

# Understanding Breast Cancer: A Comprehensive Review of Epidemiology, Risk Factors, and Treatment Strategies

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## Abstract

Breast cancer is the most common cancer among women worldwide. The term epidemiology generally deals with the branch of medicine and treatment that deals with a specific incident. Thus, considering the topic of breast cancer, this particular study deals with the distribution, determinants, and frequency of the disease. Breast cancer incidence and death data are critical to determining healthcare priorities. Women's cancer is the most common, accounting for 25.1 percent of all malignancies. According to this specific report, more than 42,000 women die from breast cancer each year. Hence, it is apparent that it is the second leading cause of death among women, especially in the US. Family history/genetics, reproductive, hormone, benign proliferative breast disease, and mammographic density are the four main risk factors for breast cancer that can be meaningfully categorized. These elements are briefly discussed, and the risk estimators are provided. Numerous screening technologies have found breast cancer; some are linked to an increased risk of breast cancer, such as ultrasound techniques and MRI scanning. Breast cancer is more common in developed countries, while relative mortality is highest in developing countries. Women's education is recommended for early detection and treatment in all nations. Health policymakers must prioritize plans to control and prevent this malignancy and increase awareness of risk factors and early detection in less developed countries.

## Keywords

Breast Cancer, Epidemiology, Risk Factors, Screening, Treatment

## 1. Introduction

Noncommunicable diseases like various types of cancer are prevailing worldwide,

thereby increasing the fatality and mortality rates worldwide. As cancer is the most common noncommunicable disease, the occurrence of breast cancer is significantly higher. Changes in lifestyle and pollution are the main contributors to the increased risk of cancer, which is now considered endemic. In 2022, 20 million new cancer cases worldwide [1], 2.3 million of those were breast cancer cases [2], and the majority of them were women, leading to 685,000 deaths [3]. However, there are differences in mortality rates in developed and developing countries [4]. According to a 2023 report, breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females worldwide. The incidence and mortality rates of breast cancer vary significantly across different regions of the world. While the incidence of breast cancer is increasing at different rates in various regions, the mortality rates in many high HDI (Human Development Index) countries have been declining. However, low HDI countries are experiencing an increase in mortality rates [5]. The epidemiology of breast cancer will help to analyze the incidence rate and mortality rates among women in developed and developing countries, creating further development in treatment.

## **2. Signs, Symptoms, and Causes of Breast Cancer**

Breast cancer is identified when a painless lump or thickening of the breast is noticeable in the human body [6]. The best way to detect breast cancer is early screening or breast mammography [7]-[9]. Mammography screening in combination with ultrasonography can improve detection, in a 2023 study they found that by combining the two methods more cancers were found than mammography alone [9]. Early medical treatment or interventions are proven to be highly efficient in reducing disease death, giving the patients a new life [10]-[13].

### **2.1. Breast Cancer Symptoms**

#### **2.1.1. Common Symptoms**

- Thickening or lumps in the breast: This is often the first noticeable sign of breast cancer. It's crucial to be familiar with the normal texture of your breasts so you can detect any changes [14].
- Abnormal discharge and appearance, and change of colors or alterations around the areola: Changes in the nipple and areola, such as discharge (especially bloody), scaling, or discoloration, can be indicative of breast cancer [14].

#### **2.1.2. Rare Symptoms**

- Nipple retraction or changes: While any change in nipple shape or direction is worth checking out, this symptom can also be caused by benign conditions [15].
- Skin dimpling or thickening: This is a more specific sign, often associated with inflammatory breast cancer [16].
- Breast or nipple pain: Pain is more frequently linked to benign breast conditions, but persistent or localized pain should be investigated [17].
- Swelling of the breast or arm: This can be a sign of advanced breast cancer or

inflammatory breast cancer [18].

- Paget's disease of the nipple: This is a rare form of breast cancer specifically affecting the nipple and areola [19].
- Mastitis-like symptoms: Inflammatory breast cancer can mimic mastitis, making it important to rule out infection [20].

Other rare symptoms include weight loss and appetite. However, immediately identify signs and early screening and treatment.

