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Global, Regional, and National Burden of Gastric Cancer in Adolescents and Young Adults, 1990–2019: A Systematic Analysis for the Global Burden of Disease Study 2019

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INTRODUCTION: **Gastric cancer is a significant global health concern, ranking as the fifth most common cancer worldwide and the third leading cause of cancer-related mortality. While improvements in health awareness and medical technology have contributed to a decline in the incidence of gastric cancer in many countries, the rate of gastric cancer in adolescents and young adults (GCAYA) has shown an upward trend. Timely and effective strategies for screening, detection, and treatment are crucial for managing the burden of GCAYA and optimizing the allocation of medical resources. To this end, our study aimed to examine the distribution of the burden of GCAYA across different factors at the global, regional, and national levels between 1990 and 2019. By identifying and analyzing these factors, we can better inform efforts to combat this growing health challenge.**

METHODS: **This study used data from the Global Burden of Disease database to analyze the global, regional, and national incidence, mortality, and disability-adjusted life years (DALY) GCAYA from 1990 to 2019. The age-standardized incidence rate (ASIR), age-standardized mortality rate, and age-standardized DALY rate (ASDR) of GCAYA were summarized and presented in a visually intuitive manner at the global, regional, and national levels. In addition, we calculated the estimated annual percentage change for each indicator of GCAYA globally, regionally, and nationally and visually displayed the results. Furthermore, we conducted an age-based analysis of adolescents and young adults with gastric cancer, comparing the age composition of deaths and the age burden of patients between 1990 and 2019. For the sake of brevity, we will use the abbreviation GCAYA to refer to gastric cancer among adolescents and young adults throughout the remainder of this article.**

RESULTS: **From 1990 to 2019, the incidence of GCAYA has slightly increased globally. The number of newly diagnosed cases rose from 47,932 (95% uncertainty interval 44,592.9–51,005.7) in 1990 to 49,007 (45,007.7–53,078.1) in 2019, while the number of deaths decreased from 35,270 (32,579–37,678.5) to 27,895 (25,710.9–30,240.4). The global ASIR showed a declining trend, decreasing from 22.4 (95% uncertainty interval 21.2–23.6) per 100,000 in 1990 to 15.6 (14.1–17.2) per 100,000 in 2019. The age-standardized mortality rate also showed a declining trend, decreasing from 20.5 (19.2–21.6) per 100,000 in 1990 to 11.9 (10.8–12.8) per 100,000 in 2019. The ASDR also showed a declining trend, decreasing from 493.4 (463.7–523.7) per 100,000 in 1990 to 268.4 (245.5–290.6) per 100,000 in 2019. From 1990 to 2019, the incidence, mortality, and DALY of gastric cancer among male adolescents and young adults were higher than those of female adolescents and young adults. In 2019, the number of male adolescents and young adults with gastric cancer was 2.1 times higher than that of female individuals (368.9 [328.2–410.3] vs 178.2 [160.5–196.9]), the number of deaths was 1.1 times higher (14,971.6 [13,643.3–16,520.5] vs 12,923.6 [11,550.3–14,339]), and the DALY were 1.1 times higher (841,920.5 [766,655.5–927,598.8] vs 731,976.3 [653,421–814,242.8]). The incidence and DALY of GCAYA were higher in regions with high-middle and middle sociodemographic index countries. The age-standardized mortality rate of GCAYA in 198 countries and territories showed a decreasing trend, with the Republic of Korea showing the greatest decrease from 1,360.5 (1,300.3–51,416.5) per 100,000 in 1990 to 298.7 (270.1–328.4) per 100,000 in 2019, with an estimated annual percentage change of −5.14 (95% confidence interval −7.23 to −2.99). The incidence and DALY of GCAYA increased with age, with the highest proportion of patients being in the 35–39 years age group. In both 1990 and 2019, the age of death from GCAYA was mainly concentrated in the 35–39 years age group, accounting for approximately half of the total population.**

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DISCUSSION: **In the past 30 years, although the total number of new cases of GCAYA has increased with population growth, the ASIR and overall disease burden have shown a decreasing trend. This indicates progress in screening, diagnosis, treatment, education, and awareness efforts. However, the distribution of this disease remains uneven in terms of sex, age, development level, region, and country. To address these challenges, global health authorities should take appropriate measures such as optimizing screening programs, strengthening awareness and screening efforts for male individuals, enhancing prevention and control among the 35–39 years age group, improving infrastructure and health care resources in developing countries, promoting international cooperation, and implementing tailored measures.**

KEYWORDS: gastric cancer; global burden of disease; adolescents and young adults; age-standardized incidence rate; age-standardized DALY rate; estimated annual percentage change

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/D83, http://links.lww.com/AJG/D84, http://links.lww.com/AJG/D90

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INTRODUCTION

Gastric cancer is one of the most common malignant tumors worldwide (1,2), and gastric cancer in adolescents and young adults (GCAYA) refers to stomach cancer that occurs in young people (usually aged 15–39 years). According to recent research, the incidence of GCAYA is unevenly distributed and has been increasing globally year by year, especially in Asian countries such as South Korea, Japan, and China (3,4), where the incidence of GCAYA is higher among young people (3). In addition, some developing countries in Africa also have a high incidence (5). The reasons for GCAYA are not fully understood, but current research suggests that it is related to factors such as dietary habits, *Helicobacter pylori* infection (6), genetic factors, environmental factors, and lifestyle (1). The United Nations and the World Health Organization have been committed to preventing and controlling the occurrence and spread of gastric cancer, with the ultimate goal of reducing the incidence and mortality of gastric cancer, improving the quality of life of patients with gastric cancer, and helping all countries around the world achieve a healthier future. Overall, the overall incidence of gastric cancer has begun to decline in many countries, and some progress has been made in controlling the overall incidence (1). However, the incidence of GCAYA has been increasing year by year and is unevenly distributed in different countries, which should be a cause for concern (7). To respond to the latest characteristics of GCAYA, targeted measures are needed to prevent and control its occurrence and protect people's health. Therefore, we need to track the changes in the latest trends and burden of GCAYA at the global, regional, and national levels, analyze the incidence trends and epidemiological characteristics of different countries, and take corresponding measures to improve the situation. This study aims to investigate the global, regional, and national burden of GCAYA in 204 countries and regions from 1990 to 2019, evaluate the trends of GCAYA in the past 30 years at the global, regional, and national levels, which can help track progress, draw resource demand maps, and help formulate and implement policies to prevent and respond to the increasing burden of GCAYA.

METHODS

Study population

The subjects of this study are adolescent and young adult patients diagnosed with gastric cancer. Although there is currently no standardized definition for GCAYA internationally, previous studies have commonly defined GCAYA as occurring in patients aged 15–39 years (8). This age range corresponds with the age grouping in the Global Burden of Disease (GBD) database, facilitating data analysis and comparison. In addition, patients within this age range have achieved stable biological and physiological maturity. Based on the aforementioned theory and previous research, this study specifically targets adolescent and young adult patients aged 15–39 years with gastric cancer.

Data collection

The gastric cancer diagnosis defined in this study corresponds to the *International Classification of Diseases (ICD-10)* codes C16-C16.9, D00.2, D13.1, D37.1 (see Supplementary Documents, ICD code pp 1478, http://links.lww.com/AJG/D90). Data were obtained from the Global Health data Exchange (http://ghdx.healthdata.org/) (9–11), exporting data using the GBD Results Tool (https://vizhub.healthdata.org/gbd-results/). The search parameters included "stomach cancer" for cause; "incidence, prevalence, deaths, years of life lost, years lived with disability, and disability-adjusted life years (DALY) for measurements; "all locations" for location; "1990–2019" for years; "number and rate" for metrics; "male, female, and both" for sex; and "age standardized, 15–39 years and corresponding 5-year bands" for age. We followed the Guidelines for Accurate and Transparent Health Estimates Reporting guidelines for cross-sectional studies.

Statistical analysis

Data provided by the GBD database were used to describe the incidence, mortality, and DALY rates of GCAYA at the global, regional, and national levels from 1990 to 2019. The age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), and age-standardized DALY rate (ASDR) of GCAYA were calculated at the global, regional, and national levels, and the world maps of ASIR, ASMR, and ASDR were plotted. The estimated annual percentage change (EAPC) of ASIR, ASMR, and ASDR of GCAYA were calculated using the formula $100 \times (\exp[\beta] - 1)$, and the 95% confidence interval was obtained from the linear regression model. The world maps of EAPC of ASIR, ASMR, and ASDR of GCAYA were plotted. Adolesgggcent and young adult patients with gastric cancer were divided into 5 age groups: 15–19 years, 20–24 years, 25–29 years, 30–34 years, and 35–39 years, and the composition of age burden in patients was compared between 1990 and 2019. The composition of age burden in deaths among patients was compared globally between 1990 and 2019. All statistics were performed using the R program (Version 4.2.3, R core team). A P value less than 0.05 was considered statistically significant.

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

RESULTS

Time and sex trends of GCAYA from 1990 to 2019

From 1990 to 2019, the total number of new cases of GCAYA worldwide showed a certain degree of fluctuation. It increased from 1990 to 2010, decreased from 2010 to 2015, and increased again from 2015 to 2019, showing an overall upward trend. The total number of new cases increased from 47,932 (95% uncertainty interval 44,592.9–51,005.7) in 1990 to 49,007 (45,007.7–53,078.1) in 2019 (Figure 1a). From 1990 to 2019, the total number of deaths due to GCAYA also showed a certain degree of fluctuation. It increased from 1990 to 2010, decreased from 2010 to 2015, and increased again from 2015 to 2019, showing an overall downward trend. The total number of deaths decreased from 35,270 (32,579–37,678.5) in 1990 to 27,895 (25,710.9–30,240.4) in 2019. The DALY due to GCAYA also showed a certain degree of fluctuation. It increased from 1990 to 2010, decreased from 2010 to 2015, and increased again from 2015 to 2019, showing an overall downward trend. The DALY decreased from 1,989,927 (1,839,468.2–2,123,565) in 1990 to 1,573,896 (1,448,735.6–1,703,548) in 2019. From 1990 to 2019, the ASIR, ASMR, and ASDR of GCAYA showed a decreasing trend (Figure 1b), decreasing from 22.4 (21.2–23.6) per 100,000 in 1990 to 15.6 (14.1–17.2) per 100,000 in 2019 for ASIR; from 20.5 (19.2–21.6) per 100,000 in 1990 to 11.9 (10.8–12.8) per 100,000 in 2019 for ASMR; and from 493.4 (463.7–523.7) per 100,000 in 1990 to 268.4 (245.5–290.6) per 100,000 in 2019 for ASDR.

From 1990 to 2019, the incidence rate, mortality rate, and DALY of GCAYA among male patients were higher than those among female patients. In 2019, the incidence rate of GCAYA among male patients was 2.1 times higher than that among female patients (368.9 [328.2–410.3] vs 178.2 [160.5–196.9]), the mortality rate of GCAYA among male patients was 1.1 times higher than that among female patients (14,971.6 [13,643.3–165,20.5] vs 12,923.6 [11,550.3–14,339]), and the DALY of GCAYA among male patients was 1.1 times higher than that among female patients (841,920.5 [766,655.5–927,598.8] vs 731,976.3 [653,421–81,4242.8]). From 1990 to 2019, the ASIR, ASMR, and ASDR of GCAYA among both male and female patients showed a decreasing trend, similar to that in the general population. However, the abovementioned indicators among male patients were consistently higher than those among female patients in all regions (Figure 1). In 2019, the ASIR of GCAYA among male patients was 2.3 times higher than that among female patients (22.4 [19.8–25.3] per 100,000 vs 9.7 [8.7–10.7] per 100,000), the ASMR of GCAYA among male patients was 2.1 times higher than that among female patients (16.6 [14.8–18.3] per 100,000 vs 7.9 [7.1–8.8] per 100,000), and the ASDR of GCAYA among male patients was 2.1 times higher than that among female patients (368.9 [328.2–410.3] per 100,000 vs 178.2 [160.5–196.9] per 100,000) (Supplementary Digital Content, see Appendix pp 1–3, http://links.lww.com/AJG/D83).

