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Global Trends in Death, Years of Life Lost, and Years Lived With Disability Caused by Breast Cancer Attributable to Secondhand Smoke From 1990 to 2019

Zejin Ou[1,2], Yunxia Gao[3], Diwei Jiang[4], Jiaxin Cui[5], Yixian Ren[2], Shihao Tang[2], Danping Duan[2], Danfeng Yu[6] and Zhi Wang[2]**

[1] Department of Central Laboratory, Guangzhou Twelfth People's Hospital, Guangzhou, China, [2] Key Laboratory of Occupational Environment and Health, Guangzhou Twelfth People's Hospital, Guangzhou, China, [3] School of Public Health, Guangzhou Medical University, Guangzhou, China, [4] School of Basic Medicine and Public Health, Jinan University, Guangzhou, China, [5] School of Public Health, Sun Yat-sen University, Guangzhou, China, [6] Department of Medical Intensive Care Unit (MICU), Guangdong Women and Children Hospital, Guangzhou, China

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***Correspondence:**
Zhi Wang
zhi_wang@outlook.com
Danfeng Yu
yudanfeng007@126.com

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Background: Secondhand smoke is an important risk factor to breast cancer patients' survival. This article aimed to describe the epidemiological changes of health loss caused by female breast cancer attributable to secondhand smoke from 1990 to 2019.

Methods: Data on breast cancer was derived from the Global Burden of Disease study 2019. The epidemiological status and trends were estimated using the number, age-standardized rate (ASR), and estimated annual percentage change (EAPC).

Results: In 2019, secondhand smoke-related breast cancer caused 168.33×10^2 death, 5242.58×10^2 years of life lost (YLLs), and 334.03×10^2 years lived with disability (YLDs) globally. The overall ASR of death and YLLs caused by breast cancer attributable to secondhand smoke presented decreasing trends from 1990 to 2019, with the respective EAPCs of –0.78 and –0.87. Meanwhile, decreasing trends occurred in most geographic regions, particularly that of YLLs in high-income North America (EAPC = –3.35). At the national level, most countries/territories had decreasing trends of death and YLLs, particularly Denmark, in which the respective EAPCs were –4.26 and –4.64. However, the ASR of YLDs showed an increasing trend globally (EAPC = 0.32). Meanwhile, increasing trends were observed in most regions and countries, particularly the Solomon Islands and Lesotho, with the respective EAPCs being 6.18 and 4.33. The changing trends were closely associated with sociodemographic development.

Conclusions: Trends in secondhand smoke-related death and YLLs caused by breast cancer declined from 1990 to 2019. However, secondhand smoke remains a challenge to

the patients' longevity and quality of life. The findings informed strategies should be strengthened the control of secondhand smoking.

Keywords: breast cancer, secondhand smoke, global burden of disease, age-standardized rate, estimated annual percentage change

INTRODUCTION

Breast cancer is the most common malignant tumor among women, and brought a substantial challenge to global health. The Global Burden of Disease study (GBDs) 2017 showed that breast cancer was the leading cause of cancer deaths and disability-adjusted life years (DALYs) for women, accounting for 601,000 deaths and 17.4 million DALYs (1). Among the related risk factors, secondhand smoke exposure is not only a well-demonstrated risk factor to the development of breast cancer (2–4), but also is an important influence factor of survival (5, 6). Globally, secondhand smoke caused more than additional 331,000 deaths and 9.3 million DALYs in 2013 (7). In Asia, secondhand smoke was a critical risk factor to DALYs caused by breast cancer (3.5%) (8). The proportion of secondhand smoke-related DALYs caused by breast cancer accounted for 1.0% in European Union (EU), and distributed heterogeneously across countries (9).

To achieve the goal of Sustainable Development Goals 2030, tobacco control had been implemented under the World Health Organization Framework Convention on Tobacco Control (WHO FCTC) since 2003 (10, 11). In recent years, the survival patterns of breast cancer and its related smoke exposure had changed (12, 13). The global age-standardized rate of death and DALYs caused by breast cancer attributable to secondhand smoke declined 5.4% and 4.9% during 2007-2017, respectively (13). However, serval countries reported the attributable YLLs of breast cancer improved slowly, substantially for tobacco exposure (14).

The GBDs accessed and quantified the burden of diseases, injuries, and risk factors, which facilitated tracking their epidemiological status and changes over time. By now, few studies reported the secondhand smoke-related health losses caused by breast cancer from a global landscape. Therefore, present work aimed to analyze health losses caused by breast cancer attributable to secondhand smoke worldwide, and estimate their trends with the updated GBDs data.

METHODS

Data Source

Secondhand smoke is also called side-stream or passive smoke exposure. According to the instruction of GBDs, the definition of secondhand smoke exposure is that non-smokers are passively exposed to average daily particulate air matter from cigarette smoke with an aerodynamic diameter of smaller than 2.5 μg (measured in $\mu g/m^3$) (7). Years of life lost (YLLs) and years lived with disability (YLDs) are the critical metrics of health loss reflecting the socioeconomic status and development of the health care system, both of which together are equal to disability-Adjusted Life-Years (DALYs). Data on secondhand smoke-related breast cancer was explored from the GBD study 2019 through the Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool). The burden included death, YLLs, and YLDs, which were extracted for age groups, sociodemographic index (SDI) areas, geographic regions, and countries/territories from 1990 to 2019. An overview of the cancer burden was comprehensively presented globally, including 21 geographic regions and 204 countries/territories. The GBDs groups summarized and estimated the risks and exposures from 46,749 cohort studies, randomized controlled trials, civil surveys, and other sources, and more details on methods were seen in the previous studies (7, 13).

Sociodemographic index (SDI) is a compound index reflecting the influence of social development to civil health. The SDI value ranged from 0 to 1, which means the lowest and highest level of educational opportunities, average per capita incomes, and fertility rates. In 2019, the SDI scales varied from 0.081 in Somalia to 0.929 in Switzerland. According to the SDI, these countries/territories and regions were categorized into five levels, including low, low-middle, middle, high-middle, and high, with the respective upper bound of SDI quintiles being 0.454743, 0.607679, 0.689504, 0.805129, and 1.

