to assess risk. It can estimate your risk of getting breast cancer in the next 5 years and over your lifetime, based on many of the factors listed above.

This tool only looks at family history in close relatives (like siblings, parents, and ADH*f*.11 Tm 0 0 0 rg 1 1 703 gs (children), t4next 5 CIS))Tj 0 g /F2 8 Tf 0, n situ (LCIS)

Other risk assessment tools, such as the **Tyrer-Cuzick model** and the **Claus model**, are based largely on family history. These tools are used mainly by genetic counselors and other health care professionals.

These tools can give you a rough estimate of your risk, but no tool or test can tell for sure if you'll develop breast cancer.

How high does my risk need to be?

There is no single definition of a higher-than-average risk of breast cancer. But most major studies have used a 1.7% risk of developing breast cancer over the next 5 years as their cut-off point. (This is the average risk for a 60-year-old woman.)

Some medical organizations recommend that doctors discuss the use of medicines to lower breast cancer risk in women at least 35 years old who have a 5-year risk of 1.7% or higher. Others might use different cutoff points.

The American Cancer Society does not have recommendations for using medicines to help lower the risk of breast cancer.

Are there reasons <u>not</u> to take one of these drugs to help reduce breast cancer risk?

All drugs have risks and side effects that must be discussed when making the decision about chemoprevention.

Most experts agree that **tamoxifen and raloxifene** should not be used to reduce breast cancer risk in women who:

- Have a higher risk of serious blood clots*
- Are pregnant or planning to become pregnant
- Are breastfeeding
- Are taking estrogen (including birth control pills or shots, or menopausal hormone therapy)
- Are taking an aromatase inhibitor
- Are younger than 35 years old

obese, or have (or are being treated for) high blood pressure or diabetes, you also have a higher risk of serious blood clots. Women with any of these conditions should ask their doctors if the benefits of taking one of these drugs would outweigh the risks.

A woman who has been diagnosed with any type of uterine cancer or atypical hyperplasia of the uterus (a kind of pre-cancer) should not take tamoxifen to help lower breast cancer risk.

Raloxifene has not been tested in pre-menopausal women, so it should only be used if you have gone through menopause.

Aromatase inhibitors are not useful for pre-menopausal women, so they should only be used if you have gone through menopause. These drugs can cause bone thinning (osteoporosis), so they're not likely to be a good option in women who already have thin or weakened bones.

Talk with your doctor about your total health picture to make the best possible choice for you.

To learn more about the use of these medicines for chemoprevention, see:

- Tamoxifen and Raloxifene for Lowering Breast Cancer Risk
- Aromatase Inhibitors for Lowering Breast Cancer Risk

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/breast-cancer/15.44</u> .outodof-breastcancer/dcis.html
- 2. <u>www.cancer.org/cancer/types/breast-cancer/non-cancerous-breast-conditions/lobular-carcinoma-in-situ.html</u>
- 3. <u>www.cancer.org/cancer/types/breast-cancer/non-cancerous-breast-conditions/hyperplasiadof-the-breast-ductal-or-lobular.html</u>
- 4. <u>www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes.html</u>
- 5. <u>bcrisktool.cancer.gov</u>

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Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for the prevention of breast

side effects.

- What kind of drugs are tamoxifen and raloxifene?
- How much do these drugs lower the risk of breast cancer?
- Are there other benefits to taking these drugs?

The effect of these drugs on breast cancer risk has varied in different studies. When the results of all the studies are taken together, the overall reduction in risk for these drugs is about 40% (more than a third).

What would this mean for me?

Although a medicine that cuts your risk by about 40% sounds like it must be a good thing, what it means for you depends on how high your risk is in the first place (your baseline risk).

For example, if you had a 5% risk of getting breast cancer in the next 5 years, you would be considered at increased risk. A 5% risk would mean that over the next 5 years, 5 of 100 women with your risk would be expected to get breast cancer. A 40% reduction in your risk would mean your risk goes down to 3%. This would be a 2% change overall.

Since the change in your overall risk depends on your baseline risk, you would benefit less if you had a lower baseline risk, and you would benefit more if your risk was higher. If you had a baseline risk of only 1.7% in the next 5 years (which is what many expert groups use as a cutoff point for being at 'increased risk'), a 40% change would mean that your risk would go down by less than 1% overall (to about 1%) in the next 5 years.

start again after the drug is stopped, they don't always, and some women go into menopause. This is more likely in women who were close to menopause when they started taking the drug.

Other, more serious side effects are rare. These include serious blood clots and cancer of the uterus.

Blood clots

Both tamoxifen and raloxifene increase your risk of developing blood clotsin a vein in your leg (deep venous thrombosis) or in your lungs (pulmonary embolism). These clots can sometimes cause serious problems, and even death. In the major studies looking at these drugs for breast cancer prevention, the overall risk of these blood clots over 5 years of treatment was less than 1%. This risk could be higher if you had a serious blood clot in the past, so these drugs are generally not recommended to lower breast cancer risk for anyone with a history of blood clots.

Because these drugs increase your risk of developing serious blood clots, there is also concern that they might also increase your risk of heart attack or stroke, although this is not clear. You might want to discuss this with your doctor, especially if you have a history of a heart attack or stroke, or if you are at increased risk for them. (See Deciding Whether to Use Medicine to Reduce Breast Cancer Risk.)

