The Epidemiology of Breast Cancer

Evelina Arzanova, Harvey N. Mayrovitz

Dr. Kiran C. Patel College of Osteopathic Medicine, Nova Southeastern University, FL, USA

Author for correspondence: Harvey N. Mayrovitz, Department of Medical Education, Dr. Kiran C. Patel College of Allopathic Medicine, Nova Southeastern University, FL, USA.
Email: mayrovit@nova.edu

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ABSTRACT

As of 2020, breast cancer has become the most diagnosed cancer globally, overtaking lung and prostate cancers**.** Breast cancer incidence is increasing globally with cases expected to reach 364,000 in the year 2040. Part of this increase may be attributed to improved detection but some, especially in lower developed countries, may be due to changes in female fertility patterns along with lifestyle changes. Developed countries have the highest incidence of breast cancer. Mortality rates vary widely from global

region to region but are highest in socio-economically low areas, reflecting a lack of access to early screening and timely treatment. Even in developed countries, the disproportionately high mortality rate among black women and white women further underscores existing health inequality. This chapter aims to provide a global epidemiological overview of breast cancer incidence and mortality.

Keywords: epidemiology of breast cancer; incidence of breast cancer; mortality from breast cancer; breast cancer; risk factors for breast cancer

Running Title: Breast Cancer Epidemiology

INTRODUCTION

Breast cancer (BC) incidence is measured by the number of new cases that occur within a population over a fixed time interval whereas its incidence rate is measured by the number of new cases within that interval divided by the number of persons at risk for BC during that time interval (1). Comparing cancer incidence rates may lead to a better understanding of cancer risk factors, facilitate the planning and prioritization of cancer control initiatives, and help evaluate specific primary prevention programs. However, both indices are used in the literature and herein will be cited accordingly. The age-standardized incidence rate (ASIR) is used to compare populations that have different age profiles. It is determined by dividing the incidence rate by the respective population in that age group and multiplying the result by 100,000 (2). The age standardized mortality rate (ASMR) is calculated similarly (2).

The incidence of BC has been growing by amounts that depend in part on a country's developmental index and the availability and utilization of BC screening methods such as self-breast examinations and mammography (3-6). Since 1997, high developmental Index countries that include the United States, Europe, and Oceania, have had an annual BC incidence rate increase of less than 0.5% (4, 5). During the same time frame middle and low human development index regions such as South America and Africa have had a greater rate of increase (7). Asian countries, including Korea and Japan, although considered to have a high human development index have also seen a rapid incidence rate increase (3). According to the World Health Organization (WHO), the human development index is measured by a country's accomplishments in three essential dimensions: health as measured by life expectancy at birth, knowledge as measured by mean and anticipated years of schooling and standard of living or quality of life as measured by gross national income (8).

During this same time interval, sub-Saharan African countries such as Nigeria, Malawi, and Seychelles have experienced the highest BC incidence rate increase of greater than 5% per year (6). Newly diagnosed BC cases have also risen in the Eastern Cape of South Africa and Zimbabwe by 3-4% annually (6). These increases are likely due to a combination of factors including the adaptation of the westernized lifestyle, delaying the onset of childbearing, shortening the breastfeeding period, and increasing the use of oral contraceptives that all contribute to BC development (2).

Studies conducted in Ireland, Denmark, Scotland, and the United States indicate an increase in the diagnosis of estrogen receptor-positive (ER+) BC and a decrease in estrogen receptor-negative (ER-) BC mainly reported in westernized countries (9-13). The change has been partially attributed to increased incidence of obesity with its associated higher body fat and greater androgen to estrogen conversion in adipose tissue. This combination is associated with an increased lifetime exposure to estrogen in women (7, 14-17). Higher and longer oral contraceptive use also contributes to this finding (18-21).

Countries with low and medium human development indexes also have been experiencing increases in cancer risk factors such as smoking, bad eating habits, excess body weight, and physical inactivity already present in high-income western countries (22). Since 2020, BC is the most diagnosed cancer globally except for skin cancers (23). In 2020, BC accounted for nearly 12% of all new cancer cases diagnosed in 7.8 million women worldwide (7, 23). The ASIR was highest in countries with a very high human development index (75.6 cases/100,000) (19). However, medium and low human development index countries had an ASIR of 27.8 cases /100,000 and 36.1 cases/100,000, respectively (19). As shown by the ASIR values in **Figure 1**, Belgium (13.2 cases/100,000), The Netherlands (100.9 cases/100,000), Luxembourg (99.8 cases/100,000), and France (90.1 cases/100,000) had the highest BC incidence rates in 2020 (7). The four countries with the lowest incidence were Nepal (13.9 cases/100,000), Mongolia (11.1 cases/100,000), The Republic of the Gambia (11 cases/100,000), and Bhutan (5.0 cases/100,000) (7). Overall, the incidence of breast cancer has doubled in the last few decades in 60/102 countries, including Argentina, Brazil, and Afghanistan (19).

Early detection of BC is inversely proportional to BC mortality; thus, screening and increased individual awareness of BC leads to better outcomes (3). In recent years, advances in BC therapy have contributed significantly to increased survival and the subsequent reduction or stabilization of BC death rates in high to medium-resource regions (3). Since the introduction of mammography in 1976 and organized breast

cancer screening guidelines in regions with high human development index, a significant increase in early-stage BC diagnosis have led to a significant decline in BC-related mortality (3).