Statistical Analysis

The data involved different age structures in multiple populations over time, thus age-standardized is a necessary and representative index. The age-standardized rate (ASR) per 100,000 population was calculated using the following formula:

$$\mathrm{ASR} = \frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} w_i} \times 100,000$$

Where a_i: the age-specific rate in the i^{th} age group; w: the number of the weight (people) in the corresponding i^{th} age group among the selected standard population; A: the number of age groups.

Estimated annual percentage change (EAPC) is a widely used index to describe the epidemiological trends in the burden of diseases in public health studies (15, 16). EAPC could not only quantify the changing speed of ASR, but also estimate their future trends. A regression line is fitted to the natural logarithm of ASR, where y is the natural logarithm of ASR, and x is the

Abbreviations: GBD, Global Burden of Disease; YLLs, years of life lost; YLDs, years lived with disability; DALYs, Disability-adjusted life years; ASR, Age-standardized rate; UI, Uncertainty interval; CI, Confidence interval; EAPC, Estimated annual percentage change; GHDx, Global Health Data Exchange; SDI, Socio-demographic index; WHO FCTC, the World Health Organization Framework Convention on Tobacco Control.

calendar year. Subsequently, EAPC and its 95% confidence interval (CI) are estimated using the linear regression model. The formulas are presented as follows:

$$y = \alpha + \beta x + \epsilon$$

$$EAPC = 100 \times (\exp(\beta) - 1)$$

The trends are judged as following standards: (1). if both the EAPC value and its 95% CI > 0, it is deemed to be an increasing trend of ASR; (2). if both the EAPC value and 95% CI < 0, it is deemed to be a decreasing trend of ASR; (3). others mean the ASR being stable over time. To analyze the influential factors of EAPC, the relationships between EAPCs and ASRs in 1990, and between ASRs and SDI in 2019 were calculated using a Pearson correlation analysis. The data and figures were analyzed using R v3.6.2 (Institute for Statistical Computing, Vienna, Austria). A *p*-value of less than 0.05 meant statistically significant.

RESULTS

Trends of Death Caused by Breast Cancer Attributable to Secondhand Smoke

Globally, breast cancer attributable to secondhand smoke was responsible for 168.33×10^2 (95% uncertainty interval [UI]: 39.56×10^2-290.39×10^2) death in 2019, with an increase of 69.98% since 1990. The overall age-standardized death rate (ASDR) declined from 0.46 in 1990 to 0.39 in 2019, by an annual average decrease of 0.78% (EAPC = −0.78, 95%CI: −0.86 to −0.71) from 1990 to 2019 (**Table 1**; **Figure 1**). The age groups of 50-59 years undertook the most frequent of death cases in 2019, and all age groups had increasing percentages, particularly those aged above 80 years (145.85%) (**Supplementary Table 1**; **Figure 2A**). Regionally, the death number ranged from 0.48×10^2 in Australasia to 37.00×10^2 in East Asia in 2019. Trends of ASDR rose in five geographic regions, especially Oceania (EAPC = 0.69, 95%CI: 0.64-0.73). On the other hand, decreasing trends occurred in fifteen regions, and the most pronounced ones appeared in high-income North America (EAPC = −3.09, 95% CI: −3.29 to −2.88), followed by Australasia and tropical Latin America (**Table 1; Figures 1** and **2C**). Among 204 countries/territories, the burden of breast cancer attributable to secondhand smoke heterogeneously varied across countries. The ASDRs varied from 0.12 in El Salvador to 2.96 in the Solomon Islands in 2019. 1990-2019, the percentages of death number significantly increased in the Solomon Islands (1162.86%) and United Arab Emirates (872.82%), but pronouncedly decreased in Denmark (−52.03%), followed by Norway and Switzerland. Ninety-one countries undertook the increasing trends, particularly Solomon Islands and Lesotho, in which the respective EAPCs were 5.65 (95%CI: 5.02-6.29) and 4.32 (95%CI: 3.79-4.85). However, ninety-nine countries had decreasing trends, particularly Denmark and Iceland, in which the EAPCs were −4.26 (95%CI: −4.42 to −4.09) and −3.94 (95% CI: −4.14 to −3.73) (**Supplementary Table 2; Figures 3A–C**).

Trends of YLLs Caused by Breast Cancer Attributable to Secondhand Smoke

In 2019, an estimated 5242.58×10^2 (95%UI: 1234.61×10^2-9029.02×10^2) YLLs number of breast cancer was attributable to secondhand smoke globally, and increased 60.83% since 1990. The overall ASR of YLLs presented a decreasing trend from 1990 to 2019, in which the EAPC was −0.87 (95%CI: −0.96 to −0.78) (**Table 2; Figure 1**). Those aged 50-54 years had the largest YLLs number (889.80×10^2), and the percentages increased in all age groups, especially the patients above 80 years (135.52%) (**Supplementary Table 1; Supplementary Figure 1A**). Among 21 regions, the YLLs number ranged from 13.44×10^2 in Australasia to 1214.48×10^2 in South Asia in 2019. Decreasing trends in the ASR of YLLs occurred in 15 regions, and the largest one occurred in high-income North America (EAPC = −3.35, 95%CI: −3.58 to −3.13). Conversely, four regions showed increasing trends, including Oceania and Central Sub-Saharan Africa (**Table 2; Figure 1** and **Supplementary Figure 1C**). Nationally, the ASRs of YLLs caused by breast cancer attributable to secondhand smoke were heterogeneous across countries, ranging from 3.79 in El Salvador to 104.76 in Solomon Islands in 2019. 1990-2019, the percentage of YLLs number drastically increased in the Solomon Islands (1256.97%), but pronouncedly decreased in Denmark (−59.19%) and Norway (−48.16%). 107 countries/territories presented decreasing trends in the ASR of YLLs from 1990-2019, and Denmark had the most pronounced one (EAPC = −4.64, 95%CI: −4.82 to −4.46), followed by Norway and Myanmar. However, seventy-six countries showed increasing trends, particularly the Solomon Islands and Lesotho, in which the respective EAPCs were 6.01 (95%CI: 5.32-6.70) and 4.42 (95%CI: 3.85-4.99) (**Supplementary Table 3; Figure 3B** and **Supplementary Figures 2A–C**).

