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Global, regional, and national burden of breast, cervical, uterine, and ovarian cancer and their risk factors among women from 1990 to 2021, and projections to 2050: findings from the global burden of disease study 2021

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Abstract

Background Female breast cancer, cervical cancer, uterine cancer, and ovarian cancer (FBCUO) pose a significant threat to global public health. Data from the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) 2021 provide critical insights that can guide the understanding and management of these cancers. Our study aims to offer comprehensive global, regional, and national estimates of the FBCUO cancer burden and its attributable risk factors from 1990 to 2021, as well as project future incidence trends up to 2050. These projections are essential for developing targeted prevention and control strategies, thereby informing more effective public health interventions.

Methods Incidence, age-standardised incidence rate (ASIR), deaths, age-standardised mortality rate (ASMR), disability-adjusted life years (DALYs), age-standardised rate of DALYs (ASDR), and the burden due to risk factors associated with FBCUO cancer were analysed from 1990 to 2021, and the Bayesian APC model was utilized for forecasting future epidemiological trajectories. All statistical analyses were performed using Join-point software (version 4.9.1.0).

Results Between 1990 to 2021, the global incidence, death, and DALYs, of female breast, cervical, uterine and ovarian cancer both to varying degrees of elevation. However, the ASMR and ASDR both showed a decreasing trend for FBCUO cancer. In 2021, diet high in red meat was a major risk factor for female breast cancer DALYs, but the attributable ASDR for diet high in red meat decreased from 1990 to 2021. Unsafe sex was the leading risk factor for cervical cancer DALYs, high body-mass index were the leading risk factor for uterine cancer and ovarian cancer. Projections indicate a global increase in the total number of female breast cancer and ovarian cancer cases from 2021 to 2050. In contrast, both cervical cancer and uterine cancer are expected to show downward trends over the same period.

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Conclusions The burden attributable to FBCUO cancers has increased significantly in female populations from 1990 to 2021, underscoring the urgent need for targeted measures to mitigate this trend. Meanwhile, Annual Percentage Change (APC) analysis indicates that the age-standardized incidence rates (ASIR) for female breast and ovarian cancers may continue to rise from 2022 to 2050. This projection highlights the importance of timely interventions to address these growing challenges.

Keywords Female breast cancer, Cervical cancer, Uterine cancer, Ovarian cancer, Risk factors, Incidence, Mortality, Disability–adjusted life years

Introduction

Cancer remains one of the most pressing challenges for public health, society, and the global economy in the twenty-first century. A recent study has underscored the disproportionate impact of cancer mortality on women, revealing that nearly half of all orphans worldwide are due to maternal deaths from breast or cervical cancer [1]. This statistic highlights the profound social and familial consequences of these diseases. According to data from the International Agency for Research on Cancer (IARC), in 2022, there were an estimated 3,294,316 new cases of breast, cervical, and ovarian cancer, representing 16.5% of all diagnosed cancers globally. Moreover, these cancers resulted in 1,220,712 deaths, accounting for 12.6% of all cancer-related fatalities [2]. The incidence and mortality rates associated with these malignancies not only pose a significant threat to women's health and longevity but also impose a considerable economic burden on healthcare systems and societies at large. Addressing this challenge requires comprehensive strategies that encompass prevention, early detection, treatment, and support for affected individuals and their families.

Regarding the risk factors for female-specific cancers—breast, cervical, uterine, and ovarian—several key elements stand out. Family history and inherited mutations in the BRCA1 and BRCA2 genes are particularly significant for breast and ovarian cancers [3]. Additionally, long-term exposure to estrogen, obesity, smoking, alcohol consumption, and physical inactivity are important contributors to the development of these malignancies [4]. The prevalence and impact of these risk factors can vary significantly across different regions and populations [5], underscoring the need for tailored prevention strategies. Understanding the latest trends and burdens associated with these risk factors is crucial for developing effective interventions and mitigating the overall impact of female-specific cancers. Comprehensive research into regional variations and population-specific influences can inform more targeted screening programs, early detection methods, and personalized treatment approaches, ultimately improving outcomes and reducing the global burden of these diseases.

In this study, we analyzed data from the 2021 Global Burden of Disease, Injuries, and Risk Factors Study (GBD) to investigate trends in the incidence, mortality, and associated risk factors for female breast, cervical, uterine, and ovarian cancers (FBCUO) at regional and national levels from 1990 to 2021. Our goal was to assess the patterns and trends in the incidence, mortality, and disability-adjusted life years (DALYs) related to these cancers within women's cancer associations. By doing so, we aim to provide valuable insights that can inform more targeted screening programs and enhance preventive measures. This will also contribute to the formulation of pertinent policies and strategies. Ultimately, our work seeks to improve women's reproductive health and the overall well-being of populations by addressing their specific needs. However, it is important to recognize the limitations of our study, due to limited data access, we used data from the GBD database for 2021 only to estimate the cancer burden in women; second, many countries in the GBD database (especially low- and middle-income countries) did not have raw data and some data were missing; and the risk factors considered were limited to those included in the database and may not have covered all relevant risk factors. In addition, our study focused on female breast, cervical, uterine, and ovarian cancers, excluding other types of female cancers and specific tumor pathologies. These may have influenced our findings.

Methods

Data source

This study leverages data from the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) 2021, which evaluates health risks associated with 371 diseases, injuries, and 88 risk factors [6]. Our analysis focused on female breast, cervical, uterine, and ovarian (FBCUO) cancers across all age groups from 1990 to 2021. However, since the GBD 2021 does not include data on FBCUO cancer burden for individuals under 15 years old, our primary focus was on those aged 15 and older.

We collected comprehensive data on incidence, mortality, and disability-adjusted life years (DALYs) for FBCUO cancers, along with their corresponding 95% uncertainty intervals (UIs). All estimates used in this study are publicly available through the GBD Results Tool at http://ghdx.healthdata.org/gbd-results-tool. The international classification of disease (ICD) codes for these four cancers, as defined in the GBD 2021, are provided in the supplementary appendix (Table S1).

All estimates for this study are stratified by age, location, population, and nation, covering the period from 1990 to 2021. The GBD database encompasses 21 GBD regions and 204 countries or territories, classified into quintiles based on the Socio-Demographic Index (SDI). The SDI is a composite measure that reflects a country's overall social and economic development, incorporating per capita income, total fertility rate (for those under 25 years), and average educational attainment (for those aged 15 years and older) [7, 8]. The regional division of the SDI can be obtained from the Institute for Health Metrics and Evaluation (IHME) at https://ghdx.healthdata.org/search/site/SDI.

Age-period-cohort (APC) model analysis

The Age-Period-Cohort (APC) model is widely recognized as an advanced research methodology that surpasses traditional analytical approaches in health and socioeconomic development studies. This model enables the determination of both net drift, representing overall time trends, and local drift, capturing specific temporal variations, while quantifying the influence of three fundamental time dimensions: age, period, and birth cohort [9–11].

To calculate the age effect, period effect, and cohort effect, we utilize intrinsic estimator (IE) methods which allow for unbiased estimation of these effects by overcoming the identification problem inherent in APC models. Specifically, the age effect is determined by analyzing the differences in AHE incidence rates across various age groups within the same period and birth cohort, reflecting changes due to biological aging or life stage. The period effect is calculated by examining deviations in AHE incidence rates during different time periods, regardless of age or birth cohort, which may be influenced by factors such as medical advancements, public health policies, or environmental changes. Lastly, the cohort effect is estimated by observing variations in AHE incidence among individuals born in different years, accounting for unique exposures or characteristics shared by a birth cohort throughout their lifetime.

In this study, we employed the APC model to analyze trends in AHE incidence across different age groups, time periods, and birth cohorts. The APC model provides a comprehensive view of AHE incidence rates and their trends, identifying shifts in disease patterns across various age groups, periods, or birth cohorts. By isolating the independent effects of age, period, and cohort, the model can hypothesize how changes in factors such as lifestyle, medical advancements, and environmental conditions influence AHE incidence, offering a more nuanced understanding of the underlying drivers of disease trends. Additionally, the APC model reveals epidemiological shifts in AHE and analyzes how socioeconomic factors impact its onset through different birth cohorts and time periods, which is crucial for understanding the broader determinants of health. Ultimately, the APC model enhances our understanding of AHE epidemiology, helping to identify potential gaps in disease prevention, control, and treatment strategies, and supports the development of more targeted and effective public health interventions.

Statistical analysis

Joinpoint regression is a statistical method used to analyze trend changes in time series data by identifying "joinpoints" that split the data into multiple phases, each with its own annual percent change (APC). In this study, we utilized the Joinpoint software (version 4.9.1.0, https://surveillance.cancer.gov/joinpoint/), developed by the National Cancer Institute's Division of Cancer Control and Population Sciences, to perform this analysis. To assess the rate trends, we applied a log-linear joinpoint regression model ($\ln y = xb$) to calculate the APC along with its 95% confidence interval (CI). The mean annual percent change (AAPC) was then computed based on the APC trends over the specified time frame. An upward trend is indicated when both the AAPC estimate and its 95% CI upper and lower bounds are greater than zero. Conversely, a downward trend is identified if both the AAPC estimate and its 95% CI limits are less than zero.

For visual representation of the results, we used the R software package (version 4.4.2) to generate the figures.

Results

Burden of female breast, cervical, uterine, ovarian cancer in 2021

In 2021, the total incidence of female breast cancer was 2.0 million (95% UI, 1.9–2.2). Total deaths were 0.6 million (0.6–0.7). Female breast cancer contributed 20.2 million (18.9–21.5) DALYs in 2021. The total incidence of cervical cancer was 0.6 million (0.6–0.7), and total deaths were 0.2 million (0.2–0.3), and cervical cancer contributed 9.9 million (9.0–10.7) DALYs in 2021. The total incidence of uterine cancer was 0.4 million (0.4–0.5), and total deaths were 0.09 million (0.08–0.10), and uterine cancer contributed 2.5 million (2.2–2.8) DALYs in 2021. The total incidence of ovarian cancer was 0.2 million (0.2–0.3), and total deaths were 0.1 million (0.1–0.2), and ovarian cancer contributed 5.1 million (4.6–5.6) DALYs in 2021 (Table S2).

In 2021, the ASIR of female breast cancer was 46.4 (95% UI, 43.3–49.6) per 100,000, cervical cancer was 15.3 (14.1–16.7) per 100,000, uterine cancer was 10.4 (9.4–11.2) per 100,000, and ovarian cancer was 6.7 (6.1–7.3) per 100,000. The ASMR of female breast cancer was 14.5 (13.5–15.6) per 100,000, cervical cancer was 6.6 (6.1–7.2) per 100,000, uterine cancer was 2.1 (1.9–2.3) per 100,000, and ovarian cancer was 4.1 (3.7–4.4) per 100,000 per 100,000. The ASDR for female breast cancer was 455.6 (426.6–485.3) per 100,000, cervical cancer was 226.3 (206.5–246.9) per 100,000, uterine cancer was 56.1 (50.1–62.4) per 100,000, and ovarian cancer was 115.1 (104.6–125.2) per 100,000 (Table S3, Figure S1, Figure S2, Figure S3, and Figure S4).

The regions with the highest ASIR for female breast cancer in 2021 were those in the High SDI quintile. Conversely, the highest ASMR and ASDR for female breast cancer in 2021 were observed in the Low SDI quintile. Specifically, Monaco recorded the highest ASIR at 163.8 (95% UI, 120.6–221.9), Palau reported the highest ASMR at 46.7 (36.9–59.3), and American Samoa had the highest ASDR at 1232.9 (966.4–1529.4) (Fig. 1 and Table S3).

The regions with the highest ASIR, ASMR, and ASDR for cervical cancer in 2021 were the Low SDI quintile. Kiribati had the highest ASIR, ASMR, and ASDR (Fig. 2 and Table S3). Meanwhile, the regions with the highest ASIR, ASMR, and ASDR for uterine and ovarian cancer in 2021 were the High SDI quintile, and the United Arab Emirates had the highest ASIR, ASMR, and ASDR for both uterine and ovarian cancer (Fig. 3, Fig. 4 and Table S3).

