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Global, regional, and national burden of breast cancer in young women from 1990 to 2021: findings from the global burden of disease study 2021

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Abstract

Aim The issue of breast cancer in young women (BCYW) has gained increasing attention over the past few decades. However, a notable gap exists in the literature concerning the comparison of the disease burden of BCYW with that of other age groups. This study presents a comprehensive analysis of the disparities in global, regional, and national burden between BCYW and their middle-aged and elderly counterparts.

Methods The breast cancer data in this study were collected from the Global Burden of Diseases, Injuries, and Risk Factors Study 2021 (GBD 2021). The age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), age-standardized prevalence rate (ASPR), and age-standardized disability-adjusted life years rate (ASDR), and the Average Annual Percent Change (AAPC) were employed to assess the disease burden of BCYW. The Bayesian Age-Period-Cohort model was used to forecast disease burden from 2022 to 2030.

Results The AAPC of ASIR of BCYW from 1990 to 2021 was 0.91 (95% CI: 0.77 to 1.05), exceeding the global average (0.49, 95% CI: 0.40 to 0.58) as well as both middle-aged (0.60, 95% CI: 0.47 to 0.73) and elderly groups (0.30, 95% CI: 0.21 to 0.39). The AAPC for ASMR of BCYW experienced a marginal increase of 0.02 (95%CI: -0.07 to 0.11) from 1990 to 2021, surpassing the rates observed in both the middle-aged group (-0.40, 95%CI: -0.47 to -0.32) and the elderly group (-0.50, 95%CI: -0.62 to -0.38). The ASIR in BCYW significantly increased in regions with low (AAPC = 1.87), low-middle (AAPC = 2.32), middle (AAPC = 1.84), and high-middle SDI (AAPC = 0.98), while it remained unchanged in regions with high SDI (AAPC = -0.02). This trend was also observed among middle-aged and older groups. The ASMR in BCYW significantly increased in regions with low (AAPC = 1.01) and low-middle SDI (AAPC = 1.25), but remained unchanged in regions with middle SDI (AAPC = 0.02), while it decreased in regions with high-middle (AAPC = -1.10) and high SDI (AAPC = -1.60). Among the middle-aged and elderly populations, there was an increase in ASMR rates observed in regions with low, low-middle, and middle SDI groups (all AAPC > 0), whereas a decrease was noted in the regions with high-middle and high SDI (all AAPC < 0). The BAPC predicts a consistent annual increase in ASIR, ASMR, ASPR, and

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ASDR of BCYW globally and in China from 2022 to 2030. Notably, China has higher ASIR and ASPR rates compared to the global average, while its ASMR and ASDR rates are lower.

Conclusion The burden of BCYW was particularly significant in regions with low-SDI, low-middle SDI, and middle SDI. Despite the progress made, China still faces considerable challenges in effectively addressing this issue. The prevention and control of BCYW must remain a priority. Different countries and regions should develop personalized, targeted intervention strategies for this population and establish public health policies tailored to the specific needs of each region.

Keywords Breast cancer in young women, Global burden of disease, Incidence, Disability-adjusted life years

Introduction

Breast cancer (BC) is a prevalent malignancy among women worldwide, ranking as the second most frequently diagnosed cancer and the fourth leading cause of cancer-related mortality globally [1]. In 2022, an estimated 2.30 million new cases of BC were reported, resulting in approximately 665,000 deaths [1]. Projections indicate that the incidence of BC will rise to 4.40 million by 2070 [2]. The 5-year survival rate for BC exceeds 90% in high-income countries, whereas it is significantly lower in low- and middle-income countries [3]. The incidence of BC was higher in high-income countries compared to low-income countries (81.00/100,000 vs. 33.80/100,000). Consequently, the burden of disability-adjusted life years (DALYs) was significantly greater in high-income countries than in low-income countries (822.01/100,000 vs. 299.36/100,000) [4]. Despite the growing availability of treatments for BC, the disease burden associated with BC continues to increase [5, 6].

Breast cancer in young women (BCYW) was unique subgroup, which was characterized by more aggressive cancer subtypes, such as triple-negative breast cancer (TNBC) and HER2-positive, advanced stages at the time of diagnosis, high grade, and poorly differentiated [7–10]. Epidemiologically, an estimated 5 to 7% of women receive a diagnosis of BC prior to reaching the age of 40 [10]. It is important to highlight that routine BC screening is generally not recommended for young women, as this poses a significant challenge to early detection efforts. The study revealed that the incidence of BC cases in women aged <40 years was 4–5% in the United States, whereas it accounted for 13% among Asian women under 40 and remained at 5% below the age of 35 [11]. Importantly, in comparison to their older counterparts, BCYW exhibit inferior rates of survival and recurrence [10, 12]. The 5-year overall survival (OS) rates for breast cancer patients were 86.34%, 89.58%, and 84.84% in the age groups of <40, 40–59, and ≥60 years, respectively [8]. In addition, the substantial risk of chemotherapy-induced premature ovarian insufficiency poses significant challenges for BCYW in terms of fertility preservation and pregnancy management [13]. Although the incidence of BCYW is relatively low, this age group plays a crucial role

in both career development and family dynamics. Consequently, the occurrence of BCYW presents significant challenges to individuals, families, and society as a whole [14]. Therefore, it is imperative to prioritize preventive and control measures specifically targeting young-onset breast cancer.

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) is a comprehensive investigation that examines the global health burden. It involves estimating the incidence, prevalence, mortality rates, DALYs, and risk factors associated with diseases. The GBD datasets were currently extensively utilized for evaluating various disease burden, particularly in the field of oncology. However, the study focusing on the disease burden of BCYW utilizing the GBD database was limited. *Yuan et al.* identified an increasing trend in the burden of BCYW globally, and significant regional disparities were observed in the GBD 2019 database [15]. However, the study did not include a comparative analysis of the burden of BC between young women and other age groups. This study aims to stratify BC into three age groups, namely younger age group (15 to 39 years), middle age group (40–59 years), and older age group (≥60 years), and compare the disparities in incidence, mortality rates, prevalence, and DALYs among these three groups at global, regional and national levels. Additionally, this study presents a projection of breast cancer disease burden across three age cohorts in the global and Chinese populations from 2022 to 2030. To the best of our knowledge, no prior studies have systematically reported on the global burden of BC across different age groups in women. This comparative analysis of the global burden of BC among three distinct age groups in women will provide a solid foundation for enhancing prevention strategies, control measures, and management approaches specifically tailored for younger breast cancer patients.

Methods

Data source

The GBD study, led by the Institute for Health Metrics and Evaluation (IHME), aims to compile all available data and employ innovative methodologies to generate comparable estimates of the world's most significant

health issues. Data about the BC burden was collected from GBD 2021, which offers a comprehensive and rigorous evaluation of the disease burden attributed to 371 diseases and injuries across 204 countries and territories from 1990 to 2021 [16]. The data were derived from vital registration systems, autopsies, censuses, household surveys, registries for specific diseases, health service contact data, and other relevant sources [16]. Each type of data was systematically identified through a comprehensive review of published studies, searches of government and international organization websites, published reports, primary data sources such as Demographic and Health Surveys, and datasets provided by GBD collaborators [17]. The GBD dataset adopts a standardized data processing protocol to systematically integrate and normalize all collected raw data. To ensure the comparability of data from diverse sources, a unified case definition standard is applied during the data standardization process. The DisMod-MR2.1 model is used for age- and gender-standardized splitting. Geographic disaggregation is conducted to generate subnational estimates. The key modeling assumptions of GBD include: cause-specific mortality modeled using CODEm (Cause of Death Ensemble modeling); non-fatal outcomes estimated via Bayesian meta-regression (DisMod-MR); and Gaussian process regression for trend estimation. Despite its strengths, the GBD has limitations, such as variations in data quality and inherent model uncertainties. The estimates of incidence, prevalence, mortality, and DALYs across different age groups, years, and locations were extracted from the Global Health Data Exchange (GHDx) query tool. The Uncertainty Intervals (UIs) is computed using a hierarchical Bayesian modeling framework through probabilistic simulation methods. The reported interval, spanning the 2.5th to 97.5th percentiles of the posterior distribution, constitutes the 95% UIs. This comprehensive uncertainty quantification integrates multiple sources of variability: (1) data quality limitations (including measurement errors and sampling biases), (2) model parameter uncertainties (particularly in prior distribution specification), and (3) inherent stochastic variations (such as spatio-temporal heterogeneity). Under the model's assumptions, this UIs represents a 95% credible interval, indicating that the true parameter values have a 95% probability of residing within the reported bounds [18].