Nevertheless, recently BC has become the fifth leading cause of mortality and the leading cause of death from cancer among women worldwide (7). BC accounted for 6.9% of all cancer-related deaths globally in 2020 (7)**.** One in 6 cancer-related deaths is due to BC, making BC the leading cause of cancer mortality in 110 countries (6). Australia/New Zealand, Northern Europe, Northern America, and China are the exception, where BC is preceded by lung cancer, and in sub-Saharan Africa, where cervical cancer mortality is highest (7)**.** In the developing world, women have a 17% higher BC mortality rate (2) due to a lack of defined early screening standards and poor or delayed access to treatment (18-21). Asia and Africa shared 63% of the 685,000 BC-related deaths in 2020, with China being the highest at 82,100 deaths (24).

BREAST CANCER RISKS

In women, non-modifiable risk factors such as female sex, age, family history and genetic mutations (BRCA 1/2), early age of menses and late age of menopause onset increase one's risk for BC (20, 25, 26). Modifiable lifestyle risk factors such as nulliparity (not having children), exposure to hormone therapy (estrogen), obesity, and alcohol consumption have also been found to increases one's risk for BC (20, 25, 26). In men, risk factors such as age, race, genetic mutations (BRCA2 >BCRA 1), elevated estradiol serum levels, obesity, gynecomastia, history of radiation exposure, diabetes and orchitis/epididymitis are associated with an increased risk for developing male breast cancer (MBC) (27).

Breast tissue consists of lobules, ducts, and connective tissue, which produce milk, carry milk from lobules to the nipple, and surround the blood vessels, lymphatic vessels, ducts, and lobules, respectively (28, 29). BC can be described based on its pattern of invasion into the surrounding tissue (28, 29). Diagnosing BC following an abnormal mammography exam, requires a biopsy of the area (30). If the presence of BC is pathologically confirmed, the neoplasm is further staged using the 8th edition of the American Joint Committee on Cancer (AJCC) tumor, nodes, and metastases (TNM) system (30). The neoplasm is further checked for the presence or absence of biological markers such as hormone receptors, including estrogen receptor, progesterone receptor, or HER2 protein (ER+/-, PR +/-, Her2+/-) production is also assigned (30). The staging then guides the treatment options, such as surgical resection, chemotherapy, and radiation (30).

Ductal carcinoma in-situ (DCIS) is a non-invasive cancer with a predicted diagnosis of 51,400 new cases in the USA for 2022 (29). Non-invasive DCIS can further progress into invasive ductal cell carcinoma (IDC) (29), which is the most commonly diagnosed BC in both men and women, with an anticipated 287,850 new cases in American women in 2022 (29). The second most common type of BC is invasive lobular carcinomas (29). The highest 5-year survival rate (99.1%) in the USA is seen in BC cases with tumors localized to the initial place of origin (31). In comparison, BC tumors with a regional lymph node spread have a 29% survival rate while women with metastatic BC have only a 6% rate of survival (31). Additionally, in the USA the 5-year survival rate in female BC is more significant than men's (86.4% vs. 77.6%) regardless of cancer stage, hormone-receptor status, HER2 status, age, year of diagnosis, and other health factors (32).

BREAST CANCER INCIDENCE AND MORTALITY RATES BY COUNTRY OR REGION

For each country or region, its BC incidence rate is presented first followed by the associated mortality rate. Prior to that it may be useful to summarize key aspects of BC risks and related factors.

Breast Cancer Incidence in the United States of America (USA)

The 1950s expansion of BC educational programs and rise in BC awareness, paired with the introduction and promotion of breast self-exams by the American Cancer Society, highlighted the beginning rise of BC incidence in the USA (33). According to the Connecticut Surveillance, Epidemiology, and End Results Programs (SEER) database, from 1950 to 1975, the USA incidence of BC cases per 100,000 increased from 66.6 cases/100,000 to 119.2 cases/100,000 (34). These numbers further increased with the introduction of mammography screening from 1975 to 1987 (34). Further, the use of postmenopausal hormone replacement therapy in women over 50 years increased women’s lifetime exposure to estrogen and contributed to the rise of invasive BC incidence from 1980 to early 2000s (4, 35, 36). In addition, from 1980 to 2008, the use of mammography screening increased by 41% in women over 50 years, increasing newly diagnosed DCIS incidence from 7 cases/100,000 in 1980 to 83 cases/100,000 in 2008 (4, 35, 36).

During the late 1990s, a study conducted by the Women's Health Initiative reported a link between postmenopausal hormone therapy use, heart disease, and BC (37). This was associated with a 13% decline in BC incidence from 1999 to 2004, in the USA (4, 35, 36). Since 2004, invasive BC incidence has increased by less than 0.5% per year, while the incidence of local BC increased by 1.1% per year from 2012 to 2016 (4).

According to the National Cancer Institute, BC is the most common cancer in US women, accounting for 15% of new annual female cancer cases today (31). The current lifelong probability of being diagnosed with BC is 12.9% (31). The median age of women at diagnosis is 63 years making up 26.5% of new cases amongst women ages 65-74 years (31). In 2022, approximately 287,850 new female and 2,710 new male invasive BC cases will be diagnosed (21). Overall, female BC incidence trends in the USA can be further observed in **Figure 2** (38).

