

Three-dimensional decomposition of breast cancer trends in perimenopausal and menopausal females: Cross-national comparative study

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Abstract

Objective

Breast cancer remains a leading cause of cancer mortality in women, disproportionately affecting perimenopausal (40–59 years) and menopausal (45–54 years) populations. This first global analysis examines incidence, mortality, prevalence, and disability-adjusted life years (DALYs) trends in these groups from 1990 to 2021.

Methods

Using the Global Burden of Disease (GBD) 2021 dataset, age-standardized rates (ASRs) and estimated annual percentage changes (EAPCs) quantified temporal trends. Socioeconomic disparities were evaluated using slope (SII) and concentration (CI) indices across Sociodemographic Index (SDI) quintiles and regions. Age-period-cohort (APC) and Bayesian age-period-cohort (BAPC) models analyzed temporal patterns, while frontier benchmarking identified optimal burden thresholds. Decomposition methods differentiated demographic, population growth, and epidemiological drivers.

Results

From 1990–2021, global breast cancer cases surged by 150.6% (menopausal) and 145.8% (perimenopausal), deaths by 82.8% (both groups), and DALYs by 85.8% (menopausal) and 84.2% (perimenopausal). ASRs for incidence and prevalence increased (EAPC: 0.44 [perimenopausal], 0.38 [menopausal]), while mortality and DALY rates declined (EAPC: -0.58 to -0.65). Burden peaked in middle-SDI regions (inverted U-shaped trend), with high-SDI areas showing declining incidence/mortality and low-SDI regions lagging. Inequality indices (SII, CI) decreased over time. Perimenopausal burden peaked at ages 55–59, with incidence/prevalence rising but mortality/DALYs falling post-2005. BAPC projections predict significant increases in all metrics by 2035.

Conclusion

This study highlights persistent socioeconomic disparities, age-specific epidemiological shifts, and rising incidence projections, underscoring the need for tailored prevention strategies and region-specific healthcare policies for perimenopausal and menopausal women.

Introduction

Breast cancer is the leading malignancy among women globally, representing the most frequently diagnosed cancer and the principal cause of cancer-related mortality. It accounts for the highest incidence rates in 157 countries and dominates mortality patterns in 112 nations, with estimated

2.3 million new cases and 666,000 deaths worldwide in 2022^{1,2}. These data indicate that currently, 1 in 20 women globally is diagnosed with breast cancer, and 1 in 70 women is likely to die from breast cancer in their lifetime. By 2050, new breast cancer cases are projected to increase by 38%, and deaths by 68%, with the fastest growth in low- and middle-income countries². Based on the age distribution of breast cancer in women, the perimenopausal (40–59 years) or menopausal (45–54 years) periods exhibit the highest incidence rates, case fatality rates, mortality rates, and disability-adjusted life years (DALYs), which suggested that the perimenopausal or menopausal period is a critical window for breast cancer risk accumulation^{3–6}.

Menopause, marked by irreversible ovarian follicular depletion, typically occurs between 45–55 years, demarcating the end of reproductive capacity⁷. Perimenopause encompasses the transitional phase from initial ovarian decline to one year after the cessation of menopause, lasting 4–6 years with significant hormonal fluctuations^{8,9}. Menopausal and perimenopausal women constitute a critical component of global population health, representing an expanding demographic cohort with increasingly complex and multifaceted healthcare demands. The global postmenopausal population surged to 1.02 billion in 2021 and is projected to reach 1.65 billion by 2050, representing 38.7% of adult females worldwide¹⁰. Studies have confirmed that the global burden of breast cancer is closely linked to women's menopausal status, with the risk of breast cancer rapidly declining after menopause^{11,12}. Perimenopause constitutes a critical transition phase in breast cancer pathogenesis, where cumulative risk transitions to clinical manifestation, due to hormonal volatility, cumulative genetic and environmental exposures¹³. The perimenopausal period also drives metabolic alterations, including the absolute weight gain, progressive visceral adipose accumulation and systemic insulin dysregulation, culminating in elevated breast cancer incidence^{14–17}. Therefore, comprehensive analysis and projection of global epidemiological trends in breast cancer among women during menopausal and perimenopausal phase are critically important. While prior investigations have examined epidemiological patterns of breast cancer, systematic research targeting the menopausal and perimenopausal period remains notably absent.

Utilizing the Global Burden of Disease (GBD) 2021 dataset, this study pioneers a comprehensive analysis of breast cancer epidemiology among perimenopausal and menopausal women across 204 countries/territories (1990–2021). We quantify incidence, mortality, prevalence, and disability-adjusted life years (DALYs), stratified by age and Sociodemographic Index (SDI), while integrating inequality metrics (Slope Index of Inequality [SII], Concentration Index [CI]), frontier analysis, and temporal trend modeling (AAPC/APC). Decomposition analysis disentangles contributions from aging, population growth, and risk factor evolution, complemented by Bayesian age-period-cohort projections to 2035. Our findings enhance our understanding of the significance of breast cancer prevalence among perimenopausal women and help uncover socioeconomic and biological determinants, guiding equitable prevention and healthcare strategies, such as early detection and treatment in these populations.

Methods

Data acquisition and sources

This study leveraged epidemiological data from the Global Burden of Disease (GBD) 2021 database, a comprehensive global repository developed by the Institute for Health Metrics and Evaluation (IHME). The GBD 2021 employs DisMod-MR 2.1 and Bayesian meta-regression models to systematically quantify 369 diseases/injuries and 88 risk factors across 204 countries and territories from 1990 to 2021¹⁸. We extracted age-standardized metrics for breast cancer among menopausal and perimenopausal women. Menopause was classified as ages 45–54, and perimenopause was considered to be the period from 40 to 59 years (extending 5 years on either side of menopause)^{4,7,19}. The analyzed metrics included incidence, prevalence, mortality, and disability-adjusted life years (DALYs), all accessed through the Global Health Data Exchange (GHDx) platform (<http://ghdx.healthdata.org/gbd-results-tool>). To enable regional comparisons, we calculated age-standardized rates using the world standard population from the Global Burden of Disease Study 2021 (GBD 2021). The reference population data, including age-specific weights, were sourced from the GBD 2021 Demographics 1950–2021 dataset²⁰.

