

Rising Global Burden of Alcohol-Attributable Breast Cancer in Women: Regional Inequalities and Temporal Trends

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Purpose: Breast cancer is the most common malignancy and a leading cause of death among women of reproductive age. Although high alcohol consumption is a known modifiable risk factor, its global and regional impact on breast cancer mortality and disability-adjusted life years (DALYs) remains insufficiently characterized.

Patients and Methods: Data on alcohol-attributable breast cancer mortality and DALYs among women aged 15–49 years were extracted across 204 countries and territories from 1990 to 2021. Temporal trends were assessed using estimated annual percentage changes (EAPC). Correlations with the sociodemographic index (SDI) were examined, and projections to 2050 were modeled to estimate future patterns.

Results: Globally, alcohol-attributable breast cancer mortality declined from 0.27 to 0.17 per 100,000 (EAPC -1.79%), and DALYs from 14.00 to 9.02 per 100,000 (EAPC -1.71%). Women aged 45–49 had the highest mortality, though rates fell significantly (EAPC -2.71%). High-SDI regions, especially Western Europe, North America, and Australasia, saw marked reductions. In contrast, low- and middle-SDI regions experienced sharp increases, with mortality rising over 300% in low-middle SDI areas and South Asia (EAPC $+2.57\%$ and $+2.87\%$, respectively). The United States, Brazil, and China recorded the highest national rates, while Gulf States had the lowest. Mortality and DALY rates correlated positively with SDI ($\rho = 0.709$ and 0.719). Projections suggest continued declines in high-SDI areas but worsening trends in low-SDI settings by 2050.

Conclusion: Despite global progress, rising alcohol-attributable breast cancer burdens in less developed regions underscore the need for targeted prevention and alcohol control efforts.

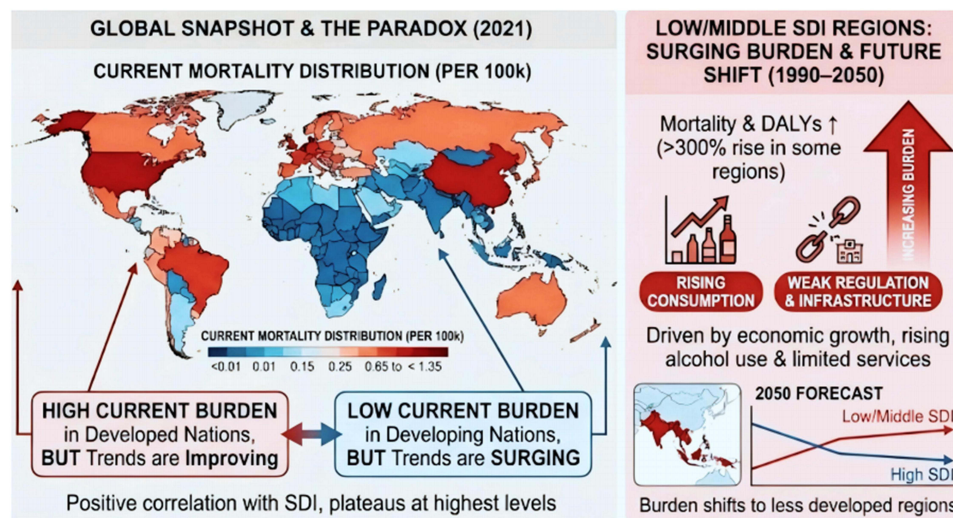
Keywords: breast cancer, alcohol consumption, disability-adjusted life years, global burden of disease, sociodemographic index

Introduction

Breast cancer is the most frequently diagnosed malignancy and a leading cause of cancer-related mortality among women worldwide, with an estimated 2.3 million new cases and 685,000 deaths in 2020 alone, according to GLOBOCAN data.¹ Among women of reproductive age, breast cancer presents a particular public health challenge, as it affects women at the peak of their social and economic contributions.² Despite notable advances in screening and treatment, substantial disparities remain in breast cancer mortality across countries and regions, reflecting differences in healthcare access, risk factor prevalence, and the effectiveness of prevention strategies.³

High alcohol consumption is an established modifiable risk factor for breast cancer, classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC).⁴ Multiple large-scale cohort studies and meta-analyses have demonstrated a dose-dependent relationship between alcohol intake and breast cancer incidence, with no level of consumption considered completely safe.^{5–8} Proposed biological mechanisms include alcohol-induced increases in circulating estrogen levels, generation of acetaldehyde leading to DNA damage, and enhanced oxidative stress.^{9,10} While the role of alcohol in breast cancer incidence is well studied, fewer investigations have quantified its contribution to breast cancer mortality and

Graphical Abstract



disability-adjusted life years (DALYs), particularly at global and national scales. Existing analyses from the Global Burden of Disease (GBD) Study have reported substantial geographic variation in alcohol-attributable cancer burden, yet they largely focus on the overall population and do not provide a comprehensive assessment of breast cancer mortality and DALYs attributable to alcohol use specifically among women of reproductive age.¹¹

To address this gap, the present study aims to provide a systematic analysis of trends in breast cancer mortality and DALYs attributable to high alcohol use among women aged 15–49 years at global, regional, and national levels between 1990 and 2021. By leveraging data from the GBD 2021 study, this work seeks to enhance understanding of temporal and geographic patterns in alcohol-attributable breast cancer burden. It further aims to support the development of targeted public health interventions and alcohol control policies to reduce breast cancer burden in this vulnerable population. In addition, the findings are intended to inform gender- and age-specific cancer prevention strategies.

Materials and Methods

Data Source

This study used data from the GBD, coordinated by the Institute for Health Metrics and Evaluation (IHME).¹² GBD 2021 provides standardized estimates of mortality, disability-adjusted life years (DALYs), and risk factor burdens for 204 countries and territories from 1990 to 2021, using data from vital registration systems, cancer registries, verbal autopsy studies, and household surveys.¹³ We extracted data on breast cancer mortality and DALYs attributable to high alcohol use among females aged 15–49 years, disaggregated into seven age groups (15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49 years), across five sociodemographic index (SDI) levels (low, low-middle, middle, high-middle, and high SDI) and 21 GBD-defined geographical regions, using the Global Health Data Exchange (GHDx) GBD Results Tool.

Case Definition

Breast cancer cases were identified using ICD-10 codes C50–C50.629 and C50.8–C50.929 and ICD-9 codes 174–175.9, V10.3, and V16.3.^{13,14} High alcohol use was defined according to the GBD comparative risk assessment framework as any alcohol consumption above the theoretical minimum risk exposure level (TMREL) for cancer outcomes, which is 0 g/day. In this context, “high alcohol use” denotes exposure above the minimum-risk level used to estimate the alcohol-attributable fraction, rather than a clinical threshold for heavy drinking. Alcohol dependence was further classified by ICD-10 codes F10.1 and F10.2 and ICD-9 code 303.90, consistent with DSM-IV criteria (requiring ≥ 3 of 7 diagnostic features within 12

months, including tolerance, withdrawal, use in larger amounts or for longer periods, unsuccessful attempts to cut down, time spent obtaining or recovering from use, abandonment of activities, and continued use despite harm).^{13,14}

Statistical Analysis

Death rates and DALY rates attributable to high alcohol use were calculated using the GBD reference population.^{15,16} Temporal trends were quantified using the estimated annual percentage change (EAPC) derived from a log-linear regression of the rate on calendar year:

$$\ln(\text{rate}_t) = \alpha + \beta \times t + \varepsilon$$

where t denotes calendar year and ε is the error term. The EAPC and its 95% CI were calculated from β as:

$$\text{EAPC} = 100 \times (e^{\beta} - 1)$$

Thus, β represents the annual change in the log rate, and EAPC represents the corresponding percent change in the rate per year. Trends were classified as increasing if the EAPC > 0 and the 95% CI excluded 0 (equivalently $p < 0.05$), decreasing if the EAPC < 0 and the 95% CI excluded 0, and stable otherwise.