For female breast cancer, the incidence, death, and DALYs numbers peaked at 55–59 years. The highest age group for the ASIR was 85–89 years, and the ASMR and ASDR)peaked at 95 + years (Fig. 5). For cervical cancer, the incidence and DALYs numbers peaked at 50–54 years, while deaths peaked at 55–59 years. The highest age group for ASIR and ASDR was 55–59 years, and ASMR peaked at 95 + years (Fig. 6). For uterine cancer, the incidence peaked at 60–64 years, while deaths and DALYs numbers peaked at 65–69 years. The highest age group for ASIR and ASDR was 70–74 years, and ASMR peaked at 95 + years (Fig. 7). For ovarian cancer, the incidence and DALYs numbers peaked at 55–59 years, while deaths peaked at 65–69 years. The highest age group for ASIR was 90–94 years, ASMR peaked at 95 + years, and ASDR peaked at 70–74 years (Fig. 8).

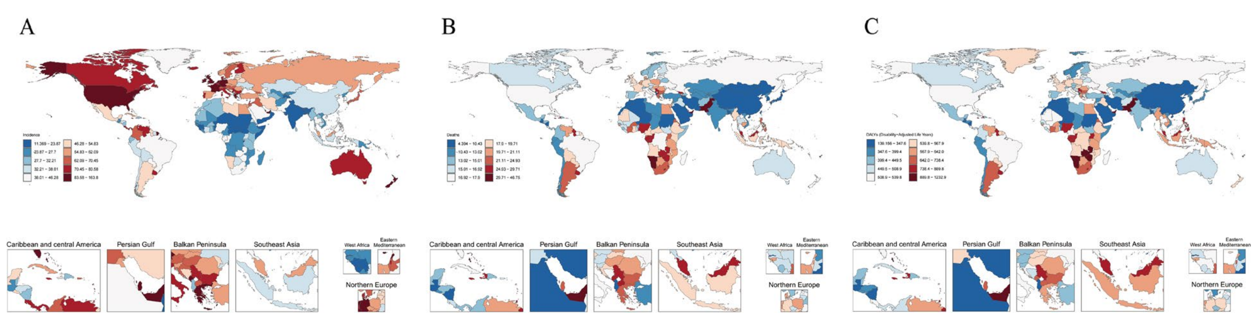

Fig. 1 Age-standardised incidence (**A**), mortality (**B**) and DALYs rate (**C**) of female breast cancer in 204 countries around the world. DALYs, disability-adjusted life-years

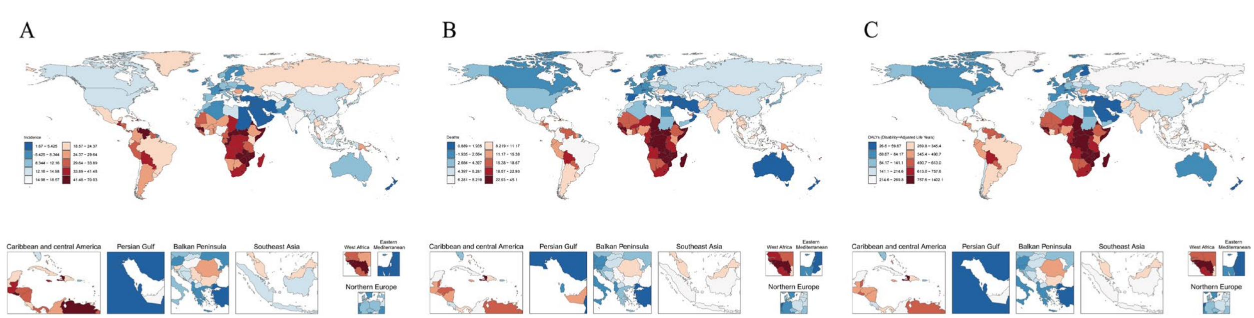

Fig. 2 Age-standardised incidence (**A**), mortality (**B**) and DALYs rate (**C**) of cervical cancer in 204 countries around the world. DALYs, disability-adjusted life-years

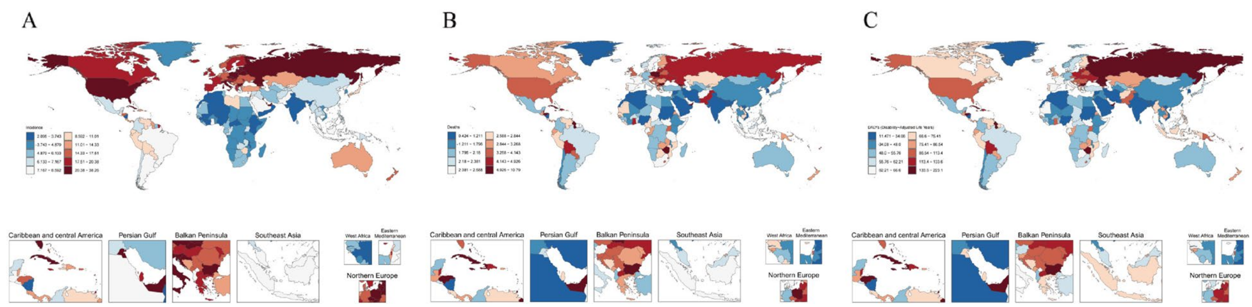

Fig. 3 Age-standardised incidence (**A**), mortality (**B**) and DALYs rate (**C**) of uterine cancer in 204 countries around the world. DALYs, disability-adjusted life-years

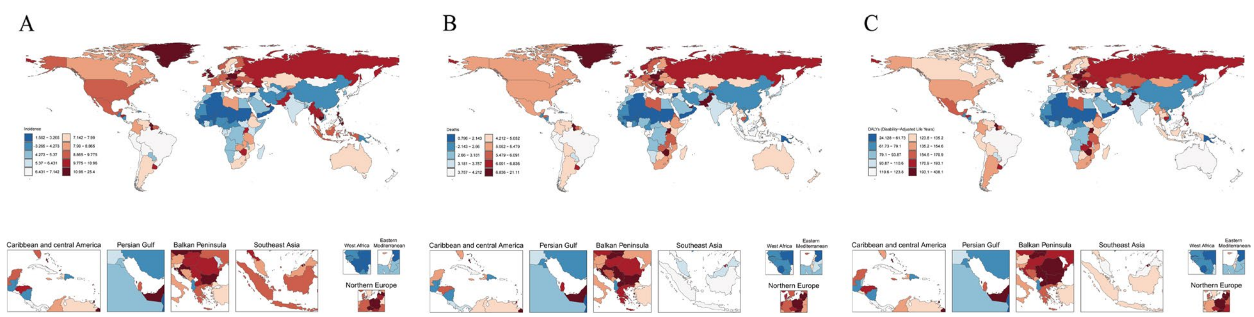

Fig. 4 Age-standardised incidence (**A**), mortality (**B**) and DALYs rate (**C**) of ovarian cancer in 204 countries around the world. DALYs, disability-adjusted life-years

The trend of female breast cancer burden from 1990 to 2021

From 1990 to 2021, the incidence number of female breast cancer increased from 0.8 million (95% UI, 0.8–0.9) to 2.0 million (1.9–2.2), marking 140.5% (126.5–156.4) increase. The number of deaths due to female breast cancer increased by 88.5% (77.6–99.9), from 0.3 million (0.3–0.3) to 0.6 million (0.6–0.7). DALYs increased from 11.0 million (10.4–11.6) to 20.2 million (18.9–21.5), an increase of 83.5% (71.5–96.5).

From 1990 to 2021, the overall global ASIR for female breast cancer has trended upward (AAPC, 0.4 [95% CI, 0.3–0.5]). Additionally, the ASIR has shown a increasing trend in all four SDI quintiles except for the high SDI region. Meanwhile, among the 204 countries and regions worldwide, only 22 countries or regions have experienced a declining trend in the ASIR of female breast cancer (Table S4).

The ASMR of female breast cancer showed an overall decreasing trend (AAPC, -0.5 [95% CI, -0.6 to -0.5]). Specifically, the ASMR for high SDI quintile (-1.5 [-1.5 to -1.4]) and high-middle SDI quintile (-0.9 [-1 to -0.8]) has decreased. In contrast, the ASMR for female breast cancer showed increasing trends across the middle, low-middle and low SDI quintiles (Table S4).

Similarly, the ASDR of female breast cancer showed an overall decreasing trend (AAPC, -0.5 [95% CI, -0.5 to -0.4]). Specifically, the ASDR for high SDI quintile (-1.5 [-1.5 to -1.4]) and high-middle SDI quintile (-0.1 [-1 to -0.9]) has decreased. In contrast, the ASMR for female breast cancer showed increasing trends across the middle, low-middle and low SDI quintiles (Table S4).

From 1990 to 2021, the incidence of female breast cancer,divided into 5-year age groups, showed a decreasing trend in 75–79 years and 80–84 years groups, and an increasing trend in other age groups. The most pronounced increase were in the 15–19 years and 20–24 years groups (there have the same AAPC, 2.2 [95% CI, 2.1–2.3]), while the most significant decrease was seen in the 80–84 years group (AAPC, -0.2 [-0.3–0.0]). Female breast cancer mortality and DALYs rate showed a decreasing trend among individuals aged ≧35 years, a flat trend in the 30–34 years group, and an increasing trend in those aged < 30 years. Mortality and DALYs rates increased most significant for ages 15–19 (ASMR AAPC, 1.4 [1.3–1.5]; ASDR AAPC, 1.4 [1.3–1.5]), and 20–24 (ASMR AAPC, 1.4 [1.2–1.5]; ASDR AAPC, 1.4[1.3–1.5]). The 75–79 years group had the most significant decrease in mortality rate (AAPC, -0.8 [-0.8 to -0.7]). DALYs rates decreased most significantly for ages 75–79 (AAPC,

