

## REVIEW

# INCIDENCE OF BREAST CANCER IN ETHNIC MINORITY GROUPS IN NORTH AMERICA AND POPULATIONS IN WESTERN EUROPE

S. Burk<sup>1,2</sup>, A. Giordano<sup>1,2</sup>

<sup>1</sup> Department of Medical Biotechnologies, University of Siena, Siena, Italy

<sup>2</sup> Sbarro Institute for Cancer Research and Molecular Medicine, Center for Biotechnology, Temple University, Philadelphia, USA

## CORRESPONDING AUTHOR:

Sharon Burk  
Department of Medical Biotechnologies  
University of Siena  
via Banchi di Sotto 55  
53100 Siena, Italy  
E-mail: s.burk@student.unisi.it  
ORCID: 0000-0003-2242-8705

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## ABSTRACT

Breast cancer (BC) is one of the most prevalent cancer types among women, and among the top for cancer deaths. Research to address this worldwide issue has been conducted to identify risk factors associated with development and treatment. It was identified that risk factors not only included age, other underlying diseases, environmental factors, but also socioeconomic factors, language barriers and ethnic background. Unfortunately, due to low socioeconomic status groups that are affected the most in the United States are African American and Hispanic women while in Western

Europe, such as in Italy, discrimination was based on geographical location rather than racial background. Previous studies indicate that discrimination and racial disparities are relevant factors affecting women battling against breast cancer. By analyzing and highlighting the pitfalls of the current medical approaches to treatment among various ethnic groups in North America and Western Europe, researchers and medical professionals will be better able to tailor treatments and improve prognosis among all BC patients, regardless of race and ethnicity.

## KEY WORDS

Breast cancer; triple negative breast cancer; minorities; racial disparities; tailored treatment.