The definition of BCYW

Currently, there is no standardized criterion for defining the age range of BCYW. In this study, we have defined BCYW as individuals below the age of 40, based on the ESO-ESMO Fifth International Consensus Guidelines for Breast Cancer in Young Women (BCY5) [19]. Due to the absence of data on BC in women under the age of 15 in the GBD database, the patients with BC in this study

were classified into three age groups: a younger age group (15 to 39 years), a middle age group (40 to 59 years), and an older age group (≥ 60 years).

Sociodemographic index (SDI)

The SDI serves as a comprehensive indicator of developmental status that is closely associated with health outcomes. It represents the geometric mean of indices ranging from 0 to 1, including the total fertility rate of individuals under 25, the average educational attainment of individuals aged 15 and above, and the lagging distribution income per capita. As a composite indicator, an SDI value of 0 represents the lowest theoretical level of health-related development, while an SDI value of 1 signifies the highest theoretical level. Moreover, based on SDI values, the GBD database classifies 204 countries and territories into five categories: low, low-middle, middle, high-middle, and high SDI regions.

Joinpoint regression

The joinpoint regression model is a crucial tool in epidemiology for analyzing time trends, combining segmented regression and time series analysis. By identifying inflection points, the research period is divided into multiple intervals, allowing for trend fitting in each interval to provide a more accurate description of disease dynamics. The joinpoint regression model encompasses both linear ($y=xb$) and log-linear ($\ln y=xb$) models. In the present study, the log-linear model was employed to examine population-based trends in age-standardized incidence, prevalence, mortality, and DALYs. Furthermore, the grid search method (GSM) was employed to determine the number and location of joinpoints, while the Monte Carlo permutation test was utilized for model optimization.

Bayesian Age-Period-Cohort (BAPC) model

To forecast the disease burden of BCYW from 2022 to 2035, we integrated global population projection data obtained from the IHME agency (<https://ghdx.healthdata.org/record/ihme-data/global-population-forecasts-2017-2100>). The BAPC model was employed to project the global and regional burden of BCYW from 2022 to 2035. The BAPC model is built upon the traditional Generalized Linear Model (GLM) framework in the Bayesian context. This model reveals the future trends of certain phenomena (such as incidence or mortality) by simultaneously considering the effects of three factors: age, period, and cohort. It assumes that the data follow a Poisson or binomial distribution and uses prior distributions such as Random Walk to smooth the effects of age, period, and cohort. A significant advantage of the BAPC model is that it directly approximates the posterior marginal distribution through the Integrated Nested

Table 1 ASIR and ASMR for breast cancer in different age groups globally and across five SDI regions from 1990 to 2021

Characteristics	Incidence			Mortality				
	No. 1990	ASIR in 1990 (/10 ⁵)	No. 2021	ASIR in 2021 (/10 ⁵)	AAPC (95% CI)	P value	No. 1990	ASMR in 1990 (/10 ⁵)
All ages								
Global	865,881 (824,338–900,794)	39.99 (38.01–41.60)	2,082,737 (1,940,351–2,225,083)	46.40 (43.26–49.56)	0.49 (0.40 to 0.58)	<0.001	350,577 (330,510–368,425)	16.60 (15.60–17.45)
Low SDI	20,117 (17,069–23,646)	15.59 (13.28–18.15)	75,294 (66,491–84,810)	24.09 (21.34–26.87)	1.41 (1.35 to 1.47)	<0.001	14,736 (12,511–17,319)	12.22 (10.48–14.13)
Low-middle SDI	52,222 (46,888–59,103)	14.72 (13.21–16.62)	235,446 (212,857–257,146)	28.29 (25.52–30.93)	2.14 (2.07 to 2.22)	<0.001	33,670 (29,972–38,287)	10.09 (8.94–11.41)
Middle SDI	123,708 (113,636–136,087)	20.55 (18.91–22.56)	539,058 (484,448–597,126)	37.16 (33.42–41.13)	1.93 (1.84 to 2.01)	<0.001	64,521 (59,296–71,144)	11.44 (10.53–12.51)
High-middle SDI	212,690 (201,932–222,708)	38.85 (36.86–40.71)	506,491 (457,359–565,100)	51.05 (46.06–57.18)	0.91 (0.76 to 1.05)	<0.001	93,258 (88,188–97,893)	17.10 (16.11–17.96)
High SDI	456,066 (434,959–466,928)	79.28 (76.17–80.97)	724,293 (661,769–756,433)	77.08 (71.83–79.93)	–0.11 (–0.28 to 0.06)	0.212	143,891 (135,642–148,567)	23.63 (22.46–24.31)
15 to 39 years								
Global	87,492 (82,551–93,414)	8.86 (8.34–9.48)	178,713 (165,382–194,715)	11.73 (10.77–12.82)	0.91 (0.77 to 1.05)	<0.001	26,780 (24,753–29,148)	2.71 (2.51–2.97)
Low SDI	3,208 (2,656–3,876)	4.11 (3.34–5.03)	14,081 (11,571–16,705)	7.31 (5.87–8.84)	1.87 (1.71 to 2.02)	<0.001	1,853 (1,531–2,257)	2.39 (1.94–2.92)
Low-middle SDI	9,143 (7,969–10,551)	4.75 (4.07–5.55)	36,701 (31,748–42,001)	9.62 (8.20–11.24)	2.32 (2.21 to 2.44)	<0.001	4,540 (3,916–5,287)	2.37 (2.01–2.79)
Middle SDI	21,310 (19,144–23,945)	6.67 (5.95–7.52)	58,721 (53,176–64,917)	11.79 (10.60–13.16)	1.84 (1.68 to 2.01)	<0.001	8,156 (7,296–9,197)	2.57 (2.28–2.91)
High-middle SDI	21,519 (19,811–23,586)	9.82 (8.90–10.86)	34,858 (30,238–40,637)	13.39 (11.49–15.75)	0.98 (0.77 to 1.18)	<0.001	6,329 (5,762–6,981)	2.89 (2.62–3.24)
High SDI	32,212 (31,367–33,089)	17.55 (16.92–18.25)	34,203 (32,902–35,593)	17.16 (16.29–18.06)	–0.02 (–0.38 to 0.34)	0.915	5,871 (5,738–6,008)	3.19 (3.10–3.29)
40 to 59 years								
Global	660,925 (609,171–707,182)	14.55 (13.45–15.56)	1,455 (1,307–1,604)	12.1 (11.16 to 12.7)	0.88 (0.81 to 0.95)	<0.001	145,935 (132,528–158,860)	12.68 (11.44–14.10)
Low SDI	45,424 (40,170–50,794)	16.00 (14.15–17.91)	145,935 (132,528–158,860)	12.1 (11.16 to 12.7)	0.88 (0.81 to 0.95)	<0.001	145,935 (132,528–158,860)	12.68 (11.44–14.10)
Low-middle SDI	115,822 (103,991–127,353)	14.59 (13.07–16.04)	145,935 (132,528–158,860)	12.1 (11.16 to 12.7)	0.88 (0.81 to 0.95)	<0.001	145,935 (132,528–158,860)	12.68 (11.44–14.10)
Middle SDI	181,470 (163,851–201,763)	12.68 (11.44–14.10)	145,935 (132,528–158,860)	12.1 (11.16 to 12.7)	0.88 (0.81 to 0.95)	<0.001	145,935 (132,528–158,860)	12.68 (11.44–14.10)
High-middle SDI	145,935 (132,528–158,860)	13.87 (12.63–15.13)	145,935 (132,528–158,860)	12.1 (11.16 to 12.7)	0.88 (0.81 to 0.95)	<0.001	145,935 (132,528–158,860)	12.68 (11.44–14.10)
High SDI	171,460 (151,342–182,071)	15.44 (14.01–16.21)	145,935 (132,528–158,860)	12.1 (11.16 to 12.7)	0.88 (0.81 to 0.95)	<0.001	145,935 (132,528–158,860)	12.68 (11.44–14.10)