To explore associations between alcohol-attributable breast cancer burden and SDI or regional indicators, we performed Spearman's rank correlation analysis, reporting ρ as the correlation coefficient and considering $p < 0.05$ statistically significant.¹⁷ For prediction, we constructed ARIMA models for deaths and DALY rates to forecast trends from 2022 to 2050.^{18–20} ARIMA model parameters (p , d , q) were determined by inspection of autocorrelation function (ACF), partial autocorrelation function (PACF), and minimization of the Akaike Information Criterion (AIC), with model adequacy assessed using residual diagnostics including the Ljung-Box test and residual plots. All analyses and figures were generated using R software with packages including forecast, ggplot2, and dplyr.

Ethics Statement

This study used aggregated, de-identified, publicly available data; thus, ethics approval and informed consent were not required.

Results

Global Trends in Alcohol-Attributable Breast Cancer Mortality and DALYs Among Women of Reproductive Age

From 1990 to 2021, the global burden of breast cancer mortality attributable to high alcohol use among women of reproductive age declined. In 1990, there were an estimated 3649 deaths (95% uncertainty interval [UI] 2748 to 4559), with a mortality rate of 0.27 per 100,000 (95% UI 0.21 to 0.34) (Table 1). By 2021, the number of deaths decreased to 3363 (95% UI 2390 to 4380), with a mortality rate of 0.17 per 100,000 (95% UI 0.12 to 0.22). The percentage change in the number of deaths was -7.85% (95% UI -19.3 to 0.53), and the EAPC in mortality rate was -1.79% (95% confidence interval [CI] -1.90 to -1.68), indicating a significant downward trend (Table 1).

A similar decreasing pattern was observed for DALYs. In 1990, breast cancer attributable to high alcohol use resulted in 187,245 DALYs (95% UI 140,166 to 233,946), with a rate of 14.00 per 100,000 (95% UI 10.48 to 17.49) (Table 2). In 2021, the DALYs decreased to 175,801 (95% UI 125,118 to 228,169), corresponding to a rate of 9.02 per 100,000 (95% UI 6.42 to 11.71). The percentage change in DALYs was -6.11% (95% UI -17.32 to 2.62), and the EAPC in DALY rate was -1.71% (95% CI -1.82 to -1.61), confirming a sustained global decline in the burden among women of reproductive age (Table 2).

Age-Specific Patterns of Alcohol-Attributable Breast Cancer Burden

Between 1990 and 2021, the burden of breast cancer mortality attributable to high alcohol use varied distinctly across different age groups among women of reproductive age. Overall, older age groups experienced a significantly higher mortality burden compared to younger age groups. Specifically, women aged 45–49 years consistently had the highest

Table 1 Global and Regional Deaths and Trends of Breast Cancer Attributable to High Alcohol Use Among Women of Reproductive Age From 1990 to 2021

Feature	Cases_1990	Rates_1990	Cases_2021	Rates_2021	Cases_change	EAPC_CI
Global	3649 (2748 to 4559)	0.27 (0.21 to 0.34)	3363 (2390 to 4380)	0.17 (0.12 to 0.22)	-7.85 (-19.3 to 0.53)	-1.79 (-1.9 to -1.68)
Age group						
15-19 years	5 (4 to 6)	0.0019 (0.0015 to 0.0025)	6 (4 to 7)	0.0018 (0.0012 to 0.0024)	9.02 (-14.89 to 34.07)	-0.41 (-0.57 to -0.25)
20-24 years	21 (16 to 25)	0.01 (0.01 to 0.01)	26 (18 to 34)	0.01 (0.01 to 0.01)	24.93 (-2.53 to 55.76)	-0.06 (-0.22 to 0.11)
25-29 years	92 (70 to 116)	0.04 (0.03 to 0.05)	92 (63 to 121)	0.03 (0.02 to 0.04)	-0.17 (-20.21 to 16.06)	-0.84 (-1.01 to -0.66)
30-34 years	319 (239 to 402)	0.17 (0.13 to 0.21)	290 (201 to 382)	0.1 (0.07 to 0.13)	-9.22 (-23.54 to 3.82)	-1.79 (-2.02 to -1.56)
35-39 years	682 (513 to 861)	0.39 (0.3 to 0.5)	588 (409 to 785)	0.21 (0.15 to 0.28)	-13.74 (-26.19 to -1.76)	-2.23 (-2.48 to -1.98)
40-44 years	1120 (831 to 1407)	0.8 (0.59 to 1)	961 (676 to 1269)	0.39 (0.27 to 0.51)	-14.22 (-26.32 to -4.27)	-2.64 (-2.79 to -2.49)
45-49 years	1410 (1020 to 1800)	1.24 (0.9 to 1.58)	1401 (985 to 1839)	0.59 (0.42 to 0.78)	-0.67 (-13.4 to 9.76)	-2.71 (-2.87 to -2.56)
SDI regions						
High SDI	2055 (1523 to 2588)	0.91 (0.67 to 1.14)	1248 (889 to 1587)	0.51 (0.37 to 0.65)	-39.3 (-46.18 to -34.34)	-2.04 (-2.15 to -1.94)
High-middle SDI	1117 (829 to 1392)	0.4 (0.3 to 0.5)	796 (548 to 1052)	0.26 (0.18 to 0.34)	-28.71 (-38.01 to -19.72)	-1.84 (-2.04 to -1.65)
Middle SDI	305 (195 to 423)	0.07 (0.04 to 0.09)	671 (464 to 902)	0.11 (0.08 to 0.15)	119.85 (86.99 to 175.77)	1.32 (1.24 to 1.4)
Low-middle SDI	91 (44 to 131)	0.03 (0.02 to 0.05)	367 (230 to 524)	0.07 (0.05 to 0.1)	304.75 (216.72 to 499.27)	2.57 (2.53 to 2.6)
Low SDI	76 (19 to 120)	0.07 (0.02 to 0.11)	277 (134 to 406)	0.1 (0.05 to 0.15)	263.67 (143.69 to 844.87)	1.11 (0.85 to 1.37)
Geographical regions						
Andean Latin America	15 (2 to 25)	0.16 (0.02 to 0.27)	39 (22 to 64)	0.22 (0.12 to 0.37)	154.18 (58.93 to 1648.79)	1.07 (0.94 to 1.19)
Australasia	70 (55 to 87)	1.31 (1.03 to 1.62)	52 (38 to 67)	0.72 (0.53 to 0.93)	-26.19 (-38.66 to -12.51)	-2.12 (-2.25 to -1.98)
Caribbean	20 (12 to 29)	0.21 (0.13 to 0.31)	32 (19 to 50)	0.27 (0.16 to 0.42)	63.31 (25.03 to 106.15)	0.88 (0.77 to 0.99)
Central Asia	36 (22 to 52)	0.21 (0.13 to 0.31)	32 (19 to 47)	0.13 (0.08 to 0.19)	-9.4 (-34.32 to 20.64)	-1.63 (-1.93 to -1.33)
Central Europe	192 (130 to 256)	0.63 (0.42 to 0.83)	138 (91 to 189)	0.54 (0.35 to 0.73)	-28.03 (-39.94 to -13.82)	-0.91 (-1.13 to -0.7)
Central Latin America	46 (27 to 68)	0.11 (0.07 to 0.16)	93 (56 to 143)	0.14 (0.08 to 0.21)	103.11 (55.86 to 169.12)	0.3 (0.14 to 0.45)
Central Sub-Saharan Africa	16 (1 to 29)	0.13 (0.01 to 0.24)	62 (9 to 102)	0.19 (0.03 to 0.31)	291.54 (131.31 to 1991.98)	1.66 (1.15 to 2.18)
East Asia	157 (86 to 244)	0.05 (0.03 to 0.07)	199 (105 to 323)	0.06 (0.03 to 0.1)	26.88 (-23.03 to 112.2)	0.59 (0.32 to 0.86)
Eastern Europe	444 (316 to 569)	0.8 (0.57 to 1.03)	309 (194 to 431)	0.64 (0.4 to 0.89)	-30.38 (-46.9 to -14.4)	-1.53 (-2.02 to -1.04)
Eastern Sub-Saharan Africa	44 (5 to 75)	0.1 (0.01 to 0.17)	173 (74 to 262)	0.16 (0.07 to 0.24)	290.19 (133.97 to 2575.21)	1.16 (0.87 to 1.44)
High-income Asia Pacific	234 (172 to 301)	0.51 (0.38 to 0.66)	204 (141 to 267)	0.54 (0.37 to 0.7)	-12.72 (-27.79 to 6.31)	-0.05 (-0.23 to 0.14)
High-income North America	671 (471 to 876)	0.9 (0.63 to 1.18)	422 (282 to 571)	0.5 (0.34 to 0.68)	-37.14 (-49.41 to -26.49)	-2.06 (-2.16 to -1.95)
North Africa and Middle East	4 (3 to 7)	0.01 (0 to 0.01)	15 (9 to 23)	0.01 (0.01 to 0.01)	236.35 (133.47 to 384.41)	2.24 (1.85 to 2.64)
Oceania	1 (0 to 1)	0.04 (0.02 to 0.08)	2 (1 to 3)	0.05 (0.02 to 0.09)	169.18 (70.93 to 395.01)	0.93 (0.58 to 1.28)
South Asia	29 (4 to 48)	0.01 (0 to 0.02)	128 (67 to 204)	0.03 (0.01 to 0.04)	343.56 (152.29 to 2683.89)	2.87 (2.69 to 3.06)
Southeast Asia	55 (18 to 81)	0.05 (0.02 to 0.07)	187 (112 to 274)	0.1 (0.06 to 0.15)	237.27 (146.91 to 672.52)	2.62 (2.56 to 2.67)
Southern Latin America	113 (83 to 147)	0.91 (0.67 to 1.18)	103 (72 to 137)	0.59 (0.41 to 0.78)	-8.5 (-25.37 to 16.83)	-1.28 (-1.45 to -1.11)
Southern Sub-Saharan Africa	37 (15 to 51)	0.28 (0.11 to 0.38)	69 (39 to 97)	0.32 (0.18 to 0.45)	84.98 (35.35 to 166.19)	0.6 (0.3 to 0.9)
Tropical Latin America	83 (53 to 118)	0.21 (0.13 to 0.3)	226 (153 to 307)	0.37 (0.25 to 0.51)	172.14 (108.79 to 256.44)	1.52 (1.28 to 1.77)
Western Europe	1329 (994 to 1666)	1.39 (1.04 to 1.74)	661 (458 to 862)	0.71 (0.49 to 0.93)	-50.22 (-57.47 to -44.11)	-2.26 (-2.38 to -2.14)
Western Sub-Saharan Africa	53 (25 to 81)	0.12 (0.06 to 0.19)	216 (123 to 331)	0.18 (0.1 to 0.28)	305.96 (161.64 to 705.98)	1.28 (1.23 to 1.34)