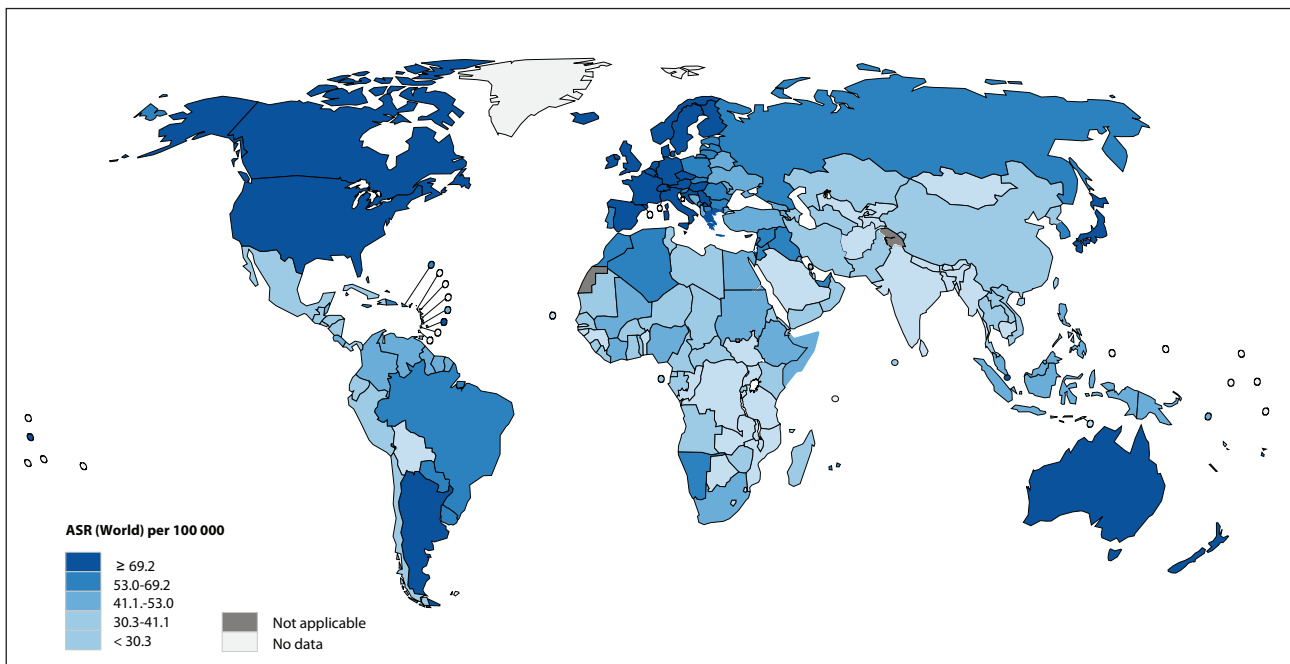
## IMPACT STATEMENT

Despite considerable advantages in research for treatments and therapies for breast cancer there is a noticeable lack of resources which emphasizes racial disparities and socioeconomic status.

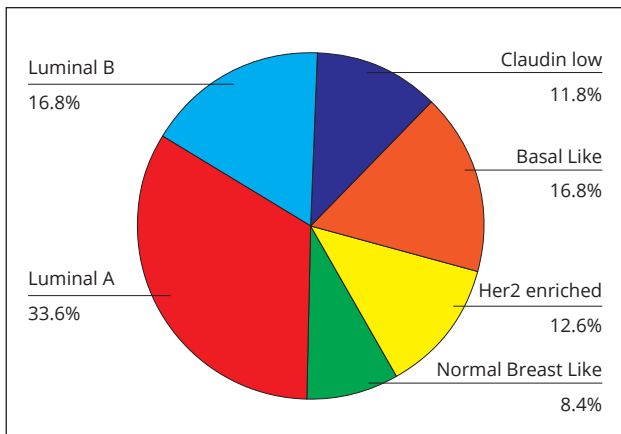
## INTRODUCTION

Breast cancer (BC) is the second-leading cause of cancer death, after lung cancer, and the most common cancer type among women worldwide at 24.5% (1). The greatest incidence, in females, is found in Asia (45.4%), followed by Europe (23.5%) and then by North America (12.5%) (1). **Figure 1** shows the estimated age-standardized incidence rates of BC across all ages. BC exhibits substantial variability among women of differing ancestries. For this reason, it is critical to analyze the incidence of BC in various ethnic groups, observe standards of care and tailor treatment and possible therapeutics in the hopes of improving quality of life and survival. The classification of breast cancers reflects the current state of knowledge; thus, it is an ever-evolving process. BC is a genetically and clinically heterogeneous disease with different biological, clinical

and molecular characteristics (2). The molecular classifications divide breast cancer into six groups: luminal A, luminal B, HER-2, basal, normal breast like and claudin-low (3). There are three main subtypes of BC that are based on immunohistochemistry cellular markers (IHC) or a combination of IHC and microarray expression methods (gene signatures): Hormone receptor positive (ER+ or PR+), HER2 positive, and Triple-negative (absence of ER, PR, and HER2 amplification) (4). **Figure 2** shows the molecular classification of breast cancers (5). More recent data for molecular classification of BC indicate prognostic associations which include intrinsic subtypes, integrative cluster subtypes, triple-negative sub-classification and mutation-based profiling (6). Triple-negative breast cancer (TNBC) accounts for 10-20% of all invasive breast cancers (7).



**Figure 1.** Breast cancer (BC) estimated age-standardized incidence rates (World) in 2020, all ages female. World map illustrating the age-standardized incidence rates in 2020 of breast cancer in women. The darker blue colored countries have a higher age-standardized rate (ASR), which include Belgium (113.2), France (99.1), Australia (96.0), United States of America (90.3), Italy (87.0), United Kingdom (87.7). While countries with lighter blue color have lower ASR. Graphic taken from International Agency for Research on Cancer, 2020, WHO.



