

;



Offered to you by:



Breast Cancer: Information for Women at Increased Risk

Introduction

If you have one or more relatives who have had breast cancer, you may be concerned about your own risk of getting breast cancer. This resource provides information on factors that increase your risk of breast cancer, on ways to reduce your risk and on the role of heredity in breast cancer.

This resource is not intended to give you a specific estimate of your breast cancer risk.

Evaluation of your breast cancer risk is available through your health care provider. Ask your physician whether referral to a familial cancer program is appropriate for you.

Terms in the text that may be unfamiliar are printed in boldface type and are defined in the “Word List” at the end of this resource.

Breast Cancer Risk Factors

Life circumstances and lifestyle practices can affect your risk of breast cancer. For the purposes of this resource, *risk factors* are divided into *major*, *moderate* and *mild*. (The categories and risk factors below are explained in the information that follows.)

**Major Risk
Factors**

Moderate Risk Factors

Mild Risk Factors

Major Risk Factors

- Age 50 or older
- Strong family history of breast cancer
- High percent of density on mammogram
- Prior breast cancer
- Carcinoma in-situ of the breast

Moderate Risk Factors

- Lesser family history of breast cancer
- Proliferative breast disease with atypia
- Radiation exposure to breasts (does not include routine chest X-ray or mammograms)

Mild Risk Factors

- Reproductive characteristics
 - Menstrual periods before age 12
 - Late onset of menopause
 - Never pregnant
 - First pregnancy after age 30
 - Never breast-fed a baby
 - Hormone therapy for 10 or more years
- Benign breast disease
- Race/ethnicity/country of origin
 - Jewish heritage
 - American Caucasian or African Amer. (compared to Hispanic Amer., Asian Amer.)
 - North American, Northern European (compared to African, Asian)
- Lifestyle variables
 - Overweight/obese
 - Alcohol intake (3 or more drinks a day)
 - Sedentary lifestyle
- Socioeconomic characteristics
 - Higher socioeconomic status
 - Urban residence
 - Never married
- Prior cancers

Major Risk Factors

The following are considered major risk factors for breast *cancer*. This means the risk is four or more times that of women of the same age without these risk factors.

Age

The *incidence* of breast cancer increases with age. This is true of most cancers that affect adults. You may have read or heard in the media that a woman's risk of breast cancer is 1 in 8. This refers to a woman's lifetime risk. This means the chance of developing breast cancer by age 30 is 1 in 249, by age 70 the chance is 1 in 24 and by age 90 the chance is 1 in 8.

Strong family history

About 15 percent of women diagnosed with breast cancer have a family history of the disease. If you have relatives who have had breast cancer, you are at some degree of increased risk. The level of increased risk is determined by the following factors:

- Number of relatives who have had breast cancer
- Closeness of biologic relationship to relatives with breast cancer
- Age of affected family members when they were diagnosed with breast cancer
- Presence of more than one primary cancer (such as breast and ovarian cancer) in the same individual in the family. (A *primary* cancer is one that originates in an area of the body for the first time and is not the result of another cancer spreading.)
- Presence of both breast and ovarian cancer in different individuals in the same family

A woman's risk may be only slightly increased if, for example, she has only one distant relative, such as a maternal aunt or grandmother whose breast cancer developed late in life. However, the risk may be significantly greater when several of a woman's close relatives develop breast cancer prior to menopause. In some families of this type, there may be an alteration in an inherited *gene* that causes an increased susceptibility to, or a high risk of developing breast cancer. In other families with multiple cases of breast cancer, no inherited pattern or genetic abnormality can be found. In such cases, the cancer is termed *familial*, rather than *inherited*. Familial and inherited risks are not the same.

Inherited genetic risk

Individuals from some families inherit and pass on altered genetic material that significantly increases the risk of breast cancer. Families with such a genetic alteration are rare and account for fewer than 10 percent of all breast cancers. If an individual in one of these rare families has a mother or father with an altered gene, that person has a 50 percent chance of having inherited the altered gene from his or her parent.

