Patient information: Factors that modify breast cancer risk in women (Beyond the Basics)

Author
Wendy Y Chen, MD, MPH
Assistant Professor of Medicine
Harvard Medical School

INTRODUCTION

About 240,000 women in the United States are diagnosed with breast cancer each year. However, not all women have the same risk of developing breast cancer during their lifetime. Studies have shown that certain factors, called risk factors, increase the likelihood that a woman will develop breast cancer. This topic review discusses the individual factors that increase a woman's risk of developing breast cancer and also reviews those factors that are thought to protect against the development of breast cancer.

RISK FACTORS

Many risk factors associated with breast cancer are not reversible, but some can be modified. The presence of breast cancer risk factors does **not** mean that cancer is inevitable; many women with risk factors never develop breast cancer. Instead, risk factors help to identify women who may benefit most from screening or other preventive measures. Individual women should work with their clinicians to determine their own personal risk of breast cancer, based upon their own circumstances.

It is important to remember that breast cancer can also occur in women who have no identifiable risk factors. The average woman has about a 10 to 15 percent chance of developing breast cancer if she lives into her 90s. On the other hand, the risk of developing breast cancer in a woman with a strong family history of the disease who has inherited one of the genes that predispose her to breast cancer is over 50 percent. All women should discuss guidelines for breast cancer screening with their clinicians, even if they have a low risk for breast cancer based upon their risk factor profile.

STANDARD RISK FACTORS

Increasing age — The primary risk factor for breast cancer in most women is older age. The incidence of breast cancer rises sharply with age until the age of 45 to 50, at which point the rise is less steep. At age 75 to 80, the incidence rates flatten out and then start to decline after this.

Gender — Breast cancer is the most common cancer in women and occurs 100 times more commonly in women than in men.

Race/ethnicity — In the United States, white women have the highest rate of breast cancer; for every 100,000 women, there are 124 cases diagnosed. The rate of breast cancer is lower in black women (113 per 100,000), American Indians/Alaska natives (92 per 100,000), and Hispanic women (90 per 100,000). It is lowest in Asian Americans/Pacific Islanders (82 per 100,000).

Weight — The impact of both weight gain and obesity is mostly associated with an increased risk of postmenopausal breast cancer. A higher body mass index (BMI) is associated with a lower risk of premenopausal breast cancer, although the mechanism behind this association is not clear.

Tall stature — Tall stature is associated with an increased risk of breast cancer. In studies, women who were at least 69 inches were more likely to develop breast cancer compared to women less than 63 inches tall.

Increased estrogen exposure

Benign breast disease — In addition to breast cancer, women can develop abnormal breast findings. These breast abnormalities can develop because of excessive growth of the glandular breast tissue (also known as proliferative lesions) or comprised of increases in fibrous tissue, ductal enlargement, or cyst formations (known as nonproliferative lesions). Women with a history of proliferative breast lesions have an increased risk for breast cancer, particularly if the cells appear abnormal (atypical hyperplasia).

Breast density on mammography — Women whose mammograms show many dense areas of tissue have an increased risk of breast cancer compared to women whose mammograms reveal mainly fat tissue.

High bone density — Bone contains estrogen receptors and is sensitive to circulating estrogen. Therefore, bone mineral density (BMD) is considered a surrogate marker to circulating estrogen levels. In studies, women with a high BMD have a higher risk of breast cancer.

Other hormonal factors

Androgens — Elevated testosterone levels in women are associated with an increased risk of breast cancer with some studies suggesting an elevated risk specifically for hormone receptor-positive disease.

Insulin — Other hormones that may influence breast cancer risk include high levels of insulin and growth factors related to the insulin pathway.

In utero exposure to diethystilbestrol — Before 1971, several million women were exposed in utero to diethylstilbestrol (DES) that was given to their mothers to prevent pregnancy complications. Whether these women are also at an increased risk for breast cancer is unclear

with one study suggesting in utero exposure increased the risk of breast cancer, while another study found there was no excess risk among these patients.

Menopausal hormonal therapy — As a woman ages, the breast's glandular tissue, the tissue in which breast cancer arises, is gradually replaced by fat. Menopausal hormonal therapy includes estrogen, which slows or reverses this process. A large clinical trial has found that long-term use of combined estrogen-progestin (approximately five years) in women ages 50 to 79 increases a woman's risk of breast cancer, as well as heart disease, stroke, and clots in the legs. The risk of breast cancer when estrogen is used alone does not appear to be increased, especially when used for a short time. (See "Patient information: Postmenopausal hormone therapy (Beyond the Basics)".)