## 2.2. Causes of Breast Cancer

Breast cancer arises from the uncontrolled growth of cells in breast tissue, often forming a lump or tumor. These cancerous cells typically originate in the lobules (milk-producing glands) or the ducts that connect the lobules to the nipple. While the exact causes of breast cancer remain unclear, several factors can increase the risk of its development [21]-[23].

### 2.2.1. Hormones and Genetics

Hormones, such as estrogen and progesterone, appear to play a significant role in many breast cancers, although the precise mechanisms are not fully understood.

The risk of breast cancer increases when a first-degree relative is a carrier. Therefore, global data on this issue estimate that 13% to 19% of people are diagnosed with breast cancer due to inheritance from first-degree relatives worldwide.

Genetic factors also contribute to breast cancer risk. Inherited gene mutations, like those in the BRCA1 and BRCA2 genes, can disrupt normal cell growth and increase susceptibility to breast cancer. However, only about 10% of breast cancers are linked to such inherited gene mutations [21]-[23].

### 2.2.2. Acquired Gene Mutations

The majority of breast cancers (around 90%) are associated with acquired gene mutations that occur during a person's lifetime, rather than being inherited. These mutations can be triggered by exposure to radiation or other carcinogens, but often arise from random occurrences within cells. Multiple acquired mutations are typically involved in the development of breast cancer [4] [21]. Genes like TP53, CDH1, PTEN, STK11, and XRCC2 have very high chances of developing breast cancer [24]-[30].

### 2.2.3. Other Risk Factors

**Body Mass Index (BMI):** Women with a higher BMI are obese and are significantly at risk for cancer. Women over 50 years, obese women, and postmenopausal women are at higher risk for cancer. An increase in body fats deregulates good hormones, thereby increasing the carcinogenic cells in the human body [31].

**Insufficient Vitamin Supplementation:** Regular intake of vitamin E, C, B-group vitamins, folic acid, and multivitamins reduces the risk of cancer in pre-menopausal and post-menopausal women. If vitamin levels in the human body are not adequately maintained, it increases the risk factor for breast cancer [32].

Age is also a factor, with the risk of breast cancer increasing as women get older.

Early detection through regular screenings and a healthy lifestyle can play a crucial role in reducing the risk of breast cancer and improving treatment outcomes [21] [24] [25].

**Alcohol Consumption.** There is a clear and well-established link between alcohol consumption and an increased risk of breast cancer. Even moderate drinking can increase the risk, and the risk increases with the amount of alcohol consumed. Binge drinking is also associated with an increased risk of breast cancer. The exact mechanisms by which alcohol increases breast cancer risk are not fully understood, but several potential explanations exist. Alcohol can increase levels of estrogen and other hormones that can promote the growth of breast cancer cells. It can also damage DNA in cells, which can lead to cancer. Additionally, alcohol may weaken the body's immune system, making it less able to fight off cancer cells. Despite the clear evidence of the link between alcohol and breast cancer, awareness of this risk remains low. Many people are unaware that even moderate drinking can increase their risk. Public health campaigns are needed to raise awareness of this important issue [33]-[36]. **Table 1** summarizes risks related to breast cancer.

**Table 1.** Risk factors associated with breast cancer.

Risk Factor	Associated Risk
<b>Family History/Genetics</b>	13% - 19% of breast cancer cases are due to inheritance from first-degree relatives.
<b>Hormones</b>	Estrogen and progesterone play significant roles in many breast cancers.
<b>Genetic Mutations</b>	Inherited mutations in BRCA1 and BRCA2 genes increase susceptibility; about 10% of breast cancers are linked to these mutations.
<b>Acquired Gene Mutations</b>	Around 90% of breast cancers are associated with acquired mutations during a person's lifetime.
<b>Body Mass Index (BMI)</b>	Higher BMI, especially in postmenopausal women, increases the risk of breast cancer.
<b>Vitamin Supplementation</b>	Insufficient intake of vitamins E, C, B-group vitamins, folic acid, and multivitamins increases risk.
<b>Age</b>	Risk increases with age.
<b>Alcohol Consumption</b>	Even moderate drinking increases the risk; the risk increases with the amount of alcohol consumed.
<b>Reproductive/Hormone Factors</b>	Includes factors like age at first menstruation, age at first childbirth, and use of hormone replacement therapy.
<b>Benign Proliferative Breast Disease</b>	Conditions like atypical hyperplasia increase the risk of developing breast cancer.
<b>Mammographic Density</b>	Higher breast density on mammograms is associated with an increased risk of breast cancer.

