



# Breast Cancer Risk Factors and Preventions

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### Abstract

The second most common malignancy among women is breast cancer. The formation of breast cancer is a multi-step process involving various cell types, and its prevention remains tough in the world. One of the best ways to avoid breast cancer is by early diagnosis. Due to early detection, the 5-year relative survival rate for patients with breast cancer is above 80% in several developed nations. Both the understanding of breast cancer and the creation of prevention measures have advanced significantly in the last ten years. By identifying breast cancer stem cells, the aetiology and processes underlying tumour drug resistance are disclosed, and numerous breast cancer-related genes are discovered. For the chemoprevention of breast cancer, people now have additional pharmacological alternatives, and biological prevention has recently been created to enhance patients' quality of life. We will cover the most important studies on breast cancer's pathophysiology, associated genes, risk factors, and preventative measures that have been conducted in recent years. These results are a modest advancement in the protracted battle against breast cancer.

**Keywords:** Pathogenesis, Breast cancer, Malignancy, Diagnosis, Risk factor, Treatment

### Introduction

One of the most prevalent malignancies in women globally, breast cancer caused 570,000 fatalities in 2015. Every year, almost 1.5 million women worldwide-25% of all cancer patients are given a breast cancer diagnosis. According to estimates, there were 252,710 new cases of breast cancer among women in America in 2017. Breast cancer is an incurable form of metastatic cancer that frequently spreads to distant organs such as the bone, liver, lung, and brain. A positive prognosis and a high survival rate can result from an early diagnosis of the illness. Mammography is a popular screening method for finding breast cancer and has been shown to significantly lower mortality. Over the past ten years, other screening techniques, such as MRI, which is more sensitive than mammography, have also been used and researched. Numerous variables can raise the risk of getting breast cancer, including sex, ageing, estrogen, family history, gene mutations, and bad lifestyle choices. Women are 100 times more likely than males to develop breast cancer, and women also experience the disease at a higher rate. Although breast cancer incidence rates rise annually in America, the fatality rates fall as a result of widespread

early detection and cutting-edge medical treatments. In recent years, biological treatments have been created and have successfully treated breast cancer. Here, we'll concentrate on recent research on the pathophysiology, associated genes, risk factors, and prevention of breast cancer.

### Pathogenesis

Breast tumours typically begin as ductal hyperproliferation, and after being repeatedly stimulated by numerous carcinogenic stimuli, they progress to benign tumours or even metastatic carcinomas. In the development and spread of breast cancer, tumour microenvironments such as stromal effects and macrophages are crucial. When only the stroma of the rat mammary gland was exposed to carcinogens, rather than the extracellular matrix or the epithelium, neoplasms might be generated. A mutagenic inflammatory microenvironment that macrophages can create can encourage angiogenesis and help cancer cells avoid immunological rejection. The difference in DNA methylation patterns between the normal and tumour-associated microenvironments suggests that the tumour microenvironment may contain epigenetic changes that can encourage the development of cancer. Cancer Stem Cells (CSCs), a new subclass of malignant cells within tumours, have recently been identified and linked to tumour genesis, escape, and recurrence. This small group of cells has the capacity to self-renew and is resistant to traditional treatments like chemotherapy and radiotherapy. They may arise from stem cells or progenitor cells in healthy tissues. Ai Hajj was the first to identify breast Cancer Stem Cells (bCSCs), and immunocompromised animals injected with as few as 100 bCSCs were able to develop new tumours.

The cancer stem cell theory and the stochastic theory are two speculative ideas for the origin and spread of breast cancer. According to the theory about cancer stem cells, all types of tumours are descended from the same stem cells or transit-amplifying cells (progenitor cells). Different tumour phenotypes can result from acquired genetic and epigenetic alterations in stem cells or progenitor cells. According to the stochastic theory, each tumour subtype originates from a particular type of cell (stem cell, progenitor cell, or differentiated cell). Any breast cell can gradually get random mutations that, when enough mutations have accumulated, will cause the cell to become a tumour cell. Both ideas have substantial facts backing them up, but neither can entirely account for the cause of human breast cancer.

### Risk factors

**Ageing:** Aside from sexual orientation, ageing is one of the most significant breast cancer risk factors because it increases the likelihood of developing the disease. In 2016, women over the ages of 40 and 60 were reported to account for 99.3% and 71.2% of all breast cancer-related fatalities in America, respectively. Therefore, women aged 40 or older must get a mammogram screening in advance.

**Family background:** Almost one-fourth of all breast cancer cases include a family history component. Women are more likely to contract this illness if their mother or sibling has the sickness. According to a UK cohort research involving over 113,000 women, women who have one first-degree cousin who has breast cancer are 1.75 times more likely to get the disease than those who don't have any

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affected relatives. Additionally, the risk increases by 2.5 times or more for women who have two or more first-degree relatives who have the disease. The mutations in breast cancer-related genes like BRCA1 and BRCA2 are partly responsible for the inherited propensity for breast cancer.

**Reproductive mechanisms:** Early menarche, late menopause, late age at first pregnancy, and low parity are reproductive characteristics that can raise the risk of breast cancer. Breast cancer risk is increased by 3% for every additional year after menopause. Each additional birth or each 1-year delay in menarche reduces the risk of breast cancer by 5% or 10%, respectively. According to a recent Norwegian cohort study, the risk ratio between late (35 years) and early (20 years) ages at first birth is 1.54.