Table 2 Global and Regional DALYs and Trends of Breast Cancer Attributable to High Alcohol Use Among Women of Reproductive Age From 1990 to 2021

Feature	Cases_1990	Rates_1990	Cases_2021	Rates_2021	Cases_change	EAPC_CI
Global	187245 (140166 to 233946)	14 (10.48 to 17.49)	175801 (125118 to 228169)	9.02 (6.42 to 11.71)	-6.11 (-17.32 to 2.62)	-1.71 (-1.82 to -1.61)
Age group						
15-19 years	388 (297 to 486)	0.15 (0.12 to 0.19)	424 (299 to 567)	0.14 (0.1 to 0.19)	9.38 (-14.23 to 33.74)	-0.4 (-0.55 to -0.25)
20-24 years	1465 (1122 to 1814)	0.6 (0.46 to 0.74)	1840 (1278 to 2445)	0.63 (0.43 to 0.83)	25.6 (-1.38 to 55.99)	-0.04 (-0.2 to 0.12)
25-29 years	6203 (4730 to 7708)	2.82 (2.15 to 3.5)	6271 (4332 to 8187)	2.16 (1.49 to 2.81)	1.09 (-18.56 to 17.31)	-0.79 (-0.96 to -0.62)
30-34 years	19517 (14588 to 24780)	10.27 (7.67 to 13.03)	18001 (12681 to 23751)	6.02 (4.24 to 7.95)	-7.77 (-22.06 to 5.54)	-1.74 (-1.96 to -1.51)
35-39 years	38055 (28376 to 48402)	21.94 (16.36 to 27.9)	33373 (23045 to 44438)	12.01 (8.3 to 16)	-12.3 (-25.02 to -0.23)	-2.17 (-2.41 to -1.93)
40-44 years	57171 (42360 to 71841)	40.77 (30.21 to 51.23)	50064 (35160 to 65362)	20.18 (14.17 to 26.35)	-12.43 (-24.03 to -2.37)	-2.56 (-2.7 to -2.42)
45-49 years	64446 (46346 to 81687)	56.63 (40.73 to 71.78)	65828 (46072 to 86328)	27.94 (19.55 to 36.63)	2.14 (-10.5 to 13.07)	-2.62 (-2.77 to -2.46)
SDI regions						
High SDI	106273 (79066 to 133654)	46.88 (34.88 to 58.95)	67276 (47818 to 87108)	27.67 (19.67 to 35.82)	-36.7 (-43.55 to -31.38)	-1.9 (-2 to -1.8)
High-middle SDI	56696 (42078 to 70417)	20.41 (15.15 to 25.35)	41167 (28392 to 54164)	13.49 (9.3 to 17.75)	-27.39 (-36.94 to -18.25)	-1.76 (-1.93 to -1.59)
Middle SDI	15594 (9936 to 21346)	3.49 (2.22 to 4.77)	34364 (23669 to 46106)	5.56 (3.83 to 7.45)	120.37 (88.74 to 176.98)	1.31 (1.23 to 1.4)
Low-middle SDI	4584 (2182 to 6608)	1.68 (0.8 to 2.42)	18640 (11565 to 26522)	3.68 (2.28 to 5.24)	306.62 (217.23 to 505.74)	2.57 (2.54 to 2.61)
Low SDI	3845 (936 to 6035)	3.44 (0.84 to 5.4)	14137 (6824 to 20790)	5.15 (2.49 to 7.58)	267.7 (145.03 to 882.89)	1.14 (0.88 to 1.4)
Geographical regions						
Andean Latin America	782 (115 to 1281)	8.25 (1.21 to 13.5)	2013 (1115 to 3251)	11.53 (6.39 to 18.63)	157.25 (60.18 to 1719.09)	1.12 (0.99 to 1.25)
Australasia	3614 (2863 to 4460)	67.34 (53.34 to 83.1)	2799 (2043 to 3630)	38.77 (28.31 to 50.28)	-22.56 (-35.08 to -8.8)	-1.95 (-2.08 to -1.82)
Caribbean	1022 (623 to 1466)	10.96 (6.68 to 15.73)	1654 (987 to 2541)	13.75 (8.21 to 21.13)	61.9 (24.12 to 104.47)	0.83 (0.72 to 0.94)
Central Asia	1837 (1121 to 2668)	10.95 (6.68 to 15.9)	1641 (984 to 2373)	6.76 (4.05 to 9.78)	-10.68 (-35.22 to 18.1)	-1.68 (-1.94 to -1.41)
Central Europe	9636 (6521 to 12724)	31.38 (21.23 to 41.43)	7081 (4651 to 9673)	27.5 (18.06 to 37.56)	-26.52 (-38.37 to -12.48)	-0.79 (-0.99 to -0.58)
Central Latin America	2423 (1450 to 3582)	5.78 (3.46 to 8.55)	4955 (3047 to 7499)	7.27 (4.47 to 11)	104.55 (58.98 to 169.13)	0.33 (0.17 to 0.49)
Central Sub-Saharan Africa	797 (50 to 1481)	6.45 (0.4 to 11.98)	3132 (448 to 5151)	9.59 (1.37 to 15.77)	292.75 (133.57 to 2010.26)	1.66 (1.15 to 2.18)
East Asia	7975 (4392 to 12469)	2.39 (1.32 to 3.74)	10381 (5597 to 16899)	3.14 (1.69 to 5.11)	30.17 (-19.65 to 117.36)	0.67 (0.4 to 0.95)
Eastern Europe	22457 (15980 to 28463)	40.61 (28.9 to 51.48)	15746 (9898 to 21800)	32.64 (20.52 to 45.19)	-29.88 (-46.65 to -13.81)	-1.47 (-1.92 to -1.03)
Eastern Sub-Saharan Africa	2263 (255 to 3816)	5.24 (0.59 to 8.84)	8928 (3642 to 13653)	8.34 (3.4 to 12.75)	294.54 (135.6 to 2704.74)	1.19 (0.91 to 1.47)
High-income Asia Pacific	12265 (8982 to 15715)	26.81 (19.64 to 34.36)	11011 (7653 to 14445)	28.95 (20.12 to 37.97)	-10.22 (-26.03 to 8.81)	0.09 (-0.1 to 0.28)
High-income North America	35645 (25304 to 46393)	47.93 (34.03 to 62.38)	23072 (15583 to 31316)	27.46 (18.55 to 37.27)	-35.27 (-47.67 to -24.64)	-1.96 (-2.07 to -1.85)
North Africa and Middle East	224 (129 to 347)	0.29 (0.17 to 0.44)	780 (475 to 1234)	0.49 (0.3 to 0.77)	248.73 (145.67 to 405.32)	2.4 (2 to 2.81)
Oceania	35 (12 to 61)	2.26 (0.77 to 3.93)	94 (40 to 159)	2.7 (1.16 to 4.59)	166.22 (71.09 to 394.43)	0.87 (0.52 to 1.22)
South Asia	1446 (216 to 2401)	0.57 (0.08 to 0.94)	6483 (3491 to 10246)	1.31 (0.71 to 2.07)	348.46 (160.83 to 2609.75)	2.91 (2.74 to 3.08)
Southeast Asia	2784 (897 to 4084)	2.32 (0.75 to 3.4)	9370 (5618 to 13835)	5.11 (3.07 to 7.55)	236.57 (149.31 to 668.38)	2.59 (2.54 to 2.65)
Southern Latin America	5620 (4155 to 7297)	45.35 (33.53 to 58.88)	5288 (3715 to 6945)	30.34 (21.31 to 39.85)	-5.91 (-22.43 to 19.81)	-1.18 (-1.35 to -1)
Southern Sub-Saharan Africa	1923 (719 to 2587)	14.46 (5.41 to 19.46)	3487 (1958 to 4903)	16.06 (9.02 to 22.58)	81.37 (33.22 to 165.23)	0.5 (0.19 to 0.81)
Tropical Latin America	4241 (2713 to 6007)	10.63 (6.8 to 15.06)	11656 (8001 to 15746)	19.23 (13.2 to 25.98)	174.85 (112.33 to 260.54)	1.56 (1.33 to 1.8)
Western Europe	67606 (50929 to 85003)	70.76 (53.3 to 88.96)	35360 (24294 to 46139)	37.95 (26.07 to 49.52)	-47.7 (-55.52 to -41.19)	-2.1 (-2.23 to -1.98)
Western Sub-Saharan Africa	2651 (1212 to 4071)	6.08 (2.78 to 9.34)	10870 (6223 to 16875)	9.07 (5.19 to 14.08)	310.05 (165.69 to 733.64)	1.3 (1.24 to 1.35)