**Figure 2.** Molecular Classification of breast cancer. Breast Cancer (BC) is a heterogeneous disease. It can be classified based on different biological, clinical and molecular characteristics. The molecular classifications can be divided into six classes: claudin low, basal like, HER2, Normal breast like, Luminal A and luminal B. Luminal A and B are characterized by a cellular marker of Estrogen Receptor (ER) positive. HER2 enriched BC subtype express HER2 protein and no ER. Basal-like BC is characterized as having no ER, no Progesterone Receptor (PR) and no HER2 present, thus it is called Triple Negative Breast Cancer (TNBC). Because of the absence of these receptors and proteins, TNBC does not respond well to hormone therapies, thus it is difficult to treat and has a poor prognosis

Among the subtypes, TNBC is associated with high mortality, early and more frequent recurrence and poor treatment response, regardless of ethnic background and social standing.

Despite the commonality of molecular characteristics among BC patients, the available treatment and therapy, overall survivorship and quality of life greatly differ among different ethnic groups especially within the United States. Due to the socioeconomic status and other economic disparities some ethnic groups, e.g., African American and Hispanic women, do not have access to routine screenings, medical care, treatment and therapies. Unfortunately, these shortcomings in treatment are not only prevalent in the US but also within some countries in Western Europe, such as Italy.

## AFRICAN AMERICAN WOMEN

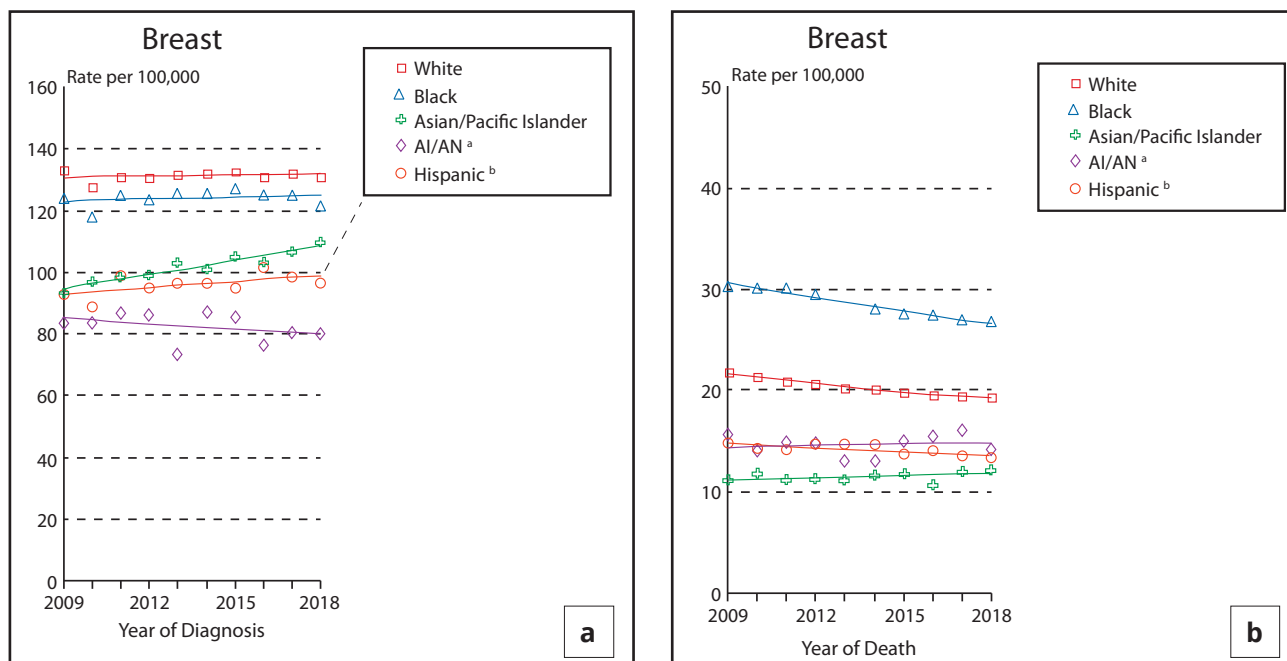
While the incidence of BC in African American (AA) women is lower when compared to European American (EA) women, the mortality rate is higher which may be caused by disparities in the socioeconomic status and in the environment-related conditions, as shown in the **figures 3 a, b** (8). The