Region and sex trends of GCAYA from 1990 to 2019

According to the sociodemographic index (SDI) quintile (11), the incidence and DALY of GCAYA in all regions of the world showed a decreasing trend. High SDI countries had the most significant decrease in ASIR and ASDR, with an EAPC of −2.12 (95% confidence interval −2.18 to −2.06) and −3.13 (−3.19 to −3.07), respectively. The ASIR decreased from 22 (95% uncertainty interval 21.2–22.4) per 100,000 in 1990 to 12.4 (11.1–13.6) per 100,000 in 2019, while the ASDR decreased from 343.2 (334.6–348.5) per 100,000 in 1990 to 145.3 (136.6–151.7) per 100,000 in 2019 (Table 1). Middle SDI countries had the least decrease in ASIR, with an EAPC of −0.77 (−1 to −0.54). The ASIR decreased from 24.5 (22.2–27.1) per 100,000 in 1990 to 18.7 (16.4–21.4) per 100,000 in 2019. Low SDI countries had the least decrease in ASDR, with an EAPC of −1.2 (−1.23 to −1.16). The ASDR decreased from 296.6 (261.9–328) per 100,000 in 1990 to 212 (189.1–237.1) per 100,000 in 2019. In 2019, regions with high-middle and middle SDI countries had higher incidence and DALY rates of GCAYA.

At the regional level, the age-standardized incidence, prevalence, mortality, and DALY rates of GCAYA were higher in male than those in female patients in 2019 (Figure 2).

At the regional level, from 1990 to 2019, the ASIR of GCAYA showed a decreasing trend worldwide. The largest decline was observed in high-income Asia Pacific, with a decrease from 61.5 (59.3–63) per 100,000 in 1990 to 28.2 (24.2–32.3) per 100,000 in 2019, representing an EAPC of −2.82 (−2.9 to −2.74). Other regions with significant declines included Eastern Europe (from 30.9 [29.8–31.5] per 100,000 in 1990 to 16.1 [14.5–17.8] per 100,000 in 2019, EAPC −2.66 [−2.85 to −2.46]), and Tropical Latin America (from 18.1 [17.2–18.7] per 100,000 to 10.2 [9.6–10.7] per 100,000, EAPC −2.03 [−2.11 to −1.95]). The smallest declines were observed in Oceania (from 13.8 [11–16.6] per 100,000 in 1990 to 12.9 [10.1–15.9] per 100,000 in 2019, EAPC −0.23 [−0.27 to −0.19]); Western Sub-Saharan Africa (from 10.2 [8.9–11.4] per 100,000 in 1990 to 8.7 [7.5–9.8] per 100,000 in 2019, EAPC −0.36 [−0.44 to −0.28]); and East Asia (from 37.1 [32.7–41.7] per 100,000 in 1990 to 30.2 [25.5–35.5] per 100,000 in 2019, EAPC −0.43 [−0.76 to 0.1]).

At the regional level, the standardized DALY for GCAYA showed a decreasing trend from 1990 to 2019 worldwide, with the largest decline observed in Western Sub-Saharan Africa, from 839.7 (816.8–856) per 100,000 to 284.7 (262.8–300.3) per 100,000. The EAPC was −3.93 (−4 to −3.85). Similarly, Western Europe exhibited a decline from 755 (725.8–770.4) per 100,000 to 330.4 (297.1–366.6) per 100,000 with an EAPC of −3.43 (−3.68 to −3.18), followed by Tropical Latin America, which decreased from 289.1 (280.9–294.2) per 100,000 to 132 (125.3–137.7) per 100,000 with an EAPC of −2.81 (−2.9 to −2.73). Among all regions, the smallest decline was observed in Andean Latin America, from 360.3 (282–441.1) per 100,000 in 1990 to 335 (255.9–422.1) per 100,000 in 2019, with an EAPC of −0.21 (−0.26 to −0.17). Australasia exhibited a decline from 248.4 (217.2–281.7) per 100,000 to 199.7 (172–229.9) per 100,000 with an EAPC of −0.58 (−0.65 to −0.51), while the Caribbean region decreased from 265.6 (239–284.4) per 100,000 to 189.6 (160.4–220.1) per 100,000 with an EAPC of −1.07 (−1.2 to −0.95) (Table 1).

Country trends of GCAYA from 1990 to 2019

In 2019, China, India, and the Russian Federation had the highest numbers of new cases of GCAYA. China had the highest number of cases at 20,855 (17,648.4–24,441.3), followed by India at 7,368 (6,275.7–8,537.3), and then the Russian Federation at 1,409 (1,187.2–1,653.3) (Supplementary Digital Content, see Appendix pp 4–13, http://links.lww.com/AJG/D83). The highest number of deaths due to GCAYA were reported in China at 8,462 (7,243.5–9,830.1), followed by India at 5,935 (5,047.9–6,941.1), and Brazil at 753 (707.0–798.5) (Supplementary Digital Content, see Appendix pp 14–23, http://links.lww.com/AJG/D83). Mongolia (43.7/100,000 [34.2–55.0]/100,000), Bolivia (Plurinational

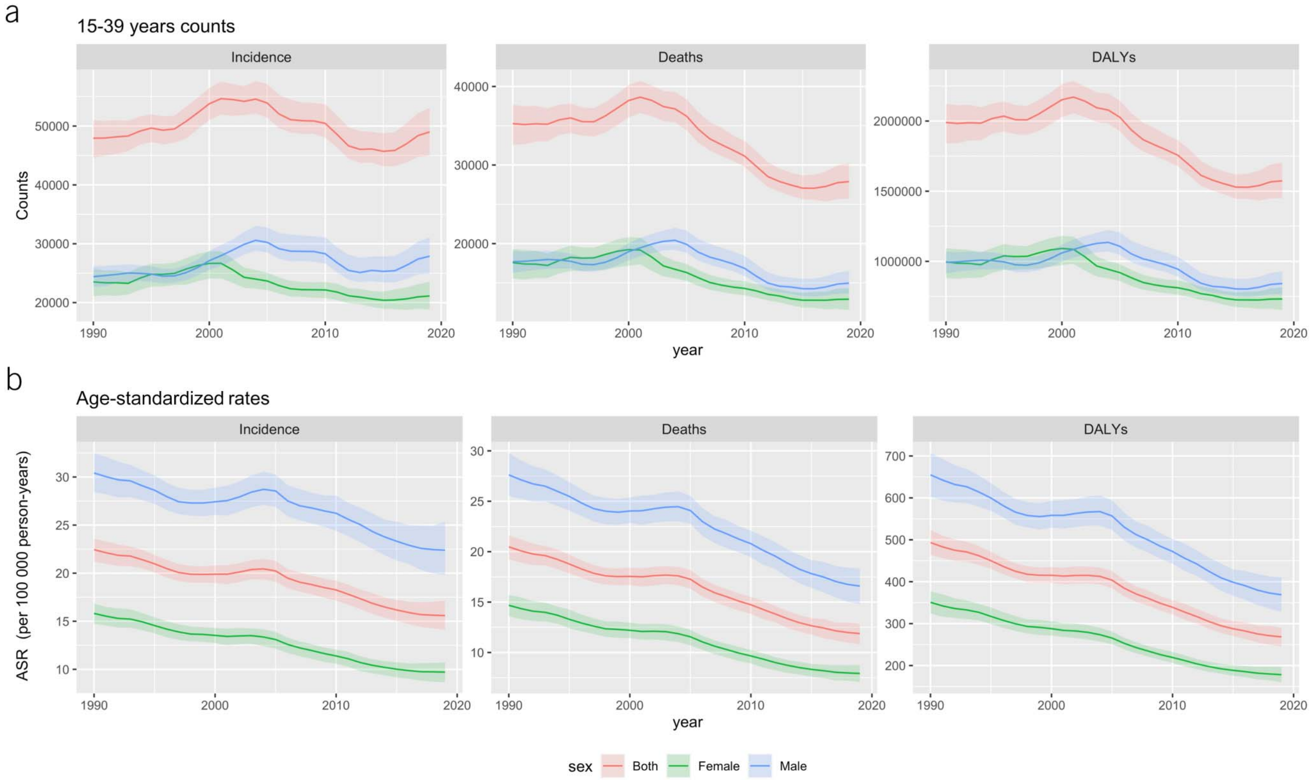

Figure 1. Global time and sex burden of GCAYA, 1990–2019. (**a**) All-age counts. (**b**) ASR, age-standardized rates; DALY, disability-adjusted life years; GCAYA, gastric cancer in adolescents and young adults.

State of Bolivia) (34.0/100,000 [26.8–42.0]/100,000), and China (30.6/100,000 [25.8–36.1]/100,000) had the highest ASIR of GCAYA, while Malawi (3.2/100,000 [2.6–3.9]/100,000), Namibia (3.4/100,000 [2.8–4.2]/100,000), and Maldives (3.7/100,000 [3.1–4.5]/100,000) had the lowest rates (Figure 3a; Supplementary Digital Content, see Appendix pp 24–38, http://links.lww.com/AJG/D83). Mongolia (46.0/100,000 [36.3–57.4]/100,000), Bolivia (Plurinational State of Bolivia) (36.1/100,000 [28.7–44.2]/100,000), and Afghanistan (29.3/100,000 [21.2–36.5]/100,000) had the highest ASMR due to GCAYA, while the United States (3.4/100,000 [3.1–3.5]/100,000), Kuwait (3.4/100,000 [2.8–4.1]/100,000), and Malawi (3.5/100,000 [2.9–4.2]/100,000) had the lowest rates (Figure 3b; Supplementary Digital Content, see Appendix pp 39–53, http://links.lww.com/AJG/D83). Mongolia (1,059.2/100,000 [816.7–1,351.3]/100,000), Bolivia (Plurinational State of Bolivia) (749.1/100,000 [572.6–946.3]/100,000), and Afghanistan (728.7/100,000 [505.3–939.3]/100,000) had the highest ASDR due to GCAYA, while Kuwait (64.8/100,000 [54.1–77.7]/100,000), the Maldives (68.1/100,000 [56.0–81.2]/100,000), and Sweden (73.4/100,000 [68.4–78.0]/100,000) had the lowest rates (Figure 3c; Supplementary Digital Content, see Appendix pp 54–68, http://links.lww.com/AJG/D83).

From 1990 to 2019, the ASIR of GCAYA in 196 of 204 countries and territories showed a downward trend for both male and female patients. Trinidad and Tobago had the greatest reduction, declining from 8.3 (7.9–8.5) per 100,000 in 1990 to 4.4 (3.4–5.7) per 100,000 in 2019, with an EAPC of −3.15 (−4.69–1.58). Austria decreased from 20.5 (19.6–21.4) per 100,000 in 1990 to 8.4 (6.8–10.2) per 100,000 in 2019, with an EAPC of −3.11 (−4.96–1.22). Maldives declined from 9.3 (7.2–10.8) per 100,000 in 1990 to 3.7 (3.1–4.5) per 100,000 in 2019, with an EAPC of −3.08 (−3.40–2.76). Honduras had the greatest increase, rising from 13.0 (10.7–15.1) per 100,000 in 1990 to 15.4 (12.6–19.6) per 100,000 in 2019, with an EAPC of 0.61 (0.13–1.09). Dominican Republic increased from 7.1 (6.2–8.1) per 100,000 in 1990 to 8.6 (6.5–11.3) per 100,000 in 2019, with an a EAPC of 0.58 (−1.00 to 2.17). Lesotho increased from 9.9 (7.9–12.0) per 100,000 in 1990 to 11.5 (8.7–14.6) per 100,000 in 2019, with an EAPC of 0.56 (−1.75 to 2.91) (Figure 3d; Supplementary Digital Content, see Appendix pp 69–84, http://links.lww.com/AJG/D83).