number of deaths, from 1410 (95% UI 1020 to 1800) in 1990 to 1401 (95% UI 985 to 1839) in 2021 (Figure 1A and Table 1). However, their mortality rate decreased substantially, from 1.24 per 100,000 (95% UI 0.90 to 1.58) to 0.59 per 100,000 (95% UI 0.42 to 0.78), with an EAPC of -2.71% (95% CI -2.87 to -2.56) (Figure 1B, C and Table 1). A similarly decreasing trend was observed among women aged 40–44 years, with an EAPC of -2.64% (95% CI -2.79 to -2.49). Smaller declines were seen among the younger groups (30–39 years), while women aged 15–19 and 20–24 years had stable trends with minimal changes in mortality rates (Figure 1B, C and Table 1).

Age-specific patterns of DALYs were broadly consistent with mortality. The greatest DALY burden occurred in older reproductive-age women (40–49 years) (Figure 1D and Table 2). Women aged 45–49 years had the highest number of DALYs, increasing slightly from 64,446 (95% UI 46,346 to 81,687) in 1990 to 65,828 (95% UI 46,072 to 86,328) in 2021, yet the DALY rate notably decreased from 56.63 per 100,000 (95% UI 40.73 to 71.78) to 27.94 per 100,000 (95% UI 19.55 to 36.63), corresponding to an EAPC of -2.62% (95% CI -2.77 to -2.46) (Figure 1D and Table 2). A significant reduction was also observed in women aged 40–44 years, with an EAPC of -2.56% (95% CI -2.70 to -2.42) (Figure 1E, F and Table 2). Younger age groups showed modest reductions, with stable or slightly declining DALY rates among women aged below 30 years. Overall, these findings highlight a pronounced age-dependent pattern in the burden of alcohol-attributable breast cancer, with older reproductive-age women bearing the highest burden but also showing the greatest reductions over the study period.

Regional Variations in Alcohol-Attributable Breast Cancer Burden

Significant regional disparities existed in breast cancer mortality and DALYs attributable to high alcohol use among women of reproductive age from 1990 to 2021. Within different SDI regions, trends varied markedly. High and high-middle SDI regions displayed substantial reductions in both mortality and DALYs. Specifically, deaths in high SDI regions decreased from 2055 (95% UI 1523 to 2588) in 1990 to 1248 (95% UI 889 to 1587) in 2021, representing a decrease of 39.3% (95% UI -46.18% to -34.34%), with a significant EAPC of -2.04% (95% CI -2.15 to -1.94) (Figure 2A, B and Table 1). Similarly, DALYs in high SDI regions declined from 106,273 (95% UI 79,066 to 133,654) to 67,276 (95% UI 47,818 to 87,108), a 36.7% reduction (95% UI -43.55% to -31.38%) with an EAPC of -1.90% (95% CI -2.00 to -1.80) (Figure 2C, D and Table 2). Conversely, middle, low-middle, and low SDI regions showed alarming increases. Notably, low-middle SDI regions had a dramatic rise in mortality of 304.75% (95% UI 216.72% to 499.27%)