Genes are present in each of the body's cells. Genes provide instructions for the body to produce proteins that, in turn, control how cells grow and function. In almost all cells of a person's body there are 46 strands (23 pairs) of genetic material called *chromosomes*. Each chromosome contains a long chain of special chemicals called *DNA* (deoxyribonucleic acid). A gene is a segment of one of these long DNA chains (see figure 1). Every person has two copies of each gene — one received from the father and one from the mother.

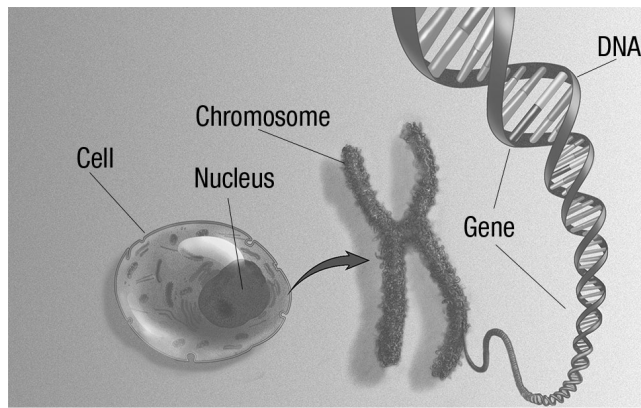


Figure 1. Each cell contains chromosomes that consist of long chains of DNA (deoxyribonucleic acid). Genes are segments of the chains of DNA.

© MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH. ALL RIGHTS RESERVED.

The order of the chemicals in each gene “spells out” a message that tells each of the body’s cells how to function. When the chemical order of a gene is altered, this can be thought of as a genetic “misspelling.” These misspellings are called *mutations*.

Mutations in certain genes called tumor suppressor genes have been linked to an increased risk for breast cancer. These genes include BRCA1 (Breast Cancer gene number 1), BRCA2, and others. Mutations in these genes cause a *genetic predisposition* to develop cancer.

The BRCA1 and BRCA2 genes are large, and many different mutations in these genes appear to cause an increased risk for breast cancer. Abnormalities (mutations) in BRCA1 and BRCA2 appear to account for approximately 40 percent of hereditary breast cancers. Mutations in these genes are also associated with an increased risk of ovarian cancer, and, to a lesser degree, an increased risk of some other cancers.

Men with a BRCA1 or BRCA2 mutation are at increased risk of developing breast cancer, however, their risk is many times less that of the risk for breast cancer in women with these mutations. Men with either a BRCA1 or BRCA2 mutation can pass the mutation on to their children.

A health care provider may suspect that a family has a mutation in one of these genes when there are numerous breast cancers in one family. This suspicion grows when those affected are diagnosed before menopause and when several generations are affected. Mutations are also the suspected cause when families have members diagnosed with ovarian cancer, breast cancer, ovarian and breast cancer (in the same woman), and male breast cancer.

Familial risk

Even if several family members have breast cancer, it does not necessarily mean an inherited gene alteration is responsible for them. Families with altered breast-cancer genes are rare. Far more often, families will have breast cancer that is *familial*. *Familial* and *inherited* risks are different. *Familial* simply means that something occurs more commonly in a family. Families share many things in addition to their genes, such as similar diets and environments, culturally influenced patterns of childbearing, even similar occupations. These factors could cause breast cancers to

occur in a family without the presence of an inherited alteration in a breast-cancer gene. Also, families may share more subtle genetic variations that may be related to the development of cancer. These are not the same as the gene mutations noted above. More than one gene may be involved and the overall cancer risk is likely much lower than in families where an alteration in a tumor suppressor gene is present. Sometimes several cases of breast cancer occur in a family by chance. This simply indicates the disease is common.

High percent of density on mammogram (breast X-ray)

X-ray images of breasts vary greatly from woman to woman. The way a breast appears on a *mammogram* depends on the relative amounts of fat tissue and fibroglandular tissue that are present. Because fibroglandular tissue appears white on a mammogram, a high percentage of white indicates a high percentage of dense breast tissue.

The ratio of fat to fibroglandular tissue in the breasts is influenced by age and menopausal status. Young, pre-menopausal women typically have more glandular tissue in their breasts, while older, post-menopausal woman usually have more fatty tissue in their breasts. A postmenopausal woman whose breasts appear nodular or dense (compared to her peers of the same age) on a mammogram has an increased risk of developing breast cancer.