The ASMR for GCAYA in 198 countries and territories have shown a decreasing trend. The Republic of Korea has exhibited the largest decline, from 52.3 (49.9–55.0) per 100,000 in 1990 to 14.0 (12.5–15.6) per 100,000 in 2019, with an EAPC of −4.46 (−6.71 to −2.17). Similarly, Singapore has experienced a significant reduction, from 20.4 (19.2–21.3) per 100,000 in 1990 to 5.5 (4.8–6.0) per 100,000 in 2019, with an EAPC of −4.36 (−5.98 to −2.70). Austria also showed a substantial decrease, from 17.2 (16.4–17.8) per 100,000 in 1990 to 5.4 (4.9–5.8) per 100,000 in 2019, with an EAPC of −3.99 (−5.72—2.23). Conversely, Honduras showed the highest increase in GCAYA, from 13.5 (11.1–15.7) per 100,000 in 1990 to 15.8 (13.1–20.0) per 100,000 in 2019, with an EAPC of 0.56 (−0.02 to −1.14). Lesotho and the Dominican Republic also demonstrated an increase, from 10.6 (8.5–12.8) per 100,000 to 12.3 (9.3–15.5) per 100,000 and from 7.6 (6.7–8.6) per 100,000 to 8.7 (6.6–11.3) per 100,000, respectively. The EAPC for Lesotho was 0.54 (−1.70 to −2.82) and that for the Dominican Republic was 0.38 (−1.11 to 1.89) (Figure 3e; Supplementary Digital Content, see Appendix pp 85–100, http://links.lww.com/AJG/D83).

The ASIR for GCAYA in 198 countries and territories showed a decreasing trend. The greatest decrease was observed in the Republic

Table 1. Region and sex burden of GCAYA, 1990–2019

Location	Sex	Incidence (95% UI) Case, 1990	ASIR (per 100,000), 1990	Incidence (95% UI) Case, 2019	ASIR (per 100,000), 2019	EAPC of ASIR (95% CI), 1990–2019	DALY (95% UI) Case, 1990	ASDR (per 100,000), 1990	DALY (95% UI) Case, 2019	ASDR (per 100,000), 2019	EAPC of ASDR (95% CI), 1990–2019
Global	Both	47,932.2 (44,592.9 to 51,005.7)	22.4 (21.2 to 23.6)	49,007.9 (45,007.7 to 53,078.1)	15.6 (14.1 to 17.2)	−1.22 (−1.35 to −1.09)	1,989,927.6 (1,839,468.2 to 2,123,565)	493.4 (463.7 to 523.7)	1,573,896.7 (1,448,735.6 to 1,703,548)	268.4 (245.5 to 290.6)	−2.11 (−2.27 to −1.95)
	Male	24,410.7 (22,659.5 to 26,200.4)	30.4 (28.4 to 32.5)	27,882.2 (24,955.9 to 31,033)	22.4 (19.8 to 25.3)	−0.96 (−1.11 to −0.81)	993,454.9 (913,630.4 to 1,069,705.3)	655 (602.3 to 706.9)	841,920.5 (766,655.5 to 927,598.8)	368.9 (328.2 to 410.3)	−1.93 (−2.11 to −1.74)
	Female	23,521.4 (21,094.6 to 25,793.2)	15.8 (14.7 to 16.8)	21,125.7 (18,841.1 to 23,540.8)	9.7 (8.7 to 10.7)	−1.76 (−1.87 to −1.65)	996,472.6 (881,582.7 to 1,093,486.4)	350.9 (324 to 377.4)	731,976.3 (653,421 to 814,242.8)	178.2 (160.5 to 196.9)	−2.46 (−2.59 to −2.34)
High SDI	Both	7,885.6 (7,655.7 to 8,114.3)	22 (21.2 to 22.4)	4,147.3 (3,824.2 to 4,509.7)	12.4 (11.1 to 13.6)	−2.12 (−2.18 to −2.06)	230,137.3 (223,570.2 to 235,720.1)	343.2 (334.6 to 348.5)	86,951.3 (82,675 to 91,738.4)	145.3 (136.6 to 151.7)	−3.13 (−3.19 to −3.07)
	Male	4,026.8 (3,848.6 to 4,189.2)	32.1 (31.2 to 32.7)	2,185 (1,995.6 to 2,399)	17.8 (15.9 to 19.8)	−2.17 (−2.24 to −2.1)	110,533.6 (104,840.3 to 114,685.2)	483.7 (473.9 to 491.2)	44,952.2 (42,131.5 to 48,480)	202.4 (191.6 to 211.2)	−3.16 (−3.22 to −3.11)
	Female	3,858.8 (3,729.1 to 3,993.9)	14.4 (13.7 to 14.8)	1,962.3 (1,762.9 to 2,203.6)	7.9 (6.8 to 8.8)	−2.24 (−2.29 to −2.19)	119,603.7 (116,107.9 to 123,149.1)	232 (223.9 to 236.7)	41,999 (39,689.3 to 44,466.9)	95.5 (88.1 to 100.7)	−3.24 (−3.32 to −3.16)
High-middle SDI	Both	12,912.5 (11,979.6 to 13,926.6)	27.3 (25.7 to 28.8)	13,170.7 (11,760.2 to 14,731.8)	18.8 (16.6 to 21)	−1.25 (−1.41 to −1.08)	535,933.5 (498,081.6 to 581,154)	636.3 (597.5 to 675.8)	337,538.3 (306,778.9 to 371,205.3)	314.1 (280.1 to 346.9)	−2.51 (−2.72 to −2.3)
	Male	7,308.5 (6,649.9 to 7,968.7)	39.3 (36.4 to 42.2)	8,300.6 (7,207.1 to 9,604.1)	28.9 (24.8 to 33.7)	−0.95 (−1.13 to −0.77)	302,098.7 (274,647.3 to 333,046.5)	908.8 (836.5 to 985.3)	205,239.7 (182,074.5 to 232,249)	467.7 (403.3 to 535.2)	−2.31 (−2.53 to −2.09)
	Female	5,604 (4,980.6 to 6,267.5)	18.2 (16.9 to 19.3)	4,870.1 (4,114.6 to 5,734)	10.5 (9.2 to 12)	−1.96 (−2.12 to −1.81)	233,834.9 (209,566.8 to 262,886.5)	415.5 (385.1 to 448.7)	132,298.6 (114,098.7 to 151,806.6)	182.2 (163 to 206.9)	−3.01 (−3.21 to −2.82)
Middle SDI	Both	16,799.6 (15,185.8 to 18,426.8)	24.5 (22.2 to 27.1)	17,804.8 (15,817.1 to 20,003)	18.7 (16.4 to 21.4)	−0.77 (−1 to −0.54)	740,557.7 (667,851.3 to 813,901.1)	597.7 (539.4 to 656.2)	530,865.2 (484,057.8 to 583,564.1)	323.4 (285.2 to 363)	−2.01 (−2.27 to −1.74)
	Male	8,680.1 (7,736.2 to 9,707.2)	31.8 (27.8 to 36.2)	10,906.3 (9,478.2 to 12,623.1)	27.2 (22.9 to 32.2)	−0.27 (−0.51 to −0.03)	378,002.8 (335,922.8 to 419,546.8)	769.5 (662.5 to 876.8)	308,625.2 (273,473 to 347,484.7)	456.7 (389.5 to 529)	−1.59 (−1.88 to −1.29)
	Female	8,119.5 (6,874.2 to 9,381.3)	17.7 (15.7 to 19.8)	6,898.5 (5,951.6 to 7,929.7)	11 (9.4 to 12.6)	−1.68 (−1.89 to −1.47)	362,554.9 (308,594.7 to 418,905.8)	432.2 (378.8 to 488.9)	222,240 (194,982.6 to 253,079.1)	200.7 (174.2 to 229.6)	−2.73 (−2.95 to −2.5)
Low-middle SDI	Both	7,868.9 (6,880.5 to 8,641.1)	14.2 (13 to 15.2)	10,019.9 (8,965.5 to 11,051)	11 (10 to 12)	−0.89 (−0.97 to −0.81)	367,978.2 (320,501.4 to 403,204.9)	371.1 (340 to 399.4)	438,416.9 (393,504.8 to 486,262.2)	259.6 (237.3 to 283.8)	−1.23 (−1.32 to −1.15)
	Male	3,399.3 (3,060.9 to 3,722.5)	16.4 (14.8 to 17.7)	4,737.3 (4,231.5 to 5,327.2)	13.2 (11.9 to 14.6)	−0.72 (−0.83 to −0.61)	157,559.2 (141,034.5 to 173,459.1)	422.9 (382.7 to 458.5)	202,616 (180,639.2 to 227,290.3)	303.2 (273.9 to 337.6)	−1.1 (−1.23 to −0.96)
	Female	4,469.6 (3,630.7 to 5,099.3)	11.9 (10.4 to 13.4)	5,282.5 (4,505.2 to 6,159.4)	8.9 (7.9 to 10.1)	−1.05 (−1.12 to −0.98)	210,419 (169,674.5 to 240,449.7)	318 (274.8 to 355.4)	235,800.9 (198,024.4 to 275,433.4)	219.4 (190.7 to 250.3)	−1.35 (−1.42 to −1.28)
