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Global, regional, and national burden of early-onset gastric cancer

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ABSTRACT

Objective: The burden of gastric cancer (GC) across different age groups needs updating. We determined the GC global, regional, and national burden profiles and changes in incidence for 3 sequential 5-year intervals from 2003 to 2017.

Methods: The latest incidence and mortality estimates of GC from 185 countries and regions were extracted from the GLOBOCAN 2022 database. The 5-year interval age-standardised incidence rates (ASIRs) were evaluated using cancer registry data from volumes X–XII of the Cancer Incidence in Five Continents (CI5). Correlation analysis was used to evaluate the relationship between ASIR or the age-standardised mortality rate (ASMR) and the Human Development Index (HDI).

Results: There was an estimated global 968,000 new GC cases and 660,000 deaths in 2022, with male predominance. GC ASIRs and ASMRs were 9.2 and 6.1 per 100,000 persons, respectively. East Asia had the highest burden, with 53.8% of cases and 48.2% of deaths among all geographic regions. There was a significant correlation between ASIR and HDI. Over three 5-year intervals from 2003 to 2017, the incidence of GC notably decreased in most countries but peaked at 2008–2012 in New Zealand, Turkey, and South Africa. Several countries in Europe, Oceania, and America suggest an increasingly concerning trend among younger individuals, especially females.

Conclusions: GC is a significant health issue, especially among males and in geographic regions with an HDI, such as eastern Asia. While the incidence of GC is decreasing in many countries due to prevention efforts and improved treatments, a rising trend persists among younger individuals. Comprehensive prevention strategies tailored to different age patterns are clearly needed.

KEYWORDS Gastric cancer; cancer burden; GLOBOCAN; incidence; mortality

Introduction

Gastric cancer (GC) ranks 5th as the most prevalent cancer globally with more than 960,000 new cases and the 5th highest cause of cancer-related mortality, accounting for nearly 660,000 deaths worldwide according to 2024 estimates[1]. The incidence of GC has wide geographic variation. The incidence of GC is 15–20-fold higher in East Asia and East Europe compared to the incidence in the African continent[1]. Because GC is often diagnosed in an advanced stage with metastases, the prognosis is poor, even in high-income countries[2,3].

Primary and secondary prevention strategies are increasingly recognized as crucial approaches for mitigating the burden of GC. The gradual decline in the global incidence and mortality rates of GC over the past 50 years has been largely attributed to improvements in general hygiene and socioeconomic conditions that limit the transmission of *Helicobacter pylori* infection[4]. Notably, high-risk geographic regions, such as Japan and the Republic of Korea, have achieved significant reductions in GC-associated mortality through the implementation of national screening programs[5,6]. However, recent studies have uncovered concerning trends, with rising incidence rates among adults < 50 years of age, especially for non-cardia GC in the United States and other affluent regions[7-9]. The reasons for GC among younger adults have not been fully elucidated but appear to be related to genetic and

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environmental factors, dietary habits, and lifestyle[10]. Focusing on early-onset GC is of essential because younger patients tend to have higher grade GC, more diffuse histologic features, increased peritoneal metastases, and signet-ring cells, all of which are associated with a worse prognosis. Moreover, young patients are often diagnosed with advanced-stage disease with progression, in part due to a lack of self-awareness regarding the potential risks of cancer. GC is preventable due to the association with modifiable risk factors. Targeted measures are needed to prevent and control the occurrence of GC.

Considering the disparities in the burden of GC across populations and the availability of more recent data, updated estimates of the global GC incidence and mortality rates GC are warranted. This study aimed to determine the global, regional, and national burden of GC using data from the 2022 International Agency for Research on Cancer (IARC) Global Cancer Observatory (GLOBOCAN) database. The changes in incidence of early (age < 50 years) and late onset (age ≥ 50 years) GC for 3 sequential 5-year intervals from 2003 to 2017 at the national level were also evaluated, which will enable effective tracking of developmental progress and assistance in the development and implementation of pertinent policies to prevent and manage the increasing burden of GC.

Materials and methods

Data sources and methods

The GLOBOCAN database was use to derive the number of new GC cases, incidence of GC, and GC-associated mortality (International Classification of Diseases, 10th revision: C16) in 185 countries grouped by gender and age, with the most recent estimates from 2022[1,11,12]. The detailed data sources and estimation methods have been described previously[12]. No inclusion or exclusion criteria were applied to the GLOBOCAN data used in the current study. The Human Development Index (HDI) for each country was developed by the United Nations Development Programme repository[13]. The cancer burden in different geographic regions of the world can be assessed by classifying the HDI into the following 4 levels: [low (< 0.604) and moderate (0.640–0.764) HDI *vs.* high (0.764–0.902) and very high (≥ 0.902)][13].

