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ORIGINAL ARTICLE

Global patterns, temporal trends and socioeconomic inequalities in the burden of breast cancer: a population-based study across 185 countries

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ABSTRACT

Objective: Breast cancer is the most frequently diagnosed cancer among women worldwide and is a leading cause of cancer-related deaths. Comparative assessments of breast cancer lifetime risks across populations are limited. This study estimated the global, regional, and national lifetime risks, temporal trends, and socioeconomic inequalities in the burden of breast cancer.

Methods: Using incidence and mortality data from GLOBOCAN 2022 (185 countries) and United Nations population and all-cause death data, lifetime risks were calculated using the adjusted for multiple primaries (AMP) method, which could adjust for multiple primary cancers, competing risks of other causes death, and life expectancy. Longitudinal data of breast cancer incidence from 2003–2017 were retrieved from the Cancer Incidence in Five Continents (CI5) Plus database. The temporal trends for breast cancer deaths were abstracted from the WHO Mortality Database. The lifetime risk of developing and dying from breast cancer were analyzed by socioeconomic characteristics, 20 predefined geographic regions and menopausal status.

Results: The overall worldwide lifetime risk of developing and dying from breast cancer was 5.51% (95% CI: 5.50%–5.52%) and 1.82% (95% CI: 1.82%–1.83%) in 2022, respectively. The estimated lifetime risks of developing breast cancer had a positive relationship with Human Development Index (HDI) levels and corresponding risks of 10.37%, 4.42%, 2.96%, and 2.91% in very high, high, middle, and low HDI regions, respectively. Very high HDI regions presented the highest lifetime risk of breast cancer death (2.70%), followed by low HDI (1.70%), medium HDI (1.54%), and high (1.38%) HDI regions. A significant correlation was identified between lifetime risks and health economics capacity. The lifetime risk of developing and dying from breast cancer primarily involved individuals ≥ 55 years of age with remaining risks of 3.77% (developing) and 1.43% (dying) from 55 years to death. The proportion of lifetime risks among individuals 0–44 years of age was higher in Africa regions compared to other regions. In surveillance data from 36 countries, a significant increasing trend in the average annual percentage change (AAPC) was noted in 32 countries, which ranged from 0.17% in the United States to 5.84% in the Republic of Korea.

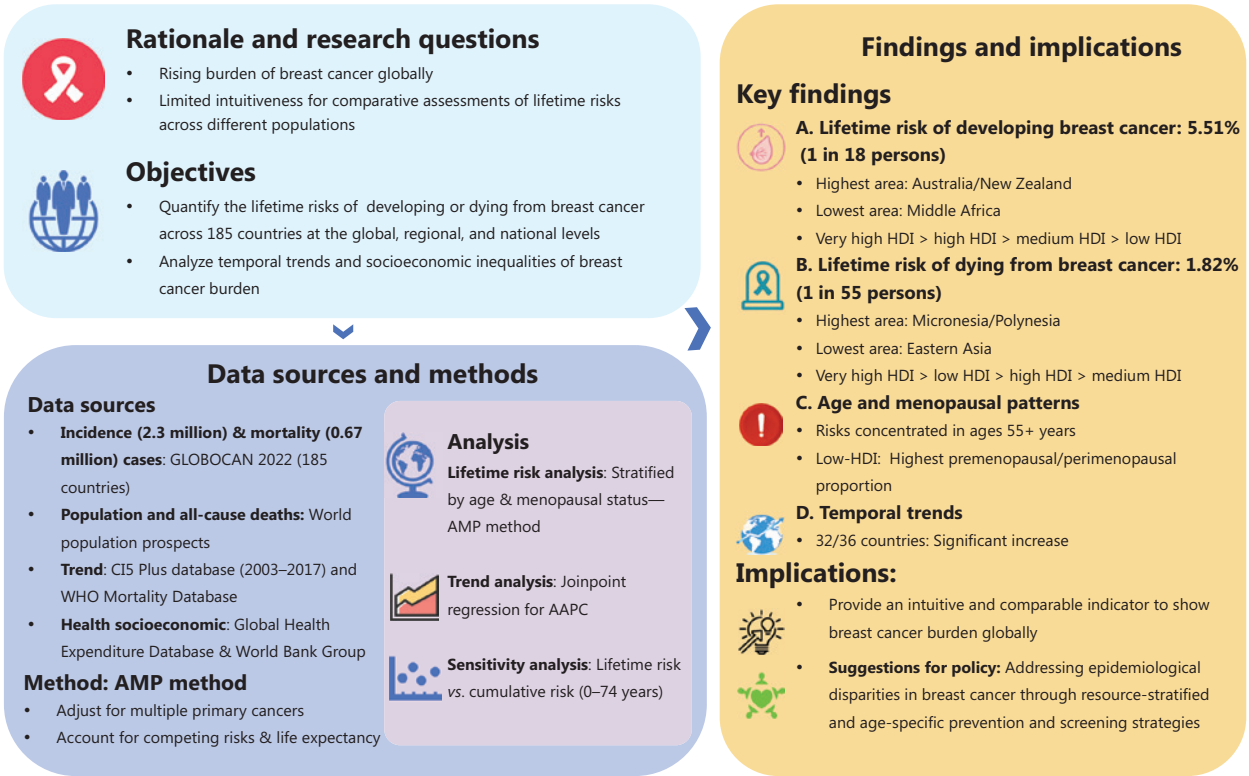
Conclusions: Globally, an estimated 1 in 18 individuals were diagnosed with breast cancer during their lifetime and approximately 1 in 55 died from the disease in 2022. Lifetime risk of breast cancer disparities reveal the socioeconomic inequalities of breast cancer. Therefore, country-tailored intervention plans for breast cancer require prioritization within precision prevention to mitigate global breast cancer inequities and burden.

KEYWORDS Breast cancer; lifetime risk; disease burden; incidence; mortality

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Introduction

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related mortality worldwide in females, comprising 23.8% of new cancer cases and 15.4% of cancer-related deaths[1,2]. In 2022, there were 2.3 million women diagnosed with breast cancer and 0.67 million deaths globally[3]. Breast cancer exerts profound multidimensional



Study Flowchart Data were obtained from GLOBOCAN 2022 (185 countries), United Nations population and all-cause mortality data from WHO, and longitudinal data on breast cancer incidence between 2003 and 2017 from CI5 Plus database. The AMP method was used to calculate lifetime risk, which accounts for multiple primary cancers, competing risks from other causes of death, and life expectancy. Analyses estimated lifetime risk across different global regions, countries, age groups, socioeconomic conditions, and menopausal status. The findings showed that the lifetime risk of developing breast cancer was 5.51% and dying from breast cancer was 1.82%. Epidemiologic disparities of breast cancer were noted in different HDI regions and healthcare resource countries globally with pronounced heterogeneity. Countries should implement precise prevention and control measures based on their respective health resources and risk profiles to reduce the global burden of breast cancer. Figure created using Microsoft Office PowerPoint and Adobe Illustrator. (AAPC, average annual percentage change; AMP method, adjusted for multiple primaries method; CI5, cancer incidence in five continents; HDI, Human Development Index).

impacts that extend beyond physical health, affecting patients' psychological, emotional, and social well-being, as well as that of their families, throughout the disease trajectory[4]. Breast cancer is a hormone-dependent malignancy of the mammary gland, exhibiting distinctly different molecular characteristics, molecular subtypes, and etiologic factors across menopausal status[5]. Because of variations in risk factors, geography, socioeconomic fabric, and accessibility to health resources across different regions, global estimates have revealed significant inequities in the breast cancer burden according to human development[6].

Accurate quantification of the global breast cancer burden at the population level is essential for developing evidence-based healthcare policies and prevention and control programs, particularly in resource-limited areas where competing priorities and systemic constraints exacerbate health disparities[7]. The lifetime risk of breast cancer represents the cumulative probability of developing or dying from breast cancer during an individual's remaining life course (usually from a given age until death)[8,9]. This indicator offers an intuitive longitudinal visualization of the global epidemiologic pattern in a population, while accounting for competing death causes and multiple primary cancers and variations in life expectancy[10]. Estimating the lifetime probability of breast cancer across regions, age groups, menopausal status, and socioeconomic levels could effectively enable more intuitive health communication and assess the impact and efficacy of breast cancer prevention and control strategies. Some studies have reported the lifetime probability of developing cancer worldwide[7,9,11]. However, evidence gaps persist in landscape of lifetime breast cancer risk globally.