Table 1 (continued)

Characteristics		Incidence			Mortality								
	No. 1990	ASIR in 1990 (/10^5)	No. 2021	ASIR in 2021 (/10^5)	AAPC (95% CI)	P value	No. 1990	ASMR in 1990 (/10^5)	No. 2021	ASMR in 2021 (/10^5)	AAPC (95% CI)	P value	
All ages													
Global	367,743 (351841–385838)	82.01 (78.47–86.04)	903,889 (837147–978939)	98.25 (91.00–106.38)	0.60 (0.47 to 0.73)	<0.001	128,927 (121802–137501)	28.80 (27.21–30.71)	235,635 (217028–255425)	25.48 (23.47–27.61)	–0.40 (–0.47 to –0.32)	<0.001	
Low SDI	10,237 (8434–12441)	34.06 (28.04–41.42)	37,544 (32191–43245)	51.35 (44.02–59.13)	1.33 (1.27 to 1.39)	<0.001	6978 (5741–8552)	23.37 (19.22–28.66)	20,621 (17664–23777)	28.64 (24.52–33.02)	0.66 (0.57 to 0.74)	<0.001	
Low-middle SDI	27,899 (24391–32059)	35.02 (30.59–40.30)	122,319 (107153–137462)	67.01 (58.69–75.35)	2.10 (2.02 to 2.19)	<0.001	16,830 (14611–19535)	21.28 (18.46–24.73)	53,914 (47030–60971)	29.73 (25.93–33.64)	1.06 (0.97 to 1.15)	<0.001	
Middle SDI	64,009 (57900–71137)	49.11 (44.42–54.60)	284,733 (252920–319930)	89.77 (79.80–100.78)	1.96 (1.83 to 2.10)	<0.001	30,294 (27278–33893)	23.37 (21.04–26.16)	80,613 (71721–90439)	25.17 (22.41–28.22)	0.26 (0.20 to 0.31)	<0.001	
High-middle SDI	96,407 (90616–102874)	90.28 (84.84–96.35)	221,554 (193867–256784)	114.29 (99.98–132.38)	0.81 (0.65 to 0.98)	<0.001	34,933 (32850–37233)	32.42 (30.48–34.57)	45,118 (40362–51004)	22.81 (20.40–25.77)	–1.10 (–1.24 to –0.97)	<0.001	
High SDI	168,714 (162834–174473)	166.57 (160.77–172.25)	236,900 (225097–248084)	156.96 (149.18–164.36)	–0.18 (–0.32 to –0.03)	0.015	39,713 (38632–40773)	39.16 (38.09–40.20)	35,133 (33789–36403)	22.79 (21.92–23.61)	–1.74 (–1.91 to –1.57)	<0.001	
≥ 60 years													
Global	410,646 (381281–430408)	155.19 (143.39–162.97)	1,000,134 (891501–1076980)	170.54 (152.08–183.62)	0.30 (0.21 to 0.39)	<0.001	194,870 (180087–205323)	76.06 (69.73–80.37)	383,743 (338494–415208)	65.22 (57.57–70.55)	–0.50 (–0.62 to –0.38)	<0.001	
Low SDI	6672 (5613–7710)	55.05 (45.99–63.78)	23,669 (20399–26861)	84.27 (72.32–95.82)	1.41 (1.31 to 1.51)	<0.001	5904 (4967–6832)	51.21 (42.68–59.53)	18,555 (16005–21077)	69.90 (59.92–79.66)	1.02 (0.89 to 1.16)	<0.001	
Low-middle SDI	15,180 (13198–17257)	44.56 (38.57–50.76)	76,426 (67773–84859)	84.69 (74.91–94.17)	2.13 (2.02 to 2.24)	<0.001	12,301 (10617–14104)	37.76 (32.41–43.42)	48,882 (43114–54630)	56.31 (49.45–63.08)	1.33 (1.19 to 1.48)	<0.001	
Middle SDI	38,390 (35003–42162)	61.77 (56.10–67.86)	195,604 (172839–218448)	110.82 (97.69–123.82)	1.91 (1.81 to 2.01)	<0.001	26,071 (23683–28775)	44.45 (40.15–49.09)	87,918 (77377–98234)	51.23 (44.91–57.31)	0.47 (0.32 to 0.62)	<0.001	
High-middle SDI	94,765 (87836–100393)	129.40 (119.50–137.27)	250,078 (219873–278346)	175.78 (154.72–195.72)	0.97 (0.86 to 1.07)	<0.001	51,996 (48148–54861)	73.45 (67.51–77.71)	95,380 (83777–104779)	66.21 (58.26–72.73)	–0.34 (–0.44 to –0.25)	<0.001	
High SDI	255,140 (234317–268311)	301.01 (277.53–316.02)	453,191 (393076–490205)	300.63 (264.65–323.26)	0.02 (–0.07 to 0.10)	0.692	98,307 (89617–103801)	113.31 (103.63–119.47)	132,467 (111505–144467)	79.25 (68.30–85.63)	–1.17 (–1.30 to –1.04)	<0.001	

Laplace Approximation (INLA) algorithm, thereby more accurately estimating the unknown parameters [20]. We utilized the BAPC model for predicting future decades' incidence and mortality.

Statistical analysis

The age-standardized rates (ASR), including the age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), age-standardized prevalence rate (ASPR), and age-standardized disability-adjusted life years rate (ASDR), were employed as indicators to assess the severity of incidence, prevalence, mortality, and DALYs, respectively. The Average Annual Percent Change (AAPC) serves as a concise indicator of the trend observed over a predetermined fixed interval, enabling the utilization of a singular numerical value to depict the annual percent change (APC) across multiple years. AAPC was computed through joinpoint regression analysis in this study. If both the AAPC estimate and its 95% CI are above zero, this indicates a statistically significant increasing trend. Conversely, if both values are below zero, a significant decreasing trend is present. However, if the 95% CI includes zero, the trend is considered stable [21]. The AAPC and its 95% CI are calculated as follows:

$$\begin{aligned}\tilde{\omega}_i &= \omega_i / \sum \omega_j \\ AAPC &= \left\{ \exp \left(\sum \tilde{\omega}_i b_i \right) - 1 \right\} \times 100 \\ AAPC_{L(\alpha)} &= \left\{ \exp \left[\log((AAPC/100) + 1) - Z_{1-\alpha/2} \sqrt{\sum \tilde{\omega}_i^2 \hat{\sigma}^2} \right] - 1 \right\} \times 100 \\ AAPC_{U(\alpha)} &= \left\{ \exp \left[\log((AAPC/100) + 1) + Z_{1-\alpha/2} \sqrt{\sum \tilde{\omega}_i^2 \hat{\sigma}^2} \right] - 1 \right\} \times 100\end{aligned}$$

ω_i as the length of each segment in the range of years, Z_α is the α^{th} quantile of the standard normal distribution, and $\hat{\sigma}^2$ denotes the estimate variance of b_i obtained from the fit of the joinpoint model.

