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Reproductive, Lifestyle, and Socioeconomic Factors Shaping Global and Regional Breast Cancer Burden

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Abstract. Breast cancer (BC) is the most commonly diagnosed cancer among women worldwide, and its burden varies substantially across regions. Based on global disease burden research, cohort studies and meta-analysis evidence, this review analyzes how reproductive, lifestyle and socioeconomic factors affect the regional distribution of BC incidence, mortality and disability-adjusted life years (DALYs). Regions with a high Socio-demographic Index (SDI) generally report higher BC incidence. This may be related to the change in reproductive patterns, the prevalence of lifestyle risk factors and the high prevalence of screening. In contrast, low-resource settings often face limited screening, delayed diagnosis, and restricted access to treatment. In general, reproductive factors mainly affect BC risk through long-term hormone exposure. Lifestyle factors affect the risk of BC through metabolic and inflammatory pathways. Therefore, the prevention and treatment of BC should be carried out synchronously in combination with lifestyle intervention, reproductive health education, national screening and standardized diagnosis and treatment.

Keywords: Breast cancer, lifestyle, socioeconomic, reproductive factor

1. Introduction

Breast cancer (BC) is one of the most common malignant tumors recognized worldwide and the main cause of cancer death in women. It seriously threatens women's lifelong health and brings a heavy operational and economic burden to the global medical system. In recent years, its incidence has continued to rise, with an average annual increase of about 1% between 2012 and 2021 [1]. With the development of accurate prediction models and the application of advanced comprehensive treatment methods, remarkable progress has been made in the prevention and control of BC. Additionally, the overall survival rate of patients in areas with sufficient medical resources has been greatly improved. However, there are population and geographical differences in the survival benefits and control effects of BC. The disease burden in many regions around the world is still very heavy. These research results show that improving early screening path and improving the accessibility of high-quality medical services is of great significance for improving the prognosis of patients and reducing preventable BC deaths.

Although the overall mortality rate has decreased significantly, there are important differences in the prognosis of BC among women of different races, regions and socioeconomic levels. For

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example, the incidence of white women is 5% higher than that of black women, but the mortality rate is 38% lower [1]. In 2021, at the national and regional levels, the incidence of BC was positively correlated with the SDI (SDI), while the mortality rate and disability-adjusted life expectancy (DALY) rates showed an inverted V-shaped trend at the national level [2]. These differences are rooted in the unfair distribution of global medical and health resources. Population screening programs are widely used in high-income countries, and standardized treatment is highly reachable. Low-income countries face serious institutional obstacles in early screening and access to basic treatment, resulting in delayed diagnosis, late-stage symptoms at the time of treatment, and a significantly low survival rate of patients. Biological factors, social factors and medical system factors together cause this prognosis gap.

However, most existing studies only focus on individual-level factors such as fertility history and lifestyle behavior, and fail to relate these factors to the more macroscopic socio-economic background and public health policies, so they cannot fully explain the difference in the burden of BC in different regions. A full understanding of these regional differences is crucial for formulating targeted interventions and narrowing the unfair gap in the outcome of BC diagnosis and treatment. To this end, this literature review aims to sort out the existing research evidence of the burden of BC at the global and regional levels, and explore the impact mechanism of reproductive factors, lifestyle factors and socioeconomic factors on regional differences in BC. This review does not measure the amount of a single comprehensive effect, but compares the relevant conclusions of population-based studies, global disease burden analysis, cohort studies and meta-analysis, while focusing on the research differences brought about by exposure definitions, population background and medical environmental conditions.

2. The current situation of BC

2.1. Indicator definition and significance

The current situation of BC is usually described by indicators such as incidence, mortality, disability-adjusted life expectancy and age-standardization rate. These indicators help to understand the burden of disease and regional differences from multiple perspectives. Specifically, the incidence rate reflects the incidence of new cases of BC in a certain population in a specific period of time, which is a key indicator for measuring the risk of disease incidence and the trend of time change. Mortality reflects the burden of disease caused by the death of BC over time in a population, which can be used to assess the severity of the disease and the effectiveness of the treatment plan. The prevalence refers to the total number of existing BC patients in a certain population at a specific point in time or period. It reflects the overall size of existing cases and the ongoing burden of the disease. In comparison, the DALYs combine the loss of healthy life expectancy caused by premature death and disability, which is more suitable for a horizontal comparison of the overall burden of disease between different countries and regions. In order to improve the comparability of data between people with different age structures, the age-standardization rate is generally used in epidemiological studies.