data from the Surveillance, Epidemiology, and End Results (SEER) database report the incidence trends across different races and ethnic groups within the United States. As a direct consequence of unhealthy living conditions in areas with low income, AA women are exposed to breast carcinogens that are present in the environment (9). AA women are consistently diagnosed at a more advanced stage of the disease and usually express a triple negative or ER-negative BC phenotype, which is more aggressive and has a poor prognosis (10). Resources such as screening and early detection procedures which could potentially improve survival rates, are less likely to be available for AA women. Friebel-Klingner (11) observed that TNBC was also less likely to be screen detected in AA women. In cases where a diagnosis is available, treatment, e.g., surgery and chemotherapy, may be economically infeasible (12).

Underlying diseases, e.g., obesity and diabetes, may potentially increase the risk to develop BC. Obesity is associated with advanced BC at diagnosis, high tumor proliferation rates, and more triple-negative phenotypes, indicating that it may adversely contribute to prognosis (13). Friebel-Klingner (11) investigated the associations of known BC risk factors, including breast density, with TNBC among black women and concluded that breast density was more strongly associated with TNBC than other subtypes, and obesity was associated with greater risk of TNBC among this group.

Therapeutics are usually tailored to a specific demographic. The majority of clinical trials groups are represented by Caucasian women. Some clinical trials neglect to take into consideration factors such as genetic background and environment-related conditions in the recruitment process, thus affecting in particular AA women. Additionally, a percentage of AA women perceive research as biased to benefit solely Caucasians (14). Multiple preclinical and clinical studies suggest inherent genetic risk factors and aberrant activation of oncogenic pathways in AA TNBC (15). In an effort to provide more inclusive therapeutics, these genetic risk factors and oncogenic pathways may be further researched with the goal to tailor precision medicine to AA TNBC.

In order to address these socioeconomic disparities and racial differences, it is critical to educate and inform with preventative screenings and to improve treatment adherence and efficacy in AA women with TNBC.



**Figures 3. a.** SEER Incidence 2009-2018 Females by Race/Ethnicity; **b.** US Mortality 2009-2018 Females by Race/Ethnicity. These graphics present the incidence and mortality rate trends in female breast cancer across different races and ethnic groups within the United States from 2009 to 2018. The incidence of female breast cancer was higher in White women followed by Black and then Asian/Pacific Islanders while the mortality rate was highest in Black women followed by White and then Hispanics. Graphics taken from National Cancer Institute: Surveillance, Epidemiology, and End Results (SEER) Program, 2020.

Source: SEER 21 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey, Georgia excluding ATL/RG), Idaho, New York and Massachusetts. Rates are age-adjusted to the 2000 US Std Population (19 age groups – Census P25-1103). Regression lines are calculated using the Joinpoint Regression Program Version 4.9, March 2021, National Cancer Institute.

<sup>a</sup> Incidence rates for American Indian/Alaska Native (AI/AN) are based on the CHSDA (Contract Health (Service Delivery Area) counties).

<sup>b</sup> Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives. Incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry.

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention. Rates are age-adjusted to the 2000 US Std Population (19 age groups – Census P26 – 1103). Regression lines are calculated using the Joinpoint Regression Program, Version 4.9, March 2021, National Cancer Institute.