Low SDI	Both	2,449.6 (1,959.3 to 2,809.9)	11.3 (10 to 12.5)	3,844.6 (3,249.9 to 4,409.1)	8.4 (7.6 to 9.3)	−1.06 (−1.09 to −1.02)	114,612.4 (92,120.9 to 131,176.8)	296.6 (261.9 to 328)	179,241.7 (154,169.2 to 207,862.9)	212 (189.1 to 237.1)	−1.2 (−1.23 to −1.16)
	Male	987.8 (845.5 to 1,124.7)	13.7 (12 to 15.3)	1,741.7 (1,490.8 to 2,047.1)	9.9 (8.8 to 11.1)	−1.13 (−1.18 to −1.07)	44,904.9 (38,871.9 to 50,998.2)	348.9 (305.7 to 390.7)	80,008.5 (68,016.2 to 92,973.3)	245.9 (214.9 to 279.9)	−1.23 (−1.28 to −1.18)
	Female	987.8 (845.5 to 1,124.7)	13.7 (12 to 15.3)	1,741.7 (1,490.8 to 2,047.1)	9.9 (8.8 to 11.1)	−1.13 (−1.18 to −1.07)	69,707.4 (49,310.6 to 84,059.2)	242.2 (198.7 to 282.4)	99,233.2 (82,817.2 to 117,551.2)	179.5 (158.5 to 204.7)	−1.08 (−1.11 to −1.05)
Andean Latin America	Both	452 (399.9 to 507.7)	29.7 (26.9 to 32.4)	633.4 (485.9 to 798.6)	22.4 (18.3 to 27.2)	−0.98 (−1.08 to −0.88)	20,956.3 (18,581.1 to 23,456.4)	716 (650.8 to 783.7)	26,011.2 (20,099.1 to 32,995.3)	461.2 (373.9 to 562.5)	−1.55 (−1.66 to −1.44)
	Male	216 (186.8 to 248.5)	34 (30.8 to 37.5)	297 (226.7 to 376.6)	26.4 (21.3 to 32.2)	−0.76 (−0.85 to −0.68)	10,178.8 (8,815.6 to 11,716.1)	823.3 (743.5 to 909.7)	13,606.8 (10,356.4 to 17,250.7)	520 (415.5 to 643.1)	−1.5 (−1.59 to −1.4)
	Female	236 (196.9 to 270.7)	25.5 (22.5 to 28.2)	336.4 (251.2 to 440.6)	18.9 (15.4 to 22.7)	−1.22 (−1.37 to −1.07)	10,777.5 (8,981.5 to 12,385.7)	613.2 (539.4 to 675.7)	12,404.4 (9,360.7 to 16,218.9)	406.1 (329.5 to 492.7)	−1.6 (−1.75 to −1.44)
Australasia	Both	74.9 (67.9 to 82.6)	10.2 (9.7 to 10.6)	74 (56.5 to 95.5)	7 (5.7 to 8.5)	−1.42 (−1.5 to −1.34)	2,200.1 (2,013.3 to 2,399.1)	161.8 (156.2 to 166.6)	1,573 (1,343.3 to 1,852.2)	84.5 (78.7 to 90)	−2.34 (−2.46 to −2.22)
	Male	38.1 (33.8 to 43.3)	14.6 (13.9 to 15.2)	38.2 (29.2 to 50.4)	9.6 (7.7 to 11.8)	−1.59 (−1.68 to −1.5)	1,111.5 (1,004.8 to 1,239.6)	224.3 (216.5 to 231.6)	785.5 (662.1 to 934.3)	112.4 (105 to 119.8)	−2.52 (−2.65 to −2.38)
	Female	36.7 (32.9 to 40.9)	6.7 (6.3 to 7.1)	35.8 (26.7 to 47.1)	4.7 (3.8 to 5.7)	−1.34 (−1.42 to −1.26)	1,088.6 (986.9 to 1,196.2)	109.5 (104.6 to 113.8)	787.4 (675.7 to 924.5)	59.2 (54.2 to 63.3)	−2.17 (−2.27 to −2.07)
Caribbean	Both	168.9 (136.4 to 191.1)	11.3 (10.3 to 12)	197.4 (153 to 241.6)	8.4 (7.3 to 9.6)	−0.9 (−1 to −0.79)	7,594.8 (6,046.1 to 8,664.8)	265.6 (239 to 284.4)	8,589.4 (6,615.2 to 10,536.8)	189.6 (160.4 to 220.1)	−1.07 (−1.2 to −0.95)
	Male	81.4 (71.5 to 92)	14.6 (13.2 to 15.6)	99.7 (78.9 to 122.9)	10.9 (9.3 to 12.5)	−0.89 (−1.02 to −0.76)	3,611.6 (3,156.3 to 4,096.9)	337.8 (305.2 to 365.6)	4,270.6 (3,363.3 to 5,314)	241.1 (204.1 to 278.9)	−1.07 (−1.22 to −0.91)
	Female	87.6 (61.4 to 105.4)	8.3 (7.5 to 9)	97.6 (67.5 to 129)	6.3 (5.4 to 7.4)	−0.87 (−0.94 to −0.8)	3,983.2 (2,743.2 to 4,860.3)	197.9 (173.7 to 219.5)	4,318.7 (2,890.3 to 5,734.2)	142.9 (117.9 to 171.7)	−1.05 (−1.13 to −0.97)
Central Asia	Both	1,008.9 (963.3 to 1,060.6)	28 (27.1 to 28.8)	744.4 (663.6 to 838.1)	16.4 (15 to 17.9)	−1.82 (−1.95 to −1.7)	46,683.6 (44,606.7 to 49,132.1)	748.1 (724.8 to 769.2)	33,383.9 (29,749.8 to 37,656.8)	400.9 (364 to 442.7)	−2.21 (−2.32 to −2.1)
	Male	608.6 (575.9 to 648)	41.8 (40.4 to 43.1)	428.4 (382.9 to 482.2)	24.1 (21.8 to 26.6)	−1.83 (−1.98 to −1.67)	28,202.5 (26,692.2 to 30,018.3)	1,111.1 (1,073.8 to 1,146)	19,285.4 (17,222.3 to 21,712.4)	581.2 (524.8 to 641.7)	−2.23 (−2.37 to −2.1)
	Female	400.3 (379.2 to 421.7)	18.4 (17.6 to 19)	315.9 (274.4 to 363.1)	10.8 (9.8 to 11.9)	−1.87 (−1.98 to −1.76)	18,481.1 (17,495.4 to 19,486.1)	476.3 (458.3 to 494)	14,098.4 (12,236.7 to 16,239.1)	261.5 (236.7 to 290.3)	−2.18 (−2.27 to −2.08)
Central Europe	Both	810 (781.6 to 841.4)	18.1 (17.6 to 18.4)	363.5 (315.4 to 417.6)	10.3 (9 to 11.6)	−1.98 (−2.04 to −1.93)	35,659.4 (34,437.3 to 37,006.7)	424.8 (415.5 to 431.7)	13,701.7 (11,901 to 15,632.6)	215.1 (187.8 to 242.4)	−2.42 (−2.48 to −2.36)
	Male	454.3 (434.5 to 473.9)	26.6 (25.9 to 27.1)	204.8 (178.7 to 232.3)	15.3 (13.4 to 17.3)	−1.93 (−1.99 to −1.87)	20,214.3 (19,359.3 to 21,127.7)	625.7 (612.5 to 637.4)	7,894.8 (6,885.2 to 8,930.9)	318 (276.2 to 362.1)	−2.4 (−2.46 to −2.33)
	Female	355.7 (340 to 371.7)	11.7 (11.2 to 12)	158.7 (133.1 to 190.1)	6.4 (5.6 to 7.3)	−2.13 (−2.18 to −2.08)	15,445.1 (14,802.9 to 16,120.8)	265.3 (257.4 to 271.3)	5,806.9 (4,877.4 to 6,851.2)	130 (113.2 to 148.7)	−2.54 (−2.59 to −2.48)
Central Latin America	Both	1,192.7 (1,150.2 to 1,234.4)	19 (18.2 to 19.6)	1,938.2 (1,604.4 to 2,314.5)	13 (11.1 to 15.2)	−1.6 (−1.69 to −1.51)	52,391.5 (50,481.8 to 54,223.8)	434.3 (420.6 to 444.8)	69,590.6 (58,198.7 to 82,570.2)	268.4 (228.7 to 315.6)	−1.91 (−1.99 to −1.83)
	Male	613.4 (589 to 638.4)	21.7 (20.7 to 22.3)	963.9 (823.8 to 1,122.7)	15.4 (13 to 18.2)	−1.49 (−1.6 to −1.38)	27,382.9 (26,298.8 to 28,476.3)	505.1 (489.1 to 518.6)	36,210 (30,705.9 to 42,343.5)	324.8 (271.9 to 386.5)	−1.82 (−1.92 to −1.71)
	Female	579.3 (552 to 604.6)	16.6 (15.7 to 17.1)	974.3 (766 to 1,209.8)	11 (9.3 to 12.8)	−1.68 (−1.78 to −1.58)	25,008.5 (23,820.4 to 26,082.4)	368.1 (354 to 378.7)	33,380.6 (26,916.1 to 40,955.4)	219.4 (187.5 to 258.1)	−1.98 (−2.06 to −1.89)
Central Sub-Saharan Africa	Both	229.9 (166.1 to 292.8)	11.9 (9.9 to 14.1)	341.7 (249.5 to 438.7)	8 (6.5 to 9.8)	−1.45 (−1.5 to −1.41)	10,587.5 (7,738.8 to 13,438.5)	313.6 (261.1 to 371.4)	15,836 (11,578.5 to 20,586.7)	204.1 (163.1 to 253.4)	−1.54 (−1.59 to −1.49)
	Male	110.2 (84.3 to 140)	16.1 (13.1 to 19.4)	182.7 (131.4 to 241.2)	10.9 (8.9 to 13.6)	−1.45 (−1.52 to −1.37)	4,881.4 (3,784.2 to 6,138.7)	424.4 (348.5 to 506.9)	8,299.6 (5,990.3 to 10,961.6)	277.2 (220.1 to 347.7)	−1.57 (−1.65 to −1.5)