Trends of YLDs Caused by Breast Cancer Attributable to Secondhand Smoke

Globally, the number of YLDs caused by breast cancer attributable to secondhand smoke was 334.03×10^2 (95%UI: 74.04×10^2-602.13×10^2) in 2019, by an increasing percentage of 123.26% since 1990. The global ASR of YLDs increased with an annual average 0.32% from 1990 to 2019 (EAPC = 0.32, 95%CI: 0.28-0.36) (**Table 2; Figure 1**). The highest YLDs number was seen in those aged 50-54 years in 2019 (51.56×10^2), and the largest increasing percentages occurred in the people above 80 years (155.79%) (**Supplementary Table 1**; **Supplementary Figure 3A**). Among 21 geographic regions, the YLDs number ranged from 0.73×10^2 in Andean Latin America to 104.36×10^2 in East Asia in 2019. Fourteen regions appeared increasing trends in the ASR of YLDs, and East Asia had the largest one (EAPC = 2.33, 95%CI: 2.25-2.40), followed by North Africa and Middle East and Southeast Asia. Whereas six regions had decreasing trends, particularly high-income North America (EAPC = −2.27,

TABLE 1 | the characteristics and trends of death caused by breast cancer attributable to secondhand smoke in global, SDI areas and geographic regions, 1990-2019.

Characteristics	1990		2019		1990-2019	
	Number×10^2 (95% UI)	ASR/100,000 (95% UI)	Number×10^2 (95% UI)	ASR/100,000 (95% UI)	Percentage (%)	EAPC (95% CI)
Global	99.03 (23.57–169.46)	0.46 (0.11–0.79)	168.33 (39.56-290.39)	0.39 (0.09-0.67)	69.98	–0.78 (–0.86-–0.71)
SDI						
Low	4.18 (1.02–7.38)	0.31 (0.08–0.55)	11.08 (2.54-19.59)	0.37 (0.08-0.65)	164.97	0.35 (0.26-0.45)
Low-middle	15.26 (3.68–26.48)	0.46 (0.11–0.80)	35.80 (8-61.94)	0.47 (0.11-0.82)	134.60	–0.09 (–0.20-0.03)
Middle	27.16 (6.41–46.65)	0.47 (0.11–0.81)	59.12 (14.48-102.13)	0.44 (0.11-0.76)	117.64	–0.39 (–0.44-–0.35)
High-middle	30.82 (7.38–52.86)	0.53 (0.13–0.90)	42.50 (10.26-73.46)	0.40 (0.10-0.69)	37.90	–1.26 (–1.39-–1.13)
High	21.55 (5.12–37.10)	0.41 (0.10–0.71)	19.72 (4.83-33.76)	0.23 (0.06-0.39)	–8.49	–2.31 (–2.43-–2.20)
Regions						
East Asia	18.95 (4.48–33.22)	0.40 (0.09–0.69)	37.00 (9.03-66.03)	0.34 (0.08-0.61)	95.23	–0.69 (–0.76-–0.63)
South Asia	13.65 (3.3–23.90)	0.45 (0.11–0.79)	36.52 (8.64-64.29)	0.48 (0.11-0.85)	167.52	–0.08 (–0.23-0.08)
Southeast Asia	12.12 (2.76–20.94)	0.77 (0.17–1.33)	26.63 (5.99-46.72)	0.75 (0.17-1.32)	119.83	–0.19 (–0.25-–0.12)
Central Asia	1.68 (0.41–2.87)	0.61 (0.15–1.04)	2.21 (0.53-3.82)	0.49 (0.12-0.85)	31.57	–0.67 (–0.78-–0.56)
High-income Asia Pacific	2.68 (0.63–4.57)	0.25 (0.06–0.42)	3.69 (0.88-6.37)	0.20 (0.05-0.35)	37.84	–0.70 (–0.80-–0.60)
Oceania	0.25 (0.06–0.45)	1.41 (0.33–2.54)	0.76 (0.18-1.38)	1.72 (0.41-3.14)	203.16	0.69 (0.64-0.73)
Australasia	0.49 (0.12–0.84)	0.42 (0.10–0.73)	0.48 (0.12-0.83)	0.21 (0.05-0.37)	–1.30	–2.61 (–2.77-–2.45)
Eastern Europe	8.92 (2.22–15.27)	0.55 (0.14–0.95)	8.60 (2.06-15.65)	0.45 (0.11-0.83)	–3.62	–1.32 (–1.67-–0.96)
Western Europe	14.92 (3.58–25.66)	0.54 (0.13–0.93)	11.29 (2.76-19.59)	0.27 (0.07-0.47)	–24.33	–2.60 (–2.69-–2.51)
Central Europe	4.52 (1.10–7.73)	0.57 (0.14–0.98)	4.97 (1.19-8.77)	0.45 (0.11-0.79)	9.96	–0.92 (–1.02-–0.83)
High-income North America	6.67 (1.6–11.59)	0.39 (0.09–0.68)	5.45 (1.31-9.41)	0.18 (0.04-0.31)	–18.35	–3.09 (–3.29-–2.88)
Andean Latin America	0.24 (0.05–0.42)	0.20 (0.05–0.36)	0.48 (0.11-0.88)	0.16 (0.04-0.29)	103.51	–1.37 (–1.57-–1.18)
Central Latin America	1.47 (0.36–2.53)	0.31 (0.08–0.53)	3.17 (0.77-5.59)	0.24 (0.06-0.43)	114.77	–1.11 (–1.26-–0.95)
Caribbean	0.51 (0.12–0.89)	0.37 (0.09–0.65)	0.82 (0.20-1.47)	0.30 (0.07-0.54)	59.77	–0.83 (–0.90-–0.76)
Tropical Latin America	2.29 (0.54–3.96)	0.45 (0.11–0.77)	3.56 (0.82-6.24)	0.27 (0.06-0.47)	55.18	–1.89 (–2.06-–1.72)
Southern Latin America	1.94 (0.46–3.35)	0.78 (0.18–1.34)	2.42 (0.57-4.21)	0.53 (0.12-0.92)	24.82	–1.62 (–1.74-–1.51)
Eastern Sub-Saharan Africa	1.08 (0.25–1.90)	0.25 (0.06–0.43)	2.68 (0.63-4.81)	0.27 (0.06-0.48)	148.34	0.19 (0.10-0.29)
Southern Sub-Saharan Africa	1.02 (0.25–1.79)	0.63 (0.16–1.11)	1.86 (0.45-3.29)	0.56 (0.14-0.99)	81.12	–0.23 (–0.36-–0.11)
Western Sub-Saharan Africa	1.30 (0.33–2.40)	0.28 (0.07–0.51)	3.53 (0.78-6.34)	0.31 (0.07-0.55)	170.66	0.31 (0.24-0.37)
North Africa and Middle East	4.02 (0.95–7.04)	0.42 (0.10–0.73)	11.33 (2.70-19.92)	0.47 (0.11-0.82)	181.51	0.38 (0.30-0.46)
Central Sub-Saharan Africa	0.29 (0.07–0.55)	0.21 (0.05–0.40)	0.90 (0.19-1.69)	0.26 (0.06-0.5)	204.78	0.62 (0.51-0.74)

