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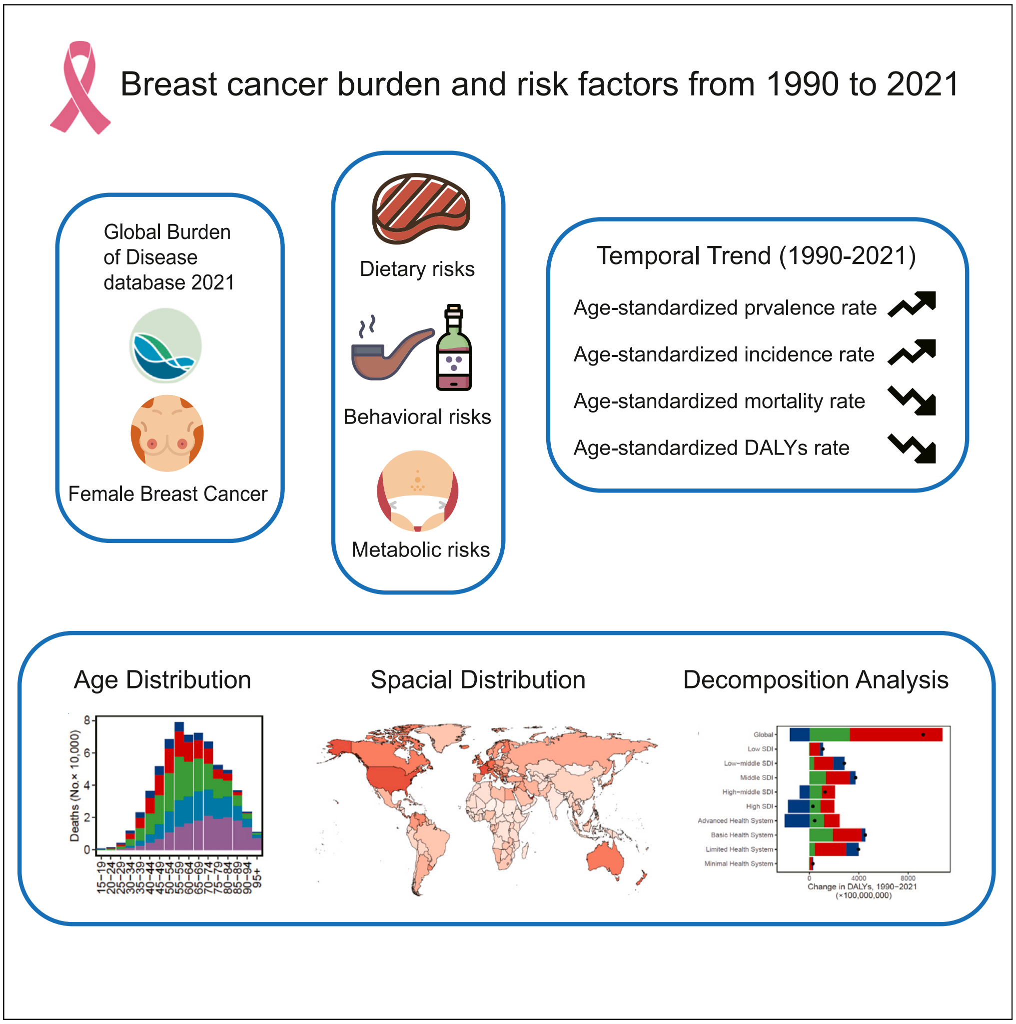

Tian Lan, Yunyan Lu, Jiawei He, Chenni Zhan, Xiaojia Wang, Xiying Shao, Zujian Hu

lan_tian_lt@163.com (T.L.)
15824113524@163.com (X.S.)
hzj_56@hotmail.com (Z.H.)

Highlights

There was an ascending trend in ASPR and ASIR during 1990–2021

ASMR and ASDR showed a downward trend over the past 32 years

Epidemiological changes influenced positively in DALYs change in the regions with lower SDI

The highest proportion of global DALYs was attributable to high red meat intake

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Global, reginal, national burden and risk factors in female breast cancer from 1990 to 2021

Tian Lan,[1,5,6,*] Yunyan Lu,[2,5] Jiawei He,[1] Chenni Zhan,[1] Xiaojia Wang,[3,4] Xiying Shao,[3,4,*] and Zujian Hu[1,*]

SUMMARY

This study was to assess the burden, trends, and risk factors associated with female breast cancer from 1990 to 2021 based on the Global Burden of Disease (GBD) 2021 study. In 2021, there were 20.32 million prevalent cases, 2.08 million incident cases, 0.66 million death cases, and 20.26 million disability-adjusted life years (DALYs). It presented an ascending trend in the age-standardized rates of prevalence and incidence over the past 32 years. The age-standardized DALYs rate (ASDR) increased slightly during 2012–2021. The DALYs increase was primarily driven by population aging and growth. High red meat intake accounted for the highest proportion of ASDR. Breast cancer burden attributed to metabolic risks increased, especially in the regions with low social-development index (SDI) and limited health systems. Dietary, behavior, and metabolic risk factors should be controlled to diminish breast cancer burden, especially in countries with lower SDI.

INTRODUCTION

Breast cancer is one of the most common and deleterious malignancies, imposing a severe burden on individuals and society alike. Female breast cancer emerged as the world's second most prevalent cancer in 2022, with approximately 2.30 million new cases, and it ranked as the fourth principal cause of cancer-specific death, with about 0.67 million fatalities.[1] In the USA, breast cancer comprised 32% of all new cancers in 2023.[2] The burden of breast cancer reveals a stark disparity across different countries.[3] Developed countries have observed a substantial 40% fall in the mortality rate over the past thirty years, whereas underdeveloped nations have unfortunately stagnated with negligible advancements.[4] To attain the United Nations (UN) Sustainable Development Goals (SDGs), specifically the objective of reducing premature mortality from noncommunicable diseases by one-third before 2030,[5] strategic measures targeting the prevention, management, and therapeutic approach to breast cancer emerge as essential steps. A comprehensive examination and analysis of global breast cancer trends is also indispensable for achieving SDGs and formulating appropriate policies.

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021, a comprehensive study of global health loss, provides updated estimations for 371 diseases and injuries across time, location, age, and sociodemographic group.[6] Previous studies on the burden of breast cancer and its associated risk factors have been performed at a global, regional, and national level utilizing data from GBD 2019.[7–9] 2020 and 2021 were the onset of the COVID-19 pandemic, precipitating delays and disruptions in breast cancer screenings, diagnosis, and treatment.[10] Therefore, the latest GBD 2021 study provides an avenue for exploring the impact of the COVID-19 pandemic on breast cancer burden. The objective of this study was to examine the impact of geographical location, age, social-development index (SDI), and health systems on global breast cancer trends regarding prevalence, incidence, mortality, and disability-adjusted life years (DALYs) from 1990 to 2021.

RESULTS

Global burden of breast cancer

In 2021, a substantial cumulative count of 20.32 million (95%UI, 19.25–21.45) prevalent cases and 2.08 million (95%UI, 1.94–2.22) incident cases were recorded, with an ASPR of 450.60 (95% UI, 427.00–476.00) and an ASIR of 46.40 (95%UI, 43.30–49.60) (Tables 1 and S1). The prevalence and incidence cases of female breast cancer increased gradually during 1990–2021, the figures in 2021 were three times higher than those recorded in 1990 (Figure 1A). Meanwhile, the ASPR exhibited an upward trajectory, as indicated by the positive values of AAPC (0.36, 95% CI, 0.33–0.38) and EAPC (0.38, 95%CI, 0.36–0.40) (Tables 2 and S2). The ASIR and ASPR shared a similar temporal trend (Figure 1B). We revealed the lowest APCs for both prevalence (2008–2021) and incidence (1995–2021) (Tables S3 and S4).