Table 1. (*continued*)

Location	Sex	Incidence (95% UI) Case, 1990	Incidence (95% UI) ASIR (per 100,000), 1990	Incidence (95% UI) Case, 2019	Incidence (95% UI) ASIR (per 100,000), 2019	EAPC of ASIR (95% CI), 1990–2019	DALY (95% UI) Case, 1990	DALY (95% UI) ASDR (per 100,000), 1990	DALY (95% UI) Case, 2019	DALY (95% UI) ASDR (per 100,000), 2019	EAPC of ASDR (95% CI), 1990–2019
	Female	119.7 (72.7 to 166)	8.2 (6.4 to 10.1)	159 (109.4 to 218.8)	5.7 (4.3 to 7.5)	−1.29 (−1.34 to −1.24)	5,706.2 (3,472.6 to 7,771.6)	216.2 (169.8 to 269.1)	7,536.5 (5,233.9 to 10,328.4)	143.9 (109.4 to 188.2)	−1.42 (−1.48 to −1.36)
East Asia	Both	18,728.6 (16,352.1 to 21,292.1)	37.1 (32.7 to 41.7)	21,313.5 (18,107.4 to 24,881.1)	30.2 (25.5 to 35.5)	−0.43 (−0.76 to −0.1)	803,978.6 (699,861.4 to 913,339.7)	895 (784.8 to 1,009.8)	492,053.5 (424,301.3 to 567,121.2)	477.9 (402.5 to 560.4)	−1.97 (−2.36 to −1.59)
	Male	10,140.7 (8,583.6 to 11,713.5)	50.5 (42.8 to 59.1)	14,289.9 (11,735.1 to 17,106.1)	46.7 (37.6 to 56.8)	0.12 (−0.21 to 0.45)	429,326.4 (360,398.5 to 495,602.9)	1,192.7 (988.8 to 1,399.6)	318,518.7 (264,304.9 to 381,142.4)	713.1 (570.7 to 867.8)	−1.47 (−1.87 to −1.08)
	Female	8,588 (6,844.4 to 10,538)	25.3 (21.3 to 29.2)	7,023.6 (5,457.3 to 8,860.2)	15.7 (12.8 to 19)	−1.59 (−1.92 to −1.26)	374,652.2 (297,341 to 455,786.4)	612.5 (511.5 to 715.6)	173,534.8 (135,075.8 to 217,806.6)	260.3 (209.9 to 318.7)	−2.99 (−3.36 to −2.63)
Eastern Europe	Both	3,516.3 (3,256.4 to 3,669.1)	30.9 (29.8 to 31.5)	2,037.2 (1,794.2 to 2,303.4)	16.1 (14.5 to 17.8)	−2.66 (−2.85 to −2.46)	139,424.1 (129,297.4 to 145,616.6)	755 (725.8 to 770.4)	62,836.1 (55,487.6 to 70,647.2)	330.4 (297.1 to 366.6)	−3.43 (−3.68 to −3.18)
	Male	1,997.4 (1,838.3 to 2,097.8)	48.3 (46.6 to 49.3)	1,108.4 (965.4 to 1,266.7)	24.3 (21 to 27.8)	−2.77 (−2.98 to −2.57)	80,407.8 (74,149.8 to 84,306.9)	1,170 (1,121.1 to 1,193.1)	35,169.1 (30,523.7 to 40,054.2)	497.3 (430.3 to 568)	−3.53 (−3.8 to −3.27)
	Female	1,518.9 (1,406.4 to 1,597.5)	20.8 (20.1 to 21.3)	928.7 (754.7 to 1,127)	10.8 (9.4 to 12.5)	−2.56 (−2.72 to −2.4)	59,016.3 (54,652.7 to 62,128.5)	489.4 (473 to 503.9)	27,667 (22,757 to 33,310.7)	216.2 (185.8 to 250.5)	−3.29 (−3.5 to −3.07)
Eastern Sub-Saharan Africa	Both	822.9 (603.2 to 969.1)	10.7 (9.3 to 11.8)	1,109.4 (908.2 to 1,387.2)	7.2 (6.3 to 8.2)	−1.53 (−1.6 to −1.46)	37,982.7 (27,789.3 to 44,853.2)	286.5 (249.2 to 320.4)	52,086.1 (42,259.6 to 65,025.2)	184.4 (160.9 to 210.6)	−1.68 (−1.75 to −1.62)
	Male	292.3 (241.8 to 339.8)	13.2 (11.2 to 15.1)	493 (404.4 to 600)	8.9 (7.6 to 10.3)	−1.49 (−1.59 to −1.4)	12,688.5 (10,602.4 to 14,731.6)	344.9 (292.5 to 394.4)	22,467.7 (18,272.8 to 27,222.2)	225.5 (192.4 to 263.3)	−1.61 (−1.71 to −1.52)
	Female	530.6 (313.8 to 664.1)	8.2 (6.7 to 9.9)	616.4 (480.7 to 878.3)	5.6 (4.8 to 7.4)	−1.48 (−1.56 to −1.41)	25,294.2 (15,081.4 to 31,658.4)	228.3 (181.4 to 273)	29,618.5 (23,153.4 to 42,528)	146.8 (124.6 to 193.5)	−1.7 (−1.78 to −1.63)
High-income Asia Pacific	Both	5,217.5 (5,006.2 to 5,429.4)	61.5 (59.3 to 63)	1,767.4 (1,550 to 2,024.3)	28.2 (24.2 to 32.3)	−2.82 (−2.9 to −2.74)	141,613.1 (135,560.6 to 146,349.3)	839.7 (816.8 to 856)	29,126.8 (27,127.5 to 31,387.7)	284.7 (262.8 to 300.3)	−3.93 (−4 to −3.85)
	Male	2,547.7 (2,384.2 to 2,705.8)	91.4 (88.2 to 93.7)	825.6 (703.3 to 968.4)	41.9 (35.6 to 49.4)	−2.8 (−2.9 to −2.7)	62,876.6 (57,582.8 to 66,569.2)	1,192 (1,160.5 to 1,215.5)	13,279.5 (11,963 to 14,819.1)	411.8 (383.7 to 434.8)	−3.85 (−3.93 to −3.76)
	Female	2,669.8 (2,547.8 to 2,796.7)	39.3 (37.3 to 40.6)	941.8 (790.8 to 1,123.7)	17 (14 to 20)	−3.08 (−3.15 to −3.01)	78,736.6 (75,680.3 to 81,876.4)	565.8 (544.1 to 579.6)	15,847.3 (14,490.7 to 17,361.5)	175.9 (159.3 to 186.9)	−4.26 (−4.36 to −4.17)
High-income North America	Both	878.1 (845.8 to 909.6)	8.5 (8.2 to 8.7)	915.2 (791.1 to 1,063.6)	6.1 (5.4 to 7)	−1.33 (−1.41 to −1.26)	25,057.6 (24,215.1 to 25,895.2)	129.3 (125.6 to 131.8)	21,101.3 (19,824.8 to 22,685.3)	77.4 (74.4 to 79.9)	−1.91 (−2.03 to −1.79)
	Male	506.7 (484.5 to 527.1)	12.3 (11.9 to 12.6)	496.3 (416.2 to 584.3)	8.4 (7.1 to 10)	−1.53 (−1.62 to −1.44)	13,778.9 (13,272.7 to 14,324.8)	181.9 (177.1 to 185.5)	10,679.1 (9,850.3 to 11,620)	102.3 (98.5 to 105.7)	−2.14 (−2.28 to −2)
	Female	371.4 (355.7 to 386.6)	5.7 (5.4 to 5.9)	419 (334.4 to 523.6)	4.2 (3.5 to 5)	−1.26 (−1.34 to −1.19)	11,278.7 (10,836 to 11,699.7)	87.7 (84.3 to 89.8)	10,422.2 (9,754.3 to 11,241.5)	55.5 (52.7 to 57.7)	−1.7 (−1.79 to −1.6)
North Africa and Middle East	Both	1,918.6 (1,633.9 to 2,195.6)	13.7 (11.9 to 15)	2,770.4 (2,340.7 to 3,276.7)	10.1 (9.1 to 11.1)	−0.94 (−1.15 to −0.73)	88,301.9 (74,307.3 to 101,533.2)	345.5 (298.3 to 379.5)	112,629.3 (93,260.5 to 134,788.3)	218.1 (196.9 to 242.4)	−1.5 (−1.69 to −1.3)
	Male	879.7 (761.1 to 1,002.6)	17.4 (14.8 to 19.1)	1,304.3 (1,121.9 to 1,536.4)	12.6 (11.3 to 13.9)	−0.98 (−1.19 to −0.77)	40,062.8 (34,819.6 to 45,645.8)	429.3 (369.6 to 472.5)	51,949.9 (43,909.9 to 61,667.3)	267.3 (240.4 to 297.5)	−1.52 (−1.73 to −1.32)
	Female	1,038.8 (760.1 to 1,260.9)	10.1 (8.7 to 11.5)	1,466 (1,117.5 to 1,802.5)	7.6 (6.7 to 8.5)	−0.88 (−1.09 to −0.67)	48,239.1 (35,006.5 to 58,460.1)	259.7 (219.1 to 296.3)	60,679.4 (45,632.1 to 75,311.1)	167.5 (144.6 to 190.6)	−1.45 (−1.63 to −1.28)
Oceania	Both	60.7 (46.4 to 76.2)	13.8 (11 to 16.6)	133.7 (98.2 to 177.5)	12.9 (10.1 to 15.9)	−0.23 (−0.27 to −0.19)	2,782.8 (2,137.5 to 3,470)	360.3 (282 to 441.1)	6,123 (4,518.5 to 8,136.8)	335 (255.9 to 422.1)	−0.21 (−0.26 to −0.17)
	Male	38.8 (28.9 to 49.9)	18.2 (14.1 to 23.1)	85.9 (63.5 to 116.8)	16.6 (12.6 to 21)	−0.33 (−0.38 to −0.29)	1,757.5 (1,313.3 to 2,253.1)	476.8 (364.2 to 609.6)	3,895.8 (2,865.1 to 5,270.3)	437.1 (329.1 to 562.2)	−0.28 (−0.33 to −0.23)
	Female	21.9 (14.4 to 30.2)	9.2 (7 to 11.8)	47.7 (28.3 to 66.3)	9 (7 to 11.8)	−0.07 (−0.11 to −0.04)	1,025.3 (662.8 to 1,411.4)	237.2 (179.2 to 307.7)	2,227.3 (1,315.4 to 3,123.7)	226.6 (172.3 to 302.1)	−0.11 (−0.15 to −0.07)
South Asia	Both	6,322.5 (5,437.8 to 7,037.2)	9.9 (8.9 to 11)	8,654.6 (7,508.3 to 9,913.3)	7 (6.2 to 8)	−1.31 (−1.39 to −1.23)	299,178.8 (256,686.9 to 333,372.9)	264.9 (237.5 to 291.5)	397,613.6 (346,381.7 to 456,557.6)	182.1 (158.7 to 207.5)	−1.36 (−1.43 to −1.28)
	Male	2,557.7 (2,243.9 to 2,877.5)	10.8 (9.5 to 11.9)	3,770.1 (3,210.1 to 4,450.8)	7.3 (6.2 to 8.7)	−1.38 (−1.47 to −1.3)	120,608.8 (105,364.7 to 136,599.5)	279.6 (244.9 to 308.6)	172,112.1 (146,571.6 to 201,389.7)	186.8 (156.8 to 220.3)	−1.4 (−1.49 to −1.32)
	Female	3,764.8 (2,997.4 to 4,369.1)	9 (7.3 to 10.7)	4,884.5 (3,928.7 to 5,982.4)	6.7 (5.5 to 8.1)	−1.18 (−1.31 to −1.06)	178,570 (144,319.6 to 207,139.7)	248.6 (206.4 to 291)	225,501.5 (178,669.3 to 277,740.3)	177.8 (142.8 to 214.7)	−1.27 (−1.41 to −1.14)
Southeast Asia	Both	2,593.4 (2,128.5 to 2,953.4)	10.9 (9.5 to 12.1)	2,241.6 (1,924.1 to 2,634.3)	6.7 (6 to 7.5)	−1.9 (−1.98 to −1.81)	119,840.2 (98,365.1 to 134,764.8)	280.5 (244.7 to 308.6)	92,751.9 (80,019.6 to 106,783.5)	153.5 (136.5 to 171.6)	−2.3 (−2.38 to −2.21)
	Male	1,212.2 (1,073.3 to 1,368)	13.7 (11.8 to 15.3)	1,257.7 (1,064.6 to 1,476.5)	8.9 (7.9 to 10.1)	−1.73 (−1.83 to −1.63)	54,615.5 (48,397.7 to 61,441.6)	347.6 (302.7 to 387.3)	50,103.1 (42,080.2 to 58,127.7)	201.6 (176.3 to 226.3)	−2.12 (−2.21 to −2.02)
	Female	1,381.2 (1,001.8 to 1,664)	8.5 (7.3 to 9.5)	983.8 (790.5 to 1,187.6)	4.9 (4.1 to 5.6)	−2.1 (−2.17 to −2.03)	65,224.7 (47,046.2 to 76,843.4)	221.8 (187.1 to 247.3)	42,648.8 (34,859.1 to 51,085.5)	112.1 (94.2 to 130.1)	−2.54 (−2.61 to −2.47)
Southern Latin America	Both	283.7 (265.8 to 300.6)	18.5 (17.9 to 19.1)	300.8 (227.4 to 388)	12.8 (10.2 to 16)	−1.29 (−1.36 to −1.23)	12,046.1 (11,369.8 to 12,739.9)	421.1 (409.3 to 432.4)	10,714.6 (9,321.9 to 12,178.1)	256.5 (242.9 to 269.8)	−1.73 (−1.78 to −1.68)
	Male	161.5 (149.1 to 175.6)	27.5 (26.6 to 28.4)	174.9 (136.6 to 218.4)	19.1 (15.2 to 23.9)	−1.29 (−1.36 to −1.21)	6,806.3 (6,298.1 to 7,367.4)	624.9 (605.2 to 644)	6,190.6 (5,353.2 to 7,047.3)	377.3 (357.4 to 397.6)	−1.78 (−1.86 to −1.71)
	Female	122.3 (113.1 to 132.1)	11.4 (10.9 to 11.9)	125.9 (90.4 to 171.1)	7.9 (6.3 to 9.8)	−1.28 (−1.37 to −1.2)	5,239.8 (4,858.4 to 5,645.5)	252.1 (242.6 to 260)	4,524 (3,944.8 to 5,147.9)	156.6 (146.3 to 166.1)	−1.62 (−1.68 to −1.55)
Southern Sub-Saharan Africa	Both	253.6 (227.9 to 278.2)	8.7 (7.9 to 9.5)	250.3 (199.3 to 310.1)	6.5 (6 to 7.1)	−1.16 (−1.49 to −0.83)	11,761.5 (10,611.6 to 12,879)	223 (204.3 to 241.6)	11,328.6 (9,035.5 to 14,000.4)	158.4 (144.3 to 175)	−1.27 (−1.59 to −0.94)
	Male	124.3 (110.4 to 142.3)	11.6 (10.2 to 13)	138.9 (110.4 to 166.8)	8.8 (8.1 to 9.5)	−1.3 (−1.72 to −0.88)	5,763.6 (5,140.4 to 6,554.5)	298.7 (265.9 to 333.4)	6,263.7 (5,102.7 to 7,511.6)	214.2 (196.6 to 234.7)	−1.47 (−1.92 to −1.02)
	Female	129.3 (109.5 to 148)	6.5 (5.7 to 7.6)	111.4 (82.5 to 149.9)	4.9 (4.3 to 5.7)	−0.83 (−1.08 to −0.57)	5,997.9 (5,070.8 to 6,893.1)	161.5 (143.1 to 184.5)	5,064.9 (3,774.2 to 6,762.5)	116.3 (100.2 to 136.1)	−0.81 (−1.02 to −0.6)
Tropical Latin America	Both	942.3 (900.9 to 982)	18.1 (17.2 to 18.7)	1,061 (998.4 to 1,130.4)	10.2 (9.6 to 10.7)	−2.03 (−2.11 to −1.95)	42,702.5 (40,809.9 to 44,733.7)	432.4 (414.9 to 446.1)	43,274.5 (40,729.2 to 45,835.5)	225.7 (214.3 to 235.9)	−2.29 (−2.36 to −2.21)

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Table 1. (continued)