In addition, some studies on the global burden of disease use socio-demographic indicators to stratify countries by level of development. The index is calculated by per capita income, education level, fertility rate and other indicators, which can be used to analyze the relationship between the BC burden and the level of socio-economic development. Therefore, these indicators reflect the incidence of the disease, the outcome of the death and the overall loss of health. In addition, they support cross-regional comparisons to build a comprehensive system for assessing the BC burden.

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2.2. Reason of the different BC distribution

From a global perspective, there are significant differences in the BC burden in different regions. Research evidence shows that the incidence and prevalence of BC are generally higher in areas with high SDI. In contrast, although the incidence rate is relatively low in some middle-sized demographic index areas, they often face problems such as insufficient diagnosis, insufficient case reporting and poor access to medical services [2]. At the same time, DALYs and mortality rate in different countries and regions show different trends [2]. This shows that the burden of BC is not only affected by the disease itself, but also closely related to the timing of the overall diagnosis and the allocation of medical resources.

From the national development level, early BC-related studies show that the higher the human development index, the higher the incidence of BC. This may be related to the higher prevalence of hormone-related and lifestyle-related risk factors, as well as the greater access to BC screening [3]. In terms of access and supply of medical services, a study conducted in the United States shows that there are significant differences in the incidence of BC, mortality and the prevalence of breast molybdenum target screening between states. These differences are closely related to demographic characteristics, the prevalence of BC risk factors, breast molybdenum target screening coverage, medical insurance policies and access to medical services [1].

In Asian countries, the level of medical system development, the implementation of national screening and the differences in diagnosis capacity will further affect the distribution characteristics of BC. The research by Weng et al. (2024) showed that among the 21 countries of the Asian National Cancer Alliance (ANCCA), only 12 countries have released national data on the age-standardized incidence (ASIR) and age-standardized mortality rate (ASMR) of BC, and each country is in screening methods, screening. There are significant differences in the coverage rate and the timeliness of diagnosis and treatment [4]. The above research results show that the regional differences in the prognosis of BC are not only due to the differences in epidemiological characteristics, but also reflect the imbalance between the cancer monitoring capacity and the operation level in various countries.

3. Risk factors for BC development

3.1. Reproductive factors

Reproductive factors can affect women's lifelong endogenous estrogen exposure level through menstruation and fertility patterns, which is an important reason for the difference in the burden of BC in the world and in various regions. This association is mainly dominated by menstrual characteristics and reproductive history, which together determine the cumulative exposure of estrogen in the human body. Increased estrogen exposure may affect the risk of BC to a certain extent through long-term hormonal stimulation of breast tissue. The earlier the menarche and the later the age of menopause, the longer the exposure to estrogen, which increases the risk of BC. The longer a woman's hormone exposure during the whole reproductive cycle will also increase the probability of malignant lesions in the breast tissue over time. A meta-analysis covering the global population in 2012 confirmed that for every year of menarche, the risk of BC increased by 5%; for every year of menopause, the risk of BC increased by 2.9% [5]. The high number of births also has a protective effect on BC. Many studies have consistently shown that the more births, the later the onset of BC. Specifically, the risk of BC can be reduced by 32% for women who have given birth 4 times or more [6]. The above research results show that the influence of reproductive-related factors

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is not only reflected in fertility, but also closely related to the number of births. It is worth noting that there are differences in the impact of such reproductive factors on different tumour subtypes, and their effect on lobular BC is more significant than that on ductal BC [5].

3.2. Lifestyles factors

Lifestyle factors are the determinants of the risk of BC that can be regulated and multi-dimensional. Existing research results consistently confirm that such factors can affect the course of BC alone or together. Among many lifestyle factors, the relationship between obesity and BC presents contradictory characteristics, and the association will change with menopause status and geographical differences [7]. A meta-analysis covering 102 observational studies found that obesity overall increases the risk of BC in postmenopausal women by 26%, and the impact is more significant in the Asian population; while in the premenopausal women, the relationship between the two is usually negatively correlated and not statistically significant, showing only in the European population. It has a statistically significant protective effect [7]. In addition to obesity, the current smoking habits are associated with a 3.3% increase in the annual incidence of early BC in women aged 40 to 49 [3]. A large cohort study by the British Biobank further shows that poor lifestyles such as unbalanced diet, smoking, alcohol consumption, lack of exercise, and abnormal body mass index can increase the risk of BC in postmenopausal women by 26% [8]. The above research results show that it is of great significance to reduce the global BC burden to carry out lifestyle interventions with obesity control, smoking cessation and increased exercise.