### 3. Pathophysiology

Breast cancer, like all malignancies, is the result of an accumulation of more dysfunctional genetic abnormalities, epigenetic changes, alterations in signal transduction, cellular metabolism, and stromal integrity. These consequences result in architectural and functional aberrations of the cellular system, such as loss of differentiation, genetic instability, and dramatically altered cellular metabolism.

### 3.1. Estrogen Receptor

In the pathophysiology of most breast tumors, the estrogen receptor plays a critical role [26]. When estrogen binds to the alpha subtype of the estrogen receptor, the intracellular domain dissociates from heat shock proteins, undergoes conformational changes, phosphorylation, dimerization, and translocates to the nucleus, where it binds to transcription repressor genes and inactivates them [27].

### 3.2. Progesterone Receptor

The progesterone receptor is becoming more well known for promoting breast cancer growth [28]. Breast cancer cells that express the progesterone receptor multiply more quickly. Progesterone receptor-positive breast cancer cells also had faster glucose absorption and higher rates of glycolysis and lipogenesis, implying that progesterone promotes the ability to use any available fuel source for survival and growth. Clinical studies in women using hormonal replacement therapy (HRT) and breast cancer risk have highlighted progesterone as a critical role in breast carcinogenesis [29].

## 4. Screening Methods for Breast Cancer

In recent years, breast cancer can be detected by several screening methods in which some screening tools can cause an increased risk of breast cancer. Meanwhile, some of the screening methods for breast cancer are mentioned below.

### 4.1. Ultrasound

Ultrasound is not commonly used as a routine breast cancer screening test. However, it can help detect breast alterations, such as lumps [33]. Ultrasound is beneficial for women with dense breast tissue, making abnormal spots on mammograms difficult to see [34]. It can also look at a questionable spot discovered on a mammogram. Ultrasound is widely available and relatively easy to obtain, and it does not expose the patient to radiation. It also tends to be less expensive than other types of testing.

### 4.2. Magnetic Resonance Imaging (MRI)

The most sensitive imaging technique for identifying breast cancer is magnetic resonance imaging (MRI). However, it has low specificity, requires intravenous gadolinium injection, and is associated with a higher false positive rate and higher expenses [34]. The American Cancer Society and other medical societies consider MRI to be an effective adjunct screening tool for carriers of the BRCA mutation and other women with a lifetime risk of breast cancer of more than 20%; however, these recommendations are based on increased incidence risk rather than increased mortality risk [33]. According to a comprehensive review, magnetic resonance imaging has a sensitivity of 75% to 100%, a specificity of 78% to 94%, and a PPV of 3% to 33% in women with thick breasts. When used in conjunction with mammography screening for women with dense breasts, MRI interpretation is

not hampered by breast density and provides more helpful information for breast masses, such as lesion vascularity, and is more successful than ultrasound in detecting breast malignancies [35].

### **4.3. Alternative Imaging Techniques**

By comparing pre- and post-contrast mammography images, dual-energy contrast enhanced spectral mammography uses readily available iodinated contrast to detect enhancing lesions within the breast [35]. Early research suggests that this method is faster and less expensive than MRI and can detect nearly all invasive tumors with fewer false positives. Similarly, nuclear medicine techniques can provide information on the more suggestive metabolic activity of breast tumors and are successful in cancer detection regardless of breast density. The use of intravenous Tc99m-sestamibi in molecular breast imaging (MBI) techniques is currently not prevalent. However, if MBI is used regularly as an auxiliary screening technique, the additional systemic radiation dose from MBI increases the lifetime risk of radiation-induced cancer. Furthermore, MBI requires the synthesis and storage of radioactive tracers close by, limiting patient access [33].