**Estrogen:** Estrogens, both endogenous and exogenous, are linked to an increased risk of breast cancer. In premenopausal women, the ovary typically produces endogenous estrogen, and ovarian removal can lower the risk of breast cancer. Hormone Replacement Treatment (HRT) and oral contraceptives are the main sources of exogenous estrogen. Since the 1960s, oral contraceptives have been extensively used, and their formulations have been improved to minimize side effects. For populations of Iranians and African American women, the OR is still greater than 1.5. But among women who cease using oral contraceptives for more than ten years, there is no increased risk of breast cancer. Exogenous estrogen or other hormones are administered to menopausal or postmenopausal women as part of HRT. A cohort study of 22,929 Asian women found that after using HRT for 4 and 8 years, respectively, HRs were 1.48 and 1.95. After two years of quitting HRT, it has been demonstrated that the risk of breast cancer considerably decreases. The HR for a new breast tumour is 3.6, and it is high among breast cancer survivors who take HRT. Due to the decline in HRT use since the Women's Health Initiative randomized controlled trial findings about the harmful effects of HRT were revealed in 2003, the incidence rate of breast cancer in America has fallen by about 7%.

**Lifestyle:** Breast cancer risk can be raised by contemporary lifestyle factors such as excessive alcohol use and dietary fat consumption. Alcohol drinking can stimulate the estrogen receptor pathways and raise blood levels of hormones associated with estrogen. An intake of 35 grams to 44 grams of alcohol per day can increase the risk of breast cancer by 32%, according to a meta-analysis based on 53 epidemiological studies, with a 7.1% rise in the RR for every additional 10 grams of alcohol per day. Overconsumption of fat, particularly saturated fat, is linked to mortality (RR=1.3) and a poor prognosis in individuals with breast cancer. The modern western diet contains too much fat. Mutagens from cigarette smoke have been found in the breast fluid of non-lactating women, despite the fact that the link between smoking and the risk of breast cancer is still debatable. Women who smoke and drink also have a higher risk of developing breast cancer (RR=1.54). As of now, mounting data shows that smoking, especially when starting young, increases the risk of developing breast cancer.

**Prevention:** There have been significant advancements in both clinical and theoretical research on breast cancer to date. In comparison to earlier preventative strategies, the current ones including screening, chemoprevention, and biological prevention are more direct and successful. Breast cancer mortality has declined. However, among females aged 20 to 59, breast cancer continues to be the primary cause of cancer death.

## Conclusion and further directions

In 140 countries, breast cancer is the most common cancer in which women are diagnosed. In the entire world, 1 in 8 women is at risk of having breast cancer in their lifetime. Breast cancer is caused by a multi-step process that has not yet had its aetiology fully understood. Breast CSCs and the tumour microenvironment have both been linked to the development of breast tumours in the last 10 years. Both genetic and environmental variables have an impact on breast cancer. Prior planning should be done to implement targeted prevention tactics against these risk factors. Almost half of breast cancer diagnoses and more than half of breast cancer fatalities occur in developing nations, despite the fact that the incidence rate of breast cancer is high in industrialized countries. Breast cancer 5-year relative survival rates vary greatly across industrialized and poor nations. In North America and Japan, the percentage is above 80%, whereas in nations in Africa like Algeria, it is only 40%. Breast cancer is a disease that may be prevented, and industrialized nations have access to enough medical resources to do so, such as annual mammograms or daily usage of chemo preventative medications. These could explain why breast cancer patients in developed nations have a higher survival rate than those in middle or low-income nations. The clinical breast examination is a reliable method of detecting breast cancer in its earliest stages, especially when taking into account the financial constraints of underdeveloped nations. Breast self-examination may also be an easy, affordable, and motivated way for women to prevent breast cancer if they are educated about the condition. People are more familiar with their bodies than any doctors are. However, the majority of women in underdeveloped nations are unaware of the significance of breast cancer prevention. Therefore, breast health promotion should receive more attention in these nations than clinical therapy.

Individual genome sequencing may now be feasible for middle-class people thanks to the decline in the price of DNA sequencing, and this could be a new strategy for avoiding breast cancer. It is advisable to perform screening, especially for inherited cancer susceptibility genes like BRCA1 or BRCA2, if a woman has a family history of breast cancer. Based on the screening results, the risk of breast cancer may then be assessed, and personal prevention recommendations might be given. Future breast cancer and other hereditary disease preventive strategies may use individual genome sequencing. Risk factors should also be treated more seriously in both low-risk and high-risk women. To reduce the incidence of breast cancer, environmental factors including ingesting exogenous estrogen, abusing alcohol, and eating an excessive amount of fat should be avoided. Despite the fact that some risk factors, such as ageing and reproductive variables, are unavoidable, precautions should be taken in advance to lower the risk. Many people in the modern world spend countless hours at tables. Physical labour is less popular than cerebral work as a form of engagement. However, compared to women who are less active, women who are physically active typically have a 25% decreased risk of breast cancer. Women from both industrialized and poor nations may find that regular exercise is an easy and affordable strategy to avoid breast cancer.

Breast cancer can be avoided. Taking chemoprevention and lowering risk factors are the two main ways to avoid breast cancer. The public still has to be made more aware of breast cancer, though. Only 4.1% of high-risk females consent to use chemopreventive medications. This hesitancy may be attributed to a lack of knowledge about breast cancer and a fear of its negative implications. Despite the fact that the Gail or IBIS models are frequently used to estimate a

woman's risk of breast cancer based on her age, family history, race, and reproductive variables, we still don't have an accurate method for calculating the risk ratio of breast cancer. Individual genome

sequencing could become a potent tool for assessing breast cancer risk as sequencing technology advances. In the future, better medications must be created with fewer side effects and a good risk-benefit ratio.

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