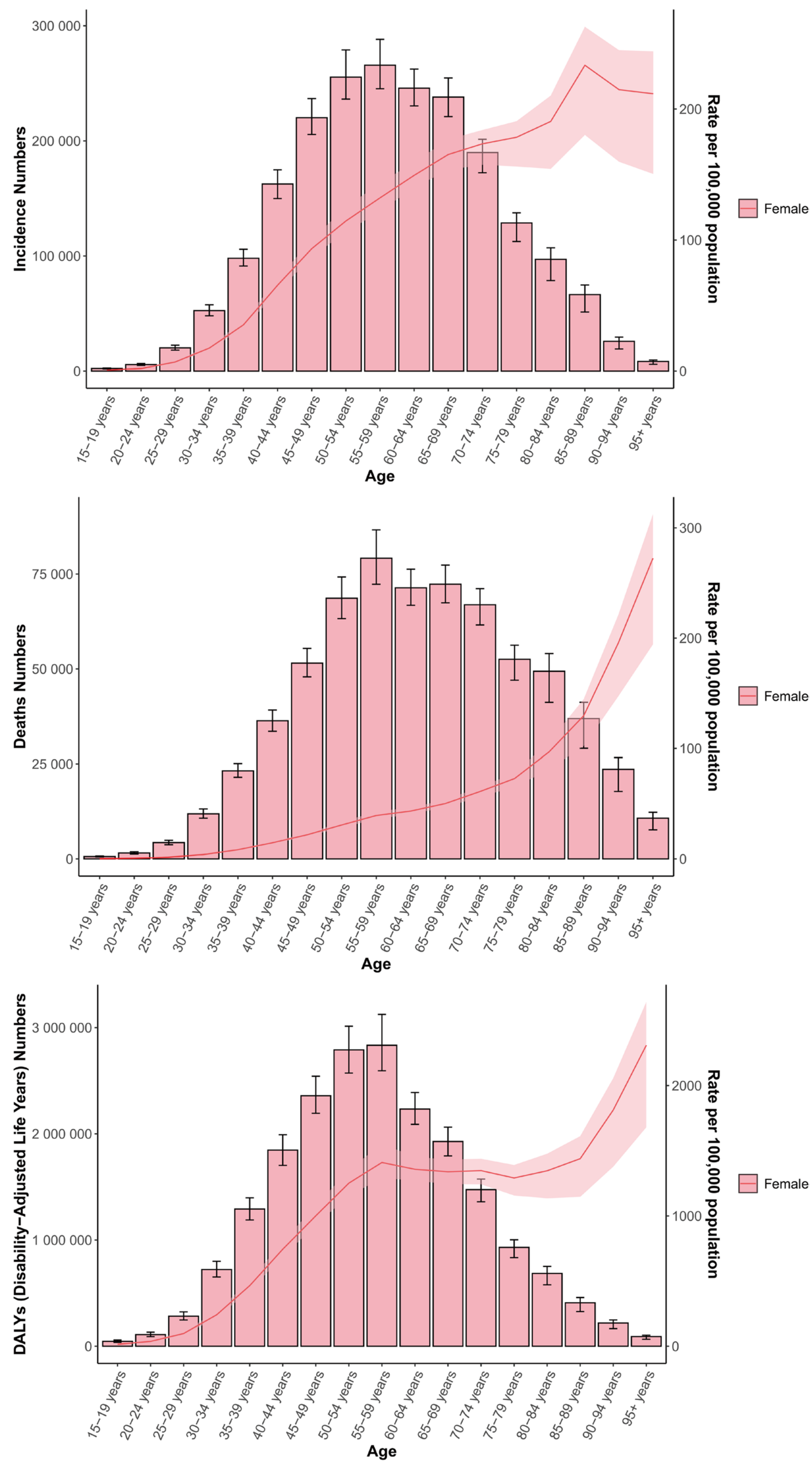

Fig. 5 The age-specific burden of female breast cancer, incidence and age-standardised incidence rate (**A**), deaths and age-standardised mortality rate (**B**), DALYs and age-standardised DALYs rate (**C**), in 2021

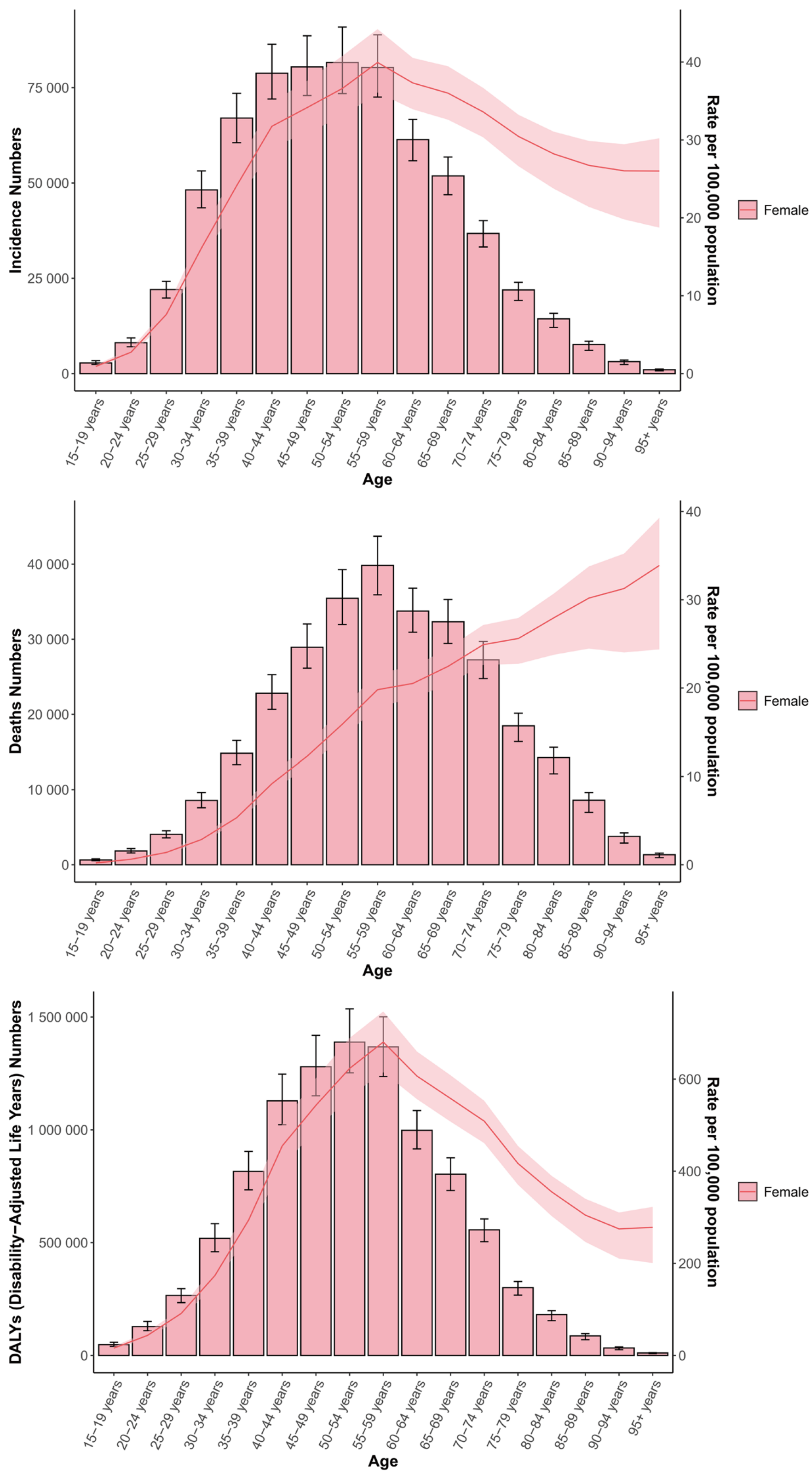

Fig. 6 The age-specific burden of cervical cancer, incidence and age-standardised incidence rate (**A**), deaths and age-standardised mortality rate (**B**), DALYs and age-standardised DALYs rate (**C**), in 2021

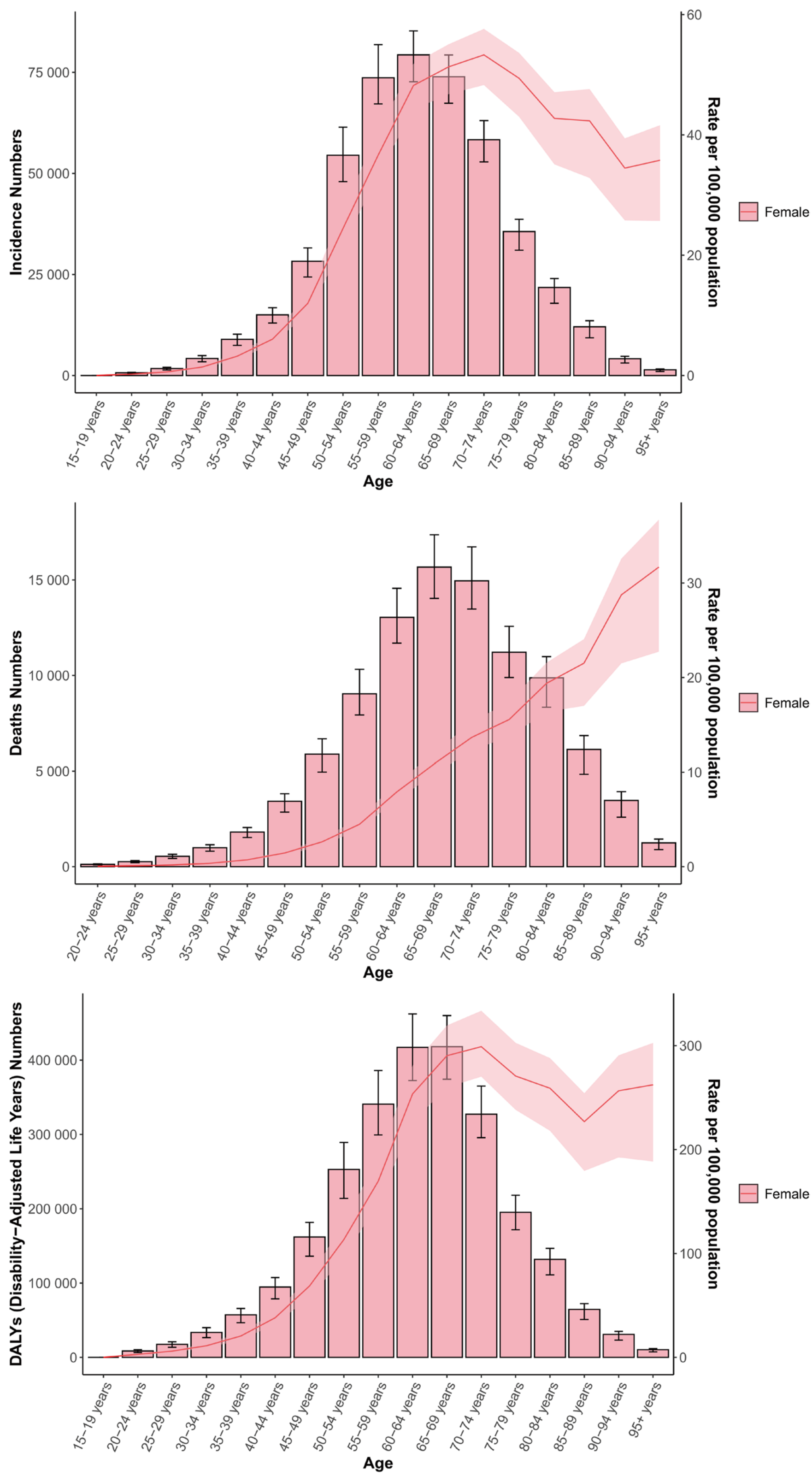

Fig. 7 The age-specific burden of uterine cancer, incidence and age-standardised incidence rate (**A**), deaths and age-standardised mortality rate (**B**), DALYs and age-standardised DALYs rate (**C**), in 2021