Table 1 lists new GC cases and deaths and assessed disparities in age-standardised rates (ASRs) per 100,000 persons using the world standard population, which allows comparisons between populations adjusted for differences in age structures. The results are delineated by gender and age groups (< 50 *vs.* ≥ 50 years) and aggregated across 21 UN-defined world regions that were categorized according to the UN 4-tier HDI in 2022. Additionally, we performed a descriptive analysis to determine the male-to-female ratio (M:F ratio) of the ASR, which was calculated as the ratio of incidence and mortality rates. Spearman's correlation test were used to evaluate the relationship between the age-standardised incidence rate or age-standardised mortality rate and the HDI. We used the terms, transitioning, emerging, and lower HDI countries/economies, interchangeably with nations classified as a low or medium HDI, and transitioned or higher HDI countries/economies for nations classified as a high or very high HDI.

CI5 volumes I–XII provide updated incidence rates at 5-year intervals from regional and national cancer registries. Gender-specific data were reported by each cancer registry. The number of selected populations and registries increased with each volume update. The most recent volume (CI5 XII) encompasses information from 455 population-based cancer registries in 70 countries and covering cancers diagnosed from 2013–2017. We evaluated the long-term GC ASIRs by different age strata (< 50 *vs.* ≥ 50 years) and gender in each selected country for at least 15 consecutive years using data aggregated by CI5 X–XII from 2003–2017. A cut-off age of 50 years was chosen based on previous studies that designated cases diagnosed at < 50 years of age as early-onset GC[14-16]. The quality of the data sources utilized has been assessed in prior studies[17-20]. Registries selected for each country must have available data among CI5 volumes X–XII. Ultimately, we performed a comprehensive assessment of incidence rate trends among 24 countries. Detailed data sources for incidence analysis, including information on registries and timeframes, are listed in **Table S1**. Confidence intervals and standard errors are provided in **Tables S2-S4**. All statistical analyses and plotted figures were performed using Python software (version 3.7.7).

Results

GC cases and deaths by world region

An estimated 968,000 cases of GC were diagnosed globally in 2022 with males and females accounting for > 627,000 and 341,000 cases, respectively. The disease claimed 660,000 lives, with males representing 65% of the fatalities. The ASRs for GC incidence and mortality were 9.2 and 6.1 new cases and deaths per 100,000 people, respectively. Geographically, > 50% of the

Table 1 New cases and deaths, age-standardised incidence and mortality rates per 100,000 persons with GC by age group and world region in 2022

Population	Incidence						Mortality					
	< 50 years			≥ 50 years			< 50 years			≥ 50 years		
	Number of cases	% of all cases	ASR	Number of cases	% of all cases	ASR	Number of cases	% of all cases	ASR	Number of cases	% of all cases	ASR
Regions												
Africa												
East Africa	2,307	22.50	0.77	7,946	77.50	18.66	1,812	20.14	0.60	7,184	79.86	16.90
West Africa	1,891	24.39	0.73	5,861	75.61	15.46	1,610	23.22	0.62	5,323	76.78	14.19
Mid-Africa	852	24.55	0.78	2,618	75.45	15.98	710	23.23	0.65	2,346	76.77	14.40
South Africa	351	17.38	0.58	1,669	82.62	14.71	254	14.85	0.43	1,456	85.15	13.09
North Africa	2,190	22.22	1.08	7,667	77.78	17.26	1,681	20.92	0.83	6,354	79.08	14.28
America												
Caribbean	460	11.00	1.28	3,720	89.00	26.87	316	9.87	0.87	2,887	90.13	20.52
Central America	2,063	13.86	1.32	12,823	86.14	31.4	1,656	14.20	1.06	10,006	85.80	24.29
South America	5,361	9.69	1.38	49,952	90.31	40.00	4,161	9.67	1.05	38,869	90.33	30.75
North America	2,946	9.93	0.96	26,729	90.07	16.83	1,114	8.33	0.36	12,253	91.67	7.05
Asia												
East Asia	27,443	5.27	1.84	493,532	94.73	72.91	12,797	4.03	0.85	305,122	95.97	42.66
West Asia	3,212	14.45	1.25	19,012	85.55	36.44	2,161	11.98	0.85	15,873	88.02	30.17
Southeast Asia	5,526	14.24	0.91	33,272	85.76	21.53	3,635	11.46	0.60	28,077	88.54	18.13
South Central Asia	19,395	17.66	1.10	90,399	82.34	23.32	15,352	16.17	0.89	79,589	83.83	20.50
Europe												
East Europe	4,368	6.58	1.57	62,032	93.42	49.41	2,744	5.65	0.97	45,804	94.35	35.19
West Europe	1,566	5.73	0.98	25,773	94.27	23.97	751	4.41	0.46	16,291	95.59	13.64
South Europe	1,307	4.24	0.92	29,540	95.76	32.45	758	3.41	0.52	21,466	96.59	21.59
North Europe	611	5.54	0.68	10,413	94.46	18.97	328	4.31	0.36	7,289	95.69	12.31
Oceania												
Australia-New Zealand	229	6.87	0.87	3,105	93.13	22.71	93	5.67	0.35	1,546	94.33	10.37
Melanesia	64	11.85	0.70	476	88.15	33.03	27	6.31	0.31	401	93.69	27.59
Micronesia	0	0.00	0.00	40	100.00	32.33	0	0.00	0.00	28	100.00	23.01
Polynesia	4	6.35	0.75	59	93.65	37.11	3	5.88	0.56	48	94.12	30.04
HDI												
Low HDI country	6,609	25.70	0.85	19,108	74.30	15.93	5,330	23.45	0.70	17,398	76.55	14.53
Medium HDI country	20,786	18.45	1.10	91,872	81.55	22.13	15,892	16.10	0.85	82,829	83.90	19.94
High HDI country	36,659	7.65	1.46	442,685	92.35	51.05	21,977	6.18	0.87	333,384	93.82	37.12
Very HDI country	18,067	5.15	1.25	332,702	94.85	43.25	8,748	4.78	0.60	174,378	95.22	21.01
World	82,146	8.48	1.24	886,638	91.52	40.92	51,963	7.87	0.79	608,212	92.13	27.28