Prior breast cancer

Women who have had cancer in one breast are at risk for developing a new (primary) cancer in the other breast or even in the same breast if a lumpectomy was done on the first cancer. The second cancer probably results from the same factors that produced the first cancer. While the *relative risks* for cancer in the other breast are moderately increased, the *absolute risks* (actual number of woman affected) are low (less than 1 in 100 women per year). Therefore, removal of the unaffected breast tissue to prevent a second cancer is generally not warranted. For women who have had breast cancer and have an inherited alteration in a gene (for example BRCA1), the risk of a second breast cancer is greatly increased compared with women whose breast cancers are not due to an inherited gene alteration.

To detect changes promptly in the remaining breast tissue, it is important to follow-up with monthly breast self-examinations, at least twice yearly examinations by a health care provider, and yearly mammograms.

Carcinoma in situ

There are two types of *carcinoma in situ* of the breast — ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS), each arising from a different type of tissue within the breast. Unlike invasive breast cancer, the cancer-like cells of carcinoma in situ have not invaded the breast tissues.

If the abnormal cells of a ductal carcinoma in situ are not removed, they may turn into an invasive cancer that may spread. Therefore, these abnormal cells should be removed by lumpectomy or mastectomy. Women who have lumpectomy may undergo radiation therapy.

The cells involved in lobular carcinoma in situ, on the other hand, do not usually grow into a cancer. Rather LCIS is a marker indicating that a woman is at increased risk of developing invasive breast cancer in other cells of either breast. Therefore, women diagnosed with LCIS should be screened regularly for breast cancer. LCIS is not removed as part of treatment, but women with LCIS should discuss their options for risk management and prevention with their doctor.

Moderate Risk Factors

The moderate risk factors below can increase the risk of breast cancer by 2.1 to 4 times over that for a woman of the same age without these risk factors.

Lesser family history

Women who have a mother or one sister with breast cancer have a moderate increase in their breast cancer risk (compared to women with no affected relatives). This is particularly true if the affected relative(s) developed breast cancer before menopause. If the affected relative(s) was diagnosed with breast cancer after menopause, the risk of breast cancer is elevated to a lesser degree.

Proliferative breast disease with atypia

Benign breast disease refers to a broad range of breast conditions. The majority of women with benign breast disease have a minimal increase in breast cancer risk. However, women with a specific type of benign breast disease called proliferative breast disease with *atypia* (also called atypical hyperplasia) have a higher risk of developing breast cancer than women with other types of benign breast disease. The presence of atypical hyperplasia can only be determined once a *biopsy* of the breast is done and breast tissue is examined under the microscope.

When atypical hyperplasia is present, breast cells show abnormalities in the number, size, shape and/or growth pattern when looked at under a microscope. The presence of atypia suggests a higher breast cancer risk and its absence a lower risk.

Radiation exposure to the breasts

Women whose breasts have been exposed to large amounts of ionizing (X-ray) radiation (for example women who received radiation treatment for Hodgkin's disease or those who survived the Hiroshima/Nagasaki atomic bomb attacks) have a moderate breast cancer risk. This is particularly true for women who received radiation to their breasts during their teenage years when the breasts are actively developing. The small amount of X-ray exposure from ordinary diagnostic X-rays (such as chest X-rays or mammograms) does not pose a significant risk.

Mild Risk Factors

The mild risk factors listed below can increase breast cancer risk by 1.1 to 2 times over the risk of a woman of the same age without these risk factors:

Reproductive characteristics

There is a mild increase in the risk of breast cancer in women for which any of the following is true:

- Early onset of menstrual periods (before age 12)
- Late onset of menopause (after age 54)
- Never pregnant
- First pregnancy after age 30
- Never breast-fed a baby
- Hormone therapy for 10 years or more, especially combination therapy (estrogen/progestin)

The reason these factors are associated with breast cancer is unclear. However, the risk is thought to be at least in part related to estrogen exposure. Each of these circumstances increases the amount of time a woman's body produces or is exposed to estrogen. In addition to its positive effects on some body systems, estrogen may stimulate the growth of breast cells. There is an increased chance that something may go wrong during cell growth and, occasionally, a cancer may occur.