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## HISPANIC WOMEN

Another minority group facing discrimination and lack of financial stability in BC treatment and therapeutics is Hispanic American women. Urban Hispanic women who survive BC are exposed to more risk factors due to low SES, unsafe neighborhood conditions, and limited access to treatment resources (9). Unfortunately, among ethnic minorities (e.g., African American and Hispanic) BC survivors, the association of neighborhood context has a significantly negative impact on health outcomes (16). Although rarely taken into account, the importance of neighborhood context may aid in examining determinants of health, survivorship and quality of life outcomes among cancer patients (16). Howell (17)

analyzed Philadelphia’s urban poor and concluded that although the financial impact and neighborhood context were not unique to urban Hispanic women, this minority group was at greater risk for poorer survivorship because of lower incomes as compared with other racial and ethnic groups. Unlike AA women, the overall rate of BC has declined for Hispanic women. However, similar to AA women, they are diagnosed with more advanced breast cancers (18). This later diagnosis creates a severe setback for these women even prior to treatment. Furthermore, there are additional factors which impede the delivery of proper treatment and care to Hispanic women: health literacy and language barrier. Health literacy is multifaceted. Ineffective communication and lack of health literacy may affect a

patient's ability to access healthcare, follow advice and receive proper treatment (9). This factor further subjects this group of individuals to discrimination. There is an increased risk for health disparities if a patient's primary language is not English and/or if they migrated to the United States (19). If a patient's primary language is Spanish, they have more difficulties with the continuity of their cancer care (20). Various measures have been put into practice in order to address this issue facing Hispanic women. For instance, the U.S Department of Health and Human Services, Office of Minority Health, has developed and established fluency standards for healthcare professionals to implement culturally and linguistically appropriate services (CLAS) (21). The main goal in discussing these issues is to establish standards and guidelines with the ultimate aim of advancing health equity, improve quality of life for all cancer patients and eliminate disparities among specific ethnic groups.

## WESTERN EUROPE - ITALY

With regard to Western European countries, Germany, France and Italy experienced the greatest incidence of BC cases (1). **Figure 4** shows the estimated number of new cases and number of deaths caused by breast cancer in European women in 2020. As stated earlier, a risk factor associated with cancer incidence may be the presence of other underlying diseases such as obesity and diabetes. A cross-sectional study conducted in 2010 provided information on the prevalence of overweight and obesity in Europe (22). Gallus (22) observed that out of the 16 European countries analyzed in the study, two Mediterranean countries, Italy and France, showed the lowest prevalence of obesity. The prevalence of obesity significantly increased with age and decreased with level of education (22). Despite the lower prevalence of obesity in Mediterranean countries, Italy and France were among the top countries with the greatest number of BC incidences, indicating that other factors contribute to the development of cancer and survivorship.

In Italy, breast cancer is the most frequent neoplasm, with almost 55,000 new cases per year (23). As in the US, in Italy certain risk factors are associated with SES and location which determine access to screening and treatment (24). Rossi's (2020) time-trend study, conducted from 1990 to 2016, showed a decrease of age-standardized mortality rate in It-

aly. Additionally, in this study, various factors were taken into account, *e.g.*, fertility rates, routine and mammographic screenings, breastfeeding and mean age at birth. These factors were compared and contrasted among the various regions in Italy and trends indicated either a decrease or increase in BC incidence (24). For instance, southern regions saw a decrease in participation in mammographic screenings while in northern regions an increase was observed. Other factors analyzed that contribute to BC development were breastfeeding and mean age at birth, which both saw an increase throughout Italy (24). Certain risk factors that influence BC incidence outcome include the stage at diagnosis and access to effective and timely treatments, which are directly correlated to individual socioeconomic and geographic differences.

In Italy, there is drastic geographic inequality between the Northern and Southern regions. In recent years this gap has been reduced. Differences in mortality rate and prevalence of risk factors are diminishing between the north and the south (24). However, between 1990 and 2017, an increase in cancer death was observed, with BC being one of the major causes of cancer death among women. This increase was likely due to the progressive aging of the Italian population (25).