ASR, age-standardised rate per 100,000 people; HDI, human development index.

global GC burden was concentrated in East Asia, accounting for 53.8% of cases and 48.2% of deaths, followed by South Central Asia (11.3% and 14.4%, respectively), East Europe (6.9% and 7.4%, respectively), and South America (5.7% and 6.5%, respectively; **Table S5**). There was a substantial disparity in the GC ASIRs across world regions, ranging nearly 5-fold from 3.4 new cases per 100,000 people in South Africa to 16.1 in East Asia. Similarly, East Asia exhibited the highest ASMR (9.2 per 100,000 people) compared to 1.7 in North America (a 5.4-fold difference). Notably, Mongolia reported the highest rates for both incidence (35.5 per 100,000 people) and mortality (31.6 per 100,000 people). The ASIRs of Japan and South Korea rank 2nd and 3rd among nations (27.6 and 27.0 per 100,000 people, respectively); the ASMRs were not as high as the ASIRs (**Tables S5-S6**).

Geographic patterns were distinct between the genders. GC was more commonly diagnosed in males. Specifically, the GC incidence rates in males ranged from < 4 per 100,000 persons in several African countries to approximately 23 per 100,000 persons in East Asian countries (**Figure 1A**). Similarly, the ASMRs were consistently higher among males compared to females across all geographic regions (**Figure 1B**). The GC male-to-female (M:F) ratio ranged from 1.13 in Mid-Africa to 2.38 in East Asia with corresponding mortality ratios being lowest in Mid-Africa (1.12) and highest in East Asia (2.55) and East Europe (2.20). This pattern persisted across age groups, with East Asia demonstrating the highest GC incidence rates for both age groups (< 50 and ≥ 50 years). Notably, Mongolia reported the highest GC incidence rates of 5.6 among individuals < 50 years of age, followed by the Republic of Korea (4.8) for people ≥ 50 years of age. The incidence rates were higher in Mongolia (154.9), Japan (132.1), and the Republic of Korea (115.8). A higher proportion of patients < 50 years died in Central America with an ASMR of 1.06 compared to patients ≥ 50 years of age due to the younger age structure in that geographic region. At the national level, Sao Tome and Principe reported the highest mortality rate for individuals < 50 years of age (3.6), while Mongolia had the highest rate for individuals ≥ 50 years of age (144.7).

