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ARTICLE

Global, Regional and National Burden of Stomach Cancer and Its Prediction in 25 Years: A Cross-Sectional Study of the Global Burden of Disease Study 2021

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Abstract

Aims/Background Given the tremendous threat of stomach cancer (SC) to global public health, detailed information and dynamic updates on the SC health burden are needed to mitigate the repercussions. In this article, we present a systematic analysis of the global burden and trends of SC using data from the Global Burden of Disease (GBD) Study 2021, aiming to provide insights for forming effective global management and prevention strategies.

Methods Stomach cancer incidence, prevalence, mortality, disability-adjusted life years (DALYs) and the corresponding age-standardized rates (ASRs) were estimated. Then, trends of the disease burden were analyzed using the estimated annual percentage changes (EAPC). Lastly, we made a unique attempt to use two powerful and versatile techniques, autoregressive integrated moving average (ARIMA) and exponential smoothing (ES) models, to provide more comprehensive and accurate forecasts for future trends in the disease burden.

Results Despite the steady decreasing trend in age-standardized rates, the total numbers of incidence, prevalence, and deaths all increased from 1990 to 2021. Subgroup analysis demonstrated great disparities in different age and gender groups, sociodemographic index (SDI) quintiles, GBD regions and countries. Both the ARIMA and ES models demonstrated a persistent rise in SC cases and a concurrent decline in ASRs, with the trend being more pronounced in males.

Conclusion Since SC is already a significant health issue globally, it is expected that the estimated disease burden will continue to rise in the future. Therefore, global coordinated efforts are needed to implement effective screening projects, consolidate preventive measures and formulate targeted treatments to alleviate the SC burden.

Key words: stomach cancer; global burden of disease; global health; epidemiology; trend analysis

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Introduction

Stomach cancer (SC), an important entity in the spectrum of gastrointestinal cancers, poses a substantial burden on global health due to its high incidence and mortality rates. In 2022, SC claimed approximately 660,000 lives, accounting for 6.8% of cancer-related deaths worldwide (Bray et al, 2024). Although temporal trends in SC morbidity and mortality have fallen in some regions over the past few decades owing to effective control of *Helicobacter pylori* (*H. pylori*) infection, improved sanitation, and rapid advancements in diagnosis and treatment (Luo et al, 2017), it is projected that there will be a 62% surge in the global burden of this malignancy by 2024 due to population aging and population growth (Song et al, 2022; Thrift et al, 2023). In addition, the incidence of gastroesophageal junction cancer, a subtype of SC, is increasing worldwide, particularly in North America, Europe, and high-income Asian countries, due to increased obesity, gastroesophageal reflux disease, and westernized lifestyle (Petrillo and Smyth, 2020). SC survival rates vary significantly by region, with the 5-year survival rate reaching 60–70% in high-incidence countries like Japan and South Korea due to early detection programs (Sekiguchi et al, 2022), while western countries exhibit a lower survival rate (33.1% in the USA and 20.7% in the UK) due to late-stage diagnoses; on global scale, advanced-stage gastric cancer remains highly lethal, evidenced by a 5-year survival rate of only 5–10% (Casamayor et al, 2018). From the economic standpoint, SC imposes substantial economic and social burdens, with combined financial costs reaching USD 20.6 billion in 2017 (Casamayor et al, 2018). Hence, a systematic analysis of worldwide patterns and trends of SC is paramount for robust policymaking and disease burden alleviation.

Persistent disparities in SC burden have been reported in previous studies, but these studies mainly focused on a certain area or country, and the extent to which global trends and patterns vary geographically and temporally still needs clarification and dynamic update. Moreover, existing studies predicting future trends of SC often rely on single models with inconsistent results (Arnold et al, 2020; Jiang et al, 2024b). Therefore, systematically analyzing the global burden of stomach cancer and predicting its future trends is of paramount importance. The goal of the current study was to analyze the temporal and regional variations in global disease burden using the most comprehensive and systematic dataset: the Global Burden of Disease (GBD) Study 2021. Further, two time series analysis techniques were utilized for predicting the cancer burden from 2022 to 2046. We are hopeful that the results stemming from this analysis will offer a comprehensive understanding of the current burden distribution, which is crucial for informing the effective allocation of healthcare resources and mitigating the impact of SC.

Methods

Study Population and Data Collection

The data available in the GBD 2021 were obtained via systematic monitoring and analyzed using modeling techniques. These data have been widely used in disease burden research. The GBD 2021 offers the most up-to-date and comprehensive depiction of distribution and trends in epidemiology for 459 health outcomes in 204 countries and territories. The International Classification of Diseases (ICD)-10 codes were applied to define SC mortality and non-fatal cases. According to GBD 2021, the ICD-10 codes for non-fatal stomach cancer are C16-C16.9, and codes for lethal stomach cancer are C16-C16.9, D00.2, D13.1 and D37.1.

The sociodemographic index (SDI) incorporated in the GBD study is a composite indicator of average per capita income, cumulative fertility rates in females younger than 25 years, and state-level educational attainment. The SDI value is proportional to the degree of health-related development. In GBD 2021, SDI values were multiplied by 100 for reporting, and based on the values, 204 countries and territories were divided into 5 regions: high, high-middle, middle, low-middle, and low.

In the present study, we obtained and analyzed GBD 2021 data on SC prevalence, incidence, mortality and disability-adjusted life years (DALYs) by sex (male and female), age (17 age groups, from 15 to ≥95 years at 5-year intervals), SDI quantiles, GBD regions and countries.

Statistical Analysis

First, specific numbers of incident cases, prevalent cases, deaths and DALYs attributed to SC in 2021 and the corresponding age-standardized rates (ASRs) were reported, both holistically and by different subgroups. Prevalence and incidence were modeled using DisMod-MR 2.1 (Disease Modeling Meta-Regression; version 2.1, Institute for Health Metrics and Evaluation, Seattle, WA, USA), a Bayesian meta-regression method that leverages disparate and limited epidemiological data to establish nonfatal outcomes and generates internally consistent incidence, prevalence, remission, and mortality estimates (Ferrari et al, 2024). For fatal diseases, causes of death were modeled via the Cause of Death Ensemble model (CODEm) (Naghavi et al, 2024). DALYs, defined as years of healthy life lost to premature death and disability, were calculated to quantify the disease burden of SC; the calculation formula is as follows:

$$\text{DALY} = \text{YLL} + \text{YLD}$$

where YLL represents total years of life lost, and YLD represents total years lived with disability (Ferrari et al, 2024). Age-standardized rate (ASR) estimates per 100,000 individuals and counts were presented in alignment with the GBD population standard framework. The 95% uncertainty interval (UI) was calculated from the 2.5th and 97.5th percentiles of an ordered set of 1000 draws.

Then, we estimated the dynamic trends of incidence, prevalence, mortality and DALYs of SC from 1990 to 2021 using an effective indicator, the estimated annual percentage change (EAPC). A linear regression model was employed on the natural logarithm of the ASRs: $y = \alpha + \beta x + \varepsilon$, where $y = ln(ASR)$, $x = calendar\ year$, α represents the intercept, β represents the slope, and ε represents the error term. The EAPC was computed using the equation: $100 \times (exp(\beta) - 1)$, with the 95% confidence interval (CI) estimated from the regression analysis (Liu et al, 2019). Specifically, the ASR was considered to exhibit an increasing trend if the EAPC estimate and the lower bound of its 95% CI were both >0. Conversely, the ASR was considered decreasing if both the EAPC estimate and the upper bound of its 95% CI were <0. Otherwise, the ASR was regarded as stable over time. Based on EAPCs, the hierarchical cluster analysis was performed by using the "hclust" function in R software (version 4.2.3, R Core Team, Vienna, Austria) to divide all

Table 1. The number of incident cases, prevalent cases, deaths and DALYs attributable to stomach cancer in 2021, and its trends from 1990 to 2021 globally.