EAPC, estimated annual percentage change; ASR, age-standardized rate; CI, confidence interval; UI, uncertainty interval; SDI, socio-demographic index.

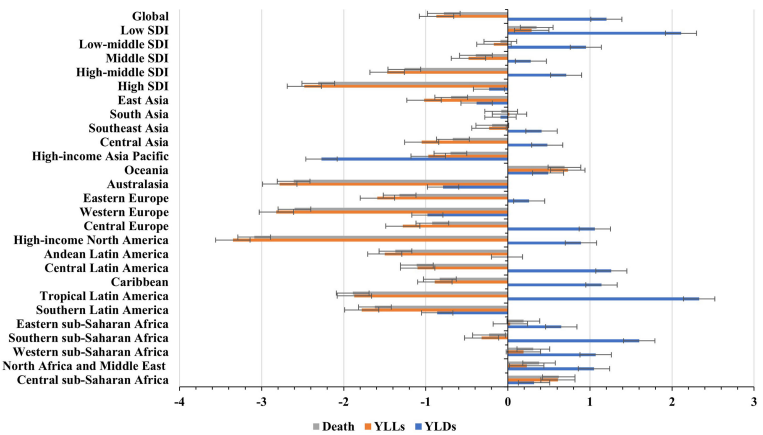

FIGURE 1 | Global trends in the ASR of death, YLLs, and YLDs caused by breast cancer attributable to secondhand smoke, and in SDI areas and geographic regions from 1990 to 2019. ASR, age-standardized rate; SDI, sociodemographic index; YLLs, years of life lost; YLDs, years lived with disability.

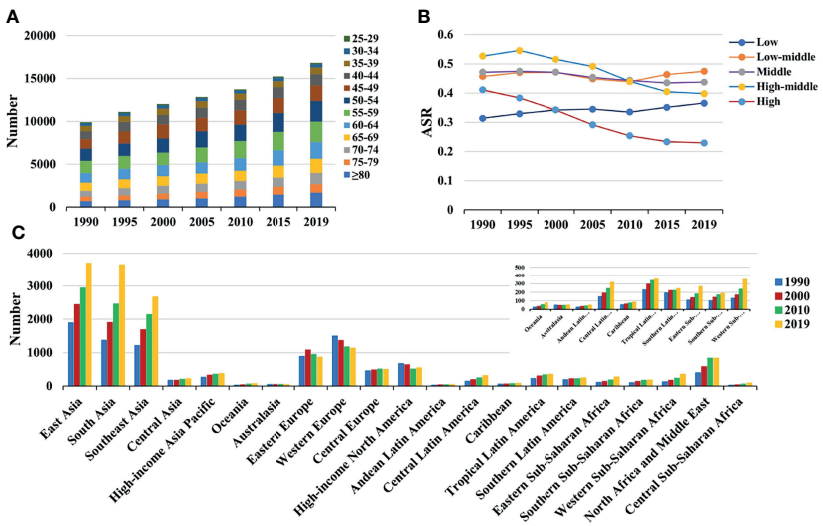

FIGURE 2 | The distribution of death caused by breast cancer attributable to secondhand smoke from 1990 to 2019. **(A)** was the death number in age groups; **(B)** was the ASDR in SDI areas; **(C)** was the death number in geographical regions. ASDR, age-standardized death rate; SDI, sociodemographic index.

95%CI: −2.46 to −2.07) (**Table 2; Figure 1** and **Supplementary Figure 3C**). Among 204 countries/territories, the ASR of YLDs ranged from 0.11 in Ethiopia to 3.01 in Solomon Islands in 2019. 1990-2019, pronounced increasing percentages were seen in Solomon Islands (1424.03%) and United Arab Emirates (1351.36%). Whereas Denmark had the largest decreasing one (−22.79%), followed by Ukraine and Georgia. 145 countries/territories showed increasing trends in ASR of YLDs caused by breast cancer attributable to secondhand smoke over the past three decades, and the Solomon Islands had the most pronounced ones (EAPC = 6.18, 95%CI: 5.66-6.70), followed by Lesotho and Saudi Arabia. On the other hand, only forty-eight countries had decreasing trends, particularly Iceland and Myanmar, in which the respective EAPCs were −2.56 (95%CI: −2.70 to −2.42) and −2.46 (95%CI: −2.71 to −2.21) (**Supplementary Table 4**; **Supplementary Figures 4A–C**).