This study used the adjusted for multiple primaries (AMP) method to quantify the lifetime risk of developing and dying from breast cancer across 185 countries using GLOBOCAN

2022 data. The global patterns and temporal trends in breast cancer using lifetime risk combined with traditional metrics, including incidence and mortality rates stratified by age, menopausal status, health socioeconomic level, and geographic region, are presented. This study will provide critical information for shaping resource-tailored breast cancer prevention and control policies, ultimately aiming to mitigate the global burden through optimized resource allocation and health system strengthening.

Materials and methods

Data source

New cases and deaths from breast cancer were collected from GLOBOCAN 2022 and classified by age group in 5-year increments (0–4, 5–9, ..., 80–84, and 85+ years of age)[1,2]. Breast cancer was defined as C50 according to the 10th revision of the International Classification of Diseases (ICD-10). Data on population size and all-cause deaths were sourced from the United Nations (World Population Prospects 2019)[12]. The global population was stratified into 20 predefined geographic regions, as classified by the 2019 Revision of World Population Prospects[12]. The Human Development Index (HDI) serves as a composite metric summarizing the following key dimensions of development: longevity, education, and standard of living. The countries were categorized in four levels based on the HDI classification from Human Development Reports, as follows: very high HDI (≥ 0.800), high HDI (0.700–0.799), medium HDI (0.550–0.699), and low HDI (< 0.550)[13]. The HDI was obtained from the United Nations Development Programme[13]. Health spending indicators serve as vital instruments for monitoring resource flows, informing health policy formulation, and enhancing health system transparency and accountability. Country-level health economic variables, including the Universal Health Coverage (UHC) Index, Current Health Expenditure (CHE) per capita, CHE as a percentage of Gross Domestic Product (GDP), Domestic General Government Health Expenditure per capita (GGHE-D), GGHE-D as a percentage of CHE, and GGHE-D as a percentage of General Government Expenditure (GGE), were extracted from the Global Health Expenditure Database (GHED) and World Bank Group to describe the landscape of economies and breast cancer lifetime risk[14,15].

Breast cancer data spanning 2003–2017 were extracted from the Cancer Incidence in Five Continents (CI5) Plus database for trend analyses of breast cancer lifetime risk[16]. The temporal trends for breast cancer death were abstracted from the WHO Mortality Database[17]. Following the exclusion of registries with incomplete age-specific and population data, the breast cancer incidence datasets from 36 countries which met quality criteria were included for the trend analysis. The Ethical Committees of the Fourth Hospital of Hebei Medical University, the National Cancer Center/Cancer Hospital, the Chinese Academy of Medical Sciences, and Peking Union Medical College waived the need for ethical approval or informed consent for this study.

Statistical analysis

The AMP method was used to calculate the lifetime risk of breast cancer, which takes into account other competing causes deaths and adjusts for the inclusion of multiple primary cancers in the incidence or mortality rates[10,18]. The breast cancer incidence, mortality, and all-cause mortality rates in 5-year age groups were used to estimate the lifetime risk of developing or dying from breast cancer at different ages. The method of probability of being diagnosed with breast cancer was calculated as follows:

$$S = \int_0^{\infty} \lambda_c(a)\hat{S}_0^*(a)da = \sum_{i=1}^{f} \frac{R_i}{R_i + M_i - D_i} \hat{S}_0^*(a_i) \times \left(1 - \exp\left(-\frac{W_i}{N_i}\left(R_i + M_i - D_i\right)\right)\right)$$

For age group i, S represents the probability of being diagnosed with or dying from breast cancer, λ_c represents the cancer incidence rate, $\hat{S}_0^*(a_i)$ represents the probability of being alive and free of cancer at age a_i, R_i signifies the breast cancer case or death count, M_i represents the annual death count, D_i represents the annual death count due to breast cancer, and W_i represents the span of age group i. The 95% confidence interval (CI) of lifetime risk was estimated based on the Poisson method. Additional details regarding this method of estimating the lifetime risk of developing or dying from breast cancers are provided in the **Supplementary materials**.

The lifetime risk of breast cancer across different age intervals, menopause status, HDI levels, and various economic indicators at the global, regional, and national levels were calculated in this study. Associations between the HDI and socioeconomic health indicators with lifetime risk of breast cancer were assessed using restricted cubic spline regression to capture potential non-linear relationships[19]. Cumulative risk refers to the probability of developing a particular disease within a specified age range assuming no other causes of death and is often calculated for 0–74 years of age as an indicator of cancer burden. Therefore, the lifetime risk of developing or dying from breast cancer was compared to the cumulative risk (0–74 years of age) in the sensitivity analysis. Joinpoint regression was performed using Joinpoint software (version 5.4.0.0; National Cancer Institute, Rockville, MD, USA) to estimate temporal trends and the models allowed for up to 3 segments (2 join-points). The average annual percentage change (AAPC) was also estimated and whether the fluctuation trend in different parts was statistically significant was investigated by comparing the AAPC to zero. Menopausal status is not routinely recording in cancer registry data, necessitating the use

of age as a proxy measure. The menopause status of females (pre-, peri-, and post-menopause) was defined as chronological age < 45 years, 45–54 years, and ≥ 55 years, respectively[20,21]. Other analyses were performed SAS software (version 9.4; SAS Institute, Cary, NC, USA) and R software (version 4.3.0; R Foundation for Statistical Computing, Vienna, Austria).

Results

Global, regional, and national lifetime risks of developing breast cancer

The overall global lifetime risks of developing breast cancer from birth to death was 5.51% (95% CI: 5.50%–5.52%). Therefore, 1 in 18 persons was diagnosed with breast cancer. **Table 1** demonstrates the probability of developing breast cancer within different age intervals globally. Among the 20 aggregated world regions, Australia/New Zealand had the highest lifetime risk of developing breast cancer (14.98%, 95% CI: 14.77%–15.18%), followed by Western Europe (13.65%, 95% CI: 13.58%–13.72%), Northern Europe (13.15%, 95% CI: 13.05%–13.25%), and North America (12.89%, 95% CI: 12.84%–12.95%). Middle Africa had the lowest lifetime risk of developing breast cancer (2.16%, 95% CI: 2.09%–2.23%; **Table 1 and Figure 1**). At a national level, Luxembourg had the highest lifetime risk of being diagnosed with breast cancer (16.62%, 95% CI: 15.03%–18.21%), followed by France (15.49%, 95% CI: 15.36%–15.62%), Australia (15.24%, 95% CI: 15.01%–15.47%), Belgium (14.91%, 95% CI: 14.60%–15.22%), and Cyprus (14.43%, 95% CI: 13.40%–15.46%). Among the world's 185 countries, 3 have a lifetime risk of developing breast cancer < 1%: Angola (0.77%, 95% CI: 0.68%–0.86%); Sierra Leone (0.54%, 95% CI: 0.42%–0.66%); and Bhutan (0.49%, 95% CI: 0.17%–0.81%) (**Table S1**).

Substantial disparities in breast cancer lifetime risk exist across the HDI levels with risk increasing at higher HDI levels (**Table 1 and Figure 2**). In countries with a very high HDI, the lifetime breast cancer risk was 10.37% (95% CI: 10.35%–10.39%). Therefore, 1 in 10 individuals was be diagnosed with breast cancer in their lifetime. In contrast, only 1 in 34 individuals in countries with a low HDI level was be diagnosed with breast cancer in their lifetime (**Table 1**). Health economics indicators also demonstrated positive associations with lifetime breast cancer risk, in which higher values correlated with higher risks. Conversely, fertility rate exhibited an inverse association with lifetime breast cancer risk (**Figures S2-S9**).

Global, regional, and national lifetime risks of dying from breast cancer

The overall global lifetime risk of dying breast cancer from birth to death was 1.82% (95% CI: 1.82%–1.83%); 1 in 55 women died from breast cancer. In the 20 regions worldwide, the regions with the highest lifetime risk of dying breast cancer were Micronesia/Polynesia (4.90%, 95% CI: 3.68%–6.12%), followed by Western Europe (3.87%, 95% CI: 3.83%–3.91%), Southern Europe (3.35%, 95% CI: 3.32%–3.39%), Northern Europe (3.25%, 95% CI: 3.20%–3.30%), and Australia/New Zealand (3.13%, 95% CI: 3.04%–3.23%) (**Table 1**). The highest lifetime risk of dying from breast cancer occurred in the Bahamas (5.83%, 95% CI: 3.96%–7.70%), based on an analysis of 185 countries worldwide in 2022. A high lifetime risk of dying from breast cancer also existed in French Polynesia, Guam, Barbados, Cyprus, and Iceland. Conversely, there were four countries, including Mongolia, Angola, Sierra Leone, and Bhutan, where the probability of dying from breast cancer was estimated to be < 0.5% (**Table S1**).

