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The global burden of breast cancer among women of reproductive age: a comprehensive analysis

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Breast cancer is the most prevalent malignant disease among women and affects women of reproductive age (15–49 years) across the globe. This study examines patterns and trends in the epidemiology of breast cancer in women of reproductive age using global burden of disease data (1990–2021), with the objective of informing targeted public health strategies. Using data from the Global Burden of Disease Study (GBD 2021), this study analyzed the temporal trends, regional disparities, and health inequalities in the burden of breast cancer among women of reproductive age across 204 countries and territories from 1990 to 2021. The analysis employed methodologies including the age-period-cohort (APC) model, decomposition analysis, the slope index of inequality (SII), and the concentration index (CIX). Additionally, the Bayesian age-period-cohort (BAPC) predictive model was utilized to forecast the global burden of breast cancer among women of reproductive age from 2022 to 2040. From 1990 to 2021, the global burden of breast cancer among women of reproductive age showed a significant upward trend, with increases of 118.7%, 121.3%, and 66.8% in the number of new cases, prevalence, and disability-adjusted life years (DALYs) lost, respectively. The most pronounced increases were observed in regions with low and low-middle sociodemographic index (SDI). APC analysis revealed that the rising incidence and prevalence rates were driven by age and period effects, while the risk of breast cancer declined among more recent birth cohorts. Decomposition analysis indicated that population aging and growth were the primary contributors to the global rise in breast cancer burden. SII and CIX analyses demonstrated that absolute health inequalities in breast cancer burden intensified during this period, while relative inequalities showed a slight decline. According to the BAPC predictive model, by 2040, the number of new breast cancer cases among women of reproductive age is expected to increase by 47.8% compared to 2022, accompanied by continued rises in age-standardized incidence, prevalence, and mortality rates. Between 1990 and 2021, the global burden of breast cancer among women of reproductive age increased significantly, with notable health inequalities across regions and populations. By 2040, new cases are projected to rise by 47.8% from 2022, underscoring an urgent global challenge in breast cancer prevention and control.

Keywords Breast cancer, Women of reproductive age, Global burden of disease, Time trends, Health inequalities, Projections

Breast cancer represents the leading malignancy affecting women worldwide, constituting an escalating public health challenge with substantial socioeconomic implications¹. Contemporary epidemiological data indicate a consistent elevation in incidence and mortality rates over recent decades, with disproportionate increases observed in developing nations. Women of reproductive age (defined as 15–49 years) constitute a distinct demographic, as this period is crucial for reproductive and family-building activities. A diagnosis of breast cancer in this group not only compromises physical health but also exerts a multifaceted impact on reproductive capacity, psychological well-being, and socioeconomic stability, thereby amplifying the disease's broader societal and individual burden².

The period from 1990 to 2021 witnessed substantial transformations in the epidemiological patterns of breast cancer among women of reproductive age, characterized by shifting geographic distributions and evolving risk factor profiles. Significant disparities in incidence and mortality rates across regions, countries, and urban-rural settings underscore the complex interplay of factors such as genetic predisposition, environmental exposures,

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lifestyle behaviors, and inequities in healthcare access³. Despite these variations, research focusing specifically on this age group remains insufficient, creating a critical gap in understanding the unique determinants and implications of breast cancer in this population. This lack of targeted analysis limits the design, implementation, and evaluation of effective, evidence-based public health interventions tailored to address the distinct challenges faced by women of reproductive age.

This study utilizes the most recent Global Burden of Disease (GBD) data, released in 2024, to systematically examine trends in the incidence, mortality, and disability-adjusted life years attributable to breast cancer among women of reproductive age from 1990 to 2021. The Global Burden of Disease database is a comprehensive and methodologically rigorous resource that provides estimates of disease burden, injuries, and risk factors that are globally comparable across countries, regions, and demographic strata, making it an indispensable tool for global health research. The present study leverages this robust dataset to conduct an in-depth epidemiological analysis of breast cancer in the specified demographic group, with the objective of offering critical insights into disease patterns and trends. This comprehensive analysis aims to provide evidence-based insights to guide public health policy formulation, optimize resource allocation, and inform the development of targeted interventions. Ultimately, this research seeks to enhance health outcomes and quality of life for reproductive-age women affected by breast cancer through the implementation of data-driven strategies. The Institute for Health Metrics and Evaluation (IHME) is responsible for the annual updates to the Global Burden of Disease (GBD) studies. These updates incorporate new datasets that become available, improve methodological performance, and adopt changes in the scientific understanding of diseases. Consequently, the results of GBD data analysis become completer and more accurate over time. The most recent iteration of the GBD, GBD 2021 (released in 2024), supersedes all previous versions (GBD 1990, 2020, 2013, 2015, 2016, 2017, and 2019).

Materials and methods

Data sources

The data used in this study were obtained from the Global Burden of Disease (GBD) 2021 database (<https://g.hdx.healthdata.org/gbd-2021>), which provides comprehensive estimates for 204 countries and territories, 371 diseases and injuries, and 88 risk factors. We downloaded the incidence number, incidence rate, prevalence number, Mortality rate, Mortality number, prevalence rate, disability-adjusted life years (DALY) number, and DALY rate for breast cancer among women of reproductive age (15–49 years). The number refers to the count of individuals affected by the disease in a given year, while the rate represents the number of cases per 100,000 population^{4–6}. The 204 countries and territories included in this analysis represent approximately 99.9% of the global population, providing comprehensive worldwide coverage.

Disease definition

According to the GBD 2021 study, diseases and injuries are typically categorized into four main levels. The first level includes communicable, maternal, neonatal, and nutritional diseases; non-communicable diseases and injuries. Breast cancer is classified under the third level of neoplasms, which falls under the second level of non-communicable diseases within the first level. The International Classification of Diseases (ICD)-11 code for breast cancer is 2C60⁷.

Age-Standardized data calculation for women of reproductive age

Age standardization was performed to eliminate the influence of population age structure on overall rates, enabling comparisons of disease burden across different years and regions. The standard population composition for the 15–49 age group was recalculated by extracting the population numbers from the standard population. The crude rates for each 5-year age group within the 15–49 range were multiplied by the corresponding population weights in the standard population and then summed to obtain the age-standardized rate for women of reproductive age.

Joinpoint model construction

The Joinpoint model was employed to explore the turning points (joinpoints) in disease prevalence trends and calculate the annual percent change (APC) between the turning points, as well as the average annual percent change (AAPC) for the entire age range, which is a weighted average of the APCs.

APC (Age-Period-Cohort) model construction

To investigate the effects of age, period, and birth cohort on the study subjects, we constructed an age-period-cohort (APC) model. The model considers age, period, and birth cohort as independent variables and the study subjects as the dependent variable, fitting a generalized linear model. Age reflects the biological changes during an individual's life course, period represents the historical events and environmental changes experienced by all age groups, and birth cohort captures the unique experiences of different birth generations.

Health inequality analysis

To examine health inequality in the global disease burden, we employed the Slope Index of Inequality (SII) and Concentration Index methods. The SII measures the absolute inequality in health variables across different socioeconomic groups, representing the health difference between the lowest and highest socioeconomic groups. The Concentration Index quantifies the degree of inequality in health variables across socioeconomic groups, ranging from –1 to 1, with 0 indicating perfect equality.

Decomposition analysis

To further investigate the factors contributing to differences in the global disease burden, we utilized decomposition analysis. This method decomposes the overall health differences into contributions from various factors, such as population growth, population aging, and epidemiological changes.

Socio-Demographic index (SDI)

The Socio-Demographic Index (SDI), developed by GBD researchers, is a composite indicator of development status closely linked to health outcomes. It is the geometric mean of the 0 to 1 indices of total fertility rate under 25 (TFU25), average educational attainment for ages 15 and older (EDU15+), and lag-distributed income per capita (LDI). A location with an SDI of 0 would have the theoretically lowest level of development relevant to health, while a location with an SDI of 1 would have the theoretically highest level (<https://ghdx.healthdat.org/record/global-burden-disease-study-2021-gbd-2021-socio-demographic-index-sdi>). We applied LOESS smoothing to visualize trends and performed Spearman's correlation tests to quantify the relationship between SDI and disease burden indicators.

BAPC model construction

The Bayesian Age-Period-Cohort (BAPC) prediction model is a statistical method based on the Bayesian framework that combines the effects of age, period, and birth cohort to forecast future trends in disease incidence, mortality, or other health indicators. We used the INLA framework within the BAPC package to predict future disease burden from 2022 to 2040.

Statistical analysis

All data processing, statistical analyses, and visualizations were performed using R version 4.4.1 (<https://www.r-project.org/>), with the following packages: dplyr, tidyverse, stringr, and arrow for data manipulation and analysis; ggplot2, ggmap, rgdal, RColorBrewer, patchwork, and ggrepel for data visualization; rgdal for geospatial analysis and stats for statistical analysis.

Results

Global trends

Between 1990 and 2021, the global burden of breast cancer among women of reproductive age showed a consistent increase. The number of incident cases rose from 256,715 (244,599–271,011) in 1990 to 561,438 (519,759–606,989) in 2021. The age-standardized incidence rate (ASIR) increased from 22.60 (21.56–23.84) per 100,000 to 27.51 (25.46–29.75) per 100,000, with an average annual percentage change (AAPC) of 0.5% (95% CI: 0.44–0.55%). During the same period, the number of prevalent cases grew from 2,170,812 (2,055,628–2,297,082) to 4,804,868 (4,464,320–5,186,300). The age-standardized prevalence rate (ASPR) increased from 191.47 (181.41–202.45) per 100,000 to 235.29 (218.54–254.04) per 100,000, with an AAPC of 0.55% (95% CI: 0.50–0.60%). The disability-adjusted life years (DALYs) rose from 3,992,794 (3,737,072–4,297,211) in 1990 to 6,659,459 (6,111,787–7,245,687) in 2021. However, the age-standardized DALY rate (ASDR) decreased from 347.91 (326.05–373.80) per 100,000 to 327.24 (300.15–356.24) per 100,000, with an AAPC of -0.38% (95% CI: -0.48 to -0.28%). Similarly, the number of deaths increased from 78,285 (73,581–84,120) in 1990 to 129,405 (119,195–140,408) in 2021, while the age-standardized mortality rate (ASMR) declined from 6.90 (6.50–7.41) per 100,000 to 6.34 (5.84–6.88) per 100,000, with an AAPC of -0.47% (95% CI: -0.57 to -0.36%) (Tables 1, 2, 3 and 4).

Patterns across five SDI regions

Between 1990 and 2021, the burden of breast cancer among women of reproductive age increased across all SDI regions, except for high SDI regions. In high SDI regions, the average annual percentage changes (AAPCs) for age-standardized incidence rate (ASIR), prevalence rate (ASPR), disability-adjusted life years (DALYs) rate, and mortality rate (ASMR) were -0.33% (95% CI: -0.45 to -0.20%), -0.24% (95% CI: -0.37 to -0.11%), -1.80% (95% CI: -1.87 to -1.73%), and -1.97% (95% CI: -2.05 to -1.90%), respectively.

In contrast, the AAPCs for ASIR in upper-middle, middle, lower-middle, and low SDI regions were 0.80% (95% CI: 0.72 to 0.89%), 1.81% (95% CI: 1.73 to 1.88%), 2.04% (95% CI: 1.98 to 2.10%), and 1.45% (95% CI: 1.31 to 1.59%), respectively. For ASPR, the AAPCs were 0.93% (95% CI: 0.85 to 1.02%), 1.99% (95% CI: 1.91 to 2.06%), 2.23% (95% CI: 2.17 to 2.28%), and 1.68% (95% CI: 1.52 to 1.84%).