Statistical analysis

We conducted geospatial visualizations and stratified comparative analyses to examine geographical patterns and interregional disparities in breast cancer burden among perimenopausal and menopausal populations. Data were stratified according to GBD-defined geographical regions and visualized using R software (v4.4.1), with the *sf* package handling geospatial processing and *ggplot2* generating visual representations of age-standardized metrics²¹. Joinpoint regression analysis was implemented to evaluate temporal trends in breast cancer incidence, prevalence, mortality, and DALYs among perimenopausal women (1990–2021). Using the segmented and broom R packages, we identified statistically significant inflection points ($p < 0.05$) in disease trends. The relationship between SDI and breast cancer burden was assessed through SDI-stratified rate calculations. Comparative analyses across SDI quintiles (low to high) evaluated socioeconomic disparities. Frontier analysis established SDI-specific theoretical minima for age-standardized rates, with the efficiency gap (deviation from optimal rates) serving as a healthcare system performance metric. Inequality was quantified using the Slope Inequality Index (SII) and Concentration Index (CI), with SII modeling prevalence gradients across SDI-ranked populations and CI evaluating inequities through Lorenz curve integration. We conducted population-based assessments of breast cancer distribution among perimenopausal women, stratifying by 5-year age intervals (40–44, 45–49, etc.). Analyses were implemented in R, with *ggplot2* visualizing epidemiological patterns. This method allocated temporal variations in breast cancer burden to three drivers: (a) demographic aging, (b) population growth, and (c) epidemiological rate fluctuations. The analysis quantified each factor's contribution to mortality and morbidity patterns^{22,23}. Using the R segmented package, we quantified AAPC in breast cancer burden among perimenopausal populations, reporting annual percentage changes with 95% confidence intervals. The BAPC model (implemented via R's INLA and BAPC packages) projected breast cancer incidence and prevalence to 2035 by integrating age, period, and cohort effects.

The analytical approach utilized anonymized population-level epidemiological data from the GBD 2021 collaborative dataset, which precluded access to individual patient records. All statistical procedures, encompassing calculation of central tendency measures (arithmetic means) with associated 95% uncertainty intervals for prevalence estimates, as well as 95% confidence intervals for EAPC and BAPC projections, were performed using R statistical software version 4.4.1. Time-dependent patterns were assessed employing a significance level of $\alpha = 0.05$, with all results presented as mean values supplemented by 95% uncertainty intervals to characterize both measurement precision and inherent model uncertainty.

Results

The global trend of breast cancer burden from 1990 to 2021

Between 1990 and 2021, the global incidence of breast cancer in menopausal and perimenopausal women rose sharply. Among menopausal women, cases increased by 150.6%, from 189,744 (95% UI: 181,921 – 198,925) to 475,583 (95% UI: 441,865 – 515,811), while perimenopausal women saw a 145.8% rise, from 367,742 (351,840 – 385,838) to 903,889 (837,146–978,939). At the same time, deaths increased by 82.8% in both groups: from 65,715 (62,120 – 70,129) to 120,135 (111,165 – 129,618) for menopausal women and from 128,926 (121,801 – 137,501) to 235,634 (217,027–255,425) for perimenopausal women. Total case counts surged by 151.1% (1,683,779–4,228,608) and 146.3% (3,308,035 – 8,147,019), respectively. Similarly, DALYs grew by 85.8% (2,770,481–5,148,783) and 84.2% (5,337,141–9,829,318), reflecting substantial disease burden escalation over three decades (Table 1). Compared with 1990, ASRs of incidence and prevalence of breast cancer among perimenopausal women increased in 2021, while the mortality rate and DALYs decreased. The EAPCs of incidence (0.44, 95% CI: 0.35 to 0.54), mortality (-0.58, -0.65 to -0.50), prevalence (0.49, 0.40 to 0.57), and DALYs (-0.53, -0.60 to -0.46). Similarly, for breast cancer in menopausal women, the corresponding EAPCs demonstrated comparable patterns: incidence (0.38, 0.27 to 0.49), mortality (-0.65, -0.71 to -0.58), prevalence (0.43, 0.32 to 0.53), and DALYs (-0.60, -0.66 to -0.53). The findings reflected improved early detection and treatment efficacy globally, though the increasing disease burden underscores the need for enhanced prevention strategies. (Table 2,3).

Trends of regions defined by Socio-demographic Index (SDI)

Globally, female breast cancer burden demonstrated significant geographical disparities in 2021, showing a general trend of decreasing incident cases, deaths, prevalent cases, and DALYs with reducing SDI. However, the middle SDI region exhibited the most substantial disease burden, featuring 151,948 (95% UI: 135,294 – 170,222) new cases in menopausal women and 284,732 (252,920 – 319,930) in perimenopausal women. Mortality data revealed 41,537 (37,121 – 46,360) deaths among menopausal women and 80,613 (71,720 – 90,438) in perimenopausal women. The region also accounted for

1,310,241 (1,179,232-1,464,898) prevalent cases in menopausal women and 2,469,028 (2,215,382-2,759,225) in perimenopausal women, with corresponding DALYs of 1,768,566 (1,582,191-1,972,009) and 3,341,043 (2,977,292-3,744,745) respectively. Geographically, South Asia, Western Europe, and High-income North America carried the highest burden of incident and prevalent cases, in contrast to Oceania, Andean Latin America, and Central Sub-Saharan Africa which demonstrated the lowest rates. Mortality and DALYs were predominantly concentrated in South Asia, East Asia, and Southeast Asia, while Oceania, Australasia, and Andean Latin America exhibited the most favorable outcomes.