Significant variations in the lifetime risk of breast cancer-associated death were noted across regions stratified by HDI levels (**Table 1 and Figure 2**). Very high HDI regions exhibited the highest lifetime risk of breast cancer-associated deaths (2.70%, 95% CI: 2.69%–2.71%); 1 in 37 women died from breast cancer. The lifetime risk of dying from breast cancer in regions with a low HDI regions was 1.70% (95% CI: 1.68%–1.73%), followed by medium and high HDI regions with lifetime risks of 1.54% (95% CI: 1.53%–1.55%) and 1.38% (95% CI: 1.38%–1.39%), respectively. Significant variations also emerged for select health economic indicators. Specifically, higher fertility rates were associated with reduced lifetime risks of dying from breast cancer (**Figures S2-S9**).

Lifetime risks of developing and dying from breast cancer according to age at diagnosis and menopausal status

The risk of developing or dying from breast cancer decreased with age. The lifetime risk of being diagnosed with or dying from breast cancer was 5.11% (95% CI: 5.09%–5.13%) and 1.74% (95% CI: 1.73%–1.75%) after 40 years of age, and 4.31% (95% CI: 4.29%–4.33%) and 1.57% (95% CI: 1.56%–1.58%) after 50 years of age, respectively (**Tables 1, S5 and Figure S10**). The lifetime risks were mainly concentrated in individuals ≥ 55 years of age (postmenopausal breast cancer). However, significant regional and country variations in risk distribution have been observed across different geographic areas. The lifetime risk of developing breast cancer had a positive correlation with increasing HDI level. The proportion of lifetime risk attributable to premenopausal (diagnosed at ≤ 44 years of age) and perimenopausal breast cancer (diagnosed between 45 and 54 years of age) was highest in regions with a low HDI. In contrast, the proportion of lifetime risk attributable to postmenopausal breast cancer (≥ 55 years of age) exhibited an inverse pattern, increasing from 56.70% in low HDI regions to 71.94% in very high HDI regions (**Tables S2 and S3**). The contributions of premenopausal breast cancer (0–44 years of

Table 1 Epidemiology of developing and dying from breast cancer within selected age intervals in 2022

Population	Cases (*n*)	ASR (per 100,000)	Birth to death (%)	40 years to death (%)	50 years to death (%)	60 years to death (%)	70 years to death (%)
Developing breast cancer							
World	2,294,713	46.80 (46.74–46.86)	5.51 (5.50–5.52)	5.11 (5.09–5.13)	4.31 (4.29–4.33)	3.18 (3.16–3.20)	1.91 (1.89–1.93)
Very high HDI	1,092,663	75.63 (75.48–75.79)	10.37 (10.35–10.39)	9.70 (9.65–9.75)	8.40 (8.35–8.44)	6.41 (6.36–6.45)	4.07 (4.03–4.11)
High HDI	737,959	38.79 (38.70–38.88)	4.42 (4.41–4.44)	4.01 (3.99–4.04)	3.20 (3.17–3.23)	2.16 (2.14–2.19)	1.13 (1.11–1.15)
Medium HDI	329,052	29.53 (29.43–29.63)	2.96 (2.94–2.97)	2.67 (2.64–2.71)	2.16 (2.13–2.19)	1.44 (1.41–1.47)	0.73 (0.70–0.75)
Low HDI	135,039	34.31 (34.12–34.50)	2.91 (2.88–2.94)	2.55 (2.49–2.61)	2.00 (1.95–2.06)	1.28 (1.22–1.33)	0.60 (0.55–0.65)
Eastern Africa	47,244	31.94 (31.64–32.24)	2.88 (2.83–2.93)	2.54 (2.44–2.63)	2.03 (1.94–2.13)	1.34 (1.25–1.43)	0.66 (0.57–0.74)
Middle Africa	14,939	26.69 (26.25–27.14)	2.16 (2.09–2.23)	1.87 (1.73–2.01)	1.47 (1.33–1.61)	0.95 (0.82–1.08)	0.45 (0.33–0.57)
Northern Africa	64,822	53.17 (52.76–53.59)	5.38 (5.32–5.44)	4.69 (4.56–4.81)	3.57 (3.44–3.69)	2.20 (2.08–2.32)	1.06 (0.95–1.16)
Southern Africa	15,815	46.16 (45.43–46.89)	3.90 (3.78–4.03)	3.60 (3.37–3.83)	2.95 (2.72–3.17)	2.03 (1.81–2.25)	1.09 (0.89–1.30)
Western Africa	54,402	42.14 (41.77–42.52)	3.12 (3.06–3.19)	2.76 (2.65–2.88)	2.16 (2.05–2.28)	1.36 (1.25–1.47)	0.63 (0.53–0.73)
Eastern Asia	480,019	37.54 (37.43–37.65)	4.60 (4.59–4.62)	4.24 (4.21–4.27)	3.37 (3.34–3.41)	2.32 (2.29–2.35)	1.29 (1.26–1.32)
South-Eastern Asia	168,536	41.73 (41.53–41.93)	4.48 (4.45–4.51)	4.05 (3.98–4.11)	3.24 (3.18–3.30)	2.14 (2.08–2.20)	1.11 (1.06–1.17)
South-Central Asia	273,902	26.70 (26.60–26.80)	2.68 (2.66–2.69)	2.41 (2.38–2.45)	1.95 (1.91–1.98)	1.29 (1.26–1.32)	0.64 (0.61–0.67)
Western Asia	62,936	45.40 (45.04–45.76)	5.37 (5.31–5.43)	4.88 (4.76–5.00)	4.02 (3.90–4.13)	2.81 (2.70–2.93)	1.59 (1.48–1.69)
Eastern Europe	163,474	58.30 (57.99–58.61)	6.75 (6.71–6.79)	6.21 (6.12–6.31)	5.23 (5.14–5.32)	3.75 (3.67–3.84)	2.00 (1.92–2.07)
Northern Europe	89,057	90.80 (90.14–91.47)	13.15 (13.05–13.25)	12.50 (12.29–12.71)	10.99 (10.78–11.20)	8.45 (8.26–8.65)	5.44 (5.27–5.62)
Southern Europe	125,303	81.76 (81.25–82.28)	11.59 (11.51–11.66)	10.74 (10.58–10.90)	9.20 (9.04–9.35)	7.05 (6.91–7.20)	4.65 (4.52–4.78)
Western Europe	180,039	89.81 (89.33–90.29)	13.65 (13.58–13.72)	12.83 (12.68–12.98)	11.28 (11.14–11.43)	9.05 (8.91–9.19)	6.25 (6.13–6.38)
Caribbean	14,422	49.57 (48.73–50.41)	6.19 (6.05–6.32)	5.66 (5.38–5.94)	4.89 (4.62–5.16)	3.78 (3.52–4.04)	2.41 (2.18–2.65)
Central America	39,835	38.28 (37.90–38.66)	4.61 (4.54–4.67)	4.20 (4.07–4.32)	3.51 (3.38–3.63)	2.53 (2.41–2.65)	1.50 (1.39–1.61)
Northern America	306,198	95.12 (94.76–95.49)	12.89 (12.84–12.95)	12.19 (12.08–12.31)	10.67 (10.56–10.79)	8.19 (8.08–8.30)	5.14 (5.04–5.24)
South America	165,427	57.16 (56.87–57.44)	6.91 (6.87–6.95)	6.33 (6.24–6.42)	5.38 (5.29–5.47)	3.98 (3.89–4.07)	2.35 (2.28–2.43)
Australia/New Zealand	25,786	100.28 (98.96–101.59)	14.98 (14.77–15.18)	14.26 (13.82–14.69)	12.56 (12.13–12.99)	9.81 (9.41–10.22)	6.48 (6.12–6.85)
Melanesia	2,294	49.21 (47.15–51.28)	4.89 (4.51–5.28)	4.36 (3.66–5.07)	3.51 (2.81–4.21)	2.36 (1.68–3.03)	1.20 (0.58–1.82)
Micronesia/Polynesia	263	67.61 (59.31–75.91)	10.54 (8.89–12.19)	9.98 (6.96–13.01)	8.76 (5.79–11.74)	7.00 (4.13–9.86)	5.05 (2.40–7.70)