Location	Sex	Incidence (95% UI) Case, 1990	Incidence (95% UI) ASIR (per 100,000), 1990	Incidence (95% UI) Case, 2019	Incidence (95% UI) ASIR (per 100,000), 2019	EAPC of ASIR (95% CI), 1990–2019	DALY (95% UI) Case, 1990	ASDR (per 100,000), 1990	DALY (95% UI) Case, 2019	ASDR (per 100,000), 2019	EAPC of ASDR (95% CI), 1990–2019
	Male	529.9 (503.5 to 555.4)	25.5 (24.3 to 26.4)	569.6 (529.4 to 610.7)	14.7 (13.7 to 15.5)	−1.96 (−2.05 to −1.87)	23,997.2 (22,808.7 to 25,239.7)	615 (588.9 to 635.7)	23,218.1 (21,658.3 to 24,703.3)	320.9 (304 to 338.2)	−2.29 (−2.37 to −2.21)
	Female	412.4 (391.7 to 433.8)	11.6 (10.9 to 12)	491.3 (453.6 to 530.5)	6.6 (6 to 7)	−2.02 (−2.08 to −1.95)	18,705.3 (17,778.3 to 19,741.6)	269.4 (257 to 279.6)	20,056.5 (18,563.4 to 21,593.8)	145.7 (135.9 to 153.9)	−2.16 (−2.22 to −2.1)
Western Europe	Both	1,913.5 (1,851.7 to 1,980.1)	16.1 (15.5 to 16.5)	1,178.2 (1,009.5 to 1,367.2)	9.4 (8.2 to 10.7)	−1.96 (−2.02 to −1.9)	63,801 (62,015.4 to 65,673.4)	289.1 (280.9 to 294.2)	27,596.8 (25,590 to 29,610.9)	132 (125.3 to 137.7)	−2.81 (−2.9 to −2.73)
	Male	1,056.8 (1,012.6 to 1,105)	23 (22.3 to 23.5)	658.3 (569.1 to 758.8)	12.8 (11.1 to 14.6)	−2.13 (−2.19 to −2.07)	34,121.3 (32,913 to 35,434.9)	406.6 (397.4 to 413.3)	14,902.5 (13,776.1 to 16,029.6)	177.3 (168.9 to 185.1)	−2.97 (−3.05 to −2.89)
	Female	856.7 (824.6 to 888.9)	11.2 (10.6 to 11.5)	519.9 (432.3 to 624.1)	6.6 (5.7 to 7.5)	−1.94 (−2.02 to −1.87)	29,679.7 (28,686.3 to 30,653.8)	198.5 (190.8 to 203.1)	12,694.3 (11,756.6 to 13,642.8)	92 (86.1 to 96.8)	−2.77 (−2.87 to −2.66)
Western Sub-Saharan Africa	Both	543.2 (453.2 to 625.9)	10.2 (8.9 to 11.4)	982.3 (791 to 1,196.8)	8.7 (7.5 to 9.8)	−0.36 (−0.44 to −0.28)	25,383.3 (21,559.3 to 29,465.4)	248.4 (217.2 to 281.7)	45,974.9 (37,044.6 to 56,552.7)	199.7 (172 to 229.9)	−0.58 (−0.65 to −0.51)
	Male	243.2 (202.6 to 282.6)	12.5 (10.7 to 14.1)	494.6 (389.7 to 612.9)	10.4 (9 to 12)	−0.47 (−0.54 to −0.4)	11,060.6 (9,180.1 to 12,858.4)	296.3 (255.1 to 337.9)	22,818.1 (17,926.4 to 28,258.3)	242.4 (207.1 to 282.4)	−0.55 (−0.62 to −0.48)
	Female	300 (241.6 to 357.1)	8.1 (6.8 to 9.3)	487.7 (385.2 to 611.9)	7 (6 to 8.1)	−0.19 (−0.31 to −0.07)	14,322.7 (11,681.6 to 17,073.4)	201.3 (169.4 to 232.1)	23,156.7 (17,981 to 29,080.4)	160.7 (135.1 to 189.7)	−0.54 (−0.64 to −0.44)

ASDR, age-standardized DALY rates; ASIR, age-standardized incidence rates; CI, confidence interval; DALY, disability-adjusted life years; EAPC, estimated annual percentage change; GCAYA, gastric cancer in adolescents and young adults; SDI, sociodemographic index; UI, uncertainty intervals.

of Korea, where the rate declined from 1,360.5 (1,300.3–51,416.5) per 100,000 in 1990 to 298.7 (270.1–328.4) per 100,000 in 2019, with an EAPC of −5.14 (−7.23 to −2.99). Singapore also experienced a considerable decrease, from 443.3 (422.9–462.8) per 100,000 in 1990 to 105.9 (96.2–114.8) per 100,000 in 2019, with an EAPC of −4.76 (−6.23 to −3.27). Similarly, Austria saw a decline in GCAYA death rates from 372.8 (359.2–384.9) per 100,000 in 1990 to 110.4 (102.6–118.3) per 100,000 in 2019, with an EAPC of −4.15 (−5.89 to 2.38). On the contrary, Lesotho showed the largest increase, from 249.7 (199.1–307.9) per 100,000 in 1990 to 300.6 (224.4–391.0) per 100,000 in 2019, with an EAPC of 0.68 (−1.82 to 3.25). In addition, the Dominican Republic also exhibited an increase in GCAYA death rates, from 181.4 (158.5–205.9) per 100,000 in 1990 to 206.9 (153.2–276.8) per 100,000 in 2019, with an EAPC of 0.39 (−1.31 to 2.11). Likewise, Zimbabwe had an increase in GCAYA death rates from 300.0 (260.6–340.7) per 100,000 in 1990 to 326.9 (251.5–415.1) per 100,000 in 2019, with an EAPC of 0.32 (0.00–0.65).

The incidence of GCAYA at different age stages

The incidence, DALY, ASIR, and ASDR of GCAYA in 1990 and 2019 were compared worldwide. The incidence rates and DALY of GCAYA increased with age, with the highest proportion of patients in the 35–39 years age group. Furthermore, the number of new cases, DALY, ASIR, and ASDR of GCAYA in 2019 were lower than those in 1990 (Figure 4).

The contribution of death numbers to different age groups in GCAYA

The age composition of GCAYA deaths globally in 1990 and 2019 indicates that in both years, most GCAYA deaths occurred in the age group of 35–39 years, accounting for approximately half of the total population. The next highest age group was between 30 and 34 years. The age groups of 20–24 and 15–19 years represented a smaller proportion in the death composition ratio. In comparison with that in 1990, the proportion of 35–39 years age group patients among the deceased slightly increased in 2019. Most of the deceased patients were in the 35–39 years age group (Figure 5).

DISCUSSION

Gastric cancer is one of the most common malignant tumors worldwide, resulting in approximately 1 million deaths annually (12,13). Although the incidence rate of gastric cancer has been declining globally, its distribution is not uniform among different regions and countries (14,15). As a subset of patients with gastric cancer, adolescent and young adult patients with gastric cancer account for a relatively low proportion but bring about a heavier disease burden. Moreover, the proportion of GCAYA varies significantly worldwide, with a higher incidence in some regions. Therefore, analyzing the disease burden of GCAYA globally, regionally, and nationally is of great importance to clinical, epidemiological, and public health studies.

According to global data from previous years, from 1990 to 2019, there was a general downward trend in the global incidence, mortality, and DALY of gastric cancer among both men and women. However, these indicators have slightly increased from 2015 to 2019. From 1990 to 2019, the standardized incidence, mortality, and DALY rates of GCAYA among both men and women showed a consistent downward trend globally, indicating progress in the prevention and treatment of GCAYA worldwide.

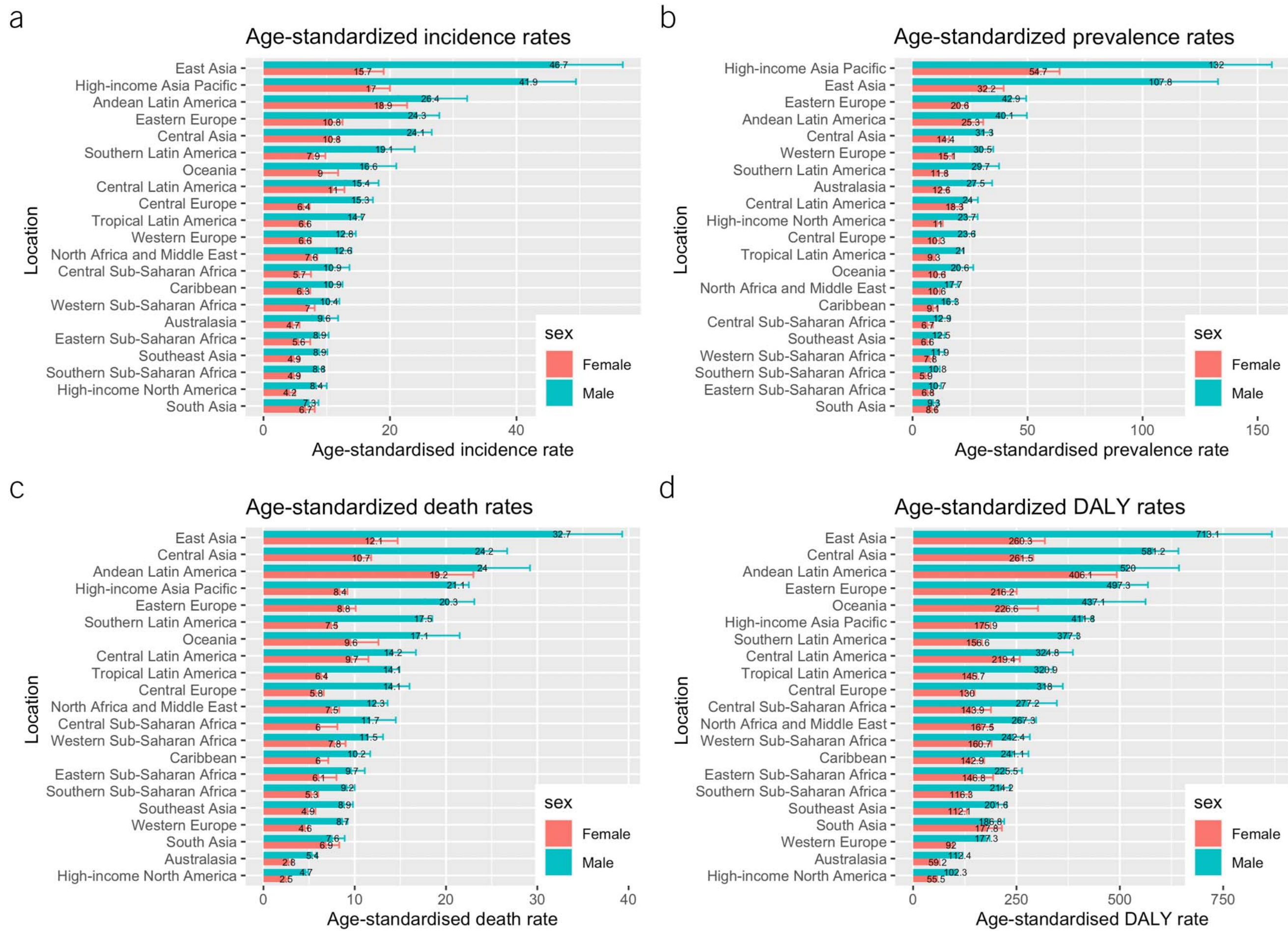

Figure 2. Age-standardized rates of GCAYA in 2019. **(a)** Age-standardized incidence rate in 2019. **(b)** Age-standardized prevalence rate in 2019. **(c)** Age-standardized mortality rate in 2019. **(d)** Age-standardized DALY rate in 2019. DALY, disability-adjusted life years; GCAYA, gastric cancer in adolescents and young adults.