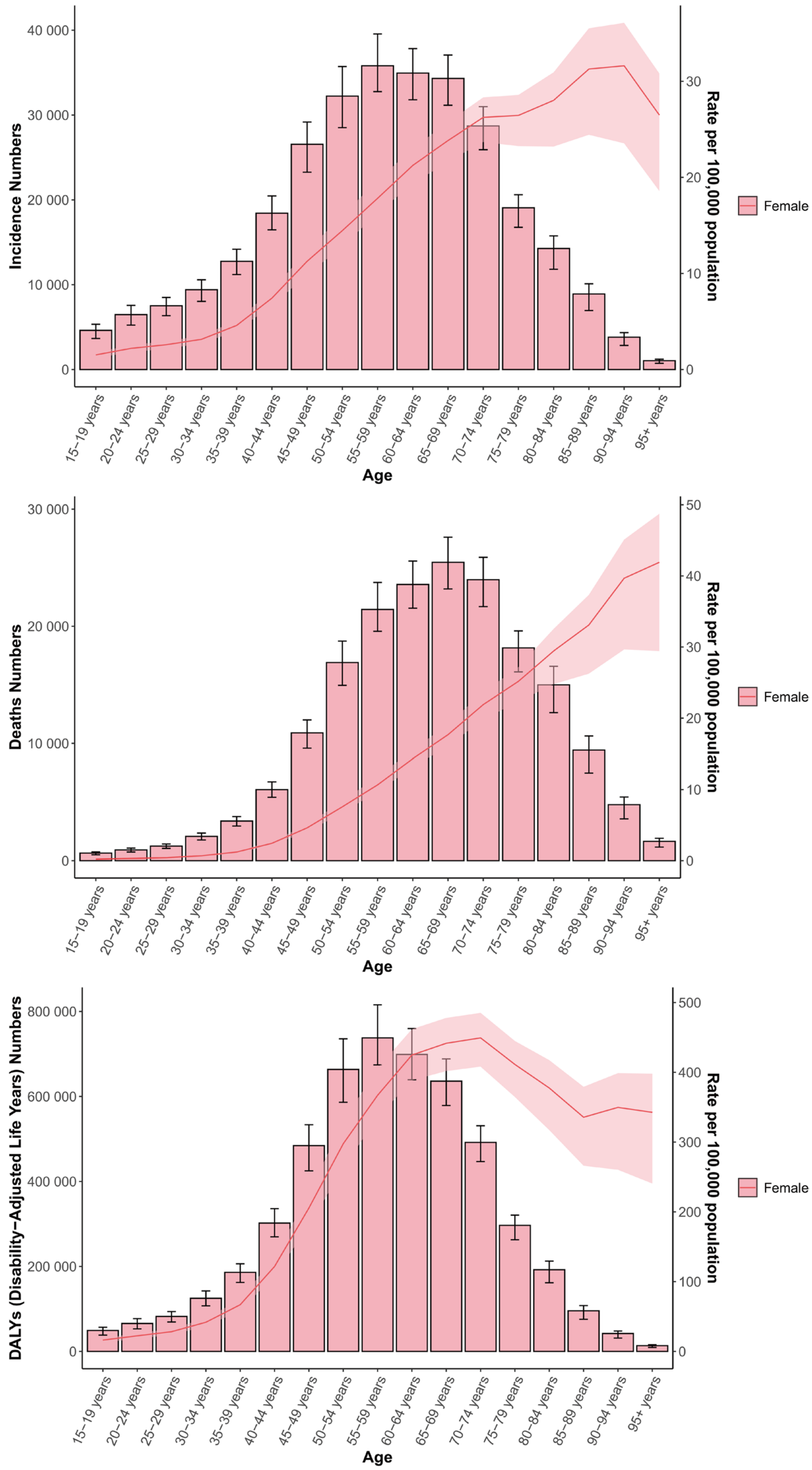

Fig. 8 The age-specific burden of ovarian cancer, incidence and age-standardised incidence rate (**A**), deaths and age-standardised mortality rate (**B**), DALYs and age-standardised DALYs rate (**C**), in 2021

-0.7 [-0.8 to -0.6]), and 80–84 (AAPC, -0.7 [-0.7 to -0.6]) (Table 1).

The trend of cervical cancer burden from 1990 to 2021

From 1990 to 2021, the incidence number of cervical cancer increased from 0.4 million (95% UI, 0.3–0.4) to 0.6 million (0.6–0.7), marking 62.9% (47.9–79.2) increase. The number of deaths due to cervical cancer increased by 40.2% (27.1–54.7), from 0.2 million (0.1–0.2) to 0.2 million (0.2–0.3). DALYs increased from 7.4 million (6.8–8.0) to 9.9 million (9.0–10.7), an increase of 33.6% (20.4–47.9).

From 1990 to 2021, the overall global ASIR for cervical cancer has trended downward (AAPC, -0.5 [95% CI, -0.6 to -0.4]). Additionally, the ASIR has shown a decreasing trend in all four SDI quintiles except for the high-middle SDI quintile. Meanwhile, among the 204 countries and regions worldwide, only 35 countries or regions have experienced a increasing trend in the ASIR of cervical cancer (Table S4).

The ASMR of cervical cancer showed an overall decreasing trend (AAPC, -1.3 [95% CI, -1.4 to -1.2]). Meanwhile, the ASMR for all SDI quintiles has decreased. At the regional and national levels, only 19 countries or regions have experienced a increasing trend in the ASIR of cervical cancer(Table S4).

Similarly, the ASDR of cervical cancer showed an overall decreasing trend (AAPC, -1.3 [95% CI, -1.4 to -1.2]), and the ASMR for all SDI quintile has decreased. At the regional and national levels, only 15 countries or regions have experienced a increasing trend in the ASDR of cervical cancer(Table S4).

From 1990 to 2021, the incidence of cervical cancer,divided into 5-year age groups, showed a increasing trend in 20–24 years group, and a decreasing trend in other age groups. The only increase were in the 20–24 years group (AAPC, 0.1 [95% CI, 0.0–0.2]), while the most significant decrease was seen in the 85–89 years (AAPC, -0.9 [-1.0 to -0.9]), and 90–94 years (AAPC, -0.9 [-0.9 to -0.8]) groups. Cervical cancer mortality and DALYs rate showed a decreasing trend among all of age groups. Mortality rate decreased most significant for ages 50–54 (AAPC, -1.5 [-1.6 to -1.3]). DALYs rates decreased most significantly for ages 45–49 (AAPC, -1.4 [-1.5 to -1.3]), and 50–54 (AAPC, -1.4 [-1.6 to -1.3]) (Table 1).

The trend of uterine cancer burden from 1990 to 2021

From 1990 to 2021, the incidence number of uterine cancer increased from 0.1 million (95% UI, 0.1–0.2) to 0.4 million (0.4–0.5), marking 147.6% (132.9–166.4) increase. The number of deaths due to uterine cancer increased by 78.1% (65.1–94.0), from 0.05 million (0.04–0.05) to 0.09 million (0.08–0.10). DALYs increased from 1.5 million (1.3–1.6) to 2.6 million (2.3–2.8), an increase of 70.7% (56.7–90.6).

From 1990 to 2021, the overall global ASIR for uterine cancer has trended upward (AAPC, 0.5 [95% CI, 0.5–0.6]). Additionally, the ASIR has shown a increasing trend in all SDI quintiles. Meanwhile, among the 204 countries and regions worldwide, only 11 countries or regions have experienced a decreasing trend in the ASIR of uterine cancer (Table S4).

The ASMR of uterine cancer showed an overall decreasing trend (AAPC,-0.8 [95% CI, -0.8 to -0.7]). Meanwhile, the ASMR for high-middle SDI quintile (AAPC, -1.2 [-1.3 to -1.1]), middle SDI quintile (AAPC, -1.2 [-1.4 to -1.1]), and low SDI quintile (AAPC, -0.1 [-0.2 to 0.0]) has decreased. A flat trend in ASMR was high SDI quintile (AAPC, 0.0 [-0.1–0.2]). Moreover, the ASMR increased for uterine cancer in low-middle SDI quintile(Table S4).

Similarly, the ASDR of uterine cancer showed an overall decreasing trend (AAPC, -0.8 [95% CI, -0.8 to -0.7]). Meanwhile, the ASDR for high-middle SDI quintile (AAPC, -1.3 [-1.4 to -1.2]), middle SDI quintile (AAPC, -1.3 [-1.4 to -1.2]), and low SDI quintile (AAPC, -0.2 [-0.3 to 0.1]) has decreased. Moreover, the ASDR increased for uterine in high SDI and low-middle SDI quintile(Table S4).

From 1990 to 2021, divided into 5-year age groups, the uterine cancer deficiency under 20 years old. Then, our focus was primarily on those aged 20 years and older. The incidence of uterine cancer, showed a increasing trend in all of age groups. The most significant increase was seen in the 55–59 years (AAPC, 0.8 [0.7–0.9]), and 60–64 years (AAPC, 0.8 [0.7–0.9]) groups. Uterine cancer mortality and DALYs rate showed a decreasing trend among individuals aged ≦94 years, a flat trend in the 95+years group. The 35–39 years group had the most significant decrease in mortality rate (AAPC, -1.7 [-1.8 to -1.5]) and DALYs rates (AAPC, -1.5 [-1.7 to -1.4]) (Table 1).

The trend of ovarian cancer burden from 1990 to 2021

From 1990 to 2021, the incidence number of ovarian cancer increased from 0.1 million (95% UI, 0.1–0.1) to 0.2 million (0.2–0.3), marking 87.8% (60.1–106.9) increase. The number of deaths due to ovarian cancer increased by 84.5% (62.5–101.1), from 0.1 million (0.09–0.10) to 0.1 million (0.1–0.2). DALYs increased from 2.9 million (2.7–3.2) to 5.2 million (4.7–5.6), an increase of 77.5% (50.9–97.1).

From 1990 to 2021, the overall global ASIR for ovarian cancer has trended downward (AAPC, -0.4 [95% CI, -0.4 to -0.3]). Meanwhile, the ASIR has shown a decreasing

Table 1 Average annual percent change in incidence, mortality, DALYs rates for different age groups in 1990 to 2021