Table 1 Continued

Population	Cases (*n*)	ASR (per 100,000)	Birth to death (%)	40 years to death (%)	50 years to death (%)	60 years to death (%)	70 years to death (%)
Dying from breast cancer							
World	665,255	12.64 (12.60–12.67)	1.82 (1.82–1.83)	1.74 (1.73–1.75)	1.57 (1.56–1.58)	1.28 (1.27–1.29)	0.91 (0.90–0.92)
Very high HDI	245,043	13.21 (13.15–13.27)	2.70 (2.69–2.71)	2.64 (2.61–2.66)	2.47 (2.45–2.49)	2.17 (2.14–2.19)	1.71 (1.69–1.73)
High HDI	195,347	9.50 (9.46–9.55)	1.38 (1.38–1.39)	1.32 (1.31–1.34)	1.17 (1.16–1.19)	0.93 (0.92–0.95)	0.63 (0.61–0.64)
Medium HDI	152,881	13.88 (13.81–13.95)	1.54 (1.53–1.55)	1.46 (1.43–1.48)	1.27 (1.25–1.29)	0.95 (0.92–0.97)	0.55 (0.53–0.58)
Low HDI	71,984	19.11 (18.97–19.25)	1.70 (1.68–1.73)	1.56 (1.51–1.60)	1.29 (1.24–1.33)	0.87 (0.83–0.92)	0.44 (0.40–0.48)
Eastern Africa	25,300	17.58 (17.36–17.81)	1.63 (1.59–1.67)	1.48 (1.40–1.55)	1.21 (1.14–1.29)	0.82 (0.75–0.89)	0.41 (0.35–0.48)
Middle Africa	8,261	15.26 (14.91–15.60)	1.27 (1.22–1.33)	1.14 (1.03–1.25)	0.93 (0.82–1.04)	0.62 (0.52–0.73)	0.31 (0.21–0.40)
Northern Africa	23,137	19.00 (18.75–19.25)	2.34 (2.29–2.39)	2.16 (2.07–2.25)	1.85 (1.76–1.94)	1.43 (1.34–1.51)	0.93 (0.85–1.01)
Southern Africa	5,693	16.57 (16.14–17.01)	1.56 (1.46–1.66)	1.47 (1.32–1.63)	1.29 (1.13–1.45)	1.01 (0.85–1.16)	0.71 (0.56–0.85)
Western Africa	28,354	22.55 (22.27–22.82)	1.72 (1.67–1.77)	1.55 (1.46–1.64)	1.25 (1.17–1.34)	0.82 (0.74–0.91)	0.40 (0.32–0.47)
Eastern Asia	97,389	6.52 (6.48–6.57)	1.13 (1.13–1.14)	1.10 (1.09–1.12)	1.00 (0.99–1.02)	0.82 (0.81–0.84)	0.59 (0.58–0.61)
South-Eastern Asia	61,228	14.85 (14.73–14.97)	1.91 (1.89–1.94)	1.82 (1.78–1.87)	1.60 (1.56–1.64)	1.23 (1.19–1.27)	0.79 (0.75–0.83)
South-Central Asia	135,348	13.41 (13.34–13.48)	1.49 (1.48–1.51)	1.42 (1.40–1.45)	1.24 (1.22–1.27)	0.92 (0.90–0.95)	0.52 (0.50–0.55)
Western Asia	21,183	15.11 (14.90–15.31)	2.24 (2.20–2.28)	2.13 (2.05–2.21)	1.90 (1.82–1.97)	1.52 (1.45–1.60)	1.07 (1.00–1.14)
Eastern Europe	49,973	14.44 (14.30–14.58)	2.10 (2.07–2.12)	2.03 (1.98–2.08)	1.87 (1.82–1.91)	1.54 (1.49–1.59)	1.02 (0.98–1.07)
Northern Europe	18,575	13.70 (13.46–13.93)	3.25 (3.20–3.30)	3.19 (3.10–3.28)	3.04 (2.95–3.13)	2.74 (2.65–2.83)	2.28 (2.20–2.36)
Southern Europe	31,594	13.81 (13.62–14.00)	3.35 (3.32–3.39)	3.30 (3.23–3.37)	3.14 (3.07–3.21)	2.83 (2.76–2.89)	2.35 (2.29–2.41)
Western Europe	44,368	15.37 (15.20–15.55)	3.87 (3.83–3.91)	3.80 (3.73–3.87)	3.64 (3.57–3.70)	3.32 (3.26–3.39)	2.79 (2.73–2.85)
Caribbean	5,778	18.17 (17.68–18.67)	2.80 (2.70–2.90)	2.68 (2.50–2.86)	2.43 (2.25–2.61)	2.02 (1.85–2.19)	1.51 (1.35–1.66)
Central America	10,670	10.05 (9.86–10.25)	1.44 (1.40–1.48)	1.38 (1.31–1.45)	1.23 (1.16–1.30)	0.96 (0.89–1.03)	0.65 (0.59–0.71)
Northern America	49,727	12.32 (12.20–12.45)	2.59 (2.56–2.62)	2.54 (2.49–2.58)	2.39 (2.35–2.44)	2.11 (2.06–2.15)	1.69 (1.65–1.73)
South America	43,253	13.80 (13.67–13.93)	2.08 (2.06–2.11)	2.00 (1.95–2.05)	1.81 (1.76–1.86)	1.49 (1.44–1.53)	1.06 (1.02–1.11)
Australia/New Zealand	4,152	12.81 (12.37–13.25)	3.13 (3.04–3.23)	3.08 (2.91–3.26)	2.93 (2.76–3.10)	2.62 (2.46–2.79)	2.16 (2.00–2.32)
Melanesia	1,179	26.77 (25.18–28.35)	3.04 (2.65–3.43)	2.83 (2.21–3.45)	2.46 (1.84–3.07)	1.90 (1.30–2.51)	1.22 (0.64–1.79)
Micronesia/Polynesia	93	22.69 (17.97–27.40)	4.90 (3.68–6.12)	4.81 (2.86–6.76)	4.48 (2.55–6.42)	3.88 (1.99–5.77)	3.14 (1.36–4.93)