The AAPCs for age-standardized DALY rates were -1.32% (95% CI: -1.41 to -1.23%) in upper-middle SDI regions, 0.02% (95% CI: -0.08 to 0.11%) in middle SDI regions, 0.98% (95% CI: 0.92 to 1.04%) in lower-middle SDI regions, and 0.68% (95% CI: 0.58 to 0.79%) in low SDI regions.

Similarly, the AAPCs for ASMR were -1.48% (95% CI: -1.58 to -1.38%) in upper-middle SDI regions, -0.06% (95% CI: -0.15 to 0.03%) in middle SDI regions, 0.93% (95% CI: 0.87 to 0.99%) in lower-middle SDI regions, and 0.63% (95% CI: 0.53 to 0.74%) in low SDI regions (Tables 1, 2, 3 and 4).

Analysis of 21 GBD regions

Between 1990 and 2021, age-standardized incidence rates (ASIRs) of breast cancer among women of reproductive age declined in Australasia, Central Asia, Eastern Europe, high-income North America, and Western Europe, while increasing in the remaining 16 GBD regions. The highest AAPCs in ASIR were observed in North Africa and the Middle East (3.39%; 95% CI: 3.24–3.54%), East Asia (2.14%; 95% CI: 2.07–2.22%), South Asia (2.02%; 95% CI: 1.87–2.17%), and Sub-Saharan Africa (2.02%; 95% CI: 1.54–2.51%). In contrast, the AAPCs for ASIR in Australasia, Central Asia, Eastern Europe, high-income North America, and Western Europe were -0.16% (95%

Location	1990		2021		EAPC, 1990-2021
	Number	ASR	Number	ASR	
Global	256715.75 (244599.77–271101.61)	22.60 (21.56–23.84)	561438.09 (519759.29–606989.93)	27.51 (25.46–29.75)	0.5 (0.44 to 0.55)
High SDI	109864.44 (106133.24–113771.40)	46.12 (44.56–47.76)	125312.96 (119245.01–131419.33)	42.42 (40.36–44.49)	-0.33 (-0.45 to -0.2)
High-middle SDI	62621.83 (57963.30–67861.82)	25.20 (23.37–27.26)	124149.85 (107985.12–143660.69)	32.37 (28.13–37.49)	0.8 (0.72 to 0.89)
Middle SDI	52868.44 (47818.45–58805.85)	14.94 (13.53–16.58)	183590.95 (165029.59–203951.82)	26.93 (24.21–29.93)	1.81 (1.73 to 1.88)
Low-middle SDI	23095.73 (20206.29–26281.60)	10.57 (9.27–11.99)	95123.05 (82566.94–107863.37)	20.25 (17.60–22.91)	2.04 (1.98 to 2.1)
Low SDI	7950.19 (6568.50–9620.63)	9.32 (7.71–11.27)	32752.16 (27291.97–38647.44)	15.07 (12.62–17.70)	1.45 (1.31 to 1.59)
Andean Latin America	933.89 (751.35–1165.02)	12.74 (10.28–15.83)	3591.19 (2627.22–4852.96)	20.84 (15.25–28.16)	1.42 (1.24 to 1.59)
Australasia	2605.48 (2279.54–2975.62)	47.58 (41.64–54.33)	3766.91 (3069.64–4539.93)	44.71 (36.40–53.95)	-0.16 (-0.31 to -0.01)
Caribbean	1994.18 (1745.85–2277.01)	25.88 (22.71–29.51)	3694.57 (2974.07–4571.79)	29.74 (23.92–36.83)	0.45 (0.36 to 0.54)
Central Asia	3231.55 (2954.01–3508.09)	25.46 (23.25–27.63)	4897.54 (4171.81–5758.36)	19.37 (16.51–22.77)	-0.84 (-0.96 to -0.72)
Central Europe	9878.29 (9190.44–10615.61)	30.29 (28.17–32.55)	11473.29 (10220.67–12886.31)	33.37 (29.69–37.51)	0.23 (0.11 to 0.36)
Central Latin America	6514.25 (6091.56–6988.68)	20.49 (19.16–21.98)	26116.26 (22114.75–30202.76)	37.31 (31.59–43.15)	1.68 (1.54 to 1.83)
Central Sub-Saharan Africa	867.47 (569.81–1283.49)	9.62 (6.33–14.18)	3991.89 (2753.33–5624.64)	15.86 (10.97–22.27)	1.65 (1.39 to 1.92)
East Asia	38491.93 (30677.24–47466.31)	13.96 (11.14–17.18)	115236.73 (86644.28–148921.33)	27.43 (20.64–35.50)	2.14 (2.07 to 2.22)
Eastern Europe	16845.11 (15806.18–17943.84)	29.91 (28.08–31.85)	18493.76 (16197.94–21047.57)	28.94 (25.33–32.95)	-0.47 (-0.64 to -0.29)
Eastern Sub-Saharan Africa	3438.07 (2659.72–4397.26)	11.12 (8.62–14.21)	14569.52 (11446.56–18504.39)	17.69 (14.03–22.29)	1.35 (1.19 to 1.5)
High-income Asia Pacific	12889.33 (11302.51–14743.79)	25.62 (22.46–29.31)	20409.33 (17796.07–23022.37)	38.93 (33.88–43.98)	1.31 (1.03 to 1.59)
High-income North America	50362.48 (48219.46–52701.72)	64.97 (62.21–68.00)	44759.35 (42027.97–47790.52)	47.20 (44.31–50.40)	-1.14 (-1.22 to -1.05)
North Africa and Middle East	7649.27 (6439.76–9173.70)	12.86 (10.85–15.39)	53147.83 (45541.45–62152.28)	33.01 (28.29–38.60)	3.39 (3.24 to 3.54)
Oceania	275.97 (194.49–382.90)	22.77 (16.12–31.45)	758.05 (535.41–1084.08)	23.97 (16.99–34.20)	-0.04 (-0.23 to 0.15)
South Asia	19737.18 (17154.59–22484.40)	9.42 (8.21–10.71)	84293.27 (71436.45–100196.12)	18.06 (15.33–21.44)	2.02 (1.87 to 2.17)
Southeast Asia	14694.10 (12109.65–17979.75)	15.66 (12.97–19.06)	51664.27 (42579.43–62992.97)	26.59 (21.92–32.41)	1.63 (1.56 to 1.7)
Southern Latin America	3085.25 (2665.49–3584.95)	26.17 (22.62–30.40)	5308.93 (4513.89–6220.81)	28.17 (23.94–33.04)	0.23 (0.12 to 0.34)
Southern Sub-Saharan Africa	1771.63 (1474.25–2103.40)	17.43 (14.51–20.66)	5149.69 (4260.45–6165.79)	24.96 (20.70–29.81)	2.02 (1.54 to 2.51)
Tropical Latin America	6060.78 (5633.84–6562.78)	18.52 (17.23–20.04)	20210.99 (18519.91–22020.50)	30.09 (27.56–32.79)	1.24 (1.14 to 1.35)
Western Europe	51955.47 (49135.33–55114.51)	51.21 (48.42–54.33)	54036.10 (50057.04–58322.41)	46.05 (42.65–49.69)	-0.3 (-0.47 to -0.12)
Western Sub-Saharan Africa	3434.09 (2664.87–4236.67)	11.22 (8.74–13.80)	15868.62 (11021.79–21831.47)	17.54 (12.24–24.03)	1.46 (1.34 to 1.58)

Table 1. Global and regional incidence of WCBA BC in 1990 and 2021, and EAPC of ASR from 1990 to 2021.

CI: -0.31 to -0.01%, -0.84% (95% CI: -0.96 to -0.72%), -0.47% (95% CI: -0.64 to -0.29%), -1.14% (95% CI: -1.22 to -1.05%), and -0.30% (95% CI: -0.47 to -0.12%), respectively.

Age-standardized prevalence rates (ASPRs) increased in 17 of the 21 GBD regions, with AAPCs ranging from 0.02% (95% CI: -0.17 to 0.20%) to 3.40% (95% CI: 3.25–3.56%). The highest AAPCs in ASPR were observed in North Africa and the Middle East, East Asia, South Asia, and Sub-Saharan Africa. The regions where ASPR decreased included Australasia, the Caucasus and Central Asia, Eastern Europe, and Western Europe.

Age-standardized disability-adjusted life years (DALYs) rates increased in 13 GBD regions, with AAPCs ranging from 0.02% (95% CI: -0.05 to 0.10%) to 1.44% (95% CI: 1.30–1.59%). The highest AAPCs were observed in North Africa and the Middle East, as well as Sub-Saharan Africa. Declines were noted in Central Asia, East

Location	1990		2021		EAPC, 1990–2021
	Number	ASR	Number	ASR	
Global	2170812.47 (2055628.69–2297082.47)	191.47 (181.41–202.45)	4804868.66 (4464320.26–5186300.68)	235.29 (218.54–254.04)	0.55 (0.5 to 0.6)
High SDI	975747.39 (935784.56–1018832.80)	409.92 (393.06–428.13)	1141454.27 (1088956.61–1194074.01)	385.50 (367.74–403.33)	-0.24 (-0.37 to -0.11)
High-middle SDI	531976.46 (493021.11–575507.01)	214.49 (199.06–231.73)	1095358.21 (959001.06–1261358.36)	285.06 (249.26–328.66)	0.93 (0.85 to 1.02)
Middle SDI	426214.28 (384979.43–473173.98)	120.47 (109.03–133.50)	1551982.96 (1399172.13–1722194.81)	227.61 (205.16–252.61)	1.99 (1.91 to 2.06)
Low-middle SDI	176297.00 (154834.71–200781.78)	80.63 (71.02–91.56)	759949.23 (663638.54–858898.95)	161.71 (141.42–182.41)	2.23 (2.17 to 2.28)
Low SDI	57952.19 (48185.49–69625.65)	67.74 (56.43–81.25)	251801.59 (211179.69–296035.75)	115.58 (97.48–135.20)	1.68 (1.52 to 1.84)
Andean Latin America	7139.06 (5765.33–8849.21)	97.29 (78.84–120.14)	29676.15 (21846.84–39815.47)	172.20 (126.81–230.99)	1.73 (1.56 to 1.89)
Australasia	23197.42 (20360.81–26338.53)	424.13 (372.35–481.42)	34371.84 (28313.95–41051.98)	407.33 (335.23–487.19)	-0.07 (-0.22 to 0.08)
Caribbean	16269.48 (14290.93–18508.16)	211.17 (185.83–239.93)	30360.69 (24691.22–37309.67)	244.29 (198.49–300.45)	0.49 (0.4 to 0.58)
Central Asia	26407.45 (24204.64–28635.40)	208.12 (190.68–225.70)	41571.18 (35686.79–48195.05)	164.49 (141.26–190.58)	-0.73 (-0.85 to -0.61)
Central Europe	83154.37 (77553.87–89452.52)	255.15 (237.90–274.55)	100555.83 (90004.81–112618.32)	292.04 (260.97–327.41)	0.38 (0.26 to 0.5)
Central Latin America	52536.22 (49135.99–56302.04)	165.20 (154.57–176.99)	218531.49 (185782.09–252503.74)	312.17 (265.34–360.74)	1.83 (1.69 to 1.96)
Central Sub-Saharan Africa	6199.16 (4151.95–8999.11)	68.40 (45.98–98.88)	30234.18 (21057.26–42047.37)	119.79 (83.71–166.01)	1.88 (1.58 to 2.18)
East Asia	320936.87 (257911.63–392396.96)	116.75 (94.01–142.40)	1015702.16 (772534.01–1299252.07)	241.32 (183.45–309.29)	2.34 (2.27 to 2.41)
Eastern Europe	140901.95 (132306.21–150251.93)	250.38 (235.17–266.89)	160186.50 (140674.68–181416.17)	250.49 (219.86–283.88)	-0.34 (-0.51 to -0.16)
Eastern Sub-Saharan Africa	24849.68 (19506.61–31296.91)	79.99 (62.97–100.51)	112605.31 (89312.05–141941.39)	136.37 (109.27–170.41)	1.65 (1.47 to 1.83)
High-income Asia Pacific	119192.42 (104510.66–135675.39)	236.37 (207.22–269.06)	188283.38 (165529.68–210810.74)	357.03 (313.12–400.62)	1.32 (1.07 to 1.57)
High-income North America	445557.35 (425130.99–467095.97)	575.40 (548.98–603.34)	407968.26 (383158.36–434336.52)	429.56 (403.38–457.39)	-1.05 (-1.13 to -0.97)
North Africa and Middle East	66038.04 (56174.92–78214.82)	111.47 (95.10–131.72)	459184.93 (396141.23–532078.46)	285.39 (246.24–330.62)	3.4 (3.25 to 3.56)
Oceania	2118.69 (1526.23–2879.53)	174.36 (126.32–235.79)	5908.85 (4263.26–8286.17)	186.66 (135.18–261.00)	0.02 (-0.17 to 0.2)
South Asia	149125.56 (129898.67–169762.36)	71.09 (62.09–80.73)	673390.55 (575113.99–794752.36)	144.26 (123.38–169.99)	2.25 (2.1 to 2.41)
Southeast Asia	113288.99 (93973.35–137315.89)	120.49 (100.52–145.20)	423192.56 (350773.58–512341.20)	217.81 (180.56–263.64)	1.85 (1.79 to 1.92)
Southern Latin America	25733.63 (22393.41–29545.04)	218.33 (190.05–250.57)	46480.37 (39697.94–54116.88)	246.51 (210.41–287.23)	0.41 (0.31 to 0.51)
Southern Sub-Saharan Africa	13673.74 (11445.29–16105.03)	134.49 (112.73–158.01)	39718.55 (33056.71–47321.01)	192.49 (160.61–228.66)	1.95 (1.5 to 2.4)
Tropical Latin America	48153.74 (44699.38–52144.03)	147.03 (136.61–159.07)	167818.68 (154127.78–182677.74)	249.87 (229.40–272.11)	1.41 (1.31 to 1.52)
Western Europe	461461.17 (434784.73–491413.84)	454.73 (428.38–484.30)	498719.71 (464291.83–537025.11)	423.28 (393.91–455.78)	-0.18 (-0.35 to -0.01)
Western Sub-Saharan Africa	24877.51 (19599.05–30476.43)	80.92 (64.09–98.72)	120407.50 (84884.87–164594.40)	132.71 (94.14–180.58)	1.64 (1.5 to 1.78)