During this period, the number of new cases, deaths, and DALY and age-standardized incidence, mortality, and DALY rates were generally higher in men than in women and were double or more. There are inherent differences in physiological structure and function between male and female patients, including notable variations in hormone levels. Early studies have highlighted the significant role of estrogens in the gastric cancer microenvironment. For instance, Zhang et al (16) found that estrogen stimulates cancer-associated fibroblasts in gastric cancer to secrete interleukin-6, thereby activating the STAT3 signaling pathway in GC cells. This provides a profound understanding of the interplay between estrogens and the tumor microenvironment and their impact on gastric cancer progression. In addition, Jukic et al (17) observed a higher frequency of androgen receptor–positive cells in the gastric cancer stroma of male patients compared with female patients, which may contribute to the increased invasiveness seen in gastric cancer of male patients. Consequently, androgen receptor could emerge as a potential therapeutic target in gastric cancer. Furthermore, Ur Rahman et al (18) discovered that low concentrations of estrogens can stimulate the expression and growth of ERα36 in gastric cancer cells, whereas high concentrations inhibit its expression and growth. This relationship between estrogen concentration and function may explain why gastric cancer is more common in male patients. In summary, further investigations into the mechanisms of action of estrogen receptor subtypes in gastric cancer development and progression hold significant importance in understanding the sex disparities in GCAYA occurrence and their implications for prevention, diagnosis, and treatment. According to the SDI quintile, both the incidence rate and DALY of GCAYA in all regions of the world have shown a declining trend. Specifically, high SDI countries have seen the most significant decrease in age-standardized incidence and DALY. These countries have better access to health care and sanitation facilities, higher living standards, and better nutrition status, all of which contribute to a more widespread and effective prevention and treatment of GCAYA (19). By contrast, the middle SDI countries have the least decline in age-standardized incidence of GCAYA. These countries have a moderate level of development and are more likely to have access to modern medical equipment and better health care than low SDI countries, potentially leading to more effective diagnosis and treatment of GCAYA at an earlier stage (20). We found that at the regional level, from 1990 to 2019, the standardized incidence rate and DALY of GCAYA all showed a downward trend at the regional level. Among them, the regions with the largest decline in incidence rate were high-income Asia Pacific, Eastern Europe, and Tropical Latin

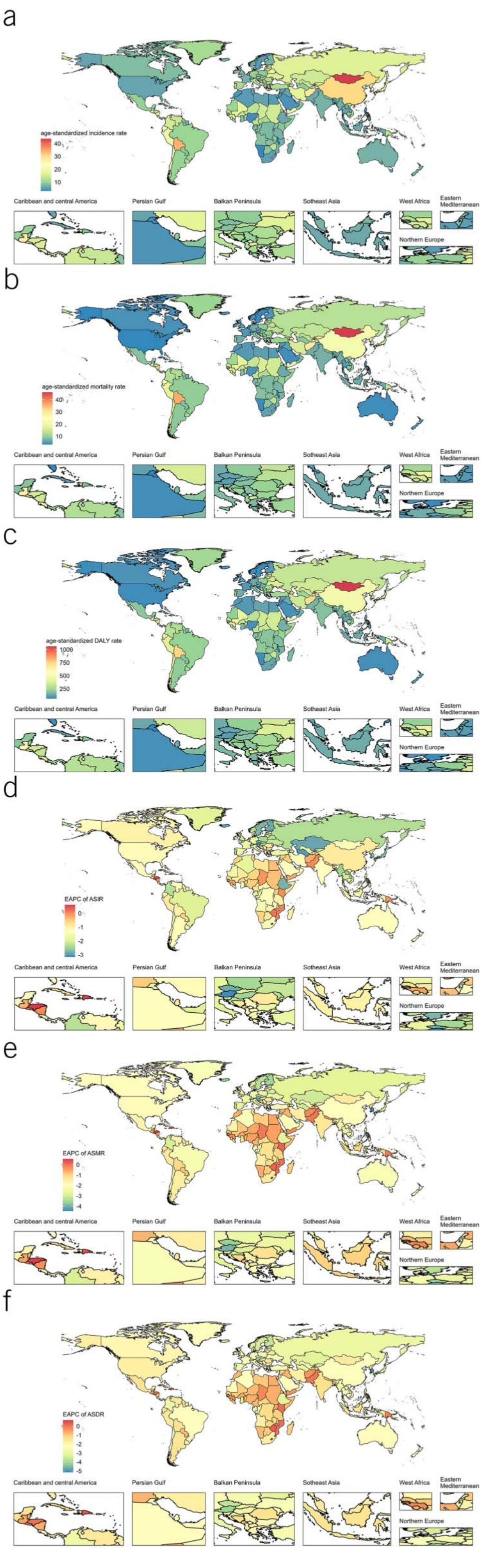

Figure 3. Country trends of GCAYA from 1990 to 2019. (**a**) Age-standardized incidence rate in 2019. (**b**) Age-standardized mortality rate in 2019. (**c**) Age-standardized DALY rate in 2019. (**d**) EAPC of ASIR from 1990 to 2019. (**e**) EAPC of ASMR from 1990 to 2019. (**f**) EAPC of ASDR from 1990 to 2019. ASDR, age-standardized DALY rates; ASIR, age-standardized incidence rates; DALY, disability-adjusted life years; EAPC, estimated annual percentage change; GCAYA, gastric cancer in adolescents and young adults.

America, while the regions with the smallest decline were Oceania, Western Sub-Saharan Africa, and East Asia. The regions with the greatest decline in DALY were Western Sub-Saharan Africa, Western Europe, and Tropical Latin America, while Andean Latin America, Australasia, and Caribbean had the smallest decline (21,22). GCAYA is unevenly distributed at the global regional level (21,23), and the reasons for the different decline in standardized incidence rate and DALY of GCAYA are multifaceted and can be attributed to changes in dietary structure, improvements in medical technology, the implementation of prevention and screening measures, and strengthened education and awareness efforts. The combined effect of these measures has helped to reduce the incidence of GCAYA and improve the cure rate. However, it is necessary to enhance the aforementioned factors in regions with a lower decline magnitude, to reduce the disease burden of GCAYA in more areas globally. Through the analysis of sex, socioeconomic status, and regional GCAYA incidence rates, it can be generally concluded that the differences in GCAYA may be attributed to various factors such as sex, culture, geography, and socioeconomic conditions. The effects and influences of these factors need to be further examined and analyzed in specific regions to ascertain their significance. On a global scale, progress has been made in the prevention and treatment of GCAYA. However, more efforts are still required, particularly in encouraging young male individuals to prioritize their health by undergoing regular checkups and screenings. It is also important to promote and educate individuals in this demographic about dietary improvements and adopting a healthy lifestyle. In countries with moderate SDI, additional measures need to be implemented and optimized to decrease the incidence rates of gastric cancer and the associated burden in terms of DALY.

We have found that at the national level, from 1990 to 2019, the ASIR of GCAYA showed a declining trend in 196 of 204 countries and territories worldwide, including both male and female individuals. Furthermore, the age-standardized death rate and DALY rate of GCAYA showed a declining trend in 198 countries and territories. Therefore, it is evident that the disease burden of GCAYA has decreased in most countries globally. This is mainly due to changes in lifestyles and diets and improvements in early screening and treatment (24). However, the magnitude of decrease varies in different countries, with some countries experiencing an increase in their burden. Therefore, it is necessary to strengthen measures to improve the disease burden in countries with a heavier burden and lower decline magnitude such as China, India (25), Russian Federation, and Brazil (26). Gastric cancer is the second leading cause of cancer death in China, and according to data from the National Cancer Center of China, the proportion of young people aged 30–39 years diagnosed with gastric cancer has increased compared with that before (27). Multiple measures can be taken, including improving public health awareness and education, enhancing basic health infrastructure, promoting disease prevention measures, strengthening medical and health services, and implementing health promotion policies. In addition, these measures should be tailored to the specific circumstances of different countries and regions. Through the implementation of these measures, disease occurrence and transmission can be reduced and people's health can be improved, thus alleviating the burden of disease. The countries with a lower decline magnitude or increasing trend in ASIR, death rate, and DALY rate are Honduras, Dominican Republic, Lesotho, and Zimbabwe. These countries can establish a sound public health system, improve medical services, prevent

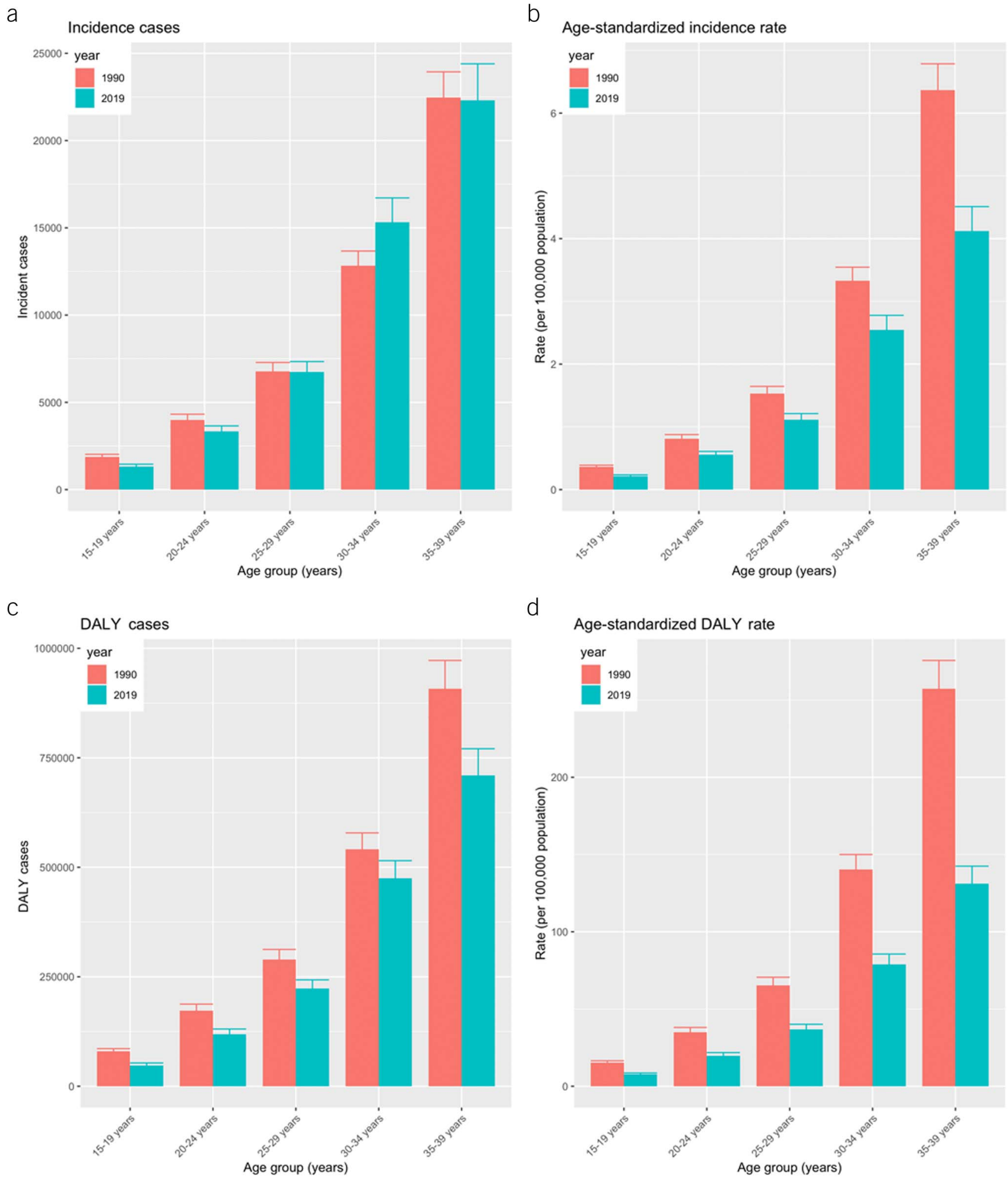

Figure 4. The incidence of gastric cancer in adolescents and young adults at different age stages. DALY, disability-adjusted life years.

chronic diseases, establish health promotion policies, and strengthen international cooperation to help improve the health of their people and reduce the disease burden of GCAYA. The countries with the highest ASIR, death rate, and DALY rate are Mongolia and Bolivia (Plurinational state of Bolivia). These 2 countries, as landlocked nations, often consume unhealthful diets containing high levels of salt, fat, and low fiber, which may lead to high incidence of gastric cancer. In addition, some regions in these countries have high levels of natural radiation, which could further increase the risk of cancer and gastric cancer for residents