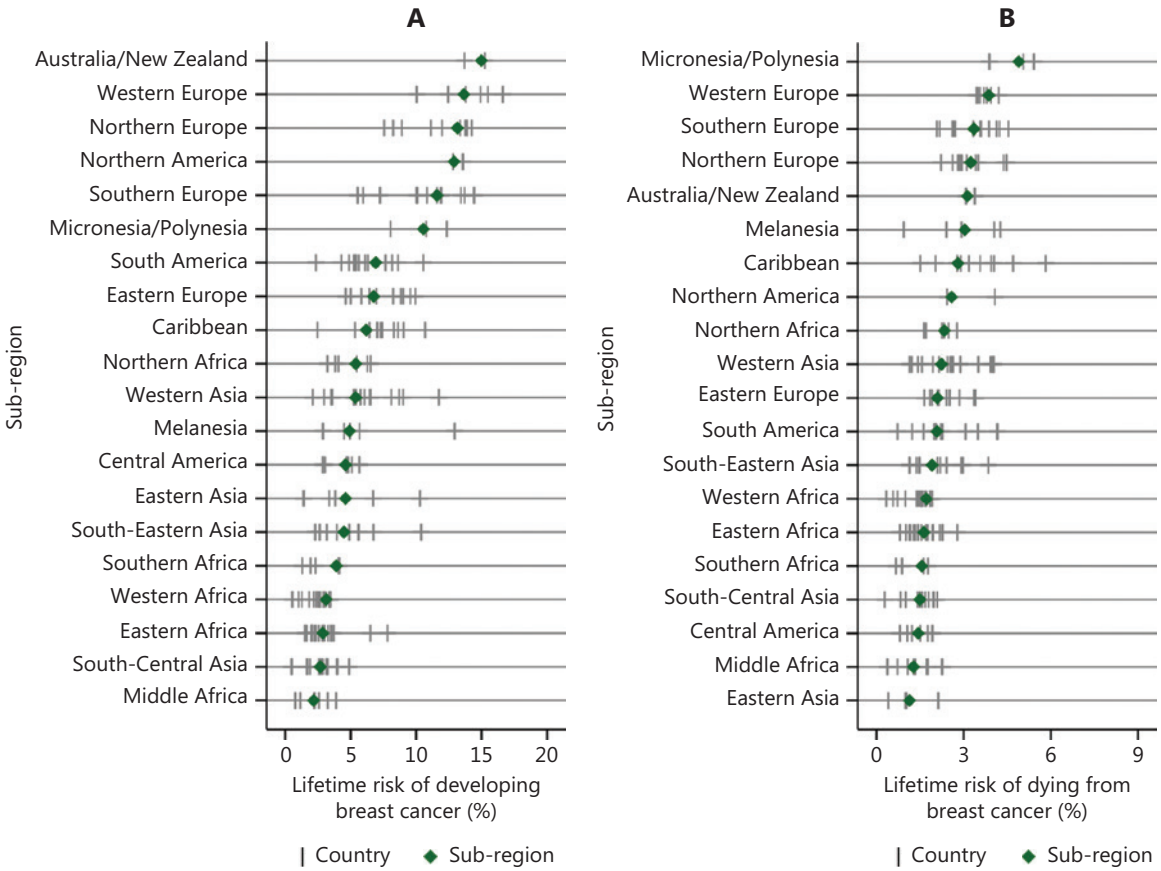


Figure 1 Lifetime risks of developing or dying from breast cancer in 2022 by region and country. A. Developing breast cancer. B. Dying from breast cancer. Green diamonds denote the average lifetime risk in each selected geographic area; vertical lines denote the estimated lifetime risk in each selected country/region.

age) and perimenopausal breast cancer (45–54 years of age) to the total lifetime risk were greatest in low-HDI regions, accounting for 15.29% and 20.59% of the lifetime risk, respectively. In contrast, the relative contributions of both age groups were lower in high- and very high-HDI regions. In contrast, the risk of postmenopausal breast cancer deaths in very high-HDI regions accounted for a substantially elevated proportion of the lifetime risk (86.67%) of the entire risk (**Table S2**). Interestingly, the risk of dying from breast cancer among individuals 0–54 years of age declined with increasing HDI level, whereas the risk among those ≥ 55 years of age had a positive association with the HDI level (**Figure 2**).

Trends in lifetime risk of developing breast cancer

Surveillance data from 36 countries were included to assess the trends in lifetime risk of developing breast cancer (22 in Europe, 6 in Asia, 6 in the Americas, and 2 in Oceania). A significant increasing trend was noted in 32 countries (19 in Europe, 6 in Asia, 5 in the Americas, and 2 in Oceania) for the lifetime breast cancer risk with the AAPC ranging from 0.17% to 5.84%. The most rapid increase occurred in the Republic of Korea (AAPC = 5.84%, 95% CI: 5.50%–6.14%), followed by Japan (AAPC = 5.21%, 95% CI: 4.74%–5.69%). Countries with an AAPC < 1.00% included New Zealand (AAPC = 0.76%, 95% CI: 0.24%–1.24%), the United Kingdom (AAPC = 0.74%, 95% CI: 0.55%–0.88%), France (AAPC = 0.63%, 95% CI: 0.31%–0.94%), the Netherlands (AAPC = 0.58%, 95% CI: 0.15%–0.92%), Germany (AAPC = 0.30%, 95% CI: 0.00%–0.71%), and the United States (AAPC = 0.17%, 95% CI: 0.04%–0.31%). Argentina was the only country with a negative AAPC, although not statistically significant. Significant increases in the lifetime risk of developing breast cancer were observed in the 0–44 and 45–54 year age groups in 22 and 20 countries, respectively, whereas an increasing trend among individuals ≥ 55 years of age was identified in 31 countries (**Figures 3 and S1**).

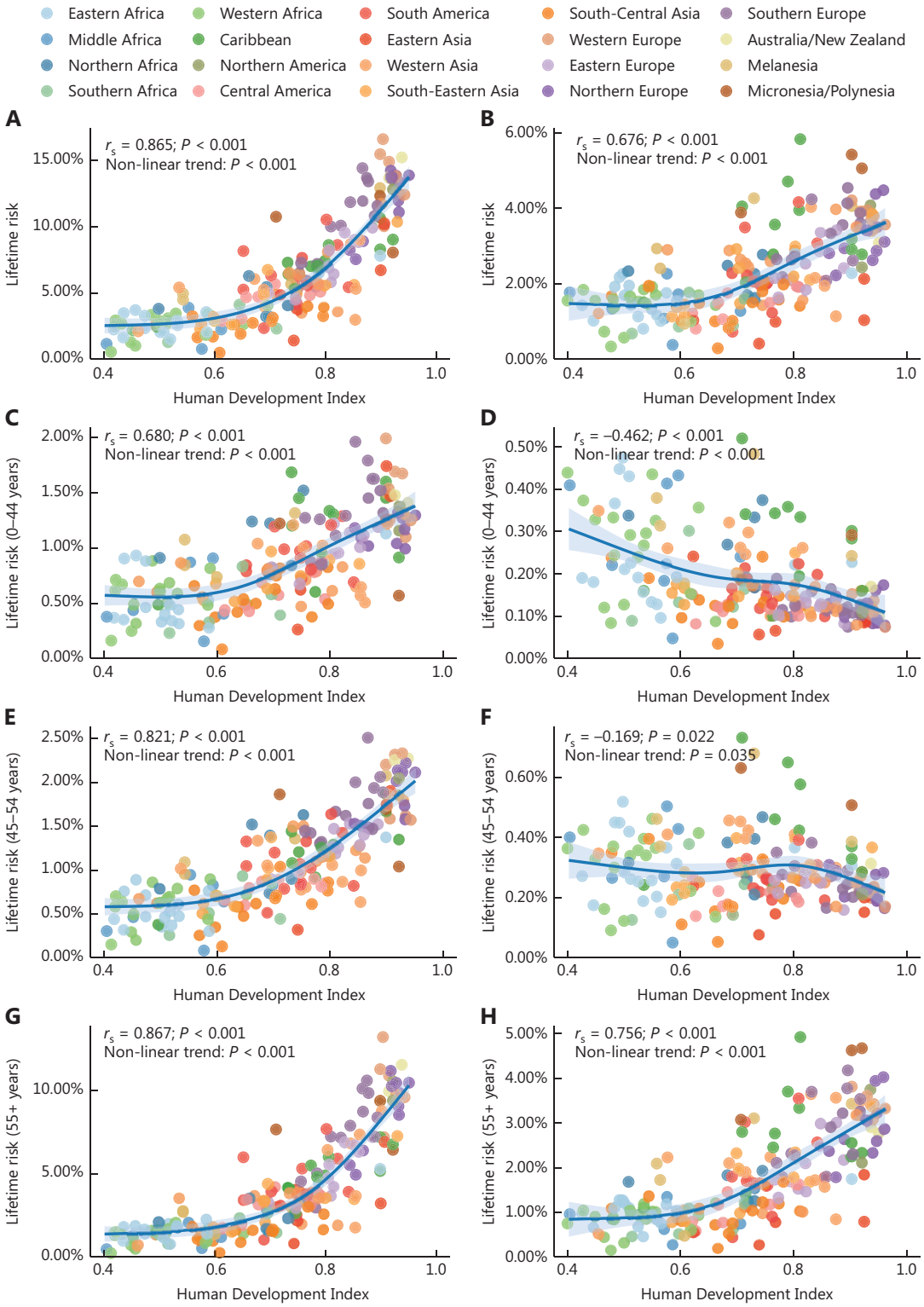


Figure 2 The correlation between the lifetime risks of developing and dying from breast cancer and the Human Development Index (HDI). A. Developing breast cancer; B. Dying from breast cancer; C. Developing breast cancer between 0 and 44 years of age (premenopausal breast cancer); D. Dying from breast cancer between 0 and 44 years of age (premenopausal breast cancer); E. Developing breast cancer between 45 and 54 years of age (perimenopausal breast cancer); F. Dying from breast cancer between 45 and 54 years of age (perimenopausal breast cancer); G. Developing breast cancer at ≥ 55 years of age (postmenopausal breast cancer); H. Dying from breast cancer at ≥ 55 years of age (postmenopausal breast cancer).