[1]Department of Breast Surgery, Hangzhou TCM Hospital Affiliated to Zhejiang Chinese Medical University, Hangzhou Hospital of Traditional Chinese Medicine, Hangzhou, Zhejiang, China
[2]Department of Cardiology, The First People's Hospital of Xiaoshan District, Xiaoshan Affiliated Hospital of Wenzhou Medical University, Hangzhou, Zhejiang, China
[3]Department of Medical Oncology (Breast Cancer), Cancer Hospital of the University of Chinese Academy of Sciences/Zhejiang Cancer Hospital, Hangzhou, China
[4]Institute of Cancer and Basic Medicine (IBMC), Chinese Academy of Sciences, Hangzhou, Zhejiang, China
[5]These authors contributed equally
[6]Lead contact
*Correspondence: lan_tian_lt@163.com (T.L.), 15824113524@163.com (X.S.), hzj_56@hotmail.com (Z.H.)
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Table 1. The age-standardized rates of prevalence, incidence, death, and DALYs for breast cancer in 1990 and 2021

Location	Age-standardized prevalence rate (×10)		Age-standardized incidence rate (×10)		Age-standardized death rate (×10)		Age-standardized DALYs rate (×10)	
	1990	2021	1990	2021	1990	2021	1990	2021
Global	40.45(37.70–43.99)	45.06(42.70–47.60)	4.00(3.80–4.16)	4.64(4.33–4.96)	1.66(1.56–1.74)	1.45(1.35–1.56)	50.38(47.59–53.22)	45.56(42.66–48.53)
Low SDI	11.49(10.04–13.34)	17.32(15.57–19.05)	1.56(1.33–1.81)	2.41(2.13–2.69)	1.22(1.05–1.41)	1.60(1.41–1.79)	38.00(32.24–44.79)	48.82(43.15–54.79)
Low-middle SDI	12.17(11.02–13.70)	22.47(20.66–24.18)	1.47(1.32–1.66)	2.83(2.55–3.09)	1.01(0.89–1.14)	1.46(1.31–1.60)	33.20(29.66–37.80)	47.81(43.01–52.58)
Middle SDI	18.21(16.62–20.15)	32.87(30.07–36.05)	2.06(1.89–2.26)	3.72(3.34–4.11)	1.14(1.05–1.25)	1.27(1.14–1.41)	37.10(33.97–40.92)	41.58(37.55–46.19)
High-middle SDI	39.23(36.40–42.95)	50.15(46.06–55.44)	3.88(3.69–4.07)	5.10(4.61–5.72)	1.71(1.61–1.80)	1.39(1.26–1.51)	53.57(50.42–56.57)	42.48(38.76–47.20)
High SDI	82.70(77.47–88.93)	82.86(79.13–86.09)	7.93(7.62–8.10)	7.71(7.18–7.99)	2.36(2.25–2.43)	1.54(1.40–1.62)	71.87(69.27–74.40)	46.71(43.71–49.36)
Advanced Health System	72.42(67.76–78.38)	77.21(74.02–80.25)	6.98(6.72–7.11)	7.30(6.86–7.58)	2.26(2.15–2.32)	1.62(1.49–1.70)	69.59(67.22–71.83)	48.85(45.96–51.62)
Basic Health System	20.06(18.21–22.36)	36.74(33.13–41.38)	2.19(1.98–2.44)	4.01(3.54–4.58)	1.16(1.05–1.28)	1.20(1.08–1.33)	37.30(33.60–41.69)	39.43(35.22–44.08)
Limited Health System	11.69(10.54–13.14)	20.46(18.67–22.39)	1.51(1.33–1.70)	2.65(2.37–2.94)	1.10(0.97–1.25)	1.49(1.33–1.65)	35.80(31.68–40.61)	47.92(42.97–53.23)
Minimal Health System	12.05(10.33–14.00)	16.84(14.30–19.85)	1.64(1.36–1.97)	2.38(1.95–2.89)	1.30(1.10–1.53)	1.67(1.37–2.00)	39.80(32.83–47.84)	50.03(40.83–61.09)
High-income Asia Pacific	37.33(33.97–41.54)	62.09(57.66–65.92)	2.88(2.73–3.02)	5.56(5.05–5.95)	0.71(0.68–0.73)	0.93(0.83–0.99)	26.28(25.18–27.51)	32.01(29.45–34.41)
High-income North America	122.75(115.87–130.53)	101.63(96.34–106.58)	12.20(11.67–12.52)	9.49(8.90–9.89)	2.81(2.65–2.90)	1.70(1.55–1.79)	88.56(84.69–92.32)	51.57(48.41–54.65)
Central Asia	31.03(28.87–33.27)	28.50(26.06–31.09)	3.54(3.33–3.72)	3.10(2.77–3.46)	1.86(1.76–1.96)	1.38(1.24–1.54)	61.87(58.41–65.12)	43.53(38.80–48.76)
East Asia	17.57(14.90–20.62)	35.73(29.08–43.60)	1.79(1.47–2.16)	3.71(2.88–4.67)	0.90(0.74–1.08)	0.84(0.66–1.04)	30.27(24.62–36.79)	28.63(22.39–36.04)
South Asia	10.41(9.38–11.65)	19.37(17.21–21.88)	1.31(1.16–1.48)	2.46(2.15–2.83)	0.94(0.82–1.06)	1.32(1.15–1.53)	31.49(27.86–35.56)	43.67(38.06–50.15)
Southeast Asia	17.05(14.83–20.00)	30.87(26.82–35.93)	2.03(1.72–2.42)	3.62(3.02–4.37)	1.34(1.12–1.61)	1.77(1.48–2.15)	44.55(37.05–54.04)	57.80(47.69–70.70)
Central Europe	43.26(40.25–47.11)	57.64(53.80–61.66)	4.54(4.36–4.73)	6.12(5.64–6.65)	2.15(2.06–2.24)	2.03(1.85–2.20)	65.42(62.69–68.30)	56.85(52.19–61.82)
Eastern Europe	39.15(36.69–42.50)	48.57(44.08–53.26)	4.06(3.94–4.18)	5.25(4.72–5.86)	1.79(1.73–1.84)	1.74(1.55–1.97)	59.90(58.00–61.87)	52.88(46.90–60.34)
Western Europe	87.71(81.71–95.35)	90.31(86.05–94.01)	8.32(7.98–8.54)	8.18(7.64–8.61)	2.91(2.76–3.00)	1.80(1.62–1.91)	87.47(84.25–90.52)	51.93(47.97–55.45)
Andean Latin America	15.17(13.21–17.39)	27.55(22.18–33.95)	1.98(1.70–2.29)	3.36(2.63–4.29)	1.22(1.04–1.42)	1.29(1.02–1.63)	38.00(32.35–44.41)	39.66(31.39–49.82)
Central Latin America	24.46(23.26–25.73)	46.67(41.15–52.33)	2.98(2.89–3.07)	5.50(4.80–6.22)	1.22(1.17–1.25)	1.41(1.23–1.58)	37.79(36.70–38.95)	45.17(39.10–50.96)
Southern Latin America	43.92(40.49–48.23)	48.44(45.40–51.54)	4.79(4.52–5.04)	5.03(4.62–5.43)	2.81(2.65–2.95)	2.06(1.87–2.23)	81.37(77.30–85.18)	58.50(53.85–62.87)
Tropical Latin America	23.47(22.36–24.78)	36.55(34.54–38.50)	3.00(2.87–3.12)	4.39(4.11–4.65)	1.66(1.58–1.73)	1.70(1.57–1.80)	50.87(48.99–52.74)	53.25(49.94–55.99)
Australasia	88.16(81.17–96.22)	88.87(81.63–96.28)	8.21(7.81–8.64)	8.09(7.25–9.00)	2.64(2.49–2.79)	1.55(1.37–1.73)	80.85(76.59–85.10)	46.72(42.18–51.78)
Caribbean	35.98(33.65–38.57)	45.32(39.49–51.29)	4.35(4.07–4.65)	5.38(4.56–6.17)	1.94(1.79–2.11)	1.96(1.65–2.31)	58.78(53.58–65.03)	59.54(49.52–70.93)
North Africa and Middle East	18.23(16.20–20.74)	45.13(41.13–49.40)	1.64(1.47–1.85)	4.84(4.31–5.45)	0.73(0.66–0.83)	1.22(1.08–1.38)	24.72(22.02–28.42)	39.61(34.71–45.40)
Oceania	23.93(20.22–28.68)	26.20(22.47–31.16)	2.99(2.38–3.72)	3.34(2.77–4.09)	1.97(1.57–2.47)	2.22(1.84–2.70)	63.93(50.33–80.82)	72.24(59.23–89.26)
Central Sub-Saharan Africa	12.54(9.60–16.00)	19.29(15.13–24.35)	1.75(1.26–2.32)	2.71(2.03–3.54)	1.40(1.03–1.82)	1.87(1.41–2.48)	42.99(30.90–57.80)	57.07(42.22–75.58)
Eastern Sub-Saharan Africa	13.49(11.46–15.85)	20.71(17.99–24.12)	1.93(1.61–2.32)	2.93(2.51–3.46)	1.56(1.30–1.87)	2.02(1.75–2.36)	47.12(38.56–57.56)	59.23(50.39–70.68)
Southern Sub-Saharan Africa	19.89(16.96–22.44)	31.25(28.54–34.14)	2.51(2.08–2.95)	4.21(3.79–4.66)	1.71(1.40–2.02)	2.49(2.26–2.75)	51.51(42.99–60.05)	72.89(65.34–81.01)
Western Sub-Saharan Africa	14.76(12.56–16.96)	24.10(19.23–30.31)	2.13(1.74–2.52)	3.46(2.69–4.44)	1.66(1.37–1.95)	2.31(1.87–2.88)	49.26(40.27–58.64)	66.82(51.65–85.49)

