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# Gastric cancer incidence, mortality, and burden in adolescents and young adults: A time-trend analysis and comparison among China, South Korea, Japan and the USA

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#### **Original research**

Gastric cancer incidence, mortality, and burden in adolescents and young adults: A time-trend analysis and comparison among China, South Korea, Japan and the USA Silin Wu<sup>1</sup>, Yao Zhang<sup>2</sup>, Yi Fu<sup>2</sup>, Jian Li<sup>2</sup>, Jisheng Wang<sup>3</sup>

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### Abstract

**Objectives** To evaluate and compare the burden of gastric cancer in adolescents and young adults (GCAYA) among China, South Korea, Japan and the USA, four countries with similar or different rates of GC incidence, development levels, and cancer control strategies. **Design** This population-based observational study collected the epidemiologic data of GCAYA from the Global Burden of Diseases Study 2019. The trend magnitude and directions over time for incidence and mortality of GCAYA were analyzed and compared among China, South Korea, Japan and the USA.

**Main outcomes and measures** Outcomes included new cases, deaths, mortality-to-incidence ratios (MIRs), disability-adjusted life-years (DALYs), and their age-standardized rates and estimated annual percentage changes (AAPCs).

**Results** There were 49 008 new cases and 27 895 deaths from GCAYA in 2019, nearly half of which occurred in China. The AAPCs for the age-standardized incidence and mortality rate were 0.3 (-0.1, 0.7), -3.6 (-3.7, -3.4), -3.2 (-3.8, -2.6), -0.1 (-0.6, 0.5) and -2.0 (-2.3, -1.6), -5.6 (-6.2, -5.0), -4.4 (-4.7, -4.1), -0.7 (-1.0, -0.3) in China, South Korea, Japan and the USA, respectively. The incidence rate for females in the USA rose by 0.4% annually. GC ranks fifth, first, fourth and ninth in China, South Korea, Japan and the USA regarding burdens caused by cancer in adolescents and young adults. The MIRs were declining constantly, with the slowest falling in the USA, becoming the highest in the four countries in 2019. **Conclusions** Although not covered by prevention and screening programs, variations in disease burden and time trends may reflect variations in GC control strategies. Given the relatively heavy burden of GCAYA and its huge socioeconomic impact, strategies—including

screening programs specific to this underserved population to further decrease the GC burden—are urgently needed.

Key words gastric cancer; adolescents; young adults; disease burden; time trend

### Strengths and limitations of this study

- We provided a comprehensive description of variations in disease burden and time trends of gastric cancer in adolescents and young adults (GCAYA) among China, South Korea, Japan and the USA.
- To compare the differences in GCAYA burden and time trends among countries with different gastric cancer control strategies may provide information to update prevention and screening programs in this underserved population.
- We were unable to analyze cardia and non-cardia gastric cancer separately, two subtypes that have different risk factors and temporal incidence trends.
- The incidence and mortality were low and volatile, especially in the USA, which means that even the smallest change could lead to a significant analytical outcome.

#### INTRODUCTION

Gastric cancer (GC) has long been a major disease burden caused by neoplasms worldwide.<sup>1</sup> Recent evidence suggests that the incidence and mortality of GC in the general population has fallen substantially,<sup>2</sup> primarily resulting from the prevention and nationwide screening programs.<sup>34</sup> On the contrary, a possible rising incidence of early-onset GC has been reported in the USA.<sup>56</sup> However, the incidence and the disease burden caused by GC in the USA was relatively smaller than that caused by other cancer types. In addition, there are no nationwide screening programs for GC in the USA. In Japan and South Korea, and in recent years in China, population screening has been performed widely, although none of them covered people younger than 40 years old.<sup>78</sup> The trends of GC incidence in youth populations have also been reported in Asian countries. In Japan, no marked changes in the incidence of GC were noted for individuals aged 30-39.9 The results from the South Korean study showed a falling trend in the 20-39 age group.<sup>10</sup> However, the end time of the analysis period in these studies was 10-30 years ago or before the implementation of nationwide screening programs. Hence, trends in recent years, and whether prevention and screening programs also influence the incidence and mortality of GC in adolescents and young adults (GCAYA), are unknown.

In this study, we conducted a comprehensive analysis of the rates and trends of incidence, mortality, and disability-adjusted life years (DALYs) for GCAYA in China, South Korea, Japan, and the USA, four countries with similar or different rates of GC incidence, development levels, and cancer control strategies. We collected all data from the Global Burden of Diseases, Injuries, and Risk Factors Study 2019 (GBD 2019). By investigating the differences in the burden and changing trends of GCAYA among the four countries, we hope

that our findings can serve as a reference for the establishment of GCAYA control measures, and help to reduce the disease burden caused by this neglected cancer type.

# **METHODS**

#### **Study Population and Data Sources**

In this study, the research subjects were adolescents and young adults (AYAs) diagnosed with GC. AYA were defined as individuals aged 15-39. We obtained all data analyzed in this study from GBD 2019, which aims to analyze health trends over time, compare variability among countries, and help establish disease control strategies globally.<sup>11</sup> We collected data from the Global Health Data Exchange (GHDx) (http://ghdx.healthdata.org/) via the freely available GBD Results Tools repository. The search parameters were "stomach cancer" for cause; "incidence, deaths, DALYs" for measurements; "China, Republic of Korea, Japan, United States of America" for location; "1990-2010" for years; "number and rate" for metrics; "male, female and both" for sex; and "15 to 39 years and corresponding 5-year bands" for age. All data in GBD 2019 are presented with a 95% uncertainty interval (UI), which was determined based on the 25th and 975th ranked values across all 1 000 draws of the uncertainty distribution.<sup>11</sup> We followed the Guidelines for Accurate and Transparent Health Estimates Reporting guidelines for cross-sectional studies.<sup>12</sup>

#### Patient and public involvement

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

#### **Statistical Analysis**

Detailed estimation methods for incidence, mortality, and DALYs have been reported in

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previous studies by GBD Collaborators.<sup>11 13</sup> We computed the age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) using the crude rates of 5-year bands from 15-39, and the GBD 2019 standard population via the direct method, expressed as the rate per 100 000 person-years. We analyzed incidence, mortality, and DALYs descriptively by gender, country and year, and we calculated the change rates between 1990 and 2019. We also calculated the mortality-to-incidence ratio (MIR)—which has previously been employed as a proxy for the 5-year survival rate across different neoplasias—as the ratio of death counts to new cases.<sup>14-16</sup> We plotted the temporal trends of these measures from 1990 to 2019. To compare the changing trends of GCAYA among the four countries, we utilized Joinpoint software (Version 4.9.0.0) to determine the average annual percentage change (AAPC) and the annual percentage change (APC) for each period, with a maximum of 2 joinpoints using a generalized linear regression model for the natural logarithm of the ASIR and ASMR. We established the statistical significance of the variation trend by their 95% confidential intervals (CIs). We considered AAPCs or APCs with a 95% CI of > 0 to represent a significant rising trend, while we deemed those with a 95% CI of < 0 to represent a significant falling trend; otherwise, they represented a stable ASIR or ASMR.<sup>17 18</sup>

## RESULTS

#### New Cases of GCAYA and Its Change Rates between 2019 and 1990

As shown in table 1, in 2019, there were an estimated 1 269 806 (1 150 487-1 399 817) new GC cases globally, 49 008 (45 008-53 078) of which were diagnosed between 15 and 39 years old. China accounted for 42.55% (20 855) of GCAYA cases, while there were fewer new GCAYA cases in South Korea, Japan and the USA than in China, with 1 921, 3 258 and 772

cases, respectively. In South Korea and Japan, new cases of GCAYA were common in females, while in China and the USA, GCAYA was much more frequently diagnosed in males. Compared with that in 1990, the new cases of GCAYA for both sexes declined by 58.51% in South Korea and 70.99% in Japan, and the degrees of reduction were similar in males and females. However, new cases in China and the USA have risen by 15.07% and 5.18%, respectively. The increase in China mainly consists of males, who represent an increase of 42.86% compared with a 17.61% decline in females. In contrast, the rise in the USA is mostly made up of females, and the changes were -0.02% in males and 14.91% in females.

# GCAYA-related Deaths and Their Change Rates between 2019 and 1990

In 2019, the number of deaths caused by GC was 957 185 (870 949-1 034 646) worldwide, and GCAYA only accounted for 2.91% (27 895, 95% UI 25 711-30 240). China contributed to 13 929 (49.93%) of the deaths caused by GCAYA, followed by South Korea (1 254, 95% UI 1 154-1 336), Japan (1 239, 95% UI 1 209-1 267), and the USA (400, 95% UI 386-415). The sex distribution was similar to that of new cases; females predominated in China and the USA, while males predominated in South Korea and Japan. In contrast to new cases, the changes in deaths between 2019 and 1990 were declining in all four countries. The most obvious changes took place in South Korea, reaching more than 80% for both sexes. The lowest decline was among females in the USA, which was only 4.52% (table 1).

#### The Age-Standardized Rates and Time Trends of GCAYA Incidence

As shown in table 2 and figure 1, for both sexes, the ASIRs of GCAYA in 2019 in China, South Korea, Japan and the USA were 3.71, 3.99, 2.55 and 0.71 per 100 000 person-years,

respectively. In Japan, the ASIR in GCAYA for females was continuously higher than that for males from 1990 to 2019, while in the USA, the opposite was true. In China, the ASIR in females was higher than that in males, but only between 1995 and 1999, while in South Korea, the ASIR in females was lower than that in males, but only between 1993 and 1998. The variability of ASIR was also found through time trend analysis among the four countries. Only in Japan did the ASIR exhibit a constant declining trend, with AAPC values of -3.6 (-3.7, -3.4), -3.5 (-3.8, -3.2), and -3.5 (-3.8, -3.3) for both sexes combined, males and females, respectively. In South Korea, there is a decreasing trend for both males (AAPC -3.4, 95% CI: -4.5, -2.2) and females (AAPC -2.7, 95% CI: -2.9, -2.5), although the ASIR in males tended to remain stable after 2016. The shifting characteristics of ASIRs in China are much more complex. For both sexes, although the change was not significant from 1990 to 2019, with an AAPC of 0.3 (-0.1, 0.7), there was a considerably falling trend from 2004-2014 (APC -1.6, 95% CI: -2.3, -0.8), but a rising trend from 1990 to 2004 (APC 0.9, 95% CI: 0.5, 1.3) and 2014 to 2019 (APC 2.4, 95% CI: 0.4-4.4). The ASIR of GCAYA in the USA was low and remained relatively stable in males; however, the ASIR in females rose by 0.4% annually from 1990 to 2019.

## The Age-Standardized Rates and Time Trends of GCAYA Mortality

In 2019, the ASMR of GCAYA for males and females combined in China, South Korea, Japan and the USA were 1.50 (1.27-1.75), 1.18 (0.94-1.47), 0.73 (0.68-0.78) and 0.30 (0.27-0.33), respectively. A decreasing trend of ASMR was observed from 1990 to 2019 in all four countries, and the annual declines were 2.0%, 5.6%, 4.4% and 0.7% in China, South Korea, Japan and the USA, respectively. The decrease started at approximately 2000 in China for

females; before that time, it had been rising for ten years (APC 0.8, 95% CI: 0.0-1.6). For males in China, among the total falling trend, there was a stable period (1997-2003). As of the writing of this paper, the downward trend has continued in China and the USA, but stabilized in South Korea and Japan from 2016 (Table 3; Figure 2).

### DALYs Caused by GCAYA and Its Change Rates between 2019 and 1990

The GBD 2019 estimated that GCAYA resulted in 475 977 (408 766-549 798), 13 267 (11 448-15 327), 15 367 (14 438-16 096) and 19 233 (18 018-20 887) DALYs in China, South Korea, Japan and the USA, respectively. The corresponding age-standardized DALY rates (ASDR) were 84.68 (71.97-98.49), 66.67 (53.05-83.09), 41.67 (38.78-44.34), and 16.85 (15.47-18.53) per 100 000 person-years. Similar to incidence and mortality, female predominance was noted in South Korea and Japan, while male predominance was witnessed in China and the USA. Between 1990 and 2019, the ASDR declined in all four countries for males, females and combined. The proportions of reduction were 38.97%, 81.44%, 77.71% and 13.98% in China, South Korea, Japan and the USA, respectively (online supplemental table 1). Compared with other malignancies in AYA, the relative burden of GCAYA in the four countries and their changes are ranked in online supplemental figure 1. In South Korea, both in 1990 and 2019, GC was the leading burden of cancer in AYA. In China, it declined from third in 1990 to fifth in 2019. GC was once the leading cause of cancer-related DALYs in AYA in Japan, and dropped to be fourth in 2019. The burden of GCAYA was relatively small in the USA, ranking tenth in 1990 and then slightly rising to ninth in 2019.

#### The MIR of GCAYA and Its Changes

In 1990, the MIRs for GCAYA in China, South Korea, Japan and the USA were 0.77, 0.65,

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0.38 and 0.52, respectively. From 1990 to 2019, the MIR declined constantly in the four countries, especially in South Korea, which had a higher MIR in 1990 but fell to 0.30, slightly higher than that in Japan (0.29). The MIR in China also exhibited a significant, decreasing trend, reaching 0.41 in 2019. The decline in the USA was the least; the MIR was 0.42 in 2019, becoming the first out of the four countries (online supplemental figure 2).