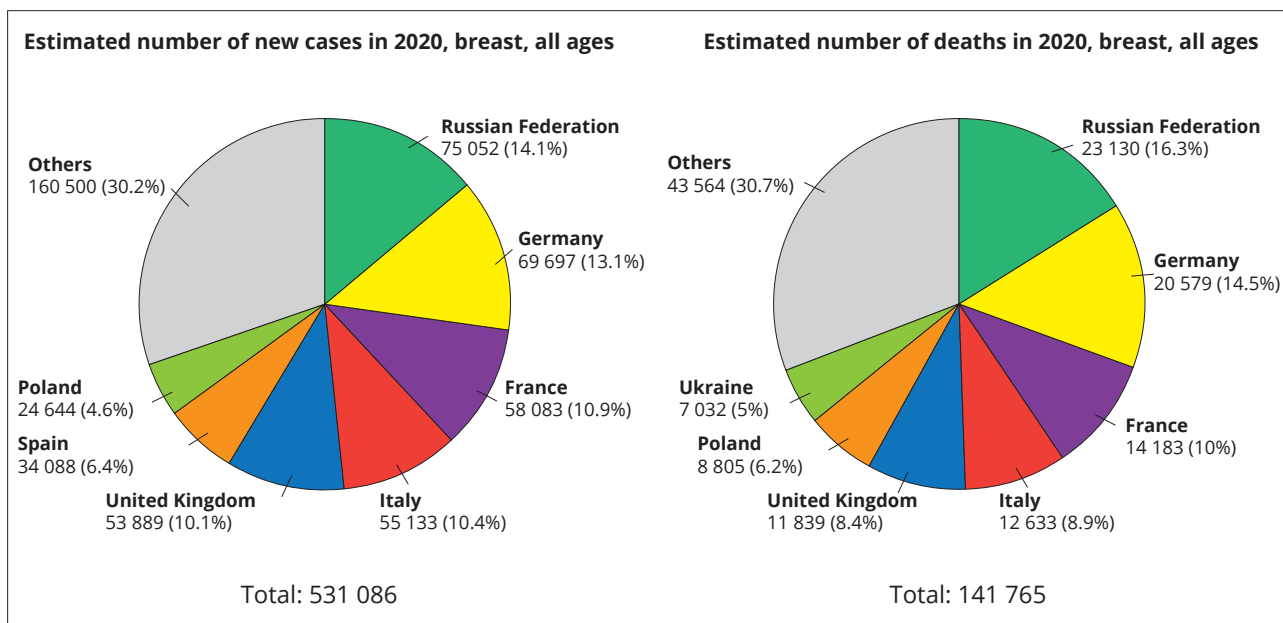
## FUTURE DIRECTIONS

Developments in personalized medicine should be encouraged and pursued. Specific areas such as accessibility to modern diagnostic technologies, improvements in surgery and introduction of innovative treatment approaches are critical to address BC and especially TNBC in order to give patients hope and thus improve their quality of life.

Previous shortcomings, *e.g.*, discrimination and inequality in treatment and therapeutics, may even further underline the need for the scientific community to collaborate globally in an effort to advance treatments that could benefit the individuals who need care, regardless of gender, race and ethnicity. The new era of personalized medicine in cancer therapy should be accessible to all.

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**Figure 4.** Estimated number of new cases and number of deaths caused by breast cancer in European women in 2020. Pie charts illustrating the incidence and mortality rates of breast cancer in women in different European countries. As observed, the estimated number of new cases in 2020 was most in the Russian Federation (14.1%), Germany (13.1%), France (10.9%) followed by Italy (10.4%) while the estimated number of deaths in 2020 showed a similar pattern with the Russian Federation (16.3%) showing the greatest percentage of mortality, followed by Germany (14.5%), Frances (10%) and Italy (8.9%). Pie chart taken from International Agency for Research on Cancer, 2020, WHO.

## ETHICS

### Fundings

This work was supported by the Sbarro Health Research Organization (SHRO).

### Conflict of interests

The authors have declared no conflict of interests.

### Availability of data and materials

The data underlying this article are available in the public domain, using various datasets primarily from Pubmed, GCO, SEER, etc.

### Authors' contribution

SB and AG worked on the conception of the work. SB worked on drafting and revising it critically for important intellectual content. AG provided approval for publication of content. SB and AG agree to be accountable for all aspects of the work.

### Ethical approval

Ethical approval was not necessary for this study because it does not involve patients.

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