### **4.4. Microwave Tomography**

Microwave tomography (MWT), divided into single-frequency and multifrequency techniques, gives quantitative information on the DPS of the breast to identify cancer tissues. In the system, one transmitting RF sensor and one receiving RF sensor were used, and both the sensors and the photographed item were submerged in water [37]. The measurement system is challenging to use in practice and requires lengthy data gathering timeframes. The findings of a clinical investigation showed that tumors as small as 1 cm in diameter could be identified, indicating that MI has the potential to identify early-stage breast cancer. For accurate and specific diagnostic results of microwave tomography, Magnetic nanoparticles have been utilized as contrast agents in breast MWI lately, and compressive sensing (CS) methods have been used to depict the magnetic contrast created within the breast.

## **5. Epidemiology of Breast Cancer Around the World**

The World Health Organization (WHO) reports that 2.26 million people were diagnosed with breast cancer in 2020. It accounts for 29% of all cancers in the United States. Countries with very high HDI (Human Development Index) are more prone to breast cancer, with an incidence rate of 75.6 per 100,000. Low HDI countries have lower incidence rates of 27.8 per 100,000 and 36.1 per 100,000. Asia and Africa have higher breast cancer rates despite some Asian countries being highly developed. Mortality rates account for 63% of breast cancer cases. Women in high-income countries have better outcomes due to advances in medical technology and facilities. Developed countries have higher survival rates than less developed countries [26].

Countries such as Asia and Africa are more prone to breast cancer though some countries of Asia are highly developed. According to 2020 reports, mortality rates account for 63% of breast cancer. It is significantly found that women from high-income countries suffer less because of advances in medical technology and medical facilities than those from low-income countries. The survival rate is also higher in highly developed countries than in low- or medium-developed countries [3].

In some developed countries such as Singapore, and Türkiye, the survival rate is 89.6%, but around 75.4% locally. On the other hand, in less developed countries like India, Saudi Arabia, Thailand and Costa Rica, the survival rate is 76.3%, and the survival rate at the local level accounts for 47.4% of breast cancer. Therefore, there is a difference in survival rates in developed countries than in developed countries [38].

According to the epidemiological data for 2019 by the US government, 268,600 women are diagnosed with breast cancer. However, 48100 women were diagnosed with ductal carcinoma in situ, resulting in 15.2% to 30% of new cancer cases. The mortality rate for breast cancer is comparatively high because 42,000 women die every year. The risk of breast cancer is relatively low in men, accounting for less than 1% in the US. Hence, it is estimated that breast cancer is the leading cause of death in women in the US after lung cancer.

In 2008, lung cancer and breast cancer were the two most dominant types of cancer worldwide. Therefore, it led to 458503 deaths worldwide. In addition to breast cancer the women also had lung cancer, and the death rate was 12.8%. Furthermore, 18.2% accounted for overall cancer deaths globally. Environmental degradation, lifestyle alteration, environmental pollution, and food habits contributed to overall death rates. Therefore, the rate of occurrence or incidence rate is lowest in less developed countries, while significantly higher in developed countries worldwide [39].

### 5.1. United States

In the United States, the lifetime risk of breast cancer is 12% of women by the age of 95. It is also found that 3% among 12% have a high chance of dying. However, comparing the two ethnic groups, the highest annual incidence rate of breast cancer is 128.6 per 100,000 whites while 112.6 per 100,000 African Americans [40]. If it is analyzed from the 1970s, it is identified that 102 cases of cancer rose significantly in the 1970s per year, while 141 points in the late 1990s [41]-[44]. Hence, the data implies a decrease in breast cancer rates. On the other hand, the age-adjusted incidence rate was steady at around 125 deaths in 2003. Contrary to the age-adjusted incidence rate, age-adjusted mortality rates or death rates also require a thorough analysis to ensure the present condition of breast cancer in developed countries. The age-adjusted death rate from breast cancer out of 100000 women rose from 31.4% in 1975 to 33.2% in 1989. On the other hand, Stapleton's group [45] state a significant decline in the death rate, around 20.5% in 2014.

According to US medical reports, breast cancer is detected as the most dreadful disease due to the constant pain and suffering experienced by patients. Therefore, cancer deaths are most common in the US.