GC cases and deaths by level of human development

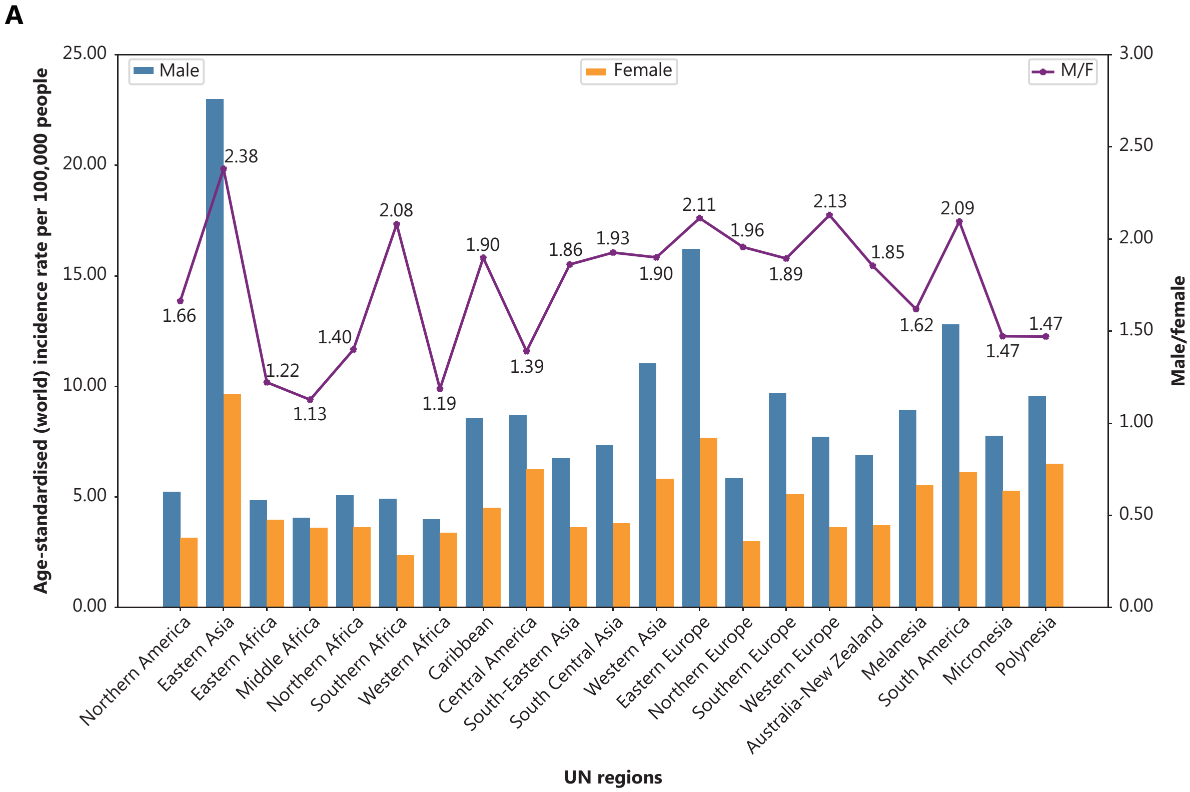
The association between the GC incidence and HDI suggests a tendency for higher incidence rates with increased HDI levels, albeit the correlation was weak ($\rho = 0.27$, $P < 0.001$). However, no significant correlation was detected between the HDI and ASMR in any country (**Table S6**). Notably, countries in transition accounted for approximately 14% of all GC cases and 18% of all deaths worldwide in 2022. The ASIRs and ASMRs were 1.5–2.5 times higher in individuals ≥ 50 years of age in transitioning countries compared to transitioned countries. However, the differences in mortality rates among individuals < 50 years of age were less pronounced. The burden of GC was especially substantial in countries with a high HDI, with the highest incidence and mortality rates observed in this group. Specifically, countries with a high HDI had incidence rates of 1.46 and 51.05 new cases per 100,000 people and mortality rates of 0.87 and 37.12 deaths per 100,000 people for individuals < 50 and ≥ 50 years of age, respectively (**Table 1**). This large contribution to the global GC burden was not unexpected because the high HDI group includes countries with the highest GC incidence and mortality rates, such as Mongolia, Japan, and the Republic of Korea.

GC incidence from 2003–2017 at 5-year intervals

Table 2 presents the GC ASIR over 3 consecutive 5-year intervals disaggregated by gender and calculated from CI5 X–XII. Notably, the GC incidence was consistently higher in males than females across all time intervals and countries. Compared to the initial 5-year span (2003–2007), the incidence rates in most nations declined in the subsequent period (2013–2017), albeit with an increase observed in South African females. However, the ASIRs for Australia, New Zealand, South Africa, and Turkey peaked during the 2008–2012 time period (7.47, 15.23, 1.29, and 16.39 per 100,000 people for males, respectively) compared to the other two 5-year intervals for males, while Turkey also had higher incidence rates in females. The Republic of Korea consistently reported the highest GC incidence for 3 sequential 5-year intervals from 2003 to 2017, averaging approximately 60 new cases per 100,000 people, closely followed by Japan with > 50 new cases per 100,000 people.

Incidence of GC in younger versus older individuals

The GC incidence rates in populations < 50 and ≥ 50 years of age are summarized in **Table 3**. **Figure S1** depicts the ASIR and confidence intervals for the younger age group. The GC