Breast Cancer Mortality in the USA

From 1950 to 1975, BC mortality in the USA increased slightly by 1.3 cases/100,000 with an overall trend as shown in **Figure 3** (39). However, from about 1990 to 2015 BC mortality declined as indicated in Figure 3 (39). This decline is likely due to increased BC awareness, increased mammography screening, and the use of adjuvant chemotherapeutic treatment options (40). In highly developed countries such as the USA, with better access to quality healthcare and established BC screening guidelines, BC tends to be diagnosed in its earliest stages with a better overall chance of survival (35).

Although there was an increase in BC diagnoses over time, deaths from invasive BC have declined for white women, with the greatest reduction between 1989 to 2009, in which mortality decreased from 33 cases/100,000 to 21 cases/100,000, respectively (36). However, black women living in the USA, despite having a 4% lower incidence rate of BC, have a 41% higher BC mortality rate than white women (40). The increased BC-related death rate in black women is due to a later stage of diagnosis, obesity, comorbidities, less access to timely and high-quality preventative care and treatment services (4, 41-43). Furthermore, some studies suggest that because black women have a higher incidence (38 cases/100,000) of triple-negative BC (ER-, PR-, HER2-) than white women (19 cases/100,000) thus, black women have a lower use and associated survival from hormonal chemotherapy treatments such as Tamoxifen (4, 42). The probability of having longer gaps between mammography screening, cancer detection, and follow-up in black women, further lead to inequitable healthcare and contribute to the lower survival rates reported (41-43).

Based on the Center for Disease Controls, National Center for Health Statistics mortality files from 2015 to 2019, the ASMR in non-Hispanic black women was the highest (28 cases/100,000) during that time (31). Followed by non-Hispanic white women (199.9 cases/100,000), non-Hispanic American Indian/Alaska Native women (17.8 cases/100,000), Hispanic women (13.7 cases/100,000), and Non-Hispanic American Indian /Alaska Native women (17.8 cases/100,000) (31). Today, the median age at

death due to BC in the USA is 69 years, with 24.1% of women dying between the ages of 65-74 years (31). The 5-year survival rate from 2012 to 2018 was 90.6% (31). According to the American Cancer Society, 43,250 women and 530 men are expected to die from BC in 2022 (21), while the projected 2040 BC mortality is expected to decrease to 30,000 deaths (44).

Breast Cancer Incidence in Canada

Canadian BC incidence trends over the years, closely correlate with those reported in the USA due to similar patterns of BC screening guideline establishments and mammography use in the North American region (45). The use of breast self-exams was widely encouraged by the Canadian Cancer Society since the early 1950s (46), followed by the establishment of formal screening guidelines in 1988 (47). In Canada's Yukon and Northwest Territories, coordinated screening programs began in 1990 and 2003, respectively. However, up until 2009, Nunavut province lacked organized screening (47). This earlier lack of established organized screening of BC in Canada contributed to mammography over screening and the rise in BC incidence between 1984 and 1991 by 2.1% (48). From 1992 to 2010, the ASIR was 114 cases/100,000 (48). After 1991, the annual incidence fluctuated with an ASIR peak of 1.57 cases/100,000 between 1992 and 2010 (48). There was a dip in the ASIR from 2002 to 2005 that was linked to a decrease in postmenopausal hormone treatments similarly to what was seen in the USA (15). However, the overall BC incidence rate significantly declined by 0.2% per year between 1991 and 2015. Nevertheless, the Canadian BC incidence has increased from 116.3 cases/100,000 in 1984 to 129 cases/100,000 in 2018 (49). The expected number of new BC cases in Canada is 28,600, which will make up 25% of all new cancer cases in Canadian women in 2022 (50).

Breast Cancer Mortality in Canada

Since the 1986 BC mortality peak in Canada, the ASMR declined by 48% from 1986 to 2019, (43 cases/100,000 in 1986 to 22 cases/100,000 in 2019) (49). This decline is similar to the rest of the developed countries which adopted the use of organized screening and improved BC treatment options (49). In 2019, BC accounted for 13% of all cancer deaths in Canadian women (51). According to the Canadian Cancer Society, BC became the most common cancer in Canadian women (excluding non-melanoma skin cancers) and was the second leading cause of death from cancer in 2021 (52). In 2022, Canada is expected to have 15,203 BC-related deaths, with a 5-year survival estimate of 76% (50).

Breast Cancer Incidence in Latin America

Incidence of BC in Latin America varies widely across countries based on their socio-economic status, healthcare coverage, availability of standard screening procedures, and use of mammography screening due to local public health expenditures and changing fertility patterns (53). As of April 2000, Argentina was the only country where breast self-exams were not part of the recommended screening exams for women, while all Latin American countries supported clinical breast exams (54). A study on the progression towards implementing national policies and standard screening procedures for BC in Argentina, Columbia, Brazil, Venezuela, and Mexico found that only Brazil and Mexico successfully incorporated BC into their public policy agenda, allocating funds to treat all stages of BC by 2010 (55). Mammography screening in Latin American varies by country, with a significant difference in the age of initiating mammography screening and the frequency of BC screening exams (54). Countries including the Bahamas, Dominican Republic, El Salvador, Guatemala, Guyana, Haiti, Honduras, Paraguay, Peru, and Trinidad and Tobago still lacked BC screening policies in 2000 (54).