The present analysis also states that 1 in 8 women in the US, 13%, is highly likely to develop breast cancer. On the other hand, it is also estimated that in 2022 287,850 new breast cancer cases are likely to develop invasive breast cancer among US women significantly. It is also estimated that women around 51,400 are more likely to create noninvasive cancer by 2022. Another notable fact is also identified that 2710 new cases of breast cancer among men are highly likely to develop at the end of 2022. Furthermore, a man's lifetime risk of breast cancer is significantly low, 1 in 833 men. In terms of incidence mortality rate, it is analyzed that 43,250 US women are expected to die at the end of 2022 from fearful breast cancer [42]. Recently, there has been a slight decrease in the death rate, accounting for 1% per year from 2013 to 2018. Therefore, the decline in death rates per year is significantly due to the advancement of treatment and the early screening process. According to data published by the American Cancer Society, 85% of breast cancers occur in women in the US who do not have any family history but occur due to genetic mutations. Society also states that the natural process of aging, apart from inherited mutations, is the risk factor for breast cancer.

## 5.2. Great Britain

The above discussion states that the epidemiology of breast cancer is higher in the US, but it is the most common form of cancer in the UK. In 2011, 49,900 women and 350 men were diagnosed with the disease, while 11600 women and 75 men died in the UK in 2012. According to the NHS, it is also estimated that in 2012 the mortality rate for women accounted for 11,600 while for men, it was 75. From these data points, it is pretty evident that the occurrence rate of breast cancer has increased significantly by 113.4 per 100,000 population in Wales. The report also states that there has been an increase in the disease in the last three decades. However, there are advances in technology and the National Health Service Breast Screening Program [43].

Breast cancer is the most common type of cancer in women in developing countries such as Argentina, Uruguay, and Brazil. Cancer probability is higher in these countries due to inadequate funding and the lack of modernized medical tools and equipment for the effective treatment of breast cancer. Modernization and advancement in medicine are the only possible solutions to reduce mortality rates among women in developing countries, but funding issues do not implement them effectively. The intensity of breast cancer is higher in Caucasian and black African women. The disease in these ethnic groups is often aggressive at younger ages. Furthermore, the genetic link is found in these communities, leading to severe death [31].

## 5.3. Europe

The European Cancer Health Indicator Project (EuroCHIP8) has revealed 86

population-based cancer registries. Only 15% of the 32 countries reported the three-cancer burden, care, and survival variables (stage at diagnosis, delay in cancer treatment, and adherence to cancer recommendations). Only 39% of the registries had information on tumor size, nodal status, and metastases. Cancer registries from more than 13 million women yielded 24,576 invasive breast cancer cases [44]. In Hungary, the age-adjusted incidence was 151.1 (95% CI 147.2 - 155.0) per 100,000, whereas, in Scotland, it was 234.7 (95 percent CI 272.4 - 242.0) per 100,000. In Scotland, one-year survival rates varied from 94.1 percent (95% CI 93.5 - 94.7 percent) to 97.1 percent (95 percent CI 96.2% - 98.1%). In Italy, one-year survival rates ranged from 97.1 percent (95% CI 96.2% - 98.1%). Scotland had many negative markers regarding tumor size, nodal status, and metastases. Adjustment for case mix was impossible due to significant differences in data completeness for case mix of prognostic variables.

#### 5.4. Sub-Saharan Africa

However, limited data on mortality and incidence are available in the sub-Saharan Africa area because it is a developing country. The incidence rate of breast cancer is significantly higher than the mortality rates in the sub-Saharan African regions [45]. The incidence rate also varies from region to region. Therefore, the incidence rate in eastern Africa 30.4%, Central Africa is 26.8%, Western Africa is 38.6%, and Southern Africa is 38.9%. It is evident from the statistics that sub-Saharan regions have lower incidence rates. However, mortality rates are significantly higher due to less developed countries that have access to medical facilities [34]. Countries do not have proper screening tools, which significantly hinders reducing cancer. Furthermore, breast and cervical cancer are the two common forms of cancer that created a substantial impact in 2018. Africa is highly focused on reducing mortality rates because it will reach 112000 deaths in 2040.