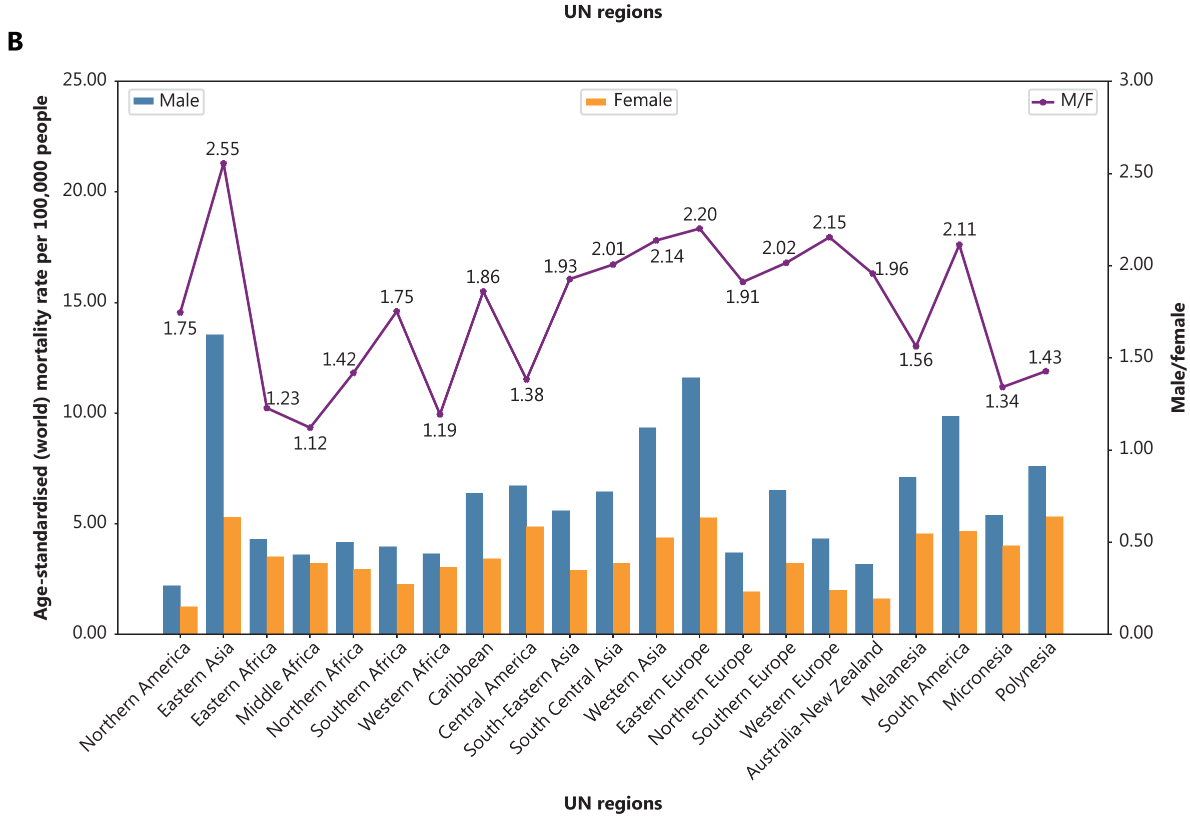


Figure 1 Age-standardised incidence (A) and mortality (B) rates per 100,000 people of GC by gender, world region in 2022. M/F, male:female age-standardised rate ratio. UN, United Nations. Data are from the GLOBOCAN database, collated by the International Agency for Research on Cancer and hosted by the Global Cancer Observatory[1].

Table 2 Age-standardised incidence rates (ASIR) per 100,000 persons with GC by gender and years

Country	Male			Female		
	2003–2007	2008–2012	2013–2017	2003–2007	2008–2012	2013–2017
Austria	11.75	10.11	9.19	6.23	4.98	4.80
Australia	6.44	7.47	6.40	3.53	3.02	3.01
Canada	7.91	7.23	6.31	3.79	3.24	2.92
China	42.66	42.59	34.32	20.22	18.56	15.53
Colombia	25.01	20.15	21.27	12.04	10.13	10.38
Denmark	7.46	6.95	7.07	3.45	3.02	3.31
France	9.01	7.95	7.55	3.41	3.52	3.24
Germany	12.72	10.64	10.02	6.67	5.64	5.15
India	9.86	8.95	7.96	4.81	4.25	4.08
Iceland	9.18	5.90	5.09	5.01	4.29	3.38
Ireland	10.23	9.62	8.79	4.88	4.55	4.22
Italy	13.91	12.20	10.03	6.93	6.18	5.55
Japan	58.67	56.52	54.83	21.34	20.32	20.02
Korea, Republic of	63.26	61.79	50.06	25.53	24.73	21.23
The Netherlands	9.31	8.24	6.55	4.13	4.02	3.39
New Zealand	14.58	15.23	11.37	9.24	8.61	7.75
Norway	7.74	6.57	6.09	4.18	3.40	3.04
Spain	11.91	11.25	9.67	5.11	5.07	4.88
Switzerland	8.33	7.79	7.72	4.30	4.01	3.74
South Africa	0.91	1.29	0.58	0.48	0.73	0.79
Türkey	14.51	16.37	14.04	7.11	7.42	6.01
Uganda	7.15	5.73	5.00	5.42	2.85	3.93
United Kingdom	9.96	8.43	7.28	4.36	3.73	3.25
United States of America	7.29	6.60	6.28	3.57	3.42	3.32

incidence rates were lower in most countries in 2013–2017 compared to 2003–2007 for patients < 50 or ≥ 50 years of age. It is noteworthy that within select nations, the ASIRs of early-onset GC for South Korea, Japan, and China consistently ranked among the top 3 for both genders across 3 sequential timeframes, despite a significant reduction observed in the 2013–2017 period compared to the 2003–2007 interval. However, increased GC incidence rates in 2013–2017 were shown in several countries with 3 and 8 countries exhibiting an increase in males and females compared to 2003–2007 among individuals < 50 years of age, respectively, although these countries had decreased incidence rates across all age groups. Notable examples include Australia, Colombia, and Ireland among both genders, and Austria, Denmark, France, South Africa, and the United States of America among women. Interestingly, the profiles in New Zealand, Turkey, and South Africa in men were similar to the profiles of all ages.