SDI, socio-demographic Index; DALYs, disability-adjusted life-years.

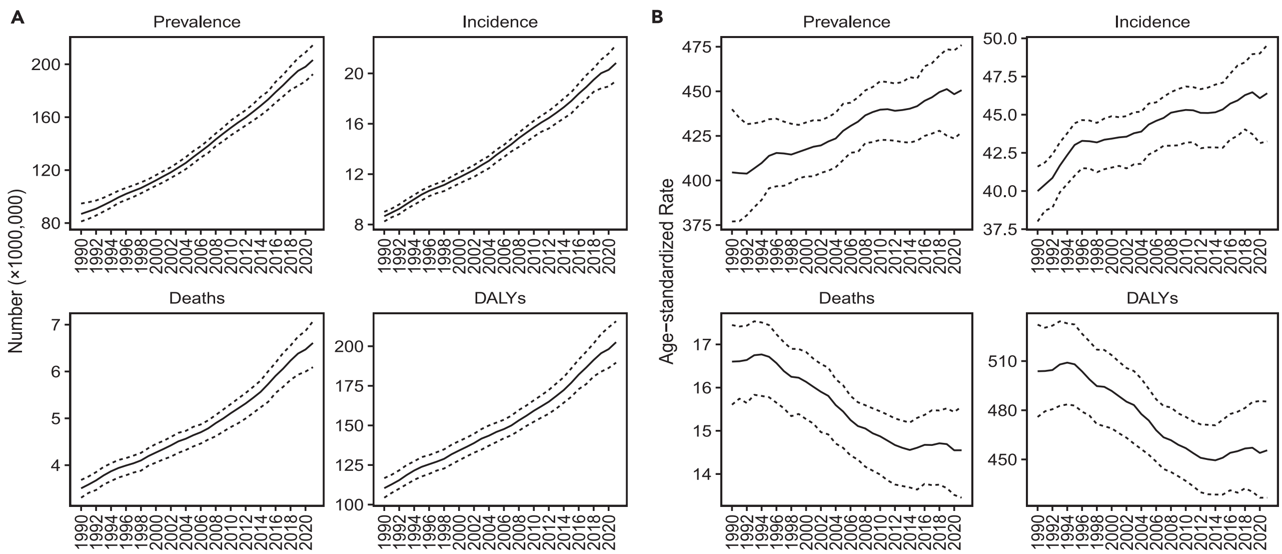

Figure 1. The temporal change of breast cancer from 1990 to 2021
The cases (A) and age-standardized rates (B) of breast cancer during 1990–2021.

Moreover, female breast cancer accounted for 0.66 million (95%UI, 0.61–0.71) death cases and 20.26 million (95%UI, 18.96–21.57) DALYs, accompanied by an ASMR of 14.50 (95% UI, 13.50–15.60) and an ASDR of 455.60 (95% UI, 426.60–485.30). Contrary to the ascending trend of death and DALYs cases, the corresponding ASRs showed a downward trend due to the negative values of AAPC and EAPC (Tables 2 and S2; Figures 1A and 1B). However, the ASMR remained stable while the ASDR increased slightly during 2012–2021 (Tables S5 and S6).

Regional burden of breast cancer

In the terms of SDI categories, the number and ASRs of prevalence and incidence augmented in conjunction with an increase of the SDI in 2021 (Table S1). The low SDI group exhibited the lowest prevalence and incidence cases, but concurrently demonstrated the highest ASMR and ASDR (Figures S1A and S2A). The largest increase in the prevalence, incidence, death, and DALYs of breast cancer was observed in the low-middle SDI classification. On the other hand, the high SDI category demonstrated the lowest EAPC and AAPC in these respective metrics (Tables 2 and S2). The detailed outcomes of joinpoint analysis across different SDI categories were presented in Tables S3, S4, S4, and S6.

In terms of health systems, both the count and ASRs of prevalence and incidence demonstrated a decline in 2021, mirroring an improvement in the health system (Tables 1 and S1; Figures S1B and S2B). ASMR (16.70, 95%UI, 13.70–20.00) and ASDR (500.30, 95%UI, 408.30–610.90) were found to be the highest in the minimal health system. Both ASPR and ASIR showed an increasing trend across all health systems (Table 2). However, ASMR and ASDR displayed a marked downward trend in advanced health systems, while exhibiting an upward trend in other health systems (Figure S2B). The specific results of the joinpoint analysis categorized by various health systems were presented in Tables S3, S4, S4, and S6.

In the term of GBD regions, the epidemiological characteristics of female breast cancer burden demonstrated significant variability during 1990–2021. The highest ASPR and ASIR were observed in high-income North America (ASPR, 1016.30, 95%UI, 963.40–1065.80; ASIR, 94.90, 95%UI, 89.00–98.90), followed by Western Europe, Australasia, and Central Europe (Table 1). Southern Sub-Saharan Africa, Western Sub-Saharan Africa, and Oceania were the top 3 GBD regions with the highest ASMR and ASDR. Regarding the ASPR and ASIR, a declining trend was observed exclusively in High-income North America and Central Asia, a stable status was found in Western Europe and Australasia, and a growing trend was identified in other GBD regions. The rapid growth of ASMR and ASDR from 1990 to 2021 was observed in North Africa and the Middle East (AAPC for ASMR: 1.61, 95%CI, 1.55–1.66; AAPC for ASDR: 1.49, 95%CI, 1.43–1.54), South Asia (AAPC for ASMR: 1.14, 95%CI, 1.08–1.19; AAPC for ASDR: 1.07, 95%CI, 1.01–1.12) and Central Sub-Saharan Africa (AAPC for ASMR: 0.96, 95%CI, 0.93–0.98; AAPC for ASDR: 0.93, 95%CI, 0.90–0.96) (Table 2).