# DISCUSSION

The majority of GC occurs in the elderly, with its peak incidence and mortality reached among the total population aged 85-89 in China.<sup>19</sup> In the USA, more than 95% of GC cases are diagnosed in individuals older than 40.<sup>20</sup> Only 3.86% of new cases and 2.91% of deaths affected AYA in 2019 worldwide. Therefore, GCAYA has traditionally been ignored by patients, physicians and policy-makers. However, compared with older patients with GC, the burden caused by GCAYA was disproportionate, given their long life expectancy and serving as the main contributors to the economy and family care. Thus, reducing the incidence and mortality in this underserved subpopulation may benefit the development of society and the economy.

The ASIR of GCAYA was much higher in the three East Asian countries, 3-5 times that in the USA. These geographic variations were also reflected in temporal trends. In Asian countries, the incidence of GCAYA showed a markedly downward trend, especially in South Korea and Japan; both had a more than 3% decrease annually. In the USA, stable incidence was observed in males, while the ASIR in females rose steadily, although by only 0.4% per year. This is consistent with the pattern in the general population, indicating that environmental risk factors may also influence AYA, as in the elderly population.<sup>21</sup> In Asian

countries, the high incidence of GC is closely linked to the high prevalence of *H. pylori* infection, which mainly contributes to cancers in the distal stomach.<sup>22</sup> In these countries, GCAYA also showed a distal predominance.<sup>23-25</sup> Hence, with the implementation of screening and eradication programs for this bacterium, the incidence of GC has fallen gradually, which has been called the 'epidemiology of an unplanned triumph'.<sup>26</sup> This 'unplanned triumph' has also been achieved in young adults.<sup>27</sup> In contrast, the risk factors associated with GC in the USA were somewhat different from those in Asian countries. These risk factors include high salt intake and obesity, the rates of which are rising in youth and are mainly associated with proximal GC.<sup>28</sup> Thus, the share of proximal GCAYA was much higher than that in Asian countries.<sup>20</sup>

In addition to the differences in risk factors, different forms of screening and early detection programs among the four countries may explain the variations in incidence and its time trends. As early as the 1960s, Japan began to implement a mass GC screening, which was expanded for all residents older than 40 in 1983.<sup>7</sup> In South Korea, GC screening started in 1999 and expanded to nationwide in 2002.<sup>8</sup> GC screening programs were launched much later in China, and the objects were limited to selected individuals with high risk factors.<sup>8</sup> In contrast, to date, there have no nationwide GC screening programs in the USA. Although these programs did not cover the AYA populations, and the effects of these programs on the incidence of GC are contradictory, the changing trends of ASIR of GCAYA in the four countries may partially reflect the effects of these programs. Because of the early establishment of GC screening and early diagnosis programs, the incidence of GCAYA

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among the entire period was not apparent, which may have resulted from the first increase after the implementation of screening programs, which in turn might detect more new cases. Next, the incidence began to decline due to the effects of these programs. How GC screening programs can decrease the incidence of GC is not clear, especially in AYA, which was not covered by these programs. This could be explained by the fact that the implementation of GC screening programs may increase the awareness of GC in the entire population. This would also encourage young people to undergo GC-specific examinations. *H. pylori* infection can be diagnosed by these examinations, leading to the eradication of this bacterium and a decrease in *H. pylori*-related GCs. Further, electronic endoscopy has been widely accepted as the first method for GC screening, which may detect more precancerous benign lesions or in situ neoplasms. Thus, in the USA without GC screening programs, the incidence of GCAYA showed a stable trend in both sexes combined, and increased steadily in females at 0.4% annually.

With regard to the mortality of GCAYA, regardless of deaths or ASMR, both showed significantly downward trends among the four countries. The changing patterns in mortality reflect shifting patterns not only in terms of incidence but also in case fatalities, which we represented with MIR in this study.<sup>29</sup> Thus, a great decline in mortality was observed in Japan and South Korea, in which there was an impressive decrease in incidence and MIR. Case fatality (MIR) was determined primarily by advancements in therapy and early detection. Under the current concept of multidisciplinary therapy for GC, modern treatment methods have significantly increased the cure rate of localized GC, and prolonged the survival of advanced GC.<sup>30</sup> However, in this study, we found that the MIR in the USA in 1990 was lower

than that of China and South Korea, but it ranked first among the four countries in 2019, despite its highly developed healthcare system. This may have stemmed from the advanced stages of GCAYA diagnosed in the USA, and increasing incidence in females, which balanced the improvement of therapy strategies. In Japan, the MIR of GCAYA was continuously the lowest during the analysis period, while in South Korea, it was gradually close to that of Japan starting in 2008. This phenomenon indicates that the most effective strategy to decrease the mortality of GCAYA is screening and early diagnosis. Therefore, according to recent studies, the prevalence of early GC rose from 28.6% in 1995 to 58.0% in 2007 in South Korea, and a 57% GC mortality rate reduction was attributed to endoscopic screening in Japan.<sup>31 32</sup>

Despite the decline in incidence and mortality of GCAYA in South Korea and Japan throughout the analysis period, the mortality tended to be stable in 2016. This implies that the effects of current prevention and screening programs for GC have reached their limitations in AYA. In addition, distinctive etiological characteristics have been recognized in GCAYA. Approximately 10% of GC cases showed familial clustering, which was more notable in GCAYA.<sup>33 34</sup> Up to 3% of GC cases are related to inherited cancer predisposition syndromes, including hereditary diffuse gastric cancer (HDGC), familial adenomatous polyposis (FAP), and Lynch syndrome, all of which predispose younger populations to GC development.<sup>35 36</sup> These hereditary factors are irreversible with current technological capabilities, and the best way to decrease the deaths caused by GC in these patients is precursor lesion detection by endoscopic surveillance and prophylactic total gastrectomy.<sup>35 37</sup> However, these specific cancer types still account for a minority of the total burdens caused by GCAYA. Other

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relevant opportunities to further improve the outcomes of GCAYA are worthwhile. Because the incidence of GC was low in AYA, endoscopic screening was considered to be associated with a low yield rate and not cost-effective.<sup>38</sup> However, the burdens caused by GC are not small in AYA. Despite the significant decrease, GC still ranked first, fourth and fifth among all cancer types in AYA in South Korea, Japan and China, respectively, with regard to DALYs. Although it was relatively small, the burden caused by GCAYA in the USA increased from the tenth in 1990 to ninth in 2019. In addition, as mentioned above, the AYA population has a long life expectancy and contributes a lot to society and the economy. Hence, prevention and screening among AYA in regions with a higher incidence of GC is worthwhile, and research into screening programs specifically in AYA is needed to determine the benefits and potential risks.

Our findings allow for a comprehensive estimation and comparison of the GCAYA burden among China, South Korea, Japan and the USA; however, several limitations exist, which were also described in studies using data from GBD 2019 and in studies on cancer incidence in AYA.<sup>10 12 13</sup> First, although GBD 2019 used many strategies to improve the data quality and comparability, bias is inevitable, which may affect the integrity and accuracy of the data that we analyzed. Second, we were unable to analyze cardia and non-cardia GC separately, two subtypes that have different risk factors and temporal incidence trends.<sup>39 40</sup> Third, the incidence and mortality were low and volatile, especially in the USA, which means that even the smallest change could lead to a significant analytical outcome, especially when determined with a very short duration. Despite these limitations, our study involved data retrieved from the GBD 2019, the best data currently available for a long time period. Our

findings highlight the health burden of GCAYA and the effects of prevention and screening programs among GCAYA, as well as the need to increase awareness and resources for this neglected subpopulation.

Overall, we have offered a comprehensive analysis and comparison of the burden and temporal trends of GCAYA in China, Korea, South Japan and the USA. In the past three decades, the incidence and mortality of GCAYA have been declining significantly in South Korea and Japan. A falling trend also appeared for females in China in recent years, while a steadily slowly rising trend has been observed for females in the USA. Although not covered by prevention and screening programs, these variations in incidence and the mortality of GCAYA may reflect variations in strategies to control GC burden among four countries. However, the effects of these programs on the GCAYA burden have limitations, and given the relatively heavy burden of this specific disease in AYA and its huge socioeconomic impact, we urgently need strategies, including screening programs or other intervention measures specific to this underserved population to further decrease the GC burden.

Author contributions Conceptualisation: LJ and W-JS. Data curation: W-SL, ZY and LK. Formal analysis: W-SL, ZY and LJ. Methodology: W-SL, W-JS and LJ. Software: LJ. Supervision: W-JS and LJ. Roles/Writing-original draft: All authors. LJ is responsible for the overall content as the guarantor.

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Competing interests None declared.
Patient consent for publication All data in this study was anonymous and retrieved from the GBD 2019 database; therefore, informed consent was waived.
Ethics approval This study was approved by the Academic Committee of the Third Hospital

of Mianyang (20190307).

**Data availability statement** Data are available in a public, open access repository. The data used in our study were available at online Global Health Data Exchange query tool (http://ghdx.healthdata.org/gbd-results-tool)

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# Figure legends

Figure 1. The temporal trends of the age-standardized incidence rate (ASIR) for gastric cancer in adolescents and young adults by sex in China, South Korea, Japan and the USA from 1990 to 2019.

Figure 2. The temporal trends of the age-standardized mortality rate (ASMR) for gastric cancer in adolescents and young adults by sex in China, South Korea, Japan and the USA from 1990 to 2019.

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Table 1. New cases ar	d deaths of gastric cancer in adolescents and young adults, and percentage changes from 1990 to 2019 in China, South Korea, Japan
and the USA.	9 N

		New cases (95% UI)			Deaths (95% UI)	<u>ب</u> ب	
		1990	2019	1990-2019 change (%)	1990	201	1990-2019 change (%)
China	Both	18 123 (15 773-20 658)	20 855 (17 648-24 441)	15.07	13 929 (12 075-15 899)	8 46 <sup>8</sup> (7 244-9 830)	-39.25
	Male	9 803 (8 267-11 346)	14 005 (11 440-16 855)	42.86	7 464 (6 224-7 464)	5 508 (4 507-6 631)	-26.21
	Female	8 320 (6 565-10 269)	6 851 (5 265-8 686)	-17.66	6 465 (5 092-7 911)	2 95 (2 256-3 758)	-54.29
Korea	Both	1 921 (1 756-2 067)	797 (637-1 005)	-58.51	1 254 (1 154-1 336)	237 204-274)	-81.10
	Male	904 (758-1 020)	352 (268-464)	-61.06	571 (477-637)	101 (81-128)	-82.31
	Female	1 017 (930-1 106)	445 (330-579)	-56.24	682 (630-735)	136 4112-165)	-80.06
Japan	Both	3 258 (3 117-3 393)	945 (806-1 108)	-70.99	1 239 (1209-1 267)	273 (256-286)	-77.97
	Male	1 626 (1 521-1 719)	462 (386-553)	-71.59	538 (524-552)	131 (12-138)	-75.65
	Female	1 632 (1 541-1 729)	483 (375-612)	-70.40	700 (682-718)	142 0133-149)	-79.71
USA	Both	772 (744-801)	812 (693-952)	5.18	400 (386-415)	343 (21-371)	-14.25
	Male	450 (430-470)	441 (360-528)	-0.02	223 (214-232)	174 (160-191)	-21.97
	Female	322 (309-336)	370 (287-473)	14.91	177 (170-184)	169 (157-182)	-4.52

Abbreviations: UI, uncertainty interval.

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Table 2. The temporal trend in the incidence rate of gastric cancer in adolescents and young adults from 1990-2019 in China, South Korea, Japan and the	
USA.	