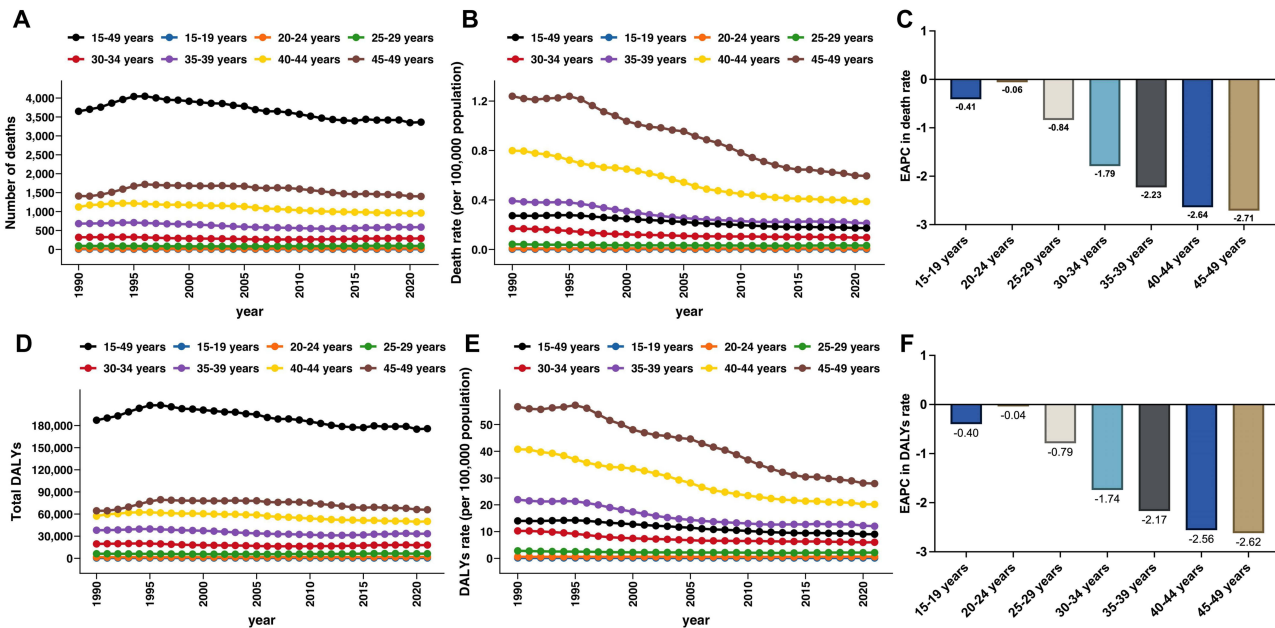


Figure 1 Global trends in breast cancer mortality and DALYs attributable to high alcohol use among women of reproductive age from 1990 to 2021. (A) Number of deaths due to breast cancer attributable to high alcohol use by age group (15–49 years overall and 5-year subgroups). (B) Age-specific death rates (per 100,000 population) over time. (C) EAPC in death rates by age group. (D) Total DALYs due to breast cancer attributable to high alcohol use by age group. (E) Age-specific DALY rates (per 100,000 population) over time. (F) EAPC in DALY rates by age group.

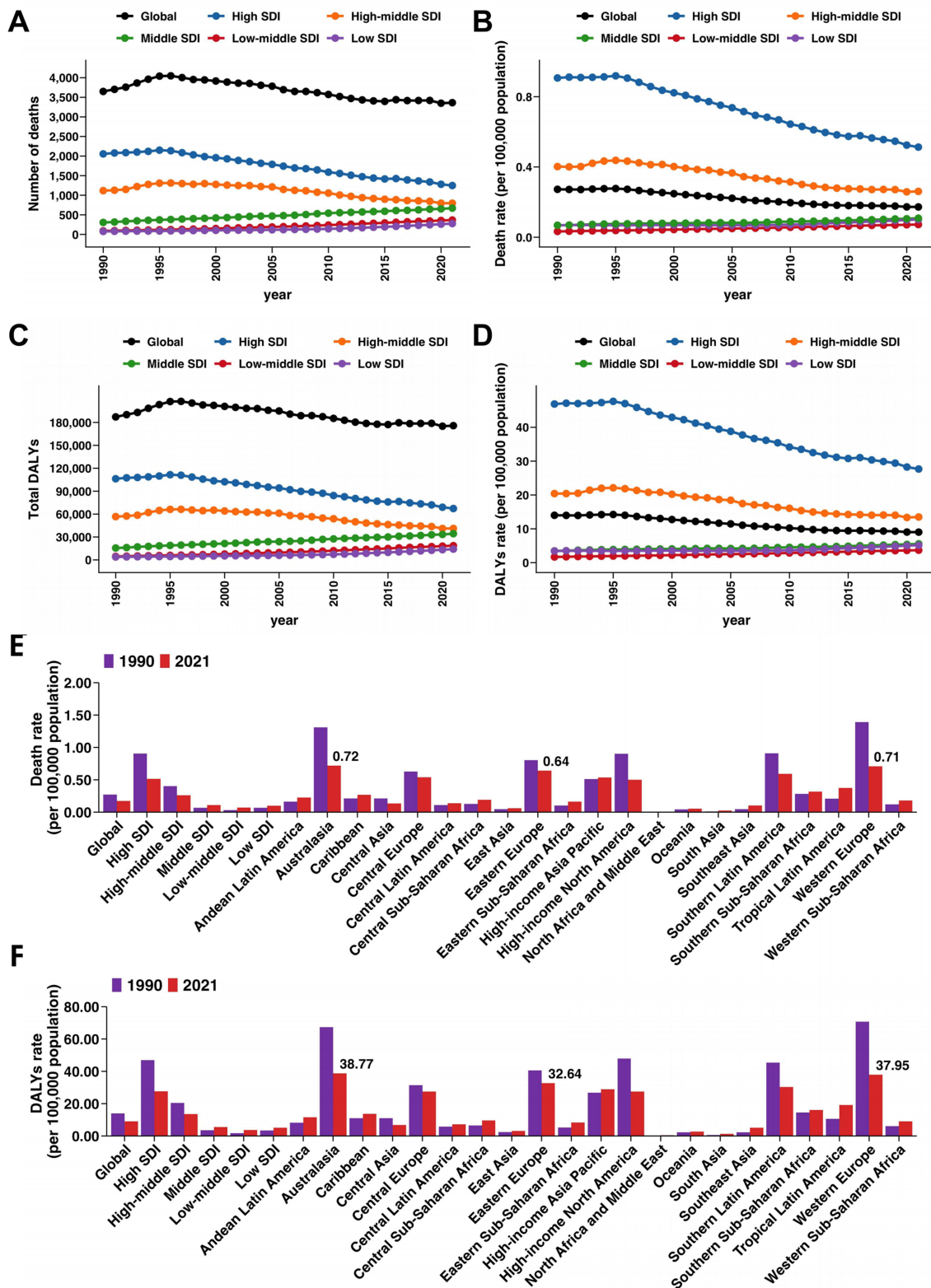


Figure 2 Regional patterns in breast cancer mortality and DALYs attributable to high alcohol use among women of reproductive age. **(A)** Number of deaths attributable to high alcohol use by Socio-demographic Index (SDI) region and globally. **(B)** Death rates (per 100,000 population) over time by SDI region and globally. **(C)** Total DALYs attributable to high alcohol use by SDI region and globally. **(D)** DALYs rate (per 100,000 population) over time by SDI region and globally. **(E)** Comparison of death rates in 1990 and 2021 by global, SDI, and regional levels. **(F)** Comparison of DALYs rate in 1990 and 2021 by global, SDI, and regional levels.

with an EAPC of 2.57% (95% CI 2.53 to 2.60). DALYs in low-middle SDI areas also sharply increased by 306.62% (95% UI 217.23% to 505.74%), and EAPC reached 2.57% (95% CI 2.54 to 2.61) (Tables 1 and 2).

Analysis of geographical regions demonstrated even greater heterogeneity. Western Europe experienced the most substantial decline, with deaths decreasing by 50.22% (95% UI -57.47% to -44.11%) from 1329 (95% UI 994 to 1666) in 1990 to 661 (95% UI 458 to 862) in 2021, and an EAPC of -2.26% (95% CI -2.38 to -2.14) (Figure 2E and Table 1). DALYs similarly decreased by 47.7% (95% UI -55.52% to -41.19%) in Western Europe, representing the most pronounced reduction globally (EAPC -2.10%; 95% CI -2.23 to -1.98) (Figure 2F and Table 2). High-income North America and Australasia also showed substantial decreases in mortality and DALYs. In stark contrast, South Asia recorded the highest increase, with deaths rising dramatically by 343.56% (95% UI 152.29% to 2683.89%) and an exceptionally high EAPC of 2.87% (95% CI 2.69 to 3.06). Southeast Asia similarly exhibited sharp increases in mortality (237.27%, 95% UI 146.91% to 672.52%; EAPC 2.62%, 95% CI 2.56 to 2.67) and DALYs (236.57%, 95% UI 149.31% to 668.38%; EAPC 2.59%, 95% CI 2.54 to 2.65) (Tables 1 and 2). These findings highlight critical regional disparities, underscoring the need for region-specific interventions and public health strategies to address the rising burden in lower-resource regions.