Based on a study analyzing the Global burden of disease data, the incidence of BC increased in all Latin American regions and the Caribbean from 1990 to 2017 (Andean Latin America 29 cases/100,000 population, Central Latin America 39.5 cases/100,000 population, Tropical Latin America 41.6 cases/100,000, Southern Latin America 52.8 cases/100,000 population, Caribbean 52.6 cases/100,000 population) (56). By 2018, the expected number of new BC cases in Latin America and the Caribbean was 199,734, making up 14.9% of all new cancer cases (57). In 2020, a total of 210, 000 new BC cases were reported in Latin America and the Caribbean, the expected number of new cases for 2040 is 309,000 (58).

Breast Cancer Mortality in Latin America

From 1990 to 2015, the Latin American ASMR increased on average 1.48 cases/100,000 per year from 12.12 cases/100,000 to 19.64 cases/100,000, respectively (59). A complete systematic epidemiological study further confirms that from 1990 to 2017, the overall percent ASMR increased by 11.3% in Andrea Latin America, 12.2% in Central Latin America, 19.6% in Southern Latin America, 14.7% in Tropical Latin America and 18.8% (56). An observed decrease in the total fertility rate, socio-economic development, and women's lifestyle changes (increased alcohol consumption, obesity, sedentary lifestyle) predispose women to greater BC-related risk factors, thus reflecting in higher incidence rates uniformly in Latin America (60).

Based on the available statistics, specifically in 2008, 14% (36,952) of global BC-related mortality occurred in Latin America (60). That year, countries such as Colombia, Ecuador, Mexico, and Peru had an estimated age-adjusted mortality rate of 10 cases/100,000, while Panama, Chile, and Venezuela had an age-adjusted mortality rate of 13 cases/100,000 (60). Regions such as Argentina and Uruguay, which have a much higher incidence rate than other Latin American countries, had an age-adjusted mortality rate of 24 cases/100,000 (60). BC further accounted for 15% of total deaths due to BC in Latin America, with 53,000 deaths in 2018 (57). In 2020, a total of 57,000 women died from BC in Latin America, that number is expected to nearly double by 2040 with a total BC-related mortality of 92,700 women (61).

Breast Cancer Incidence in Africa

Limited BC related epidemiological data is available for African countries (62) due to a lack of quality cancer registries and number of registrations (63). In fact, from 1978 to 1982, there were no reported cancer registries based on the lack of African representatives in the Cancer Incidence in Five Continents Volume V (64). However, despite a slow progression, cancer registries and their quality have been slowly improving in areas such as Nigeria, which established its National System of Cancer Registries in 2009 (64). Similarly, Uganda established two cancer institutes (Uganda Cancer Institute and Kampala Cancer Registry) since then (65). By 2014, there were 25 population-based cancer registries covering 10.5% of the sub-Saharan African population (64), and in 2006, 11% of the population-based cancer registries were reported in Africa (63). The importance of having cancer registries lies in their ability to offer a systematic collection, storage, understanding, and calculation of cancer incidence and mortality rates along with other epidemiologically significant factors and estimate regional disease burden (64).

According to the Global Burden of Disease data estimates, the percent increase of BC incidence based on the ASIR from 1990 to 2017 was 24.4 % in Central sub-Sahara Africa, 39.4% in Western sub-Sahara Africa, 24.1% in Eastern Subsabra Africa and 30.3% in Southern sub-Sahara Africa (56). In 2018, the ASIR ranged from 6.9 cases /100,000 in Gambia to 69.6 cases/100,000 in Mauritius, with an overall ASIR for Africa of 37.9 cases/100,000 (66). By 2020, BC became the most common cancer diagnosed among African women, with 186,598 new cases (67).

In 2020, the five participating countries with the highest BC ASIR ranged from 20.0 cases/100,000 in Zambia and 22.2 cases/100,000 in Uganda to 49.0 cases/100,000 in Nigeria, 52.6 cases/100,000 in South Africa, and 57.6 cases/100,000 in Namibia (68). That same year, a total of 186,000 new BC cases were

recorded in Africa and that number is expected to nearly double by 2040, with a projected estimate of 337,000 (69).

In general, BC incidence rates continue to increase in Africa due to women delaying childbirth, having fewer children, adopting westernized lifestyles such as delaying marriage, and decreasing the length of breastfeeding (66). In contrast to non-African geographical regions, where BC is more frequent in women over 50 years, African incidence rates are growing in younger premenopausal women ages 30-49 (66). Factors such as African women's short overall life expectancy of 66 years (70) exaggerate the incidence rates of younger women compared to the global female life expectancy of 71 years (70, 71). The low median age of the African female population leads to a more significant proportion of BC diagnoses among younger women (71, 72).

Breast Cancer Mortality in Africa

From 1990 to 2017, the percent change in BC ASMR in regions of Africa was: 17.5% in Central sub-Sahara Africa, 13% in Southern sub-Sahara Africa, 7.2% in Northern Africa and the Middle East, 8.4% in Western sub-Sahara Africa, and 3.4% in Eastern sub-Sahara Africa (56). In 2018, Nigeria was the leading country in absolute BC burden with 11,564 deaths, followed by 9,254 deaths in Egypt (66).