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Country	Sex	Sex ASIR (per 100 000 95%UI)		Trends 1		Trends 2		Trends 3		1990-2019
		1990	2019	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)	AAPC (95% CI)
China	Both	3.62 (3.13-4.18)	3.71 (3.12-4.35)	1990-2004	0.9 (0.5, 1.3)	2004-2014	-1.6 (-2.3, -0.8)	2014-2019	2.4 (0.4-4.4)	0.3 (-0.1, 0.7)
	Male	3.79 (3.12-4.45)	4.88 (3.94-5.90)	1990-1997	-1.9 (-3.6, -0.1)	1997-2003	5.5 (2.3, 8.8)	2003-2019	-0.1 (-0.6, 0.4)	0.6 (-0.2, 1.4)
	Female	3.44 (2.69-4.29)	2.49 (1.89-3.17)	1990-2000	1.8 (0.9, 2.6)	2000-2006	-6.1 (-8.3, -3.9)	2006-2019	-0.7 (-1.2, -0.1)	-1.0 (-1.6, -0.4)
Korea	Both	9.59 (8.39-10.83)	3.99 (2.96-5.30)	1990-1994	0.0 (-4.4, 4.5)	1994-2019	-3.7 (-4.0, -3.4)	5 5 5		-3.2 (-3.8, -2.6)
	Male	8.90 (7.14-10.77)	3.32 (2.27-4.82)	1990-1995	1.8 (-1.6, 5.3)	1995-2017	-5.0 (-5.4, -4.7)	2017-2019	2.5 (-12.0, 19.3)	-3.4 (-4.5, -2.2)
	Female	10.29 (8.76-11.96)	4.74 (3.22-6.70)	1990-2019	-2.7 (-2.9, -2.5)			5 5 5		-2.7 (-2.9, -2.5)
Japan	Both	7.07 (6.61-7.53)	2.55 (2.15-3.02)	1990-2001	-5.3 (-5.7, -4.9)	2001-2019	-2.5 (-2.7, -2.3)	3		-3.6 (-3.7, -3.4)
	Male	6.94 (6.31-7.57)	2.46 (2.03-2.96)	1990-2002	-5.2 (-5.5, -4.9)	2002-2017	-2.6 (-2.8, -2.4)	2017-2019	0.2 (-4.6, 5.2)	-3.5 (-3.8, -3.2)
	Female	7.20 (6.62-7.83)	2.65 (2.02-3.41)	1990-2002	-5.1 (-5.4, -4.9)	2002-2011	-1.8 (-2.3, -1.2)	2011-2019	-3.1 (-3.6, -2.6)	-3.5 (-3.8, -3.3)
USA	Both	0.71 (0.67-0.75)	0.71 (0.60-0.85)	1990-2013	0.1 (-0.1, 0.2)	2013-2016	2.9 (-2.2, 8.2)	2016-2019	-4.0 (-6.4, -3.4)	-0.1 (-0.6, 0.5)
	Male	0.83 (077-0.88)	0.77 (0.63-0.94)	1990-2013	-0.2 (-0.3, -0.1)	2013-2016	3.4 (-1.6, 8.6)	2016-2019	-5.0 (-7.3, -2.7)	-0.4 (-0.9, 0.2)
	Female	0.59 (0.56-0.63)	0.65 (0.50-0.84)	1990-2019	0.4 (0.3-0.5)		ת ט ר ו			0.4 (0.3-0.5)

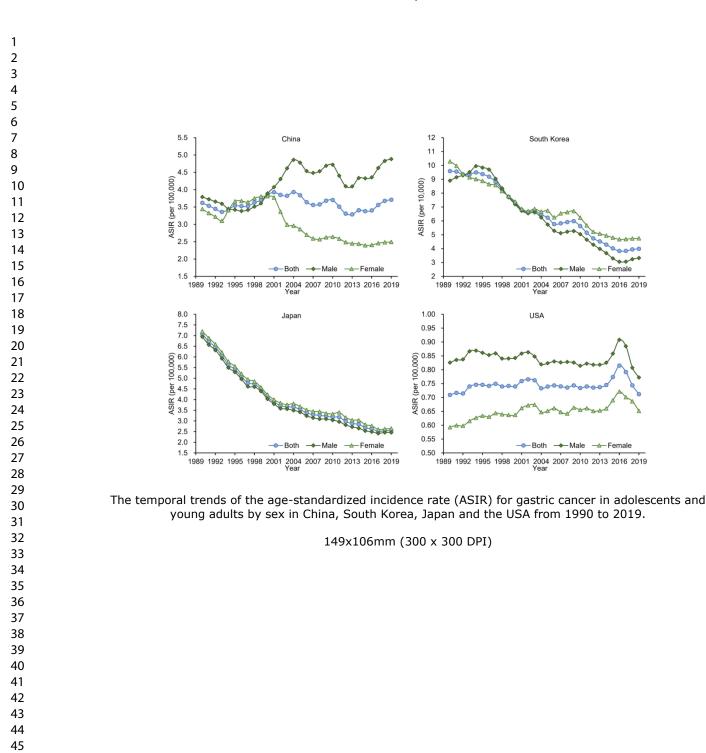
Abbreviations: UI, uncertainty interval; AAPC, average annual percentage change; APC, annual percentage change; ASIR, age-standardized incidence rate.

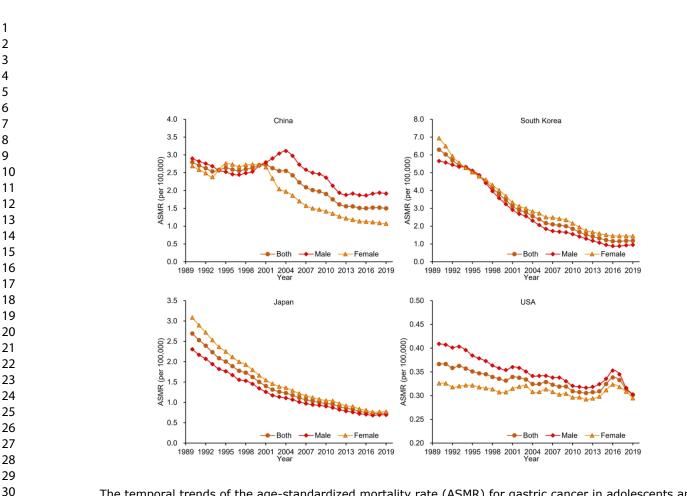
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-	Table 3. The temporal trend in the mortality rate of gastric cancer in adolescents and young adults from 1990-2019 in the Bina, South Korea, Japan and the	
I	USA.	

J <b>S</b> A.								, )		
Country	Sex	ex ASMR (per 100 000 95%UI)		Trends 1		Trends 2		Trends 3		1990-2019
		1990	2019	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)	AAPC (95% CI)
China	Both	2.80 (2.41-3.23)	1.50 (1.27-1.75)	1990-2003	0.0 (-0.4, 0.3)	2003-2013	-5.1 (-5.7, -4.4)	2013-2019	-0.8 (-2.0, 0.5)	-2.0 (-2.3, -1.6)
	Male	2.90 (2.38-3.40)	1.91 (2.31-1.56)	1990-1997	-2.7 (-4.8, -0.5)	1997-2003	3.8 (0.0-7.8)	2003-2019	-3.5 (-4.1, -2.9)	-1.8 (-2.7, -0.9)
	Female	2.69 (2.10-3.35)	1.07 (0.80-1.36)	1990-2000	0.8 (0.0-1.6)	2000-2007	-7.9 (-9.5, -6.3)	2007-2019	-3.3 (-3.9, -2.8)	-3.1 (-3.6, -2.6)
Korea	Both	6.29 (5.58-7.01)	1.18 (0.94-1.47)	1990-1995	-4.6 (-6.7, -2.4)	1995-2016	-6.8 (-7.0, -6.5)	2016-2019	0.9 (-4.0, 6.1)	-5.6 (-6.2, -5.0)
	Male	5.66 (4.58-6.70)	0.95 (0.67-1.33)	1990-1994	-1.1 (-5.1, 3.0)	1994-2016	-7.8 (-8.1, -7.5)	2016-2019	1.9 (-4.5, 8.7)	-6.0 (-6.8, -5.2)
	Female	6.94 (5.99-7.95)	1.44 (1.07-1.90)	1990-2016	-5.8 (-6.0, -5.6)	2016-2019	0.5 (-4.3, 5.5)	5		-5.2 (-5.7, -4.7)
Japan	Both	2.69 (2.60-2.78)	0.73 (0.68-0.78)	1990-2003	-5.6 (-5.8, -5.4)	2003-2017	-3.8 (-4.0, -3.6)	2017-2019	-0.0 (-3.9, 3.9)	-4.4 (-4.7, -4.1)
	Male	2.30 (2.21-2.40)	0.69 (0.64-0.74)	1990-2003	-5.2 (-5.5, -5.0)	2003-2017	-3.6 (-3.8, -3.4)	2017-2019	1.0 (-3.3, 5.5)	-4.0 (-4.3, -3.7)
	Female	3.08 (2.97-3.19)	0.77 (0.72-0.82)	1990-2003	-5.9 (-6.1, -5.7)	2003-2017	-4.1 (-4.3, -3.9)	2017-2019	-0.6 (-4.6, 3.6)	-4.7 (-4.9, -4.4)
USA	Both	0.37 (0.35-0.39)	0.30 (0.27-0.33)	1990-2013	-0.8 (-0.9, -0.7)	2013-2016	3.6 (0.3, 6.9)	2016-2019	-3.6 (-5.2, -2.0)	-0.7 (-1.0, -0.3)
	Male	0.41 (0.39-0.41)	0.30 (0.27-0.34)	1990-2013	-1.2 (-1.2, -1.1)	2013-2016	4.2 (0.0, 8.7)	2016-2019	-5.0 (-7.0, -3.0)	-1.0 (-1.5, -0.6)
	Female	0.33 (0.31-0.35)	0.29 (0.27-0.29)	1990-2013	-0.4 (-0.5, -0.3)	2013-2016	2.9 (-1.6, 7.6)	2016-2019	-2.7 (-4.8, -0.5)	-0.3 (-0.8, 0.2)
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Abbreviations: UI, uncertainty interval; AAPC, average annual percentage change; APC, annual percentage change; ASMR, age-standardized mortality rate.





The temporal trends of the age-standardized mortality rate (ASMR) for gastric cancer in adolescents and young adults by sex in China, South Korea, Japan and the USA from 1990 to 2019.

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# 36/bmjopen-2022-061038 on **Supplementary material** Gastric cancer incidence, mortality, and burden in adolescents and young adults: A time-trend analysis and comparison among China, South Korea, ıly 2022. Japan and the USA Supplementary Table 1. Disability-adjusted life years and its age-standardized rate of gastric cancer in adolescents and young adults, and percentage changes from 1990 to 2019 in China, South Korea, Japan and the USA. Supplementary Figure 1. Rank changes in disability-adjusted life years attributable to cancers in adolescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019. Supplementary Figure 2. The temporal trends of the mortality-to-incidence ratio (MIR) for gastric cancer in addlescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019. This supplementary material has been provided by the authors to give readers additional information about their work. en onl .com/ on July 2, 2024 by guest. Protected by copyright For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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	Supplementary Table 1. Disability-adjusted life years and its age-standardized rate of gastric cancer in adolescents and young adults, and
	percentage changes from 1990 to 2019 in China, South Korea, Japan and the USA.

China Both 7 Male 4 Female 3 Korea Both 7 Male 3 Female 3 Japan Both 6 Male 3	1990 779 909(677 182-888 574) 416 551(347 977-482 273) 363 358(286 546-444 289) 71 475(65 771-76 040) 32 299(26 954-35 969) 39 176(36 174-42 144)	2019 475 977(408 766-549 798) 308 971(253 584-370 090) 167 005(128 595-211 925) 13 267(11 448-15 327) 5 667(4 542-7 129) 7 600(6 275-9 166)	1990-2019 change (%) -38.97 -25.83 -50.04 -81.44 -82.45	155.81(134.03-180.06)	2019 2019 2019 84.68(71.97-98.49) 107.71(87.92-129.65) 60.78(46.34-77.16) 66.67(53.05-83.09) 53.75(37.93-75.89)	1990-2019 change (%) -45.65 -49.77 -59.56 -81.27 -83.08
Male4Female3KoreaBoth7Male3Female3JapanBoth6Male3	416 551(347 977-482 273)         363 358(286 546-444 289)         71 475(65 771-76 040)         32 299(26 954-35 969)         39 176(36 174-42 144)	308 971(253 584-370 090) 167 005(128 595-211 925) 13 267(11 448-15 327) 5 667(4 542-7 129)	-38.97 -25.83 -50.04 -81.44 -82.45	155.81(134.03-180.06)         160.93(132.64-188.95)         150.31(117.82-187.10)         355.99(345.64-397.32)	84.68(71.97-98.49)         107.71(87.92-129.65)         60.78(46.34-77.16)         66.67(53.05-83.09)	-45.65 -49.77 -59.56 -81.27
Male4Female3KoreaBoth7Male3Female3JapanBoth6Male3	416 551(347 977-482 273)         363 358(286 546-444 289)         71 475(65 771-76 040)         32 299(26 954-35 969)         39 176(36 174-42 144)	308 971(253 584-370 090) 167 005(128 595-211 925) 13 267(11 448-15 327) 5 667(4 542-7 129)	-25.83 -50.04 -81.44 -82.45	160.93(132.64-188.95)         150.31(117.82-187.10)         355.99(345.64-397.32)	107.71(87.92-129.65)           60.78(46.34-77.16)           66.67(53.05-83.09)	-49.77 -59.56 -81.27
Female3KoreaBoth7Male3Female3JapanBoth6Male3	363 358(286 546-444 289)         71 475(65 771-76 040)         32 299(26 954-35 969)         39 176(36 174-42 144)	167 005(128 595-211 925)         13 267(11 448-15 327)         5 667(4 542-7 129)	-50.04 -81.44 -82.45	150.31(117.82-187.10) 355.99(345.64-397.32)	66.67(53.05-83.09)	-59.56 -81.27
KoreaBoth7Male3Female3JapanBoth6Male3	71 475(65 771-76 040) 32 299(26 954-35 969) 39 176(36 174-42 144)	13 267(11 448-15 327) 5 667(4 542-7 129)	-81.44 -82.45	355.99(345.64-397.32)	66.67(53.05-83.09)	-81.27
Male3Female3JapanBoth6Male3	32 299(26 954-35 969) 39 176(36 174-42 144)	5 667(4 542-7 129)	-82.45			
Female     3       Japan     Both     6       Male     3	39 176(36 174-42 144)			317.60(256.55-376.87)	53.75(37.93-75.89)	-83.08
Japan Both 6 Male 3	``````````````````````````````````````	7 600(6 275-9 166)			7	
Male 3			-80.60	395.55(340.82-453.79)	81.26(60.40-107.51)	-79.44
	68 962(67 305-70 575)	15 367(14 438-16 096)	-77.71	150.80(145.59-155.88)	9 41.67(38.78-44.34)	-72.37
Female 3	30 060(2 926-30 838)	7 399(6 918-7 778)	-75.39	129.57(124.13-135.22)	39.53(36.57-42.24)	-69.49
i cinare 3	38 903(37 868-39 888)	7 969(7 481-8 388)	-75.92	172.44(166.00-178.83)	43.88(40.67-46.82)	-74.55
USA Both 2	22 359(21 568-23 174)	19 233(18 018-20 887)	-13.98	20.53(19.50-21.61)	ද දි 16.85(15.47-18.53)	-17.92
Male 1	12 413(11 915-12 931)	9 778(8 984-10 690)	-21.23	22.80(21.50-24.17)	פי 17.09(15.33-18.96)	-25.35
Female 9	9 946(9 548-10 360)	9 455(8 787-10 223)	-4.93	18.28(17.23-19.40)	16.62(15.21-18.34)	-9.08