3.3. Socioeconomic factors

Socio-economic factors will further shape the distribution pattern of BC burden in different populations by affecting the screening, diagnosis and treatment of the population. A recent global study shows that the burden of BC in women of childbearing age is closely related to SDI [2]. At the global and national levels, the SDI is positively correlated with the incidence and prevalence of BC, but the correlation with mortality and DALY rate is more complex. The screening effect is one of the reasons for this phenomenon. Women in areas with high SDI usually have access to more complete screening and diagnosis services, which will improve the case detection rate and then increase the incidence and prevalence of statistical records. At the same time, the increase in the burden of BC in areas with medium and low levels of SDI is more significant, highlighting the long-standing health inequality among countries and regions [2]. Part of the reason is that women in areas with low SDI are often diagnosed with advanced cancer, and the paths for timely and effective treatment are more limited, which ultimately leads to poorer prognosis and heavier burden. In addition, between 1990 and 2021, the absolute inequality of BC burden continued to increase, which means that although the global relative disparity has released, resource-poor areas still bear a heavier disease burden [2]. Therefore, socio-economic factors should not only be regarded as the background variable of BC research, but also an important influencing factor that determines the distribution of disease burden and the difference in prognosis.

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4. Comparative synthesis of reproductive, lifestyle, and socioeconomic evidence

4.1. Rationale for synthesis strategy

To more accurately analyze the independent and joint effects of reproductive, lifestyle, and socioeconomic factors on BC risk and disease burden, ideal research should be conducted using unified population-based data and combine with registry data or Electronic Health Records (EHR) [2, 9]. Under the same data framework, the definitions of exposure and outcome, stratification by menopausal status, and confounder adjustment methods can be unified. Firstly, this can make the comparison of relative effects between different factors clearer. Secondly, overall influence on treatment outcomes and the distribution of disease burden can be analyzed deeper.

However, this research only uses outcomes from published papers rather than original individual-level data from a single source. Different studies have differences in population scope, exposure definition, reference group setting, menopausal status stratification, and covariate adjustment. So, it is not suitable to conduct strict total effect estimation or unified joint model analysis. Based on this point, this review will use a narrative comparative synthesis. First, this review evaluates the comparability among current studies, and then integrate qualitative comparison with semi-quantitative evidence synthesis to discuss how different factors might influence BC risk and disease burden differences. This may inform future population-based studies with unified original data.

4.2. Comparative assessment of parity-related evidence

Current research overall supports that higher parity is associated with a lower BC risk. However, due to differences in exposure definition, reference group setting, and menopausal status stratification across different studies, current evidence is more suitable for comparative assessment rather than directly strict pooled effect analysis. Song et al. found that women with parity ≥ 4 had a significantly lower BC risk, with an adjusted HR of 0.69 （95% CI: 0.49–0.98） [6]. Takeuchi et al. also reported, after performing a pooled analysis of nine Japanese population cohorts, that in postmenopausal women, parity ≥3 was negatively associated with BC risk compared to nulliparous women, with an adjusted HR of 0.63 and a statistically significant overall trend (P for trend: 0.03) [9]. A population-based cohort study by Wang et al. also indicated a negative relationship between parity and BC incidence, and reported that adjusted HR is 0.63 when parity was treated as an ordinal categorical variable [10]. Overall, current evidence consistently shows that higher parity has a certain protective effect against BC. However, the magnitude of effect requires further validation within a more unified data framework regarding exposure definitions and population stratification (Table 1).