Table 2. Global and regional prevalence of WCBA BC in 1990 and 2021, and EAPC of ASR from 1990 to 2021.

Asia, Eastern Europe, the Caucasus and Central Asia, high-income Asia-Pacific, high-income North America, Southern Latin America, and Western Europe.

Similarly, age-standardized mortality rates (ASMRs) increased in 12 GBD regions, with AAPCs ranging from 0.04% (95% CI: -0.05 to 0.13%) to 1.47% (95% CI: 1.00–1.94%). The highest AAPCs were recorded in Sub-Saharan Africa and North Africa and the Middle East. In contrast, ASMRs declined in Central Asia, East Asia, Eastern Europe, the Caucasus and Central Asia, high-income Asia-Pacific, high-income North America, Southern Latin America, Tropical Latin America, and Western Europe (Tables 1, 2, 3 and 4).

Location	1990		2021		EAPC, 1990–2021
	Number	ASR	Number	ASR	
Global	3992794.45 (3737072.99–4297211.12)	347.91 (326.05–373.80)	6659459.91 (6111787.74–7245687.69)	327.24 (300.15–356.24)	-0.38 (-0.48 to -0.28)
High SDI	1078666.35 (1040772.86–1120023.81)	452.63 (436.73–470.01)	791735.03 (748403.20–837604.93)	269.20 (254.46–284.83)	-1.8 (-1.87 to -1.73)
High-middle SDI	962550.32 (887009.68–1052380.37)	384.36 (354.82–419.23)	1049179.39 (931683.50–1184651.63)	274.78 (243.77–310.56)	-1.32 (-1.41 to -1.23)
Middle SDI	1087398.83 (979131.86–1216348.10)	304.67 (274.89–340.05)	2202113.75 (1984729.78–2443177.82)	323.73 (291.78–359.18)	0.02 (-0.08 to 0.11)
Low-middle SDI	615747.52 (535423.93–707621.03)	279.15 (243.57–319.64)	1818680.64 (1572636.03–2089027.93)	385.56 (333.99–441.83)	0.98 (0.92 to 1.04)
Low SDI	243403.83 (200091.29–296331.39)	281.81 (232.03–342.72)	791378.41 (658840.08–938445.60)	360.67 (302.00–425.62)	0.68 (0.58 to 0.79)
Andean Latin America	21299.92 (17178.66–26500.18)	287.70 (233.08–356.09)	46001.47 (34142.72–61679.78)	266.69 (197.98–357.61)	-0.47 (-0.62 to -0.33)
Australasia	27579.78 (24545.55–30743.83)	502.84 (447.73–560.20)	22563.62 (19331.79–26062.66)	268.30 (229.63–310.26)	-2.14 (-2.22 to -2.07)
Caribbean	32198.76 (27786.66–38097.51)	415.35 (359.19–490.03)	52167.52 (39938.80–67626.78)	421.13 (322.02–546.53)	0.06 (-0.03 to 0.15)
Central Asia	62358.52 (57738.09–66772.63)	484.43 (448.43–518.69)	73810.70 (63280.72–86210.16)	291.28 (249.83–340.06)	-1.68 (-1.81 to -1.56)
Central Europe	148286.62 (140190.53–156885.12)	453.90 (429.10–480.24)	100674.15 (90755.73–111110.52)	293.62 (264.37–324.38)	-1.56 (-1.68 to -1.44)
Central Latin America	92211.26 (87279.05–97343.96)	286.89 (271.58–302.78)	223779.84 (189764.93–258390.33)	320.08 (271.39–369.59)	0.18 (0.03 to 0.32)
Central Sub-Saharan Africa	27031.97 (17969.10–39040.57)	296.11 (197.31–425.64)	100234.74 (69657.58–141402.53)	394.96 (275.50–555.51)	0.96 (0.76 to 1.15)
East Asia	729314.95 (578765.06–904473.82)	261.61 (207.92–323.77)	910804.60 (684539.12–1179341.55)	218.20 (164.13–282.51)	-0.88 (-1 to -0.77)
Eastern Europe	269866.20 (254860.32–286541.54)	476.43 (450.09–505.74)	200253.27 (173889.19–233756.20)	314.20 (272.74–366.78)	-1.85 (-2.04 to -1.67)
Eastern Sub-Saharan Africa	108325.41 (82719.63–139755.33)	344.50 (263.63–444.06)	358568.71 (281115.91–457695.85)	430.07 (340.46–544.54)	0.56 (0.43 to 0.69)
High-income Asia Pacific	119116.50 (112187.75–126857.89)	238.43 (224.15–254.28)	115601.27 (105948.99–126580.51)	221.65 (202.56–243.57)	-0.41 (-0.57 to -0.26)
High-income North America	416992.09 (398934.74–436728.29)	535.81 (512.54–561.25)	271142.97 (253553.13–289030.75)	287.15 (268.50–306.16)	-2.08 (-2.19 to -1.97)
North Africa and Middle East	123151.71 (103486.68–149370.42)	206.76 (174.14–250.31)	474651.02 (400790.20–564485.38)	294.60 (248.75–350.36)	1.44 (1.3 to 1.59)
Oceania	6663.93 (4576.76–9371.38)	546.30 (377.10–765.90)	19250.47 (13395.94–27613.20)	607.04 (423.81–868.89)	0.35 (0.24 to 0.47)
South Asia	564642.58 (489421.10–644209.29)	266.93 (232.05–303.65)	1681616.05 (1418169.78–2004231.06)	358.91 (303.20–426.87)	0.83 (0.72 to 0.94)
Southeast Asia	359832.68 (292682.69–446219.81)	380.27 (311.35–468.62)	874747.81 (715124.46–1076332.65)	450.77 (368.62–554.36)	0.45 (0.38 to 0.53)
Southern Latin America	60389.86 (53146.49–68713.51)	511.77 (450.53–582.10)	65704.85 (56704.34–75346.79)	349.34 (301.27–400.92)	-1.21 (-1.35 to -1.07)
Southern Sub-Saharan Africa	43516.07 (36282.69–51343.32)	424.27 (354.15–499.62)	104454.09 (86428.70–125754.98)	503.53 (417.41–604.80)	1.38 (0.9 to 1.87)
Tropical Latin America	120198.57 (112260.57–128857.69)	364.24 (340.52–390.10)	267046.04 (247622.72–287477.39)	398.13 (369.08–428.72)	0.02 (-0.05 to 0.1)
Western Europe	559375.83 (533951.45–586420.89)	552.17 (526.97–578.98)	329990.52 (308440.56–353311.59)	282.54 (264.01–302.61)	-2.21 (-2.29 to -2.13)
Western Sub-Saharan Africa	100441.24 (78719.87–122599.48)	324.46 (255.29–394.76)	366396.21 (257379.98–496796.00)	401.69 (283.65–542.85)	0.69 (0.59 to 0.79)

Table 3. Global and regional dalys of WCBA BC in 1990 and 2021, and EAPC of ASR from 1990 to 2021.

Country-Level variations across 204 nations

Between 1990 and 2021, the global burden of breast cancer among women of reproductive age exhibited significant regional disparities. The highest increases in the estimated annual percentage change (EAPC) for incidence rates were observed in Turkey (7.43%), South Korea (3.85%), and Lesotho (3.81%). Conversely, the largest declines were recorded in Ukraine (-2.28%), Armenia (-2.09%), and Belgium (-1.41%).

Similarly, trends in prevalence rates mirrored those of incidence. Turkey (7.28%), Equatorial Guinea (3.85%), and South Korea (3.85%) showed the highest increases in prevalence EAPC, while the most pronounced declines were observed in Ukraine (-2.11%), Armenia (-1.86%), and Belgium (-1.25%).