Sensitivity analysis comparing lifetime and cumulative risks (0–74 years of age)

Sensitivity analyses compared the lifetime and conventional cumulative risks (0–74 years of age). Lifetime risk was calculated based on actual country-specific life expectancy, whereas the cumulative risk was conventionally truncated at 74 years of age. Significant differences and a linear correlation were noted with life expectancy variations. The cumulative risk (0–74 years of age) overestimated the lifetime risk of developing breast cancer in countries with a lower life expectancy, whereas the cumulative risk generated an underestimate in countries with higher life expectancy. The cumulative risk (0–74 years of age) for mortality was significantly lower than the lifetime risk of dying from breast cancer (**Figure S11**).

Discussion

In this study the global lifetime risk of developing and dying from breast cancer among women was estimated in 185 countries in 2022, analyzing variations across different HDI levels, regions, countries, and age groups. Overall, the lifetime risk of developing and dying from breast cancer globally was 5.51% (1 in 18 women) and 1.82% (1 in 55 women), respectively. This study identified substantial disparities in lifetime risk of breast cancer, which was significantly correlated with HDI level and healthcare resource availability. The lifetime risk of breast cancer in very high-HDI regions was 3.56 times higher compared to low-HDI regions. Notably, pre- and peri-menopausal breast cancer deaths accounted for a disproportionately higher proportion of the total lifetime breast cancer risk in low-HDI regions or regions with limited health resources compared to other regions. In contrast, postmenopausal breast cancer risk constituted a greater proportion in very high-HDI regions. Among countries with continuous cancer surveillance data, most exhibited an increasing trend in lifetime risk of developing breast cancer. The significant global inequities in breast cancer risk reflected structural determinants of health disparities, including uneven socioeconomic resource distribution, variable implementation of risk factor prevention strategies, and profound gaps in healthcare access and quality across nations.

The lifetime risk of breast cancer offers an accurate, comparable, and intuitive measure of disease burden across populations compared to conventional epidemiologic indicators. Although the AMP method, which adjusts for age-specific incidence, all-cause mortality, and multiple primaries, relies on several assumptions that are unlikely to hold exactly and remain reasonable approximations for macro-level policy calculations. The AMP method assumes that the risk of developing a new primary breast cancer is equivalent between individuals without a prior breast cancer diagnosis and the general population and mortality rates for non-breast cancer are the same as those individuals without previous breast cancer and the general population. Nevertheless, factors, such as smoking and social deprivation, influence cancer incidence and non-cancer mortality, meaning that these assumptions cannot be expected to hold exactly in every population subgroup. It should also be emphasized that the lifetime risk obtained is an artificial construct and may not accurately reflect the actual lifetime risk from birth for any individual, particularly in the context of abrupt changes in incidence rates, such as the introduction of population screening programs and changes in reproductive patterns. However, the lifetime risk of breast cancer based on AMP method remains a reasonable approximation for the purpose of population-level estimation. Notably, our study revealed that in countries with a lower life expectancy, the cumulative risk (0–74 years of age) overestimated the lifetime risk of developing breast cancer, whereas in countries with higher life expectancy the cumulative risk produced an underestimate. A sensitivity analysis was performed under the assumption that global incidence and mortality rates for breast cancer remained unchanged, while life expectancy and age-specific mortality rates were set to levels observed in Japan. The estimated lifetime risk of developing breast cancer rose by approximately 37.23% (from 5.51% to 7.57%). In contrast, when life expectancy and age-specific mortality were aligned with the estimates in South Africa (life expectancy = 65 years) the lifetime risk showed a reduction of 29.98% (from 5.51% to 3.86%; **Figure S12**). These findings underscore the substantial impact of life expectancy on lifetime risk estimates.

Our study demonstrated that significant variations in lifetime risk of breast cancer across different global regions/countries reflect pronounced inequities in disease burden and signified an increasing trend in most regions. These findings are consistent with previous assessments of disease burden by incidence and mortality[22]. Approximately 1 in 7 individuals in Australia and New Zealand was diagnosed with breast cancer in their lifetime, whereas approximately 1 in 46 individuals in Middle Africa was diagnosed across the entire lifespan. Similarly, 1 in 20 individuals in Micronesia/Polynesia died from breast cancer compared to 1 in 89 in East Asia. Temporal trend analyses across 36 countries indicated that lifetime risk continued to rise between 2003 and 2017 in most countries, which is consistent with other studies reporting an increase in breast cancer burden[5,23]. The rising burden and disparate distribution of breast cancer is largely attributable to different conditions in risk factors, demographic and socioeconomic transitions, and the coverage of screening strategies.

Disparities in lifetime risk of breast cancer are shaped by the interplay of multiple biological and socioeconomic determinants. Well-established breast cancer risk factors include gynecologic characteristics, reproductive patterns, pharmaceutical exposures, modifiable lifestyle factors, environmental influences, dietary habits, iatrogenic exposure to diagnostic

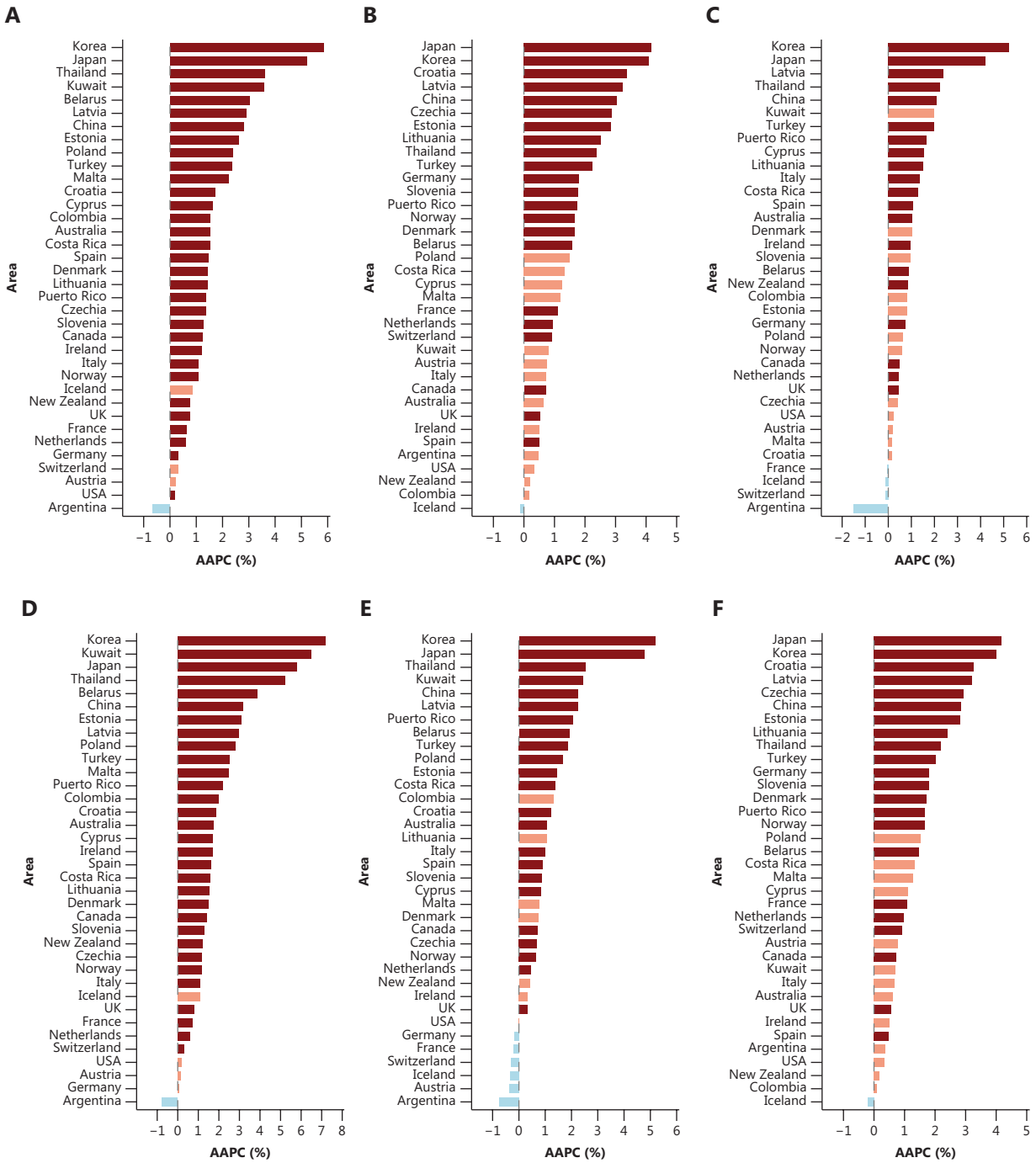


Figure 3 Continued

radiation, and genetic predisposition, such as BRCA1/BRCA2 mutations[24,25]. The increased breast cancer burden in very high-HDI countries is attributed to the prolonged prevalence of reproductive, endocrine, and lifestyle-related risk factors[26]. An estimated a quarter of breast cancer cases in high-income countries are attributable to modifiable risk factors, highlighting a significant potential for prevention. Our analyses also indicated that a significant correlation existed between trends in declining fertility and elevated breast cancer risk (**Figure S8**). A previous study showed that each additional