Table 1. Methodological comparison of parity-related evidence across included studies

Study	Population	Exposure definition	Reference group	Adjusted HR (95% CI)	Key comparability issue
Song 2025	US women ≥35 years	>4 deliveries	≤4 deliveries	0.69 (0.49–0.98)	Overall women, not menopausal-specific
Wang 2022	Population-based cohort	Parity (ordinal: 0, 1–3, ≥4 children)	Per one-category increase	0.63 (0.44–0.91)	Ordinal parity effect, not directly equivalent to binary comparisons in the other studies

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Table 1. (continued)

Takeuchi 2021	Japanese postmenopausal women	≥3 births	Nulliparous	0.63 (0.39–1.04)	Postmenopausal subgroup only

4.3. Cross-factor comparison of lifestyle and socioeconomic evidence

Compared with reproductive factors, lifestyle and socioeconomic factors have stronger heterogeneity in relative evidence. Therefore, it is more suitable to use comparative synthesis rather than formal pooled analysis. Among lifestyle factors, current studies mostly showed that obesity, physical inactivity, sedentary behaviour, smoking, and some unhealthy dietary patterns are associated with higher BC risk. However, obvious variations exist across studies in terms of exposure definitions, comparison methods, and populations. For instance, the association between obesity and BC risk is more significantly influenced by menopausal status. Postmenopausal women often show a higher risk, while premenopausal women have a more complex pattern [7]. Besides, current smoking is associated with increased early-onset BC incidence [3]. In addition, healthier overall lifestyle patterns are associated with lower postmenopausal BC risk [8]. In some studies, sedentary behaviour [10], high perceived stress, and certain unhealthy dietary patterns also indicate a higher risk [11]. Overall, current lifestyle evidence better supports directional conclusions, meaning multiple modifiable and preventable factors may collectively contribute to higher BC risk. Furthermore, the specific effect size of these factors remains difficult to uniformly quantify based on current studies.

Regarding socioeconomic factors, current evidence indicates their effects are more likely observed in risk distribution, case detection, diagnosis, and disease burden variations, instead of only influencing disease occurrence. Some cohort studies indicate that higher education levels are related to higher BC incidence risk [12]. However, this pattern may partly reflect differences in screening uptake, access to diagnostic services, reproductive patterns, and lifestyle factors, rather than a direct biological effect [2]. From the analysis of SDI and burden patterns earlier, socioeconomic factors influence the distribution of BC burden among different populations through screening, diagnosis, treatment access, and health inequalities. Therefore, similar to lifestyle factors, current evidence on socioeconomic factors is more suitable for explanation via mechanisms of action and social structure, rather than being used directly to produce a single pooled estimate.

4.4. Implications for BC burden

Reproductive, lifestyle and socioeconomic factors jointly contribute to BC disease burden through hormonal pathways, metabolic-inflammatory pathways and healthcare access pathways. Reproductive factors are primarily associated with long-term hormonal exposure and underlying genetic susceptibility, while lifestyle factors highlight the cumulative risk effect of modifiable behaviours like smoking and sedentary behaviours. In contrast, socioeconomic factors shape the distribution of BC burden across different populations and regions via screening, diagnostic and treatment access. Therefore, BC disease burden reflects the combined effect of reproductive, lifestyle, and socioeconomic factors rather than a single cause.

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5. Public health implications and prevention strategies

BC prevention and control require differentiated strategies aligned with regional social development levels. In high-SDI regions that face relatively high BC incidence, priority should be given to lifestyle intervention, obesity management, physical activity promotion and reproductive health education. These measures are especially applicable to areas with late marriage and late childbearing, low fertility, common sedentary lifestyle and high obesity rate. In areas with medium SDI, policy work should focus on expanding screening coverage, improving early diagnosis capacity, and improving the public's awareness of BC symptoms and risk factors. In areas with low SDI, in order to reduce BC mortality and disability adjustment life expectancy, it is necessary to improve the tumour registration system, provide affordable diagnostic services, ensure access to basic treatment, and establish a referral network for severe cases. However, if access to medical services is not improved at the same time, it is difficult to significantly reduce mortality by relying on health education alone. Overall, these targeted strategies require cross-sectoral collaboration from relevant health, education and government departments to effectively reduce the global BC burden.

6. Conclusion

The regional differences in BC burden are formed by the combination of reproductive factors, lifestyle factors and socio-economic factors. In high-income areas, late childbearing and reduced breastfeeding rates are more common, and reproductive factors seem to have a relatively important impact in such areas. Lifestyle factors such as obesity and lack of exercise can aggravate BC burden in different regions. Socio-economic factors such as limited screening and treatment pathways in poor areas have further increased regional difference. Various factors together cause the uneven distribution of BC burden, and vulnerable areas are under heavier disease pressure. This review is limited by heterogeneity in study design, exposure definitions, and analytical methods. Future studies using harmonized population-based data are needed to clarify how these factors interact and to inform more targeted prevention strategies.

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