Location	1990		2021		EAPC, 1990-2021
	Number	ASR	Number	ASR	
Global	78285.12 (73580.99–84119.97)	6.90 (6.50–7.41)	129405.59 (119195.22–140408.42)	6.34 (5.84–6.88)	-0.47 (-0.57 to -0.36)
High SDI	20913.55 (20342.56–21484.32)	8.79 (8.55–9.03)	14780.43 (14199.84–15370.06)	4.97 (4.78–5.18)	-1.97 (-2.05 to -1.9)
High-middle SDI	18956.08 (17531.33–20689.62)	7.66 (7.10–8.34)	20261.42 (18057.43–22813.50)	5.24 (4.67–5.91)	-1.48 (-1.58 to -1.38)
Middle SDI	21350.55 (19280.15–23874.12)	6.08 (5.50–6.79)	43250.70 (39025.64–47938.71)	6.32 (5.70–7.01)	-0.06 (-0.15 to 0.03)
Low-middle SDI	12151.76 (10604.30–13936.22)	5.60 (4.90–6.40)	35573.56 (30893.15–40563.39)	7.60 (6.61–8.64)	0.93 (0.87 to 0.99)
Low SDI	4813.34 (3965.51–5859.06)	5.69 (4.69–6.91)	15413.94 (12890.64–18190.80)	7.16 (6.02–8.42)	0.63 (0.53 to 0.74)
Andean Latin America	422.57 (342.11–523.63)	5.81 (4.72–7.16)	906.97 (673.26–1212.08)	5.27 (3.91–7.04)	-0.55 (-0.69 to -0.4)
Australasia	539.01 (482.13–599.38)	9.87 (8.83–10.97)	419.08 (361.92–478.90)	4.95 (4.27–5.66)	-2.36 (-2.44 to -2.27)
Caribbean	635.56 (549.56–748.02)	8.29 (7.18–9.73)	1037.51 (795.77–1339.02)	8.35 (6.40–10.79)	0.04 (-0.05 to 0.13)
Central Asia	1214.60 (1125.10–1301.15)	9.69 (8.97–10.38)	1454.91 (1245.28–1700.19)	5.76 (4.93–6.73)	-1.72 (-1.85 to -1.59)
Central Europe	2968.68 (2811.47–3136.60)	9.11 (8.63–9.63)	1977.96 (1790.74–2178.76)	5.68 (5.14–6.27)	-1.69 (-1.81 to -1.57)
Central Latin America	1784.89 (1693.06–1884.10)	5.66 (5.37–5.98)	4317.57 (3658.18–4968.76)	6.16 (5.22–7.09)	0.09 (-0.05 to 0.23)
Central Sub-Saharan Africa	542.28 (360.79–781.00)	6.05 (4.03–8.68)	2003.05 (1395.59–2822.73)	8.02 (5.60–11.27)	0.94 (0.75 to 1.14)
East Asia	14153.64 (11244.75–17507.73)	5.16 (4.11–6.38)	17407.32 (13179.39–22518.19)	4.11 (3.11–5.31)	-1.05 (-1.17 to -0.93)
Eastern Europe	5382.97 (5089.21–5694.31)	9.59 (9.07–10.14)	3958.34 (3427.38–4617.05)	6.16 (5.33–7.18)	-1.95 (-2.14 to -1.75)
Eastern Sub-Saharan Africa	2118.24 (1618.73–2734.80)	6.92 (5.29–8.92)	6926.43 (5470.65–8787.94)	8.50 (6.78–10.71)	0.51 (0.39 to 0.64)
High-income Asia Pacific	2287.05 (2170.99–2410.37)	4.54 (4.31–4.80)	2156.55 (2004.70–2329.68)	4.04 (3.74–4.38)	-0.59 (-0.75 to -0.43)
High-income North America	7938.15 (7677.74–8214.07)	10.26 (9.92–10.62)	4999.35 (4738.97–5268.70)	5.26 (4.99–5.54)	-2.23 (-2.34 to -2.11)
North Africa and Middle East	2405.91 (2019.91–2908.39)	4.11 (3.45–4.96)	9052.87 (7648.95–10745.52)	5.64 (4.76–6.69)	1.32 (1.17 to 1.47)
Oceania	130.74 (90.19–183.54)	10.95 (7.58–15.33)	380.11 (265.33–542.99)	12.11 (8.47–17.26)	0.35 (0.24 to 0.47)
South Asia	11173.26 (9708.81–12707.18)	5.37 (4.68–6.09)	32832.57 (27816.43–38889.24)	7.05 (5.99–8.34)	0.75 (0.64 to 0.87)
Southeast Asia	7143.85 (5842.42–8820.69)	7.68 (6.32–9.44)	17512.72 (14298.35–21636.36)	8.99 (7.34–11.10)	0.42 (0.35 to 0.49)
Southern Latin America	1215.49 (1070.73–1380.79)	10.33 (9.10–11.73)	1290.61 (1119.58–1474.25)	6.83 (5.92–7.81)	-1.32 (-1.46 to -1.19)
Southern Sub-Saharan Africa	845.06 (705.02–994.67)	8.40 (7.01–9.87)	2081.50 (1722.39–2497.67)	10.12 (8.39–12.12)	1.47 (1 to 1.94)
Tropical Latin America	2385.16 (2232.56–2554.53)	7.34 (6.87–7.85)	5270.97 (4893.83–5664.18)	7.83 (7.27–8.41)	-0.05 (-0.13 to 0.02)
Western Europe	10996.84 (10554.35–11438.29)	10.83 (10.39–11.27)	6170.27 (5849.37–6496.49)	5.21 (4.93–5.48)	-2.43 (-2.51 to -2.34)
Western Sub-Saharan Africa	2001.16 (1574.69–2440.63)	6.60 (5.21–8.03)	7248.95 (5115.49–9815.09)	8.09 (5.73–10.92)	0.66 (0.56 to 0.76)

Table 4. Global and regional deaths of WCBA BC in 1990 and 2021, and EAPC of ASR from 1990 to 2021.

For disability-adjusted life years (DALYs), Turkey (4.63%), Lesotho (3.67%), and Zimbabwe (3.67%) experienced the largest EAPC increases between 1990 and 2021. In contrast, Armenia (-3.49%), Denmark (-3.34%), and Norway (-3.00%) showed the most substantial decreases.

Regarding mortality, Turkey (4.39%), Lesotho (3.65%), and Zimbabwe (3.65%) exhibited the most significant increases in EAPC. Conversely, the largest declines in mortality EAPC were noted in Denmark (-3.63%), Armenia (-3.52%), and Norway (-3.22%) (Fig. 1A–H).

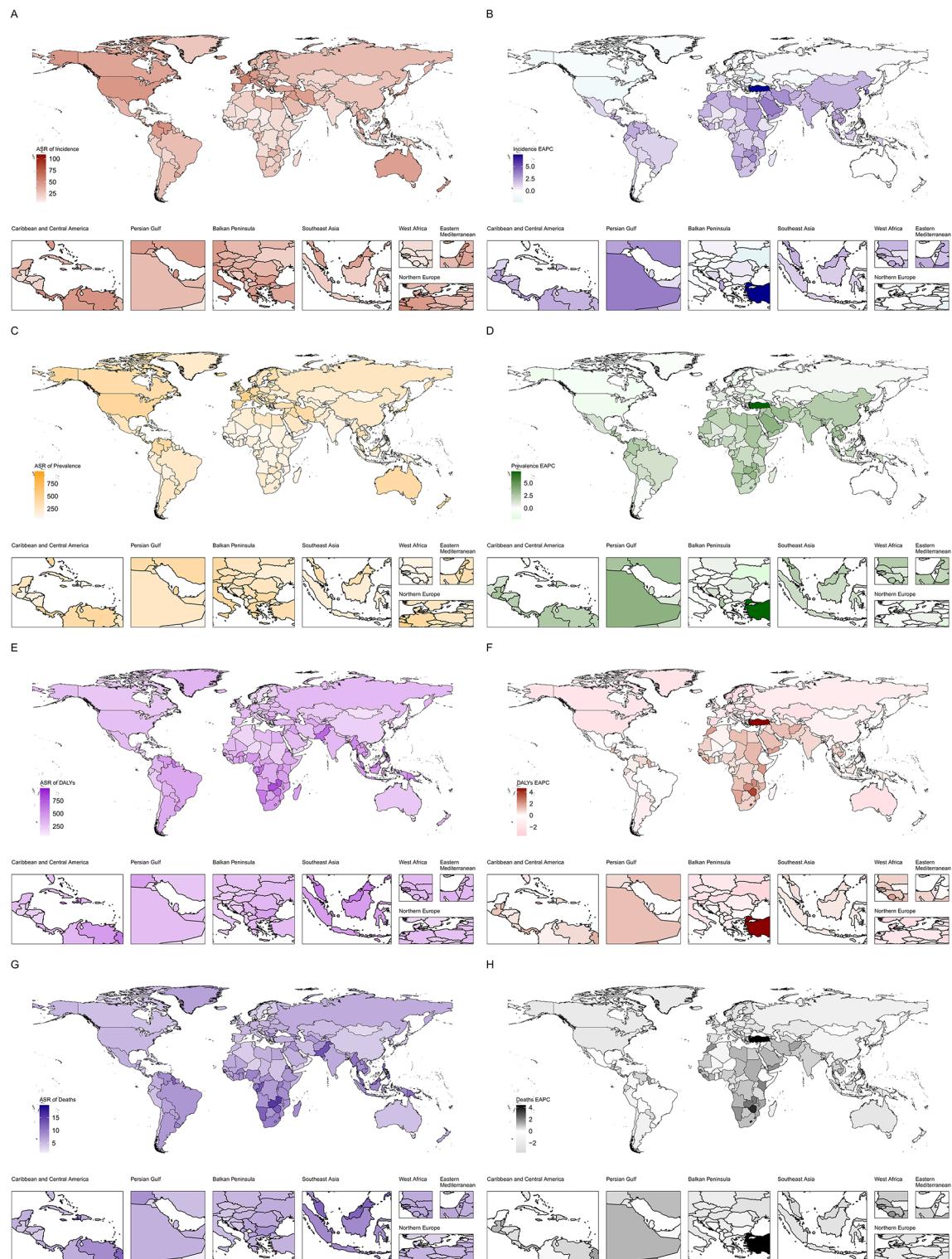


Fig. 1. Global geographical distribution of changes in breast cancer burden among women of reproductive age, 1990–2021. (A) Age-standardized incidence rates of breast cancer among women of reproductive age in 204 countries/territories. (B) EAPC in incidence of breast cancer among women of reproductive age in 204 countries/territories. (C) Age-standardized prevalence rates of breast cancer among women of reproductive age in 204 countries/territories. (D) EAPC in prevalence of breast cancer among women of reproductive age in 204 countries/territories. (E) Age-standardized DALY rates of breast cancer among women of reproductive age in 204 countries/territories. (F) EAPC in DALYs of breast cancer among women of reproductive age in 204 countries/territories. (G) Age-standardized Mortality rates of breast cancer among women of reproductive age in 204 countries/territories. (H) EAPC in Mortality of breast cancer among women of reproductive age in 204 countries/territories.

Trends in incidence, prevalence, dalys, and mortality rates of breast Cancer among women of reproductive age from 1990 to 2021

Joinpoint regression analysis was used to examine the trends in incidence, prevalence, disability-adjusted life years (DALYs) rate, and mortality rate of breast cancer among women of reproductive age from 1990 to 2021 (Fig. 2). The results revealed similar fluctuating trends in incidence and prevalence, both showing an overall upward trajectory. The average annual percentage change (AAPC) for incidence was 0.64%, while that for prevalence was 0.67%. Specifically, these two metrics increased from 1990 to 1996, then declined until 2000, rose again until 2009, followed by another increase from 2013 to 2019, and continued to rise thereafter.

In contrast, DALYs rate and mortality rate showed an overall downward trend. The AAPC for DALYs rate was -0.18% , and for mortality rate, it was -0.26% . The DALYs rate increased between 1990 and 1995, then experienced multiple phases of decline until a rebound began in 2012. Similarly, mortality remained stable from 1990 to 1995, followed by a similar declining phase, before increasing again after 2012.

These findings suggest that although the incidence and prevalence of breast cancer have risen, the overall disease burden and mortality rates have decreased. This likely reflects advancements in early diagnosis and improvements in treatment strategies for breast cancer.

Age-Period-Cohort analysis of breast Cancer in women of reproductive age

The Age-Period-Cohort (APC) model was employed to analyze the effects of age, period, and birth cohort on the incidence and prevalence of breast cancer among women of reproductive age (Fig. 3; Table 5). The results demonstrated that the age effect significantly influenced both the incidence and prevalence of breast cancer in this population ($P < 0.001$). Compared with the 15–19 years age group, the relative risk (RR) of incidence and prevalence increased progressively with age in the 20–24, 25–29, 30–34, 35–39, 40–44, and 45–49 years age groups. The incidence and prevalence RRs peaked in the 45–49 years age group at 6.045 (95% CI: 6.024–6.067) and 6.281 (95% CI: 6.273–6.289), respectively (Fig. 4).

The period effect analysis revealed a general upward trend in the RRs for both incidence and prevalence of breast cancer from 1992 to 2017 ($P < 0.001$). By 2017, the incidence RR reached 1.548 (95% CI: 1.542–1.555), and the prevalence RR reached 1.561 (95% CI: 1.559–1.564).