However, the EAPCs of ASRs for breast cancer incidence, mortality, prevalence, and DALYs among menopausal and perimenopausal women globally followed an inverted U-shaped curve relative to SDI levels, peaking in low-middle SDI regions before declining. Specifically, menopausal women showed EAPCs of 2.04 (95% CI: 1.99–2.10) for incidence, 1.00 (0.93–1.06) for mortality, 2.19 (2.13–2.25) for prevalence, and 1.02 (0.95–1.08) for DALYs. Similarly, perimenopausal women demonstrated corresponding EAPCs of 2.10 (2.05–2.16) for incidence, 1.08 (1.01–1.14) for mortality, 2.23 (2.17–2.29) for prevalence, and 1.09 (1.02–1.15) for DALYs. Meanwhile, the ASRs of incident has shown a stable decreasing trend in high SDI, from 166.57(160.77-172.25) to 156.96(149.18-164.36) in perimenopausal women and from 176.87(170.92-182.94) to 166.15(157.67-174.38) in menopausal women, with the EAPCs of -0.27(-0.47 to -0.08) and - 0.31(-0.51 to -0.11). Similar declining trends were also observed in the age-standardized prevalence rates in high SDI: from 1657.59(1,566.69-1,755.87) to 1,605.66(1,527.92-1,682.86) in menopausal women and from 1,582.35(1,490.09-1,686.92) to 1,545.71(1475.47-1,617.79) in perimenopausal women, with the EAPCs of -0.18(-0.36,0.01) and - 0.12(-0.30 to 0.06). Notably, high-SDI regions demonstrated more pronounced declines in ASRs of both mortality and DALYs for breast cancer among menopausal and perimenopausal women. For menopausal women, mortality ASRs decreased from 40.44 (95% UI: 39.33–41.56) to 23.11 (22.28–23.93), with an EAPC of -1.96 (-2.03 to -1.89), while DALYs declined from 1,753.19 (1,692.97-1,819.56) to 1,048.00 (993.04-1,108.18), showing an EAPC of -1.81 (-1.88 to -1.74). Similarly, perimenopausal women experienced mortality ASR reductions from 39.16 (38.09–40.20) to 22.79 (21.92–23.61) [EAPC: -1.88 (-1.95 to -1.81)], with DALYs decreasing from 1,653.01 (1,595.98-1,714.45) to 1,002.40 (949.92-1,058.28) [EAPC: -1.74 (-1.81 to -1.67)]. Geographically, the most significant increases in incidence and prevalence rates were observed in North Africa and the Middle East, Southern Sub-Saharan Africa, and East Asia, while the most substantial decreases occurred in High-income North America, Central Asia, and Australasia. For mortality rates and DALYs, the greatest increases were concentrated in Southern Sub-Saharan Africa, North Africa and the Middle East, and Southeast Asia, whereas the most pronounced reductions were seen in Australasia, Western Europe, and High-income North America (Table 1–3, Fig. 1).

Additionally, our study systematically analyzed the associations between SDI and breast cancer burden across 21 regions and 204 countries, revealing distinct patterns by menopausal status. Among perimenopausal women, incidence rates showed a positive correlation with SDI levels, while mortality rates followed an inverted U-shaped trajectory, initially rising then sharply declining with increasing SDI. Regional analyses confirmed this nonlinear relationship, with high-SDI regions exhibiting the highest

incidence but lowest mortality rates (Fig. 2A-B, Figure S2A-B). Temporal trend analysis demonstrated diverging patterns: high-SDI regions experienced slight incidence declines versus modest increases elsewhere, while mortality trends showed decreasing ASRs in high and high-middle SDI areas contrasted with stable increases in low-middle and low-SDI regions. As of 2021, the highest SDI quintiles maintained the lowest mortality ASRs (Fig. 2C, Figure S2C).

Our inequality analysis revealed significant socioeconomic disparities in breast cancer burden among perimenopausal women, with higher ASRs concentrated in nations with greater socioeconomic development. The SII showed notable reductions between 1990 and 2021: incidence decreased from 119.01 (95% CI: 104.37-133.65) to 103.31 (90.98-115.64), mortality shifted from 22.91 (17.71–28.12) to -4.51 (-9.51 to 0.49), prevalence remained stable (1,111.61 to 1,101.49), while DALYs transitioned from positive (983.98) to negative values (-113.53). Correspondingly, CIs declined across all metrics, with incidence/prevalence CIs falling from 0.35 to 0.24 and mortality/DALYs CIs reversing from positive (0.14) to negative values (-0.04/-0.02), indicating progressive reduction in health inequalities from 1990 to 2021 (Fig. 3A-B, Figure S3A-B).

To quantify achievable prevalence reductions through developmental optimization, we constructed an SDI-ASR efficiency frontier (1990–2021). Countries below this frontier (Fig. 3C/S3C) demonstrated untapped potential, measured as effective differences between their current ASRs and frontier-optimal rates. Using 2021 data, we calculated effective differences for each country and region relative to the frontier. Out of 204 countries and territories, the top 15 countries with the largest effective difference in incidence with an breast cancer gap from the frontier among perimenopausal women were Monaco, Bahamas, Bahrain, France, Lebanon, Bermuda, Andorra, New Zealand, Barbados, Montenegro, Cyprus, Costa Rica, Italy, Qatar, Cook Islands. For the largest effective difference in mortality, the top 15 countries were Nauru, American Samoa, Tonga, Fiji, Bahamas, Micronesia (Federated States of), Marshall Islands, Cook Islands, Namibia, Saint Vincent and the Grenadines, Malaysia, Congo, Kiribati, Pakistan, Tokelau. These countries exhibited elevated ASRs of breast cancer among perimenopausal women compared to nations with comparable sociodemographic development levels. The distribution of the top 15 countries with the highest prevalence rates closely mirrored that of incidence rates, while the pattern of DALYs exhibited greater similarity to mortality rates. Frontier analysis revealed that the 15 countries with the largest efficiency gaps in incidence and prevalence all belonged to high and high-middle SDI regions, whereas those with the greatest mortality and DALYs rate efficiency disparities were predominantly concentrated in low and low-middle SDI regions.

Demographic patterns of perimenopausal breast cancer cases

Age-stratified analyses of breast cancer burden among perimenopausal women revealed distinct distribution patterns and temporal trends. As demonstrated in Fig. 4A and Figure S4A, the proportion of disease burden escalated progressively with age, with the oldest subgroup (55–59 years) consistently exhibiting the highest shares of incidence, mortality, prevalence, and DALYs across most geographical

regions. Longitudinal assessment (1990–2021) showed universal increases in incidence and prevalence rates across all age groups, contrasted by steady declines in both mortality and DALY rates. These opposing trends were most pronounced in the 55-59-year cohort (Fig. 4B and Figure S4B), suggesting age-specific differentials in detection and management efficacy.

Decomposition of global burden in perimenopausal women

Global decomposition analysis revealed differential demographic impacts on perimenopausal breast cancer burden. While population growth and aging contributed positively to incidence, mortality, prevalence and DALYs in most SDI regions, high and high-middle SDI areas (particularly Eastern/Western Europe) exhibited inverse associations with all indicators (Fig. 4C, S4C). This divergence suggests distinct epidemiological transitions across development spectrums.