36/bmjopen-2022-06103ge 2019 South & Control &

Change

-81.44%

-19.95%

-14.50%

-35.97%

-44.26%

-56.59% -48.67%

-62.46%

-36.88%

-14.79%

-62.64%

26.23% 93.90%

-12.48%

-7.60%

-47.10%

-27.32%

-76.01%

-76.20%

-22.69%

-40.75%

-2.87%

-69.69%

-18.80% -77.88%

-0.22% -10.94%

Change -37.71%

-32.70% -14.39%

9.37%

-52.12%

-51.25%

-25.18% -32.37%

-13.98%

-25.87%

-57.47%

1.41%

28.11% -24.96%

-8.19%

7.17%

-22.85% 55.50%

12 38% -16 32%

-6 66%

-31 52%

-57.46% -23.37%

-13.38%

-20.80%

-39.13%

-15.91%

-68.11%

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	China 1990		China 2019			South Korea 1990		South	n <b>Ge</b> rea (
Rank	Cancer type		Cancer type	Change	Rank	Cancer type		Cancer type Stomach cancer	• O
1	Liver cancer		Leukemia	-43.35%	1	Stomach cancer		oronneron oenroon	
2	Leukemia		Liver cancer	-58.76%	2	Leukemia		Leukemia	Ņ
3 4	Stomach cancer	200	Tracheal, bronchus, and lung cancer	-11.12%	3	Tracheal, bronchus, and lung cancer	> /	Liver cancer	-
4 5	Tracheal, bronchus, and lung cancer Brain and central nervous system cancer	$\sim$	-Colon and rectum cancer Stomach cancer	21.07%	4	Brain and central nervous system cancer Colon and rectum cancer	>//	Breast cancer Colon and rectum cancer	ر د
6	Colon and rectum cancer	7	-Brain and central nervous system cancer	-38.97%	5	Liver cancer		Brain and central nervous sys	
7	Breast cancer		Breast cancer	0.27%	7	Breast cancer	/ \	Tracheal, bronchus, and lung	
8	Nasopharynx cancer	1	Non-Hodgkin lymphoma	9.66%	8	Non-Hodgkin lymphoma	-	Non-Hodgkin lymphoma	00
9	Non-Hodgkin lymphoma	10	Cervical cancer	-1.61%	9	Cervical cancer		Cervical cancer	N
10	Cervical cancer	-	Pancreatic cancer	59.32%	10	Pancreatic cancer		Pancreatic cancer	Ň
11	Esophageal cancer		Nasopharynx cancer	-48.79%	11	Gallbladder and biliary tract cancer		Ovarian cancer	
12	Pancreatic cancer		Esophageal cancer	-39.08%	12	Ovarian cancer		Gallbladder and biliary tract of	
13	Hodgkin lymphoma	1	Ovarian cancer	1.36%	13	Uterine cancer		Kidney cancer	9
14	Ovarian cancer	+	Kidney cancer	103.02%	14	Esophageal cancer		Thyroid cancer	2
15	Uterine cancer	V	Lip and oral cavity cancer	-8.01%	15	Lip and oral cavity cancer		Lip and oral cavity cancer	2
16	Bladder cancer	X	Gallbladder and biliary tract cancer	-10.20%	16	Nasopharynx cancer		Malignant skin melanoma	<sup>o</sup>
17	Lip and oral cavity cancer	A	-Bladder cancer	-30.63%	17	Kidney cancer		Nasopharynx cancer	a
18	Gallbladder and biliary tract cancer	71	Uterine cancer	-44.69%	18	Larynx cancer		Hodgkin lymphoma	wnloaded
19	Kidney cancer		Multiple myeloma	82.61%	19	Non-melanoma skin cancer		Uterine cancer	ă
20	Malignant skin melanoma	X	Malignant skin melanoma	-12.38%	20	Malignant skin melanoma	X	Esophageal cancer	<b>_</b>
21 22	Larynx cancer Testicular cancer	LAT	Testicular cancer	-2.82%	21	Hodgkin lymphoma		Testicular cancer	2
22	Thyroid cancer	X	Non-melanoma skin cancer	6.00%	22	Bladder cancer		Bladder cancer	from
24	Non-melanoma skin cancer	X	Hodgkin lymphoma	-72.84%	23 24	Thyroid cancer		Multiple myeloma	
25	Multiple myeloma		Thyroid cancer	-19.49% -45.66%	24	Testicular cancer Multiple myeloma		Non-melanoma skin cancer Prostate cancer	http:
	Other pharynx cancer	_							
20					26				0
	Prostate cancer	$\rightarrow$	Mesothelioma	6.49%	26 27	Prostate cancer Mesothelioma		Larynx cancer	~
27		$\geq$	Prostate cancer	6.49% -6.89% -43.39%	26 27 28	Prostate cancer Mesothelioma Other pharynx cancer		Conter pharynx cancer Mesothelioma	o://b
27	Prostate cancer	$\times$	Prostate cancer Other pharynx cancer	-6.89%	27	Mesothelioma		Other pharynx cancer	//br
27	Prostate cancer Mesothelioma Japan 1990	$\times$	Prostate cancer Other pharynx cancer Japan 2019	-6.89% -43.39%	27	Mesothelioma Other pharynx cancer USA 1990		Other pharynx cancer Mesothelioma USA 2	2009
27 28 Rank	Prostate cancer Mesothelioma Japan 1990	$\times$	Prostate cancer Other pharynx cancer	-6.89%	27 28	Mesothelioma Other pharynx cancer USA 1990	~~	Other pharynx cancer Mesothelioma	2009
27 28 Rank 1	Prostate cancer Mesothetioma Japan 1990 Cancer type Stomach cancer Leukemia	$\times$	Prostate cancer Other pharynx cancer Japan 2019 Cancer type	-6.89% -43.39% Change -66.32% -39.26%	27 28	Mesothelioma Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia	<u> </u>	Other pharynx cancer Mesothelioma USA 2 Cancer type	2009
27 28 Rank 1 2 3	Prostate cancer Mesothelioma Japan 1990 c Cancer type Stomach cancer Leukemia Colon and rectum cancer	$\times$	Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer	-6.89% -43.39% Change -66.32% -39.26% -42.71%	27 28 Rank 1 2 3	Nesothelioma Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia Brain and central nervous system cancer		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys	//bngopen.
27 28 Rank 1 2 3 4	Prostate cancer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Colon and rectum cancer Breast cancer	X	Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer	-6.89% -43.39% Change -66.32% -39.26% -42.71% -77.72%	27 28 Rank 1 2 3 4	Mesothelioma Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia Brain and central nervous system cancer Non-Hodgkin lymphoma		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys Colon and rectum cancer	2000 en.
27 28 1 2 3 4 5	Prostate cancer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Colon and rectum cancer Breast cancer Tracheal, bronchus, and lung cancer	X	Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stormach cancer Brain and central nervous system cancer	-6.89% -43.39% Change -66.32% -39.26% -42.71% -77.72% -11.78%	27 28 Rank 1 2 3	Nesothelioma Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia Brain and central nervous system cancer Non-Hodyšin lymphoma Tracheal, bronchus, and lung cancer		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys Colon and rectum cancer Non-Hodgkin lwrphoma	//bngopen.emj.
27 28 1 2 3 4 5 6	Prostate cancer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Coton and rectum cancer Breast cancer Tracheal, bronchus, and lung cancer Non-Hodgkin lymphoma	XXX	Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system cancer Tracheal, bronchus, and lung cancer	-6.89% -43.39% Change -66.32% -39.26% -42.71% -77.72% -111.78% -56.37%	27 28 Rank 1 2 3 4	Mesothelioma Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia Brain and central nervous system cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung cancer Colon and rectum cancer		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys Colon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung	//bngopen.emj.
27 28 1 2 3 4 5 6 7	Prostate cancer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Colon and rectum cancer Breast cancer Tracheal, bronchus, and lung cancer Non-Hodgkin lymphoma Brein and central nervous system cancer	XXX	Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system cancer Tracheal, bronchus, and lung cancer Orevical cancer	-6.89% -43.39% Change -66.32% -39.26% -42.71% -77.72% -11.78% -56.37% -56.37% -56.93%	27 28 Rank 1 2 3 4	Nesotheliama Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia Brain and central nervous system cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung cancer Colon and rectum cancer Malignant skin melanoma		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys Colon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung Cervical cancer	//bngopen.emj.eer
27 28 1 2 3 4 5 6 7 8	Prostate cancer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Colon and rectum cancer Breast cancer Breast cancer Tracheal, bronchus, and lung cancer Non-Hodgkin lymphoma Brain and central nervous system cancer Liver cancer		Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system cancer Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin (ymphoma	-6.89% -43.39% -66.32% -39.26% -42.71% -77.72% -11.78% -56.37% -5.93% -59.14%	27 28 1 2 3 4 5 6 6 7 8	Nesothelioma Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia Brain and central nervous system cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung cancer Colon and rectum cancer Colon and rectum cancer Cervical cancer		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys Colon and rectum cancer Non-Hodgkin lwmphoma Tracheal, bronchus, and lung Cervical cancer Malignant skin melanoma	//bngopen.emj.
27 28 1 2 3 4 5 6 7 8 9	Prostate cancer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Colon and rectum cancer Breast cancer Tracheal, bronchus, and lung cancer Non-Hodgkin lymphoma Brein and central nervous system cancer Liver cancer Ovarian cancer		Prostate cancer Other pharynx cancer Japan 2019 Cancer type -Leukemia Breast cancer Colon and reotum cancer Stomach cancer Brain and central nervous system cancer Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma Ovarian cancer	-6.89% -43.39% -66.32% -39.26% -42.71% -77.72% -11.78% -56.37% -59.14% -42.03%	27 28 1 2 3 4 5 6 7 8 9	Nesotheliama Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia Brain and central nervous system cancer Non-Hodgikn lymphoma Tracheal, bronchus, and lung cancer Colon and rectum cancer Malignant skin melanoma Cervical cancer Hodgikn iymphoma		Other phaynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys Colon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung Cervical cancer Malignant skin melanoma Stomach cancer	1/bngopen.stemj.cer
27 28 1 2 3 4 5 6 7 8 9 10	Prostate cancer Mesothetioma Japan 1990 Cancer type Stomach cancer Leukemia Colon and rectum cancer Breast cancer Non-Hodgkin lymphoma Brein and central nervous system cancer Liver cancer Dvarian cancer Cervical cancer		Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stormach cancer Brain and central nervous system cancer Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Uver cancer	-6.89% -43.39% -66.32% -39.26% -42.71% -77.72% -11.78% -56.37% -59.14% -42.03% -59.8%	27 28 1 2 3 4 5 5 6 7 8 9 10	Nesothelioma Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia Brain and central nervous system cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung cancer Colon and rectum cancer Malignant skin melanoma Cervical cancer Hodgkin lymphoma Stomach cancer		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys Colon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung Carvical cancer Malignant skin melanoma Stomach cancer Ovarian cancer	1/bngopen.stemj.cer
27 28 1 2 3 4 5 6 7 8 9 10 11	Prostate cencer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Coton and rectum cancer Breast cancer Tracheal, bronchus, and lung cancer Non-Hodgkin lymphoma Brain and central nervous system cancer Liver cancer Ovarian cancer Ovarian cancer Panoreatic cancer		Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stormach cancer Brain and central nervous system cancer Tracheel, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Pancreatic cancer	-6.89% -43.39% -66.32% -39.26% -42.71% -77.72% -11.78% -56.37% -59.14% -42.03% -59.14% -42.03%	27 28 1 2 3 4 4 5 6 7 8 9 9 10 11	Nesothelioma Other pharynx cancer USA 1990 Cancer type Breast.cancer Leukemia Brain and central nervous system cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung cancer Colon and rectum cancer Colon and rectum cancer Malignant skin melanoma Cervical cancer Hodgkin lymphoma Stomach cancer	XXX	Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys Colon and rectum cancer Non-Hodgkin lymphoma Cervical cancer Malignant skin melanoma Stomach cancer Ovarian cancer Hodgkin hymphoma	://bngopen.etemj.etem/ on
27 28 1 2 3 4 5 6 7 8 9 10 11 12	Prostate cancer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Cofon and rectum cancer Breast cancer Tracheal, bronchus, and lung cancer Non-Hodgkin lymphoma Brein and contral nervous system cancer Liver cancer Ovarian cancer Cervical cancer Pancreatic cancer Pancreatic cancer		Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stormach cancer Brain and central nervous system cancer Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Uver cancer Pancreatic cancer Luer cancer	-6.89% -43.39% -66.32% -39.26% -42.71% -77.72% -11.78% -56.37% -59.14% -42.03% -59.89% -39.78% -39.78%	27 28 1 2 3 4 5 5 6 7 8 9 10 11 12	Nesotheliama Other pharynx cancer USA 1990 Cancer type Breast cancer Leakemia Brain and central nervous system cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung cancer Colon and rectum cancer Malignant skin melanoma Cervical cancer Hodgkin lymphoma Stomach cancer Ovarian cancer Testicular cancer		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemiä Brain and central nervous sys Golon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung Cervical cancer Malignant skin melanoma Stomach cancer Ovarian cancer Nodgkin lymphoma Pancreatic cancer	://bngopen.etemj.etem/ on
27 28 1 2 3 4 5 6 7 8 9 10 11 12 13	Protatie cancer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Colon and rectum cancer Breast cancer Tracheal, bronchus, and lung cancer Non-Hodgkin lymphoma Brain and certiral nervous system cancer Ovarian cancer Cervical cancer Pancreatic cancer Pancreatic cancer Testicular cancer Galibtadder and bilary tract cancer		Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system cancer Tracheal, bronchus, and lung cancer Carvical cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Liver cancer Liver cancer Lip and oral cavity cancer Testicular cancer	-6.89% -43.39% -66.32% -99.26% -42.71% -77.72% -56.37% -59.14% -59.14% -59.89% -59.14% -59.89% -59.26% -11.60%	27 28 1 2 3 4 4 5 6 7 8 9 9 10 11	Nesothelioma Other pharynx cancer USA 1990 Cancer type Breast.cancer Leukemia Brain and central nervous system cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung cancer Colon and rectum cancer Colon and rectum cancer Malignant skin melanoma Cervical cancer Hodgkin lymphoma Stomach cancer		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemia Brain and central nervous sys Colon and rectum cancer Non-Hodgkin lwmphoma Tracheal, bronchus, and lung Cervical cancer Malignant skin melanoma Stomach cancer Ovarian cancer Hodgkin lymphoma Pancreatic cancer Liver cancer	1/bngopen.stemj.cer
27 28 <b>Rank</b> 1 2 3 4 5 6 7 8 9 10 11 12 13 14	Prostate cancer Mesothelioma Japan 1990 Cancer type Stomach cancer Leukemia Cofon and rectum cancer Breast cancer Tracheal, bronchus, and lung cancer Non-Hodgkin lymphoma Brein and contral nervous system cancer Liver cancer Ovarian cancer Cervical cancer Pancreatic cancer Pancreatic cancer		Prostate cancer Other pharynx cancer Japan 2019 Cancer type Leukemia Breast cancer Colon and rectum cancer Stormach cancer Brain and central nervous system cancer Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Uver cancer Pancreatic cancer Luer cancer	-6.89% -43.39% -66.32% -39.26% -42.71% -77.72% -11.78% -56.37% -59.14% -42.03% -59.89% -39.78% -39.78%	27 28 <b>Rank</b> 1 2 3 4 5 6 7 8 9 10 11 12 13	Nesothelioma Other pharynx cancer USA 1990 Cancer type Breast cancer Leukemia Brain and central nervous system cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung cancer Colon and rectum cancer Colon and rectum cancer Cervical cancer Hodgkin lymphoma Stomach cancer Ovarian cancer Dati cancer Pancreatic cancer		Other pharynx cancer Mesothelioma USA 2 Cancer type Breast cancer Leukemiä Brain and central nervous sys Golon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lung Cervical cancer Malignant skin melanoma Stomach cancer Ovarian cancer Nodgkin lymphoma Pancreatic cancer	://bngopen.temj.tem/ on July
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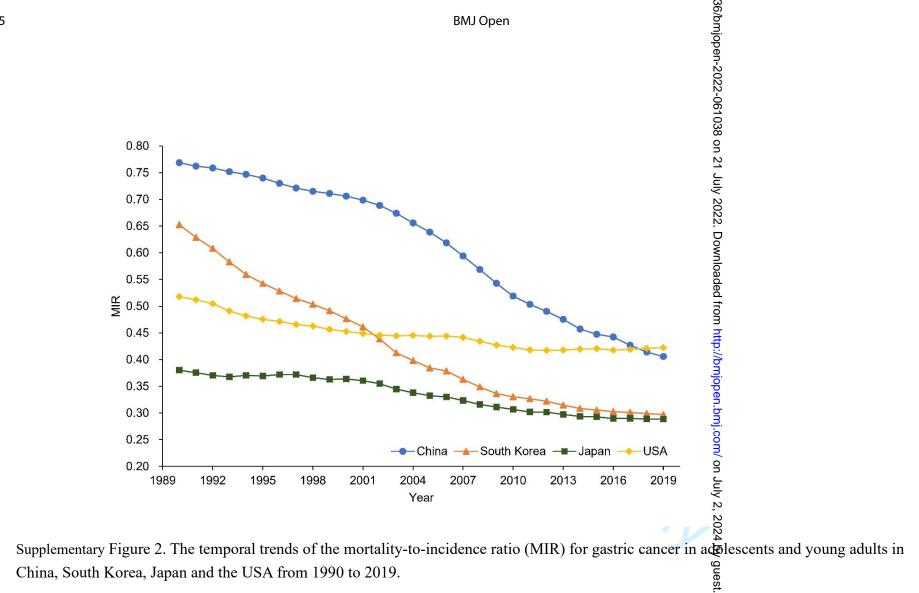
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44 45 46 Supplementary Figure 1. Rank changes in disability-adjusted life years attributable to cancers in adolescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019.