	Incidence			Prevalence			Deaths			DALYs		
	Number of incident cases (95% UI)	Age-standardized incidence rate/per 100,000 population (95% UI)	EAPC (95% CI)	Number of prevalent cases (95% UI)	Age-standardized prevalence rate/100,000 (95% UI)	EAPC (95% CI)	Number of deaths (95% UI)	Age-standardized mortality rate/100,000 population (95% UI)	EAPC (95% CI)	Number of DALYs (95% UI)	Age-standardized DALYs rate/100,000 population (95% UI)	EAPC (95% CI)
Global	1,230,233 (1,052,350–1,409,970)	14.33 (12.23–16.41)	–1.81 (–1.87–1.75)	2,393,213 (2,059,698–2,771,476)	27.58 (23.75–31.89)	–1.24 (–1.32–1.16)	954,374 (821,751–1,089,577)	11.2 (9.62–12.73)	–2.26 (–2.34–2.18)	22,786,633 (19,576,344–26,118,869)	262.75 (226.08–301.02)	–2.54 (–2.62–2.46)
Sex												
Female	397,312 (344,272–446,653)	8.63 (7.47–9.7)	–2.24 (–2.31–2.18)	694,957 (606,527–783,245)	15.23 (13.29–17.16)	–1.85 (–1.93–1.77)	329,822 (287,083–368,393)	7.13 (6.22–7.97)	–2.56 (–2.65–2.48)	7,512,286 (6,716,178–8,393,835)	165.57 (148.13–185.02)	–2.8 (–2.89– –2.71)
Male	832,921 (687,723–1,006,469)	20.94 (17.22–25.19)	–1.61 (–1.68–1.53)	1,698,257 (1,404,777–2,052,649)	41.41 (34.19–49.83)	–0.97 (–1.06–0.88)	624,551 (514,019–750,101)	16.03 (13.24–19.12)	–2.11 (–2.2– –2.02)	15,274,347 (12,568,802–18,643,478)	371.24 (305.91–451.15)	–2.41 (–2.5– –2.33)
Age												
15–19 years	728 (601–810)	0.12 (0.1–0.13)	–2.7 (–2.82– –2.59)	1934 (1589–2152)	0.31 (0.25–0.34)	– 2.26 (–2.39–2.13)	461 (382–506)	0.07 (0.06–0.08)	–3.26 (–3.36–3.17)	33,685 (27,876–36,950)	5.4 (4.47–5.92)	–3.26 (–3.35–3.17)
20–24 years	2038 (1745–2240)	0.34 (0.29–0.38)	–2.13 (–2.22–2.04)	5516 (4684–6110)	0.92 (0.78–1.02)	–1.59 (–1.69–1.48)	1278 (1106–1390)	0.21 (0.19–0.23)	– 2.89 (–2.94–2.84)	87,074 (75,348–94,686)	14.58 (12.62–15.86)	–2.89 (–2.94–2.83)
25–29 years	5281 (4464–5798)	0.9 (0.76–0.99)	–1.78 (–1.9– –1.65)	18,106 (15,225–19,977)	3.08 (2.59–3.4)	–1.28 (–1.41–1.15)	2873 (2463–3144)	0.49 (0.42–0.53)	– 2.65 (–2.75–2.55)	181,945 (155,872–199,220)	30.92 (26.49–33.86)	–2.64 (–2.74–2.55)
30–34 years	13,217 (11,232–14,851)	2.19 (1.86–2.46)	–1.98 (–2.14–1.81)	43,823 (36,990–49,609)	7.25 (6.12–8.21)	–1.56 (–1.72–1.39)	7208 (6195–8025)	1.19 (1.02–1.33)	– 2.8 (–2.97– –2.62)	420,455 (361,553–467,946)	69.56 (59.81–77.41)	–2.79 (–2.96–2.61)
35–39 years	20,776 (17,794–23,551)	3.7 (3.17–4.2)	–2.64 (–2.83–2.44)	59,113 (50,176–67,640)	10.54 (8.95–12.06)	– 2.14 (–2.34–1.94)	12,453 (10,870–14,028)	2.22 (1.94–2.5)	– 3.21 (–3.41–3.01)	664,377 (579,300–747,627)	118.46 (103.29–133.3)	–3.21 (–3.4– –3.01)
40–44 years	32,344 (27,977–37,370)	6.47 (5.59–7.47)	–2.61 (–2.74–2.48)	84,108 (72,291–98,135)	16.81 (14.45–19.62)	–1.88 (–2.01–1.74)	20,821 (18,172–23,740)	4.16 (3.63–4.75)	– 3.17 (–3.29–3.06)	1,006,284 (877,843–1,146,824)	201.16 (175.48–229.25)	–3.17 (–3.29–3.06)
45–49 years	50,737 (43,456–60,094)	10.72 (9.18–12.69)	–2.34 (–2.47– –2.2)	123,711 (104,712–147,059)	26.13 (22.11–31.06)	–1.67 (–1.8– –1.53)	33,778 (29,146–39,697)	7.13 (6.16–8.38)	– 2.91 (–3.05–2.77)	1,465,216 (1,263,610–1,722,583)	309.44 (266.86–363.79)	–2.9 (–3.04– –2.76)
50–54 years	85,483 (72,588–102,838)	19.21 (16.31–23.11)	–2.55 (–2.73–2.38)	203,237 (171,028–248,416)	45.68 (38.44–55.83)	–1.91 (–2.1– –1.73)	58,512 (50,065–69,725)	13.15 (11.25–15.67)	– 3.09 (–3.28–2.91)	2,258,788 (1,933,764–2,692,795)	507.68 (434.63–605.23)	–3.09 (–3.27– –2.9)
55–59 years	123,232 (104,531–145,418)	31.14 (26.41–36.75)	–2.47 (–2.58–2.37)	285,460 (241,995–343,896)	72.14 (61.15–86.9)	–1.83 (–1.96– –1.7)	84,565 (72,233–98,411)	21.37 (18.25–24.87)	– 3.04 (–3.14–2.94)	2,871,707 (2,447,571–3,346,393)	725.68 (618.5–845.63)	–3.03 (–3.13–2.93)
60–64 years	139,740 (120,440–161,958)	43.66 (37.63–50.6)	–2.15 (–2.22–2.09)	304,251 (260,191–353,993)	95.06 (81.3–110.61)	–1.46 (–1.56–1.36)	101,033 (87,297–116,997)	31.57 (27.28–36.56)	– 2.71 (–2.76–2.66)	2,953,643 (2,550,400–3,417,710)	922.88 (796.88–1067.87)	–2.7 (–2.75– –2.66)
65–69 years	185,153 (157,412–214,943)	67.12 (57.07–77.92)	–1.95 (–2.03–1.87)	378,417 (320,020–439,688)	137.19 (116.02–159.4)	–1.2 (–1.28– –1.12)	136,724 (117,359–157,329)	49.57 (42.55–57.04)	– 2.52 (–2.63–2.41)	3,369,997 (2,891,421–3,877,770)	1221.71 (1048.22–1405.79)	–2.51 (–2.61– –2.4)

Table 1. Continued.