The Burden of Breast Cancer Attributable to Secondhand Smoke-Related With SDI

Among five SDI areas, the middle SDI area had the largest health loss caused by breast cancer attributable to secondhand smoke, followed by low-middle and high-middle areas. The ASDR ranged from 0.23 in the high SDI area to 0.47 in the low-middle one.1990-2019, decreasing trends in the ASR of death and YLLs caused by breast cancer attributable to secondhand

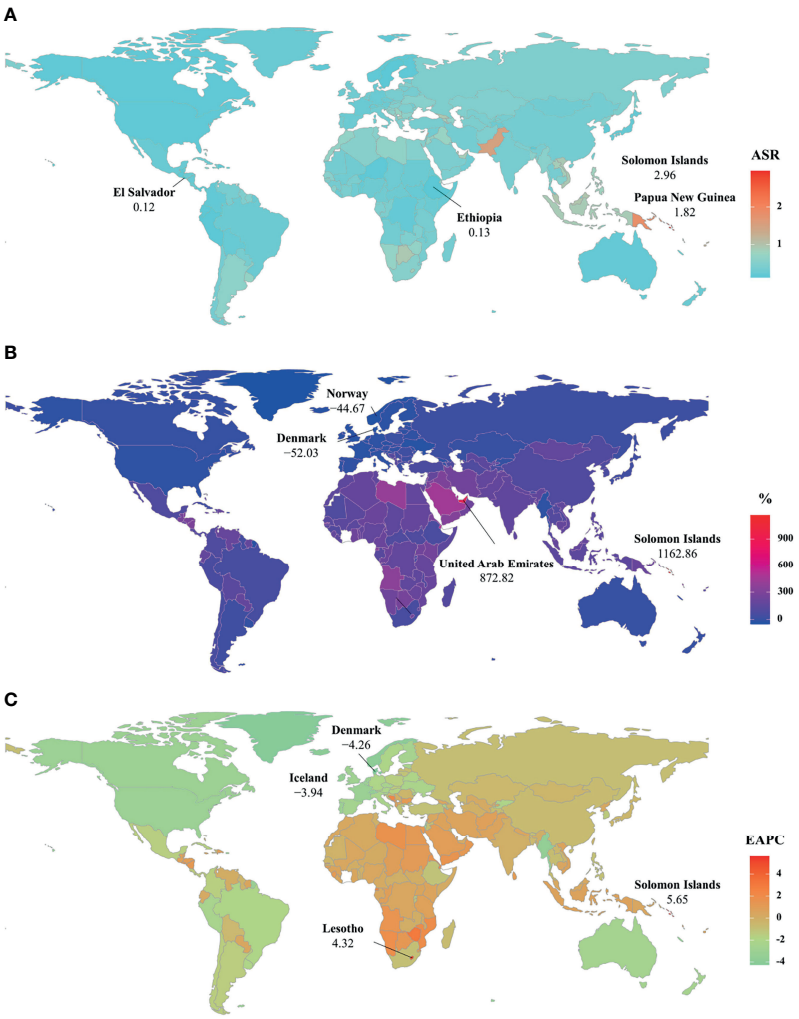

FIGURE 3 | The distribution of ASRs, percentages, and EAPCs of death caused by breast cancer attributable to secondhand smoke at the national level. **(A)** was the ASDR in 2019; **(B)** was the percentage changes in death number between 2000 and 2019; **(C)** was the EAPCs of death, respectively. Countries/territories with an extreme value were annotated. ASDR, age-standardized death rate; EAPC, estimated annual percentage change.

smoke occurred in most SDI areas, particularly high SDI one, with the respective EAPCs being −2.31 (95%CI: −2.43 to −2.20) and −2.48 (95%CI:−2.61 to −2.36). However, increasing trends of death and YLLs appeared in the low SDI area. On the other hand, increasing trends of YLDs occurred in most SDI areas, except the high SDI one (EAPC = −0.86, 95%CI: −0.97 to −0.75). The most pronounced increasing one was seen in the middle SDI area (EAPC = 1.60, 95%CI: 1.56 to 1.63), followed by low and low-middle SDI ones. (**Tables 1**, **2; Figures 1**, **2B**). Negative correlations were found between ASRs of death and YLLs and SDI among regions in 2019. Whereas positive correlation was found between ASRs of YLDs and SDI ($\rho = -0.15$, $p < 0.001$; $\rho = -0.17$, $p < 0.001$; $\rho = 0.67$, $p < 0.001$, respectively; **Figures 4A–C**).

The ASRs in 1990 is considered as the disease reservoir at baseline. EAPCs of death, YLLs and YLDs had negative relationships with their corresponding ASRs in 1990 at the national level ($\rho = -0.14$, $p = 0.04$; $\rho = -0.14$, $p = 0.043$; $\rho = -0.48$, $p < 0.001$, respectively; **Figures 5A–C**).

DISCUSSION

Secondhand smoke is an important risk factor to the development and survival of breast cancer. Based on the pooled analysis, both passive and active smoking were demonstrated to equally elevate the risk of breast cancer for women (17). It was estimated that passive smoke exposure caused two-fold breast cancer mortality among never smokers (Hazard ratios = 2.12, 95% CI = 1.24-3.63) (6). The potential mechanisms included the changes in DNA methylation (18), hormone-receptor status (19), genetic susceptibility (20), and hormone levels (particularly premenopausal) (21). Meanwhile,

TABLE 2 | the characteristics and trends of YLLs and YLDs caused by breast cancer attributable to secondhand smoke in global, SDI areas and geographic regions, 1990-2019.