Despite the high and increasing BC mortality rates in sub-Sahara Africa, the prevalence of BC screening is low, with an overall prevalence of 12.9% in 39,646 women ages 15-49 years old recorded in 2020 (73), however women ages 45-49 have the highest mortality rate due to BC (66). Late-stage presentation of BC is largely to blame for low survival rates in sub-Saharan Africa, where 77% of all newly diagnosed BC cases are in stage III/IV (7). Furthermore, in a study of 2,156 women diagnosed with BC and tracked for three years until January 2019, a significant difference in survival rates was observed among white African women compared to black African women (74). The overall BC 3-year survival rate was 50% in Namibia, with a 90% survival rate for white women, but only a 56% survival rate for black women. In South Africa mixed-race women had a 3-year survival rate of 76% compared to a 59% survival rate for black women (74). The highest determinants for increased survival were determined to be early diagnosis and treatment improvements, with an overall improvement in survival by 22% in Nigeria, Zambia, and Uganda (74). In 2020, the recorded overall BC-related ASMR was 88.8 cases/100,000, ranging from 56.6 cases/100,000 in the Republic of Congo to 139.4 cases/100,000 in Zimbabwe (67). To summarize, 416,000 women are expected to die from BC in sub-Saharan Africa from 2020 to 2029, yet at least a third of these deaths might be avoided with early diagnosis of BC and effective treatments (74).

Breast Cancer Incidence in Europe

England and the Netherlands established their national BC screening programs in the mid-1980s, similarly to other highly developed countries (3). Implementation of organized mammography screening programs, supported by the European Council, increased by 2006 (75). Additionally, since 2007, most European countries have switched from film to digital mammography screening that has a higher sensitivity for detecting BC neoplasm in dense breasts (76). Other studies of 14 European countries from 1980 to 2018 have demonstrated a decline in BC-related mortality (76). The decline was somewhat age-dependent and was between 1.5% to 5.4% in women aged 50-59, 0.2% to 8.1% in women aged 60-69, and a 0% to 7.1% in women aged 70-79 years. Another study completed in Western Europe is consistent with the findings that the use of mammography screening along with broader availability of organized screening programs reduces BC-related mortality in women aged 50-74 years by 25-30% (75).

Although the incidence of BC has increased in European nations secondary to the improvements of BC screening and awareness, mortality has been declining as observed in other highly developed countries (75-78). Further, studies support that a similar trend of increased BC incidence was seen across Europe during the early 1990s and 2000s when the use of hormone replacement therapy began, with a subsequent decline when the use of such therapies declined in highly developed countries (79, 80). Denmark, where the BC incidence rate decreased by 1.2% annually from 2002 to 2010, serves an example of that decline (62).

From 1999 to 2003, BC accounted for 26% of all cancer incidents in Denmark, Iceland, Finland, Norway, Sweden, and Greenland (81). From 1993 to 2007, BC incidence rates declined by 0.3% in Austria, while Croatia had a stable increase in incidence of 2.2% during the same time (62). In Malta and Croatia, incidence rates increased by 0.5% and 2.2% respectively from 1993 to 2007 (62). Meanwhile, Slovenia's incidence rate declined from 5.7% in 1997 to 0.9% by 2010 (62). In France, incidence trends began to decline in 2009 by 1.2% (62).

In Belarus, the Czech Republic, Poland, Slovakia, incidence rates increased by 1.7%–2.2% per year from 1993 to 2007/2008 (62). In Russia, where data reported might not be accurate due to a lack of organized screening programs and BC registries, the BC ASIR increased from 33.1 cases/100,000 to 54.2 cases/100,000 from 1993 to 2019 (82). By 2020, Belgium had the highest incidence rate of BC in the world with an ASIR of 113.2 cases/100,000 followed by the Netherlands (100.9 cases/100,000),

Luxemburg (99.8 cases/100,000), and France (99.1 cases/100,000) (7). Overall, the number of new BC cases in Europe was 531,000 in 2020, which is predicted to increase to 568,000 by 2040 (83).

Breast Cancer Mortality in Europe

As previously mentioned, in Europe, the increase in incidence of BC inversely correlates with mortality (82). While incidence rates continue to increase, BC-related death rates are decreasing due to adequate healthcare, increased BC screening and earlier diagnosis of BC in women since the 1990s (82). Northern European countries have seen a decrease in mortality since the mid-1990s except Latvia which had a stable 0.1% decline per year since 2002 (62). Denmark has had a 2.9% annual decrease in mortality rates from 1996 to 2012, however it has one of the highest BC mortality rates overall (62). Western European countries such as Germany, the Netherlands, France, and Austria had a decreasing BC-related mortality rate since 2003 (62). Based on the reports from six cancer registries, the BC-mortality rate also declined in Switzerland by 1% since 2000 (62). In Eastern Europe, mortality has been increasing in places such as Russia, Estonia, Romania and Hungary from 1993 to 1997 the latest for which data was found (3).