National Patterns of Alcohol-Attributable Breast Cancer Mortality and DALYs

National patterns of alcohol-attributable breast cancer mortality in 2021 revealed enormous global disparities, with age-standardized death rates spanning from virtually zero in nations such as Kuwait and Oman (0.006 per 100 000) and the Maldives (0.007) to a peak of 378.52 per 100 000 in the United States, followed by Brazil (219.57) and China (187.81) (Figure 3A and Supplementary Table S1). Between 1990 and 2021, most high-income countries achieved substantial declines—Denmark reported a -71.8% change in deaths (EAPC -4.29), Finland -60.4% (EAPC -3.37), Italy -58.1% (EAPC -2.67), Germany -54.4% (EAPC -2.50), and the United Kingdom -47.6% (EAPC -2.31)—reflecting the combined impact of stronger alcohol policies and advances in early detection and treatment (Supplementary Table S1). In stark contrast, low- and middle-income countries experienced dramatic increases: Libya's attributable deaths surged by 11183.6% (EAPC 13.99) from a very low baseline, Nepal by 1866.4% (EAPC 10.09), the Solomon Islands by 835.9% (EAPC 8.83), Cambodia by 1376.3% (EAPC 8.63), and Myanmar by 1354.9% (EAPC 9.80). Pakistan (+690.6%, EAPC 6.97), Angola (+665.2%, EAPC 7.71), and Niger (+454.5%, EAPC 6.42) also reported marked rises (Supplementary Table S1). These divergent trends underscore a widening divide: while advanced economies continue to drive down alcohol-related breast cancer mortality, many developing regions confront a rapidly growing burden, highlighting the urgent need for tailored alcohol control measures coupled with strengthened cancer screening and treatment infrastructure in high-growth settings.

Between 1990 and 2021, age-standardized DALY rates for alcohol-attributable breast cancer among reproductive-aged women ranged from near zero in several Gulf States (eg, Kuwait 0.34 per 100 000; Maldives 0.34) to 20718.54 per 100 000 in the United States, followed by 11324.53 in Brazil and 9836.77 in China (Figure 3B and Supplementary Table S2). High-income countries achieved marked reductions: Denmark saw a -69.9% change (EAPC -4.05), Germany -51.5% (EAPC -2.35), Finland -57.6% (EAPC -3.10), Italy -56.7% (EAPC -2.58), and the United Kingdom -45.2% (EAPC -2.15) (Supplementary Table S2). Conversely, low- and middle-income countries experienced dramatic surges, with Libya's DALYs jumping by 10981.8% (EAPC 13.96) from a minimal baseline, Nepal by 1854.2% (EAPC 10.07), the Solomon Islands by 812.3% (EAPC 8.69), Cambodia by 1379.9% (EAPC 8.63), and Myanmar by 1296.7% (EAPC 9.63) (Supplementary Table S2). Pakistan (+712.3%, EAPC 7.07), Angola (+671.1%, EAPC 7.75), and Niger (+450.4%, EAPC 6.42) also recorded substantial rises (Supplementary Table S2). These divergent DALY trends mirror mortality patterns and further underscore the urgent need for strengthened alcohol control policies, early detection programs and treatment capacity, particularly in rapidly industrializing and resource-limited settings.

Correlation of Breast Cancer Burden with SDI and Regional Indicators

A strong positive correlation was observed between SDI and the burden of breast cancer attributable to high alcohol use among women of reproductive age at both regional and national levels. At the regional level, mortality and DALY rates increased with SDI, with Spearman's ρ values of 0.709 ($P < 0.001$) and 0.719 ($P < 0.001$), respectively (Figure 4A and B). The burden was highest in regions with elevated SDI, such as Western Europe, High-income North America, and

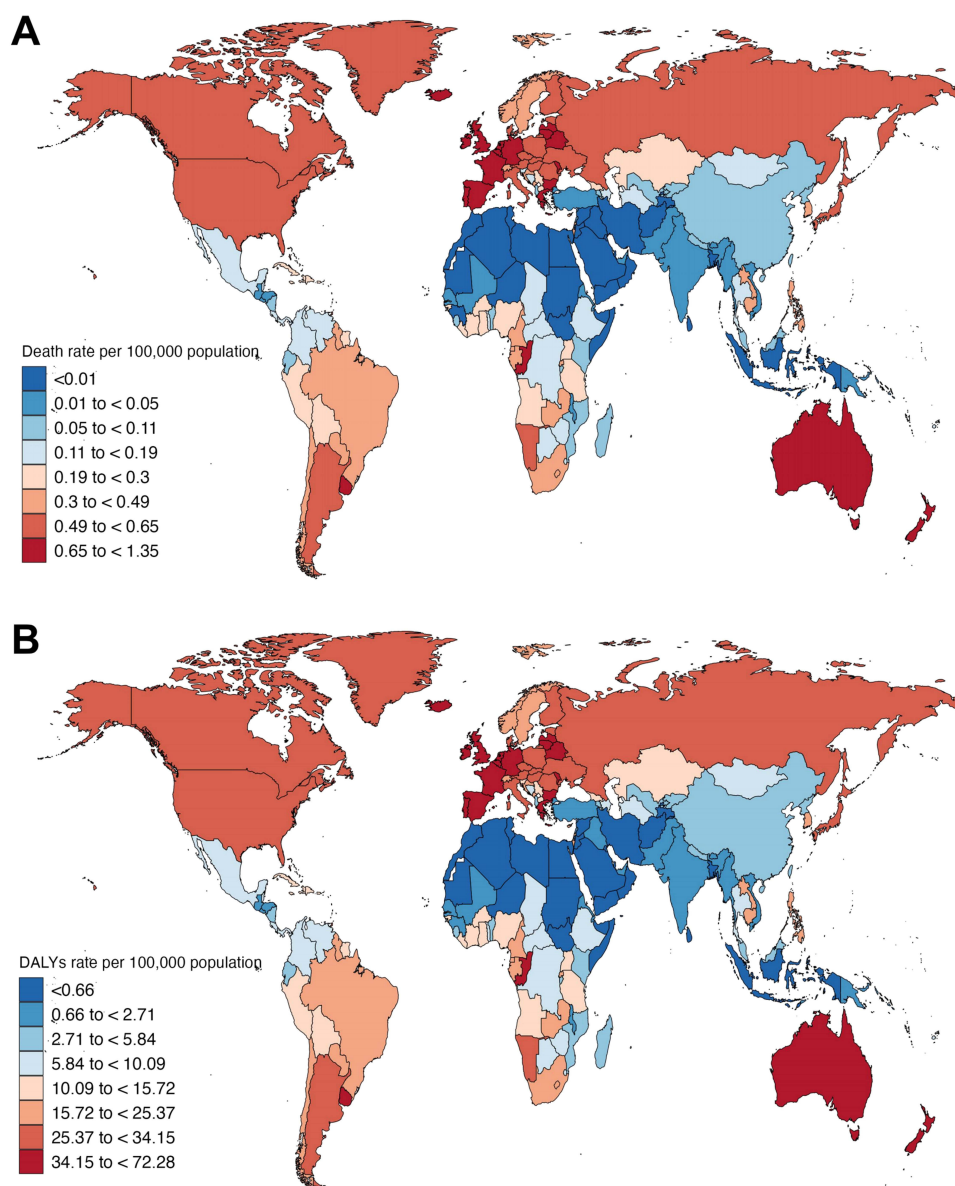


Figure 3 Global distribution of breast cancer mortality and DALYs attributable to high alcohol use among women of reproductive age in 204 countries. **(A)** Breast cancer deaths attributable to high alcohol use among women of reproductive age rates by country in 2021. **(B)** Breast cancer DALYs attributable to high alcohol use among women of reproductive age rates by country in 2021.