In the GBD dataset, regions are delineated according to geographical proximity and epidemiological similarity. These regions are subsequently aggregated into super-regions based on patterns of cause-of-death distributions [22]. The seven GBD super-regions are central Europe, eastern Europe, and central Asia; high income; Latin America and the Caribbean; north Africa and the Middle East; south Asia; southeast Asia, east Asia, and Oceania; and sub-Saharan Africa.

The analyses were performed using R software (version 4.4.0) and the Joinpoint Regression Program

(version 5.0.2). A p-value < 0.05 was considered statistically significant.

Results

Global burden and trend of BCYW

The global number of female breast cancer cases increased from 865,881 (95% uncertainty interval (UI): 824,338 to 900,794) in 1990 to 2,082,737 (95%UI: 1,940,351 to 2,225,083) in 2021. Additionally, the ASIR rose from 39.99/100,000 in 1990 to 46.40/100,000 in 2021. However, the number of BCYW escalated from 87,492 in 1990 to 178,713 in 2021, with an ASIR increase from 8.86/100,000 in 1990 to 11.73/100,000 in 2021 (Table 1). From 1990 to 2021, The AAPC of ASIR for BCYW was 0.91 (95% confidence intervals (CI): 0.77 to 1.05), higher than the global average (0.49, 95% CI: 0.40 to 0.58), as well as surpassing that of both middle-aged (0.60, 95% CI: 0.47 to 0.73) and elderly groups (0.30, 95% CI: 0.21 to 0.39) (Table 1).

The global ASMR for BC was decreased from 16.60/100,000 in 1990 to 14.55/100,000 in 2021. However, there was little change in the ASMR for BCYW, which remained at 2.71 per 100,000 in 1990, and 2.73 per 100,000 in 2021. Conversely, the ASMR were decreased among middle-aged individuals from 28.80/100,000 in 1990 to 25.48/100,000 in 2021, and among elderly individuals from 76.06/100,000 to 65.22/100,000 during the same period. The AAPC for ASMR of BCYW increased by a marginal value of 0.02 (95%CI: -0.07 to 0.11) between 1990 and 2021. The AAPC for ASMR during this time frame was -0.43 (95%CI: -0.51 to -0.34). The AAPC for ASMR in the middle-aged group was -0.40 (95%CI: -0.47 to -0.32), while in the elderly group it was -0.50 (95%CI: -0.62 to -0.38) (Table 1).

From 1990 to 2021, the AAPC for ASPR for BCYW showed a significant increase of 0.96 (95% CI: 0.82 to 1.10). The AAPC for all ages ASPR was observed to be 0.37 (95% CI: 0.29 to 0.44). The middle-aged group exhibited an AAPC of 0.60 (95% CI: 0.45 to 0.75), while the elderly group had an AAPC of 0.11 (95% CI: 0.04 to 0.19). The AAPC of ASDR for BCYW was 0.09 (95% CI: 0.01 to 0.18) from 1990 to 2021, whereas it was -0.33 (95% CI: -0.40 to -0.25) for the middle age group and -0.42 (95% CI: -0.54 to -0.30) for the elderly population (Table S1).

Additionally, the joinpoint regression analysis revealed significant shifts in the ASIR of BCYW in 1996, 1999, 2005, 2012, and 2019 (Fig. 1). Unfortunately, the ASMR of BCYW has consistently experienced an upward trajectory from 2007 to 2021, while there is a significant downward trend observed among the middle-aged and elderly demographics (Fig. 1). The trends in ASPR and ASDR in BCYW from 1990 to 2021 do not align with those observed in the middle-aged and older age groups (Fig. S1).

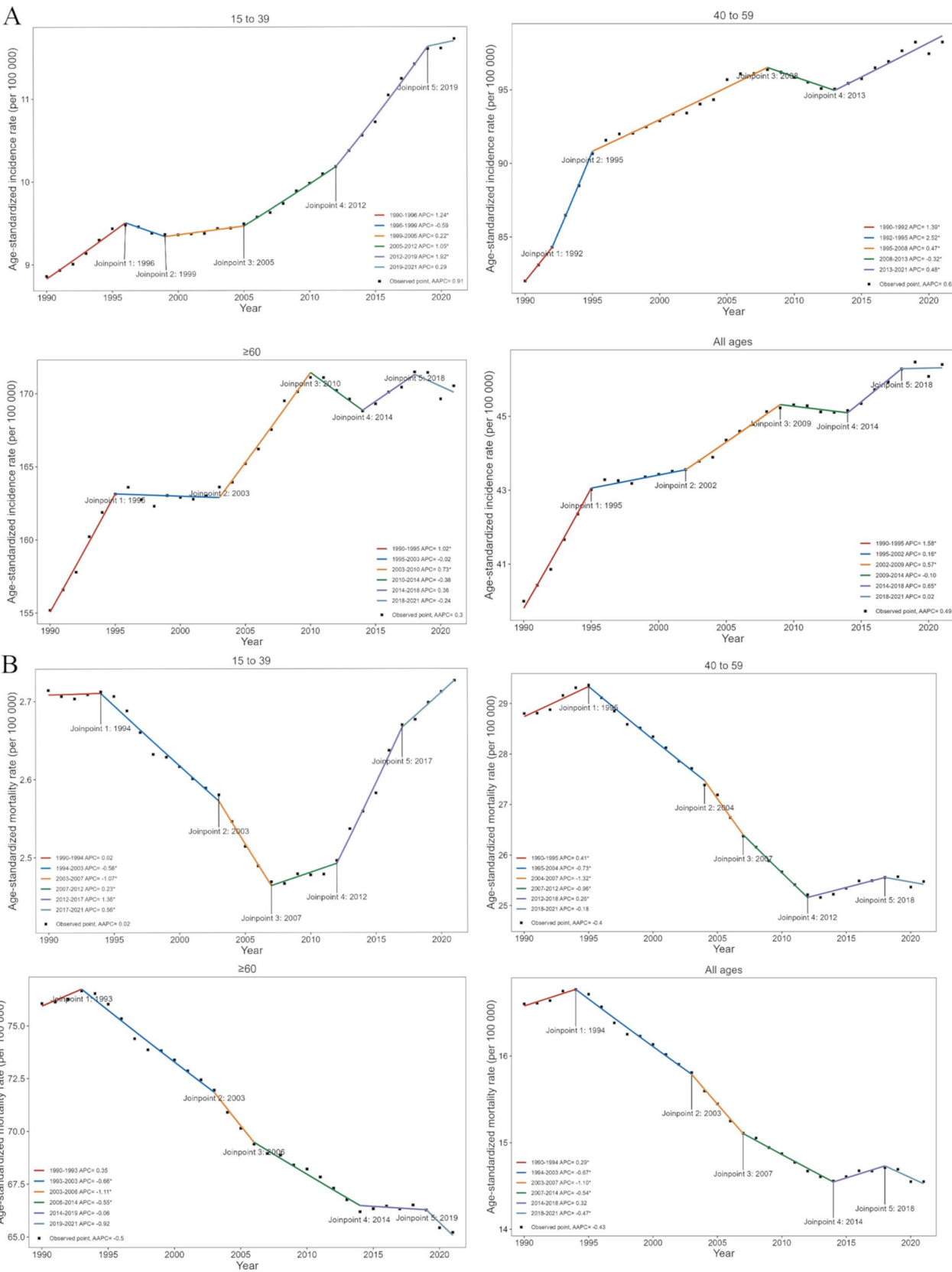


Fig. 1 (See legend on next page.)

(See figure on previous page.)

Fig. 1 Joinpoint regression analysis was conducted to examine the ASIR and ASMR for breast cancer across different age groups from 1990 to 2021. **(A)** The ASIR for the 15 to 39 years group, 40 to 59 years group, ≥ 60 years group, and all ages group. **(B)** The ASMR for the 15 to 39 years group, 40 to 59 years group, ≥ 60 years group, and all ages group

The findings suggest that, although the proportion is relatively small, there is a more pronounced trend of increasing disease burden in BCYW compared to other age groups affected by breast cancer.