Benign breast disease

There are many types of benign breast disease and all types can only be diagnosed after a breast biopsy. Women with benign breast disease have a slightly increased risk of developing breast cancer. As mentioned earlier, this risk is significantly higher if the type of benign breast disease has been diagnosed as lobular carcinoma in situ (LCIS) or as proliferative breast disease with atypia. Women who undergo breast biopsies showing other types of benign breast disease have only a slight increase in breast cancer risk.

Race/ethnicity/country of origin

Women of Jewish ancestry are somewhat more likely to develop breast cancer than are non-Jewish women. Part of this risk may be due to genetic factors because Jewish women of central European origin are more likely to have mutations in BRCA1 and BRCA2 genes. The full reason for the increased risk in Jewish women is not clear.

Breast cancer is about twice as common among Caucasian Americans (110 cases per 100,000 women per year) and African Americans (96 cases per 100,000) than it is among Hispanics (59 cases per 100,000) or Asians (53 cases per 100,000). In general, breast cancer rates are highest in residents of North America and Northern Europe and lowest in Asia and Africa. The reasons for these differences are not clearly understood.

Lifestyle variables

Lifestyle variables, such as weight, physical activity, smoking and diet are factors that play a role in breast cancer risk. More importantly, they are aspects of your life you can control.

Body weight

Weight gain and obesity have been shown to increase the risk for breast cancer as well as the risk for other cancers and chronic diseases. Current data suggest that reasonable weight loss can lower your risk of breast cancer.

Exercise/activity

Women who are physically inactive (sedentary) have a mildly increased risk of breast cancer.

Diet

- *Dietary fat* — The relationship between dietary fat intake and breast cancer risk is a controversial issue. Some studies suggest that women who consume excess quantities of dietary fat are at a greater risk of developing breast cancer, while other studies show no excess risk. Recent studies suggest that high-fat diets may decrease survival rates for those who already have breast cancer.
- *Dietary fiber* — There appears to be no clear association between dietary fiber intake and breast cancer risk.
- *Vitamins/dietary supplements* — Data regarding vitamin and mineral supplementation is inconclusive, however, research continues in this area.
- *Alcohol* — Women who consume three or more alcoholic drinks a day are at an increased risk for breast cancer. It is not known whether discontinuing alcohol consumption reduces the risk of breast cancer.

Bottom line: An active lifestyle and a healthful diet are the basis for a healthful weight, which is associated with a reduction in the risk of breast cancer.

Socioeconomic characteristics

Some socioeconomic factors have been associated with an increased risk of breast cancer. These factors include having higher socioeconomic status, living in urban areas, and having never married. Although the reasons why these factors increase breast cancer risk are not clear, they are thought to be linked to dietary, reproductive, and/or behavioral characteristics. For example, women of higher socioeconomic status may be at an increased risk because they are more likely to delay their first pregnancy, or more likely to use hormone therapy than women of lower socioeconomic levels.

History of other cancers

Women who have had separate cancers of the ovaries, *endometrium*, colon, or rectum are more likely to develop cancer of the breast than are women who have never had these cancers. The reason for this small increased risk may be because these cancers share one or more causes or risk factors. For example, being inactive and being overweight have been associated with an increased risk of both breast cancer and *colorectal* cancers.

Another way that two separate cancers might occur in the same woman is through an inherited genetic process. The breast cancer genes BRCA1 and BRCA2 (explained previously) have been linked to the development of cancers besides breast cancer. A woman who carries an altered

BRCA1 gene may develop breast cancer, she may develop another cancer associated with the BRCA1 gene or she may develop more than one of these cancers.

Genetic Testing

Testing for specific gene alterations or mutations (genetic testing) is possible when the gene's location (on the chromosome) and its chemical sequence are known. Testing for mutations in BRCA1 and BRCA2 is available, but the process is complex. In some families where breast cancers appear to be associated with BRCA1 or BRCA2, evaluation of these genes does not show an identifiable alteration. This suggests that the tests, as they are now being done, do not have a 100 percent detection rate. In addition, there are probably other genes not yet identified that also predispose people to breast and other cancers.