National burden of breast cancer

At the national level, there was significant heterogeneity observed in disease burden across 204 countries. China, India, and the United States of America emerged as the top 3 countries with the highest number of prevalence, incidence, death cases, and DALYs in 2021 (Tables S7 and S8; Figure S3). The relatively higher ASPR and ASIR were observed in the Arabian peninsula (United Arab Emirates, Qatar, and Bahrain), Western Europe (Monaco, Fance), and the United States of America (Tables S7 and S8; Figures 2A and 2C). Meanwhile, Parkistan, some Oceania countries (American Samoa, Palau, Nauru, Tonga), and several Southern Sub-Saharan Africa countries (Namibia, Zambia, Zimbabwe) demonstrated relatively higher ASMR and ASDR (Tables S7 and S8; Figures 2E and 2G). Based on the AAPC of ASIR, 169 countries showcased an upward trend, 28 countries displayed a downward trend, and 7 countries remained stable. Most of the countries that exhibited a decline

Location	AAPC for Prevalence	AAPC for Incidence	AAPC for Deaths	AAPC for DALYs
Global	0.36 (0.33–0.38)	0.50 (0.46–0.55)	−0.41 (−0.45 to −0.36)	−0.31 (−0.34 to −0.29)
Low SDI	1.34 (1.32–1.36)	1.42 (1.40–1.44)	0.89 (0.86–0.92)	0.82 (0.80–0.85)
Low-middle SDI	2.01 (1.99–2.03)	2.13 (2.10–2.17)	1.21 (1.19–1.24)	1.18 (1.16–1.21)
Middle SDI	1.96 (1.93–1.99)	1.95 (1.93–1.98)	0.35 (0.32–0.38)	0.37 (0.34–0.40)
High-middle SDI	0.78 (0.75–0.82)	0.88 (0.84–0.94)	−0.67 (−0.70 to −0.62)	−0.74 (−0.78 to −0.69)
High SDI	0.01 (−0.03 to 0.06)	−0.09 (−0.15 to −0.04)	−1.38 (−1.43 to −1.34)	−1.40 (−1.43 to −1.37)
Advanced Health System	0.20 (0.15–0.26)	0.13 (0.08–0.18)	−1.06 (−1.09 to −1.01)	−1.15 (−1.18 to −1.10)
Basic Health System	2.04 (2.01–2.08)	1.98 (1.95–2.01)	0.14 (0.12–0.17)	0.20 (0.18–0.22)
Limited Health System	1.82 (1.80–1.84)	1.83 (1.80–1.87)	0.98 (0.95–1.02)	0.94 (0.91–0.97)
Minimal Health System	1.10 (1.09–1.12)	1.21 (1.19–1.22)	0.81 (0.80–0.83)	0.75 (0.73–0.76)
High-income Asia Pacific	1.71 (1.62–1.78)	2.27 (2.20–2.36)	0.86 (0.78–0.92)	0.64 (0.58–0.70)
High-income North America	−0.63 (−0.67 to −0.57)	−0.84 (−0.90 to −0.76)	−1.63 (−1.67 to −1.58)	−1.74 (−1.78 to −1.70)
Central Asia	−0.19 (−0.25 to −0.11)	−0.19 (−0.27 to −0.11)	−0.92 (−1.02 to −0.82)	−1.04 (−1.11 to −0.94)
East Asia	2.40 (2.33–2.46)	2.42 (2.37–2.47)	−0.21 (−0.24 to −0.18)	−0.15 (−0.18 to −0.12)
South Asia	2.01 (1.96–2.05)	2.07 (2.00–2.14)	1.14 (1.08–1.19)	1.07 (1.01–1.12)
Southeast Asia	1.95 (1.93–1.97)	1.91 (1.87–1.95)	0.88 (0.86–0.91)	0.83 (0.80–0.85)
Central Europe	0.94 (0.88–0.99)	0.94 (0.86–1.00)	−0.17 (−0.21 to −0.12)	−0.51 (−0.57 to −0.45)
Eastern Europe	0.70 (0.64–0.77)	0.82 (0.74–0.91)	−0.20 (−0.31 to −0.08)	−0.48 (−0.57 to −0.36)
Western Europe	0.08 (0.02–0.13)	−0.06 (−0.15 to 0.02)	−1.56 (−1.61 to −1.52)	−1.70 (−1.75 to −1.65)
Andean Latin America	1.99 (1.85–2.11)	1.76 (1.60–1.89)	0.17 (0.05–0.28)	0.14 (0.01–0.27)
Central Latin America	2.15 (2.11–2.20)	2.02 (1.97–2.08)	0.48 (0.42–0.55)	0.59 (0.52–0.67)
Southern Latin America	0.32 (0.26–0.38)	0.19 (0.11–0.26)	−0.99 (−1.05 to −0.93)	−1.04 (−1.11 to −0.98)
Tropical Latin America	1.45 (1.37–1.50)	1.21 (1.13–1.28)	0.07 (0.03–0.13)	0.16 (0.06–0.25)
Australasia	0.01 (−0.04 to 0.07)	−0.03 (−0.09 to 0.04)	−1.69 (−1.76 to −1.59)	−1.75 (−1.80 to −1.68)
Caribbean	0.76 (0.70–0.83)	0.70 (0.65–0.76)	0.04 (−0.03 to 0.11)	0.02 (−0.05 to 0.07)
North Africa and the Middle East	3.02 (2.97–3.07)	3.55 (3.48–3.61)	1.61 (1.55–1.66)	1.49 (1.43–1.54)
Oceania	0.32 (0.28–0.35)	0.33 (0.27–0.39)	0.37 (0.33–0.41)	0.38 (0.32–0.44)
Central Sub-Saharan Africa	1.41 (1.38–1.43)	1.45 (1.42–1.47)	0.96 (0.93–0.98)	0.93 (0.90–0.96)
Eastern Sub-Saharan Africa	1.42 (1.39–1.44)	1.36 (1.35–1.38)	0.85 (0.83–0.86)	0.75 (0.73–0.77)
Southern Sub-Saharan Africa	1.40 (1.28–1.50)	1.57 (1.45–1.68)	1.18 (1.07–1.28)	1.04 (0.91–1.17)
Western Sub-Saharan Africa	1.58 (1.57–1.60)	1.56 (1.53–1.59)	1.06 (1.04–1.08)	0.98 (0.95–1.00)

Table 2. The temporal estimated trends of prevalence, incidence, death, and DALYs associated with breast cancer during 1990–2021

AAPC, Average Annual Percent Change; SDI, socio-demographic Index; DALYs, disability-adjusted life-years.

in ASPR and ASIR were situated in Central Asia (Tajikistan, Kyrgyzstan), North America (United States of America, Canada), and North Europe (Denmark, Sweden) (Tables S8 and S9; Figures 2B, 2D, S4A, and S4B). According to AAPC of ASMR, a rise is observed in 131 countries, a decrease is seen in 63 countries, and stability is noted in 10 countries (Figure 2F). The global distribution of the AAPC for ASDR was familiar with that observed for ASMR (Figure 2H). ASMR and ASDR increased dramatically in Egypt, Turkey, Lesotho, Mauritius, and United Arab Emirates, with the relevant AAPCs and EAPCs exceeding 2.00 (Tables S8 and S9; Figures S4C and S4D). To be specific, Turkey stood out as the fastest-growing country in terms of ASPR, ASIR, ASMR, and ASDR.