	Incidence			Prevalence			Deaths			DALYs		
	Number of incident cases (95% UI)	Age-standardized incidence rate/per 100,000 population (95% UI)	EAPC (95% CI)	Number of prevalent cases (95% UI)	Age-standardized prevalence rate/100,000 (95% UI)	EAPC (95% CI)	Number of deaths (95% UI)	Age-standardized mortality rate/100,000 population (95% UI)	EAPC (95% CI)	Number of DALYs (95% UI)	Age-standardized DALYs rate/100,000 population (95% UI)	EAPC (95% CI)
70–74 years	192,015 (162,607–221,305)	93.28 (79–107.51)	–1.68 (–1.82–1.55)	359,649 (306,931–413,967)	174.72 (149.11–201.11)	– 0.86 (–1.01–0.71)	147,156 (125,392–169,150)	71.49 (60.92–82.18)	– 2.26 (–2.42– –2.1)	2,989,198 (2,546,846–3,438,906)	1452.2 (1237.3–1670.68)	–2.25 (–2.41– –2.1)
75–79 years	149,233 (126,471–169,400)	113.15 (95.9–128.45)	–1.4 (–1.51– –1.29)	241,659 (206,969–272,274)	183.24 (156.93–206.45)	– 0.68 (–0.81–0.54)	124,396 (105,677–141,627)	94.32 (80.13–107.39)	–1.89 (–2.01–1.77)	2,019,663 (1,713,388–2,297,943)	1531.39 (1299.16–1742.39)	–1.89 (–2.01–1.77)
80–84 years	115,220 (97,519–128,648)	131.56 (111.35–146.89)	–1.08 (–1.14–1.01)	164,987 (140,929–183,410)	188.38 (160.91–209.41)	– 0.31 (–0.42–0.19)	106,338 (90,306–118,763)	121.41 (103.11–135.6)	–1.47 (–1.53–1.42)	1,350,350 (1,145,189–1,509,215)	1541.79 (1307.55–1723.18)	–1.48 (–1.53–1.42)
85–89 years	75,040 (61,735–83,880)	164.12 (135.02–183.46)	–0.66 (–0.74–0.59)	84,779 (68,913–95,332)	185.42 (150.72–208.5)	0.08 (–0.05–0.21)	72,362 (60,172–80,757)	158.27 (131.61–176.63)	–1.11 (–1.21–1.02)	730,929 (606,085–815,508)	1598.64 (1325.59–1783.63)	–1.11 (–1.21–1.02)
90–94 years	31,292 (25,089–35,222)	174.92 (140.25–196.89)	–0.44 (–0.49–0.38)	29,846 (23,329–33,906)	166.84 (130.41–189.53)	0.45 (0.32–0.58)	33,554 (26,958–37,645)	187.56 (150.69–210.43)	– 0.92 (–0.97–0.87)	295,210 (237,668–331,641)	1650.2 (1328.54–1853.84)	–0.91 (–0.96–0.86)
95+ years	8705 (6135–10,063)	159.72 (112.56–184.64)	0.03 (–0.05–0.1)	4617 (3238–5327)	84.72 (59.41–97.74)	0.15 (0.08–0.22)	10,862 (7689–12,553)	199.3 (141.08–230.31)	– 0.42 (–0.49–0.35)	88,112 (62,651–101,719)	1616.65 (1149.49–1866.3)	–0.48 (–0.55– –0.4)
SDI region												
High-middle SDI	387,196 (315,957–457,286)	19.62 (16.02–23.13)	–1.75 (–1.84–1.65)	749,747 (610,195–903,200)	38.28 (31.13–46.09)	– 0.72 (–0.84–0.61)	295,105 (244,787–343,611)	14.93 (12.4–17.36)	– 2.47 (–2.59–2.35)	6,901,607 (5,703,610–8,141,888)	353.18 (291.89–416.78)	–2.79 (–2.91–2.66)
High SDI	239,119 (215,071–256,938)	11.16 (10.21–11.91)	–2.4 (–2.46– –2.34)	592,767 (542,982–629,774)	29.39 (27.2–31.24)	–1.99 (–2.1– –1.89)	153,539 (136,670–165,354)	6.83 (6.18–7.34)	– 2.79 (–2.81–2.76)	2,897,404 (2,654,584–3,101,177)	146.1 (135.56–155.89)	–3.15 (–3.18–3.13)
Low-middle SDI	110,396 (97,098–126,222)	7.68 (6.71–8.77)	–0.82 (–0.86–0.78)	157,615 (139,220–179,612)	10.34 (9.11–11.79)	– 0.69 (–0.73–0.66)	107,456 (94,064–122,211)	7.71 (6.69–8.76)	– 0.89 (–0.94–0.85)	2,953,125 (2,599,859–3,357,038)	192.56 (169.42–219.14)	–1.08 (–1.12–1.04)
Low SDI	41,388 (32,600–46,956)	8.13 (6.44–9.22)	–1.11 (–1.16–1.06)	57,598 (45,194–65,610)	10.22 (8.07–11.56)	–1.1 (–1.15– –1.05)	41,192 (32,515–46,864)	8.46 (6.71–9.6)	–1.1 (–1.15– –1.04)	1,198,903 (940,407–1,371,290)	209.77 (165.6–238.95)	–1.35 (–1.4– –1.29)
Middle SDI	451,465 (368,224–542,292)	16.91 (13.79–20.28)	–1.79 (–1.88– –1.7)	834,461 (673,685–1,015,061)	30.06 (24.25–36.54)	– 0.93 (–1.01–0.84)	356,459 (294,160–423,770)	13.72 (11.31–16.22)	– 2.42 (–2.54– –2.3)	8,820,717 (7,336,337–10,567,624)	320.24 (266.07–382.87)	–2.75 (–2.86–2.63)

DALYs, disability-adjusted life years; UI, uncertainty interval; CI, confidence interval; SDI, sociodemographic index; EAPC, estimated annual percentage change.

45 GBD regions into four groups: minor increase, remained stable or showed a minor decrease, significant decrease, and significant increase.

Finally, we adopted the autoregressive integrated moving average (ARIMA) model and the exponential smoothing (ES) model in the time series analysis for disease burden prediction. The ARIMA model is well-suited for long-term forecasting by modeling complex dependencies in time series, while the ES model is particularly effective for short-term predictions and adaptive trend smoothing (Xian et al, 2023). All data collection, analysis and image drawing were performed using R software (version 4.2.3, R Core Team, Vienna, Austria), freely available from the R Foundation for Statistical Computing at https://www.r-project.org.

Results

Global Trends of Stomach Cancer Burden From 1990 to 2021

Fig. 1 shows a visual chart of the temporal trend of global SC burden. From 1990 to 2021, the global incident cases of SC increased by 25.41% (**Supplementary Table 1**), reaching 1,230,233 (95% UI: 1,052,350–1,409,970) cases in 2021 (Table 1). Despite this rise, the age-standardized incidence rate (ASIR) declined by 42.12%, from 24.76 (95% UI: 22.58–27.00) to 14.33 (95% UI: 12.23–16.41), with an EAPC of –1.81 (95% CI: –1.87– –1.75) (**Supplementary Table 1**). A similar paradoxical trend was observed for prevalence (**Supplementary Table 2**) and mortality (**Supplementary Table 3**). While absolute prevalent cases increased to 2,393,213 (95% UI 2,059,698–2,771,476) and deaths increased to 954,374 (95% UI 821,751–1,089,577), the corresponding ASR (age-standardized rate of prevalence [ASPR]: EAPC = –1.24 [95% CI: –1.32– –1.16]; age-standardized mortality rate [ASMR]: EAPC = –2.26 [95% CI: –2.34– –2.18]) demonstrated significant reductions (Table 1). This divergence likely reflects the interplay between population structure and individual disease burden. The increase in absolute numbers reflected the challenges posed by population expansion and aging, while declining ASRs highlighted the true impact of medical advancements and public health interventions. The number of DALYs cases showed a minor reduction of 1.94% and the age-standardized DALYs rate (ASDR) presented a more prominent decrease of 53.06% (EAPC = –2.54 [95% CI: –2.62– –2.46]) (**Supplementary Table 4**), which further highlights the improvements in health status and the successful control of diseases. More detailed results of estimated incidence (**Supplementary Table 1**), prevalence (**Supplementary Table 2**), mortality (**Supplementary Table 3**), and DALYs (**Supplementary Table 4**) and their trends can be found in the supplementary files.