Australasia, while Sub-Saharan Africa and South Asia had the lowest rates. The association was non-linear, showing a steep rise in mortality and DALY rates as SDI surpassed 0.6, followed by a plateau or slight decline at the highest SDI levels. At the national level, similar positive correlations were found (mortality: $\rho = 0.553$, $P < 0.001$; DALYs: $\rho = 0.562$, $P < 0.001$), although greater heterogeneity was noted (Figure 4C and D). Countries with high SDI generally bore a heavier burden, yet notable variations existed—for instance, Monaco reported one of the highest burdens despite its very high SDI, while some Eastern European and Latin American countries showed intermediate rates. Conversely, low-SDI countries exhibited a wide range of burdens, suggesting that factors beyond socio-demographic status, such as alcohol consumption patterns, screening programs, and health system capacity, likely influenced the observed disparities.

Predicted Trends in Alcohol-Attributable Breast Cancer Burden, 2022–2050

Using the ARIMA model, we forecasted global and regional trends in breast cancer deaths attributable to high alcohol use among women of reproductive age (15–49 years) from 2022 to 2050. The global number of deaths is projected to

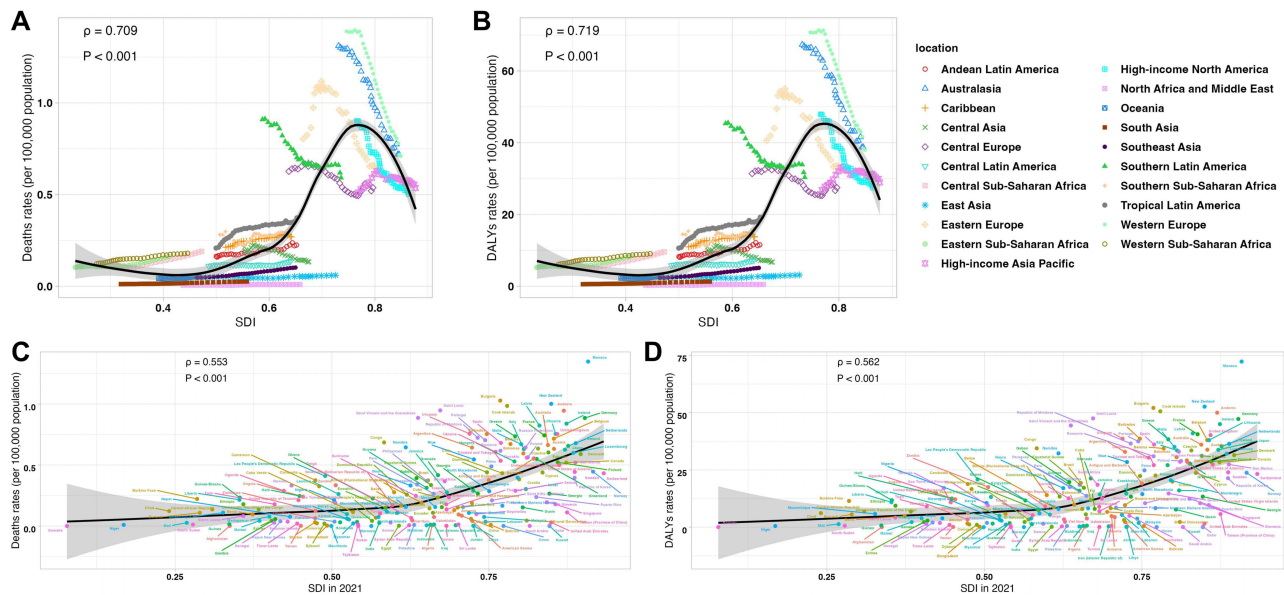


Figure 4 Correlations between breast cancer mortality and DALYs attributable to high alcohol use among women of reproductive age, temporal trends, and socio-demographic development. **(A)** Relationship between deaths and SDI at the regional level. **(B)** Relationship between DALYs and SDI at the regional level. **(C)** Relationship between deaths and SDI at the national level. **(D)** Relationship between DALYs and SDI at the national level.

show a modest overall decline from 3649 in 2021 to 3143 by 2050 ([Supplementary Table S3](#)). However, the 95% uncertainty interval widens substantially over time, ranging from -1386 to 7671 in 2050. It is important to note that negative values in these forecasts do not represent actual negative case counts, which are biologically implausible, but instead reflect the statistical uncertainty inherent in the model projections—especially in contexts where declining trends intersect with wide variability in input data or small case numbers. Across SDI regions, high and high-middle SDI areas are predicted to experience significant reductions in mortality, with deaths decreasing to 161 and 319 respectively by 2050. Conversely, middle, low-middle, and low SDI regions are forecast to see increasing trends, with deaths in these regions projected to rise to 1013, 708, and 715 respectively by 2050, indicating a shift in burden toward less developed regions ([Figure 5A, B](#) and [Supplementary Table S3](#)).

Age- and region-specific predictions highlight persistent inequalities in alcohol-attributable breast cancer mortality. Women aged 45–49 years are expected to continue contributing the largest share of deaths globally, while mortality among younger age groups (under 30 years) will likely remain low and relatively stable over time. Regional analysis indicates that Western Sub-Saharan Africa, Western Europe, and North Africa and the Middle East may bear a disproportionate share of the mortality burden by 2050. In contrast, regions such as Australasia and the Caribbean are predicted to maintain low case numbers ([Figure 5C](#) and [Supplementary Table S3](#)). These findings emphasize the need for targeted, region-specific interventions and sustained public health efforts to address alcohol-related breast cancer mortality, particularly in low-SDI and low-middle SDI settings where the burden is projected to grow.

Discussion

This study provides a comprehensive global and regional assessment of breast cancer mortality and DALYs attributable to high alcohol use among women of reproductive age over the past three decades, with projections extending to 2050. The findings highlight substantial geographic inequalities in the burden, marked by sustained declines in high-income and high-SDI settings and worrying increases in low- and middle-SDI regions. These contrasting trends reflect both the successes of established public health interventions and persistent gaps in global alcohol control and cancer prevention strategies.

In high-SDI countries, including much of Western Europe, North America, and Australasia, reductions in alcohol-attributable breast cancer mortality and DALYs are consistent with strengthened alcohol policies, declines in per capita consumption, and widespread access to early detection and effective treatment.^{21–23} Measures such as taxation,