Burden of breast cancer by age, health system, and social-development index

There was a global upward trend in the age-specific rates of prevalence, incidence, death, and DALYs as age increased (Figures S5A–S5D). The highest number of prevalence, incidence, death, and DALYs cases were found in the 55–59 age group (Figures S5E–S5H and S5A–S5D). The proportion of low and low-middle SDI categories in death and DALYs was higher compared to that percentage in prevalence and incidence. When examining the health system scale, a greater proportion of limited and minimal health systems was identified in relation to death and DALYs cases compared to prevalence and incidence cases (Figure S6).

On the SDI scale, the ASR trends among distinct SDI categories were illustrated in Figure S7. The correlation between ASPR and SDI exhibited a similar pattern to the relationship observed between ASIR and SDI. In both cases, a positive relationship was observed (Figures S7A and S7B).

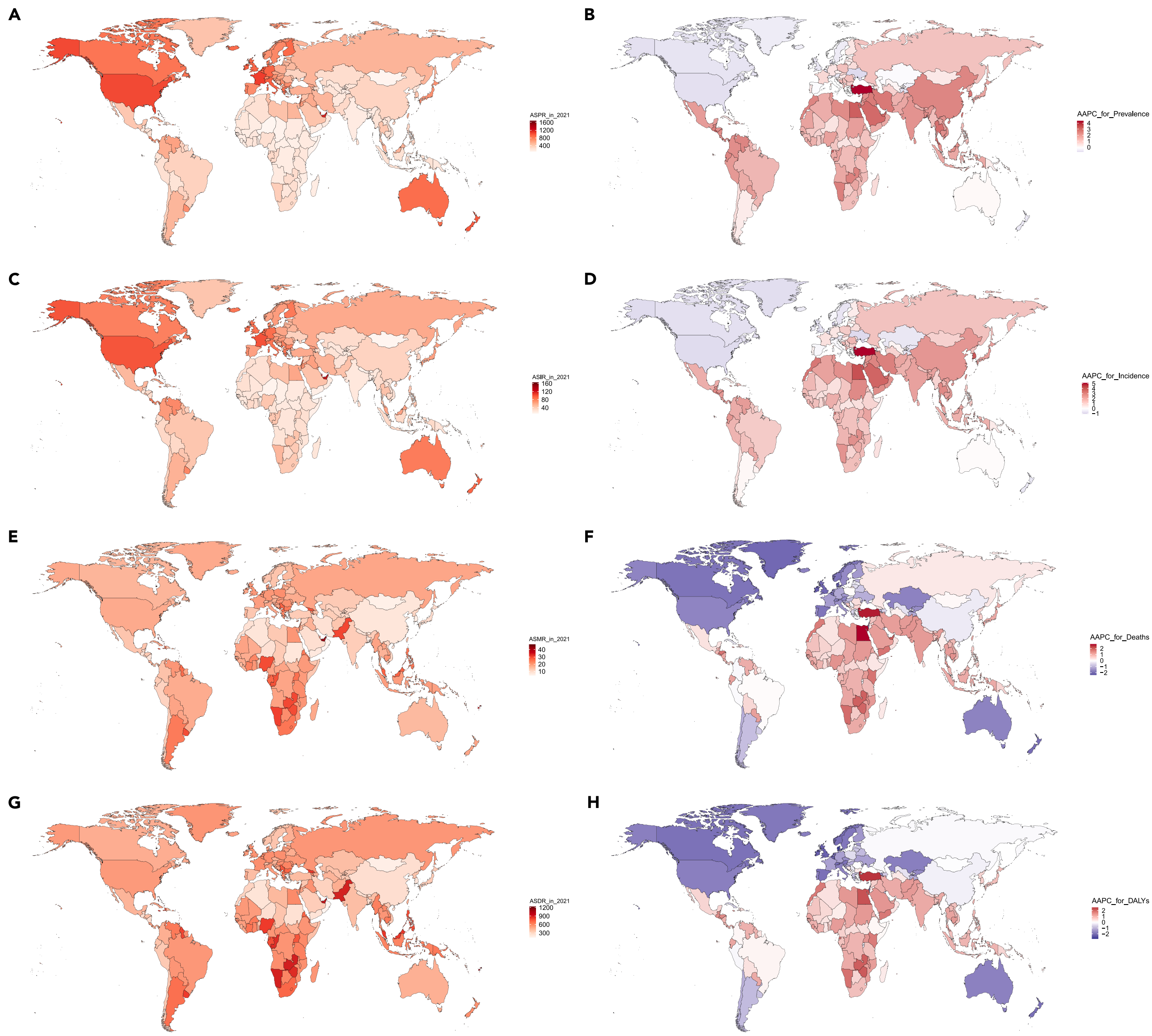

Figure 2. The global distribution of the age-standardized rates and AAPC for breast cancer

Age-standardized prevalence (A), incidence (C), death (E), and DALYs (G) rates for breast cancer in 2021. AAPC for age-standardized prevalence (B), incidence (D), death (F), and DALYs (H) rates. DALYs, disability-adjusted life-years. AAPC, Average annual percent change.

The fitted curve between ASRs (ASMR and ASDR) and SDI also shared an analogous shape (Figures S7C and S7D). A relative horizontal curve was observed in the GBD regions with an SDI below 0.5, an ascending curve in the GBD regions with an SDI of 0.5–0.7, and a declined curve in the GBD regions with SDI above 0.7. At the national level, there was a positive association between ASRs of prevalence and incidence and SDI (Figures 3A and 3B). The relationship between ASRs (ASMR and ASDR) and SDI presented a curved pattern resembling an inverted "V" (Figures 3C and 3D). A positive correlation was shown in countries with an SDI below 0.7, but an inverse relationship was found in nations with an SDI above 0.7. In the low and low-middle SDI countries, the relationship between the temporal change (EAPCs and AAPCs) and SDI presented a positive linkage. However, it revealed an inverse correlation in the middle, high-middle, and high SDI countries (Figure S8).

Breast cancer epidemiological drivers and risk factors

The changes in prevalence, incidence, death, and DALYs in breast cancer were explored by decomposition analysis at the whole world, as well as across various health systems and SDI categories (Figures 4, S9A and S9B). Globally, population growth accounted for 56.01% of the growth in incidence, followed by population aging at 26.72%, and changes in epidemiology at 17.27% (Figure 4A; Table S10). Both population growth and aging made positive contributions to the DALYs. However, the contribution of epidemiological changes had a negative impact on the