Different SDI regional burden and trend of BCYW

From 1990 to 2021, the ASIR in BCYW significantly increased in regions with low SDI, low-middle SDI, middle SDI, and high-middle SDI ($AAPC > 0$, $P < 0.05$), while it remained unchanged in regions with high SDI ($P > 0.05$). This trend was also observed among middle-aged and older groups (Fig. 2; Table 1).

Between 1990 and 2021, the ASPR in BCYW significantly increased in regions with low SDI, low-middle SDI, middle SDI, and high-middle SDI ($AAPC > 0$, $P < 0.05$), while it remained unchanged in regions with high SDI ($P > 0.05$). This trend was also observed among the middle-aged group. Additionally, a rising prevalence was found among the elderly group ($AAPC > 0$, $P < 0.05$) (Fig. 2, Table S1).

During the period from 1990 to 2021, the ASMR in BCYW significantly increased in regions with low SDI and low-middle SDI ($AAPC > 0$, $P < 0.05$). However, it remained unchanged in regions with middle SDI ($P > 0.05$), while it decreased in regions with high-middle SDI and high SDI ($AAPC < 0$, $P < 0.05$). Among the middle-aged and elderly populations, there was an increase in ASMR rates observed in regions with low SDI, low-middle SDI, and middle SDI groups ($AAPC > 0$, $P < 0.05$), whereas a decrease was noted in the regions with high-middle SDI and high SDI ($AAPC < 0$, $P < 0.05$) (Fig. 2; Table 1).

Between 1990 and 2021, the ASDR was significantly increased in regions with low SDI and low-middle SDI, as well as middle SDI ($AAPC > 0$, $P < 0.05$). Conversely, it decreased in regions with high-middle SDI and high SDI ($AAPC < 0$, $P < 0.05$). Among the middle-aged and elderly populations, a similar trend was observed for AAPC (Fig. 2, Table S1).

During the period from 1990 to 2021, regions with a high SDI exhibited the highest values of ASIR and ASPR in BCYW, while regions with low-middle SDI showed the highest values of ASMR and ASDR in BCYW (Fig. S2). The analysis examined the proportions of ASIR, ASMR, ASPR, and ASDR across three age groups in five distinct SDI regions from 1990 to 2021. The results revealed that BCYW displayed the highest values for these four indicators in low and low-middle SDI regions, while the lowest values were observed in the high SDI region (Fig. S3, S4). The correlation coefficients between ASIR, ASMR,

ASPR, ASDR of BCYW and SDI were found to be 0.57 ($P < 0.05$), -0.20 ($P < 0.05$), 0.61 ($P < 0.05$), and -0.17 ($P < 0.05$), respectively (Fig. S5, S6).

Regional burden and trend of BCYW

The regions with the highest ASIR for BCYW in 2021 were high-income North America (19.39/100,000), Western Europe (18.47/100,000), and Australasia (16.63/100,000). Conversely, Central Sub-Saharan Africa (6.34/100,000), Western Sub-Saharan Africa (7.53/100,000), and Andean Latin America (8.38/100,000) had the lowest ASIR for BCYW in 2021 (Table S2). The regions experiencing the most significant increases in AAPC of ASIR for BCYW between 1990 and 2021 were North Africa and Middle East (3.03, 95%CI: 2.87 to 3.19, $P < 0.05$), South Asia (2.04, 95%CI: 2.13 to 2.75, $P < 0.05$), and Central Latin America (1.95, 95% CI: 1.71 to 2.19, $P < 0.05$). On the other hand, the most substantial declines in AAPC were observed in Central Asia (-0.73, 95% CI: -0.91 to -0.56, $P < 0.05$), High-income North America (-0.55, 95% CI: -1.10 to -0.01, $P < 0.05$), and Western Europe (-0.20, 95%CI: -0.65 to -0.24, $P > 0.05$) (Table S2).

In 2021, Oceania (5.38/100,000), Eastern Sub-Saharan Africa (4.10/100,000), and Southern Sub-Saharan Africa (3.93/100,000) had the highest ASMR for BCYW among all regions. On the other hand, High-income Asia Pacific (1.48/100,000), Australasia (1.74/100,000), and East Asia (1.75 /100,000) had the lowest ASMR for BCYW in that year (Table S2). The regions with the highest increases in AAPC of ASMR for BCYW between 1990 and 2021 were South Asia (1.23, 95%CI: 0.92 to 1.54, $P < 0.05$), North Africa and the Middle East (1.08, 95%CI: 0.95 to 1.21, $P < 0.05$), and Eastern Sub-Saharan Africa (0.91, 95% CI: 0.76 to 1.06, $P < 0.05$). Conversely, significant declines in AAPC were observed in Western Europe (-2.16, 95% CI: -2.45 to -1.88, $P < 0.05$), Australasia (-2.05, 95% CI: -2.36 to -1.73, $P < 0.05$), and High-income North America (-1.72, 95%CI: -2.24 to -1.20, $P < 0.05$) (Table S2).

The regions exhibiting the most substantial increases in AAPC of ASPR for BCYW between 1990 and 2021 were North Africa and the Middle East (3.10, 95%CI: 2.94 to 3.27, $P < 0.05$), South Asia (2.55, 95%CI: 2.27 to 2.83, $P < 0.05$), and East Asia (2.21, 95% CI: 1.92 to 2.50, $P < 0.05$) (Table S3). The regions with the most significant increases in AAPC of ASDR for BCYW between 1990 and 2021 were South Asia (AAPC: 1.29, 95%CI: 1.00 to 1.58, $P < 0.05$), North Africa and the Middle East (AAPC: 1.22, 95%CI: 1.09 to 1.34, $P < 0.05$), and Eastern Sub-Saharan Africa (0.94, 95% CI: 0.79 to 1.10, $P < 0.05$) (Table S3).