There is no simple, routine, reliable and inexpensive test for these alterations. As a result, testing is being done in only a few laboratories in the United States. Your health care provider can tell you more about the benefits and limitations of testing. She or he can explain how such testing may be used by an individual or family to help make choices about medical care. Information is also available about ongoing research to learn more about genetic risk factors for breast cancer and other cancers.

Genetic counseling

An important issue related to genetic testing for cancer is the potential psychological impact of learning more about the risk for cancer for oneself or family members. Each family member may have different reactions to information provided by genetic testing. Family tensions may develop as the information about risk is shared. Some individuals decide not to be tested because of concerns about what might happen if employers or insurance companies learn that they carry an altered cancer susceptibility gene. Health-care providers trained to deal with these issues are called genetic counselors. *Genetic counseling* can help you make a thoughtful decision about whether to proceed with genetic testing.

Breast Cancer Risk Reduction

Lifestyle-related risk factors

Research has identified some risk factors that predispose a woman to developing breast cancer. While you cannot control some of the risk factors, there are others you can control or influence. For example, age, ethnic and racial background, and family history cannot be changed, but risk factors, such as the use of hormone therapy, the age at which you have your first baby and the decision whether to breast-feed are controllable to some degree. While controllable, these risk factors involve personal decisions and circumstances that make general recommendations impractical.

Other lifestyle-related risk factors such as obesity and inactivity are ones you can control. As mentioned before, an active lifestyle coupled with a healthful diet can work together to help you

maintain a healthful weight. Data indicate that maintaining a healthful weight and/or losing weight (if you are overweight) are associated with a reduction in breast cancer risk.

It is important to remember that the presence of one or more risk factors does not mean a person will definitely develop breast cancer. Rather, it means a person has a higher risk of developing cancer than someone in the general population. Many people who have breast cancer risk factors remain cancer-free. This is also true for women who carry the altered breast cancer genes, although more than half of women with mutations in BRCA1 and BRCA2 will develop breast cancer sometime during their lives.

Medication to reduce risk

The medication tamoxifen has been shown to lower the risk of breast cancer in women who have never had breast cancer. Tamoxifen has possible side effects you should discuss with your physician before deciding to take it. There is still uncertainty regarding which groups of women should take tamoxifen to reduce their risk and at what age they should take it. Research is being done to determine whether other medicines can safely lower the incidence of breast cancer in women at increased risk. However, it may take years before the results of these studies are available. Ask your health-care provider about current information on medications that decrease risk for breast cancer.

Surgery to reduce risk

Removal of the breasts to prevent breast cancer (so-called *preventive* or *prophylactic* mastectomy) is an option for some women who are at high risk for breast cancer. For example, women who have an altered BRCA1 or BRCA2 gene may have as much as an 85 percent chance of developing breast cancer. In this case, the benefits of breast removal may outweigh the disadvantages. Information from a Mayo Clinic study suggests that preventive removal of the breasts may lower the risk of breast cancer by about 90 percent. The procedure eliminates much, but not all, of the risk of developing breast cancer. While this procedure may be warranted (in a select group of fully informed women), it is not an approach recommended routinely.

Another surgery that can reduce cancer risk in high-risk women is removal of the ovaries (oophorectomy). Oophorectomy decreases breast cancer risk by about 50 percent in high-risk women if done prior to menopause.

A woman must decide for herself whether changing her behavior, taking a medication or having surgery is worthwhile. This decision may be influenced by a woman's perception of the level of her cancer risk, her experiences with cancer in herself or loved ones, her personal philosophy of life and her lifestyle.

Early Diagnosis With Careful Monitoring

It is currently not possible to prevent all breast cancers, but early diagnosis can significantly increase a woman's chance of successful treatment of cancer. Physical examination and regular mammograms increase the chance of finding breast cancer before it spreads. A breast cancer

found by mammogram, before it can be felt on physical examination, is more likely to be cured by current therapies than one that is large enough to be felt.