Projected patterns of global breast cancer burden in perimenopausal women

Using joinpoint regression analysis, we identified distinct temporal patterns in breast cancer burden among perimenopausal women. The incidence trajectory showed four distinct phases: a rapid initial increase (1990–1995; APC = 2.064), followed by more gradual growth (1995–2008; APC = 0.462), a modest decline (2008–2012; APC = -0.384), and subsequent resurgence (2012–2021; APC = 0.432). Mortality and DALY rates exhibited different dynamics, beginning with a moderate rise (1990–1995; APC = 0.474) before transitioning to a steep decline (1995–2003; APC = -0.709), which accelerated further (2003–2012; APC = -1.097) before stabilizing at a slower rate of decrease (2013–2021; APC = -0.148). Notably, prevalence trends demonstrated strong concordance with incidence patterns, while DALY rates closely tracked mortality trends, suggesting differential underlying drivers for case identification versus outcome measures. (Fig. 5A, Figure S5A).

Our Age-Period-Cohort analysis revealed significant temporal patterns in breast cancer burden among perimenopausal women. The net drifts demonstrated distinct trajectories: incidence (0.3725832) and prevalence (0.4343787) showed increasing trends, while mortality (-0.6270664) and DALYs (-0.573548) exhibited significant declines (all $p < 0.05$). Age effects consistently rose across all indicators. Period effects displayed divergent patterns - incidence and prevalence rate ratios (RRs) remained > 1.0 post-2005, reflecting growing disease burden, whereas mortality and DALYs RRs stabilized below 1.0 after 2005, indicating sustained improvements. Cohort effects similarly showed reduced burden for women born after 1956, suggesting positive impacts of evolving diagnostic and therapeutic approaches (Fig. 5B, Figure S5B).

Global disease burden prediction for female breast cancer to 2035

The BAPC projections, which was utilized to project future trends in ASRs and case counts of breast cancer among perimenopausal women from 2022 to 2035, forecast substantial increases by 2035, with incident cases, deaths, prevalent cases, DALYs, incidence rates, and prevalence rates all exhibiting marked growth. Concurrently, mortality rates and DALY rates are projected to maintain a steady upward trajectory, reflecting persistent challenges in disease management despite advancements in detection and care. (Fig. 6, Figure S6).

Discussion

This pioneering study, utilizing the latest 2021 GBD dataset, presents the first global assessment of breast cancer patterns specifically among perimenopausal and menopausal populations, revealing a high disease burden, significant disparities in SDI levels, and variations across age groups. According to our findings, global breast cancer burden among menopausal and perimenopausal women showed substantial increases in absolute cases but declining age-standardized mortality and DALYs from 1990–2021, with the heaviest burden in middle-SDI regions following an inverted U-shaped pattern. High-SDI areas achieved better outcomes while low-SDI regions lagged, persisting geographic disparities. Inequality decreased over time, though development-related gaps remained in incidence versus mortality. The disease peaks at 55–59 years, with incidence/prevalence rising and mortality/DALYs falling post-2005. Projections derived from BAPC analysis paint a sobering picture: by 2035, perimenopausal women will face substantially greater breast cancer burden, and the sustained upward trends highlight critical healthcare system challenges that persist despite medical advancements. These findings underscore the necessity for tailored prevention strategies and optimized treatment protocols, especially for vulnerable perimenopausal women in underserved areas.

Our analysis reveals that in 2021, approximately 476 thousand menopausal and 904 thousand perimenopausal women developed breast cancer globally, representing a 150% increase since 1990. While incidence and prevalence rates continued to rise, significant declines were shown in mortality and DALYs. These trends align with previously published data on breast cancer patterns among women across all age groups globally^{6,24}, which demonstrate global improvements in screening and treatment efficacy. However, persistent geographical disparities emerge: higher SDI regions consistently exhibit elevated breast cancer incidence and disease burden follows an inverse U-shaped pattern across SDI levels, peaking in middle-SDI regions. Factors arising from rapid social development (such as a diet high in red meat, high alcohol use, high BMI, high fasting plasma glucose, low physical activity, secondhand smoke, and smoking) were related to this result^{5,25,26}, along with increased detection rates resulting from developed clinical infrastructure and implemented mass screening protocols. Such sustained high prevalence signals the critical importance of maintaining prevention-focused policies, particularly through population-level lifestyle interventions and accessible screening programs, even in settings with advanced therapeutic capabilities.

Additionally, high-SDI areas show declining age-standardized rates (particularly in mortality), whereas lower SDI regions face rising burdens. We found the highest incidence and prevalence rates were

predominantly observed in South Asia, Western Europe, and High-income North America, while Oceania, Andean Latin America, and Central Sub-Saharan Africa showed the lowest prevalence. Mortality and DALY burdens were most prevalent in South Asia, East Asia, and Southeast Asia, contrasting with Oceania, Australasia, and Andean Latin America, which had the most favorable outcomes. Frontier analysis also revealed that the 15 countries with the largest efficiency gaps in incidence and prevalence all belonged to high and high-middle SDI regions, whereas those with the greatest mortality and DALYs rate efficiency disparities were predominantly concentrated in low and low-middle SDI regions. The decline in incidence and prevalence ASRs of breast cancer among menopausal and perimenopausal women in high-SDI regions may be attributed to advanced medical technology systems, effective tertiary prevention measures, and improved population-wide health literacy^{27–30}. These factors collectively enhance breast cancer screening coverage and early detection rates. The rising incidence in low-middle SDI regions also may be driven by exposure to region-specific pollutants under certain climatic conditions and occupational hazards and lifestyle transitions typical of early industrialization phases. Furthermore, compared to high-SDI regions, low-SDI regions demonstrate distinct behavioral risk patterns. At the same time, sociocultural determinants also significantly influence the accessibility and efficacy of cancer treatment among perimenopausal female populations. High-SDI populations benefit from systematic interventions such as regular mammography screenings and stress management programs, while low-SDI groups face compounded modifiable risks, including gender inequality, chronic occupational stress, physical inactivity, and high-sugar diets. These multilayered disparities ultimately create divergent disease risk profiles across SDI levels^{31–34}. In addition, variations in the impact of breast cancer in perimenopausal women are also influenced by economic and social factors, underscoring the importance of strategic allocation of health resources and medical interventions to mitigate the burden of breast cancer^{35,36}. To mitigate these disparities, global health strategies must prioritize scalable, low-resource screening solutions, particularly clinical breast exams and decentralized community screening in low- and middle-income regions. Region-specific policies should emphasize infrastructure development for mobile mammography units and task-shifting to train community health workers in early detection³⁷. Moreover, Systematic incorporation of breast cancer care within primary healthcare frameworks can significantly improve early case identification and treatment initiation timelines, particularly in resource-constrained settings³⁸. In addition, gender equity advancement directly enhances women's health capital and living standards through improved resource allocation and social empowerment.