Age group	Female breast cancer, % (95% CI)			Cervical cancer, % (95% CI)			Uterine cancer, % (95% CI)			Ovarian cancer, % (95% CI)		
	ASIR AAPC	ASMR AAPC	ASDR AAPC	ASIR AAPC	ASMR AAPC	ASDR AAPC	ASIR AAPC	ASMR AAPC	ASDR AAPC	ASIR AAPC	ASMR AAPC	ASDR AAPC
15–19 years	2.2 (2.1 to 2.3)	1.4 (1.3 to 1.5)	1.4 (1.3 to 1.5)	-0.1 (-0.2 to -0.1)	-1.0 (-1.1 to -0.9)	-1.0 (-1.1 to -0.9)	NA	NA	NA	0.7 (0.6 to 0.8)	0.3 (0.2 to 0.4)	0.3 (0.2 to 0.4)
20–24 years	2.2 (2.1 to 2.3)	1.4 (1.2 to 1.5)	1.4 (1.3 to 1.5)	0.1 (0.0 to 0.2)	-0.7 (-0.9 to -0.6)	-0.7 (-0.8 to -0.5)	0.2 (0.1 to 0.3)	-1.5 (-1.5 to -1.4)	-1.4 (-1.5 to -1.4)	0.9 (0.9 to 1.0)	0.5 (0.4 to 0.6)	0.5 (0.4 to 0.6)
25–29 years	1.6 (1.5 to 1.7)	0.7 (0.6 to 0.8)	0.7 (0.6 to 0.8)	-0.1 (-0.1 to 0.0)	-0.9 (-1.0 to -0.7)	-0.8 (-0.9 to -0.7)	0.4 (0.3 to 0.5)	-1.3 (-1.4 to -1.2)	-1.2 (-1.3 to -1.2)	0.8 (0.7 to 0.9)	0.4 (0.3 to 0.4)	0.4 (0.3 to 0.5)
30–34 years	1.0 (0.8 to 1.1)	0.0 (-0.1 to 0.1)	0.0 (-0.1 to 0.2)	-0.3 (-0.4 to -0.2)	-1.2 (-1.2 to -1.1)	-1.1 (-1.2 to -1.1)	0.5 (0.4 to 0.5)	-1.4 (-1.5 to -1.2)	-1.3 (-1.4 to -1.1)	0.5 (0.4 to 0.5)	0.1 (0.0 to 0.1)	0.1 (0.0 to 0.1)
35–39 years	0.5 (0.4 to 0.7)	-0.4 (-0.5 to -0.2)	-0.3 (-0.5 to -0.2)	-0.4 (-0.5 to -0.3)	-1.3 (-1.4 to -1.2)	-1.2 (-1.3 to -1.1)	0.3 (0.2 to 0.4)	-1.7 (-1.8 to -1.5)	-1.5 (-1.7 to -1.4)	0.1 (0.0 to 0.2)	-0.4 (-0.5 to -0.2)	-0.3 (-0.5 to -0.2)
40–44 years	0.4 (0.3 to 0.4)	-0.6 (-0.7 to -0.4)	-0.5 (-0.7 to -0.4)	-0.4 (-0.5 to -0.3)	-1.3 (-1.5 to -1.2)	-1.3 (-1.4 to -1.2)	0.4 (0.2 to 0.5)	-1.4 (-1.6 to -1.3)	-1.3 (-1.4 to -1.2)	-0.2 (-0.3 to -0.1)	-0.6 (-0.7 to -0.5)	-0.6 (-0.7 to -0.5)
45–49 years	0.3 (0.2 to 0.4)	-0.7 (-0.8 to -0.6)	-0.6 (-0.7 to -0.5)	-0.5 (-0.6 to -0.4)	-1.4 (-1.6 to -1.3)	-1.4 (-1.5 to -1.3)	0.6 (0.4 to 0.7)	-1.2 (-1.3 to -1.0)	-1.0 (-1.2 to -0.9)	-0.4 (-0.5 to -0.2)	-0.7 (-0.8 to -0.6)	-0.7 (-0.8 to -0.6)
50–54 years	0.4 (0.3 to 0.6)	-0.6 (-0.7 to -0.6)	-0.6 (-0.6 to -0.5)	-0.6 (-0.8 to -0.4)	-1.5 (-1.6 to -1.3)	-1.4 (-1.6 to -1.3)	0.6 (0.4 to 0.7)	-1.2 (-1.3 to -1.1)	-1.1 (-1.2 to -1.0)	-0.6 (-0.6 to -0.5)	-0.8 (-0.9 to -0.8)	-0.8 (-0.8 to -0.7)
55–59 years	0.6 (0.5 to 0.7)	-0.5 (-0.5 to -0.4)	-0.4 (-0.5 to -0.3)	-0.6 (-0.7 to -0.4)	-1.4 (-1.5 to -1.2)	-1.3 (-1.5 to -1.2)	0.8 (0.7 to 0.9)	-1.0 (-1.1 to -0.9)	-0.8 (-0.9 to -0.7)	-0.5 (-0.5 to -0.4)	-0.7 (-0.7 to -0.6)	-0.6 (-0.7 to -0.6)
60–64 years	0.7 (0.6 to 0.8)	-0.5 (-0.5 to -0.4)	-0.4 (-0.4 to -0.3)	-0.7 (-0.8 to -0.6)	-1.3 (-1.5 to -1.2)	-1.3 (-1.4 to -1.2)	0.8 (0.7 to 0.9)	-0.7 (-0.8 to -0.6)	-0.6 (-0.7 to -0.5)	-0.5 (-0.5 to -0.4)	-0.6 (-0.7 to -0.6)	-0.6 (-0.7 to -0.6)
65–69 years	0.5 (0.4 to 0.6)	-0.6 (-0.6 to -0.5)	-0.5 (-0.6 to -0.4)	-0.7 (-0.8 to -0.6)	-1.2 (-1.3 to -1.2)	-1.2 (-1.3 to -1.1)	0.5 (0.4 to 0.7)	-0.7 (-0.9 to -0.6)	-0.6 (-0.8 to -0.5)	-0.6 (-0.7 to -0.6)	-0.7 (-0.8 to -0.7)	-0.7 (-0.7 to -0.7)
70–74 years	0.2 (0.1 to 0.3)	-0.6 (-0.7 to -0.5)	-0.6 (-0.6 to -0.5)	-0.8 (-0.8 to -0.7)	-1.1 (-1.2 to -1.1)	-1.1 (-1.2 to -1.1)	0.4 (0.2 to 0.5)	-0.7 (-0.8 to -0.6)	-0.6 (-0.8 to -0.5)	-0.6 (-0.7 to -0.5)	-0.6 (-0.7 to -0.5)	-0.6 (-0.7 to -0.5)
75–79 years	-0.1 (-0.2 to 0)	-0.8 (-0.8 to -0.7)	-0.7 (-0.8 to -0.6)	-0.8 (-0.9 to -0.8)	-1.1 (-1.2 to -1.0)	-1.1 (-1.1 to -1.0)	0.2 (0.2 to 0.3)	-0.7 (-0.8 to -0.6)	-0.6 (-0.7 to -0.5)	-0.7 (-0.8 to -0.5)	-0.7 (-0.8 to -0.5)	-0.7 (-0.8 to -0.5)
80–84 years	-0.2 (-0.3 to 0)	-0.7 (-0.8 to -0.7)	-0.7 (-0.7 to -0.6)	-0.8 (-0.8 to -0.7)	-0.9 (-1.0 to -0.9)	-0.9 (-1.0 to -0.9)	0.2 (0.1 to 0.2)	-0.6 (-0.7 to -0.5)	-0.5 (-0.6 to -0.5)	-0.7 (-0.9 to -0.5)	-0.7 (-0.8 to -0.5)	-0.7 (-0.8 to -0.5)
85–89 years	0.1 (0 to 0.3)	-0.6 (-0.7 to -0.5)	-0.5 (-0.6 to -0.4)	-0.9 (-1.0 to -0.9)	-1.0 (-1.1 to -1.0)	-1.0 (-1.1 to -1.0)	0.4 (0.2 to 0.5)	-0.4 (-0.4 to -0.3)	-0.3 (-0.4 to -0.2)	-0.5 (-0.8 to -0.3)	-0.5 (-0.7 to -0.3)	-0.5 (-0.7 to -0.3)
90–94 years	0.2 (0.1 to 0.3)	-0.3 (-0.4 to -0.2)	-0.3 (-0.4 to -0.2)	-0.9 (-0.9 to -0.8)	-1.1 (-1.1 to -1.0)	-1.1 (-1.1 to -1.0)	0.2 (0.1 to 0.3)	-0.3 (-0.4 to -0.2)	-0.3 (-0.3 to -0.2)	-0.4 (-0.6 to -0.2)	-0.4 (-0.6 to -0.2)	-0.4 (-0.6 to -0.2)
95 + years	0.2 (0 to 0.3)	-0.1 (-0.3 to 0.0)	-0.2 (-0.3 to 0.0)	-0.6 (-0.8 to -0.5)	-0.8 (-0.9 to -0.7)	-0.9 (-1.0 to -0.8)	0.4 (0.3 to 0.6)	0.1 (-0.1 to 0.2)	0.0 (-0.1 to 0.2)	-0.1 (-0.2 to 0.0)	-0.1 (-0.2 to 0.0)	-0.2 (-0.3 to 0.0)

AAPC average annual percent change, *CI* confidence interval, *DALYs* disability-adjusted life-years trend in high SDI and high-middle SDI quintiles. Other three SDI quintiles has trended upward (Table S4).

The ASMR of ovarian cancer showed an overall decreasing trend (AAPC,-0.6 [95% CI, -0.7 to -0.6]). Meanwhile, the ASMR for high SDI quintile (AAPC, -1.3 [-1.4 to -1.2]), and high-middle SDI quintile (AAPC, -0.7 [-0.8 to -0.6]) has decreased. Additionally, the ASMR increased for ovarian cancer in middle SDI, low-middle SDI, and low SDI quintiles(Table S4).

Similarly, the ASDR of ovarian cancer showed an overall decreasing trend (AAPC, -0.6 [95% CI, -0.6 to -0.5]). Meanwhile, the ASDR for high-middle SDI quintile (AAPC, -1.5 [-1.6 to -1.4]), high-middle SDI quintile (AAPC, -0.9 [-1.0 to -0.8]). Additionally, the ASDR increased for ovarian cancer in middle SDI, low-middle SDI, and low SDI quintiles(Table S4).

From 1990 to 2021, the incidence of ovarian cancer,divided into 5-year age groups, showed an increasing trend in individuals aged ≦39 years, and a decreasing trend in those aged ≧40 years. The most pronounced increase was in the 20–24 years group (AAPC, 0.9 [95% CI, 0.9–1.0]), while the most significant decrease was seen in the 75–79 years (AAPC, -0.7 [-0.8 to -0.5]), and 80–84 years (AAPC, -0.7 [-0.9 to -0.5]) groups. Ovarian cancer mortality and DALYs rate showed a increasing trend in individuals aged ≦34 years, and a decreasing trend in those aged ≧35 years. The 20–24 years group had the most significant increase in mortality rate and DALYs rates with same AAPC (0.5 [0.4–0.6]). Mortality and DALYs rate decreased most significant for ages 50–54 (AAPC, -0.8 [-0.9 to -0.8]; -0.8 [-0.8 to -0.7]) (Table 1).

Disability-adjusted life years from female breast cancer attributable to risk factors

In 2021, female breast cancer was estimated to cause 5.1 million (95% UI, 1.6–8.0) DALYs attributable to risk factors exposure. Table 2 illustrates the contribution of 7 factors across overall global, five SDI quintiles, and 21 GBD regions in 2021 to DALYs caused by female breast cancer.Diet high in red meat is the primary risk factor for female breast cancer DALYs (11.9% [95% UI, 0.0–25.3]), followed by Alcohol use (2.7% [1.9–3.7)]) and Low physical activity (2.0% [0.4–3.6)]) (Table 2).

Diet high in red meat is the leading risk factor across all of five SDI quintiles and 21 GBD regions. Moreover, risk factor proportions varied across different SDI quintiles. Alcohol use was the second highest risk factor in high (6.5% [4.6–8.6]), high-middle (3.2% [2.2–4.4]) and low SDI quintiles (1.6% [0.9–2.3]). However, in middle and low-middle quintiles, Low physical activity was the second greatest contributor to DALYs from female breast cancer (Table 2).

Similarly, in 2021, diet high in red meat was the leading risk factor for attributable ASDR for female breast cancer globally, with an ASDR of 54.0 (95% UI, 0–115.1) per 100,000. This was consistent across all SDI quintiles and 204 countries and territories. High alcohol use was the second highest risk factor for female breast cancer ASDR of 12.4 (8.7–16.5) per 100,000. However, in middle SDI and low-middle SDI quintiles low physical activity was the second highest risk for ASDR. Details on the attribution of 7 risk factors to ASDR by 5 SDI quintiles and 204 countries or territories level are provided in Table S5.

Disability-adjusted life years from cervical, uterine and ovarian cancer attributable to risk factors

About cervical cancer, in 2021, cervical cancer was estimated to cause 9.9 million (95% UI, 9.0–10.8) DALYs attributable to risk factors exposure. Table 3 illustrates the contribution of 2 factors across overall global, five SDI quintiles, and 21 GBD regions in 2021 to DALYs cause by cervical cancer. Unsafe sex is the primary risk factor for cervical cancer DALYs (100% [95% UI, 100–100]), followed by Smoking (7.3% [4.3–10.5]) (Table 3).

Unsafe sex is the leading risk factor across all of five SDI quintile and 21 GBD regions, and of all percent and 95% UI were 100% (100–100). Smoking was the second highest risk factor in other SDI quintiles, and as SDI decreased, the proportion of DALYs from smoking gradually reduced (Table 3).

Similarly, in 2021, unsafe sex was the leading risk factor for attributable ASDR for cervical cancer globally, with an ASDR of 226.2 (95% UI, 206.4–246.6) per 100,000. This was consistent across all SDI quintiles and 204 countries and territories. Smoking was the second highest risk factor for cervical cancer ASDR of 16.2 (9.8–23.8) per 100,000. Details on the attributable of 2 risk factors to ASDR by 5 SDI quintiles and 204 countries or territories level are provided in Table S6.