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Supplementary Figure 2. The temporal trends of the mortality-to-incidence ratio (MIR) for gastric cancer in adolescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019.

# Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

# Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below. Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation. Upload your completed checklist as an extra file when you submit to a journal. In your methods section, say that you used the STROBE cross sectional reporting guidelines, and cite them as: von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Page Reporting Item Number Title and abstract Title #1a Indicate the study's design with a commonly used term in the title or the abstract Abstract #1b Provide in the abstract an informative and balanced summary 2.3

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1 2			of what was done and what was found			
3 4 5	Introduction					
6 7 9 10 11 12 13	Background /	<u>#2</u>	Explain the scientific background and rationale for the	4		
	rationale		investigation being reported			
	Objectives	<u>#3</u>	State specific objectives, including any prespecified	4,5		
14 15			hypotheses			
16 17 18 19	Methods					
20 21 22	Study design	<u>#4</u>	Present key elements of study design early in the paper	5		
23 24 25	Setting	<u>#5</u>	Describe the setting, locations, and relevant dates, including	5		
26 27 28			periods of recruitment, exposure, follow-up, and data collection			
29 30	Eligibility criteria	<u>#6a</u>	Give the eligibility criteria, and the sources and methods of	5		
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33 34 35		<u>#7</u>	Clearly define all outcomes, exposures, predictors, potential	5		
36 37			confounders, and effect modifiers. Give diagnostic criteria, if			
38 39 40			applicable			
40 41 42 43	Data sources /	<u>#8</u>	For each variable of interest give sources of data and details of	5		
44 45	measurement		methods of assessment (measurement). Describe			
46 47			comparability of assessment methods if there is more than one			
48 49 50			group. Give information separately for for exposed and			
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3 4	variables		analyses. If applicable, describe which groupings were chosen,	
5 6 7			and why	
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16 17 18	methods		interactions	
19 20 21	Statistical	<u>#12c</u>	Explain how missing data were addressed	n/a
22 23 24	methods			
25 26	Statistical	<u>#12d</u>	If applicable, describe analytical methods taking account of	6
27 28 29	methods		sampling strategy	
30 31	Statistical	<u>#12e</u>	Describe any sensitivity analyses	n/a
32 33	methods			
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49 50 51 52	Participants	<u>#13b</u>	Give reasons for non-participation at each stage	n/a
53 54 55	Participants	<u>#13c</u>	Consider use of a flow diagram	n/a
56 57 58	Descriptive data	<u>#14a</u>	Give characteristics of study participants (eg demographic,	6,7
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Page	35	of	35
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1 2			clinical, social) and information on exposures and potential	
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8 9	Descriptive data	<u>#14b</u>	Indicate number of participants with missing data for each	n/a
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16			Give information separately for exposed and unexposed	
17 18 19			groups if applicable.	
20 21 22	Main results	<u>#16a</u>	Give unadjusted estimates and, if applicable, confounder-	n/a
23 24			adjusted estimates and their precision (eg, 95% confidence	
25 26 27			interval). Make clear which confounders were adjusted for and	
28 29			why they were included	
30 31 32	Main results	<u>#16b</u>	Report category boundaries when continuous variables were	6-10
33 34 35			categorized	
36 37	Main results	<u>#16c</u>	If relevant, consider translating estimates of relative risk into	n/a
38 39 40			absolute risk for a meaningful time period	
41 42 43	Other analyses	<u>#17</u>	Report other analyses done—e.g., analyses of subgroups and	6-10
44 45			interactions, and sensitivity analyses	
46 47 48	Discussion			
49 50	Key results	<u>#18</u>	Summarise key results with reference to study objectives	10
51 52	- ,			-
53 54 55	Limitations	<u>#19</u>	Discuss limitations of the study, taking into account sources of	14,15
56 57			potential bias or imprecision. Discuss both direction and	
57 58 59			magnitude of any potential bias.	
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1 2	Interpretation	<u>#20</u>	Give a cautious overall interpretation considering objectives,	10-15
3 4			limitations, multiplicity of analyses, results from similar studies,	
5 6 7			and other relevant evidence.	
8 9 10	Generalisability	<u>#21</u>	Discuss the generalisability (external validity) of the study	15
11 12 13			results	
14 15	Other Information			
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18	Funding	<u>#22</u>	Give the source of funding and the role of the funders for the	15,16
19 20 21			present study and, if applicable, for the original study on which	
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# Gastric cancer incidence, mortality, and burden in adolescents and young adults: A time-trend analysis and comparison among China, South Korea, Japan and the USA

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## **Original research**

Gastric cancer incidence, mortality, and burden in adolescents and young adults: A time-trend analysis and comparison among China, South Korea, Japan and the USA Silin Wu<sup>1</sup>, Yao Zhang<sup>2</sup>, Yi Fu<sup>2</sup>, Jian Li<sup>2</sup>, Jisheng Wang<sup>3</sup>

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# Abstract

**Objectives** To evaluate and compare the burden of gastric cancer in adolescents and young adults (GCAYA) among China, South Korea, Japan and the USA, four countries with similar or different rates of GC incidence, development levels, and cancer control strategies. **Design** This population-based observational study collected the epidemiologic data of GCAYA from the Global Burden of Diseases Study 2019. The trend magnitude and directions over time for incidence and mortality of GCAYA were analyzed and compared among four countries.

Main outcomes and measures Outcomes included new cases, deaths, mortality-to-incidence ratios (MIRs), disability-adjusted life-years (DALYs), and their age-standardized rates and estimated annual percentage changes (AAPCs).

**Results** There were 49 008 new cases and 27 895 deaths from GCAYA in 2019, nearly half of which occurred in China. The AAPCs for the age-standardized incidence and mortality rate were 0.3 (-0.1, 0.7), -3.6 (-3.7, -3.4), -3.2 (-3.8, -2.6), -0.1 (-0.6, 0.5) and -2.0 (-2.3, -1.6), -5.6 (-6.2, -5.0), -4.4 (-4.7, -4.1), -0.7 (-1.0, -0.3) in China, South Korea, Japan and the USA, respectively. The incidence rate for females in the USA rose by 0.4% annually. GC ranks fifth, first, fourth and ninth in China, South Korea, Japan and the USA regarding burdens caused by cancer in adolescents and young adults. The MIRs declined constantly in South Korea and China, and the MIR in the USA became the highest in 2019.

**Conclusions** Although not covered by prevention and screening programs, variations in disease burden and time trends may reflect variations in risk factors, cancer control strategies and treatment accessibility of GC among the four countries. Investigating the reasons behind

the varying disease burden and changing trends of GCAYA across countries will inform recommendations for prevention measures and timely diagnosis specific to this underserved population to further decrease the GC burden.

Key words gastric cancer; adolescents; young adults; disease burden; time trend

# Strengths and limitations of this study

- We provided a comprehensive description of variations in the incidence and mortality of gastric cancer in adolescents and young adults (GCAYA) among China, South Korea, Japan and the USA.
- Our study uses the average annual percentage change (AAPC) and the annual percentage change (APC) to quantify and compare secular trends in the incidence and mortality of GCAYA.
- This study analyses the mortality-to-incidence ratios (MIRs) of GCAYA and their changing trends among China, South Korea, Japan and the USA.
- We were unable to analyze cardia and noncardia gastric cancer separately, two subtypes that have different risk factors and temporal incidence trends.
- The incidence and mortality were low and volatile, especially in the USA, which means that even the smallest change could lead to a significant analytical outcome.