Geographic Disparities of Stomach Cancer Burden

Substantial heterogeneity was found across regions (Fig. 2, **Supplementary Fig. 1**). The largest number of new cases was detected in Asia (913,055 [95% UI: 751,620–1,089,660]), particularly in China, Japan and India. China alone accounted for more than half of all global incident and prevalent cases (**Supplementary Tables 1,2**), 46.62% of global deaths (**Supplementary Table 3**) and 46.70% of

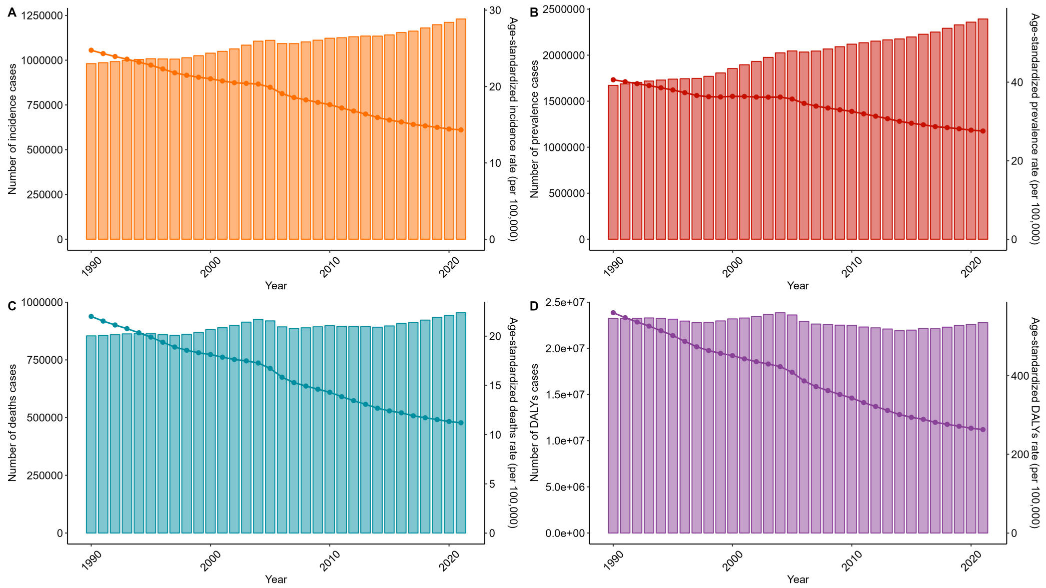

Fig. 1. Changes in stomach cancer burden from 1990 to 2021. The columns represent numbers of incidence (A), prevalence (B), deaths (C) and DALYs (D) cases, while the dots represent the corresponding age-standardized rates. DALYs, disability-adjusted life years.

global DALYs (**Supplementary Table 4**). On a regional basis, East Asia bore the highest ASIR of 28.64 (95% UI: 22.23–35.55), exceeding the global average by 100%, whereas the lowest ASIRs were found in Northern Africa (5.01 [95% UI: 3.51–6.03]), North America (5.23 [95% UI: 4.9–5.46]), and South Asia (5.7 [95% UI: 4.92–6.84]). As for SC mortality, the lowest ASMRs were reported in North America (2.95 [95% UI: 2.72–3.1]), Australasia (3.91 [95% UI: 3.49–4.25]) and Northern Africa (4.95 [95% UI: 3.51–5.96]), and the highest ASMRs were recorded in Andean Latin America (21.33 [95% UI: 17.3–26.08]), East Asia (21.26 [95% UI: 16.59–26.22]) and Western Pacific Region (18.94 [95% UI: 15.3–22.87]). Specifically, Mongolia, Afghanistan and Bolivia ranked at the top three for the highest ASIR, ASMR and ASDR. **Supplementary Figs. 2,3** depict the SC burden trends on the world map.

A hierarchical clustering analysis was conducted based on combined EAPC values of ASRs to identify similar changing trends across all 54 GBD regions. Fig. 3 clearly showed that the majority of regions were categorized into "significant decrease", including Eastern Sub-Saharan Africa, Eastern Africa and World Bank Lower Middle Income. 7 regions were categorized into "significant increase", including World Bank High Income, Advanced Health System, European Region, Europe & Central Asia-WB, Europe, Eastern Europe and High-income Asia Pacific.

Subgroup Heterogeneity of Stomach Cancer Burden

The burden of SC varied significantly across different subgroups, including age (**Supplementary Fig. 4**), sex (**Supplementary Fig. 5**), and SDI regions (**Supplementary Fig. 6**). These differences reflected the complex interactions be-

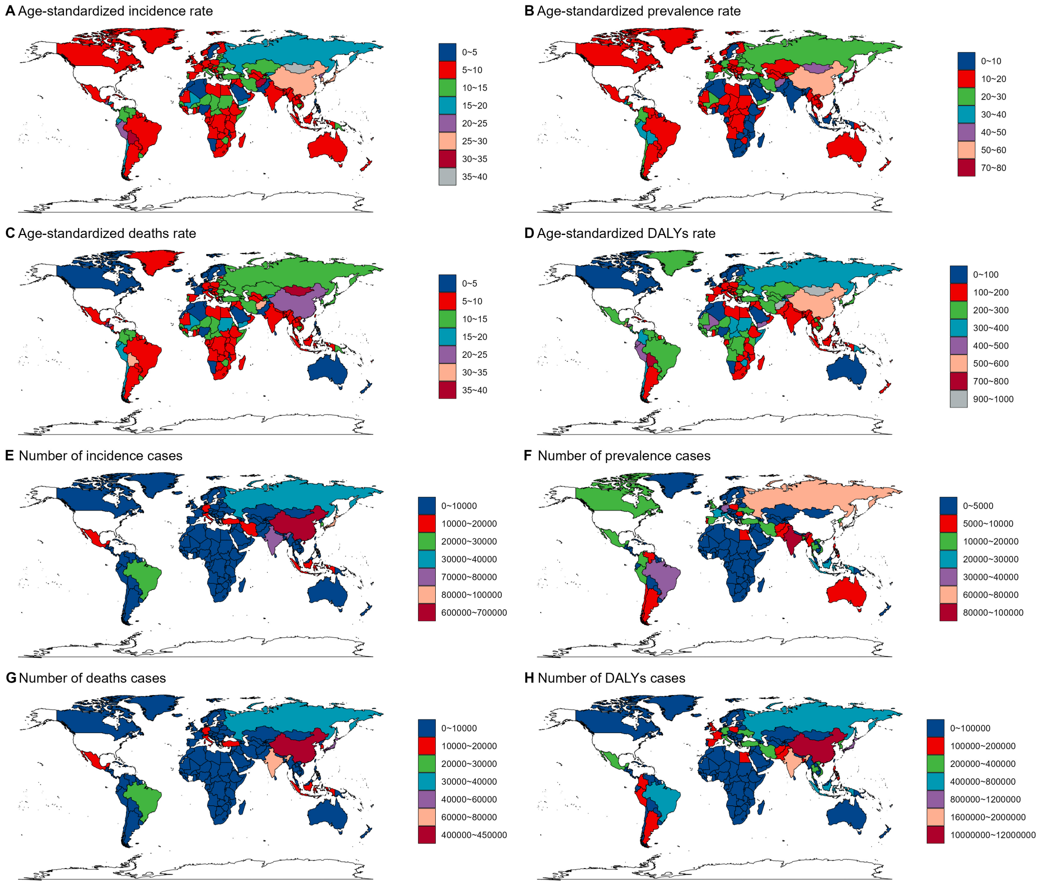

Fig. 2. World maps depicting stomach cancer burden in 2021. Age-standardized rates of stomach cancer incidence rate (A), prevalence rate (B), deaths rate (C), DALYs rate (D), number of incidence cases (E), prevalence cases (F), deaths cases (G) and DALYs cases (H) in 204 countries around the world. DALYs, disability-adjusted life years.

tween biological, demographic, and socio-economic factors, which can shape the overall disease burden in distinct populations.