The recommended program for careful monitoring of women at significantly increased risk includes monthly breast self-examination, twice-a-year breast examinations by your health-care provider and once-a-year mammograms. Your health-care provider can advise you about the age at which you should begin having mammograms.

Candidates for careful monitoring may include:

- Women with prior cancers of the breast, colon, rectum, ovary or endometrium
- Women with breast biopsies showing atypical hyperplasia
- Women with prior carcinoma in-situ of the breast
- Women with a strong family history of breast cancer

Conclusion

Learning what factors increase your risk of breast cancer, and knowing which ones you can control, may help you reduce your risk of breast cancer. By knowing your risk, you can adjust your level of monitoring for breast cancer to improve your chances of detecting a breast cancer when it is most likely to be successfully treated.

Word List

Absolute risk: The actual number of breast cancer occurrences among 100 women of a certain age over the next five years.

Atypia: A set of features in the appearance of cells, as observed through a microscope, in which cells are abnormal in size, shape and number.

Biopsy: A procedure in which a tissue sample is removed from the body for examination under a microscope to find out if cancer or other abnormal cells are present.

Cancer: A general term for more than 100 different diseases in which cancerous or malignant cells develop. Some malignant cells exist quietly within the body for years without causing problems. Others grow rapidly and may invade and destroy surrounding normal tissue. When a cancer spreads, it usually travels through the lymph system or bloodstream to distant areas of the body. Cancers are named according to the organ or tissue in which they begin.

Carcinoma in situ: A disorder in which malignant-appearing cells are present in an organ but have not invaded underlying tissues. This is the earliest stage at which cancer can be found. While ductal carcinoma in situ of the breast is considered to be a cancer that hasn't become invasive yet, lobular carcinoma in situ of the breast is considered to be a risk factor for cancer development, but is not a cancer itself.

Chromosome: Chromosomes are long strands of DNA. Every cell contains 23 pairs of chromosomes. One of the pair is inherited from the father and one from the mother.

Colorectal: Pertaining to the colon and rectum.

DNA: The abbreviation for deoxyribonucleic acid, one of two substances (the other is RNA) found inside almost all cells, that contains genetic information which controls cell growth, division and function.

Endometrium: Lining of the uterus (womb).

Gene: A gene is a segment of DNA that contains the information needed to carry out the specific functions of a cell. This information passes from parents to children.

Genetic predisposition: Increased likelihood of developing a disease because of a gene mutation. A genetic predisposition does not mean that the person will definitely develop the disease, but rather that an increased likelihood of the disease exists.

Genetic counseling: Genetic counseling is a communication process that deals with the human problems associated with the occurrence or risk of occurrence of a genetic disorder in a family.

Genetic testing: The process by which a blood or tissue sample is examined for gene alterations, that can increase the likelihood of disease or illness.

Incidence: The number of new cases of a disease diagnosed every year per 100,000 people. For example, the average incidence of breast cancer among adult women in the United States is 109 cases out of 100,000 women every year.

Mammogram: An X-ray technique to examine the breasts. It is the best way to find the earliest changes associated with breast cancer, when the cancer is too small to be felt on physical examination.

Mutation: A permanent change or alteration in the genetic material, usually in a single gene. This type of change may cause the gene to function improperly permitting illness or disease to develop.

Relative risk: The ratio of risk associated with a specific risk factor in one group of individuals compared to the risk in another group that does not have that risk factor. To say that women are 100 times more likely to develop breast cancer than men means that a woman's relative risk of breast cancer is 100 times that of a man's. This measure of risk tells you nothing about the actual number of women who develop breast cancer during a particular period of time.

Risk factor: A risk factor is an identifiable characteristic that influences the chances that a person will develop a specific illness. Thus, being female is a risk factor for breast cancer, as women are 100 times more likely to develop breast cancer than are men. Some risk factors, like gender, cannot be changed. Other risk factors relate to lifestyle choices, such as alcohol consumption, and can be modified.

This material is for your education and information only. This content does not replace medical advice, diagnosis or treatment. New medical research may change this information. If you have questions about a medical condition, always talk with your health care provider.

© 2002 Mayo Foundation for Medical Education and Research (MFMER). All rights reserved. MC1972-11rev0917