Discussion

Several major findings were derived from this study. There was a wide variation in the global burden of GC with a higher

Table 3 Age-standardised incidence rates per 100,000 (< 50 and ≥ 50 years of age) persons with GC by gender and years

Country	< 50 years						≥ 50 years					
	Male			Female			Male			Female		
	2003–2007	2008–2012	2013–2017	2003–2007	2008–2012	2013–2017	2003–2007	2008–2012	2013–2017	2003–2007	2008–2012	2013–2017
Austria	1.02	0.92	0.90	0.77	0.77	0.85	10.73	9.20	8.28	5.47	4.21	3.95
Australia	0.51	0.83	0.74	0.44	0.52	0.50	5.94	6.64	5.66	3.09	2.50	2.51
Canada	0.63	0.89	0.62	0.79	0.78	0.39	7.28	6.34	5.69	3.01	2.46	2.52
China	4.03	3.46	3.12	2.75	2.83	2.37	38.63	39.13	31.20	17.47	15.73	13.16
Colombia	2.88	2.73	2.92	1.72	2.29	2.30	22.13	17.42	18.35	10.32	7.85	8.08
Denmark	0.85	0.65	0.71	0.56	0.49	0.58	6.60	6.30	6.37	2.89	2.53	2.73
France	0.93	0.86	0.90	0.55	0.50	0.61	8.08	7.09	6.66	2.85	3.03	2.63
Germany	1.33	1.10	1.13	1.01	0.82	0.91	11.39	9.53	8.89	5.66	4.81	4.24
India	1.62	1.41	1.14	0.91	0.86	0.83	8.24	7.54	6.82	3.90	3.39	3.25
Iceland	0.66	0.53	0.55	0.73	0.45	0.34	8.52	5.37	4.55	4.27	3.83	3.04
Ireland	0.81	0.75	0.89	0.56	0.67	0.59	9.42	8.87	7.90	4.32	3.88	3.63
Italy	1.20	1.17	0.93	1.03	0.89	0.81	12.70	11.04	9.09	5.90	5.30	4.74
Japan	5.23	3.64	3.15	3.47	2.81	2.68	53.44	52.89	51.68	17.87	17.51	17.34
Korea, Republic of	8.37	7.87	6.36	6.23	6.09	5.46	54.89	53.93	43.70	19.31	18.64	15.77
The Netherlands	0.84	0.77	0.68	0.59	0.69	0.57	8.46	7.47	5.87	3.54	3.32	2.82
New Zealand	2.02	2.37	1.77	2.17	1.94	1.45	12.56	12.85	9.60	7.07	6.67	6.31
Norway	0.55	0.67	0.51	0.58	0.39	0.52	7.19	5.89	5.58	3.61	3.01	2.52
Spain	1.24	1.15	0.86	0.93	0.77	0.81	10.66	10.10	8.81	4.18	4.29	4.08
Switzerland	0.91	1.02	0.86	0.89	0.75	0.82	7.42	6.76	6.86	3.41	3.26	2.92
South Africa	0.08	0.48	0.00	0.05	0.23	0.07	0.83	0.80	0.58	0.43	0.50	0.71
Türkey	2.32	1.95	2.07	1.86	1.45	1.39	12.20	14.41	11.96	5.25	5.98	4.62
Uganda	0.85	0.87	0.72	1.13	0.34	0.49	6.30	4.86	4.28	4.29	2.51	3.44
United Kingdom	0.70	0.65	0.65	0.49	0.54	0.43	9.26	7.79	6.62	3.87	3.19	2.81
United States of America	0.84	0.80	0.81	0.61	0.61	0.67	6.45	5.80	5.47	2.96	2.80	2.64

incidence and mortality in East Asia and in males. Countries with a higher HDI known to have a higher prevalence of established risk factors for GC tend to have a higher incidence globally. Moreover, the overall decreased GC incidence rates were reported in most countries, although increased GC incidence rates occurred in individuals < 50 years of age in some countries, especially in women. Clearly, much work remains to be done in the fight against cancer.