Beyond menopausal hormonal therapy, the administration of exogenous hormones as oral contraceptives or for the purpose of ovulation induction is not clearly associated with an increased risk of breast cancer.

Reproductive factors

Age at time of menses starts and at menopause — Both a younger age when menses begins and a later age at onset of menopause increase the breast cancer risk. This is likely due to the overall exposure to estrogen in a woman’s lifetime.

Pregnancy and breastfeeding — Women who have never given birth are more likely to develop breast cancer after menopause than women who have given birth multiple times. In addition, the younger a woman is at her first full-term pregnancy the lower her risk of breast cancer. Breastfeeding has been found to be protective against developing breast cancer.

Abortion is not associated with a risk of breast cancer.

Personal history of breast cancer — Women with a prior history of cancer in one breast have an increased risk of developing cancer in the other breast. If a woman has a prior history of ductal carcinoma in situ (DCIS), this risk is as high as five percent in the next 10 years. However, if there is a personal history of an invasive breast cancer, the risk is one percent per year for premenopausal women and 0.5 percent per year for postmenopausal women.

Family history — Family history is an important risk factor for breast cancer, although a history of breast cancer involving a first-degree relative is only reported by 20 percent of women with breast cancer. Overall, less than 10 percent of all breast cancers are associated with inherited genetic mutations. One of the main factors responsible for this elevated risk is an inherited genetic mutation in one of two genes, called BRCA1 and BRCA2. For women who have a BRCA1 or BRCA2 mutation, the lifetime risk of breast cancer ranges from 50 to 85 percent. Genetic testing for the BRCA mutation is discussed in detail elsewhere. (See "Patient information: Genetic testing for breast and ovarian cancer (Beyond the Basics)".)

LIFESTYLE FACTORS

A number of modifiable risk factors have been identified that are associated with an increased risk of breast cancer. These include the following:

Physical inactivity — While there is no direct evidence that inactivity is associated with an increased risk of breast cancer, physical exercise appears to protect against breast cancer in both premenopausal and postmenopausal women.

Alcohol — There appears to be a significant relationship between alcohol consumption and an increased risk of breast cancer, which begins with alcohol intake as low as three drinks per week. The risk appears to increase with greater alcohol consumption and additive with the use of menopausal hormone therapy. There does not appear to be a difference by type of alcohol (wine versus beer versus liquor).

Smoking — Both passive and active tobacco smoking has been associated with an increased risk of breast cancer, especially among premenopausal women. This risk is associated with early initiation, longer duration, and/or higher pack-years of smoking. It also appears to be higher in genetically susceptible subgroups.

DIETARY FACTORS

A number of dietary factors have been reported to increase the risk of breast cancer. Among them, alcohol intake has the strongest association to breast cancer incidence.

Dietary pattern — While some studies have shown that high consumption of a diet composed predominantly of fruits and vegetables resulted in a lower risk of breast cancer, there was no influence on the risk of breast cancer among women who reported a high intake of red/processed meats, refined grains, sweets, and high-fat dairy.

Dietary fat intake — An association between high intake of dietary fat and breast cancer has been seen in some studies, although the overall effect appears modest at best.

Consumption of red meat — Eating more than five servings of red meat per week may be associated with an increased risk of hormone-positive premenopausal breast cancer.

Calcium/Vitamin D — Diets low in calcium and vitamin D have been associated with an increased breast cancer risk in premenopausal but not in postmenopausal women. However, one study of women who supplemented their diet with vitamin D and calcium did not show a difference in the number of women diagnosed with breast cancer.

Antioxidants — There is no evidence for an effect of intake of vitamin A, E, or C or beta-carotene on breast cancer risk.

Soy/Phytoestrogens — Phytoestrogens are naturally occurring plant substances with a chemical structure similar to estrogen. They consist mainly of isoflavones (found in high concentrations in soy beans and other legumes) and lignans (found in a variety of fruits, vegetables, and cereal products). There is low quality evidence that soy-rich diets in Western women prevent breast cancer.

Caffeine — A number of studies have failed to show any association between caffeine intake and breast cancer risk.

ENVIRONMENTAL FACTORS

Geopgraphic residence — Within the United States, geographic clusters with a high incidence of breast cancer have been described. Although these clusters are most likely due to regional differences in established breast cancer risk factors, studies are ongoing to better understand them.

Exposure to ionizing radiation — Exposure to ionizing radiation of the chest at a young age, as occurs with treatment of Hodgkin lymphoma or in survivors of atomic bomb or nuclear plant accidents, is associated with an increased risk of breast cancer.