Reports of BC mortality in Southern Europe (62) Indicate that Italy had a variable mortality rate that increased from 1993 to 1999 by 4.6% annually then followed a steady decline of 0.8% per year from 2000 to 2007. Further, Croatia was reported to have a stable annual mortality rate increase of 2.2% per year from 1993 to 2007. Spain's mortality rate declined 2.1% per year from 1993-1995 followed by an increase of 2.8% per year between 1996-2002 then declined 1.3% until 2007. A more recent study completed in 27 European countries, reported that from 2012 to 2017 the overall BC-related mortality decreased by 3.9% from 15.0 cases/100,000 in 2012 to 14.4 cases/100,000 in 2017 (77). According to 2020 data, the total number of deaths due to BC in Europe was 142,000, while that number is projected to increase to 171,000 by 2040 (84).

Breast Cancer Incidence in Asia

The 48 countries comprising Asia differ broadly in BC incidence trends over time (85). From 1990 to 2017, ASIR increased by 54% in Central Asia, 89.5% in East Asia, and 76.7% in South Asia (56). Per year changes in ASIR from 1993 to 2007 amounted to 4.8% in Thailand, 3.0% in Japan and 4.1% in China from 1993 to 2001 but 1.6% from 2001 to 2007 (62). Despite the increasing incidence, in 2006, only 8% of the total Asian population was covered by population-based cancer registries (63). Studies conducted in 2010 found that population-based cancer registries in Asia increased to 20%, but with only four registries to cover the entire populations of Japan, Korea, Singapore and Taiwan, and China (86).

Thus, for a region that has nearly 60% of the world's population (87), the reported numbers might be lower than the exact due to inadequate tracking of new BC cases (63).

In 2012, 651,000 Asian women were diagnosed with BC, making up 38.8% of global BC cases (85). In 2018, 10% of all cancers in Asia were due to BC (845,400 total cases) (88). By 2040 the number of new BC cases in Asia is expected to reach 1.34 million (89).

Breast Cancer Mortality in Asia

From 1990 to 2017 ASMR increased by 15% in South Asia, 13.9% in Central Asia, 14.9% in Southeastern Asia, and 8.6% in Eastern Asia (56). More specifically, it has been reported that from 1997 to 2001 and 2007 to 2009, the BC-related mortality in rural China increased by 20%, while the urban regions reported a 7% drop (90). It was suggested that efforts to expand the availability of high-quality screening, diagnosis, and treatment and primary prevention methods focusing on weight loss have been suggested to help China minimize BC-related mortality. This study further suggested that BC management in Asia is also complicated by a lack of awareness, proper diagnostic equipment, healthcare competition, and reliance on traditional approaches.

Overall, BC ASMR is predicted to increase by 2030 in East Asia by 7% since 1990 from 9.10 cases/100,000 to 9.88 cases/100,000 and 35% in South Asia from 13.4 cases/100,000 to 18.1 cases/100,000 in women ages 50-80 years (91). Imminent lifestyle changes such as reducing red meat consumption, better glycemic control, and increased activity paired with improved access to treatment and earlier diagnoses may reduce the current projected mortality trends in Asia and the rest of the world (91).

Breast Cancer Incidence in Oceania

BC incidence in Australia increased steadily in women ages 50-69 years with the start of mammography screening in 1984 (3). By 1992, mammography became available to all women over the age of 40, and the incidence rates further reflected a more significant increase with a broader female age variation (3). New Zealand had a similar increase in incidence reported from 1978 to 1992 (3). Like other highly developed regions, Oceania had a drop in incidence rates after the declining use of postmenopausal hormone therapy in the early 2000s (92). From 1990 to 2017, ASIR data reported separately for Oceania and Australasia indicated an overall increase of 40.7% and 84.7% respectively (56). In 2018, 13.9% of all new cancer cases were due to BC in Australasia, Melanesia, Micronesia, and Polynesia (88). The 2020

BC ASIR was 99 cases/100,000 in New Caledonia, Australia (96 cases/100,000), followed by New Zealand (93 cases/100,000) and Samoa (81.4 cases/100,000), while the lowest was in Vanuatu (30.4 cases/100,000), Guam (41.3 cases/100,000), Papua New Guinea (35.9 cases/100,000) and Solomon Islands (48.2 cases/100,000) (93). The overall number of new BC cases in Oceania was 25,700 in 2020. The expected number of new cases in 2040 is estimated at 34,800 new BC cases (94).

Breast Cancer Mortality in Oceania

BC mortality in Australia rose steadily from the early 1970s to the 1980s but declined in the late 1980s and early 1990s (95). The decrease was 4.2% in women aged 25-49 and 3.2% in women aged 50–69. The observed decline was due to increased efforts in breast screening between 1988 and 1994 and a subsequent increase in BC awareness (95). In 2018, BC accounted for 7% of all cancer mortalities reported in Australasia, Melanesia, Micronesia, and Polynesia (88). The 2018, ASMR was highest in Fiji (41 cases/100,000), Papua New Guinea (27.7 cases/100,000), Samoa (25.6 cases/100,000), and French Polynesia (20.6 cases/100,000), while the lowest ASMR was in Vanuatu (9.5 cases/100,000) (93). In 2020, 4,990 women died from BC in Oceania, that number is expected to be 7,910 by 2040 (96).