Cancers of the uterus

Because **tamoxifen** acts like estrogen in the uterus, it can increase your risk of cancers of the uterus, including <u>endometrial cancer</u>² and <u>uterine sarcoma</u>³. It's also linked to a higher risk of endometrial pre-cancers. The increased risk seems to affect women over 50, but not younger women.

The overall increase in the risk of uterine cancer with tamoxifen use is low (less than 1%), and it goes back to normal within a few years of stopping the drug.

If you have had a hysterectomy (surgery to remove the uterus), you are not at risk for endometrial cancer or uterine sarcoma and do not have to worry about these cancers.

If you are taking tamoxifen, tell your doctor if you have any abnormal vaginal bleeding or spotting, especially after menopause, as these are possible symptoms of uterine cancer.

Raloxifene does not act like estrogen in the uterus and is not linked to an increased risk

of uterine cancer.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-hormone-receptor-status.html</u>
- 2. www.cancer.org/cancer/types/endometrial-cancer.html
- 3. <u>www.cancer.org/cancer/types/uterine-sarcoma.html</u>

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Aromatase Inhibitors for Lowering Breast Cancer Risk

Aromatase inhibitors (Als) are drugs used to lower breast cancer risk in some postmenopausal women. For post-menopausal women with a higher-than-average risk of breast cancer, these drugs may be an option instead of tamoxifen or raloxifene.

- What are aromatase inhibitors?
- Can aromatase inhibitors lower the risk of breast cancer?
- What are the risks and side effects of aromatase inhibitors?

What are aromatase inhibitors?

Aromatase inhibitors (Als) lower estrogen levels by stopping an enzyme in fat tissue (called **aromatase**) from changing other hormones into estrogen. (Estrogen can fuel the growth of breast cancer cells.)

These drugs don't stop the ovaries from making estrogen. They only lower estrogen levels in women whose ovaries aren't making estrogen (such as women who have already gone through menopause). Because of this, they are used mainly in women who have gone through menopause already. The AIs that have been shown in studies to lower breast cancer risk include:

- Anastrozole (Arimidex)
- Exemestane (Aromasin)

Like tamoxifen, these drugs are more often used to treat hormone receptor-positive breast cancer than to lower breast cancer risk.

When used to lower breast cancer risk, these drugs are typically taken for 5 years. They are pills taken once a day.

Can aromatase inhibitors lower the risk of breast cancer?

In large studies, both anastrozole and exemestane have been shown to lower breast cancer risk in postmenopausal women who are at increased risk.

While these drugs are not FDA approved to lower breast cancer risk, some expert groups include them as options (along with tamoxifen and raloxifene) to reduce breast cancer risk in post-menopausal women at increased risk. For example, they might be a reasonable option for women who have an increased risk of blood clots and therefore should not take tamoxifen or raloxifene.

What are the risks and side effects of aromatase inhibitors?

The most common side effects of Als are symptoms of menopause, such as hot

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Sharma P. Selective estrogen receptor modulators and aromatase inhibitors for breast

Preventive Surgery to Reduce Breast Cancer Risk

For women at very high risk of breast cancer

For women in this group, removing both breasts (known as a **bilateral prophylactic mastectomy**) before cancer is diagnosed can greatly reduce (but not eliminate) the risk of getting breast cancer.

Unfortunately there's no way to know for sure ahead of time if a woman will benefit from this surgery. Most women with a *BRCA1* or *BRCA2* gene mutation will develop breast cancer at some point. Having a prophylactic mastectomy before the cancer develops might add many years to their lives. But not all women with *BRCA1* or *BRCA2* mutations develop breast cancer. For some women the surgery might not have been helpful. Although they might still get some important benefits from the surgery such as peace of mind, they would also have to deal with its aftereffects, which might include physical and emotional side effects.

For women already diagnosed with breast cancer

Some women who have already been diagnosed with breast cancer choose to have the other breast removed at the same time of surgery to remove the breast with cancer. This operation (known as a **contralateral prophylactic mastectomy**, or CPM) can help lower their risk of developing a second breast cancer.

This is more likely to be a good option for women who also have other factors that increase their risk of getting another breast cancer, such as a *BRCA1* or *BRCA2* mutation or a strong family history of breast cancer.

But for women who don't have a family history or other risk factors for breast cancer, the benefit of CPM is less clear. Having breast cancer does raise your risk of getting cancer in the other breast, but this risk is still usually low, and many women overestimate this risk. And while CPM lowers the risk of getting cancer in the other breast, it does not increase most women's chances of living longer.

Other issues might also be important when considering a CPM. For example, after a mastectomy, the breasts may no longer look the same, even if a woman has <u>breast</u> reconstruction². Removing both breasts (possibly followed by reconstruction) can help the breasts look more symmetrical after treatment.

Before having this type of surgery, it's very important to talk with a member of your cancer care team or a genetic counselor so that you understand how much you might benefit from it, versus the likelihood of risks and side effects. You might also want to get a second medical opinion, as well as talk to others who have had this surgery, before deciding if it's right for you.

Prophylactic oophorectomy (removal of the ovaries)

Women with a BRCA1