Uterine cancer was estimated to cause 0.9 million (95% UI, 0.6–1.2) DALYs attributable to risk factors exposure. High body-mass index is the only risk factor for uterine cancer across overall global, five SDI quintiles, and 21 GBD regions in 2021. As SDI decreased, the proportion of DALYs from high body-mass index gradually reduced (Table 3). Similarly, in 2021, high body-mass index was the only risk factor attributable ASDR for uterine cancer globally, with an ASDR of 19.2 (13.8–25.4) per 100,000. Furthermore, the higher the SDI quintile, the greater the impact of high body-mass index (Table S7). Meanwhile, ovarian cancer was estimated to cause 0.6 million (0.2–0.9) DALYs attributable to risk factors exposure. Table 3 illustrates the contribution of 2 factors across overall global, SDI quintile, and 21 GBD regions in 2021 to DALYs cause by ovarian

Table 2 Percentage contribution of risk factors to all-age DALYs of female breast cancer in 2021, for SDI, and by regions

Location	Risk factors						
	Alcohol use, %(95% UI)	Diet high in red meat, %(95% UI)	High body-mass index, %(95% UI)	High fasting plasma glucose, %(95% UI)	Low physical activity, %(95% UI)	Secondhand smoke, %(95% UI)	Smoking, %(95% UI)
Global	2.7 (1.9 to 3.7)	11.9 (0.0 to 25.3)	5.1 (-0.2 to 10.0)	4.0 (-1.2 to 9.5)	2.0 (0.4 to 3.6)	1.2 (-0.3 to 2.8)	1.5 (1.2 to 1.9)
High SDI	6.5 (4.6 to 8.6)	13.6 (0.0 to 28.8)	7.9 (-0.3 to 15.3)	4.9 (-1.4 to 11.5)	2.7 (0.5 to 4.6)	0.7 (-0.2 to 1.5)	3.1 (2.3 to 3.8)
High-middle SDI	3.2 (2.2 to 4.4)	13.4 (0.0 to 28.5)	7.4 (-0.2 to 14.6)	4.2 (-1.2 to 9.8)	2.1 (0.4 to 3.6)	1.5 (-0.4 to 3.4)	1.9 (1.4 to 2.3)
Middle SDI	1.3 (0.9 to 1.8)	11.5 (0.0 to 24.6)	4.4 (-0.2 to 8.5)	3.9 (-1.1 to 9.3)	2.1 (0.4 to 3.6)	1.5 (-0.4 to 3.4)	0.9 (0.7 to 1.2)
Low-middle SDI	0.9 (0.6 to 1.3)	9.6 (0.0 to 20.6)	2.4 (-0.3 to 4.9)	3.7 (-1.1 to 8.5)	1.7 (0.3 to 3.0)	1.3 (-0.3 to 2.9)	0.7 (0.6 to 0.9)
Low SDI	1.6 (0.9 to 2.3)	10.3 (0.0 to 21.7)	1.3 (-0.4 to 2.8)	2.7 (-0.8 to 6.5)	1.2 (0.3 to 2.2)	0.9 (-0.2 to 2.0)	0.6 (0.5 to 0.8)
Andean Latin America	3.0 (1.8 to 4.6)	13.3 (0.0 to 28.1)	4.9 (-0.4 to 9.3)	3.7 (-1.0 to 8.6)	1.4 (0.3 to 2.6)	0.6 (-0.1 to 1.4)	1.0 (0.7 to 1.2)
Australasia	9.0 (6.6 to 11.5)	13.7 (0.0 to 29)	8.3 (-0.3 to 16.0)	4.6 (-1.4 to 10.5)	3.3 (0.7 to 5.9)	0.5 (-0.1 to 1.1)	3.2 (2.4 to 4.0)
Caribbean	2.1 (1.3 to 3.1)	13.1 (0.0 to 27.8)	5.3 (-0.4 to 10.1)	4.7 (-1.4 to 11.1)	2.6 (0.5 to 4.6)	0.7 (-0.2 to 1.7)	1.9 (1.4 to 2.5)
Central Asia	1.6 (1.0 to 2.4)	13.6 (0.0 to 28.8)	6.1 (-0.4 to 11.7)	3.5 (-1.0 to 8.2)	1.3 (0.3 to 2.3)	1.6 (-0.4 to 3.6)	0.6 (0.4 to 0.8)
Central Europe	4.6 (3.1 to 6.5)	13.7 (0.0 to 28.9)	9.0 (-0.3 to 17.5)	5.4 (-1.6 to 12.5)	2.3 (0.5 to 4.1)	1.0 (-0.2 to 2.3)	3.5 (2.7 to 4.4)
Central Latin America	1.5 (0.9 to 2.2)	13.5 (0.0 to 28.5)	5.7 (-0.4 to 10.9)	5.1 (-1.5 to 12.0)	2.0 (0.4 to 3.5)	0.9 (-0.2 to 2.0)	1.4 (1.1 to 1.8)
Central Sub-Saharan Africa	2.6 (0.6 to 4.0)	9.0 (0.0 to 19.3)	2.2 (-0.3 to 4.6)	3.4 (-1.0 to 8.1)	1.3 (0.3 to 2.5)	0.8 (-0.2 to 1.8)	0.4 (0.3 to 0.6)
East Asia	1.0 (0.6 to 1.6)	13.6 (0.0 to 28.8)	5.7 (-0.2 to 11.5)	3.7 (-1.1 to 8.7)	1.9 (0.3 to 3.3)	2.2 (-0.5 to 5.0)	0.8 (0.6 to 1.1)
Eastern Europe	4.5 (2.9 to 6.4)	13.6 (0.0 to 28.9)	9.5 (-0.3 to 18.2)	3.6 (-1.0 to 8.3)	1.7 (0.3 to 3.0)	1.2 (-0.3 to 2.6)	1.6 (1.2 to 2.0)
Eastern Sub-Saharan Africa	2.3 (1.2 to 3.2)	11.8 (0.0 to 25.2)	1.1 (-0.4 to 2.7)	1.8 (-0.5 to 4.1)	1.0 (0.2 to 1.8)	0.8 (-0.2 to 1.8)	0.7 (0.5 to 0.8)
High-income Asia Pacific	6.3 (4.4 to 8.2)	13.4 (0.0 to 28.5)	4.6 (-0.1 to 9.2)	4.2 (-1.3 to 9.7)	2.9 (0.5 to 5.0)	0.9 (-0.2 to 2.0)	1.5 (1.1 to 2.0)
High-income North America	6.1 (4.2 to 8.4)	13.7 (0.0 to 28.9)	9.3 (-0.3 to 17.8)	6.1 (-1.8 to 14.3)	2.4 (0.5 to 4.3)	0.5 (-0.1 to 1.0)	3.5 (2.7 to 4.4)
North Africa and Middle East	0.1 (0.1 to 0.2)	13.0 (0.0 to 27.6)	4.8 (-0.5 to 9.0)	5.0 (-1.5 to 11.6)	2.9 (0.6 to 5.0)	1.6 (-0.4 to 3.5)	1.0 (0.7 to 1.3)
Oceania	0.4 (0.2 to 0.6)	13.2 (0.0 to 27.8)	5.1 (-0.2 to 10.2)	4.5 (-1.3 to 10.3)	2.6 (0.5 to 4.7)	1.9 (-0.5 to 4.3)	2.5 (1.8 to 3.3)
South Asia	0.3 (0.2 to 0.5)	6.5 (0.0 to 14.3)	1.4 (-0.3 to 3.1)	4.1 (-1.2 to 9.5)	1.5 (0.3 to 2.7)	1.2 (-0.3 to 2.7)	0.5 (0.4 to 0.7)
Southeast Asia	0.9 (0.6 to 1.3)	11.6 (0.0 to 24.9)	4.0 (-0.1 to 8.1)	3.1 (-0.9 to 7.5)	2.0 (0.4 to 3.6)	1.9 (-0.5 to 4.3)	0.8 (0.6 to 1.1)
Southern Latin America	5.9 (4.1 to 7.8)	13.6 (0.0 to 28.9)	8.0 (-0.3 to 15.2)	4.8 (-1.4 to 10.9)	1.7 (0.4 to 3.1)	1.0 (-0.2 to 2.3)	4.0 (3.0 to 5.0)
Southern Sub-Saharan Africa	2.9 (1.9 to 3.9)	13.5 (0.0 to 28.6)	5.5 (-0.4 to 10.4)	3.6 (-1.0 to 8.4)	2.5 (0.5 to 4.2)	1.4 (-0.3 to 3.0)	1.5 (1.1 to 1.9)
Tropical Latin America	3.0 (2.1 to 4.1)	13.6 (0.0 to 28.8)	5.0 (-0.4 to 9.8)	4.3 (-1.3 to 10.1)	2.6 (0.5 to 4.6)	0.7 (-0.2 to 1.6)	2.9 (2.1 to 3.6)
Western Europe	7.7 (5.6 to 10)	13.6 (0.0 to 28.9)	7.8 (-0.3 to 15.6)	4.1 (-1.1 to 9.8)	2.9 (0.6 to 5.1)	0.6 (-0.1 to 1.4)	3.4 (2.6 to 4.3)
Western Sub-Saharan Africa	2.9 (1.9 to 4.0)	12.0 (0.0 to 25.5)	3.0 (-0.3 to 6.3)	2.8 (-0.8 to 6.6)	1.6 (0.3 to 2.9)	0.6 (-0.1 to 1.3)	0.3 (0.2 to 0.3)

cancer. Same with uterine cancer, high body-mass index also is the primary risk factor for ovarian cancer DALYs 9.3 (2.3–16.5), and they have the same trend. Occupational exposure to asbestos was the second highest risk factor for ovarian cancer DALYs 1.9 (0.9–3.1). Similarly, in 2021, high body-mass index was the leading risk factor for attributable ASDR for ovarian cancer globally, with an ASDR of 10.6 (2.5–18.6) per 100,000. This was consistent across all SDI quintiles and 204 countries and territories. Occupational exposure to asbestos was the second highest risk factor for ovarian cancer ASDR of 2.1 (1.0–3.4) per 100,000. Details on the attribution of 2 risk factors to ovarian cancer ASDR by 5 SDI quintiles and 204 countries or territories level are provided in Table S8.

Table 3 Percentage contribution of risk factors to all-age DALYs of cervical cancer, uterine cancer, and ovarian cancer in 2021, for SDI, and by regions