CONCLUSION

Breast cancer incidence is increasing globally with cases expected to reach 364,000 in the year 2040. Part of this increase may be attributed to improved detection but some, especially in lower developed countries, may be due to changes in female fertility patterns along with lifestyle changes (97). Increased awareness, early detection and improved treatments in highly developed regions have significantly contributed to decreasing breast cancer related mortality. However, lack of resources and limited access to quality healthcare continue to disproportionately affect lower socioeconomic regions of the world where breast cancer mortality is high. Better organized screening programs, establishment of breast cancer registries, and more widespread use of mammography screening in lower developmental regions of the world can increase early-stage breast cancer diagnosis, reduce breast cancer-related mortality, and help reduce future global breast cancer burden.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest with respect to research, authorship and/or publication of this chapter.

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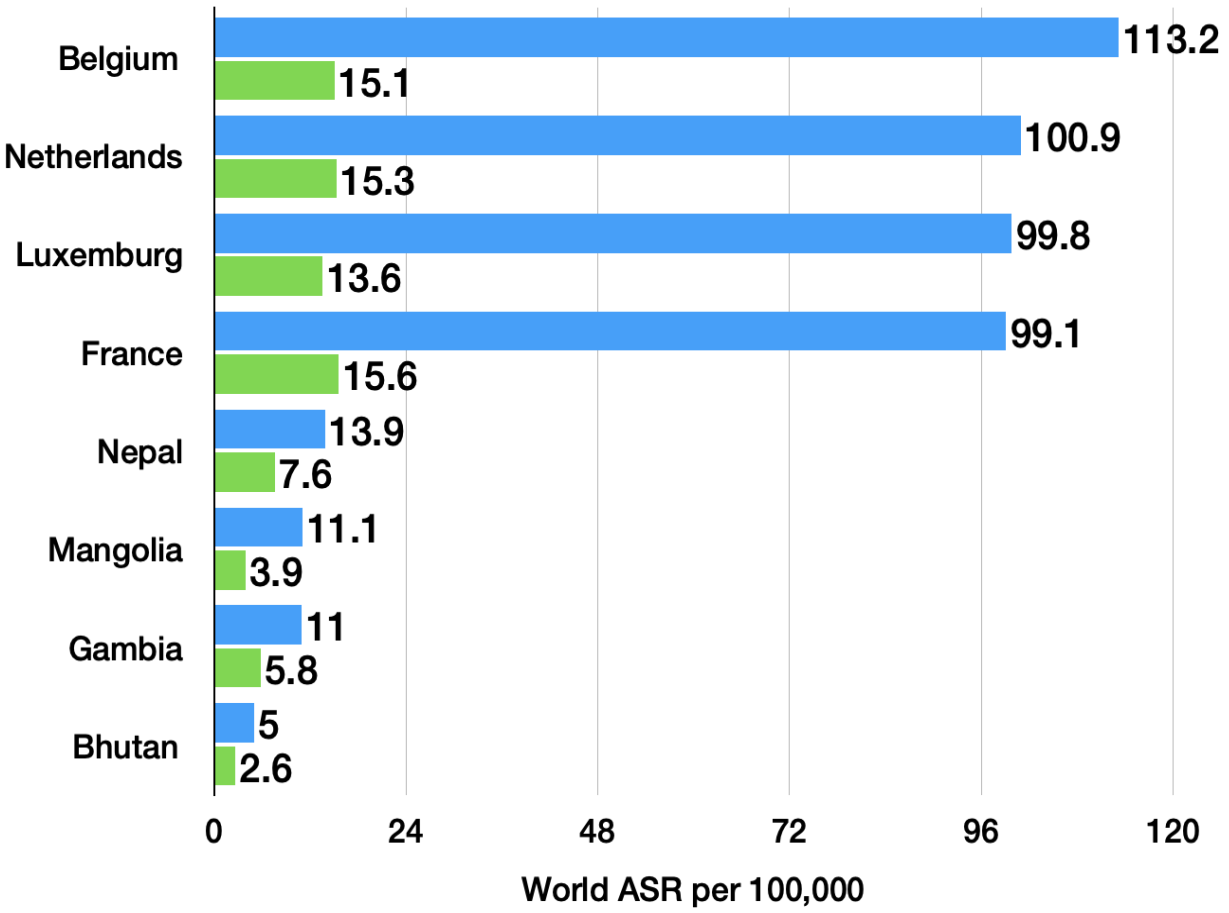

Figure 1. Age-standardized global incidence rates and mortality rates for female breast cancer. Data are for the year 2020 with the top four and bottom four countries. Blue is for ASIR (age-standardized incidence rate), and green is for ASMR (age standardized mortality rate). Graphs based on data from (7).