Characteristics	YLLs				YLDs			
	2019		1990-2019		2019		1990-2019	
	Number×10^2 (95% UI)	ASR/100,000 (95% UI)	Percentage (%)	EAPC (95%CI)	Number×10^2 (95% UI)	ASR/100,000 (95% UI)	Percentage (%)	EAPC (95%CI)
Global	5242.58 (1234.61-9029.02)	12.28 (2.89-21.14)	60.83	–0.87 (–0.96- –0.78)	334.03 (74.04-602.13)	0.78 (0.17-1.41)	123.26	0.32 (0.28-0.36)
SDI								
Low	390.17 (90.65-692.44)	11.48 (2.64-20.27)	161.40	0.29 (0.19-0.39)	10.18 (2.34-19)	0.31 (0.07-0.58)	226.28	1.05 (0.98-1.13)
Low-middle	1193.14 (266.32-2063.49)	14.99 (3.35-25.89)	120.20	–0.17 (–0.30- –0.04)	40.88 (9.37-75.75)	0.52 (0.12-0.96)	216.27	1.07 (0.96-1.19)
Middle	1914.45 (469.83-3297.88)	13.76 (3.38-23.68)	101.78	–0.48 (–0.53- –0.42)	110.61 (24.3-200.67)	0.80 (0.18-1.45)	261.14	1.60 (1.56-1.63)
High-middle	1213.73 (294.18-2099.64)	11.94 (2.90-20.63)	25.45	–1.47 (–1.60- –1.33)	101.72 (22.47-184.5)	1.00 (0.22-1.81)	113.14	0.65 (0.58-0.72)
High	526.99 (129.86-903.45)	7.09 (1.75-12.24)	–18.96	–2.48 (–2.61- –2.36)	70.46 (15.31-130.46)	0.92 (0.20-1.72)	27.79	–0.86 (–0.97- –0.75)
Regions								
East Asia	1103.57 (266.85-1960.46)	10.29 (2.48-18.3)	70.24	–1.02 (–1.11- –0.92)	104.36 (22.86-193.17)	0.98 (0.21-1.81)	305.77	2.33 (2.25-2.40)
South Asia	1214.48 (288.49-2148.51)	15.10 (3.58-26.7)	154.26	0.02 (–0.14-0.18)	38.34 (8.91-70.88)	0.48 (0.11-0.89)	255.43	1.14 (0.99-1.28)
Southeast Asia	923.26 (208.25-1625.36)	24.96 (5.63-43.9)	106.51	–0.23 (–0.29- –0.16)	36.97 (8.59-69.19)	1.01 (0.23-1.89)	219.73	1.26 (1.22-1.29)
Central Asia	71.67 (17.13-123.55)	14.96 (3.6-25.76)	29.17	–1.05 (–1.17- –0.93)	3.60 (0.80-6.65)	0.76 (0.17-1.41)	69.32	–0.01 (–0.05-0.03)
High-income Asia Pacific	97.45 (23.58-165.61)	6.52 (1.59-11.01)	8.87	–0.97 (–1.10- –0.85)	15.42 (3.55-29.13)	0.98 (0.23-1.86)	82.39	0.89 (0.75-1.03)
Oceania	28.48 (7.04-51.62)	58.02 (14.07-105.51)	206.12	0.73 (0.68-0.78)	0.76 (0.17-1.45)	1.59 (0.36-3.02)	244.74	1.06 (1.02-1.11)
Australasia	13.44 (3.3-23.57)	6.63 (1.61-11.63)	–12.33	–2.78 (–2.95- –2.62)	1.90 (0.41-3.58)	0.92 (0.19-1.73)	48.62	–0.98 (–1.09- –0.87)
Eastern Europe	245.76 (59.23-446.97)	14.21 (3.44-25.78)	–12.30	–1.59 (–1.95- –1.23)	17.66 (3.9-33.37)	1.02 (0.23-1.9)	31.24	0.26 (0.10-0.41)
Western Europe	284.60 (70.58-490.9)	8.30 (2.07-14.39)	–34.36	–2.82 (–2.92- –2.73)	37.75 (8.12-70.2)	1.09 (0.24-2.04)	12.61	–0.79 (–0.94- –0.64)
Central Europe	117.66 (28.28-209.62)	12.17 (2.93-21.72)	–9.82	–1.28 (–1.37- –1.19)	9.37 (2.08-17.39)	0.97 (0.21-1.81)	42.53	0.49 (0.37-0.6)
High-income North America	144.73 (35.04-251.18)	5.47 (1.32-9.52)	–28.67	–3.35 (–3.58- –3.13)	21.13 (4.24-40.13)	0.77 (0.15-1.47)	0.69	–2.27 (–2.46- –2.07)
Andean Latin America	15.25 (3.59-28.02)	4.93 (1.16-9.06)	86.87	–1.50 (–1.69- –1.31)	0.73 (0.16-1.4)	0.24 (0.05-0.46)	234.25	0.48 (0.32-0.64)

(Continued)