The birth cohort effect analysis indicated that the 1947 birth cohort had the highest RRs for incidence and prevalence, at 2.134 (95% CI: 2.119–2.150) and 2.149 (95% CI: 2.143–2.154), respectively. However, as birth years advanced, the RRs for both metrics gradually declined. By the 2002 birth cohort, the incidence and prevalence RRs decreased to 0.607 (95% CI: 0.582–0.634) and 0.606 (95% CI: 0.597–0.615), respectively (Supplementary Figs. 1–3).

Association between breast Cancer burden and SDI from 1990 to 2021

A further analysis was conducted to explore the correlation between the burden of breast cancer among women of reproductive age and the Sociodemographic Index (SDI) in 22 regions in 2021. The results indicated a significant positive correlation between SDI and both incidence and prevalence rates ($P < 0.001$), with the disease burden exhibiting a logarithmic upward trend as SDI increased. High SDI regions, such as High-income North America and Australasia, showed incidence and prevalence rates far exceeding expected values, whereas low SDI regions, such as Southern Sub-Saharan Africa and Andean Latin America, had rates well below expected values (Fig. 5A, B).

The DALY rate demonstrated a wave-like trend with SDI ($P < 0.001$), peaking at an SDI of approximately 0.75. Regions like Oceania and Eastern Europe exhibited DALY rates and mortality rates far above expectations, while regions such as East Asia and North Africa and the Middle East had rates significantly below expectations (Fig. 5C, D).

A similar analysis was conducted at the national level across 204 countries or territories, revealing a significant positive correlation between SDI and both incidence and prevalence rates ($P < 0.001$), with a linear upward trend in disease burden as SDI increased. High SDI countries such as Monaco and the Bahamas exhibited incidence and prevalence rates well above expected values, whereas middle-to-low SDI countries such as Mongolia and Oman had rates substantially below expectations (Fig. 5E, F).

In contrast, DALY and mortality rates followed an inverted V-shaped trend with SDI ($P < 0.001$). Countries such as Nauru and American Samoa had DALY rates far exceeding expected values, while Mongolia and Oman had rates significantly below expectations (Fig. 5G, H).

Overall, these findings suggest a strong correlation between the burden of breast cancer among women of reproductive age and SDI globally, while highlighting substantial variations between countries and regions.

Decomposition analysis of changes in breast Cancer burden from 1990 to 2021

Globally, the total DALYs attributable to breast cancer among women of reproductive age increased by 2,666,665 from 1990 to 2021. Decomposition analysis revealed that population aging and growth in population size were the primary drivers of the rising global breast cancer burden. Population size growth accounted for 73.7% of the increase in DALYs, while population aging contributed 37.95%. In contrast, changes in epidemiology partially offset the rising burden, reducing the number of DALYs by 11.65%. These findings highlight that, despite the positive impact of epidemiological improvements, the rapid growth in population size and aging remain the key drivers behind the escalating global breast cancer burden (Fig. 4 and Supplementary Table 5).

Further analysis across regions with different Sociodemographic Index (SDI) levels revealed significant variations in the changes in breast cancer burden. In high-SDI regions, the DALYs associated with breast cancer among women of reproductive age decreased by 286,931, primarily driven by epidemiological improvements, which contributed to a 170.93% reduction. Conversely, in upper-middle-SDI regions, the breast cancer burden experienced a slight increase, although this rise was also largely attributed to epidemiological changes.

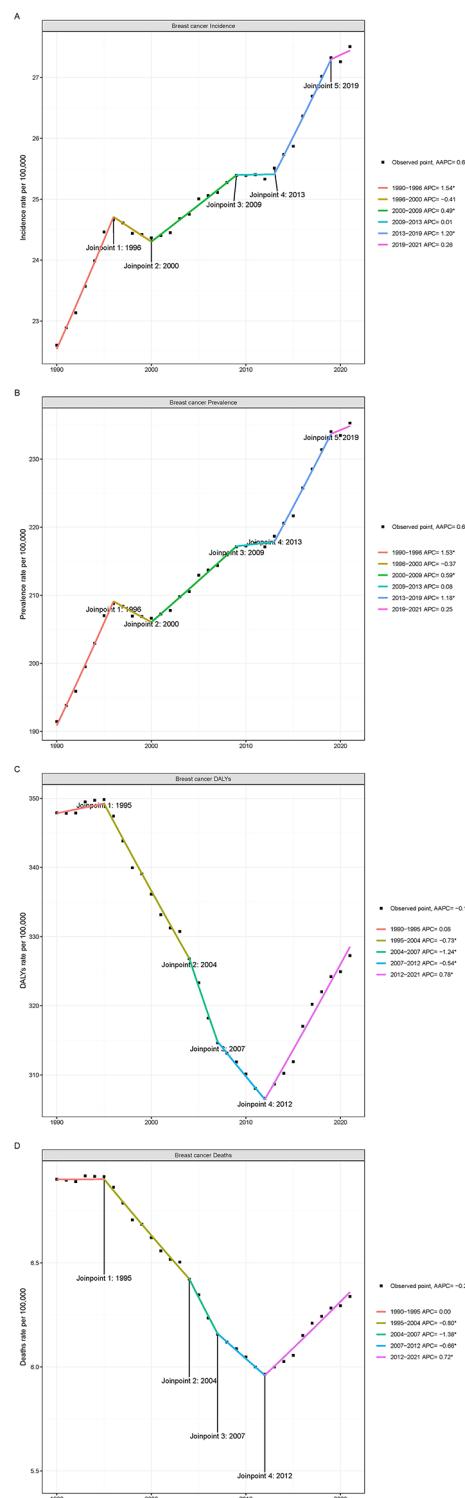


Fig. 2. Temporal trends of breast cancer burden among women of reproductive age from 1990 to 2021. (A) Incidence rate of breast cancer per 100,000 women of reproductive age from 1990 to 2021. (B) Prevalence rate of breast cancer per 100,000 women of reproductive age from 1990 to 2021. (C) DALYs rate of breast cancer per 100,000 women of reproductive age from 1990 to 2021. (D) Mortality rate of breast cancer per 100,000 women of reproductive age from 1990 to 2021.

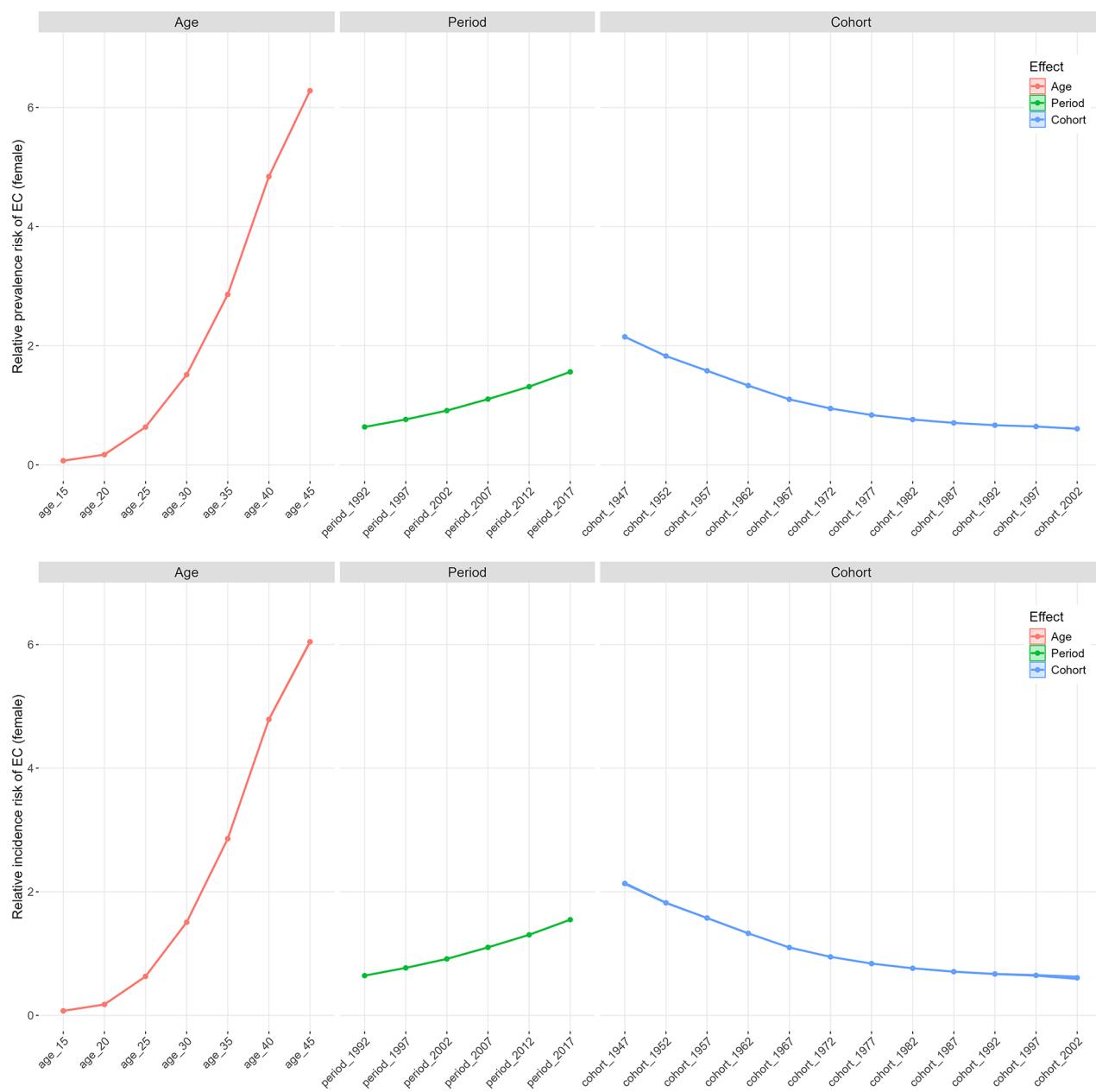


Fig. 3. Age-Period-Cohort analysis of breast cancer risk among women of reproductive age. **(A)** Relative prevalence risk of Breast cancer by age, period, and cohort. **(B)** Relative incidence risk of Breast cancer by age, period, and cohort.

In contrast, the most substantial increases in breast cancer burden were observed in lower-middle-SDI and low-SDI regions, with increases of 1,202,933 and 547,974 DALYs, respectively. In these regions, population size growth was the predominant contributor to the rising burden, while the impact of epidemiological changes was relatively minor.

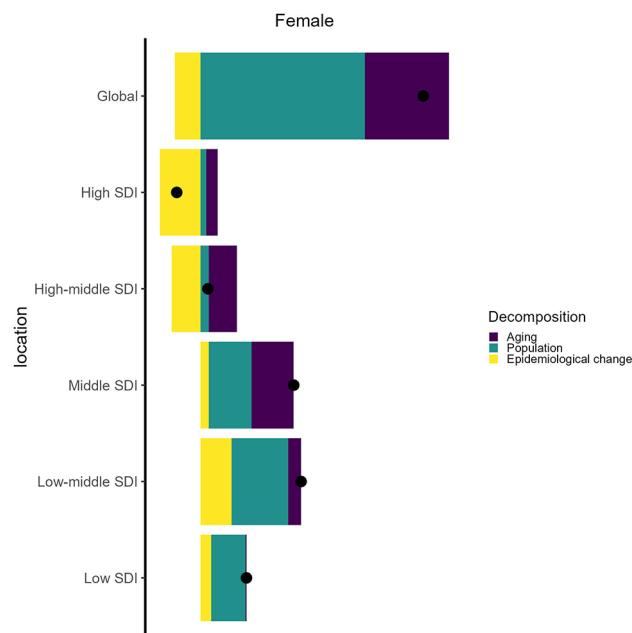
Trends in health inequalities of global breast Cancer burden among women of reproductive age from 1990 to 2021

The health inequalities in the burden of breast cancer among women of reproductive age in 1990 and 2021 were analyzed using the Slope Index of Inequality (SII) and Concentration Index (CI).