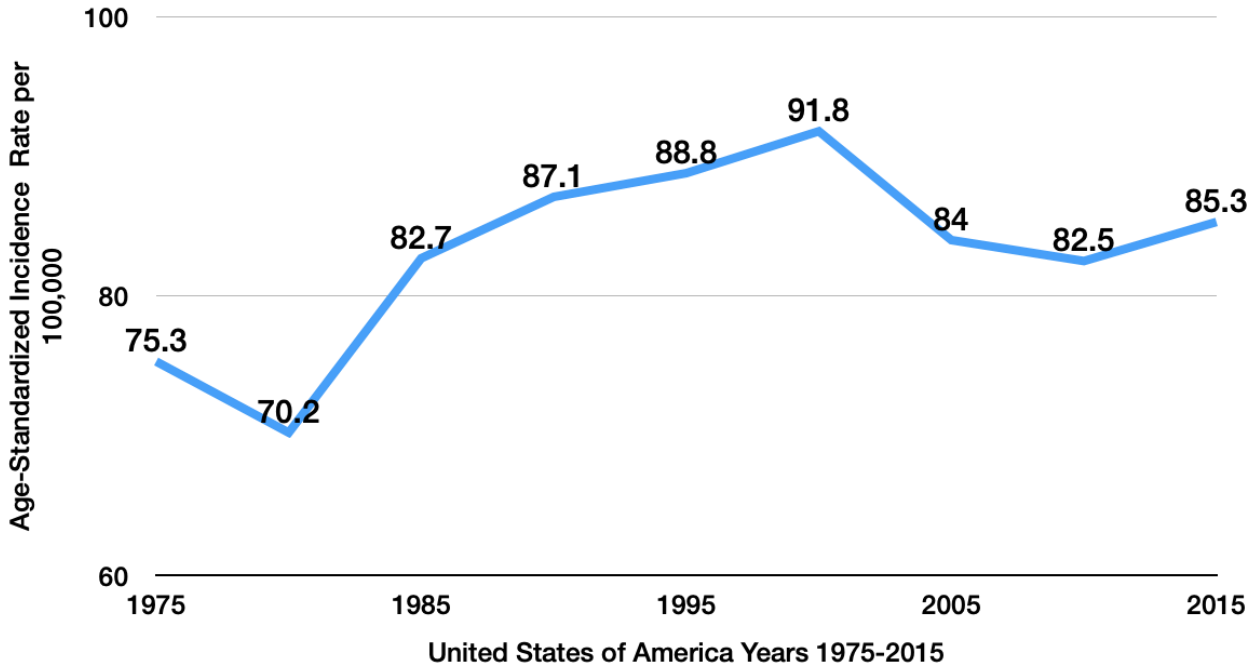

Figure 2. Female breast cancer incidence rate in the USA. Values are the mean age-standardized incidence rate (ASIR). Data are mean values of ASIR (38).

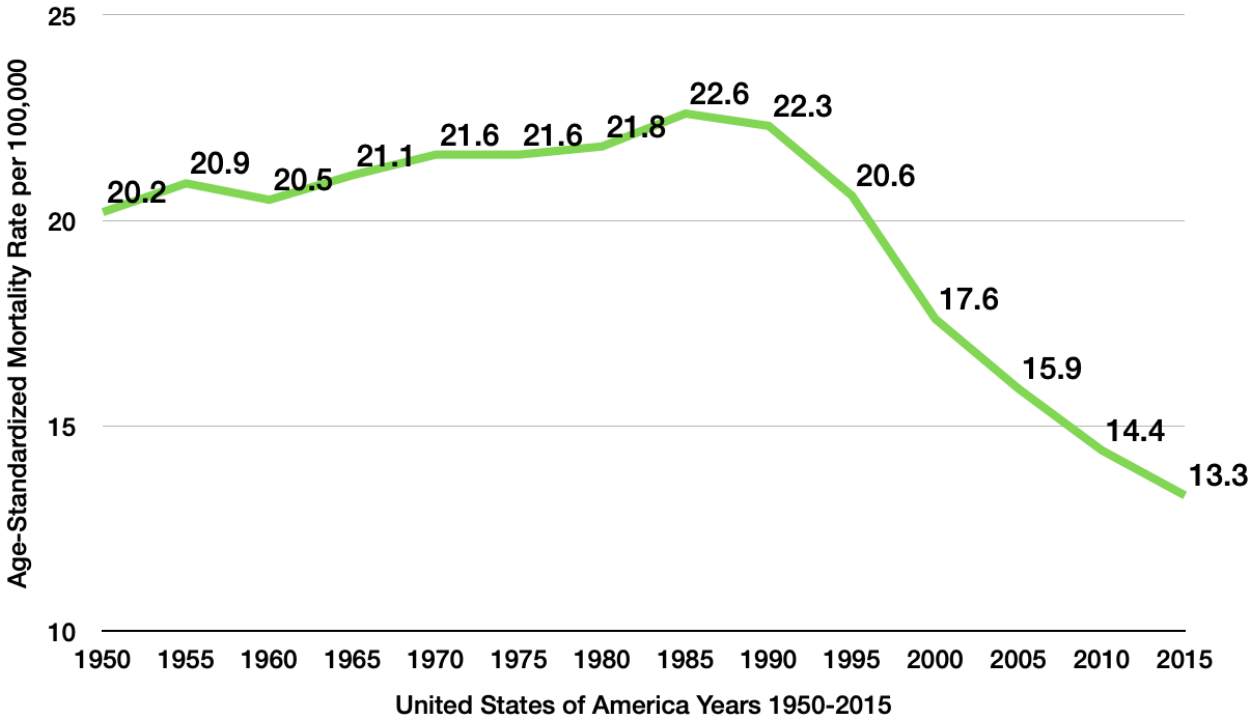

Figure 3. Breast Cancer Related Mortality Rate in the USA. Values are the mean age-standardized mortality rate (ASMR). The decline in the ASMR between 1990 and 2015 is evident from the graphic. Data are mean values of ASMR (39).