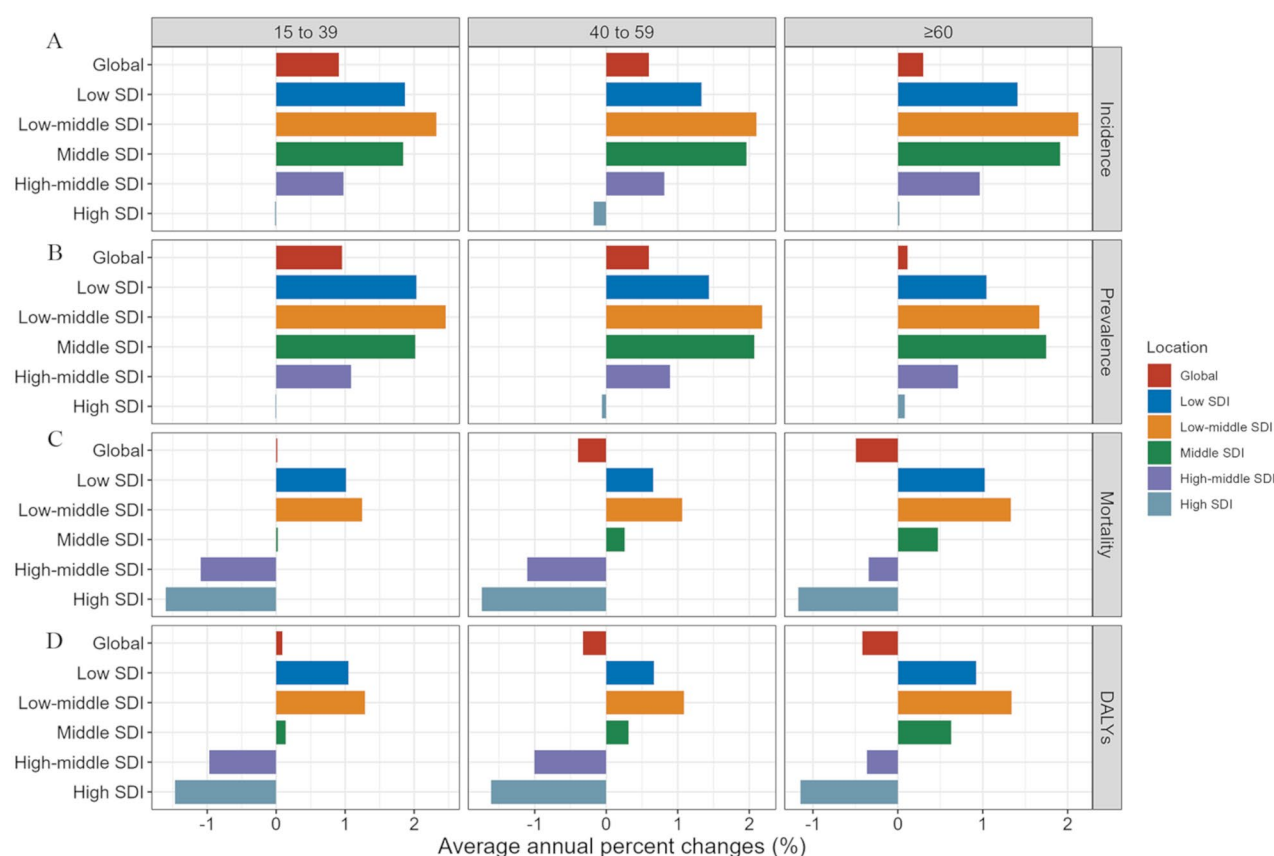


Fig. 2 The AAPCs of ASIR (A), ASMR (B), ASPR (C), and ASDR (D) in different age groups globally and across five SDI regions from 1990 to 2021

Among all GBD super-regions in 2021, high-income regions exhibited the highest ASIR of BCYW (17.84/100,000). However, the South Asia region recorded the highest ASMR (3.2/100,000). Notably, high-income regions also had the peak ASPR (157.58/100,000), whereas the Sub-Saharan Africa region showed the highest ASDR burden (207.62/100,000). Importantly, high-income regions showed decreasing AAPCs for ASIR, ASMR, ASPR, and ASDR (Table S4, Table S5).

The correlation coefficients of ASIR, ASMR, ASPR, and ASDR in BCYW from high-income GBD regions were 0.86 ($P < 0.05$), -0.11 ($P < 0.05$), 0.87 ($P < 0.05$), and -0.07 ($P < 0.05$), respectively. It is worth mentioning that ASMR and ASDR in the other two age groups exhibit a positive correlation with the high-income GBD region, indicating distinct characteristics of breast cancer among young individuals compared to the other two age groups (Fig. S7, S8).

National burden and trend of BCYW

The countries with the highest ASIR for BCYW in 2021 were Monaco (51.92/100,000), Bahamas (33.18/100,000), and Cook Islands (30.74/100,000). On the other hand, Guatemala (2.82/100,000), Gambia (3.27/100,000), and Oman (3.52/100,000) had the lowest ASIR for BCYW in

2021 (Fig. 3, Table S6). The countries exhibiting the highest increase in AAPC of ASIR between 1990 and 2021 were Turkey (6.49, 95%CI: 5.41 to 7.58, $P < 0.05$), Thailand (3.72, 95%CI: 3.00 to 4.45, $P < 0.05$), and Equatorial Guinea (3.63, 95%CI: 2.81 to 4.45, $P < 0.05$), the most significant declines in AAPC were observed in Saint Kitts and Nevis (-3.27, 95% CI: -3.16 to -2.32, $P < 0.05$), Armenia (-2.08, 95% CI: -2.58 to -1.58, $P < 0.05$), Ukraine (-1.69, 95% CI: -2.74 to -0.62, $P < 0.05$) (Fig. 3, Table S6).

The countries exhibiting the highest rates of ASMR per 100,000 individuals were Tokelau (9.53), Palau (8.95), and Niue (8.90), while those with the lowest rates were Oman (0.44), Norway (1.15), and Mongolia (1.16) (Fig. 3, Table S6). The countries with the highest increase in AAPC of ASMR between 1990 and 2021 were Turkey (3.64, 95%CI: 2.67 to 4.62, $P < 0.05$), Zimbabwe (2.79, 95%CI: 2.08 to 3.51, $P < 0.05$), and Lesotho (2.65, 95%CI: 2.22 to 3.07, $P < 0.05$). Conversely, the most significant declines in AAPC were observed in Saint Kitts and Nevis (-4.18, 95%CI: -4.71 to -3.65, $P < 0.05$), Armenia (-3.50, 95%CI: -3.97 to -3.02, $P < 0.05$), and Luxembourg (-3.43, 95% CI: -4.92 to -1.92, $P < 0.05$) (Fig. 3, Table S6).

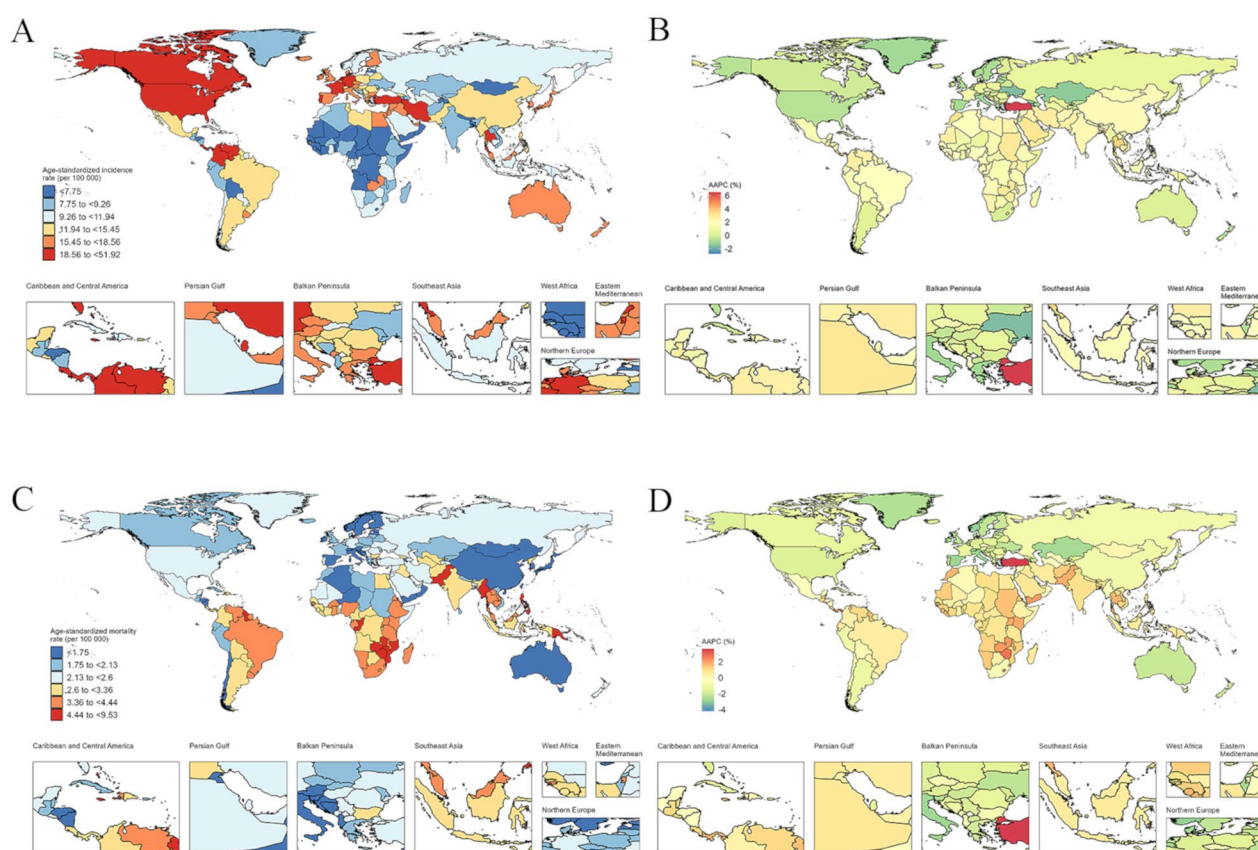


Fig. 3 ASIR (A) and ASMR (C) of breast cancer in young women in 204 countries and territories in 2021. AAPC of ASIR (B) and AAPC of ASMR (D) of breast cancer in young women in 204 countries and territories from 1990 to 2021