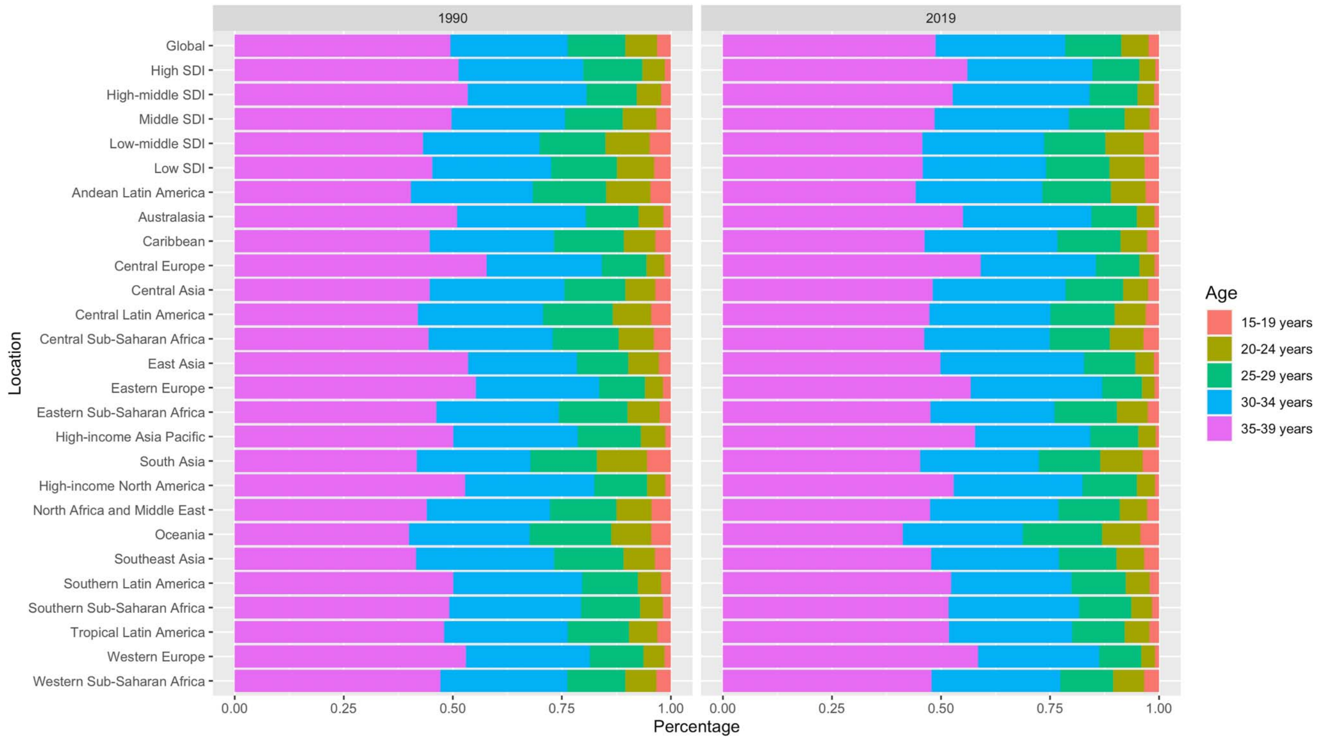

Figure 5. The contribution of death numbers to different age groups in gastric cancer in adolescents and young adults.

who are exposed to high-intensity natural radiation for prolonged periods. Furthermore, the health care services in these countries are relatively backward, and many patients with gastric cancer may not receive timely diagnosis or treatment. Therefore, it is necessary to adopt multifaceted intervention measures, including strengthening health education, promoting healthy diets, improving lifestyle habits, and enhancing medical services, to reduce the disease burden of GCAYA in these countries.

According to age groups of 15–19 years, 20–24 years, 25–29 years, 30–34 years, and 35–39 years, both the incidence and DALY rates of GCAYA increased with age from 1990 to 2019, with the highest proportion of patients in the 35–39 years age group. However, in 2019, the incidence count, DALY count, standardized incidence rate, and standardized DALY rate of GCAYA all decreased compared with those in 1990. In addition, the age distribution of GCAYA deaths was mainly concentrated in the 35–39 years age group, accounting for approximately half of the entire population, followed by the 30–34 years age group. The 20–24 and 15–19 years age groups accounted for a smaller proportion of deaths. Thus, the disease burden of GCAYA mainly affects the 35–39 years age group. Most guidelines for gastric cancer screening developed by international cancer associations or health management departments recommend that screening should start at the age of 50 years or older for adults. However, the screening age may vary depending on different countries' situations (28–30). For example, the American Cancer Society recommends that screening should start at the age of 40 years for adults in 2021 (31), while the Chinese health management department suggests starting at the age of 35 years (31). Few health management departments focus on the early screening and intervention of GCAYA. Although screening GCAYA for those younger than 40 years may increase the workload of health management departments, high-risk individuals in the younger age may be subjected to screening, such as patients with gastric cancer or related diseases history in families. For these groups, strengthening screening and early diagnosis, controlling preventive factors, and improving research and clinical practice are necessary. For countries with a high incidence of GCAYA, relevant institutions and professional teams could be established to reduce the incidence of GCAYA and improve treatment outcomes. In terms of disease burden, although other age groups have a lower proportion, different strategies should also be adopted for different age groups to reduce the overall disease burden of GCAYA.

There have been numerous studies on the analysis of the burden of gastric cancer on the general population. However, there is a lack of analysis specifically focused on the burden of GCAYA. Li et al (8) conducted an analysis of GCAYA using data from the International Agency for Research on Cancer Global Cancer statistics in 2020. They found that the incidence rates of GCAYA have decreased in some countries, and most countries have witnessed a decrease in mortality rates. These findings are consistent with our own research results. In addition, they compared the incidence and mortality rates of GCAYA with those of older patients with gastric cancer and discovered that although the diagnostic rates for GCAYA are much lower compared with those among the older population, the disease burden caused by GCAYA remains considerable due to the longer life expectancy of these individuals. However, their study did not present data for all countries globally. In our study, we aim to further refine the data presentation and visualization analysis of the burden of GCAYA for all countries worldwide, providing more comprehensive and intuitive results. Furthermore, Song et al (32,33) analyzed GBD data and found that climate and geographical changes worldwide have also led to a significant burden of noncommunicable diseases. However, their research did not specifically analyze the burden of more specific diseases such as schizophrenia and cancer. In our study, we focus on a more specific analysis of the burden of GCAYA, a specific type of cancer. In addition, Alvarez et al (34) discovered in their research that in 2019, cancer among adolescents and young adults accounted for a significant portion of the overall disease burden for this age group. The age-standardized DALY for cancer among adolescents and young adults differed from that of children and adults, indicating the need for further analysis of the burden structure of cancer in this population. Alvarez et al (34) also found that gastric cancer was one of the 4 major cancers contributing to the combined DALY burden in both male and female patients among all cancers in adolescents and young adults. However, their research did not further analyze GCAYA based on temporal, regional, national, and sex factors nor did it provide detailed data support. Therefore, in this study, we aim to expand on the aforementioned studies and provide a more detailed analysis of the factors mentioned earlier to optimize measures for reducing the burden of GCAYA globally. We also aim to provide more professional and detailed data support for addressing this issue.

The GBD 2019 Cancer Risk Factor Collaborators include only "behavioral risks" and "dietary risks" as recorded factors contributing to gastric cancer (see Supplementary Appendix 2, pp 154–155, http://links.lww.com/AJG/D84) (35). Insufficient data exist to comprehensively document other risk factors or provide detailed subcategorization of the recorded ones. Therefore, we have compiled findings from studies by Thrift et al (36), Machlowska et al (37), and Aaron et al (14), summarizing the risk factors of gastric cancer in the general population. These studies indicate that risk factors of gastric cancer include *H. pylori* infection, high body fat content, smoking, high intake of salt and processed meats, viral infections (such as Epstein-Barr virus), family history, low socioeconomic status, low physical activity level, radiation exposure, obesity, and the presence of gastroesophageal reflux disease. Furthermore, individual risk of gastric cancer is influenced by a combination of factors such as age, sex, and genetic predisposition. Future research on risk factors of GCAYA could use the aforementioned risk factors, collecting corresponding data to determine the contribution of each factor to GCAYA. This represents a direction for further investigation into the causative factors of GCAYA. The general incompleteness of the GBD database limits this study. Some countries and regions may not have sufficient data to accurately assess their disease burden, resulting in significant bias in the data from these areas. In addition, data quality issues may also affect the analysis of the GBD database. Despite multiple levels of verification and correction, in some countries and regions, lack of sufficient capacity and resources may prevent accurate assessment of their disease burden, leading to data bias. Time limitations are also a limiting factor for the GBD database. Although the GBD database is updated annually, the latest data may not reflect recent disease trends and health risk factors due to the timeliness of some data. Finally, the GBD database also has shortcomings regarding regional specificity. Although the GBD database provides global data, these data may not be representative enough for some regions. For example, cultural, social, and environmental factors in different regions may all affect disease burden, but the GBD database may not accurately reflect these differences. Therefore, our research results should also take into account the limitations of the GBD database to avoid misinterpretation or misuse of the data and should be analyzed in conjunction with other data sources and the corresponding situations in the relevant regions. In future studies, our attention will be directed toward the aforementioned data, with a particular focus on the corresponding regions. We aim to conduct further research and elucidate the precise mechanisms contributing to the disparities observed in GCAYA. This will enable us to implement more targeted measures to mitigate the burden of GCAYA in specific geographical areas.

In summary, over the past 30 years, although the number of new cases of GCAYA worldwide has generally increased in line with population growth, the ASIR of GCAYA has decreased and the overall burden of GCAYA has decreased as well. This suggests that significant progress has been made globally in addressing this disease challenge, which is due to various factors such as improved screening, diagnosis, and treatment and education and awareness campaigns. However, GCAYA still faces several challenges globally, including uneven distribution based on factors such as sex, age, socioeconomic status, region, and country. The burden of disease is heavier among male patients, and the age group of 35–39 years bears a significant burden of GCAYA, accounting for approximately half of the affected population. The burden of GCAYA is also heavier in countries with high-middle and middle SDI. The countries with the heaviest burden of GCAYA are primarily located in landlocked developing countries, such as Mongolia and Bolivia (Plurinational state of Bolivia). To address these challenges, global health authorities should make appropriate adjustments, such as optimizing screening programs, strengthening awareness campaigns and screening efforts for male individuals, enhancing prevention and control measures for the 35–39 years age group, and improving infrastructure and investing more medical resources in developing countries. A primary preventive measure to reduce the incidence of gastric cancer in the adolescent and young adult population involves the implementation of treatment and eradication of *H. pylori* infection. This approach has been successfully implemented in various countries including Japan (38) and the United States (39), resulting in a significant reduction in individual risk of developing gastric cancer. Furthermore, a secondary preventive measure involves the use of upper gastrointestinal endoscopy for screening in young individuals. This method enhances the detection rate of gastric cancer and is considered cost-effective in developed countries (40). Its potential implementation and dissemination in other countries, based on their specific contexts, could lead to an overall improvement in the detection rate of gastric cancer in the adolescent and young adult population. International cooperation should also be strengthened to facilitate cooperation and mutual learning on prevention and treatment measures among countries with different levels of development. Moreover, tailored measures should be adopted based on different cultural, regional, and habitual factors of individual countries. In conclusion, to meet the global challenge posed by the burden of GCAYA, it is necessary to explore more appropriate measures and strategies to further reduce the burden of disease and address the problem of uneven distribution.

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CONFLICTS OF INTEREST

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STOMACH

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Study Highlights

WHAT IS KNOWN

- ✓ Gastric cancer poses a heavy burden worldwide.
- ✓ There is limited documentation on the systematic analysis of the burden of gastric cancer in adolescents and young adults (GCAYA).

WHAT IS NEW HERE

- ✓ The burden of GCAYA has shown a slight increasing trend in recent years.
- ✓ The burden of GCAYA is higher in male populations compared with female populations.
- ✓ Countries with a heavy burden of GCAYA are predominantly concentrated in landlocked developing nations.

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