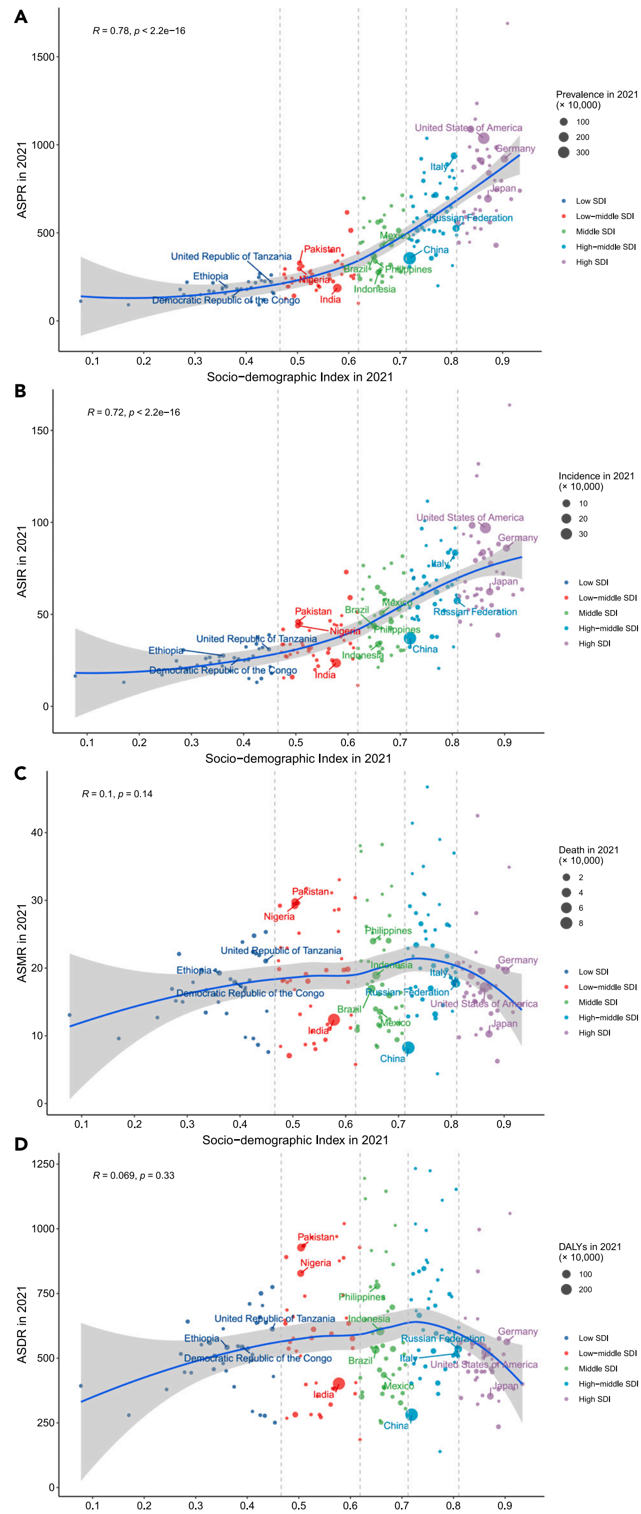

Figure 3. The relationship between age-standardized rates and SDI

(A–D) The correlation between the age-standardized prevalence (A), incidence (B), death (C), and DALYs (D) rates of breast cancer and SDI in 2021. SDI, socio-demographic index.

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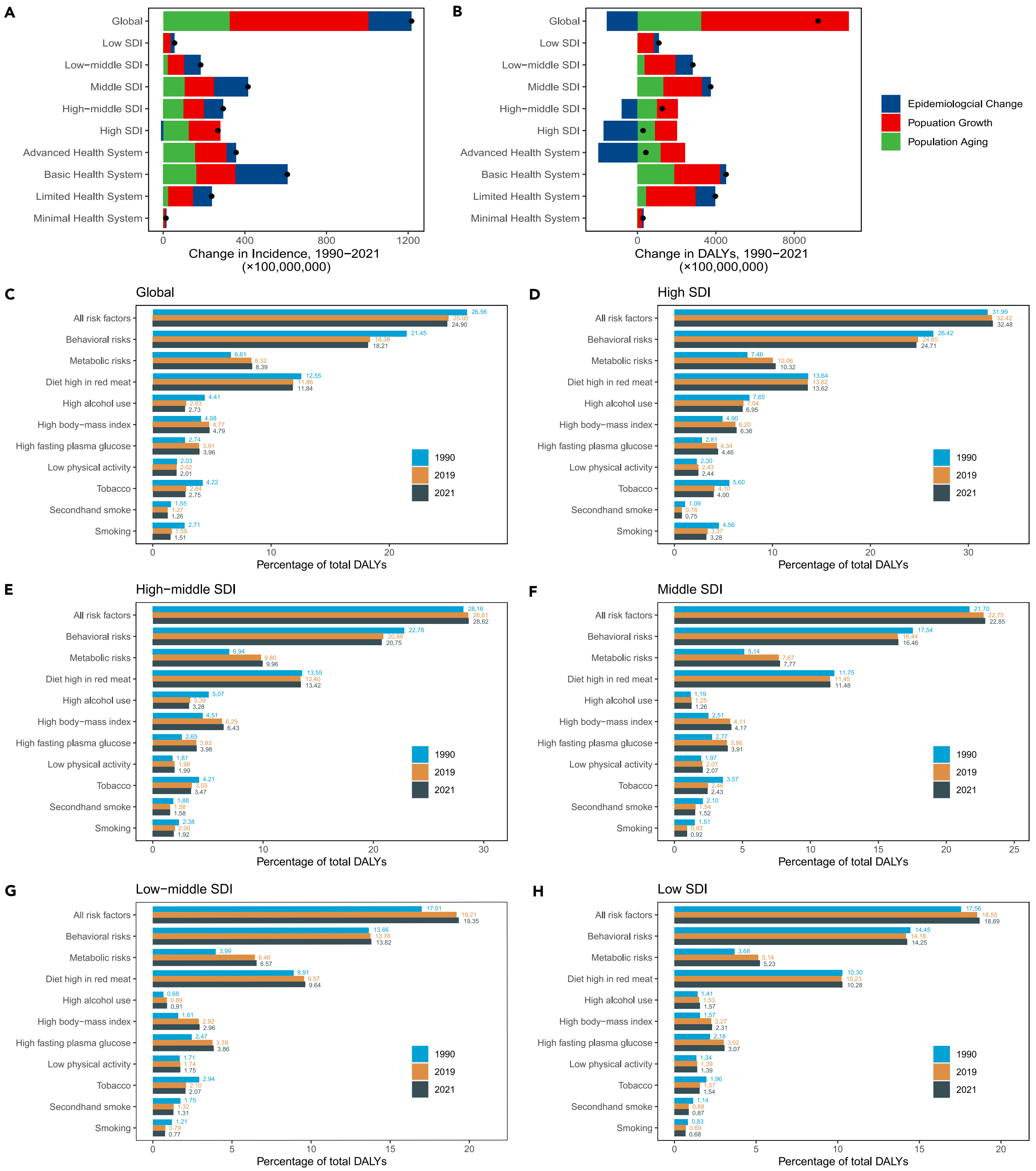

Figure 4. The decomposition analysis and the distribution of risk factors attributed to breast cancer

The change in incidence (A) and DALYs (B) associated with breast cancer across various SDI categories and health systems through decomposition analysis. The black dots represent the overall changes attributed to epidemiological factors, population growth, and population aging. The distribution of risk factors attributed to breast cancer in the world (C) and various SDI categories (D–H) in 1990, 2019, and 2021.