The burden of SC showed dramatic disparities across age groups, with elderly populations bearing the brunt of the disease. Individuals aged 65 and older accounted for 47.59% of global DALYs (**Supplementary Table 4**), reflecting the cumulative impact of aging and prolonged exposure to risk factors. The highest ASRs were all recorded in age groups over 80: ASIR and ASDR peaked in the 90–94 age group, while the maximum ASMR was recorded in those aged 95 and older (**Supplementary Fig. 4**). These trends underscore the challenges of managing SC in aging populations, where comorbidities and late-stage diagnoses are common. In contrast, individuals in the younger age groups (15–19 years) have experienced the steepest declines in ASIR (EAPC = –2.7% [95% CI: –2.82– –2.59]) and ASDR (EAPC = –3.26 (95% CI: –3.35– –3.17]) (**Supplementary Table 1**, **Supplementary Fig. 7**), likely due to reduced *H. pylori* transmission and improved sanitation in recent decades. However, the rising prevalence among the oldest groups (90–94 years: EAPC = 0.45 [95% CI: 0.32–0.58]; 95+ years: EAPC = 0.15 [95% CI: 0.08–

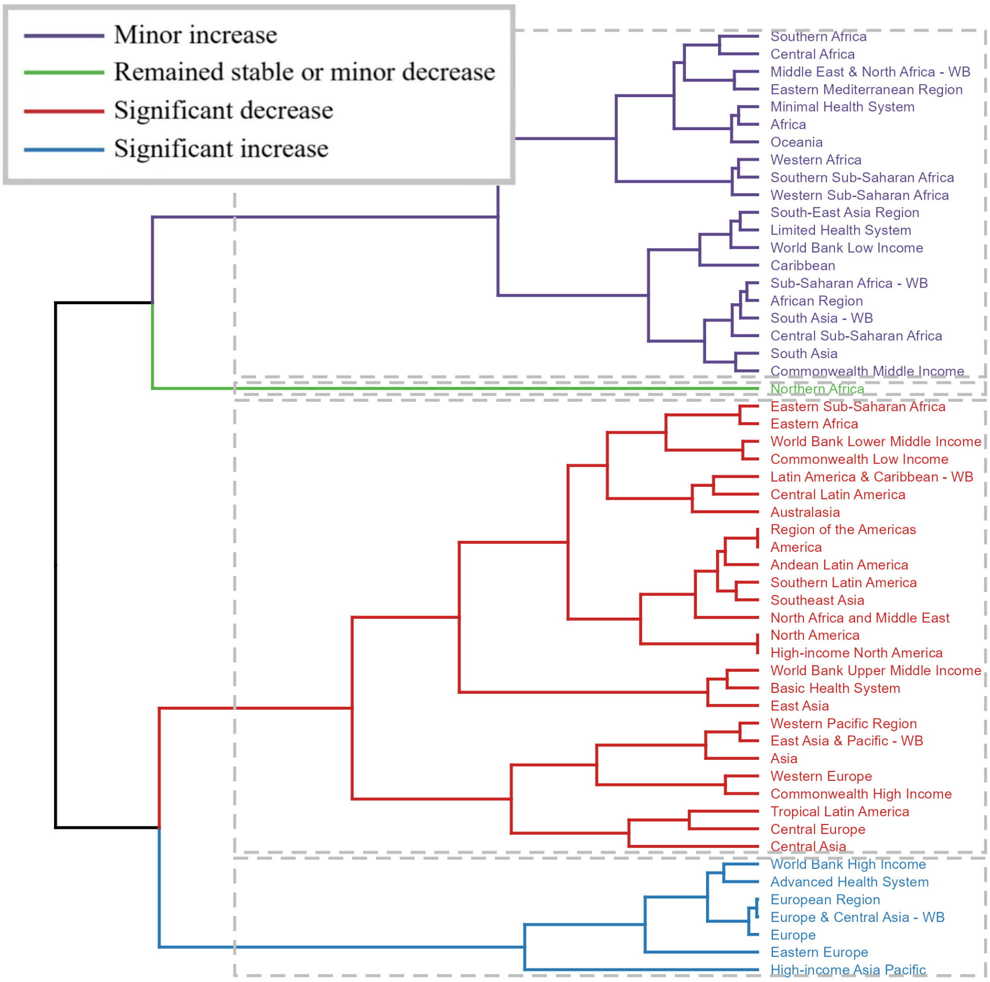

Fig. 3. Results of cluster analysis based on the EAPC values of the age-standardized rates for stomach cancer from 1990 to 2021. EAPC, estimated annual percentage change.

0.22]) (**Supplementary Table 2**) highlights the growing burden of SC in an aging global population (**Supplementary Fig. 7**).

In terms of sex disparities, men faced higher SC burden globally compared to women, with ASIRs of 20.94 [95% UI: 17.22–25.19] vs. 8.63 [95% UI: 7.47–9.70] (**Supplementary Table 1**), ASPR (41.41 [95% UI: 34.19–49.83] vs. 15.23 [95% UI: 13.29–17.16]) (**Supplementary Table 2**), ASMR (16.03 [95% UI: 13.24–19.12] vs. 7.13 [95% UI: 6.22–7.97]) (**Supplementary Table 3**), and ASDR (371.24 [95% UI: 305.91–451.15] vs. 165.57 [95% UI: 148.13–185.02]) (**Supplementary Table 4**) in men being more than two times higher than in women. Despite alleviation of the relevant disease burden in both sexes, ASRs among males exhibited a steeper decline when compared to females (**Supplementary Fig. 8**). Furthermore, from 1990 to 2021, men exhibited a more pronounced increase in the ASIR-to-ASMR ratio (15.04% [from 1.13 to 1.30]) when compared to women (10.00% [from 1.10 to 1.21]). This trend revealed that although men historically bear a higher SC burden, accelerated declines in their ASRs and increased ASIR-to-ASMR ratio signal the potential success of public health interventions tailored to male-dominated risk profiles.

Socioeconomic development further shapes the SC burden. As shown in Fig. 4, from 1990 to 2021, the middle SDI region, including India and South Africa, witnessed the sharpest rise of 48.56%, 84.33%, 25.51% and 7.46% in incidence, prevalence, death and DALY cases, respectively. Despite the largest absolute cases in the middle SDI region, the corresponding ASRs generally showed an inverted "U" relationship with SDI, with the rate reaching peak in the high-middle SDI group (**Supplementary Fig. 6**). This phenomenon may be explained by how economic development in these regions led to lifestyle changes that initially exacerbate the burden of SC, yet effective prevention and treatment strategies were still insufficient to mitigate this increased risk. High-SDI regions, such as South Korea and Japan, achieved the fastest declines in SC burden (ASIR: EAPC = –2.40 [95% CI: –2.46– –2.34] [**Supplementary Table 1**]; ASMR: EAPC = –2.79 [95% CI: –2.81– –2.76] [**Supplementary Table 3**]), owing to advanced screening programs and widespread access to treatment. A transient rise in ASPR within high-middle and middle SDI regions between 2000 and 2004, likely due to expanded screening programs, was followed by accelerated declines as interventions took effect, demonstrating the importance of sustained public health efforts.

Predictions of the Stomach Cancer Burden From 2022 to 2046

We adopted the ARIMA model and the exponential smoothing (ES) model in time series to make a quantitative forecast of the SC burden, and the results are exhibited in Figs. 5,6. According to the ARIMA model, the number of incidence cases would increase steadily over the next 25 years and reach a new record of 997,973.75 (95% UI: 917,389.68–1,078,557.83) male cases and 553,273.27 (95% UI: 361,788.51–744,758.04) female cases by 2025, with the growth rate similar in both sexes. With regard to ASRs, ASIRs were predicted to decline continually. Compared to females, ASIR for males tends to decline at a more rapid rate (50.87% vs. 25.81%). A similar pattern of changes was also observed in ASMR (male 70.75% vs. female 25.11%) and ASDR (male 85.19% vs. female 6.39%), with a faster rate of decline in males. As for ASPR, both sexes present a similar decline rate from 2022 to 2046 (**Supplementary Table 5**).

The ES model showed a minor change in predicted disease burden in females for the next 25 years. The projected trends indicate a continued rise in the absolute numbers of male incidence cases, prevalence cases, and deaths, however, the rate of increase shows a progressive decline over time. An opposite trend was found in ASRs for males, which declined over time at a progressively slower rate. The predicted changing rates of ASIR, ASPR, ASMR, and ASDR for males were 6.30%, 6.11%, 9.72%, and 11.16%, respectively (**Supplementary Table 6**).

The divergence between ARIMA and ES forecasts for SC burden likely stemmed from structural differences in model assumptions. The ARIMA model captures linear trends and autocorrelations, while the ES model assigns decaying weights to past obserbations, prioritizing recent data. Both models struggle with long-term trends and external factors infuencing cancer burden (Xian et al, 2023).