For DALY rates, the SII increased from 635 in 1990 to 723 in 2021, indicating a worsening degree of inequality in DALY rates over time. However, the CI for DALYs decreased from 0.33 in 1990 to 0.14 in 2021, suggesting that the distribution of DALYs across socioeconomic groups became more equitable (Fig. 6A and B).

For prevalence rates, the SII rose significantly from 577 in 1990 to 1,131 in 2021, reflecting a marked increase in inequality. Despite this, the CI for prevalence decreased from 0.56 in 1990 to 0.44 in 2021, indicating

Factor	Incidence		Prevalence	
Age (years)	RR (95% CI)	P	RR (95% CI)	P
15-19	0.072(0.071-0.074)	<0.001	0.070(0.069-0.070)	<0.001
20-24	0.176(0.174-0.178)	<0.001	0.172(0.171-0.173)	<0.001
25-29	0.630(0.625-0.635)	<0.001	0.634(0.633-0.636)	<0.001
30-34	1.507(1.498-1.515)	<0.001	1.514(1.511-1.517)	<0.001
35-39	2.859(2.846-2.872)	<0.001	2.861(2.856-2.866)	<0.001
40-44	4.790(4.772-4.808)	<0.001	4.840(4.833-4.846)	<0.001
45-49	6.045(6.024-6.067)	<0.001	6.281(6.273-6.289)	<0.001
Period				
1992	0.643(0.640-0.646)	<0.001	0.636(0.635-0.638)	<0.001
1997	0.768(0.765-0.771)	<0.001	0.762(0.761-0.763)	<0.001
2002	0.913(0.910-0.916)	<0.001	0.911(0.910-0.912)	<0.001
2007	1.100(1.096-1.103)	<0.001	1.104(1.102-1.105)	<0.001
2012	1.303(1.298-1.308)	<0.001	1.313(1.311-1.314)	<0.001
2017	1.548(1.542-1.555)	<0.001	1.561(1.559-1.564)	<0.001
Birth cohort				
1947	2.134(2.119-2.150)	<0.001	2.149(2.143-2.154)	<0.001
1952	1.821(1.811-1.831)	<0.001	1.827(1.824-1.831)	<0.001
1957	1.575(1.567-1.583)	<0.001	1.580(1.577-1.583)	<0.001
1962	1.328(1.321-1.334)	<0.001	1.331(1.329-1.334)	<0.001
1967	1.098(1.092-1.104)	<0.001	1.100(1.098-1.102)	<0.001
1972	0.947(0.941-0.952)	<0.001	0.946(0.945-0.948)	<0.001
1977	0.837(0.832-0.843)	<0.001	0.836(0.834-0.838)	<0.001
1982	0.762(0.755-0.768)	<0.001	0.760(0.758-0.763)	<0.001
1987	0.706(0.699-0.714)	<0.001	0.705(0.702-0.707)	<0.001
1992	0.669(0.661-0.678)	<0.001	0.666(0.663-0.669)	<0.001
1997	0.647(0.634-0.659)	<0.001	0.644(0.639-0.648)	<0.001
2002	0.607(0.582-0.634)	<0.001	0.606(0.597-0.615)	<0.001

Table 5. RRs of WCBA BC incidence and prevalence for females due to age, period and birth cohort effects.**Fig. 4.** Decomposition analysis of DALYs for Breast Cancer among women of reproductive age globally and in 5 SDI regions.

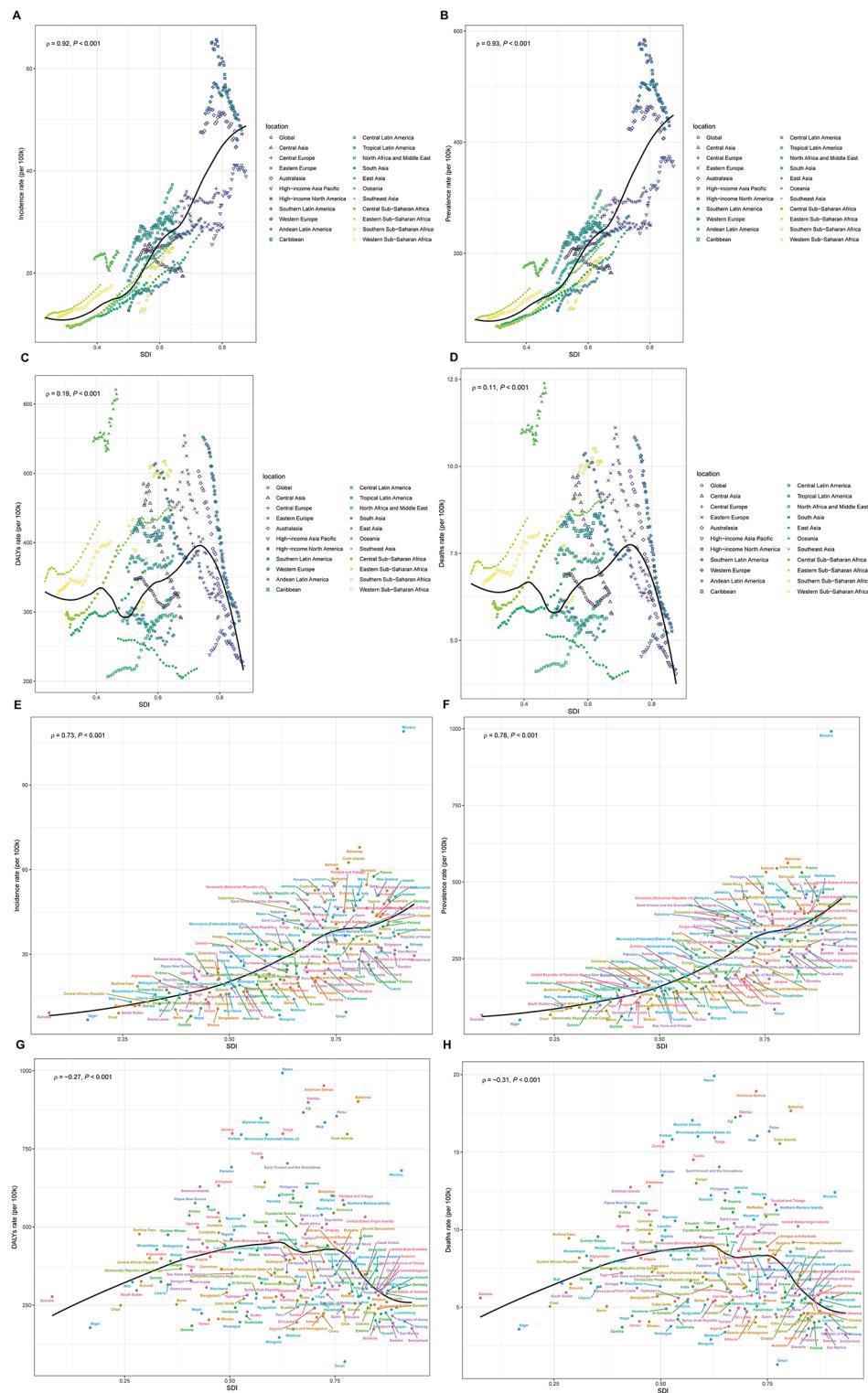


Fig. 5. The correlation between breast cancer burden and SDI in different regions and countries among women of reproductive age in 2021. (A) Scatter plot of the correlation between breast cancer incidence rate and SDI in 22 regions in 2021. (B) Scatter plot of the correlation between breast cancer prevalence rate and SDI in 22 regions in 2021. (C) Scatter plot of the correlation between breast cancer DALY rate and SDI in 22 regions in 2021. (D) Scatter plot of the correlation between breast cancer death rate and SDI in 22 regions in 2021. (E) Scatter plot of the correlation between breast cancer incidence rate and SDI in 204 countries or territories in 2021. (F) Scatter plot of the correlation between breast cancer prevalence rate and SDI in 204 countries or territories in 2021. (G) Scatter plot of the correlation between breast cancer DALY rate and SDI in 204 countries or territories in 2021. (H) Scatter plot of the correlation between breast cancer death rate and SDI in 204 countries or territories in 2021.

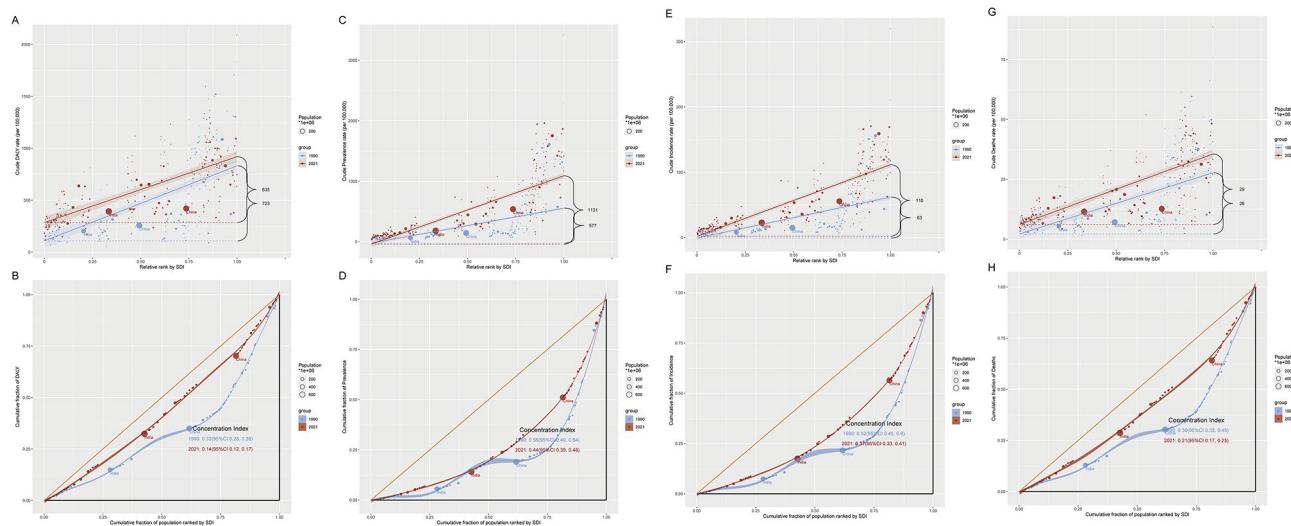


Fig. 6. Health inequality analysis of breast cancer burden among women of reproductive age in 1990 and 2021. (A) Slope index of inequality for DALY rate. (B) Concentration index for DALY. (C) Slope index of inequality for prevalence. (D) Concentration index for prevalence. (E) Slope index of inequality for incidence rate. (F) Concentration index for incidence rate. (G) Slope index of inequality for death rate. (H) Concentration index for death rate.

some improvement in the distribution of prevalence rates across socioeconomic groups, although significant disparities persist (Fig. 6C and D).

For incidence rates, the SII increased from 63 in 1990 to 110 in 2021, highlighting a worsening inequality in incidence rates. The CI for incidence, however, decreased from 0.52 in 1990 to 0.37 in 2021, showing a trend toward more equitable distribution, albeit with remaining disparities (Fig. 6E and F).

For mortality rates, the CI declined from 0.39 in 1990 to 0.21 in 2021, indicating a movement toward more equitable distribution of mortality rates among socioeconomic groups, though a certain degree of inequality still exists (Fig. 6G and H).

These findings reveal a complex pattern of health inequalities in the burden of breast cancer, with certain aspects improving in terms of equity, while others, such as prevalence and incidence rates, have seen worsening inequalities. This analysis underscores the need for targeted public health interventions to address these disparities.