Projected future global and Chinese burden of BCYW

The BAPC model was employed to forecast the global and Chinese ASIR, ASMR, ASPR, and ASDR in three age groups from 2022 to 2035. The findings revealed a consistent annual increase in all four indicators of BCYW both globally and in China. Notably, China exhibited higher ASIR and ASPR rates compared to the global average (Fig. 4), while ASMR and ASDR rates were lower than the global average (Fig. 4). In the 40–59 age group, China exhibits higher ASIR and ASPR compared to the global average level, with a faster growth trend than the global level. However, China's ASMR and ASDR are lower than the global level. In the elderly group, China's ASIR and ASPR will gradually surpass the global average level, while ASMR and ASDR remain lower than the global level (Fig. S9).

Discussion

The incidence of BCYW may be relatively low, and the proportion of cases may also be relatively small; however, it remains a profoundly debilitating disease for individuals, families, and societies. The present study aimed to compare and analyze the distinct characteristics of ASIR,

ASMR, ASDR, and DALYs associated with breast cancer across three different age groups. Additionally, it sought to examine the unique features of BCYW worldwide, thereby providing valuable evidence for its prevention and control.

In this study, it was observed that the AAPC of ASIR in young breast cancer patients was higher at 0.91 compared to the middle-aged group (0.60) and the elderly group (0.30). Furthermore, the 2021 ASIR for all three age groups was highest in the high SDI region across the five SDI regions. The significant utilization of mammography screening in regions with high SDI was a prominent factor contributing to the upward trajectory of breast cancer. The extent of breast cancer screening varies considerably among different nations. Well-established breast cancer screening programs were present in Europe, the United States, Singapore, Australia, and New Zealand. Nevertheless, numerous countries in Latin America, Central and Western Asia as well as North Africa either lack comprehensive screening programs or have not yet adopted them [23]. It is worth noting that there are currently no national recommendations or guidelines for breast cancer screening in any sub-Saharan African country [23].

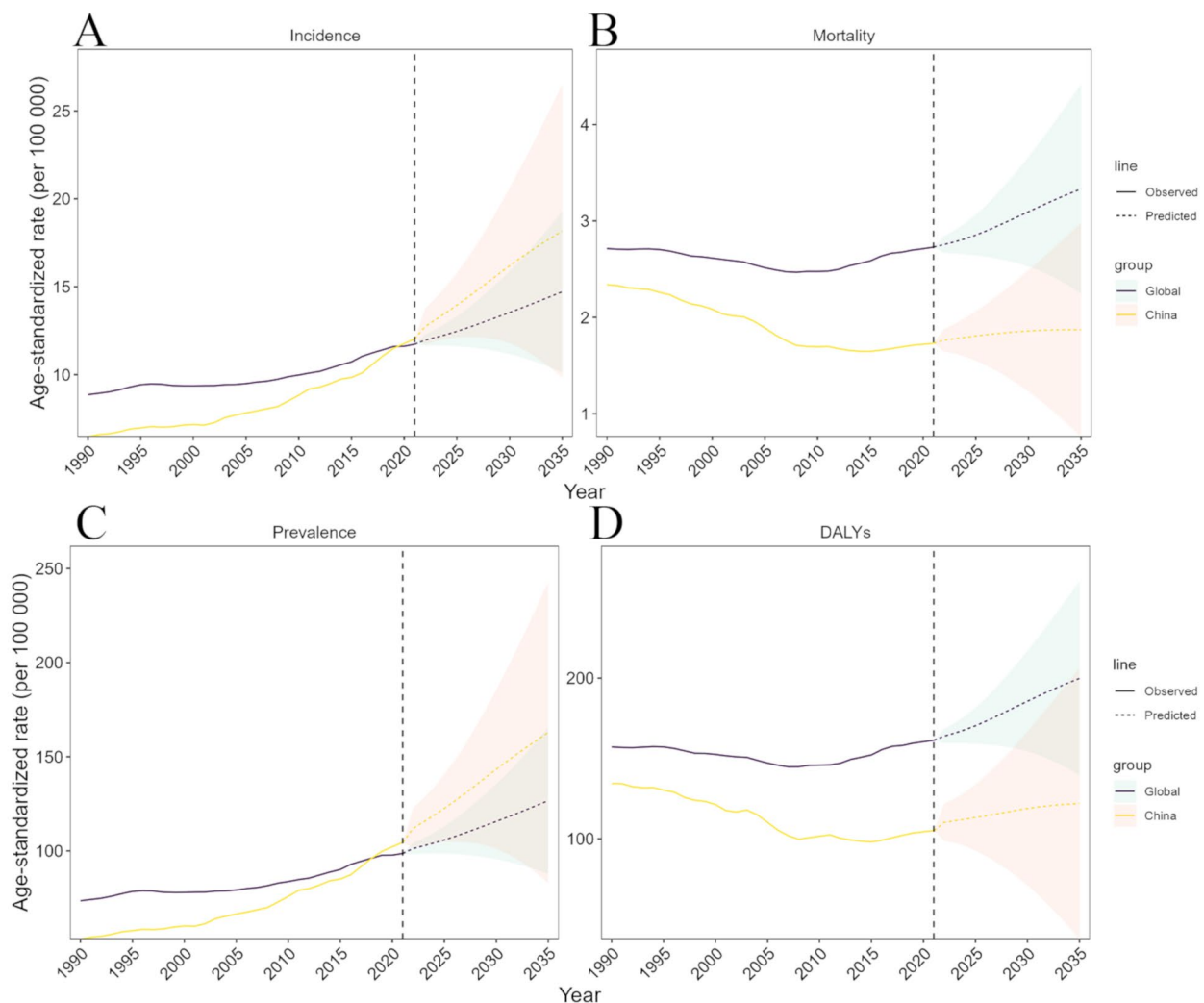


Fig. 4 Projections of ASIR (A), ASMR (B), ASPR (C), and ASDR (D) for breast cancer among individuals aged 15–39 years globally and in China from 2022 to 2035

Only 14.30% of women aged 18 to 39 in the United States underwent mammographic screening [24]. These indicate that younger women are less inclined to engage in routine screening compared to older women. Consequently, public health policies may need to emphasize the development of tailored screening approaches for younger populations while enhancing awareness and encouraging greater participation in screening programs. In China, the Chinese National Breast Cancer Screening Program (CNBCSP) and the Chinese breast cancer Multimodality Independent Screening Trial (MIST) were developed and implemented in 2008 to carry out two comprehensive pilot projects for breast cancer screening [25, 26]. Moreover, reproductive, hormonal, and behavioral risk factors additionally contribute to the elevated incidence of breast cancer in certain transitioning countries [27].