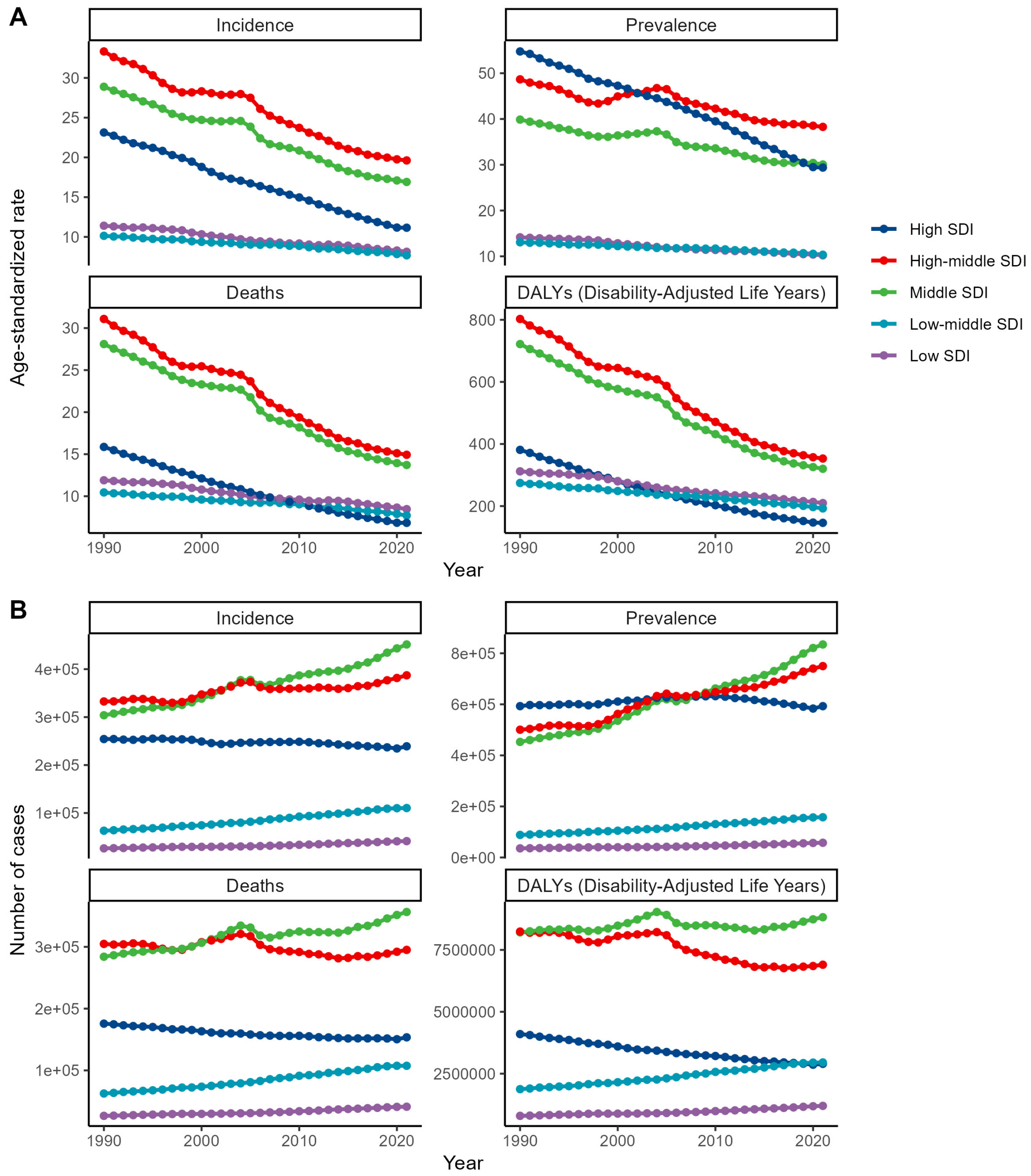

Fig. 4. Temporal trends of stomach cancer burden in different SDI quantiles from 1990 to 2021. (A) Temporal trends of ASRs of stomach cancer incidence, prevalence, deaths and DALYs from 1990 to 2021. (B) Temporal trends of the numbers of stomach cancer incidents, prevalence, deaths and DALYs cases from 1990 to 2021. ASR, age-standardized rate; DALYs, disability-adjusted life years; SDI, sociodemographic index.

Discussion

To the best of our knowledge, this is the most thorough study to comprehensively investigate and predict global burden of SC using the latest updated GBD 2021 dataset. Despite the steady decreasing trend in the ASRs, the total number of incident cases, prevalent cases, and deaths all increased significantly from 1990 to 2021, and a continued rise of all these variables was predicted to persist for the next 25 years, making SC a significant entity of global disease burden that necessitates immediate action.

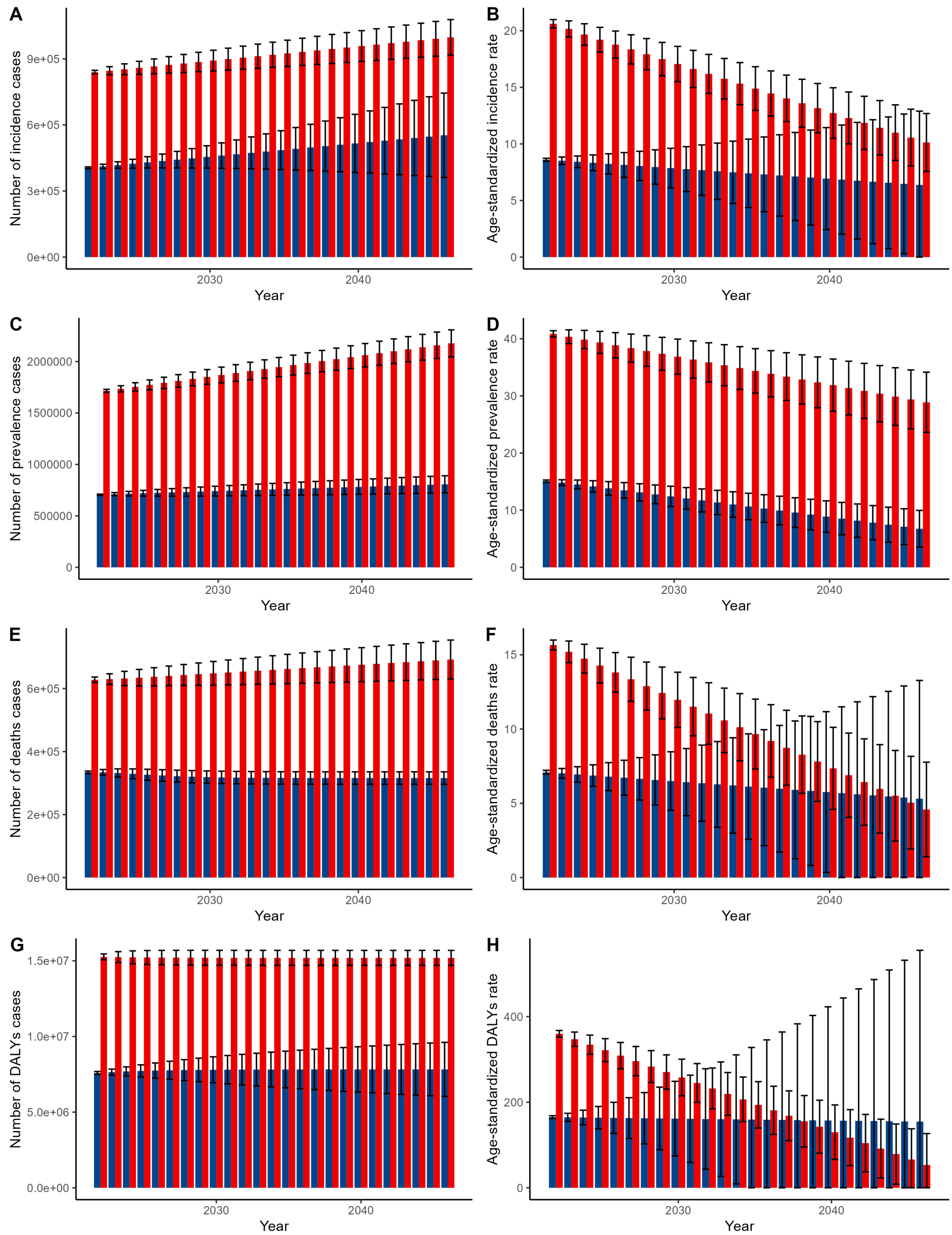

Fig. 5. Prediction of stomach cancer burden leading up to 2046 by ARIMA model. Predicted trends in stomach cancer incidence cases (A), age-standardized incidence rate (B), prevalence cases (C), age-standardized prevalence rate (D), deaths cases (E), age-standardized deaths rate (F), DALYs cases (G), and age-standardized DALYs rate (H) in both sexes by ARIMA model. The blue-colored bar represents females, while the red represents males. ARIMA, autoregressive integrated moving average; DALYs, disability-adjusted life years.