Projections of breast Cancer burden among women of reproductive age globally and in China for 2040

Using the Bayesian Age-Period-Cohort (BAPC) prediction model, this study projected the epidemiological trends of breast cancer among women of reproductive age globally from 2022 to 2040. The results indicate that over the next two decades, the number of cases, age-standardized incidence rate (ASIR), age-standardized prevalence rate (ASPR), disability-adjusted life years (DALYs), and deaths due to breast cancer are expected to continue rising.

Specifically, by 2040, the number of new breast cancer cases is projected to reach 3,154,846, representing a 47.8% increase from 2022. The ASIR is expected to increase from 23.93 per 100,000 in 2022 to 25.95 per 100,000. Similarly, the number of prevalent cases is projected to rise from 20,945,142 in 2022 to 31,825,636 in 2040, with the ASPR increasing from 234.58 per 100,000 to 257.23 per 100,000.

In terms of DALYs, the global burden of breast cancer is predicted to reach 28,924,255.05 by 2040, with the age-standardized DALY rate increasing from 232.24 per 100,000 in 2022 to 247.38 per 100,000. The number of deaths is also expected to rise from 676,638 in 2022 to 975,756 in 2040, accompanied by a slight increase in the age-standardized mortality rate (Fig. 7 and Supplementary Table 6).

These findings suggest that the burden of breast cancer among women of reproductive age will continue to intensify globally over the next two decades, posing significant challenges for the prevention and control of this disease. Strategic public health interventions and improved access to early detection and treatment will be critical in mitigating this growing burden.

Discussion

This study highlights the heavy and growing global burden of breast cancer among women of reproductive age. From 1990 to 2021, incidence and prevalence rates continued to rise. While advancements in early detection and treatment have resulted in slight decreases in global age-standardized DALYs and mortality rates, absolute burden has escalated due to demographic drivers such as population growth and aging. Decomposition analysis revealed that population expansion accounted for 73.7% of the increase in DALYs, while improvements in

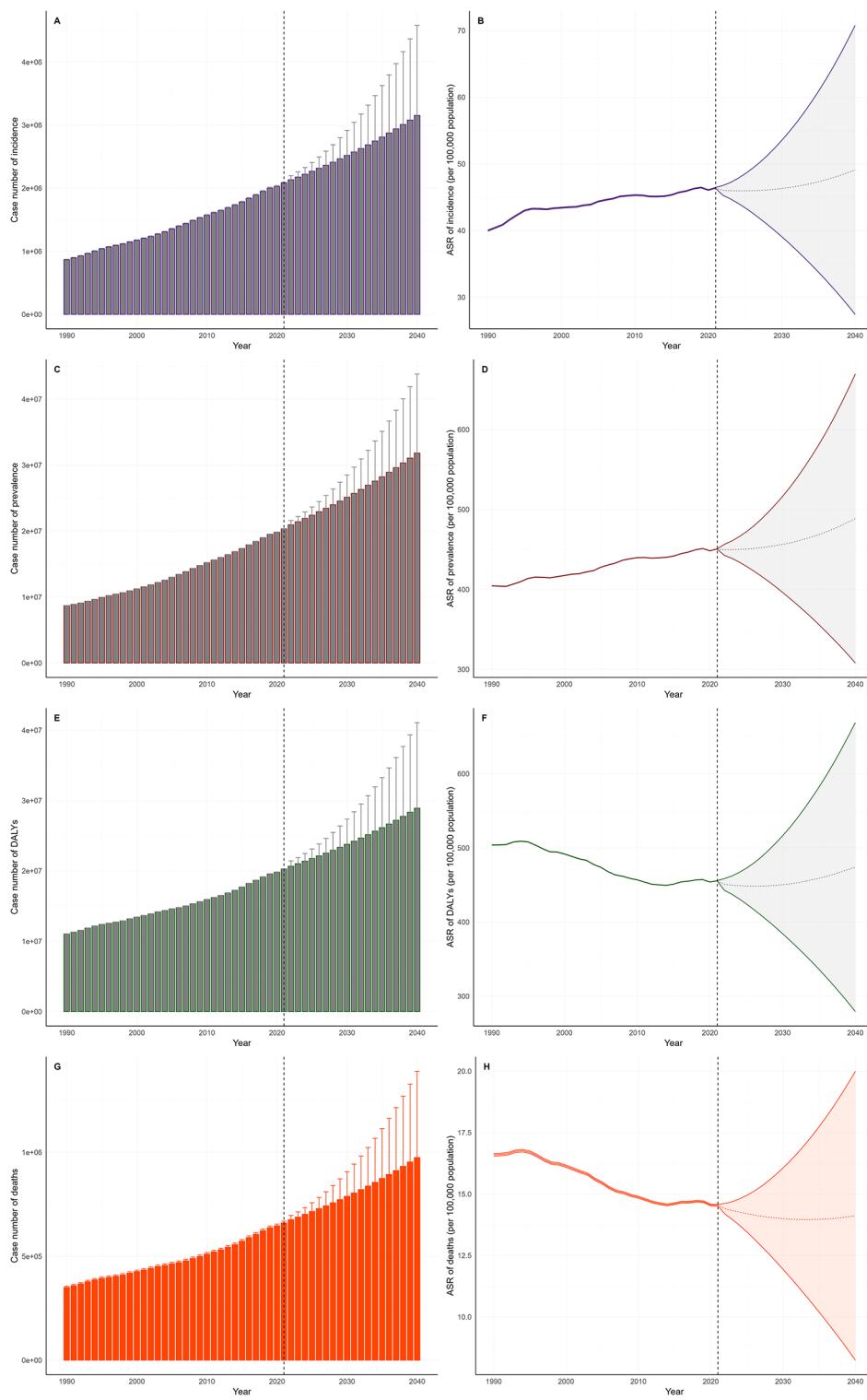


Fig. 7. Projected burden of breast cancers among women of reproductive age globally in 2040. (A, B) Incidence of breast cancers among women of reproductive age globally in 2040. (C, D) Prevalence of breast cancers among women of reproductive age globally in 2040. (E, F) Disability-adjusted life years (DALYs) due to breast cancers among women of reproductive age globally in 2040. (G, H) Mortality of breast cancers among women of reproductive age globally in 2040.

epidemiological patterns offset 11.65% of the burden. These findings underscore the need for integrated strategies targeting both demographic and epidemiological factors to manage the rising breast cancer burden.

At the SDI regional level, areas such as High-income North America and Australasia exhibited incidence and prevalence rates significantly exceeding expectations. These findings reflect increased exposure to risk factors, including obesity, delayed childbearing, and reduced breastfeeding rates⁸, as well as enhanced case detection due to advanced healthcare infrastructure and widespread screening programs. These high rates highlight the need to continue emphasizing prevention strategies, including lifestyle interventions and early diagnostic measures, to address the growing burden despite advanced medical systems. Interestingly, Oceania and Eastern Europe exhibited disproportionately high DALYs and mortality rates. These trends may reflect disparities in healthcare quality or accessibility, leading to delayed diagnoses or suboptimal management, despite higher SDI levels. Studies have suggested that improving care delivery and treatment affordability in similar regions could help address this imbalance⁹.

In contrast, economically underdeveloped regions such as Sub-Saharan Africa and Andean Latin America exhibited incidence and prevalence rates significantly below expected levels. While this could partially reflect reduced exposure to certain risk factors, it is more likely attributable to underdiagnosis and limited access to screening and healthcare services. This “hidden burden” highlights the importance of expanding healthcare accessibility and diagnostic capacity in low-SDI regions. Bridging these healthcare disparities is fundamental to facilitating early detection and minimizing advanced-stage presentations, which significantly contribute to elevated mortality rates and increased disability-adjusted life years. DALY rates exhibited a wave-like trend, peaking at an SDI of approximately 0.75. This reflects the dual impact of increasing disease prevalence in developing regions and effective disease management capabilities in high-SDI regions. DALY rates in countries such as East Asia, North Africa, and the Middle East were below expectations, likely due to improvements in early detection and treatment programs. However, disproportionately high DALY rates in countries such as Nauru and American Samoa highlight the need for targeted interventions in areas with moderate SDI levels but limited healthcare accessibility and quality.

At the national level, high-SDI countries such as Monaco and the Bahamas exhibited incidence and prevalence rates far exceeding expectations. This epidemiological pattern correlates with previously documented trends in high-SDI regions, reflecting the confluence of lifestyle modifications, enhanced screening capabilities, and improved diagnostic technologies. In contrast, middle-to-low SDI countries such as Mongolia and Oman exhibited significantly lower burden metrics, likely reflecting underreporting and limited healthcare access. DALY and mortality rates exhibited an inverted V-shaped relationship with SDI, further reinforcing the need to address healthcare access and resource allocation inequities across the SDI spectrum.

For the implications and recommendations, first, addressing inequities in low-SDI regions. Expand access to affordable and culturally appropriate screening programs to improve early detection rates. Strengthen healthcare infrastructure and workforce training in low-SDI countries, particularly in rural and underserved areas. Second, focusing on prevention in high-SDI regions. Implement robust public health campaigns targeting modifiable risk factors such as obesity and sedentary lifestyles. Integrate breast cancer prevention and screening into existing healthcare systems to ensure sustainability. Third, improve healthcare services in middle-SDI regions. Improve the quality and affordability of treatment in regions with unexpectedly high DALYs and mortality rates, such as Oceania and Eastern Europe. Promote regional cooperation to share best practices and technologies in cancer management. Finally, global collaboration. International organizations such as WHO can focus on narrowing disparities by providing financial and technical assistance to middle-to-low SDI countries. Establish a global database to monitor trends and evaluate the effectiveness of implemented interventions.

The regional differences in the burden of breast cancer among women of reproductive age reflect inequalities in healthcare infrastructure, socioeconomic development, and public health programs. In high-SDI regions, age-standardized incidence, DALY, and mortality rates have declined, driven by widespread screening programs, early detection, and advanced therapeutic interventions¹⁰. In contrast, low- and middle-SDI regions have experienced sustained increases in breast cancer age-standardized metrics, primarily due to limited preventive healthcare resources and delayed diagnoses¹¹. To address this situation, priority should be given to promoting low-cost screening technologies, such as clinical breast examinations and community-based screening programs, in low- and middle-income regions to alleviate disparities in health resources. Policies in specific regions should prioritize expanding healthcare access, particularly through affordable and accessible screening technologies. For instance, mobile mammography units and community-based screening programs may prove effective in resource-limited settings¹². Moreover, integrating breast cancer management into primary healthcare systems can enhance early detection and timely treatment¹³.

The Age-Period-Cohort (APC) analysis revealed that age significantly affects breast cancer incidence and prevalence among women of reproductive age ($P < 0.001$). The relative risks (RRs) of incidence and prevalence increased steadily with age, peaking in the 45–49 age group. The RRs for incidence (6.045, 95% CI: 6.024–6.067) and prevalence (6.281, 95% CI: 6.273–6.289) in this group highlight the amplified risk associated with reproductive aging. This pattern aligns with the cumulative exposure to risk factors over time, such as hormonal changes, genetic predisposition, and environmental exposures¹⁴. These findings underscore the importance of age-specific interventions. For younger women, targeted education and lifestyle modifications, such as promoting physical activity and reducing alcohol consumption, could mitigate long-term risks¹⁵. For older women, enhanced screening programs and regular clinical evaluations can facilitate early detection and timely intervention, especially in resource-limited settings where diagnostic delays are prevalent.

Period effect analysis identified an increasing risk of breast cancer between 1992 and 2017, with incidence RR reaching 1.548 (95% CI: 1.542–1.555) and prevalence RR at 1.561 (95% CI: 1.559–1.564) in 2017. This upward trend likely reflects the cumulative impact of social and environmental changes over time, including rising obesity rates, decreased physical activity, and delayed childbearing¹⁶. Advances in diagnostic technologies and

expanded screening opportunities during this period may also have contributed to the noticeable increase in prevalence and incidence due to improved case detection. These findings highlight the necessity of public health initiatives to address modifiable risk factors. Governments and healthcare providers should prioritize campaigns promoting healthy lifestyles, such as balanced diets and weight management, and expanding access to preventive services, particularly in low- and middle-income regions where these programs are still underdeveloped. Furthermore, addressing systemic barriers to healthcare access, such as cost and geographic availability, could help alleviate the growing breast cancer burden over time¹⁷.