Location	Risk factor of cervical cancer		Risk factor of uterine cancer	Risk factor of ovarian cancer	
	Smoking, %(95% UI)	Unsafe sex, %(95% UI)	High body-mass index, %(95% UI)	High body-mass index, %(95% UI)	Occupational exposure to asbestos, %(95% UI)
Global	7.3 (4.3 to 10.5)	100.0 (100.0 to 100.0)	34.3 (25.0 to 44.2)	9.3 (2.3 to 16.5)	1.9 (0.9 to 3.1)
High SDI	19.3 (11.6 to 27.3)	100.0 (100.0 to 100.0)	38.7 (28.3 to 49.5)	11.3 (2.8 to 20.3)	4.3 (2.1 to 6.6)
High-middle SDI	12.2 (7.5 to 17.4)	100.0 (100.0 to 100.0)	39.3 (28.4 to 50.8)	11.6 (2.8 to 20.8)	2.3 (1.1 to 3.8)
Middle SDI	6.1 (3.5 to 9.0)	100.0 (100.0 to 100.0)	30.8 (22.2 to 39.7)	8.6 (2.0 to 15.5)	0.9 (0.4 to 1.5)
Low-middle SDI	5.3 (3.0 to 7.9)	100.0 (100.0 to 100.0)	26.9 (18.8 to 34.8)	6.3 (1.4 to 11.4)	0.4 (0.2 to 0.7)
Low SDI	4.0 (2.3 to 5.9)	100.0 (100.0 to 100.0)	21.9 (15.1 to 28.6)	4.3 (0.7 to 8.2)	0.1 (0.0 to 0.2)
Andean Latin America	6.0 (3.4 to 9.0)	100.0 (100.0 to 100.0)	40.2 (29.0 to 52.0)	12.4 (3.2 to 22.3)	1.2 (0.5 to 2.4)
Australasia	20.4 (12.3 to 29.5)	100.0 (100.0 to 100.0)	42.3 (30.8 to 54.4)	13.4 (3.5 to 23.3)	8.2 (4.0 to 13.1)
Caribbean	10.2 (6.0 to 15.2)	100.0 (100.0 to 100.0)	37.2 (26.7 to 48.7)	11.5 (3.1 to 20.1)	0.7 (0.3 to 1.2)
Central Asia	4.8 (2.7 to 7.1)	100.0 (100.0 to 100.0)	41.5 (30.2 to 53.6)	12.8 (3.3 to 22.9)	1.4 (0.6 to 2.2)
Central Europe	24.1 (15.5 to 33.5)	100.0 (100.0 to 100.0)	41.5 (30.2 to 53.5)	12.9 (3.3 to 23.1)	2.3 (1.1 to 3.7)
Central Latin America	8.3 (4.9 to 12.1)	100.0 (100.0 to 100.0)	43.3 (31.4 to 55.4)	13.9 (3.7 to 24.5)	1.2 (0.6 to 1.9)
Central Sub-Saharan Africa	2.8 (1.6 to 4.3)	100.0 (100.0 to 100.0)	25.8 (17.4 to 33.9)	6.1 (1.2 to 10.6)	0.0 (0.0 to 0.0)
East Asia	5.9 (3.3 to 8.9)	100.0 (100.0 to 100.0)	27.1 (19.1 to 36.3)	7.0 (1.4 to 13.5)	1.0 (0.4 to 1.8)
Eastern Europe	13.4 (8.3 to 19.1)	100.0 (100.0 to 100.0)	45.6 (33.3 to 57.7)	15.1 (4.2 to 26.1)	2.4 (1.1 to 4.0)
Eastern Sub-Saharan Africa	4.0 (2.3 to 6.0)	100.0 (100.0 to 100.0)	22.8 (15.8 to 29.9)	5.1 (0.9 to 9.7)	0.0 (0.0 to 0.0)
High-income Asia Pacific	11.3 (6.2 to 16.9)	100.0 (100.0 to 100.0)	19.1 (13.3 to 25.0)	3.7 (0.4 to 7.2)	1.9 (0.9 to 3.3)
High-income North America	23.2 (13.9 to 33)	100.0 (100.0 to 100.0)	44.8 (33.0 to 56.7)	14.6 (4.0 to 25.2)	3.5 (1.7 to 5.5)
North Africa and Middle East	5.2 (3.0 to 7.7)	100.0 (100.0 to 100.0)	48.0 (35.7 to 60.2)	16.7 (4.7 to 28.2)	1.2 (0.4 to 2.4)
Oceania	15.8 (9.5 to 22.4)	100.0 (100.0 to 100.0)	35.4 (25.3 to 45.9)	10.3 (2.6 to 18.6)	0.0 (0.0 to 0.1)
South Asia	4.4 (2.4 to 6.8)	100.0 (100.0 to 100.0)	20.6 (14.2 to 26.9)	4.4 (0.8 to 8.2)	0.2 (0.1 to 0.5)
Southeast Asia	5.4 (3.2 to 8.0)	100.0 (100.0 to 100.0)	23.1 (15.9 to 30.1)	5.5 (1.1 to 10.1)	0.2 (0.1 to 0.5)
Southern Latin America	24.7 (15.9 to 33.6)	100.0 (100.0 to 100.0)	43.9 (31.9 to 56.0)	14.2 (3.8 to 25)	2.9 (1.4 to 4.7)
Southern Sub-Saharan Africa	8.1 (4.8 to 12.0)	100.0 (100.0 to 100.0)	45.2 (33.4 to 56.9)	15.5 (4.4 to 26.7)	2.1 (0.9 to 3.8)
Tropical Latin America	15.6 (9.0 to 22.7)	100.0 (100.0 to 100.0)	39.2 (28.1 to 51.4)	11.6 (2.8 to 21.2)	2.6 (1.3 to 4.1)
Western Europe	22.6 (14.2 to 31.3)	100.0 (100.0 to 100.0)	36.4 (26.1 to 47.7)	10.5 (2.4 to 19.4)	6.5 (3.2 to 10.1)
Western Sub-Saharan Africa	1.8 (1.0 to 2.8)	100.0 (100.0 to 100.0)	30.2 (21.4 to 39.8)	8.2 (1.9 to 15.1)	0.0 (0.0 to 0.0)

The trend of risk factors of female breast cancer burden from 1990 to 2021

The attributable DALYs for female breast cancer increased from 2.9 million (95% UI, 1.2–4.4) in 1990 to 5.1 million (1.6–8.0) in 2021.From 1990 to 2021, the age-standardized death rate (ASDR) for female breast cancer attributable to a diet high in red meat decreased (AAPC, -0.7 [95% CI, -1.1 to -0.2]). However, increasing trends were observed in the low-middle and low SDI quintiles, while the middle SDI quintile showed a flat trend (Table S9).Additionally, the ASDR for female breast cancer attributable to alcohol use also decreased (AAPC, -2.0 [-2.9 to -1.1]).Most countries and SDI quintiles exhibited a downward trend for this risk factor, with the exception of the low-middle SDI quintile.Low physical activity levels in most SDI quintiles, countries, and regions either declined or remained stable (Table S9).

In 2021, smoking was a major risk factor for female breast cancer DALYs across all SDI quintiles. Despite this, the ASDR for female breast cancer attributable to smoking either decreased or remained stable from 1990 to 2021.Overall, other risk factors for female breast cancer generally showed decreasing or stable trends globally and within the five SDI quintiles (Table S9).

The trend of risk factors of cervical, uterine and ovarian cancer burden from 1990 to 2021

The attributable DALYs for cervical cancer increased from 7.4 million (95% UI, 6.8–8.1) in 1990 to 9.9 million (9.0–10.8) in 2021. Over this period, the age-standardized death rate (ASDR) for cervical cancer attributable to unsafe sex (AAPC, -1.3 [95% CI, -1.5 to -1.1]) and smoking (AAPC, -2.5 [-3.3 to -1.8]) both showed a decreasing trend. All SDI quintiles exhibited the same downward trend for these two risk factors. In 2021, unsafe sex was the leading risk factor for cervical cancer DALYs globally, across all five SDI quintiles, and in all 21 GBD regions. However, in most countries and regions, the trend for these risk factors was either decreasing or stable (Table S10).

The attributable DALYs for uterine cancer rose from 0.4 million (95% UI, 0.3–0.5) in 1990 to 0.9 million (0.6–1.2) in 2021. Between 1990 and 2021, the ASDR for uterine cancer attributable to high body-mass index (AAPC, 0.3 [-0.6 to 1.2]) remained relatively stable. Notably, at the global level, within the five SDI quintiles, and among the 204 countries or territories, most countries and regions experienced an increase or stability in the trend, with exceptions including Czechia (-1 [-1.5 to -0.4]), Estonia (-0.7 [-1.3 to -0.1]), Greenland (-1.3 [-2.3 to -0.2]), Hungary (-0.9 [-1.4 to -0.3]), Kazakhstan (-1 [-1.6 to -0.4]), Slovakia (-0.7 [-1.2 to -0.2]), Turkmenistan (-0.9 [-1.9 to 0.0]), and the United States Virgin Islands (-0.8 [-1.4 to -0.2]) (Table S11).

The attributable DALYs for ovarian cancer grew from 0.3 million (95% UI, 0.1–0.4) in 1990 to 0.6 million (0.2–0.9) in 2021. From 1990 to 2021, the ASDR for ovarian cancer attributable to occupational exposure to asbestos (AAPC, -1.5 [95% CI, -3.6 to 0.8]) and high body-mass index (AAPC, 0.5 [-0.7 to 1.7]) remained stable. This trend was observed in all SDI quintiles, except for the middle and low-middle SDI quintiles regarding the high body-mass index risk factor. Due to data limitations for some regions and years, ASDR results are not available for certain areas (Table S12) (Fig. 9).

Fig. 9 Changes in total attributable DALYs for female breast, cervical, uterine and ovarian cancer in global and 5 SDI quintiles regions (1990–2021). DALYs, disability–adjusted life–years; SDI, Socio–demographic Index

Global disease burden prediction for female breast, cervical, uterine and ovarian cancer to 2050

The Bayesian Age-Period-Cohort (BAPC) model was employed to forecast the future trends in the age-standardized incidence rates (ASIR) and the number of cases for female breast cancer, cervical cancer, uterine cancer, and ovarian cancer from 2022 to 2050. Projections indicate a global increase in the total number of female breast cancer and ovarian cancer cases from 2021 to 2050. In contrast, both cervical cancer and uterine cancer are expected to show downward trends over the same period (Fig. 10).

Discussion

This study provides a comprehensive estimation of the incidence, deaths, and DALYs for female-specific cancers, female breast cancer, cervical cancer, uterine cancer, and ovarian cancer, and investigates their global temporal trends, with projections to 2050. From 1990 to 2021, the global burden of these cancers generally increased, although epidemiological trends varied by country or region. Notably, the age-standardized DALYs rate decreased for all four cancers. Annual increases in the age-standardized incidence rate were observed for female breast cancer and uterine cancer, while cervical cancer and ovarian cancer showed stable or decreasing trends. Additionally, the age-standardized mortality rate decreased across all four cancers. Female breast cancer and cervical cancer were the most prevalent globally, followed by uterine cancer and ovarian cancer, with significant regional disparities in the burden of these cancers, collectively referred to as FBCUO (Female Breast, Cervical, Uterine, and Ovarian) cancers. The age-standardized incidence rates of female breast, ovarian, and uterine cancers generally showed an upward trend with increasing Socio-Demographic Index (SDI), whereas both the age-standardized incidence and DALY rates for cervical cancer exhibited downward trends with increasing SDI. There is notable age-related heterogeneity in the prevalence of FBCUO cancers, with varying risk factors among the different cancers; however, high body-mass index (BMI) is the most common risk factor, except for cervical cancer, where it has not been identified as significant. By 2050, the age-standardized incidence rates (ASIR) for

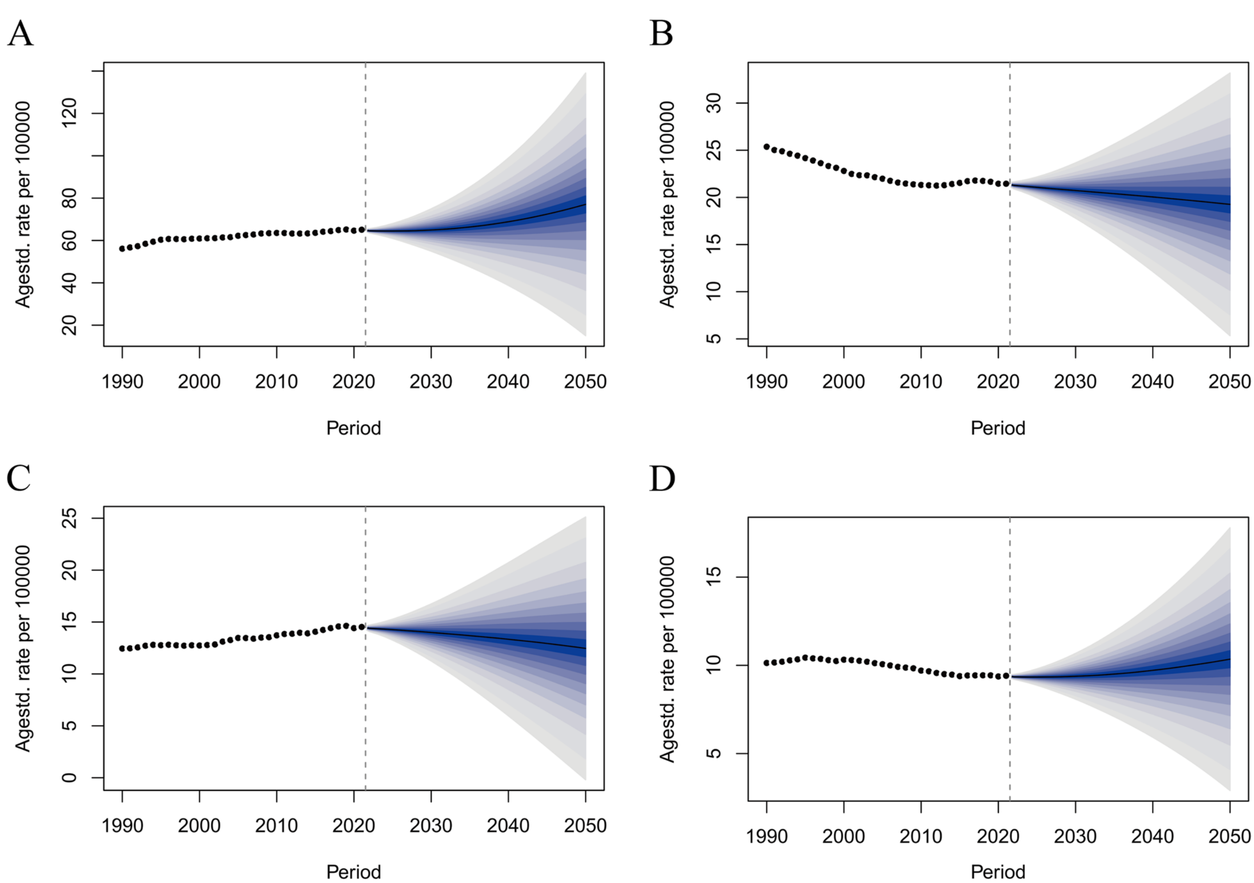

Fig. 10 Projections of the Age-Standardized Incidence Rates (ASIR) and Number of Cases for Female Breast Cancer (**A**), Cervical Cancer (**B**), Uterine Cancer (**C**), and Ovarian Cancer (**D**) from 2022 to 2050

female breast cancer and ovarian cancer are projected to gradually increase, while those for cervical and uterine cancer are expected to decrease. These variations reflect regional heterogeneity, likely influenced by differences in the distribution of risk factors for FBCUO cancers, levels of economic development, and access to healthcare.