Our findings were generally in line with those found in the 2022 GLOBOCAN database (Bray et al, 2024). From 1990 to 2022, SC dropped from the second to the fifth leading cause of cancer-related deaths. In the present study, we discovered that the mortality of SC decreased at a faster rate than the incidence, and the same

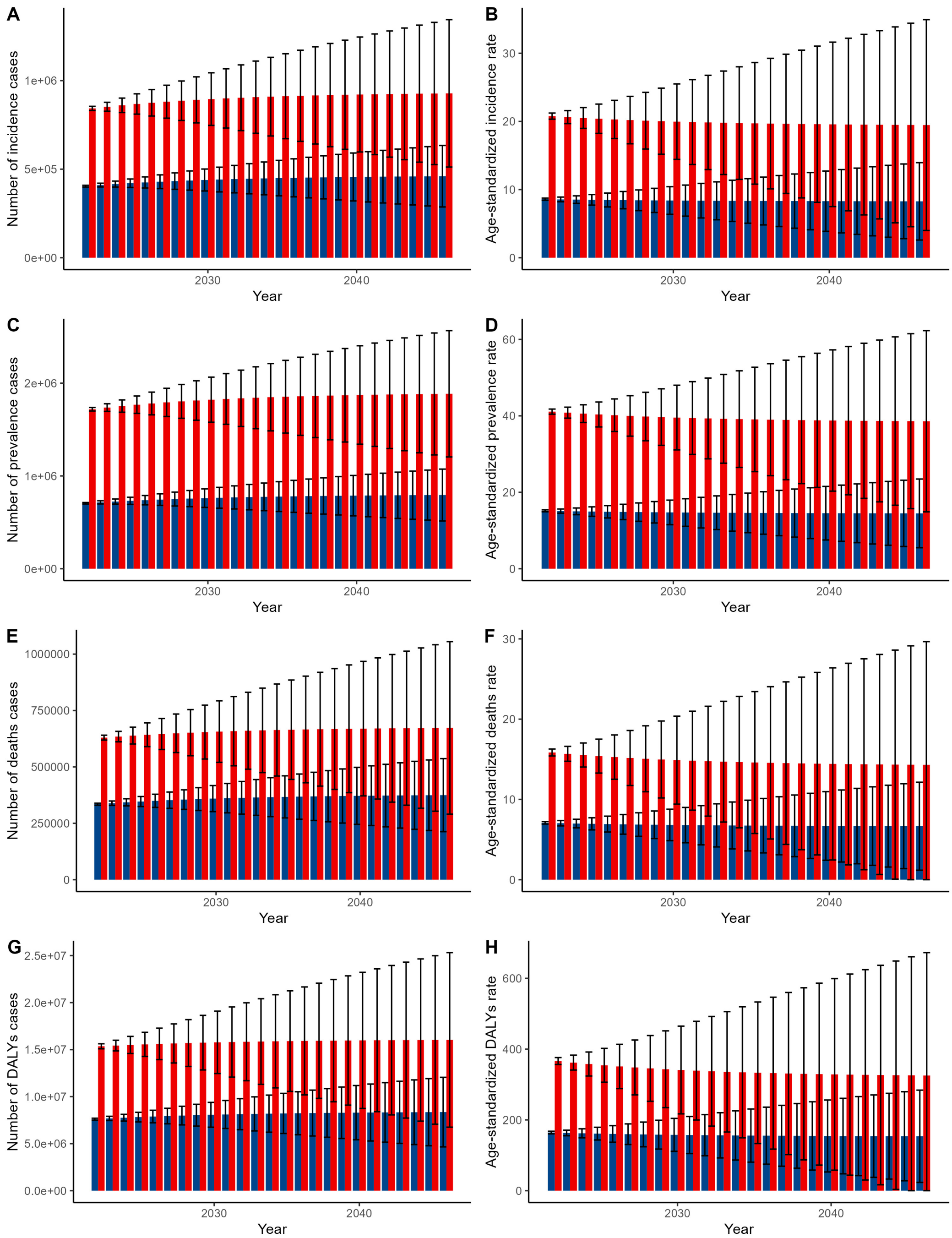

Fig. 6. Prediction of stomach cancer burden leading up to 2046 by ES model. Predicted trends in stomach cancer incidence cases (A), age-standardized incidence rate (B), prevalence cases (C), age-standardized prevalence rate (D), deaths cases (E), age-standardized deaths rate (F), DALYs cases (G) and age-standardized DALYs rate (H) in both sexes by ES model. The blue-colored bar represents females, while the red represents males. DALYs, disability-adjusted life years; ES, exponential smoothing.

observation has been reported in previous studies (GBD 2017 Stomach Cancer Collaborators, 2020; Petrillo and Smyth, 2020). This may be attributed to optimization of diagnostic tools and treatments, along with an ever-expanding and aging population.

Despite the decreasing ASRs, the world still faces many challenges in reducing the SC burden. The effectiveness of preventing and treating *H. pylori* in reducing the SC burden has been confirmed by numerous studies (Jiang et al, 2024a; Lee et al, 2016), especially in some developed countries, where the declining trend of SC has leveled off in the middle-aged population due to low and stable prevalence of *H. pylori* infection (GBD 2017 Stomach Cancer Collaborators, 2020; Ferro et al, 2014). Chen et al (2024) found a significant reduction in *H. pylori* prevalence in Western Pacific, Southeast Asian, and African regions, where the SC prevalence also showed the same downward trend in our study. Concerningly, the emergence of antibiotic-resistant *H. pylori* strains has been jeopardizing the efficacy of current treatments in approximately 10% to 30% of patients (Mannion et al, 2021; Tshibangu-Kabamba and Yamaoka, 2021). Therefore, enhanced surveillance of rational antibiotic use in parallel with monitoring therapeutic efficacy is required. Moreover, researchers found that the East Asian type cytotoxin-associated gene A (*CagA*) strains harboring glutamic acid-proline-isoleucine-tyrosine-alanine (EPIYA) segments (EPIYA-A, EPIYA-B and EPIYA-D), which were associated with increased risks for developing SC, have been increasing (Ansari and Yamaoka, 2022). Over the last decades, mass population-based screening of *H. pylori* infection was recommended but only launched in a few developed countries due to a lack of resources and inadequate cancer awareness. Hence, along with formulating tailored and personalized treatment, and arousing awareness of cancer prevention, more comprehensive screening methods, especially noninvasive and low-cost methods like the urea breath test, *H. pylori* stool antigen test, and serological testing, should be incorporated into efforts for reducing SC burden (Best et al, 2018).