TABLE 2 | Continued

Characteristics	YLLs				YLDs			
	2019		1990-2019		2019		1990-2019	
	Number×10^2 (95% UI)	ASR/100,000 (95% UI)	Percentage (%)	EAPC (95%CI)	Number×10^2 (95% UI)	ASR/100,000 (95% UI)	Percentage (%)	EAPC (95%CI)
Central Latin America	98.99 (23.93-174.6)	7.40 (1.79-13.07)	99.02	–1.10 (–1.25- –0.95)	6.02 (1.36-11.47)	0.45 (0.1-0.86)	227.12	0.41 (0.27-0.55)
Caribbean	24.22 (5.70-44.03)	9.09 (2.14-16.56)	49.11	–0.89 (–0.96- –0.81)	1.40 (0.31-2.58)	0.52 (0.11-0.96)	90.42	–0.09 (–0.13- –0.06)
Tropical Latin America	105.04 (23.89-184.41)	7.82 (1.78-13.7)	42.65	–1.87 (–2.03- –1.71)	5.77 (1.31-10.93)	0.43 (0.10-0.81)	127.98	–0.38 (–0.60- –0.16)
Southern Latin America	57.86 (13.71-100.98)	13.62 (3.23-23.7)	10.83	–1.78 (–1.88- –1.67)	3.82 (0.80-7.32)	0.89 (0.19-1.72)	73.33	–0.23 (–0.33- –0.12)
Eastern Sub-Saharan Africa	95.15 (22.67-171.11)	8.28 (1.95-14.89)	142.92	0.03 (–0.07-0.14)	2.40 (0.54-4.60)	0.22 (0.05-0.41)	199.99	0.71 (0.62-0.81)
Southern Sub-Saharan Africa	56.12 (13.38-99.37)	15.69 (3.77-27.7)	68.29	–0.32 (–0.46- –0.17)	1.87 (0.43-3.49)	0.53 (0.12-0.99)	103.56	0.28 (0.17-0.39)
Western Sub-Saharan Africa	123.35 (27.15-223.57)	9.30 (2.05-16.72)	176.59	0.19 (0.12-0.27)	3.32 (0.72-6.46)	0.26 (0.06-0.51)	238.93	0.95 (0.89-1.01)
North Africa and Middle East	389.44 (92.71-689)	14.70 (3.5-25.93)	173.73	0.23 (0.14-0.31)	20.68 (4.66-38.67)	0.79 (0.18-1.48)	360.23	2.11 (2.04-2.18)
Central Sub-Saharan Africa	32.05 (6.71-60.26)	8.27 (1.74-15.63)	201.79	0.61 (0.51-0.71)	0.76 (0.17-1.51)	0.20 (0.05-0.40)	260.33	1.20 (1.06-1.33)

EAPC, estimated annual percentage change; ASR, age-standardized rate; CI, confidence interval; UI, uncertainty interval; SDI, socio-demographic index; YLLs, years of life lost; YLDs, years lived with disability.

passive smoke exposure probably stimulated the malignant performance of cancer, including cell malignancy, tumor angiogenesis, and metastatic activity (22–25).

Despite the overall incidence of breast cancer growing steadily, improvements in the survival of the patients had been achieved over the past decades (12, 26). The findings in the present work showed the decreasing trend in the death and YLLs caused by breast cancer attributable to secondhand smoke during the period 1990-2019. The achievements benefited from the early screening, improved regimens and healthcare systems, and the management of related risk factors (1, 12, 27). Meanwhile, a large reduction in the prevalence of daily smoke exposure had been achieved globally (28, 29), particularly cost-effective smoke-free policies for reducing secondhand smoke exposure under the forced measures of WHO FCTC (30, 31). Additionally, decreasing trends in secondhand smoke exposure were observed during 2011-2018 (32), and it was estimated that 1 in 14 breast cancer cases could be prevented without secondhand smoke exposure (33). Sociodemographic status strongly influenced the prevalence of smoking and second-hand smoke exposure (34). The upward trends of YLDs caused by breast cancer attributable to secondhand smoke were seen globally, and in most regions and countries. The improved patients' survival could prolong the lifespan with disability. Passive smoke had a high risk of early-onset breast cancer, probably related to genetic polymorphisms (35).

Among SDI quintiles, the middle and high-middle SDI areas undertook the largest burden caused by breast cancer attributable to secondhand smoke, mainly related with the huge population size, and rapid population growth and aging (1, 7). Meanwhile, several low-income and middle-income countries faced the challenge of worsening smoke epidemics (36). Because of poor policy guidance and health awareness, cigarette consumption remains to be unfavorable in low- and middle-income countries (37). Furthermore, the poor medical resource and healthcare system drove the increasing trends in the low SDI area (38). At the national level, downward trends of death and YLLs commonly occurred in the high SDI countries, particularly the high-income North America and Western Europe, where existed sound health systems, early disease screening, and strict tobacco control policies. In high-income North America, the implementation of home smoking bans had significantly reduced the exposure of secondhand smoke at home (39). Denmark, Iceland, and Norway presented the most pronounced decreasing trends, were the highest score of the implementation of tobacco control policies (40). On the other hand, increasing trends were mostly seen in the south Pacific and sub-Saharan Africa countries, where the new diagnosed cases of breast cancer were much more than in the past, lack of cancer prevention and control programs (41, 42), low awareness of cancer risk, and weak implementation of smoke-free policies in public places (43, 44).