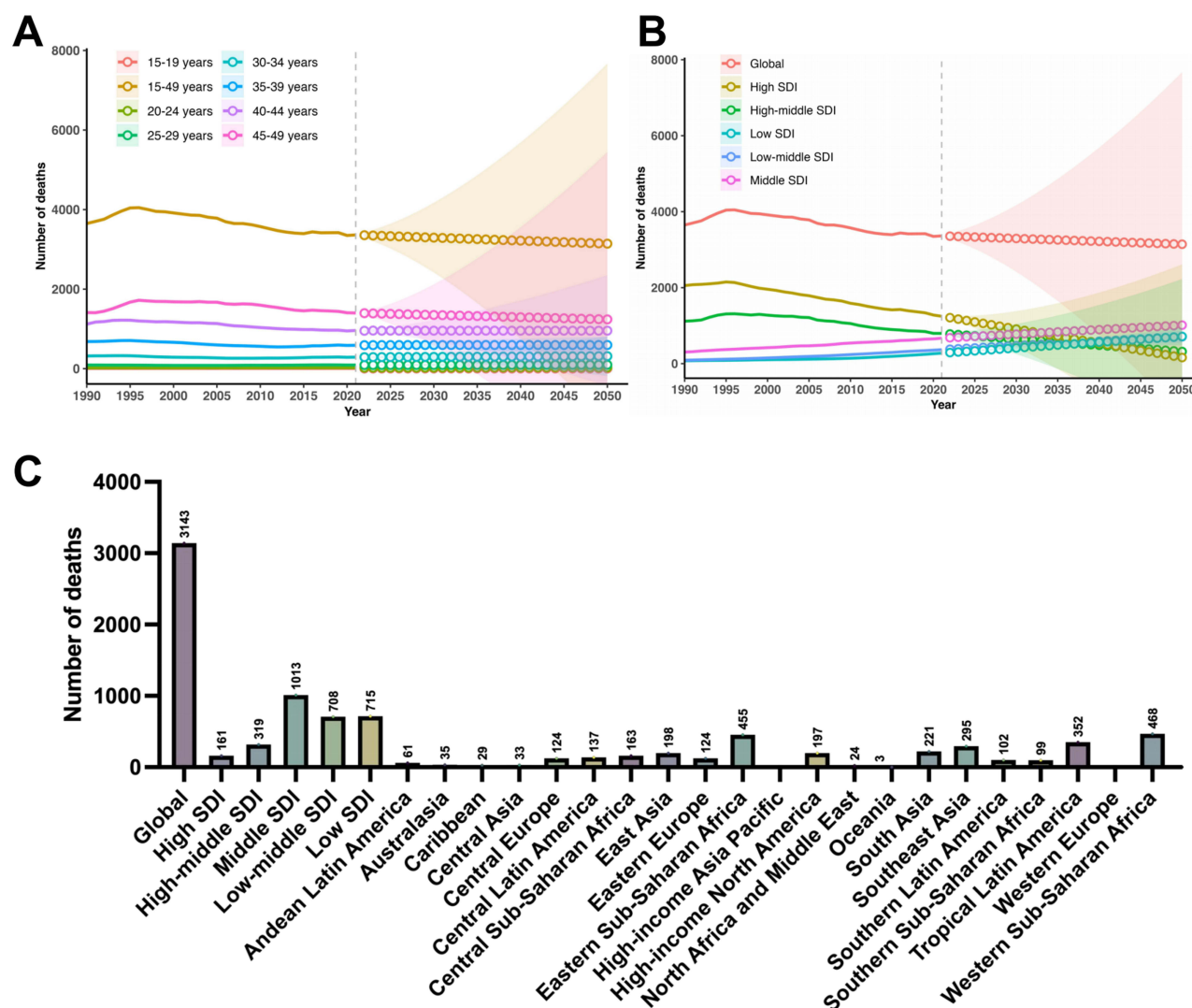


Figure 5 Projected breast cancer deaths attributable to high alcohol use among women of reproductive age (15–49 years) from 1990 to 2050, by age group and region. **(A)** Trends and projections in the number of deaths by 5-year age group. **(B)** Trends and projections in the number of deaths by SDI region. **(C)** Predicted number of deaths in 2050 by global, SDI region, and 21 GBD geographic regions.

restrictions on marketing and availability, and public education campaigns have helped curb harmful drinking patterns.²⁴ Simultaneously, advances in breast cancer screening and treatment—spanning mammography, endocrine therapies, and targeted agents—have improved outcomes.²⁵ Together, these interventions illustrate how coordinated policy and health system approaches can mitigate modifiable cancer risks. Conversely, our analysis shows that low- and middle-SDI regions face a growing burden. Rising alcohol consumption, fuelled by economic growth, urbanisation, shifting cultural norms, and expansion of the global alcohol industry into emerging markets, contributes to these trends. Weak regulatory environments, limited enforcement of alcohol control measures, and inadequate cancer screening and treatment services have compounded the challenge. Without urgent, context-specific action, these regions are likely to experience widening disparities in cancer outcomes, placing further strain on health systems.

The study's age-specific findings reinforce the cumulative nature of alcohol-related breast cancer risk.^{9,26} Women aged 40–49 years consistently bore the greatest burden, reflecting longer exposure periods. While high-SDI countries have achieved significant reductions in mortality and DALYs in this group, trends are stable or rising in many resource-limited settings. Preventing harmful alcohol use across the life course and strengthening early detection will be critical to reversing these patterns.²⁷ The observed positive correlations between alcohol-attributable breast cancer burden and SDI

at regional and national levels reflect complex interactions between socio-demographic development, alcohol use patterns, and health system capacity. Although historically higher SDI was associated with higher burden, this relationship appears to plateau or reverse at the highest SDI levels, likely reflecting the impact of public health measures. Substantial heterogeneity in low- and middle-SDI countries underscores the influence of contextual factors beyond socio-economic development alone.²⁸

This analysis benefits from the strengths of the GBD framework, including standardised methodology and broad geographic and temporal coverage. The use of robust statistical techniques, such as EAPC estimation and ARIMA forecasting, provides insight into trends and likely future trajectories. However, limitations include uncertainty in estimates from data-sparse settings, the inability to account for synergistic risk factor interactions, and the ARIMA model's assumption that historical trends will persist, without accounting for future policy or behavioural changes.^{27,29,30}

From a policy perspective, our findings have implications for both global and national cancer control strategies by supporting the integration of alcohol control into breast cancer prevention, particularly for women of reproductive age.³¹ At the national level—especially in low- and middle-income countries where the alcohol-attributable burden is projected to rise—embedding evidence-based alcohol policies within cancer control plans may be a cost-effective approach to reducing future mortality and DALYs, including pricing/tax measures, restrictions on alcohol marketing and availability, and clearer health warning labels.^{32,33}

The findings of this study have important clinical and public health implications. Integrating alcohol-use assessment and brief counseling into routine breast health and primary care may help identify harmful drinking early and support risk reduction. In addition, pronounced regional disparities underscore the need to strengthen prevention and screening capacity in low- and middle-SDI settings, where rising alcohol use and limited access to early detection contribute to poorer outcomes. In these regions, evidence-based alcohol control measures (eg, taxation and marketing restrictions) should be implemented alongside expanded mammography and early detection programs. In addition, future projections were generated using ARIMA models based on historical trends. Such models inherently assume continuity of past patterns and may not fully capture the potential impact of future changes in alcohol control policies, screening practices, or population-level behavioral shifts, which could alter the projected burden.

From a broader perspective, the metabolic mechanisms linking alcohol intake to breast cancer progression, including hormonal and oxidative pathways, suggest potential avenues for pharmacologic and lifestyle-based interventions aimed at mitigating risk. Incorporating alcohol-related risk evaluation into existing cancer risk stratification tools could improve personalized prevention strategies. Collectively, these results emphasize that reducing harmful alcohol use is not only a behavioral and policy challenge but also an essential component of comprehensive cancer control and women's health promotion.

Conclusion

In conclusion, our findings underscore the need for intensified global efforts to reduce harmful alcohol use and its contribution to breast cancer burden among women of reproductive age. Prioritising evidence-based alcohol control policies, alongside expansion of breast cancer prevention, screening, and treatment services in low- and middle-SDI regions, will be essential to narrowing inequities and achieving global cancer control targets.

Data Sharing Statement

The data are available from the Global Burden of Disease Results Tool of the Global Health Data Exchange (<http://ghdx.healthdata.org/>).

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of The Affiliated Hospital of Yangzhou University in line with the Declaration of Helsinki (Approval number: 2025081405). As a result of the secondary data analysis in this study, the review board waived informed consent. Additionally, this article does not contain any personal information about patients. All authors are in agreement with the manuscript.

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Author Contributions

L.D. made a significant contribution to the conception and study design, data analysis and interpretation, and drafted the manuscript. H.Y. contributed to data interpretation, literature review, and manuscript drafting and revision. W. L. supervised the study, provided methodological input, and critically revised the manuscript. All authors took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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