Our results suggested that the highest SC burden was in people aged over 80, a finding consistent with previous reports (GBD US Health Disparities Collaborators, 2023; Jiang et al, 2024a; Xie et al, 2022; Yu et al, 2024; Zhang et al, 2023). A rising trend in SC prevalence among the oldest age groups was observed in our study. This trend is particularly concerning given the limited treatment options and poorer outcomes often observed in elderly patients (Smyth et al, 2016). Addressing this challenge will require innovations in geriatric oncology care, including tailored screening protocols and multidisciplinary treatment approaches. The heavy burden in the elderly population may be influenced in part by the expanding proportion of aging people in the population and inadequate development of elderly care facilities at a national level. It is essential that health services adapt to new demands. Also, there have been some worrying results indicating an increasing trend of SC in individuals under 50 years in low-incidence countries including the UK and the USA (Arnold et al, 2020; Machlowska et al, 2020; Wang et al, 2024; Wong et al, 2021), and the reasons for which have not yet been clarified (Zhang et al, 2023). Based on emerging evidence, it can be hypothesized that lifestyle-driven epidemiological shifts, particularly the escalating prevalence of obesity attributed to excessive ultra-processed food and alcohol, may accelerate the initiation of carcinogenesis in younger populations. Meanwhile, improved screening and diagnostic methods potentially amplify disease burden detection, creating an observable incidence elevation (Arnold et al, 2020; Liu et al, 2024). The indicators studied in our study all suggested that men suffered more than twice the disease burden compared to women, regardless of geographical differences. The gender differences in SC were due to not only more frequent exposure to risk factors like smoking and drinking by men, but also underlying biological sex differences, including different levels of estrogen and chromosomal structure. Studies have found the connections of female reproductive factors and menopausal hormone therapy with decreased risk of SC (Baek et al, 2022; Jang et al, 2022; Quaas et al, 2022; Song et al, 2024). Underlying mechanisms of estrogen's protective effect include inhibition of caspase-12 expression, which leads to enhanced immune response to bacterial pathogens, interactions with cellular receptors in the gastric mucosa and upregulated expression of trefoil factor family genes, which safeguard the gastric mucosa (Song et al, 2024). Additionally, the X chromosome was recently found to be a protective factor of SC in large-scale studies (Ishigaki et al, 2020; Oh et al, 2020). The physiological differences between males and females may imply a novel pathophysiological mechanism and potential therapeutic target for SC. In addition, studies have found that SC exhibited distinct genetic susceptibilities across global populations, influenced by regional molecular heterogeneity (Alsina et al, 2023; Jin et al, 2020). Asian cohorts exhibited prevalent mutations in FAT Atypical Cadherin 4 (*FAT4*), Piccolo presynaptic cytomatrix protein (*PCLO*), and Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (*PIK3CA*), while African American patients demonstrated higher frequencies of Tumor Protein p53 (*TP53*), Low-Density Lipoprotein Receptor Related Protein 1B (*LRP1B*), and AT-Rich Interaction Domain 1A (*ARID1A*) alterations. Caucasians often harbored Erb-B2 Receptor Tyrosine Kinase 4 (*ERBB4*) and Cadherin 1 (*CDH1*) mutations, with germline *CDH1* variants strongly linked to hereditary diffuse gastric cancer (López et al, 2023; Machlowska et al, 2020). These mutations collectively drive gastric carcinogenesis by disrupting critical signaling pathways and genomic integrity (López et al, 2023; Machlowska et al, 2020).

A recent study found that Asians bear the heaviest burden of SC, especially in men from several South-Central Asian nations (Bray et al, 2024). Similar to this, we also found the highest incidence number in China and the largest ASIR in East Asia. Since Asia is a large continent composed of numerous countries where SC burden varies prominently, several studies have investigated SC burden distribution and trends in Asian countries (Jiang et al, 2024a; Sekiguchi et al, 2022; Tang et al, 2024; GBD 2019 Asia and All Cancers Collaborators, 2024; Zhang et al, 2024). From 1990 to 2019, among the five regions of Asia, the most significant reduction in ASIR was noted in the high-income Asia Pacific (Zhang et al, 2024), which was in line with our finding. Notably, despite the high incidence and prevalence rate in some Asian countries like South Korea and Japan, these countries ranked relatively lower in mortality rate, and the rate of decline in mortality in some of them was leading on a global scale. South Korea has been implementing nationwide SC screening programmes over the last decades, with a participation rate up to 50% in 2011. Individuals over 40 were recommended to receive upper gastrointestinal series or upper endoscopy at a 2-year interval (Jun et al, 2017). In the USA, recent studies call for prevention strategies focusing on high-risk ethnic groups, such as Asian and African American populations (Huang et al, 2022; Zhu et al, 2020).

When compared to China, the USA had lower SC mortality and DALY rates (Qiu et al, 2021). This may imply the efficacy of national evidence-based prevention and large-scale early detection programs for SC in these countries. China has also begun to implement measures to narrow the gap in the SC burden between urban and rural areas (GBD 2017 Stomach Cancer Collaborators, 2020). To bolster the SC elimination efforts, it is necessary to distill the SC screening and prevention strategies from successful cases and adapt them appropriately based on varying conditions across countries. In our study, both ARIMA and ES models projected an increase in SC case numbers alongside a concurrent decline in the corresponding ASRs. This paradoxical trend likely reflects population aging combined with improved early detection and preventive measures. This trend yields critical public health insights, highlighting the need to prioritize resource allocation and implement cost-effective screening programs tailored to demographic shifts.

This study has some limitations. First, since the data used in this study were extracted from a global database, the results were inevitably affected by data quality due to disparities in medical practices, data collection and case registration across countries and regions. For example, in low-income regions and conflict zones, incomplete vital registration systems and limited healthcare access often lead to disease underreporting or misclassification. Variations in diagnostic practices and reporting frequencies in different regions can also introduce biases. Second, we were unable to investigate the burden of distinct subtypes of SC due to data deficiency. Researchers have found that, although the incidence of distal SC associated with *H. pylori* infection has dropped, that of gastroesophageal junction cancers has shown a conspicuous increase (Casamayor et al, 2018; Petrillo and Smyth, 2020). This change was probably ascribed to increased autoimmune gastritis and gastric flora alteration (Morgan et al, 2022). Hence, refined and further research concerning dynamic changes of different types of SC and possible causes are needed. In addition, the present assessment lacks a detailed investigation in different provinces and states, between urban and rural areas. Considering the vast territory and huge discrepancy of disease burden in many countries, more data and comprehensive analyses are needed to inform the formulation of more accurate and geographically tailored prevention and treatment strategies. Finally, we adopted two powerful and versatile time series analysis techniques for SC burden prediction, but biases due to data quality, along with the inability to account for complicated influencing factors like lifestyle or dietary changes, may lead to inconsistencies between the estimated and actual future changes. Further, the large error bars in both ARIMA and ES models reflect the increased uncertainty in long-term predictions. ARIMA's reliance on time-series autocorrelation and ES's emphasis on recent trends contribute to this uncertainty, which is further affected by limited data and the inherent variability in health indicators over time. Thus, great caution is needed when interpreting our results. In order to improve the reliability of long-term projections, future researches that incorporate additional external variables, such as demographic shifts and healthcare interventions, and advanced forecasting techniques are needed.

Conclusion

In summary, this paper comprehensively assesses the current global SC burden and projects its trends up to 2046. Although the ASRs showed a significant decline between 1990 and 2021, the absolute numbers of SC incidence, prevalence and death cases dramatically increased in the same period. The SC burden varied widely across sex, age groups, SDI regions and geographical locations. Stomach cancer remains a substantial disease burden globally, especially in older men in Asia, and populations from the middle to high-middle SDI regions. We also projected that the global SC burden will continue to rise for the next 25 years, indicating the exigency for implementing SC screening and prevention policies.

Key Points

- This comprehensive study analyzed the global burden of stomach cancer (SC) from 1990 to 2021, revealing a paradoxical trend of increasing absolute case numbers alongside declining age-standardized rates (ASRs).
- Geographical disparities in the burden of SC were evident, with East Asia, particularly China, bearing the highest incidence and mortality rates, while regions like Northern Africa and North America reported the lowest.
- This study projected a continued rise in SC cases over the next 25 years, despite declining ASRs, highlighting the need for targeted public health interventions and resource allocation.
- The findings emphasize the urgent need for global, coordinated efforts to implement effective screening, prevention, and treatment strategies to mitigate the rising burden of SC, particularly in high-risk regions and populations.

Availability of Data and Materials

All data used in this study are available at: https://vizhub.healthdata.org/gbd-results/.

Author Contributions

XL: Conceptualization, Methodology, Software, Formal analysis, Writing—original draft, Visualization. QL: Conceptualization, Writing—review and editing. YY: Conceptualization, Methodology, Data curation, Writing—review and editing. ZZ: Formal analysis, Data curation. HZ: Conceptualization, Methodology, Project administration, Writing—review and editing, Supervision. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2025.0023.

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