The GC burden varied across geographic regions at the population level, which is generally consistent with previous studies[21,22]. The observed variations in GC burden can be partially attributed to demographic factors, notably the substantial populations of China and India, which contribute to a higher number of cases in Asia. The incidence of GC exhibited a significant elevation in East Asia, while the incidence of GC was lower and comparable to the Africa rates in North America and North Europe. The distribution of GC subtypes (non-cardia and cardia GC) varied among different racial groups. The between-group differences in GC incidence can be largely elucidated by variations in modifiable risk factors, such as tobacco consumption, *H. pylori* infection, dietary patterns, and lifestyle behaviors. These factors interact with intrinsic racial and ethnic disparities, including genetic predispositions and gene-environment interactions[23,24]. *H. pylori* infection has emerged as a pivotal risk factor with approximately 90% of non-cardia GC cases associated with this bacterium[25]. Globally, the prevalence of *H. pylori* infection exhibits regional discrepancies with notably high rates in Central and South America (approximately 60%), parts of Asia (e.g., approximately 55% in China and the Republic of Korea), and East Europe (approximately 50%)[26]. Cytotoxin-associated gene A (CagA) stands out as the most extensively researched *H. pylori* virulence factor, exerting a more potent influence on the risk of non-cardia GC compared to CagA+ *H. pylori* strains. Notably, East Asian CagA+ *H. pylori* strains harbor EPIYA motif variant D (EPIYA-D), which exhibits a binding affinity to the pro-oncogenic SHP2 phosphatase twice as strong as the EPIYA-C motif found in Western strains. This phenomenon contributes to an elevated risk of peptic ulcer or GC among individuals infected with East Asian CagA strains when compared to those infected with Western-type CagA strains[27,28]. Notably, nearly all *H. pylori* isolates in Japan include virulent strains of CagA and vacA[29]. Recent sero-prevalence data underscore the high *H. pylori* infection rates in China (46.1%) and the Republic of Korea (42.5%) among East Asia[30,31]. However, South Africa presents an intriguing paradox, with a high *H. pylori* prevalence but relatively lower GC incidence, which suggested various factors, such as the predominance of East Asia-type CagA strains, co-infections with parasites, antioxidant-rich diets, and limitations in data collection systems[32-34]. These findings offer insight into the significant disparities in the GC ASIR across HDI levels. The increase in GC burden with increase in HDI can be attributed to the fact that geographic regions with a relatively higher HDI tend to have a higher prevalence of *H. pylori*. However, Mongolia has the highest ASIR despite a low HDI. Mongolia exhibits a notably high prevalence of *H. pylori* infection, ranging from 67%–76% among individuals presenting with gastric complaints or diagnosed with early-stage GC[35]. Despite the high prevalence of GC in Mongolia, a screening program has just been implemented and no satisfying results have been achieved[36,37]. The current early cancer detection efforts are suboptimal and the scarcity of diagnostic tools, coupled with ineffective treatment protocols, frequently results in the late-stage diagnosis of gastrointestinal cancers. This delay in detection is likely contributing to an elevated mortality rate within the country. Additionally, cultural and dietary factors have a significant impact on the GC incidence apart from the different prevalence of two different CagA+ *H. pylori* strains (*vide supra*). Drinking tea with salt every day and a lower vegetable and fruit consumption were identified as high-risk factors for GC in Mongolia[36]. A higher GC incidence has been reported in Koreans and Japanese who lived in the United States of America[38]. Notable lifestyle factors contributing to GC risk include the consumption of salted and smoked foods, as well as obesity[39,40].

Significant gender disparities in the GC incidence exist with higher incidence and mortality rates noted in men compared to women across different age groups (< 50 and ≥ 50 years of age). This gender discrepancy can be attributed to various factors. Men typically exhibit higher rates of exposure to established risk factors, such as smoking, *H. pylori* infection, and alcohol consumption. These factors are known to contribute to the progression of preneoplastic lesions over an extended period, thereby increasing the incidence of GC among older individuals[41]. In contrast to our findings, several studies focusing on GC in young women (< 40 years of age) have reported a higher incidence compared to men. However, the GC ASIR and ASMR in women gradually declined below the GC ASIR and ASMR in men ≥ 40 years of age[42,43]. The underlying reasons for this discrepancy remain unclear, although two potential explanations have been proposed. One previous study demonstrated a correlation between a high incidence of diffuse-type GC and expression of estrogen receptors, which is linked to a poor prognosis in young women[44]. However, as women reach menopausal age (approximately 45 years), estrogen levels gradually decrease, approaching the estrogen levels in age-matched men[45]. The high-risk age group for developing GC in men is typically characterized by individuals ≥ 50 years of age[46]. Consequently, the GC incidence and mortality rates vary across different age groups. To enhance our understanding of the GC burden and to formulate effective preventive strategies, future corollary studies should consider categorizing GC into various subtypes based on additional age cut-off points.