Night shift work — Night shift work is recognized by International Agency for Research on Cancer and the World Health Organization (IARC/WHO) as a probable carcinogen. Women who work at night have a higher risk of breast cancer compared to women who do not do night-shifts. The primary reason for this remains under study but may be tied to the hormone melatonin, which is normally produced at night.

Miscellaneous factors — Organochlorines include polychlorinated biphenyls (PCBs), dioxins, and organochlorine pesticides such as dichlorodiphenyltrichloroethane (DDT). These compounds are weak estrogens, highly lipophilic, and capable of persisting in body tissues for years. However, an association with breast cancer has not been demonstrated. In addition, cosmetic breast implants, electromagnetic fields, electric blankets, and hair dyes have not been associated with breast cancer risk.

MEDICATIONS

Several medication classes may have a modifying effect on breast cancer risk although their association to breast cancer is weak at best.

Nonsteroidal anti-inflammatory drugs — The data are mixed in showing an association between nonsteroidal anti-inflammatory drugs and breast cancer risk. While some studies show that patients who used aspirin or ibuprofen had a lower risk of breast cancer, others have not.

Bisphosphonates — Oral bisphosphonates are commonly used for the treatment of osteoporosis and for women with breast cancer with evidence of bone loss attributed to aromatase inhibitors. Whether their use is a true protective factor against breast cancer is unclear.

REDUCING BREAST CANCER RISK

Although screening mammography does not reduce the risk of developing breast cancer, screening significantly decreases the risk of dying from breast cancer. (See "Patient information: Breast cancer screening (Beyond the Basics)".)

Lifestyle changes — A number of lifestyle changes may reduce breast cancer risk:

- Planning for first birth before the age of 30
- Breastfeeding for at least six months
- Avoidance or limited duration of use of postmenopausal hormone therapy
- Avoidance of unnecessary exposure to radiation (eg, inappropriate use of computed tomography)
- Avoidance or cessation of smoking
- Limiting alcohol intake

- Maintenance of a healthy weight
- Limiting nocturnal shift work
- Adopting a physically active lifestyle. This should include at least 150 minutes of weekly moderate intensity activity, 75 minutes of weekly vigorous intensity activity, or at least some physical activity above one's usual routine, in addition to limiting sedentary behavior.

Medication — Women at an increased risk of developing breast cancer should discuss whether chemoprevention is right for them. This topic is discussed separately. (See "Patient information: Medications for the prevention of breast cancer (Beyond the Basics)".)

ESTIMATING RISK

Although breast cancer risk assessment tools are available, their accuracy for individual women is only modest, partly because not all important risks have been identified and partly because accurate risk stratification requires strong risk factors and most risk factors for breast cancer are relatively weak and common in the population. (See "Patient information: Breast cancer screening (Beyond the Basics)".)

WHERE TO GET MORE INFORMATION

Your healthcare provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our web site (www.uptodate.com/patients). Related topics for patients, as well as selected articles written for healthcare professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient information: Breast cancer (The Basics)
Patient information: Breast cancer screening (The Basics)
Patient information: Common breast problems (The Basics)
Patient information: Genetic testing for breast and ovarian cancer (The Basics)
Patient information: Ductal carcinoma in situ (DCIS) (The Basics)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Patient information: Breast cancer screening (Beyond the Basics)
Patient information: Genetic testing for breast and ovarian cancer (Beyond the Basics)
Patient information: Medications for the prevention of breast cancer (Beyond the Basics)
Patient information: Postmenopausal hormone therapy (Beyond the Basics)
Patient information: Risks and benefits of alcohol (Beyond the Basics)
Patient information: Nonhormonal treatments for menopausal symptoms (Beyond the Basics)

Professional level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

Factors that modify breast cancer risk in women
Breast imaging: Mammography and ultrasonography
Breast masses and other common breast problems
Genetic risk assessment for individuals at risk for hereditary breast and ovarian cancer syndromes
Genetic testing for hereditary breast and ovarian cancer syndrome
Management of hereditary breast and ovarian cancer syndrome and patients with BRCA mutations
BRCA1 and BRCA2: Prevalence and cancer risks for breast and ovarian cancer
Screening for breast cancer: Strategies and recommendations

The following organizations also provide reliable health information.

- National Cancer Institute

1-800-4-CANCER
(www.nci.nih.gov)

- People Living With Cancer: The official patient information website of the American Society of Clinical Oncology

(www.cancer.net/portal/site/patient)

- National Comprehensive Cancer Network

(www.nccn.com)

- American Cancer Society

1-800-ACS-2345
(www.cancer.org)

- National Library of Medicine

(www.nlm.nih.gov/medlineplus/healthtopics.html)

- Susan G. Komen Breast Cancer Foundation

(www.komen.org)

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