Cohort effects indicated a significant decline in breast cancer RRs in more recent birth cohorts. Women born in 1947 had the highest RRs for incidence (2.134, 95% CI: 2.119–2.150) and prevalence (2.149, 95% CI: 2.143–2.154), which gradually decreased in subsequent cohorts, with the 2002 cohort showing significantly reduced RRs for incidence (0.607, 95% CI: 0.582–0.634) and prevalence (0.606, 95% CI: 0.597–0.615). This downward trend may reflect advances in healthcare accessibility, public health awareness, and strategies to reduce early-life risks in recent cohorts. Cohort findings emphasize the long-term benefits of early-life interventions. Investments in future health services, such as childhood diet programs, have been shown to play a critical role in adult health outcomes¹⁸. These findings also suggest that promoting widespread health education and preventive measures targeting young women could reduce the future burden of breast cancer.

The analysis of health inequalities in the global burden of breast cancer among women of reproductive age from 1990 to 2021 reveals a nuanced and evolving pattern of disparities. The Slope Index of Inequality (SII) and Concentration Index (CI) provide complementary insights into the absolute and relative distribution of breast cancer burden across socioeconomic gradients. These trends underscore the need for targeted interventions to address persistent gaps.

First, from 1990 to 2021, the SII for the disability-adjusted life years (DALY) rate increased from 635 to 723, indicating a continuous widening of absolute inequality in DALY distribution. This suggests that the absolute burden of breast cancer has become increasingly concentrated among specific populations, likely those with lower socioeconomic development or limited access to healthcare services. Conversely, the CI for DALYs decreased from 0.33 to 0.14, reflecting improvements in the relative distribution across socioeconomic strata. While global health initiatives have attenuated relative inequalities, the absolute disease burden persists disproportionately in resource-constrained regions, primarily driven by demographic expansion and systemic healthcare infrastructure deficiencies. Second, breast cancer prevalence exhibited the most significant increase in absolute inequality, with the SII rising from 577 in 1990 to 1131 in 2021. This highlights the widening absolute gap in disease prevalence between high-resource and low-resource populations. Meanwhile, the CI for prevalence decreased modestly from 0.56 to 0.44, indicating some progress in reducing relative disparities. However, the high absolute SII underscores persistent challenges faced by low-SDI regions, where rising prevalence may reflect delayed diagnoses, limited treatment opportunities, and insufficient public health resources. Third, the SII for incidence increased from 63 in 1990 to 110 in 2021, suggesting a gradual expansion of absolute inequality. Meanwhile, the CI for incidence decreased from 0.52 to 0.37, reflecting relative improvements in the equitable distribution of new cases. These findings suggest that global efforts to promote early detection and prevention have partially alleviated relative disparities but have not adequately addressed the underlying determinants of breast cancer incidence in resource-poor areas. Finally, for mortality, the CI decreased from 0.39 in 1990 to 0.21 in 2021, reflecting improvements in relative equity. However, persistent inequalities in mortality rates may be attributed to disparities in treatment accessibility and quality, particularly in regions where late-stage diagnoses remain common due to delayed detection.

These findings have significant implications and call for concrete actions to address health inequalities in the burden of breast cancer. Targeted public health interventions are essential in regions with high absolute inequality in DALYs and prevalence, particularly in low- and middle-SDI areas, where efforts to improve early diagnosis and access to affordable treatment options are crucial. For instance, a community outreach program in rural Ghana significantly improved women's knowledge, attitudes, and practices regarding breast cancer, demonstrating the effectiveness of targeted community campaigns¹⁹. Strengthening healthcare infrastructure, including investments in diagnostic facilities and cancer treatment centers, is also vital for reducing delays in care and improving outcomes, especially in regions with significant prevalence disparities. Policymakers should prioritize equitable resource allocation to ensure underserved populations benefit from advancements in cancer care. Moreover, international collaboration, such as technical assistance from WHO and financial aid from high-income countries, can help bridge resource gaps and foster global progress. Finally, ongoing monitoring of health inequality indices (SII and CI) is critical to provide valuable feedback on the effectiveness of interventions, enabling policymakers to adjust strategies as needed and ensure sustained improvements in addressing these disparities. By addressing these priorities, it is possible to reduce disparities and improve outcomes for women of reproductive age facing the burden of breast cancer.

The projections for 2040 indicate a continued rise in the burden of breast cancer among women of reproductive age, underscoring the need for targeted actions with short-, medium-, and long-term goals to address this escalating trend. In the short term, the focus should be on promoting low-cost screening technologies and enhancing medical training to address current diagnostic capacity gaps. In the medium to long term, efforts should aim to strengthen the resilience of healthcare systems by advancing precision medicine technologies and advocating for universal health coverage policies.

First, global collaboration is crucial to reducing cost barriers to cancer diagnosis and treatment in low-income countries. Mechanisms such as international aid, subsidized drug pricing, and public-private partnerships can play a pivotal role in supporting these efforts. Second, addressing the shortage of healthcare workers through targeted capacity-building programs, including oncology-specific training for medical professionals, can significantly improve care delivery in resource-constrained settings. Third, expanding investments in cancer research is essential to developing cost-effective screening tools and tailored treatment methods. For instance,

studies have shown that low-cost biomarkers for breast cancer detection could revolutionize public health outcomes in regions with limited diagnostic resources²⁰.

Finally, women of reproductive age face unique social and familial responsibilities that significantly affect their physical and mental health, potentially intensifying the burden of breast cancer²¹. These women often experience the dual pressures of caregiving, professional obligations, and societal expectations, which increase psychological stress and negatively impact lifestyle factors such as diet, exercise, and sleep²². Chronic stress is closely linked to physiological changes, including hormonal imbalances, immunosuppression, and increased inflammation, all of which contribute to cancer development and progression²³.

Caregiving responsibilities often result in delayed medical visits or missed preventive screenings, leading to late-stage diagnoses and poorer treatment outcomes. In addition to caregiving, occupational responsibilities impose another layer of stress. Many women struggle to balance demanding careers and family obligations, often in workplaces that lack flexibility or adequate support. Prolonged exposure to workplace stress elevates cortisol levels, leading to metabolic disorders such as obesity and insulin resistance, both of which are established risk factors for breast cancer²⁴. Furthermore, limited workplace health benefits, such as insufficient paid leave, exacerbate disparities by restricting access to preventive care, thereby increasing the overall breast cancer burden.

Parenting during critical child-rearing years adds another dimension of emotional and physical strain. Mothers frequently prioritize their children's needs over their own health, resulting in poor dietary choices and neglect of self-care. The psychological stress associated with raising children, especially in regions with limited institutional support, contributes to chronic stress and emotional exhaustion. Studies indicate that these cumulative burdens not only diminish quality of life but also increase the risk of stress-related illnesses, including cancer²⁵. To mitigate these multifaceted pressures, targeted policies and interventions are essential. Flexible work arrangements, remote work options, and paid caregiving leave can help women balance professional and family responsibilities more effectively. Workplace wellness programs focusing on stress management, physical activity, and mental health support can enhance overall well-being and potentially reduce breast cancer risk.

Improving healthcare services is equally vital. Governments and healthcare providers should prioritize affordable, community-based preventive services, including regular breast cancer screenings. Public education campaigns emphasizing self-care, balanced nutrition, and regular exercise can empower women to prioritize their health despite demanding schedules. Family and community support systems are another critical area of focus. Encouraging equitable distribution of caregiving and household responsibilities within families can alleviate the burden on women. Community-based childcare and eldercare programs can provide essential relief, enabling mothers to dedicate more time to their health and well-being. Implementation of comprehensive psychosocial support interventions is essential for mitigating the psychological burden associated with concurrent caregiving responsibilities and occupational demands among affected women. Accessible counseling services, stress management programs, and support groups for working mothers and caregivers can help women maintain their health while fulfilling their responsibilities.

Addressing these systemic challenges through well-designed policies and support mechanisms can reduce breast cancer risk and improve overall health outcomes for women of reproductive age. Prioritizing these interventions is essential to easing the disproportionate burdens faced by this vulnerable population and fostering equitable health care and well-being.

Limitation

This study provides a comprehensive and in-depth examination of breast cancer in a special population of women of childbearing age. It employs descriptive, trend, decomposition, health inequality, and predictive analyses to elucidate the epidemiological characteristics of breast cancer in this demographic. The findings of this study inform global public health policymaking and healthcare resource allocation. While this study has notable strengths, it is not without limitations. First, the quality and availability of data vary across countries, especially in low- and middle-income areas. This may result in an underestimation of the burden due to factors such as underdiagnosis, misclassification, and limited health reporting systems. Additionally, it is important to note that there are significant differences between the data provided by the Global Burden of Disease (GBD) Study and the International Agency for Research on Cancer (IARC). For instance, the number of new cases reported for the 15–49 age group in 2022 by IARC (668,417) significantly exceeds GBD's estimate of 561,438, illustrating a potential discrepancy that may affect comparisons between the two datasets. While this study relies on GBD data for its global burden analysis, future studies should consider these differences when interpreting cancer incidence estimates, especially in regions with incomplete or inconsistent reporting systems. Secondly, the Global Burden of Disease framework employs statistical modelling to address data gaps, which may introduce potential bias. Despite the use of sophisticated methods to minimise these biases, the estimates remain contingent upon the assumptions and quality of the input data. Thirdly, the Global Burden of Disease study aggregates long-term data, which may obscure short-term fluctuations or recent trends in the burden of breast cancer. Fourth, while the analysis explores trends and inequalities, it does not sufficiently consider contextual factors such as health care policies, socioeconomic changes, and cultural influences, which may have a complex impact on observed patterns. In addition, projections extending to 2040 are based on historical trends and covariates, which may not fully account for potential future changes in health care innovation or policy shifts.

Conclusions

This study systematically evaluated the temporal trends, regional disparities, and health inequalities in the global burden of breast cancer among women of reproductive age from 1990 to 2021 and projected the epidemiological trends for the next 20 years. The results indicate a significant increase in the burden of breast cancer over the past 32 years, with the most pronounced growth observed in middle- and low-SDI regions, likely due to unequal access to prevention, diagnostic, and treatment resources. In terms of age patterns, the global burden was highest

in 2021 among women aged 45–49. Decomposition analysis revealed that population aging and growth were the primary drivers of the increasing burden globally and across SDI regions, while changes in epidemiological patterns partially mitigated this trend. Frontier analysis highlighted significant disparities in the burden of breast cancer across SDI groups, with middle- and low-SDI countries showing substantial gaps compared to the frontier, suggesting underutilization of health services or deficiencies in disease prevention and control measures. Health inequality analysis showed that from 1990 to 2021, absolute inequalities in the global burden of breast cancer worsened, while relative inequalities improved. Projections based on the BAPC model predict that by 2040, the global burden will further intensify, with new cases expected to increase by 47.8% compared to 2022, alongside continuing rises in age-standardized incidence, prevalence, and mortality rates.

Data availability

The data used for the analyses in the study are publicly available at <https://ghdx.healthdata.org/gbd-2021>.

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Author contributions

Conceptualization, Y.C.; F.D. and Y.Y.; Data management, Y.C. and Y.Y.; Methodology, Y.C.; Software, Y.C.; Supervision, J.Q.; Writing-original draft, Y.C.; Writing-criticism and editing, Y.C.; Y.Y. and J.Q.; Visualization, Y.C. and Y.Y.; All authors have read and agreed to the published version of the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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