Additionally, from the perspective of age distribution, the proportion of disease burden escalated progressively with age, with the oldest subgroup (55–59 years) consistently exhibiting the highest shares of incidence, mortality, prevalence, and DALYs across most geographical regions. Longitudinal assessment (1990–2021) showed universal increases in incidence and prevalence rates across all age groups, contrasted by steady declines in both mortality and DALY rates. These opposing trends were most pronounced in the 55-59-year cohort. Considering the global average menopause onset occurs at age 51, the 55–59 age group universally qualifies as postmenopausal across all geographic regions and ethnic populations. The European Prospective Investigation into Cancer and Nutrition (EPIC) study, one

of the largest prospective cohort studies with over 500,000 participants, demonstrated particularly strong associations between adiposity indicators (BMI ≥ 30 kg/m²; waist circumference > 88 cm) and postmenopausal breast cancer risk³⁹. Some analytical study on female cancers also confirmed the relationship between obesity and breast cancer^{5,16,40}. In addition, perimenopausal or postmenopausal women often exhibit unhealthy lifestyle habits, such as alcohol consumption and irregular or poor dietary patterns⁴¹, which may be associated with depressive states during the postmenopausal period⁴². All these factors have been confirmed as risk factors for breast cancer^{5,43}. Other factors like elevated circulating IGFBP7 and an elevated IGFBP7/IGF1 ratio also showed significant positive relationships with advancing age, obesity (specific to IGFBP7), all-cause mortality, and cancer occurrence among postmenopausal women⁴⁴. Targeted psychological support for perimenopausal women is crucial to address their emotional volatility, stress responses, and anxiety disorders. Concurrently, implementing menopause-specific mental health initiatives requires healthcare system reforms to deliver specialized services, including screening protocols and therapeutic interventions for menopause-related psychological distress.

This investigation acknowledges three primary limitations: (1) The breast cancer burden estimates are intrinsically dependent on GBD 2021 data quality and completeness, with particular constraints arising from fragmented healthcare datasets in certain lower SDI regions that may compromise regional burden estimation accuracy; (2) The dichotomous categorization of menopausal status (restricted to 45–49 and 50–54 age cohorts) imposes analytical constraints on longitudinal pattern detection; (3) Heterogeneity in international diagnostic classifications and evolving screening practices introduces cross-temporal comparability challenges. These data quality considerations necessitate cautious interpretation of the identified perimenopausal breast cancer burden trajectories.

Conclusion

In conclusion, this first global analysis of menopausal and perimenopausal breast cancer reveals rising global burden (1990–2021). Middle-SDI regions bear the highest burden, with persistent geographic disparities. While high-SDI areas show improving trends, low-SDI regions lag behind. Projections indicate escalating incidence through 2035 despite diagnostic advances, particularly for perimenopausal women aged 55–59. The findings highlight critical needs for age-specific interventions and equitable healthcare policies to address socioeconomic and regional inequalities in breast cancer management. Additionally, Investigating breast cancer in perimenopausal populations hold transformative potential, bridging biomedical science with societal imperatives. The research paradigm extends beyond clinical outcomes to intersect with health economics of aging populations, ethical AI applications in menopausal care, and structural determinants of women's health equity, demanding cross-sectoral policy integration.

Declarations

Ethics approval and consent to participate

This study was exempted from institutional review board review because it analyzed only publicly available, de-identified datasets.

Consent for publication

Not applicable.

Availability of data and materials

No datasets were generated or analysed during the current study.

Competing Interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Authors' contributions

Xia Wang—formal analysis, methodology, resources, software, writing-original draft; Rui Yang: conceptualization, methodology, funding acquisition, visualization, writing-original draft, writing-review & editing; Chaofei Shen, Xiang Xu—data curation—funding acquisition; Siang Lv; conceptualisation; Fangjun Chen: investigation, methodology, validation; Jun Wu—conceptualisation—funding acquisition—project administration—supervision.