## INTRODUCTION

Gastric cancer (GC) has long been a major disease burden caused by neoplasms worldwide.<sup>1</sup> Recent evidence suggests that the incidence and mortality of GC in the general population has fallen substantially,<sup>2</sup> primarily resulting from the prevention and nationwide screening programs.<sup>34</sup> On the contrary, a possible rising incidence of early-onset GC has been reported in the USA.<sup>56</sup> However, the incidence and disease burden caused by GC in the USA were relatively smaller than those caused by other cancer types. In addition, there are no nationwide screening programs for GC in the USA. In Japan and South Korea, and in recent years in China, population screening has been performed widely, although none of them covered people younger than 40 years old.<sup>78</sup> The trends of GC incidence in youth populations have also been reported in Asian countries. In Japan, no marked changes in the incidence of GC were noted for individuals aged 30-39.9 The results from the South Korean study showed a falling trend in the 20-39 age group.<sup>10</sup> However, the end time of the analysis period in these studies was 10-30 years ago or before the implementation of nationwide screening programs. Hence, trends in recent years and whether prevention and screening programs also influence the incidence and mortality of GC in adolescents and young adults (GCAYA), are unknown.

Given that adolescents and young adults represent the main proportion of people who contribute substantially to the economy and have an important role in caring for their families, GCAYA carries a disproportionate burden than GC among older patients due to its greater impact on life expectancy.<sup>11 12</sup> Variations in cancer incidence among different populations may reflect differences in the prevalence of risk factors and screening strategies. Variations in mortality reflect variations not only in incidence but also in case fatality, which can be

affected by differences in early diagnosis and accessibility to treatment.<sup>13</sup> Therefore, we conducted a comprehensive analysis of the rates and trends of incidence, mortality, and disability-adjusted life years (DALYs) for GCAYA in China, South Korea, Japan, and the USA, four countries with similar or different rates of GC incidence, development levels, and cancer control strategies. We collected all data from the Global Burden of Diseases, Injuries, and Risk Factors Study 2019 (GBD 2019). By investigating the differences in the burden and changing trends of GCAYA among the four countries, we hope that our findings can serve as a reference for the establishment of GCAYA control measures and help to reduce the disease burden caused by this neglected cancer type.

### **METHODS**

## **Study Population and Data Sources**

In this study, the research subjects were adolescents and young adults (AYAs) diagnosed with GC. AYA were defined as individuals aged 15-39. We obtained all data analyzed in this study from GBD 2019, which aims to analyze health trends over time, compare variability among countries, and help establish disease control strategies globally.<sup>14</sup> We collected data from the Global Health Data Exchange (GHDx) (<u>http://ghdx.healthdata.org/</u>) via the freely available GBD Results Tools repository. The search parameters were "stomach cancer" for cause; "incidence, deaths, DALYs" for measurements; "China, Republic of Korea, Japan, United States of America" for location; "1990-2019" for years; "number and rate" for metrics; "male, female and both" for sex; and "15 to 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.<sup>15</sup>

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# Definitions

The definition of GCAYA is not always consistent across studies, yet most authors adopted 40 years as the upper limit to categorize patients as having early-onset GC.<sup>12</sup> Therefore, in this study, we defined GCAYA as patients diagnosed between the ages of 15 and 39 years. The rationale for using this age range relates to biological and physiological maturity and relative stability; these individuals have not yet experienced the effects of hormonal and immune response decline or chronic medical conditions that can influence oncologic decision-making as it would in the care of older patients.<sup>16</sup> The DALY is a summary measure that quantifies the overall burden of disease, which represents the sum of years of life lost due to premature death and years lived with disability. One DALY can be regarded as the loss of 1 year in full health.

# Patient and public involvement

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

## **Statistical Analysis**

Detailed estimation methods for incidence, mortality, and DALYs have been reported in previous studies by GBD Collaborators.<sup>14 17</sup> We computed the age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) using the crude rates of 5-year bands from 15-39, and the GBD 2019 standard population via the direct method, expressed as the rate per 100 000 person-years. We analyzed incidence, mortality, and DALYs descriptively by gender, country and year, and we calculated the change rates between 1990 and 2019. We also calculated the mortality-to-incidence ratio (MIR)—which has previously been employed

as a proxy for the 5-year survival rate across different neoplasias—as the ratio of death counts to new cases.<sup>18-20</sup> We plotted the temporal trends of these measures from 1990 to 2019. To compare the changing trends of GCAYA among the four countries, we utilized Joinpoint software (Version 4.9.0.0) to determine the average annual percentage change (AAPC) and the annual percentage change (APC) for each period, with a maximum of 2 joinpoints using a generalized linear regression model for the natural logarithm of the ASIR and ASMR. We established the statistical significance of the variation trend by their 95% confidential intervals (CIs). We considered AAPCs or APCs with a 95% CI of > 0 to represent a significant rising trend, while we deemed those with a 95% CI of < 0 to represent a significant falling trend; otherwise, they represented a stable ASIR or ASMR.<sup>21 22</sup>

# RESULTS

## New Cases of GCAYA and Its Change Rates between 2019 and 1990

In 2019, there were an estimated 1 269 806 new GC cases globally, 49 008 (3.86%) of which were diagnosed between 15 and 39 years old. China accounted for 42.55% (20 855) of GCAYA cases. As shown in table 1, in South Korea and Japan, new cases of GCAYA were common in females, while in China and the USA, GCAYA was much more frequently diagnosed in males. Compared with that in 1990, the new cases of GCAYA declined by 58.51% in South Korea and 70.99% in Japan, and the degrees of reduction were similar in males and females. However, new cases in China and the USA have risen by 15.07% and 5.18%, respectively. The increased number of new cases in China contributed to male cases, while in the USA it contributed to female cases.

## GCAYA-related Deaths and Their Change Rates between 2019 and 1990

In 2019, the number of deaths caused by GC was 957 185 worldwide, and GCAYA accounted for only 2.91% (27 895). China contributed to 13 929 (49.93%) of the deaths caused by GCAYA. The sex distribution was similar to that of new cases; females predominated in China and the USA, while males predominated in South Korea and Japan. In contrast to new cases, the number of deaths between 2019 and 1990 declined in all four countries. The most obvious changes occurred in South Korea, reaching more than 80% for both sexes. The lowest decline was among females in the USA, which was only 4.52% (table 1).

# The Age-Standardized Rates and Time Trends of GCAYA Incidence

As shown in table 2 and figure 1, for both sexes, the ASIRs of GCAYA in 2019 in China, South Korea, Japan and the USA were 3.71, 3.99, 2.55 and 0.71 per 100 000 person-years, respectively. Consistent with the sex variations in new cases, the ASIRs were higher for females than for males in Japan and South Korea, while the opposite was true in the USA and China. The variability of ASIR was also found through time trend analysis among the four countries. Only in Japan did the ASIR exhibit a constant declining trend, with AAPC values of -3.6 (-3.7, -3.4) for both sexes. In South Korea, there was a decreasing trend for both males (AAPC -3.4, 95% CI: -4.5, -2.2) and females (AAPC -2.7, 95% CI: -2.9, -2.5), although the ASIR in males tended to remain stable after 2016. The shifting characteristics of ASIRs in China are much more complex. The changing trends were not significant from 1990 to 2019, with an AAPC of 0.3 (-0.1, 0.7), resulting from a considerably falling trend from 2004-2014 (APC -1.6, 95% CI: -2.3, -0.8) but a significantly rising trend from 2014 to 2019 (APC 2.4, 95% CI: 0.4-4.4). The ASIR of GCAYA in the USA was low and remained relatively stable in males; however, the ASIR in females rose by 0.4% annually from 1990 to 2019.

The Age-Standardized Rates and Time Trends of GCAYA Mortality In 2019, the ASMRs of GCAYA in China, South Korea, Japan and the USA were 1.50 (1.27-1.75), 1.18 (0.94-1.47), 0.73 (0.68-0.78) and 0.30 (0.27-0.33), respectively. A decreasing

trend of ASMR was observed from 1990 to 2019 in all four countries, and the annual decline rates were 2.0%, 5.6%, 4.4% and 0.7% in China, South Korea, Japan and the USA, respectively. The decrease started at approximately 2000 in China for females; before that time, it had been rising for ten years (APC 0.8, 95% CI: 0.0-1.6). For males in China, among the total falling trend, there was a stable period (1997-2003). The downward trend continued in China and the USA untill 2019, but stabilized in South Korea and Japan from 2016 (Table

3; Figure 2).

# DALYs Caused by GCAYA and Its Change Rates between 2019 and 1990

The GBD 2019 estimated that GCAYA resulted in 475 977, 13 267, 15 367 and 19 233 DALYs in China, South Korea, Japan and the USA, respectively. The corresponding agestandardized DALY rates (ASDR) were 84.68, 66.67, 41.67, and 16.85 per 100 000 personyears. Similar to incidence and mortality, female predominance was noted in South Korea and Japan, while male predominance was witnessed in China and the USA. Between 1990 and 2019, the ASDR declined in all four countries. The proportions of reduction were 38.97%, 81.44%, 77.71% and 13.98% in China, South Korea, Japan and the USA, respectively (online supplemental table 1). Compared with other malignancies in AYA, the relative burden of GCAYA in the four countries and their changes are ranked in online supplemental figure 1. In South Korea, both in 1990 and 2019, GC was the leading burden of cancer in AYA. In China, it declined from third in 1990 to fifth in 2019. GC was once the leading cause of cancer-

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related DALYs in AYA in Japan and dropped to fourth in 2019. The burden of GCAYA was relatively small in the USA, ranking tenth in 1990 and then slightly rising to ninth in 2019.

# The MIR of GCAYA and Its Changes

In 1990, the MIRs for GCAYA in China, South Korea, Japan and the USA were 0.77, 0.65, 0.38 and 0.52, respectively. From 1990 to 2019, the MIR declined constantly in South Korea, which had a higher MIR in 1990 but fell to 0.30, slightly higher than that in Japan (0.29). The MIR in China also exhibited a significant, decreasing trend, reaching 0.41 in 2019. The changing trend of MIR in the USA was not obvious; however, the MIR was 0.42 in 2019, becoming the first out of the four countries. Japan had the lowest MIR throughout the analyzed period, although the decreasing trend was slight (online supplemental figure 2).

# DISCUSSION

The majority of GC occurs in elderly individuals, with its peak incidence and mortality reached among the total population aged 85-89 in China.<sup>23</sup> In the USA, more than 95% of GC cases are diagnosed in individuals older than 40.<sup>24</sup> Only 3.86% of new cases and 2.91% of deaths affected AYA in 2019 worldwide. GCAYA has traditionally been ignored by patients, physicians and policy-makers. However, compared with older patients with GC, the burden caused by GCAYA was disproportionate, given their long life expectancy and serving as the main contributors to the economy and family care. Thus, reducing the incidence and mortality in this underserved subpopulation may benefit the development of society and the economy.

We found that nearly half of new cases and deaths of GCAYA occurred in China, which was attributed to it having the world's largest population and a higher incidence rate. The ASIR of GCAYA was much higher in the three East Asian countries, 3-5 times that in the

USA. These geographic variations were also reflected in temporal trends. In Asian countries, the incidence of GCAYA showed a markedly downward trend, especially in South Korea and Japan; both had a more than 3% decrease annually. In the USA, a stable incidence was observed in males, while the ASIR in females rose steadily, although by only 0.4% per year. This is consistent with the pattern in the general population, indicating that environmental risk factors may also influence AYA, as in the elderly population.<sup>25</sup> In Asian countries, the high incidence of GC is closely linked to the high prevalence of *H. pylori* infection, which mainly contributes to cancers in the distal stomach.<sup>26</sup> In these countries, GCAYA also showed a distal predominance.<sup>27-29</sup> Hence, with the implementation of screening and eradication programs for this bacterium, the incidence of GC has fallen gradually, which has been called the 'epidemiology of an unplanned triumph'.<sup>30</sup> The effectiveness of the eradication of *H. pylori* infection to decrease the incidence of GC was also validated in many recent well-designed interventional trials.<sup>31</sup> Although H. pylori infection is primarily considered a risk factor for the development of GC in older populations, the etiological role of H. pylori infection in GCAYA has also been elucidated.<sup>32 33</sup> Therefore, this 'unplanned triumph' has also been achieved in young adults.<sup>34</sup> In addition, modern practices of food preservation and refrigeration have increased the consumption of fresh fruits and vegetables, which are protective factors for GC.35 In contrast, the risk factors associated with GC in the USA were somewhat different from those in Asian countries. Some authors have suggested that increased salt intake and obesity may contribute to an increased incidence of GCAYA.636 These risk factors are mainly associated with proximal GC, which cannot be distinguished in this study; however, the increasing trend in GCAYA is consistent with the dramatic shift in

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the location of GC that has occurred in the United States, with a marked increase in diffusetype GC of the proximal stomach.<sup>24 37 38</sup>

In addition to the differences in risk factors, different forms of screening and early detection programs among the four countries may explain the variations in incidence and its time trends. As early as the 1960s, Japan began to implement a mass GC screening, which was expanded for all residents older than 40 in 1983.<sup>7</sup> In South Korea, GC screening started in 1999 and expanded nationwide in 2002.8 GC screening programs were launched much later in China, and the objects were limited to selected individuals with high-risk factors.<sup>8</sup> In contrast, to date, there have been no nationwide GC screening programs in the USA. The effects of these programs on the incidence of GC are contradictory, and recently published welldesigned studies have shown that screening programs effectively decrease the GC incidence.<sup>39</sup> <sup>40</sup> Although these programs did not cover the AYA populations, the changing trends of the ASIR of GCAYA in the four countries may partially reflect the effects of these programs. Because of the early establishment of GC screening and early diagnosis programs, the incidence of GCAYA decreased steadily in South Korea and Japan during the analysis period. In China, the change among the entire period was not apparent, which may have resulted from the first increase after the implementation of screening programs, which in turn might detect more new cases. Next, the incidence began to decline due to the effects of these programs. How GC screening programs can decrease the incidence of GC is not clear, especially in AYA, which was not covered by these programs. This could be explained by the fact that the implementation of GC screening programs may increase the awareness of GC in the entire population. This would also encourage young people to undergo GC-specific examinations.