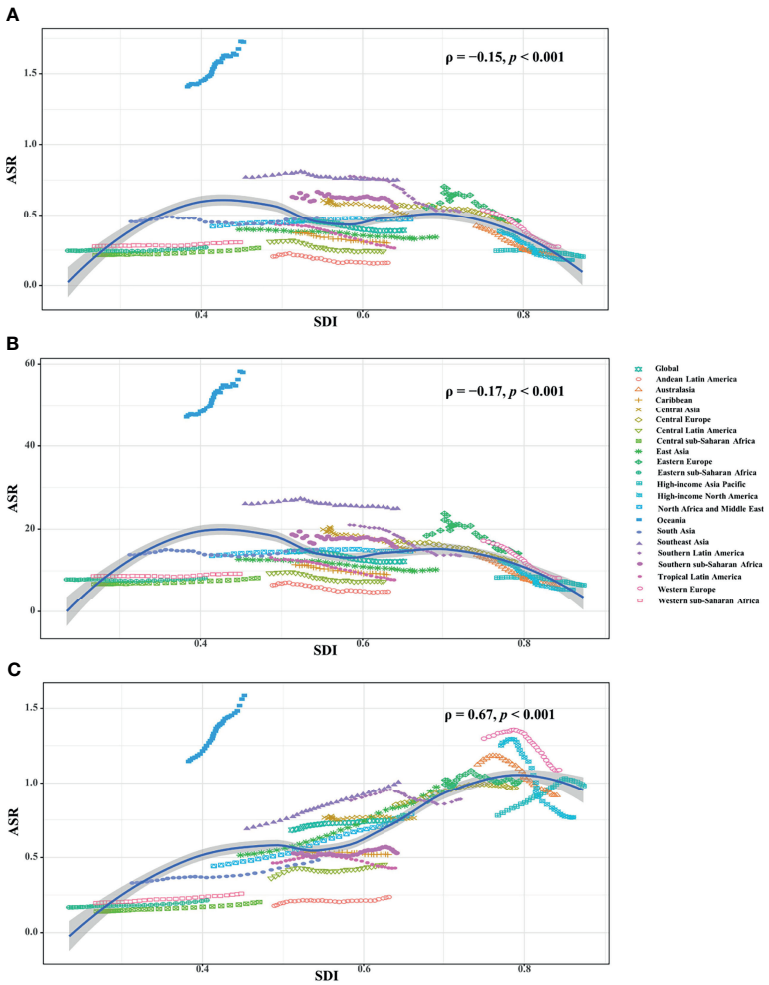

FIGURE 4 | Correlation analysis between ASRs and SDI in 2019 among regions. The ASRs of death **(A)** and YLLs **(B)** negatively related with SDI, but that of YLDs **(C)** positively related with SDI. The correlations were calculated with Pearson correlation analysis. ASR, age-standardized rate; SDI, socio-demographic index; YLLs, years of life lost; YLDs, years lived with disability.

Several limitations should be interpreted in this work. First, the GBD estimations of passive smoking exposure were mainly based on the data from multiple sources, including cross-sectional survey, self-reported data, history recall, and so on. The potential bias was inevitable, including underreported cases, incomplete testing, and the technology varied across countries over time (7, 13, 38). Second, data on the intensity of secondhand smoke exposure could not be quantified and categorized, thus analysis on the association between the exposure and health loss. Third, individual heterogeneity was prone to different subtypes of breast cancer, including genetic background, hormone, and physiological status (pre/postmenopausal). However, the lack of related data failed to explain the findings further. Fourth, several countries lack vital registration data, but the GBD collaborators applied multi statistical models to estimate the settings with sparse data. Last but not least, age is an important factor in breast cancer. However, due to the limitation of ASR estimates, the trends were demonstrated only using the percentage changes in the absolute number in age groups.

CONCLUSIONS

1990-2019, trends of secondhand smoke-related death and YLLs due to breast cancer declined worldwide, and in most regions and countries, highlighting that the advance in the current management and treatment of the disease. Healthcare systems need to be improved to cope with the increasing trends in disability caused by the disease. Meanwhile, disparities and inequities of health care existed among regions and countries, suggesting global efforts need to be taken to promote health equity. Secondhand smoke exposure is a modifiable risk factor,

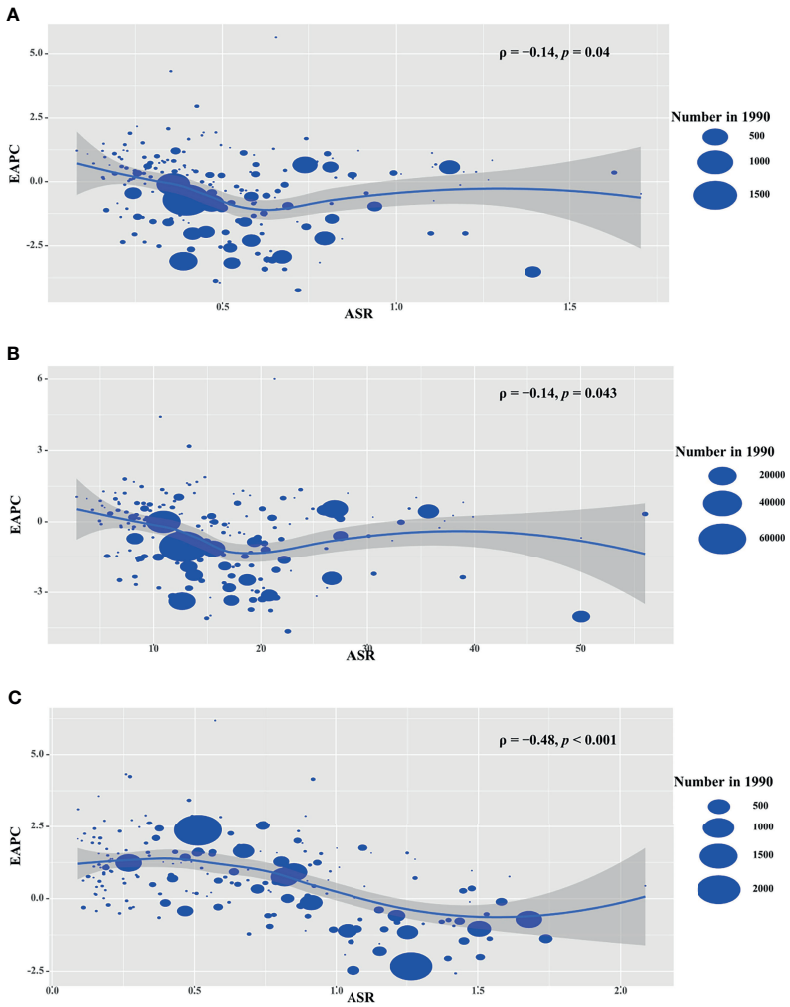

FIGURE 5 | Correlation analysis between EAPCs and ASRs in 1990 among countries. The ASRs of death **(A)**, YLLs **(B)**, and YLDs **(C)** had negative correlations with ASR, respectively. The correlations were calculated with Pearson correlation analysis. The symbols were the countries/territories in the corresponding regions. ASR, age-standardized rate; YLLs, years of life lost; YLDs, years lived with disability.

and governments should adopt cost-effective measures to reduce the related burden through the implementation of enhanced smoke-free policies in public places.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**. Further inquiries can be directed to the corresponding authors.

AUTHOR CONTRIBUTIONS

ZO: Project administration and drafting. DJ, ST, and YR: Data analysis and validation. DY and YG: Data analysis and visualization. JC and DD: Data collection and collation. ZW: supervision and drafting and editing. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2022.853038/full#supplementary-material

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