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Tables

Tables 1 to 3 are available in the supplementary files section

Figures

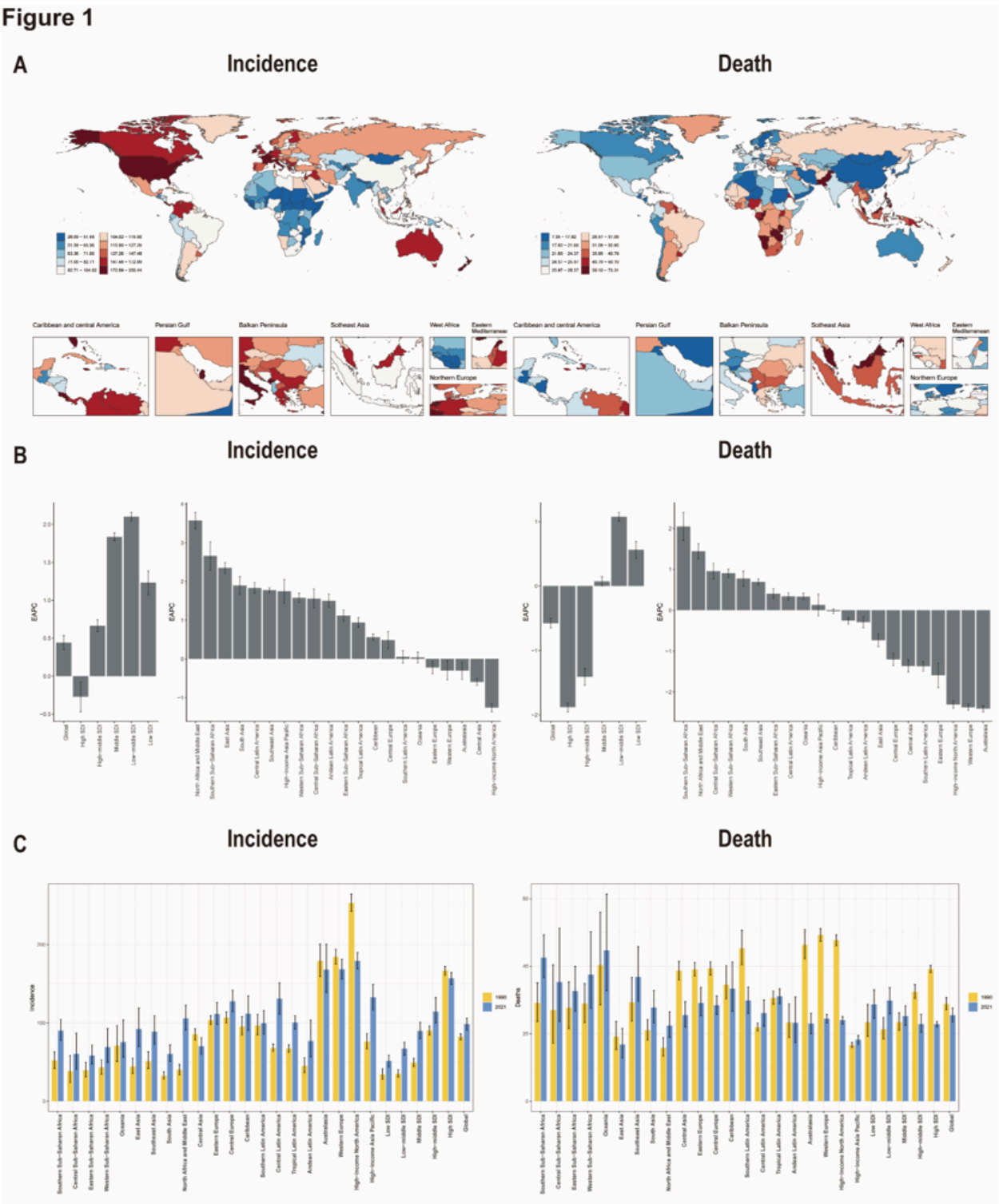


Figure 1

The global burden distribution of breast cancer in perimenopausal women through three panels: (A) Heatmaps displaying EAPCs for incidence (left) and mortality (right) worldwide; (B) Bar plots visualizing the same EAPC data; (C) Comparative bar charts showing ASRs for incidence (left) and mortality (right) across 21 regions in 1990 versus 2021.

Figure 2

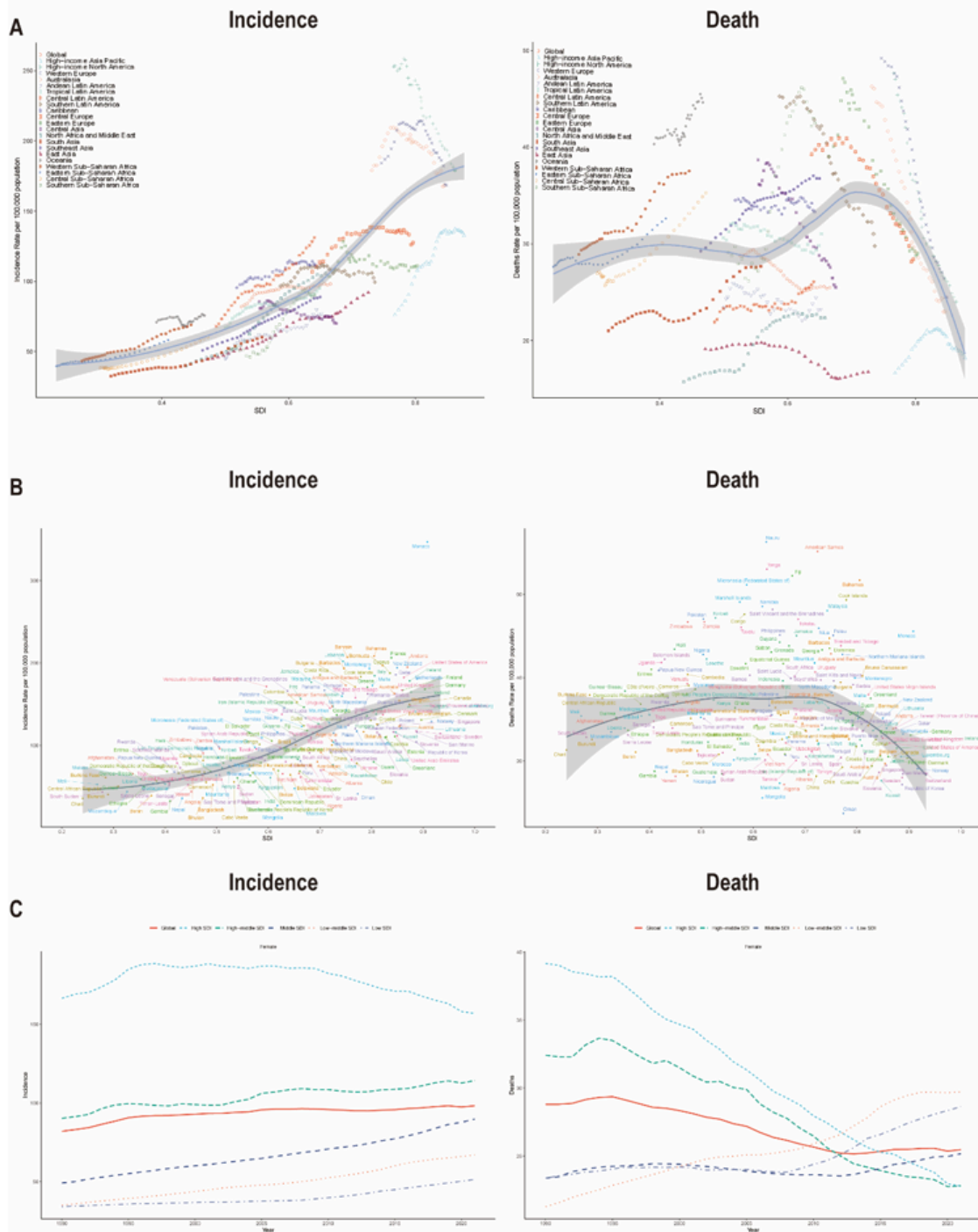


Figure 2

SDI-related disease burden patterns: (A) SDI correlations with incidence(left) and mortality (right) across 27 GBD regions; (B) The Country-level (204 nations) of incidence(left) and mortality (right)-SDI relationships in 2021; (C) Time trends (1990-2021) of incidence(left) and mortality (right) by SDI region.