Despite disparities in the GC burden, a declining incidence has been demonstrated for 3 sequential 5-year intervals from 2003 to 2017 that can be attributed to shifts in lifestyle, improvements in food storage and hygiene practices, and a significant reduction in the prevalence of *H. pylori* infection[3]. Notably, a parallel decrease in the population risk for *H. pylori* corresponds to the declining GC incidence rates in Asia and some European countries[47,48]. However, the limited availability of accurate *H. pylori* prevalence data in Africa hampers robust comparisons with other geographic regions[34]. Furthermore, ongoing tobacco control interventions have effectively curtailed smoking prevalence, which interacts synergistically with *H. pylori* infection to elevate GC risk. Similarly, large-scale initiatives targeting salt intake reduction have also influenced GC incidence rates[49,50]. Early detection efforts through the aforementioned screening programs, coupled with advancements in GC treatment strategies, have contributed to improved patient outcomes and are key factors driving the sustained decline in GC incidence, especially notable in countries like Japan and the Republic of Korea, which historically have had the highest incidence rates but considerably lower mortality rates. National GC screening programs have been implemented, featuring biennial screenings for individuals ≥ 40 years of age, utilizing upper gastrointestinal series or upper endoscopy. These programs have been ongoing for several decades and were initiated in 2002 and 2016 in the Republic of Korea and Japan, respectively[51,52]. Currently, GC screening has been included in the China National Cancer Screening Programmes[53]. However, launching endoscopic screening program in a huge population can be cost-prohibitive and requires the capabilities of local physicians and access to available technology. A recent study introduced the GC risk score, an effective GC risk assessment tool designed for widespread public use. This innovative tool can be seamlessly incorporated into existing health management or physical examination frameworks, enabling personalized endoscopic screening based on stratified risk levels[54]. Likewise, Mongolia has recently launched a nationwide screening initiative aimed at identifying early-stage GC cases. The potential for expanding and sustaining these screening efforts is promising, particularly with advancements in diagnostic technologies. Such initiatives are expected to enhance tailored prevention strategies for GC, potentially decreasing the occurrence and related fatalities.

Decreased GC incidence rates have been noted across most countries and age groups, which is consistent with findings from previous studies[55]. Peak GC incidence rates were apparent in New Zealand, South Africa, and Turkey during 2008–2012 period. This observation can be attributed to various factors. The limited coverage of cancer registration data in South Africa, with only one geographic region included in the calculations, may have introduced a potential bias in the ASRs during the early time period. In addition to the scarcity of detailed data records in New Zealand a potential explanation for the peak GC incidence rate during 2008–2012, as suggested by a population-based study conducted from 2009–2013, is the increasing registration rates among the Māori population. Compared to the non-Māori population, who constitute nearly 85% of the New Zealand population, Māori individuals are more likely to be exposed to higher GC risks due to factors, such as elevated smoking rates, increased seroprevalence of *H. pylori* infection, and a greater likelihood of having more than two individuals sharing a bedroom during childhood[56]. With implementation of continuous tobacco control measures and the promotion of fish consumption, New Zealand has shown promising results in significantly reducing the GC ASIR in 2013–2017. Previous analyses utilizing CI5 Plus data indicated an increasing trend in the GC incidence from 1998 to 2012 in Turkey among males and females across age groups (< 50 and ≥ 50 years of age)[55]. Previous analyses utilizing CI5 Plus data in Turkey indicated an increasing trend in GC incidence from 1998 to 2012 among males and females across age groups (< 50 and ≥ 50 years of age)[57].

In contrast to the overall declining GC incidence rates in individuals < 50 years of age, increased GC incidence rates were noted, especially in low-incidence countries in Europe, Oceania, and America, and in females. This phenomenon among young people may be attributed to several factors, including rising obesity rates and modern lifestyles associated with dysbiosis of the gastric microbiome, rather than *H. pylori* infection, which has shown a decline in prevalence among younger individuals. Notably, the incidence rates of obesity are higher among females and in populations residing in countries following a Western diet, indicating a higher risk of cardia GC compared to males[58,59]. Additionally, factors such as immigration from high-risk geographic regions to low-risk areas and a growing willingness among young individuals to undergo invasive diagnostic endoscopy may contribute to the observed increases in GC rates[21].

This study had several limitations. First, the GLOBOCAN estimates of GC in 2022 based on the best available data, which were obtained from selected registries (usually in major cities) and may not accurately reflect the overall burden in some countries. Second, substantial random variation might occur because data analysis in some countries was based on a small number of patients and the analysis may lack sufficient statistical power. Third, we did not apply the annual percent change and average annual percent change to reflect the detailed trend of GC incidence in specific periods owing to the limited availability of data. Data for analyzing ASIR trends can be derived from CI5Plus but were only available up through 2012, which may not accurately represent the trends in recent years. Therefore, to keep the consistency of data versions and utilize the best and most recent available data, only the CI5 X–XII database was applied. The calculated results in the current study show approximated overall changes in the GC incidence. Fourth, analysis of the GC burden for detailed information on the staging and different subtypes was not available.

Conclusions

In summary, GC continues to impose a significant burden, especially among males and in countries with high HDI levels, such as countries in East Asia. There was a decreasing GC incidence in most countries, which may be attributed to the implementation of early prevention measures and advances in effective therapeutic interventions. Despite the relatively lower GC incidence rates among younger individuals compared to elders, there has been an increased GC incidence observed across several countries throughout for 3 sequential 5-year intervals from 2003 to 2017, which presents challenges to national productivity given the longer life expectancy of these individuals. This finding underscores the necessity for comprehensive prevention strategies tailored to address specific patterns of the GC prevalence.

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Conflict of interest statement

No potential conflicts of interest are disclosed.

Author contributions

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Performed the analysis: Nuopei Tan.
Wrote the paper: Nuopei Tan.

Data availability statement

All data used in this study is publicly available from the Global Cancer Observatory (GCO) [https://gco.iarc.fr].

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