Our study indicates a global rise in the age-standardized incidence rate of FBCUO cancers from 1990 to 2021, primarily driven by increases in female breast, uterine, and ovarian cancers. This finding aligns with previous studies [2, 3, 12], underscoring the need for heightened attention to the cancer burden in this population. Notably, high BMI emerged as a common risk factor for female breast, uterine, and ovarian cancers, consistent with its demonstrated effects on inflammatory, metabolic, and hormonal pathways [13, 14], which may be closely related to the increased incidence of these three cancers. Additionally, our results identified multiple risk factors for each type of cancer: female breast cancer is influenced by a diet high in red meat, high alcohol use, high BMI, high fasting plasma glucose, low physical activity, secondhand smoke, and smoking; cervical cancer is associated with smoking and unsafe sex; uterine cancer is linked solely to high BMI; and ovarian cancer is affected by high BMI and occupational exposure to asbestos. These findings highlight the importance of addressing specific risk factors to develop targeted prevention and control strategies for each type of cancer. Besides, researchers revealed numbers of adverse life-style behaviors (like high alcohol use, low physical activity, unsafe sex, and obesity and so on) arising from rapid social development are associated with increased FBCUO cancers though diverse mechanisms [15, 16]. At the same time, unsafe sex is the most important risk factor for cervical cancer, posing a significant threat to women's health. Therefore, targeted interventions focusing on modifiable risk factors can effectively reduce the incidence of these cancers. Additionally, the incidence of FBCUO cancers varies across different SDI regions. Specifically, female breast, uterine, and ovarian cancers are often more prevalent in high SDI quintile compared to low SDI quintile, which may be related to improvements in breast cancer screening and routine gynecological examinations brought about by socioeconomic development. These findings underscore the importance of addressing region-specific risk factors and enhancing preventive measures in both high and low SDI settings to mitigate the burden of FBCUO cancers [17].

From 1990 to 2021, the age-standardized DALYs rates for FBCUO cancers showed a general decreasing trend, however, significant variations were observed across different SDI regions. Female breast cancer exhibited a declining trend in high and high-middle SDI quintiles but increased in the other three regions, likely due to differences in socio-economic development and access to effective treatments, indicating that countries or regions with lower socio-economic development lack adequate methods for managing breast cancer. Uterine cancer, on the other hand, showed an increasing age-standardized DALYs rate (ASDR) in high SDI regions, possibly because higher BMI levels (i.e., obesity) are more common in more developed areas, highlighting the need for targeted interventions to reduce this risk factor. Ovarian cancer followed a similar pattern to breast cancer, with higher ASDR rates in areas of low economic development. As the fifth leading cause of cancer-related deaths in women and the deadliest gynecological cancer [18], ovarian cancer has been treated historically with surgical removal of the ovaries and fallopian tubes [19], which significantly impacts patients' quality of life and may contribute to elevated DALYs. Additionally, the UK Collaborative Trial of Ovarian Cancer Screening found that neither multimodal screening nor transvaginal ultrasound screening significantly reduced ovarian cancer mortality compared to no screening [20], underscoring the critical need for effective screening methods to improve prevention, cure rates, and survival rates. These findings highlight the importance of region-specific strategies to address the varying trends in FBCUO cancers, emphasizing the need for targeted interventions, particularly in low socioeconomic regions, to improve treatment access and outcomes, as well as addressing modifiable risk factors like BMI. Additionally, from 1990 to 2021, the trends in age-standardized mortality rates (ASMR) for FBCUO cancers were similar to those observed for ASDR. Moreover, the patterns across different SDI quintiles mirrored those of the ASMR, suggesting that these trends may be influenced by the same factors.

Additionally, a systematic study concluded that delays and barriers to cancer treatment are more common in middle-income areas and below [21]. Our findings indicate that the incidence of breast and ovarian cancer, as well as the associated DALYs, are significantly higher among women in poorer or lower-status regions, such as Africa and the Middle East, compared to other regions. This suggests that sociocultural factors also play a crucial role in influencing the prevalence and effectiveness of cancer treatment in women. Furthermore, both breast and ovarian cancers have shown increasing trends in middle SDI, low-middle SDI, and low SDI quintiles, consistent with findings from other studies [22, 23]. Similarly, research has shown that women with low income and education levels rarely undergo routine breast examinations [24], which significantly increases their risk of developing malignant breast cancer compared to women who receive regular check-ups [25, 26]. To effectively address the regional disparities in female cancers, it is essential to implement policy reforms aimed at reducing poverty and inequity by improving income distribution, health education, and the social status of women [27].

In 2021, FBCUO cancers had the highest age-standardized incidence rates (ASIR), ASMR, and ASDR worldwide, followed by cervical cancer. With socioeconomic progress, our results show a decline in both ASMR and ASDR for breast cancer from 1990 to 2021, which is consistent with other studies [28]. In 2023, the World Health Organization (WHO) launched the Global Breast Cancer Initiative Framework, aiming to reduce breast cancer mortality by 2.5% and prevent 2.5 million breast cancer deaths by 2040. However, our findings indicate a global upward trend in breast cancer ASIR, suggesting that current predictive measures for breast cancer are still inadequate. Additionally, we project that the ASIR of breast cancer will continue to rise by 2050, underscoring the need for further research to identify more effective prevention methods and reduce the incidence of breast cancer.

Regarding cervical cancer, our study shows that from 1990 to 2021, the ASIR, ASMR, and ASDR of cervical cancer have been declining. The main risk factors for cervical cancer are unsafe sex and smoking, with unsafe sex being the most significant factor. At the same time, our projections show that the incidence of cervix will decline by 2050. This trend may be attributed to the introduction of the HPV vaccine. To further reduce the incidence of cervical cancer, it is essential to strengthen HPV vaccination programs and utilize high-performance detection methods for cervical cancer screening to achieve "early detection, early diagnosis, and early treatment." In addition, in 2021, the ASIR, ASMR, and ASDR for cervical cancer increased as the SDI decreased. This trend is consistent with a recent study that found a rapid increase in cervical cancer rates among women in some low-income areas, rising at an annual rate of 4.4% since 2007 [29]. Therefore, countries or regions with low SDI quintile should actively promote HPV vaccination and publicize health knowledge about safe sex to reduce the incidence of cervical cancer and alleviate the associated social and economic burdens.

Overall, although FBCUO cancers originate in different tissues, they share common risk factors such as obesity, age, and age at menarche. While our study did not explicitly demonstrate these risk factors, broader risk prediction models are needed to support prevention and treatment strategies for FBCUO cancers. Additionally, the ASIR of FBCUO cancers is higher among younger middle-aged and young women, possibly due to factors like higher levels of physical activity, greater life stress, and poorer lifestyle habits. Therefore, initiatives promoting more physical activity, healthy weight management, positive lifestyle habits, and stress reduction in women's lives are essential. Strengthening community-based public health education on women's cancers will also play a crucial role in addressing these issues.

Our study shows that the incidence, mortality, and DALYs rates of FBCUO cancers differ across age groups from 1990 to 2021. For breast cancer, there is a downward trend in incidence among women aged 75 and above, while the ASIR with the highest annual average percentage change (AAPC) occurs in the age groups 15–19 and 20–24 to 34 years. This trend can significantly impact the normal lives of young women, affecting aspects such as work, marriage, and childbearing, and the ASMR and age-standardized DALY rate (ASDR) were also higher in these younger age groups. Cervical cancer has shown a downward trend across all age groups, closely related to the introduction of the HPV vaccine. Uterine and ovarian cancers exhibit similar trends to breast cancer, posing significant challenges for society and the health of women, who often play crucial roles in caring for children, managing families, and performing important work [1]. Therefore, it is particularly important to develop safer and more effective treatment programs to reduce adverse events in women. Historically, clinical trials have shown that women experience more severe adverse reactions to treatments for female tumors, including chemotherapy and biotherapy [30], highlighting a significant gender difference in treatment responses. One study found that the care needs of many young gynecological cancer patients are not being adequately met [31], making these women more susceptible to tumor-related depression.

Our study has several limitations. First, we only utilized GBD data from 2021 to estimate the burden of cancer among women, whereas the original data for many countries, especially for low- and middle-income countries, are incomplete and some of them are missing. In addition, the risk factors considered were limited to those included in the GBD database, which may not encompass all relevant risk factors. This may have influenced the results of our study. Second, our study focused on female breast, cervical, uterine, and ovarian cancers, excluding other types of female cancers and specific tumor pathological features. Third, given that the data cover 204 countries or regions worldwide, different diagnostic and treatment methods across countries, regions, and years may impact the comparability of results, making it important to interpret the disease burden findings with caution. Fourth, due to data access, we used data on female cancers from only one database, GBD, and did not include other databases. Finally, our predictions for the age-standardized incidence of FBCUO cancers extend only from 2022 to 2050 and are limited to incidence rates, without including mortality or DALYs rates beyond this period. Therefore, continued observation and research are necessary to better understand the future trends of FBCUO cancers.

In conclusion, female cancers pose a significant threat to women's health. From 1990 to 2021, the global incidence of cancer in women has continued to rise, despite a downward trend in disability-adjusted life years (DALYs). This trend varies across countries, highlighting the need for tailored approaches. Over the past 30 years, healthcare providers have observed that social factors associated with globalization may be contributing to the increasing number of women at risk for gynecological tumors. The heterogeneity at the national level underscores the importance of robust and nuanced healthcare and public health policies. To achieve a substantial reduction in the incidence of female cancers by 2050, the global health response must consider the specific needs and challenges faced by women as a group. By addressing these issues comprehensively, we can work towards a healthier future for women worldwide.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Authors' contributions
Shiling Sun and Wenfu Song conceived the study. Wenfu Song designed the protocol. Wenfu Song, Yingying Li, Liutong Zhang and Yaxuan Yao analysed the GBD data. Wenfu Song, Ping Gao, Xutao Guan, Bing Wang, Yaqiong Guo and Yi Wang contributed to the statistical analysis and interpretation of data. Wenfu Song drafted the manuscript, and other authors revised the manuscript. Shiling Sun and Wenfu Song accessed and verified the underlying data. Yingying Li and Shiqing Jiang revised the manuscript according to the reviewers' comments and made the final modifications and approvals of the manuscript. All authors have read and approved the final version off the manuscript.

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Data availability
The data used in this study can be derived from the GBD 2021 (Available at: https://ghdx.healthdata.org/gbd-2021).

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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