Figure 3

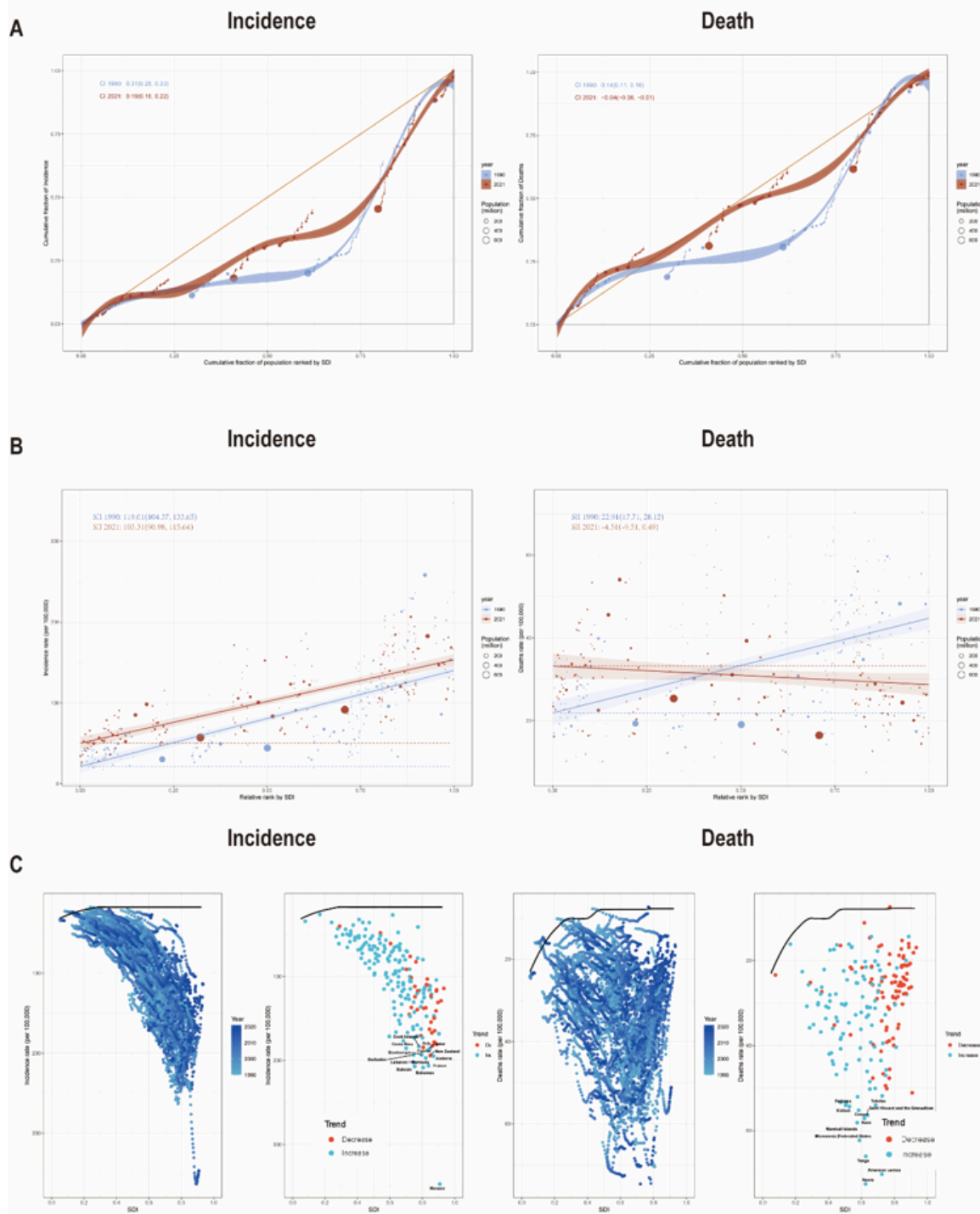


Figure 3

Global inequalities in breast cancer burden among perimenopausal women (1990-2021). Health inequality metrics through regression (A) and concentration curves (B) for incidence (left) and mortality (right) rates. (C) Frontier analysis of SDI relationships, in which temporal evolution is color-graded with light blue (1990) and dark blue (2021). The efficiency frontier for incidence and mortality rates is demarcated by a solid black line, with individual countries/territories plotted as colored data points.

(left) and mortality (right) rates; (C) Bar charts quantify the relative contributions of demographic shifts, epidemiological changes, and population growth to global incidence (left) and mortality (right) trends through decomposition analysis.