However, achieving a consensus on the necessity of breast cancer screening for young women remains elusive [28]. Some researchers posit that screening can enhance the detection rate of breast cancer in young individuals and subsequently improve their survival outcomes. It has been observed that BCYW (<40 years) have a higher risk of dying from breast cancer compared to older counterparts (≥ 40 years) (cHR 1.39, CI 1.34–1.45) [10]. On the contrary, some scholars argue that the potential disadvantages of screening young women for breast cancer outweigh its advantages. The potential drawbacks of screening for young women include limited sensitivity, false positive results, unwarranted psychological distress, and the risk of radiation-induced cancer, all of which can unnecessarily compromise their well-being [28–31]. The screening for young women was recommended for those who present high-risk factors, such as being carriers of BRCA 1/2 gene mutations, having a history of

chest irradiation, or having a history of benign breast disease [29]. At present, the American College of Obstetricians and Gynecologists (ACOG) [32] and the American College of Radiology (ACR) [33] recommend initiating mammography breast cancer screening for average-risk women at the age of 40, while the U.S. Preventive Services Task Force (USPSTF) [31] suggests commencing screening at the age of 50, women aged between 40 and 49 are encouraged to make an informed decision regarding their own screening.

The AAPC of ASMR in the middle-aged group and the elderly group were -0.40% and -0.50% , respectively, while that in young breast cancer patients was 0.02% . Similar patterns were identified for the AAPC of ASPR and ASDR. The findings indicate that the global disease burden of BCYW is a matter of concern, underscoring the urgent need for heightened attention and more comprehensive disease management strategies targeting this population. In recent years, the advancement of treatments has significantly enhanced the survival rates for breast cancer. However, there still exist notable disparities in survival rates among different countries. The 5-year survival rate for breast cancer in countries such as the United States, the United Kingdom, and Canada was 85% or above. In countries like China, Turkey, Singapore, and Brazil, the 5-year survival rate ranges from 80 to 84% . Cuba and Estonia have a 5-year survival rate of 70 – 79% , while Thailand (69%) and India (66%) still exhibit significantly lower rates [3]. The age factor plays a significant role in determining breast cancer survival. The 10-year relative survival rate for breast cancer patients under 40 in France was 74.60% from 1990 to 1999, compared to 79.40% for patients aged 50–74. In the period of 2000–2008, the rate increased to 78.30% for patients under 40 and reached 88.30% for those aged between 50 and 74 [34]. Furthermore, our study findings revealed that the region with the highest SDI exhibited the highest ASIR and ASPR for BCYW in 2021 among the five SDI regions, while demonstrating the lowest ASMR and ASDR. The observed decrease in mortality rates in most high-income countries aligns with the widely accepted notion that economic development facilitates advancements in medical technology, improves access to healthcare services, and aids disease prevention and treatment [35, 36]. In addition, the fertility preservation and pregnancy desire of young breast cancer patients also require the expertise of multidisciplinary professionals to provide specialized assistance [37]. However, the prevention and treatment of young breast cancer in low SDI regions continue to encounter significant challenges. First, it is essential to provide comprehensive training for healthcare professionals and enhance public awareness regarding breast cancer. Second, international cooperation should be strengthened to optimize the allocation of

health resources efficiently. Finally, regionally appropriate public health policies must be developed, along with the establishment of suitable screening and treatment protocols [38]. The increasing disease burden of BCYW has placed significant strain on medical resources, precipitated family economic crises, disrupted career trajectories, inflicted psychological trauma, and further exacerbated the loss of social productivity. Consequently, region-specific intervention strategies are essential to tackle the unique epidemiological patterns of BCYW. In low and low-middle SDI regions, priorities should focus on raising disease awareness, enhancing screening participation among young women, and optimizing the allocation of healthcare resources to control the rising incidence. By contrast, in high-SDI countries, reinforcing and expanding current prevention efforts are critical to sustaining the declining trend in incidence rates.

China, with its substantial population, ranks among the nations with a significant disease burden related to breast cancer. The median age at diagnosis of breast cancer in China was 45–49 years, which was significantly lower than the range of 62 to 64 years observed in the United States [39, 40]. The findings of this study suggest that there will be a higher incidence and prevalence of breast cancer among young Chinese individuals compared to the global average. Therefore, proactive measures for effective management are necessary. The CNBCSP was currently conducting the largest population-based breast cancer screening cohort study ever conducted in China. It includes a total of 1,226,714 women aged 35–69 years (including 398,184 urban women and 828,530 rural women) who were enrolled in this program between 2009 and 2011 [26]. Additionally, the program also identified significant differences in screening efficacy and cancer distribution patterns between urban and rural populations. Consequently, it is imperative to develop tailored screening protocols for specific demographic groups to enhance breast cancer detection rates. Furthermore, comprehensive cost-benefit analyses are required to evaluate the health economic implications of various screening methodologies [26]. Notably, the disparity in survival rates between breast cancer patients in urban and rural areas of China was also remarkable [41]. Additionally, the MIST program enrolled a total of 33,234 women aged from five regions in China between 2008 and 2010 [25]. The Chinese government has implemented a series of policies and measures aimed at mitigating the impact of malignant tumors on individuals' life and health. Since 2015, the Chinese government has executed a range of mid- to long-term strategic plans in the healthcare sector. In both the China Mid- and Long-term Chronic Disease Prevention and Control Plan (2017–2025) and the Healthy China 2030 strategy, cancer survival rates are acknowledged as a pivotal metric for evaluating

healthcare system efficacy [41]. The government aims to implement a range of policies aimed at safeguarding public health and alleviating the burden of disease.

Distinguished from previous studies [15], this study innovatively categorized breast cancer patients by age group. The findings revealed that the disease burden among BCYW exhibited a significantly more pronounced upward trend compared to other age groups. Additionally, the prediction and comparison of the disease burden of BC in China for 2022 and 2030, contrasted with global data across three age groups, offers more targeted and robust scientific evidence for the development of precise prevention strategies for BCYW. However, our study had several limitations. Firstly, the lack of robust population-based cancer registries in many low- and middle-income countries may lead to inaccurate estimations of breast cancer burden within these nations. Secondly, the absence of clinical data, treatment interventions, and other relevant information in GBD data hinders a comprehensive analysis of the disease burden associated with breast cancer. Thirdly, our projections of future breast cancer burdens are solely based on current patterns without considering potential impacts from unpredictable factors, significant advancements in medical technology, changes in policy measures, and other relevant variables.

In conclusion, the ASIR, ASMR, ASPR, and ASDR of AAPC in BCYW were found to be higher compared to those in middle-aged and elderly breast cancer patients. Moreover, the burden of BCYW was particularly significant in regions with low-SDI, low-middle SDI, and middle SDI regions. Therefore, it is essential to clearly define specific objectives for the prevention and treatment of BCYW and to develop targeted public health policies and interventions. Concurrently, enhancing international collaboration, optimizing the allocation of healthcare resources, and establishing a comprehensive screening and treatment framework are crucial to reducing the disease burden associated with BCYW. Despite progress made, China still faces considerable challenges in effectively addressing this issue, emphasizing the need for continued implementation of existing policies and measures to safeguard people's lives and health.

Abbreviations

ASR	Age-standardized rates
ASIR	Age-standardized incidence rate
ASMR	Age-standardized mortality rate
ASPR	Age-standardized prevalence rate
ASDR	Age-standardized disability-adjusted life years rate
AAPC	The Average Annual Percent Change
BAPC	Bayesian Age-Period-Cohort
BCYW	Breast cancer in young women
CI	Confidence intervals
DALYs	Disability-adjusted life years
SDI	Sociodemographic index
TNBC	Triple-negative breast cancer
UI	Uncertainty interval

Supplementary Information

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Supplementary Material 1

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Author contributions

YF and SW designed this study, WW and JL performed software and database, WW, YS, and CR performed data collection, data analysis, and data interpretation, WW, YS, HB, and JL drafted the article, WW, SW, CR, and JL revised the article, YF and SW approved the final version to be published. All authors reviewed the manuscript.

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Data availability

Data availability The data are available from the GBD Results Tool of the GHDx (ghdx.healthdata.org/gbd-results-tool).

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Conflict of interest

The authors declare that no competing interests exist.

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