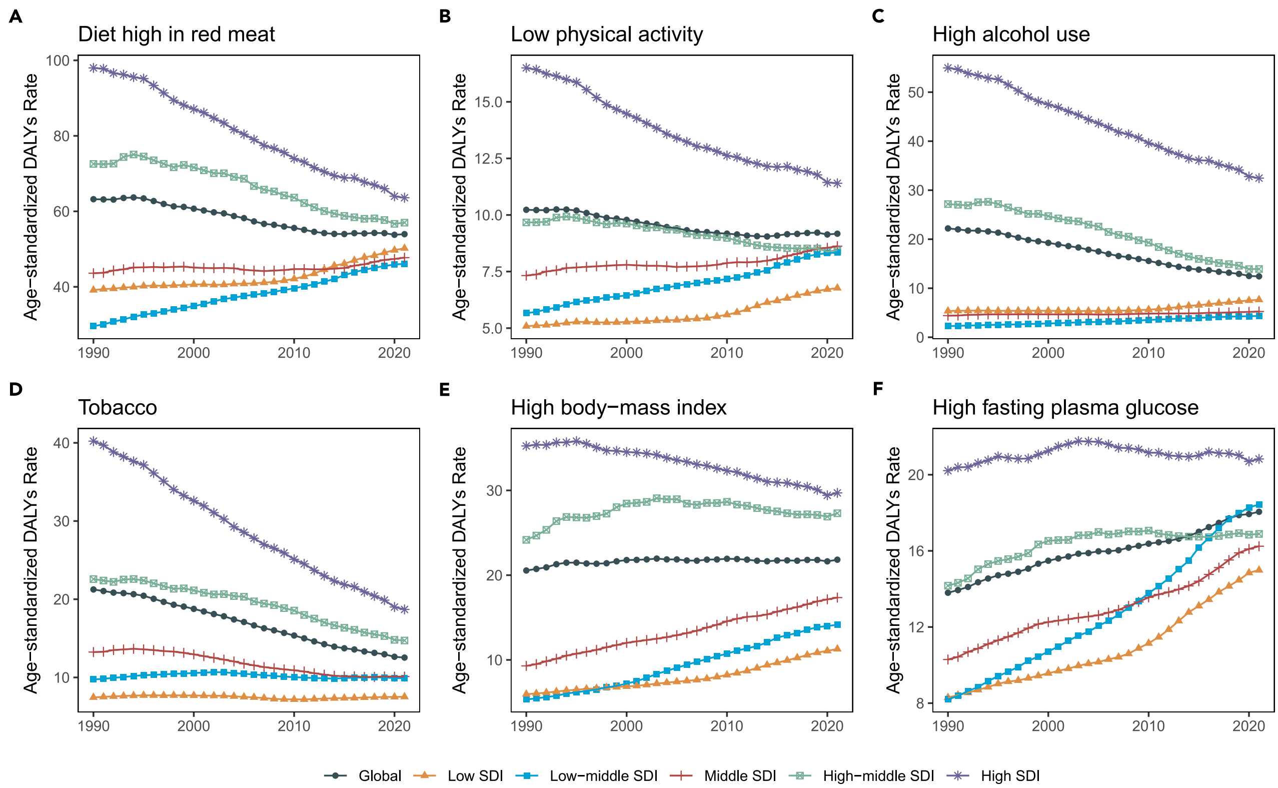

Figure 5. The temporal variation of breast cancer by different risk factors and SDI

(A–F) The age-standardized DALYs rates of breast cancer attributable to a diet high in red meat (A), low physical activity (B), high alcohol use (C), tobacco (D), high body-mass index (E), and high fasting plasma glucose (F) from 1990 to 2021 across different SDI categories.

DALYs (Figure 4B). At the SDI level, epidemiological changes influenced positively in the DALYs change in the low (23.06%), low-middle (30.85%), and middle (11.92%) SDI categories, but it played a negative role in high-middle and high SDI categories. In addition, epidemiological change was most pronounced for the total DALYs in the limited (24.87%) and minimal (21.97%) health systems. At the GBD regional level, we revealed a substantial disparity in the contributions of the three determinants to the change in prevalence, incidence, death, and DALYs (Figures S9C–S9F; Table S10).

Behavioral risks made the largest contribution (18.21%) to the DALYs globally in 2021. Metabolic risks, including high body mass index and high fasting plasma glucose, were responsible for 8.39% of total DALYs (Figure 4C). It was noteworthy that the proportion of metabolic risks in total DALYs increased numerically during 1990–2021. We also revealed the contribution of risk factors to the total DALYs at different SDI groups and health systems (Figures 4D–4H and S10).

Female breast cancer DALYs attributable to risk factors (level 3) varied by various SDI quintiles and health systems in 2021. 11.84% of the global breast cancer DALYs were attributable to a diet high in red meat, while 2.01% were ascribed to low levels of physical activity. The temporal trends of breast cancer DALYs associated with high red meat and low physical activity exhibited similarity. In low, low-middle, and middle SDI groups, there was a gradual increase of the DALYs for breast cancer attributed to these two dietary risks (Figures 5A and 5B). We observed an upward trend of the DALYs related to these two dietary risks in minimal and limited health systems (Figures S11A and S11B).

Alcohol use and tobacco resulted in 2.73% and 2.75% of total breast cancer DALYs, respectively. There was a dramatic decline in breast cancer associated with these two behavioral risks in the high and high-middle SDI groups, and a stable trend in the other SDI categories (Figures 5C and 5D). Although the worldwide DALYs of these diseases decreased from 1990 to 2021, it was notable that breast cancer DALYs related to high alcohol use increased slightly in the low SDI group and among minimal and limited health systems (Figures S11C and S11D).

High body mass index and high fasting plasma glucose accounted for 4.79% and 3.96% respectively of all the breast cancer DALYs in 2021. It demonstrated a noticeable increased trend of breast cancer associated with these two metabolic risks in the low, low-middle, and middle SDI groups (Figures 5E and 5F). Except for the relatively stable DALYs associated with these two risk factors in advanced health systems, there was a significant upward trend observed in other health systems (Figures S11E and S11F). The patterns of female breast cancer deaths related to aforesaid risk factors were consistent with that of DALYs (Figures S12 and S13).

DISCUSSION

In our study, we presented the spatiotemporal trends of female breast cancer and its associated risk factors over the past 32 years based on the latest GBD 2021 study. There was a total of 20.32 million prevalent cases, 2.08 million incident cases, 0.66 million deaths, and 20.26 million DALYs attributed to female breast cancer worldwide in 2021. In contrast to the ascending trend observed in ASPR and ASIR, ASMR and ASDR showed a downward trend globally. Based on the joinpoint analysis, our findings indicated that ASMR remained stable while ASDR increased slightly during 2012–2021. The paramount frequencies of prevalence, incidence, mortality, and DALYs were discernibly concentrated in the women aged 55–59.

We quantified the respective contributions of population aging, population growth, and epidemiological alterations to the disease burden through the decomposition analysis. It revealed that population aging and growth can be attributed to approximately 85% of the changes in prevalence and incidence, thereby further corroborating previous findings.[11] The remaining 15% change was attributed to actual prevalent and incident growth, which may be elucidated by organized mammographic screening programs, heightened public health awareness, as well as increased dietary, metabolic, and behavioral risk factors.[12–14] The incidence surge may primarily derive from estrogen receptor (ER) positive breast cancer, rather than its ER negative counterpart.[15,16] There were two plausible interpretations. Obesity was correlated with an approximate 40% escalation in the relative risk for ER positive postmenopausal breast cancer.[17] The ER positive breast cancer, known for its comparatively favorable prognosis, could be preferentially identified through regular mammographic screening.[18] In contrast to the positive contributions of population growth and aging, the epidemiological changes had a negative impact on the alteration of death and DALYs. The potential explanations may stem from three elements: the evolution in surgical philosophy, advancements in systemic treatment, and improvements in psychological and complementary therapies.[19–21]

Discrepancies in SDI and the health system resulted in different breast cancer burdens. There was an upward trajectory of ASPR, ASIR, ASMR, and ASDR in the low, low-middle, and middle SDI groups and the limited and minimal health system. ASPR and ASIR increased over the preceding 32 years in the high-middle SDI in the low SDI categories and the basic health system. The reproductive, lifestyle, and environmental risk factors may be the main reasons for the increased disease incidence.[22] Therefore, it is imperative to enhance the public awareness, improve the global health framework, and allocate medical resources efficiently. Academic publications should be coupled with mainstream media announcements to achieve increased public awareness.[23] To ensure the general public's understanding of health matters, online patient education materials should be composed at or below a 6th-grade reading level.[24] In addition, the healthcare paradigms established in China and Rwanda, such as the "Two cancers" screening program and Women's Cancer Early Detection Program, could potentially serve as replicable models for implementation in the resource-constrained countries.[25,26]

We demonstrated that the ASRs of female breast cancer evidenced a numerical decline in 2019–2020. At the beginning of 2020, the World Health Organization proclaimed COVID-19 as an immense challenge and a public health emergency for global health systems. The number of breast imaging, biopsy, and breast surgery declined significantly after the COVID-19 outbreak.[27] The COVID-19 pandemic resulted in the deferral of preventive measures, early detection, and initial intervention initiatives, contributing to this observable decrement in epidemiological trends.[28] Meanwhile, individuals diagnosed with breast cancer may have a higher susceptibility for contracting COVID-19. Patients with pre-existing malignancy who contracted COVID-19 had a higher mortality rate, not directly attributable to cancer, compared to their counterparts without cancer.[29] Moreover, there was a slight increase in the ASRs of global breast cancer cases during 2020–2021. The forthcoming data from GBD 2023 is anticipated to attain a more comprehensive understanding of the long-term consequences of the pandemic.