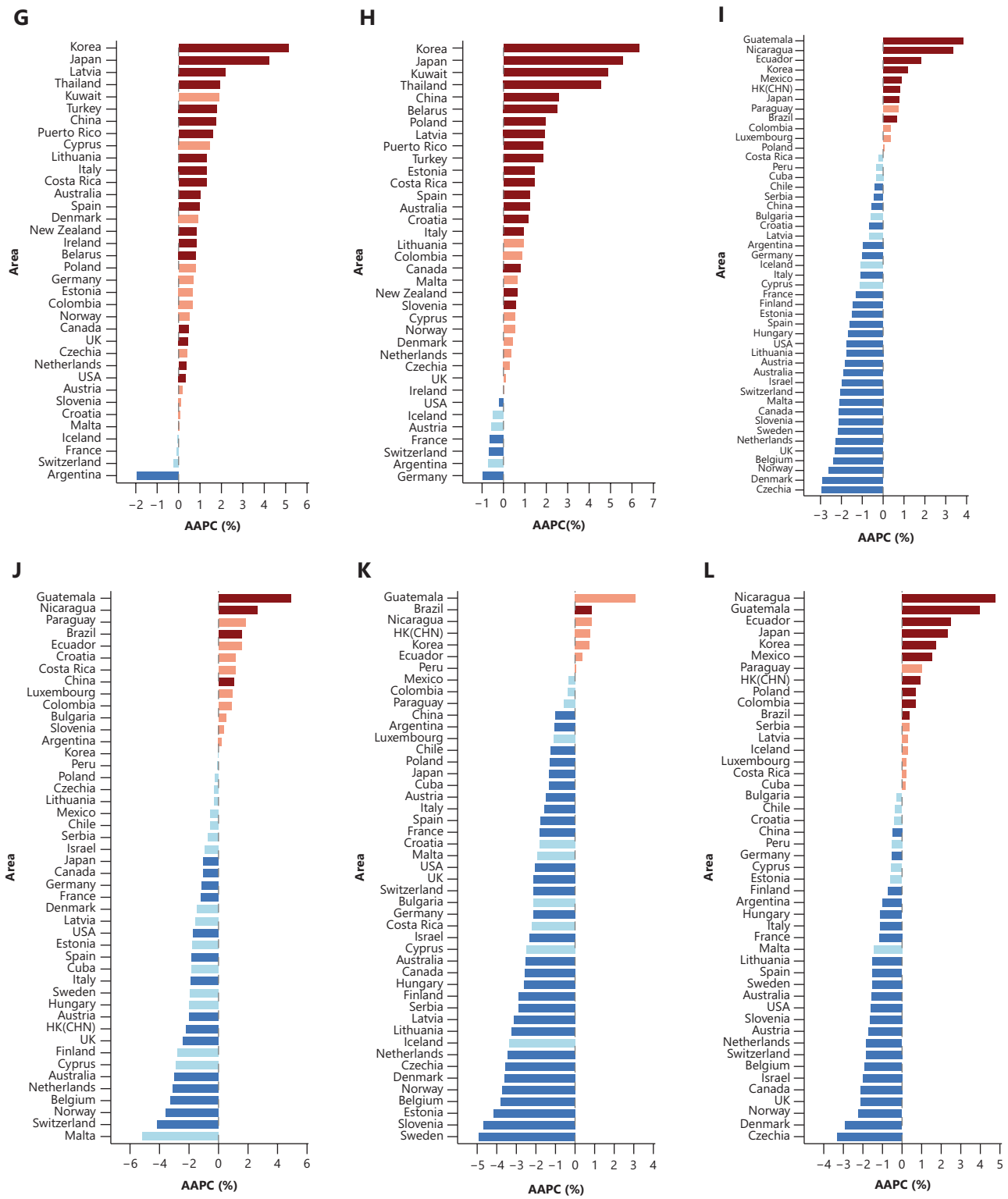


Figure 3 The average annual percent change (AAPC) for lifetime risks of developing breast cancer, age-standardized incidence rate (ASIR), and age-standardized mortality rate (ASWR) in 2003–2017 by country and menopausal status. A. Developing breast cancer from birth to

death; B. Developing breast cancer between 0 and 44 years of age (premenopausal breast cancer); C. Developing breast cancer between 45 and 54 years of age (perimenopausal breast cancer); D. Developing breast cancer at ≥ 55 years of age (postmenopausal breast cancer); E. Age-standardized incidence rate of breast cancer; F. Age-standardized incidence rate of breast cancer between 0 and 44 years of age (premenopausal breast cancer); G. Age-standardized incidence rate of breast cancer between 45 and 54 years of age (perimenopausal breast cancer); H. Age-standardized incidence rate of breast cancer at ≥ 55 years of age (postmenopausal breast cancer); I. Age-standardized mortality rate of breast cancer; J. Age-standardized mortality rate of breast cancer between 0 and 44 years of age (premenopausal breast cancer); K. Age-standardized mortality rate of breast cancer between 45 and 54 years of age (perimenopausal breast cancer); L. Age-standardized mortality rate of breast cancer at ≥ 55 years of age (postmenopausal breast cancer). Dark red bars represent countries with a statistically significant increasing trend (AAPC > 0, P < 0.05). Light red bars represent countries with an increasing trend that is not statistically significant (AAPC > 0, P ≥ 0.05). Light blue bars represent the countries with a decreasing trend that is not statistically significant (AAPC < 0, P ≥ 0.05).

child reduces breast cancer risk by approximately 10.5%[27]. Fertility rates remain low in high-income regions and high in Sub-Saharan Africa, which had a lower lifetime risk of developing breast cancer. Increased breast cancer burden in less developed regions is primarily driven by factors, such as environmental carcinogen exposure, chronic inflammatory states resulting from infectious diseases, and dietary insufficiency[28]. Reducing the breast cancer burden requires not only addressing these modifiable macro-level risk factors but also strengthening critical mediators, such as organized breast cancer screening, public health policies, and socioeconomic mechanisms.

Differentials in lifetime risk of dying from breast cancer across regions are determined in part by inequalities in breast cancer screening coverage and diagnostic accuracy, which lead to variable rates of early detection across regions. Our research indicated that low-HDI regions had the highest proportion of lifetime risk of dying relative to developing breast cancer. Globally, pronounced inequalities in lifetime risk of dying from breast cancer are driven by low public awareness, insufficient screening coverage, delayed diagnosis, and inadequate access to timely and effective treatment. A study reported that 67.5% of patients were diagnosed at stages III-IV with a 5-year survival rate of only 33.5%. In contrast, countries, such as the United States or Canada, have achieved early detection rates of 60–80% and survival rates of approximately 90%[28,29]. An estimated 40% of this disparity is attributable to delayed diagnosis, while 30% is attributed to inadequate treatment. A key factor was detected and treated at an early stage (I or II) in > 60% of cases in all geographic areas that achieved a reduction in breast cancer mortality from 1990 to 2020[4]. Although effective screening implementation helps reduce mortality, maintaining such programs in resource-limited regions remains challenging. Furthermore, access to timely and effective treatment following diagnosis is often inadequate in these regions[30,31]. Equitable access to early detection and management is a public health imperative, fundamental to securing sustained gains in survival and well-being for the entire breast cancer population. Countries with a high burden of breast cancer mortality may need combination of strategies to reach the early detection threshold (60%)[32].