*H. pylori* infection can be diagnosed by these examinations, leading to the eradication of this bacterium and a decrease in *H. pylori*-related GCs. Furthermore, electronic endoscopy has been widely accepted as the first method for GC screening, which may detect more precancerous benign lesions or in situ neoplasms. Thus, in the USA without GC screening programs, the incidence of GCAYA showed a stable trend in both sexes combined and increased steadily in females at 0.4% annually.

With regard to the mortality of GCAYA, regardless of deaths or ASMR, both showed significant downward trends among the four countries. The changing patterns in mortality reflect shifting patterns not only in terms of incidence but also in case fatalities, which we represented with MIR in this study.<sup>13</sup> Thus, a great decline in mortality was observed in Japan and South Korea, in which there was an impressive decrease in incidence and MIR. Case fatality (MIR) was determined primarily by advancements in therapy and early detection. Under the current concept of multidisciplinary therapy for GC, modern treatment methods have significantly increased the cure rate of localized GC and prolonged the survival of advanced GC.<sup>41</sup> However, in this study, we found that the MIR in the USA in 1990 was lower than that of China and South Korea, but it ranked first among the four countries in 2019, despite its highly developed healthcare system. This may have stemmed from the advanced stages of GCAYA diagnosed in the USA, increasing incidence in females, and the striking health disparities observed in cancers,<sup>42</sup> which balanced the improvement of therapy strategies. In Japan, the MIR of GCAYA was continuously the lowest during the analysis period, while in South Korea, it was gradually close to that of Japan starting in 2008. This phenomenon indicates that the most effective strategy to decrease the mortality of GCAYA is

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screening and early diagnosis. Therefore, according to recent studies, the prevalence of early GC rose from 28.6% in 1995 to 58.0% in 2007 in South Korea, and a 57% GC mortality rate reduction was attributed to endoscopic screening in Japan.<sup>43 44</sup>

Despite the decline in incidence and mortality of GCAYA in South Korea and Japan throughout the analysis period, the mortality tended to be stable in 2016. This implies that the effects of current prevention and screening programs for GC have reached their limitations in AYA. In addition, distinctive etiological characteristics have been recognized in GCAYA. Approximately 10% of GC cases showed familial clustering, which was more notable in GCAYA.<sup>45 46</sup> Up to 3% of GC cases are related to inherited cancer predisposition syndromes, including hereditary diffuse gastric cancer (HDGC), familial adenomatous polyposis (FAP), and Lynch syndrome, all of which predispose younger populations to GC development.<sup>47 48</sup> HDGC is an autosomal dominant syndrome arising from germline mutations in the tumor suppressor gene CDH1 and is characterized by the development of gastric cancers, predominantly the diffuse type and occurs in females at a young age.<sup>47 49</sup> These characteristics are consistent with diffuse gastric cancer and female predominance, reflecting the hereditary factors may contribute to the carcinogenesis of GCAYA. These hereditary factors are irreversible with current technological capabilities, and the best way to decrease the deaths caused by GC in these patients is precursor lesion detection by endoscopic surveillance and prophylactic total gastrectomy.<sup>47 50</sup> However, these specific cancer types still account for a minority of the total burdens caused by GCAYA. Other relevant opportunities to further improve the outcomes of GCAYA are worthwhile. Because the incidence of GC was low in AYA, endoscopic screening was considered to be associated with a low yield rate and not

cost-effective.<sup>51</sup> However, the burdens caused by GC are not small in AYA. Despite the significant decrease, GC still ranked first, fourth and fifth among all cancer types in AYA in South Korea, Japan and China, respectively, with regard to DALYs. Although it was relatively small, the burden caused by GCAYA in the USA increased from tenth in 1990 to ninth in 2019. In addition, as mentioned above, the AYA population has a long life expectancy and contributes greatly to society and the economy. Hence, prevention and screening among AYA in regions with a higher incidence of GC is worthwhile, and research into screening programs specifically in AYA is needed to determine the benefits and potential risks.

Our findings allow for a comprehensive estimation and comparison of the GCAYA burden among China, South Korea, Japan and the USA; however, several limitations exist, which were also described in studies using data from GBD 2019 and in studies on cancer incidence in AYA.<sup>10 15 17</sup> First, although GBD 2019 used many strategies to improve the data quality and comparability, they were obtained from selected registries and might not be accurate in reflecting the overall burden in some countries, particularly for countries where data are not available or are of poor quality, which may affect the integrity and accuracy of the data that we analyzed. Second, we were unable to analyze cardia and noncardia GC separately, two subtypes that have different risk factors and temporal incidence trends.<sup>52 53</sup> Third, the incidence and mortality were low and volatile, especially in the USA, which means that even the smallest change could lead to a significant analytical outcome, especially when determined with a very short duration. Despite these limitations, our study involved data retrieved from the GBD 2019, the best data currently available for a long time period. Our

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findings highlight the health burden of GCAYA and the effects of prevention and screening programs among GCAYA, as well as the need to increase awareness and resources for this neglected subpopulation.

Overall, we have offered a comprehensive analysis and comparison of the burden and temporal trends of GCAYA in China, Korea, South Japan and the USA. In the past three decades, the incidence and mortality of GCAYA have been declining significantly in South Korea and Japan. A falling trend also appeared for females in China in recent years, while a steadily slowly rising trend has been observed for females in the USA. Although not covered by prevention and screening programs, these variations in incidence and mortality of GCAYA may reflect variations in risk factors, cancer control strategies and treatment accessibility of GC among the four countries. Although GC is much less frequently diagnosed in AYA than in older populations, its effects remain considerable due to the long life expectancy of these individuals. Investigating the reasons behind the varying disease burden and changing trends of GCAYA across countrieswill inform inform recommendations for prevention measures and timely diagnosis specific to this underserved population to further decrease the GC burden.

Author contributions Conceptualisation: LJ and W-JS. Data curation: W-SL, ZY and LK. Formal analysis: W-SL, ZY and LJ. Methodology: W-SL, W-JS and LJ. Software: LJ. Supervision: W-JS and LJ. Roles/Writing-original draft: All authors. LJ is responsible for the overall content as the guarantor.

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Competing interests None declared.

Patient consent for publication All data in this study were anonymous and retrieved from the GBD 2019 database; therefore, informed consent was waived.

Ethics approval This study was approved by the Academic Committee of the Third Hospital of Mianyang (20190307).

Data availability statement Data are available in a public, open access repository. The data used in our study are available at the online Global Health Data Exchange query tool Lien (http://ghdx.healthdata.org/gbd-results-tool)

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## Figure legends

Figure 1. The temporal trends of the age-standardized incidence rate (ASIR) for gastric cancer in adolescents and young adults by sex in China, South Korea, Japan and the USA from 1990 to 2019.

Figure 2. The temporal trends of the age-standardized mortality rate (ASMR) for gastric cancer in adolescents and young adults by sex in China, South Korea, Japan and the USA from 1990 to 2019.

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		New cases			Deaths		
		1990	2019	1990-2019 change (%)	1990	2019	1990-2019 change (% -39.25
China	Both	18 123	20 855	15.07	13 929	8 462	-39.25
	Male	9 803	14 005	42.86	7 464	5 508	
	Female	8 320	6 851	-17.66	6 465	2 955	-54.29
Korea	Both	1 921	797	-58.51	1 254	237	-81.10
	Male	904	352	-61.06	571	101	-82.31
	Female	1 017	445	-56.24	682	136	-80.06
Japan	Both	3 258	945	-70.99	1 239	273	-77.97
	Male	1 626	462	-71.59	538	131	-75.65
	Female	1 632	483	-70.40	700	142	-79.71
USA	Both	772	812	5.18	400	343	-14.25
	Male	450	441	-0.02	223	174	-21.97
	Female	322	370	14.91	177	169	-4.52
							-26.21 -54.29 -81.10 -82.31 -80.06 -77.97 -75.65 -79.71 -14.25 -21.97 -4.52

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Table 2. The temporal trend in the incidence rate of gastric of	cancer in adolescents and young adults fi	rom 1990-2019 in Ghina, South Korea, Japan and the
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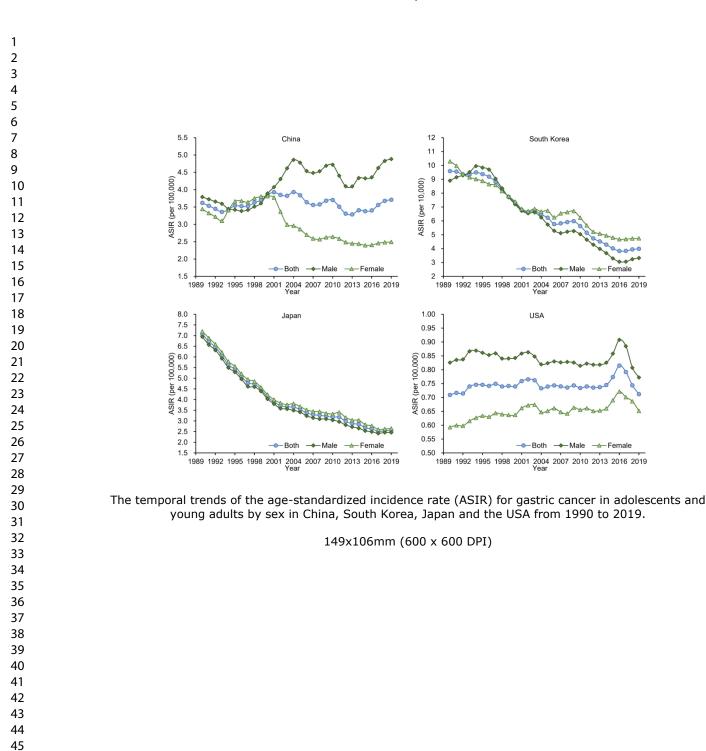
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Country	Sex	ASIR (pe	er 100 000)	Trends 1	1	Trends 2	1	Trends 3	July	1990-2019
		1990	2019	Years	APC (95% CI)	Years	APC (95% CI)	Years	ARC (95% CI)	AAPC (95% CI)
China	Both	3.62	3.71	1990-2004	0.9 (0.5, 1.3)	2004-2014	-1.6 (-2.3, -0.8)	2014-2019	2.4 (0.4-4.4)	0.3 (-0.1, 0.7)
	Male	3.79	4.88	1990-1997	-1.9 (-3.6, -0.1)	1997-2003	5.5 (2.3, 8.8)	2003-2019	-0ad (-0.6, 0.4)	0.6 (-0.2, 1.4)
	Female	3.44	2.49	1990-2000	1.8 (0.9, 2.6)	2000-2006	-6.1 (-8.3, -3.9)	2006-2019	-07 (-1.2, -0.1)	-1.0 (-1.6, -0.4)
Korea	Both	9.59	3.99	1990-1994	0.0 (-4.4, 4.5)	1994-2019	-3.7 (-4.0, -3.4)		n http:	-3.2 (-3.8, -2.6)
	Male	8.90	3.32	1990-1995	1.8 (-1.6, 5.3)	1995-2017	-5.0 (-5.4, -4.7)	2017-2019	2.5(-12.0, 19.3)	-3.4 (-4.5, -2.2)
	Female	10.29	4.74	1990-2019	-2.7 (-2.9, -2.5)	1 CL			pen.bmj.cor	-2.7 (-2.9, -2.5)
Japan	Both	7.07	2.55	1990-2001	-5.3 (-5.7, -4.9)	2001-2019	-2.5 (-2.7, -2.3)		nj.con	-3.6 (-3.7, -3.4)
	Male	6.94	2.46	1990-2002	-5.2 (-5.5, -4.9)	2002-2017	-2.6 (-2.8, -2.4)	2017-2019	0.29(-4.6, 5.2)	-3.5 (-3.8, -3.2)
	Female	7.20	2.65	1990-2002	-5.1 (-5.4, -4.9)	2002-2011	-1.8 (-2.3, -1.2)	2011-2019	-3 <sup><u>L</u></sup> <sub>N</sub> (-3.6, -2.6)	-3.5 (-3.8, -3.3)
USA	Both	0.71	0.71	1990-2013	0.1 (-0.1, 0.2)	2013-2016	2.9 (-2.2, 8.2)	2016-2019	-4 <sup>N</sup> / <sub>4</sub> (-6.4, -3.4)	-0.1 (-0.6, 0.5)
	Male	0.83	0.77	1990-2013	-0.2 (-0.3, -0.1)	2013-2016	3.4 (-1.6, 8.6)	2016-2019	-5 (-7.3, -2.7)	-0.4 (-0.9, 0.2)
	Female	0.59	0.65	1990-2019	0.4 (0.3-0.5)				est. P	0.4 (0.3-0.5)

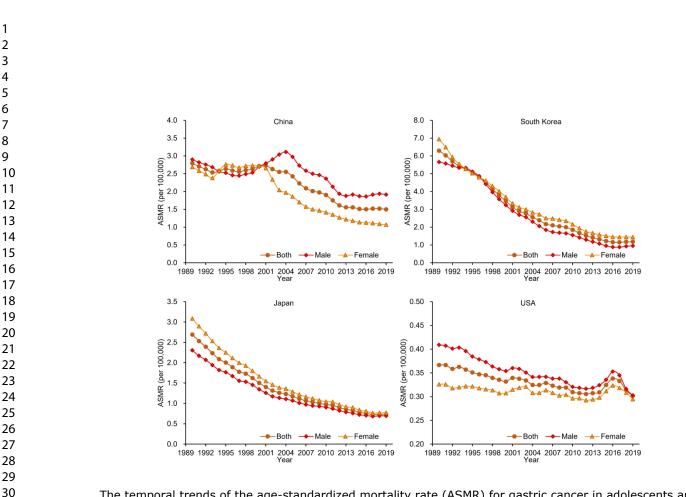
Abbreviations: AAPC, average annual percentage change; APC, annual percentage change; ASIR, age-standardized incidence rate of the py copyright.