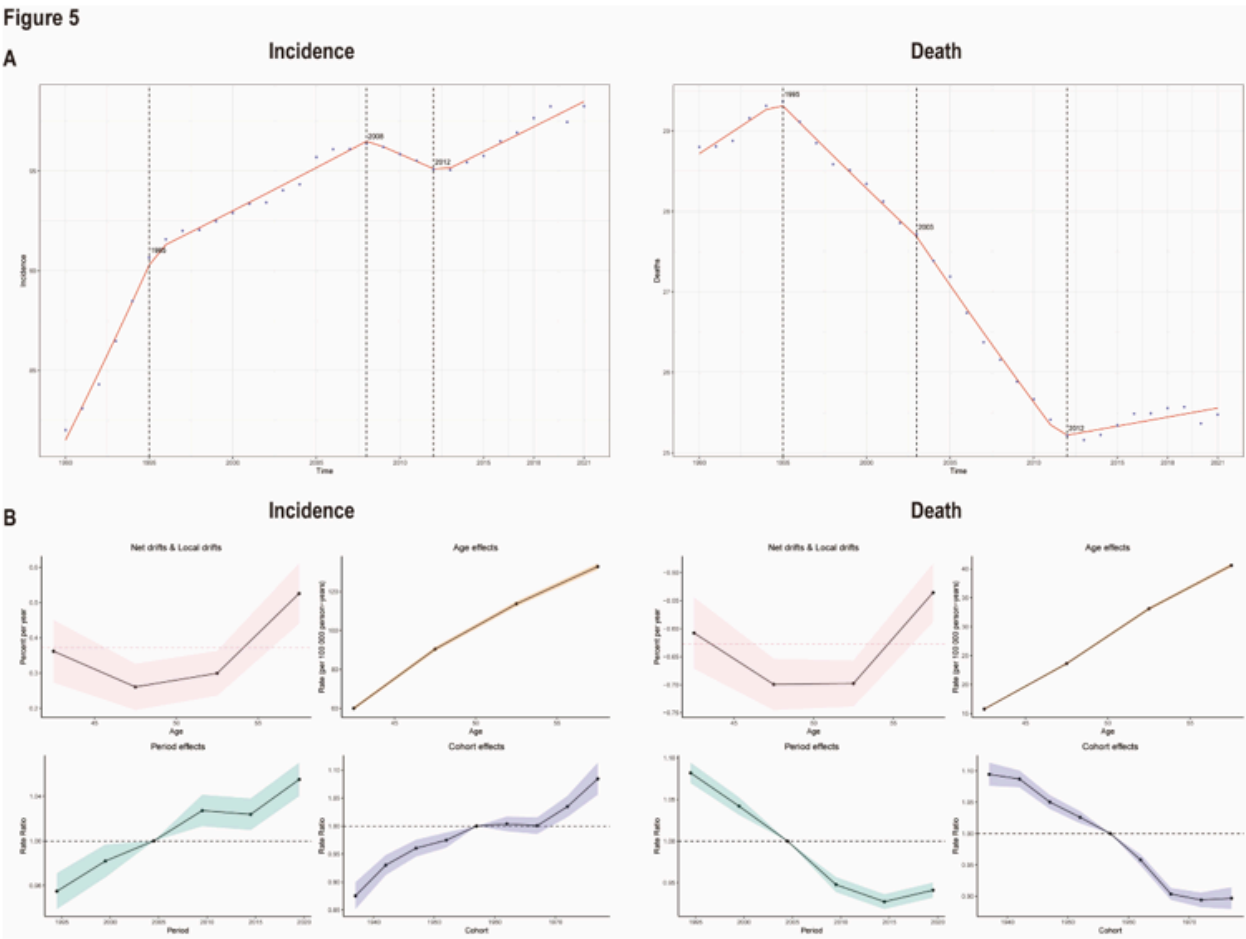


Figure 5

Joinpoint regression and Age-Period-Cohort modeling to evaluate temporal patterns in breast cancer burden among perimenopausal women. (A) Temporal trend plots showing AAPC trajectories for incidence (left panel) and mortality (right panel) between 1990-2021; (B) APC decomposition with: (i) Net/local drift values >0 signaling burden escalation (upper left), (ii) Age-specific effect curves (upper right), and (iii) Period/cohort rate ratios >1 indicating elevated risk (lower panel).

Figure 6

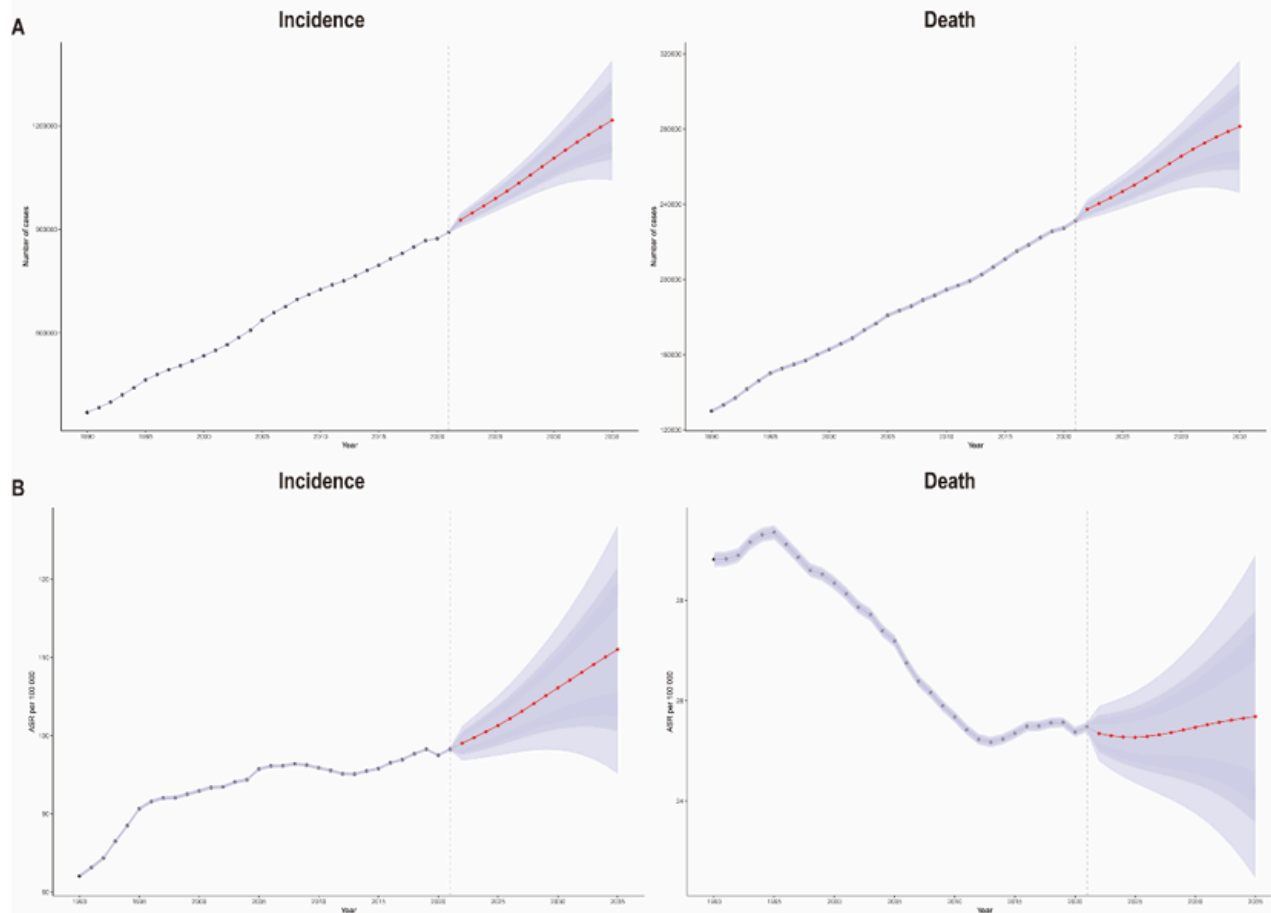


Figure 6

Future trajectories of breast cancer burden in perimenopausal populations (A) Age-standardized rate (ASR) projections for incidence (left) and mortality (right); (B) Absolute case number estimations for incidence (left) and mortality (right).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryFigure.docx](#)
- [Table11.28.xlsx](#)