### 6. Treatment of Breast Cancer

Breast cancer treatment has significantly improved over the years. However, treating breast cancer can be challenging because it has different forms (heterogeneity). Breast cancer is divided into four main types based on the proteins found in the cancer cells: Luminal A, Luminal B (HR+/HER2+), HER2+, and Triple-negative. Most breast cancers (84%) are either Luminal A or Luminal B. Luminal A and B are hormone receptor-positive (HR+), meaning the cancer cells have receptors that hormones like estrogen can bind to and promote growth. Therefore, hormone therapy is the foundation of treatment for HR+ breast cancer. HER2+ breast cancers have a high level of the protein HER2, which promotes the growth of cancer cells. For early-stage HER2+ breast cancer, the standard treatment is a combination of chemotherapy and drugs that target the HER2 protein. Triple-negative breast cancers lack the three receptors that the other types have (estrogen receptors, progesterone receptors, and HER2). This type tends to be more aggressive and challenging to treat. Standard chemotherapy remains the primary treatment

for triple-negative breast cancer. See **Table 2** for a detailed summary of the treatment of breast cancer.

**Table 2.** A detailed summary of breast cancer treatments.

Subtype	Description	Treatment	References
Luminal A (HR+BC)	Most common subtype, hormone receptor positive (HR+), growing in premenopausal women.	Endocrine therapy: Aromatase inhibitors, Tamoxifen, Luteinizing hormone blockers, Fulvestrant.	[46] [47]
HER2+	HER2-positive breast cancer.	Neoadjuvant treatment with chemotherapy and anti-HER2-targeted therapy: Trastuzumab, Pertuzumab, Ado-trastuzumab emtansine, Lapatinib.	[48]
Luminal B (HR+/HER2+)	Hormone receptor positive and HER2-positive.	Combination of endocrine therapy and HER2-targeted therapy.	[46] [47]
Triple-Negative Breast Cancer (TNBC)	More aggressive and difficult to treat, lacks expression of ER, PR, and HER2.	Standard chemotherapy: Taxanes, Anthracyclines, Platinum medicines, with or without Bevacizumab.	[49]

## 7. Preventive Measures

You can take preventative measures to lower your risk of breast cancer. These include maintaining a healthy weight, limiting alcohol consumption, and getting regular physical activity. **Table 3** summarises the preventative measures for breast cancer that can be done at home without physician supervision.

### 7.1. Weight Control

Premenopausal weight gain and being overweight or obese after menopause raises the risk of breast cancer. According to a meta-analysis, the risk of breast cancer increases by 12 percent for every 5 kg/m<sup>2</sup> increase in BMI. Two extensive observational studies show that losing weight before or after menopause reduces the incidence of postmenopausal breast cancer. Weight control can also help prevent diabetes and cardiovascular disease [50]-[52].

### 7.2. Alcohol

For each increase in alcohol use, the risk of breast cancer is projected to increase by 7% to 10%. Compared to nondrinkers [51]. Women who consumed the most alcohol (at least 27 units per week) were 51% more likely to get breast cancer, it is crucial to remember that lifestyle prevention applies to women of all ages, not just those in their forties and fifties [52].

### 7.3. Dietary Components

According to a new review study, in pre and postmenopausal women, moderate to vigorous physical activity decreases breast cancer risk by 25% compared to sedentary women [53]. Recreational physical activity, lifetime physical activity, postmenopausal physical activity, and moderate to vigorous physical exercise had the

highest inverse relationships with breast cancer risk (Table 3).

**Table 3.** Preventative measures for breast cancer.

Preventive Measure	Description	References
Weight Control	Premenopausal weight gain and being overweight or obese after menopause raise the risk of breast cancer.	[50] [51]
Alcohol Consumption	Increased alcohol use raises the risk of breast cancer.	[51] [52]
Dietary Components	Moderate to vigorous physical activity decreases breast cancer risk by 25% compared to sedentary women.	[53]

## 8. Conclusions

In conclusion, breast cancer remains a significant global health challenge, with incidence and mortality rates varying across regions and populations. While developed countries generally have higher incidence rates, developing countries experience disproportionately higher mortality rates due to limited access to healthcare and advanced treatment options.

The complexity of breast cancer, with its diverse subtypes and risk factors, necessitates a multifaceted approach to prevention, early detection, and treatment. Public health initiatives focusing on education, awareness, and risk reduction strategies are crucial, particularly in less-developed regions. Further research into the molecular mechanisms of breast cancer and the development of targeted therapies remain essential for improving patient outcomes globally.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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