This study identified dietary risk (high red meat intake and low physical activity), behavioral risk (alcohol use and tobacco), and metabolic risk (high body mass index and high fasting plasma glucose) as significant risk factors for breast cancer, leading to a substantial portion of the disease burden. First, among all the risk factors, high red meat intake was the largest proportion of total ASMR and ASDR. High red meat intake, one prominent characteristic of the Western diet, was strongly associated with an elevated risk of both obesity and breast cancer.[30] Second, we demonstrated that the temporal trend of breast cancer burden related to behavioral risks was a more flattened or declining trajectory compared to that associated with other risk factors. Yet the hazards posed by tobacco and alcohol consumption to breast cancer cannot be overlooked. Third, the ASMR and ASDR of breast cancer attributed to metabolic risks were increased globally, especially in the low, low-middle, and middle SDI categories. BMI stood as the prevailing metric utilized to assess adiposity.[31] Cancer associated with obesity constituted a significant proportion, accounting for up to 55% of all cancer cases among women.[32] Moreover, metformin, an oral antidiabetic medication, shown potential as a therapeutic option for breast cancer in clinical practice according to several adjuvant and metastatic clinical trials.[33] The notable lifestyle changes over the past three decades encompassed unhealthy dietary practices, unfavorable behavior habits, and low physical activity, resulting in a rise in metabolic disorders, particularly in rapidly developing nations. Mediterranean diet, ketogenic diet, and low-carbohydrate diet may promote metabolic health and should be popularized, as they offer protection against cancer by mitigating hyperinsulinemia and hyperglycemia.[34]

In conclusion, the cases of prevalence, incidence, death, and DALYs of breast cancer increased globally from 1990 to 2021. It presented an ascending trend in ASPR and ASIR, while ASMR and ASDR showed a downward trend over the past 32 years. The ASDR increased slightly during 2012–2021. Further investigation should be warranted due to the highest annual percentage changes of ASRs observed in Turkey. Dietary, behavior, and metabolic risk factors should be controlled to diminish breast cancer burden, especially in countries with lower SDI or limited health systems. Our study offered compelling evidence concerning the global breast cancer burden, which was helpful for effective measure implementation, optimal resource allocation, and extensive international collaboration.

Limitations of the study

In the current study, we conducted a thorough investigation of the female breast cancer burden and its attributable risk factors from 1990 to 2021 at the global, regional, and national scales. Our findings provided valuable insights for governments, policymakers, and oncologists in shaping public policies, allocating limited resources, and reducing the overall burden of breast cancer. However, it is crucial to recognize and address several limitations. First, the variations in data collection methods and the quality of data sources across different countries unavoidably influence the reliability of our findings. But two vital improvements, the updated Bayesian algorithm, and the non-zero floor were used to reduce stochastic variation in the GBD 2021 study.[35] Second, the absence of clinicopathological parameters for breast cancer in the GBD 2021 database precluded us from exploring the spatiotemporal trends of different subtypes of the disease.

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Tian Lan (lan_tian_lt@163.com).

Materials availability

This study did not generate new unique reagents.

Data and code availability

- All data reported in this article will be shared by the lead contact upon request.
- This article does not report the original code.
- Any additional information required to reanalyze the data reported in this article is available from the lead contact upon request.

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AUTHOR CONTRIBUTIONS

Conceptualization, T.L., XY.S., and ZJ.H.; formal analysis, T.L., YY.L., JW.H., and CN.Z.; writing – original draft, T.L. and YY.L.; writing – review and editing, T.L. and YY.L.; visualization, T.L. and YY.L.; supervision, T.L., XY.S., and ZJ.H.

DECLARATION OF INTERESTS

The authors declare no competing interests.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS
- METHOD DETAILS
  - Data sources
- QUANTIFICATION AND STATISTICAL ANALYSIS

SUPPLEMENTAL INFORMATION

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and algorithms		
R Version 4.2.2	R Foundation, USA	https://www.r-project.org/
R studio 2024.04.2	Posit, USA	https://posit.co/downloads/

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

All data used in this study were obtained from the Global Burden of Disease (GBD) database.

METHOD DETAILS

Data sources

The data (the number and corresponding age-standardized rate of prevalence, incidence, deaths, and DALYs) pertaining to breast cancer was obtained from the GBD 2021 database (https://ghdx.healthdata.org/gbd-2021). The SDI, which ranged from 0 to 1, functioned as a comprehensive index of the overall fertility rate, educational attainment, and per capita income. Countries and territories were systematically categorized into five sub-regions based on their respective SDI classifications: low, lower-middle, middle, upper-middle, and high tiers. Furthermore, there were four distinct health system tiers, namely advanced, basic, limited, and minimal health systems.

QUANTIFICATION AND STATISTICAL ANALYSIS

All estimations derived from the GBD 2021 study were evaluated, accompanied by a 95% uncertainty interval (UI). Age-standardized rates (ASRs, per 100,000 population), including age-standardized prevalence rate (ASPR), age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), and age-standardized disability-adjusted life years rate (ASDR), were calculated based on the following formula.

$$ASR = \frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} w_i} \times 100000$$

In this equation, a_i denoted the age specific rate of age group i in the population, w_i was the number of persons in the age group i. ASRs manifested the more precise epidemiological assessments by accounting for variations in age structures. The trends in ASRs can effectively serve as reliable indicators of diseases change, as supported by previous literatures.[36,37] We computed the estimated annual percentage change (EAPC) and average annual percentage change (AAPC) of ASRs to assess these trends. The supposition was a linear correspondence between the natural logarithm of ASRs and temporal progression. This relationship was encapsulated by the following equation.

$$Y = a + \beta X + \varepsilon$$

Y represented ln (ASR), X symbolized the year, and ε was synonymous with the error term. The EAPC was ascertained as 100×(exp(β)-1), while the 95% confidence interval (CI) was deduced concomitant with this linear regression framework. The joinpoint analysis was conducted to determine the annual percentage change (APC) and the correlated 95% CI, utilizing the jpCommand software (Version 5.02) alongside the R package "nih.joinpoint". The equation used to calculate AAPC was set as follows,

$$AAPC = \left\{ \exp\left(\frac{\sum w_i b_i}{\sum w_i} \right) \right\} \times 100$$

where b represented the coefficient for the segment, w_i denoted the length of the segment, i referred to the specific ith segment.

A decomposition analysis, inspired by Das Gupta's methodology, was employed to deepen the understanding of discrepancies in disease burden.[38] This methodology ascribed variations in prevalence, incidence, deaths, and DALYs to the combined influences of three elements, such as epidemiological changes, population aging, and population size. Pearson's correlation analysis was conducted to evaluate the interrelation between the ASRs estimates and SDI in 2021. All statistical visualizations and computations were conducted using the R program (Version 4.2.2, R core team).