The relationship between lifetime risk and health services serving as indicators revealed significant inequalities in the burden of breast cancer worldwide. Health system characteristics associated with measuring health economic inequality include the UHC Index, CHE per capita, CHE as a percentage of GDP, GGHE-D per capita, GGHE-D as a percentage of CHE, and GGHE-D as a percentage of GGE (**Figures S2-S9**). Within resource-constrained low-HDI areas, disparities in breast cancer burden could be attributed to limited political commitment to health investment, insufficient health initiatives, and a shortage of feasible implementation plans. Infrastructure remains a barrier for breast cancer prevention in low- and middle-HDI areas. For example, radiation therapy facilities are available in only 23 of the 52 African nations, highlighting a continent-wide accessibility crisis[33]. Furthermore, these regions face multiple systemic challenges, including limited availability of cancer drugs, inadequate transportation infrastructure to medical facilities, a severe shortage of qualified healthcare professionals, and sociocultural and religious barriers that restrict women's access to healthcare services[34]. Therefore, differentiated prevention and control strategies tailored to HDI levels and health resource availability are imperative. In very high-HDI countries with abundant health resources where screening and treatment accessibility is high, populations focus on enhancing screening precision, mitigating psychological repercussions, and minimizing radiation exposure and subsequent risk of secondary primary cancers. Multipronged strategies are needed to reduce the breast cancer burden for individuals in low- and middle-HDI regions with limited health resources. These strategies include raising public health awareness, implementing government-organized screening programs by mammography and/or ultrasound to improve the proportion of cases with an early diagnosis and treatment, which is pivotal in reducing the disease burden[34-38].

The lifetime risk of breast cancer varies substantially with age, which provides critical evidence for the age of onset in

breast cancer screening programs and establishing national prevention and control strategies in different countries, particularly in limited-resource areas. The remaining lifetime risk is 1 in 20 for women 40 years of age, 1 in 23 women 50 years of age and 1 in 31 for women aged 60 years of age. Overall, the risk of developing and dying from breast cancer is relatively low before 40 years of age and increases thereafter. Notably, significant cross-national variations exist in age-specific breast cancer risks. Low-HDI regions with limited health resources, such as low-HDI regions in Africa, have a heavier burden of pre- and peri-menopausal breast cancer that is influenced by younger population structures as well as genetic and environmental factors that together contribute to an earlier onset of breast cancer[34]. Similarly, Olopade identified a high incidence of premenopausal breast cancer linked to *BRCA1* mutations among young women in Africa that was associated with a poor prognosis[39]. In low-HDI regions 20.62% and 15.29% of the total lifetime risk of developing and dying from breast cancer occurred between 0 and 44 years of age, respectively. In contrast, these two proportions were significantly lower (11.86% and 4.81%) in very high-HDI regions, such as Australasia, Europe, and North America, where the risk of postmenopausal breast cancer is notably elevated. Accordingly, screening strategies should be tailored to regional health resource availability and breast cancer burden. In regions with an increased lifetime risk of dying from breast cancer, such as Africa and Asia, initiating screening at 40 or 45 years of age is recommended to facilitate early detection and timely intervention. In very high-HDI regions, such as Australia/New Zealand, Europe, and North America, greater emphasis may be focused on screening after 50 years of age to align with epidemiologic patterns and optimize resource allocation. The age-specific and menopausal status-stratified risk estimates provided in this study form a critical evidence base for developing screening guidelines, particularly in resource-limited areas. Each country should balance the benefits and risks of screening, including overdiagnosis, potential psychosocial harms, and false-positive results.

This study had several strengths. First, the lifetime risk was estimated by applying the AMP method, which could effectively consider life expectancy and the competing risks of other causes of death and multiple primary cancers. The AMP method corrects for cancer registries that publish data on all primary cancers arising each individual but does not overstate lifetime risk when compared to the "current probability" method (**Table S4**). Conventional cumulative risks (0–74 years of age) may underestimate cancer risks in populations with a higher life expectancy or lower competing death risks[40]. The lifetime risk of developing and dying from breast cancer provides an intuitive metric for comparative assessment of cancer burden across populations. The lifetime risk of developing and dying from breast cancer also provides the evidence-based information for developing long-term healthcare planning and cancer control. Second, by integrating GLOBOCAN 2022, all-cause mortality data from the United Nations, and WHO Global Health Expenditure data, our study provides a comprehensive global comparison of the lifetime risks of breast cancer incidence and mortality across regions with varying geographic and socioeconomic characteristics[10,18]. Finally, we systematically reported the age-specific lifetime risk probabilities and risks stratified by age and menopausal status in various regions/countries, providing essential information for developing targeted breast cancer prevention and control strategies[35].

However, our study had some limitations. First, because the AMP method is based on three assumptions, this method is applicable to population-level rather than individual-level estimation. While this assumption may not hold in the presence of shared risk factors, such as smoking or social deprivation, the resulting impact on national-level aggregate estimates is expected to be limited and is based on cross-sectional estimates rather than cohort estimates of risk. It is important to note that changes in breast cancer incidence, mortality, and all-cause death, combined with the implementation of both organized and opportunistic screening programs and evolving lifestyle factors across regions, might contribute to dynamic changes in lifetime risk over time, which were not accounted for in our study. Rising incidence trends can lead to underestimation of future risk, while declining mortality rates can produce overestimation of lifetime risk. Although we assessed trends in breast cancer risk for selected regions between 2003 and 2017, the predominantly high socioeconomic level of the included countries limits the extrapolation of these trends to all global regions and nations[23,41]. Despite these assumptions, the AMP method provides a more precise lifetime risk estimate than the cumulative risk (0–74 years of age) and the current probability (first primaries only) because the AMP method corrects for multiple primaries and covers the full lifespan. The GLOBOCAN 2022 data utilized cancer registry data and national population statistics from countries worldwide to systematically calculate region- and country-specific incidence and mortality rates. Data accuracy is dependent on the availability and quality of the source information in each country. Cancer registry coverage in many low-HDI regions are limited, requiring modelling to estimate location- and year-specific rates[42]. Even areas with cancer registry data, heterogeneity in representativeness and quality could lead to appreciable uncertainty. Currently, only one in three countries currently able to report high-quality data. Excluding countries with low-quality data confirmed the stability of the global lifetime risk estimates but country-specific results for data-limited countries should still be interpreted with caution (**Table S6**). Third, due to the lack of specific pathologic subtype records in the database, our study did not conduct analyses and assessments based on different types of breast cancer. The epidemiologic impact of cancer demonstrates marked heterogeneity across national varies, notably in populous

nations, such as China and Russia, where demographic variations substantially influence disease distribution patterns. Consequently, the risk estimates in our study only reflect aggregate population-level metrics rather than characterizing region-specific risk profiles. Finally, individual-level data of menopausal status was not collected in the cancer database, so the status was estimated using age-based thresholds based on WHO recommendations. Given that the timing of menopause varies across individuals due to biological, genetic, and environmental influences, applying a fixed age cut-off might lead to the degree of misclassification bias.

Conclusions

This study provides visual evidence of global burden of breast cancer and its inequality distribution worldwide. Compared with the cumulative risk (0–74 years of age), the AMP-derived lifetime risk directly quantifies the risk of developing or dying from breast cancer across the full lifespan, accounting for multiple primaries and competing risks. The global estimates in 2022 indicated that 1 in 18 individuals was diagnosed with breast cancer in their lifetime and 1 in 55 died from the disease with the probability of developing breast cancer increasing globally. Epidemiologic disparities of breast cancer are observed in different HDI regions and healthcare resource countries globally with cancer lifetime risk providing an evidence-based foundation for developing tailored prevention and control strategies across different global regions and countries.

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Conflict of interest statement

No potential conflicts of interest are disclosed.

Author contributions

Conceived and designed the analysis: Di Liang and Rongshou Zheng.
Collected the data: Rongshou Zheng, Weijia Kong, Hengna Lin.
Contributed data or analysis tools: Weijia Kong, Hengna Lin, Jie Li.
Performed the analysis: Weijia Kong, Yaxiong Nie.
Wrote the paper: Di Liang, Rongshou Zheng, Weijia Kong.

Data availability statement

All data can be obtained from public databases. The cancer data are available at https://gco.iarc.fr/today/. Population, all-cause mortality, and life expectancy data are available at https://population.un.org/wpp/. Any other requests for the full dataset are available from the corresponding authors.

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