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Table 3. T JSA.	`he tempo	ral trend ir	the mortal	ity rate of gas	tric cancer in adol	escents and ye	oung adults from	1990-2019 in	36/bmjopen-2022-0610 South Kor	ea, Japan and th
Country	Sex	ASMR (p	er 100 000)	Trends 1		Trends 2		Trends 3	21 July	1990-2019
		1990	2019	Years	APC (95% CI)	Years	APC (95% CI)	Years	20 APC (95% CI)	AAPC (95% C
China	Both	2.80	1.50	1990-2003	0.0 (-0.4, 0.3)	2003-2013	-5.1 (-5.7, -4.4)	2013-2019	<b>Q</b> 0.8 (-2.0, 0.5)	-2.0 (-2.3, -1.6)
	Male	2.90	1.91	1990-1997	-2.7 (-4.8, -0.5)	1997-2003	3.8 (0.0-7.8)	2003-2019	3.5 (-4.1, -2.9)	-1.8 (-2.7, -0.9)
	Female	2.69	1.07	1990-2000	0.8 (0.0-1.6)	2000-2007	-7.9 (-9.5, -6.3)	2007-2019	व इं3.3 (-3.9, -2.8)	-3.1 (-3.6, -2.6)
Korea	Both	6.29	1.18	1990-1995	-4.6 (-6.7, -2.4)	1995-2016	-6.8 (-7.0, -6.5)	2016-2019	<b>3</b> .9 (-4.0, 6.1)	-5.6 (-6.2, -5.0)
	Male	5.66	0.95	1990-1994	-1.1 (-5.1, 3.0)	1994-2016	-7.8 (-8.1, -7.5)	2016-2019	<u>.</u> .9 (-4.5, 8.7)	-6.0 (-6.8, -5.2)
	Female	6.94	1.44	1990-2016	-5.8 (-6.0, -5.6)	2016-2019	0.5 (-4.3, 5.5)		pen.b	-5.2 (-5.7, -4.7)
Japan	Both	2.69	0.73	1990-2003	-5.6 (-5.8, -5.4)	2003-2017	-3.8 (-4.0, -3.6)	2017-2019	<u>3</u> . <u>9</u> 0.0 (-3.9, 3.9)	-4.4 (-4.7, -4.1)
	Male	2.30	0.69	1990-2003	-5.2 (-5.5, -5.0)	2003-2017	-3.6 (-3.8, -3.4)	2017-2019	g.0 (-3.3, 5.5)	-4.0 (-4.3, -3.7)
	Female	3.08	0.77	1990-2003	-5.9 (-6.1, -5.7)	2003-2017	-4.1 (-4.3, -3.9)	2017-2019	<u>u</u> <u>v</u> <u>v</u> <u>v</u> <u>v</u> <u>v</u> <u>v</u> <u>v</u> <u>v</u> <u>v</u> <u>v</u>	-4.7 (-4.9, -4.4)
USA	Both	0.37	0.30	1990-2013	-0.8 (-0.9, -0.7)	2013-2016	3.6 (0.3, 6.9)	2016-2019	No. 10, 10, 10, 10, 10, 10, 10, 10, 10, 10,	-0.7 (-1.0, -0.3)
	Male	0.41	0.30	1990-2013	-1.2 (-1.2, -1.1)	2013-2016	4.2 (0.0, 8.7)	2016-2019	ву ца 5.0 (-7.0, -3.0)	-1.0 (-1.5, -0.6)
	Female	0.33	0.29	1990-2013	-0.4 (-0.5, -0.3)	2013-2016	2.9 (-1.6, 7.6)	2016-2019	2.7 (-4.8, -0.5)	-0.3 (-0.8, 0.2)

Abbreviations: AAPC, average annual percentage change; APC, annual percentage change; ASMR, age-standardized mortality rate





The temporal trends of the age-standardized mortality rate (ASMR) for gastric cancer in adolescents and young adults by sex in China, South Korea, Japan and the USA from 1990 to 2019.

149x108mm (600 x 600 DPI)

# 36/bmjopen-2022-061038 on **Supplementary material** Gastric cancer incidence, mortality, and burden in adolescents and young adults: A time-trend analysis and comparison among China, South Korea, ıly 2022. Japan and the USA Supplementary Table 1. Disability-adjusted life years and its age-standardized rate of gastric cancer in adolescents and young adults, and percentage changes from 1990 to 2019 in China, South Korea, Japan and the USA. Supplementary Figure 1. Rank changes in disability-adjusted life years attributable to cancers in adolescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019. Supplementary Figure 2. The temporal trends of the mortality-to-incidence ratio (MIR) for gastric cancer in addlescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019. This supplementary material has been provided by the authors to give readers additional information about their work. en on .com/ on July 2, 2024 by guest. Protected by copyright

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ercentage ch	hanges				,e-stanuaru	nzed rate	of gastric cancer in adolescents and young a	duits, and
		5 from 1990 DALYs	0 to 2019 :	in China, South Korea	a, Japan and ASDR	1 the USA	· 21 	
Country Sex		1990	2019	1990-2019 change (%)	1990	2019		
China Bot		779 909	475 977	-38.97	155.81	84.68	-45.65	
Mal		416 551	308 971	-25.83	160.93	107.71	-49.77 d	
		363 358	167 005	-50.04	150.31	60.78	1990-2019 change (%)       -45.65       -49.77       -59.56       -81.27       -83.08       -79.44       -72.37       -69.49       -74.55       -17.92       -25.35	
Korea Bot	oth	71 475	13 267	-81.44	355.99	66.67	-81.27	
Mal	ale	32 299	5 667	-82.45	317.60	53.75	-83.08	
Fen	emale	39 176	7 600	-80.60	395.55	81.26	-79.44	
Japan Bot	oth	68 962	15 367	-77.71	150.80	41.67	-72.37	
Mal	ale	30 060	7 399	-75.39	129.57	39.53	-69.49 On L	
Fen	emale	38 903	7 969	-75.92	172.44	43.88	-74.55	
USA Bot	oth	22 359	19 233	-13.98	20.53	16.85	-17.92	
Mal	ale	12 413	9 778	-21.23	22.80	17.09	-25.35 Gu	
Fen	emale	9 946	9 455	-4.93	18.28	16.62	0.00	
obreviations: ASD	DR, age-st	andardized DA	LYs rate; DAL	Ys, disability-adjusted life years.			-9.08 Protected by copyright.	

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Rank Cancer type 1 Liver cancer	Concer tune	Change	South Korea 1990 Rank Cancer type		en-2022-06103 South Sorrea 20 Cancer type O	Change
	Cancer type	Change -43.35%	1 Stomach cancer	Sto	omach cancer	-81.44%
2 Leukemia	Liver cancer	-58.76%	2 Leukemia	Leu	ukemia N	-68.11%
3 Stomach cancer	Tracheal, bronchus, and lung cancer	-11.12%	3 Tracheal, bronchus, and lung cancer 4 Proin and control papeous system cancer		ver cancer -	-19.95%
Tracheal, bronchus, and lung cancer     Brain and central nervous system cancer	Colon and rectum cancer Stomach cancer	21.07% -38.97%	Brain and central nervous system cancer     Colon and rectum cancer		east cancer C	-14.50% -35.97%
6 Colon and rectum cancer	Brain and central nervous system can	-13.19%	6 Liver cancer	Bra	ain and central nervous system cancer	-44.26%
7 Breast cancer 8 Nasopharynx cancer	Breast cancer	0.27% 9.66%	7 Breast cancer 8 Non-Hodgkin lymphoma	Tra	acheal, bronchus, and lung oncer	-56.59% -48.67%
9 Non-Hodgkin lymphoma	Non-Hodgkin lymphoma Cervical cancer	-1.61%	9 Cervical cancer		n-Hodgkin lymphoma	-62.46%
10 Cervical cancer	Pancreatic cancer	59.32%	10 Pancreatic cancer		ncreatic cancer N	-36.88%
11 Esophageal cancer 12 Pancreatic cancer	Nasopharynx cancer Esophaceal cancer	-48.79% -39.08%	11 Gallbladder and biliary tract cancer 12 Ovarian cancer		arian cancer Ilbladder and biliary tract caler	-14.79% -62.64%
13 Hodgkin lymphoma	Ovarian cancer	1.36%	13 Uterine cancer		iney cancer	26.23%
14 Ovarian cancer	Kidney cancer	103.02%	14 Esophageal cancer	Thy	yroid cancer	93.90%
15 Uterine cancer 16 Bladder cancer	Lip and oral cavity cancer	-8.01%	15 Lip and oral cavity cancer 16 Nasopharynx cancer		and oral cavity cancer	-12.48%
17 Lip and oral cavity cancer	Gallbladder and biliary tract cancer Bladder cancer	-10.20% -30.63%	16 Nasopharynx cancer 17 Kidney cancer		ilignant skin melanoma	-7.60% -47.10%
18 Gallbladder and biliary tract cancer	Uterine cancer	-44.69%	18 Larynx cancer	Ho	dgkin lymphoma	-27.32%
Kidney cancer     Malignant skin melanoma	Multiple myeloma Malianant skip molonomo	82.61% -12.38%	19 Non-melanoma skin cancer 20 Malignant skin melanoma		erine cancer <u>O</u>	-76.01% -76.20%
21 Larynx cancer	Malignant skin melanoma Testicular cancer	-12.38%	20 Malignant skin melanoma 21 Hodgkin lymphoma		ophageal cancer	-76.20%
22 Testicular cancer	Non-melanoma skin cancer	6.00%	22 Bladder cancer	Bla		-40.75%
23 Thyroid cancer 24 Non-melanoma skin cancer	Hodgkin lymphoma	-72.84%	23 Thyroid cancer 24 Testicular cancer		Itiple myeloma	-2.87%
25 Multiple myeloma	Thyroid cancer Larynx cancer	-19.49% -45.66%	24 Testicular cancer 25 Multiple myeloma		n-melanoma skin cancer	-69.69% -18.80%
26 Other pharynx cancer	Mesothelioma	6.49%	26 Prostate cancer	Lar	rynx cancer	-77.88%
27 Prostate cancer 28 Mesothelioma	Prostate cancer Other pharynx cancer	-6.89% -43.39%	27 Mesothelioma 28 Other pharynx cancer		her pharynx cancer	-0.22% -10.94%
Japan 1990	Japan 2019		USA 1990	ivie	USA 2029	-10.0478
Japan 1990						
					0	
Rank Cancer type	Cancer type	Change	Rank Cancer type	Pre	Cancer type 号	Change
					0	Change -37.71% -32.70%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer	Cancer type Leukemia Breast cancer Colon and rectum cancer	Change -66.32% -39.26% -42.71%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer	Leu Brai	Cancer type O east cancer O ukemia	-37.71% -32.70% -14.39%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer	Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer	Change -66.32% -39.26% -42.71% -77.72%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma	Leu Bra Colu	Cancer type O east cancer O ukemia in and central nervous system cancer ion and rectum cancer	-37.71% -32.70% -14.39% 9.37%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma	Cancer type Leukemia Breast cancer Colon and rectum cancer	Change -66.32% -39.26% -42.71% -77.72%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer	Leu Brai Colu	Cancer type O east cancer O ukemia	-37.71% -32.70% -14.39%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and ractum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain do central nervous system cancer	Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system can Tracheal, bronchus, and lung cancer Cervical cancer	Change -66.32% -39.26% -42.71% -77.72% -77.72% -711.78% -56.37% -5.93%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma	Leu Brai Colu Non Trai	Cancer type sast cancer ukemia in and central nervous system tancer ion and rectum cancer n-todgkin tymphoma cheal, bronchus, and lung Goer rotac cancer	-37,71% -32,70% -14,39% 9,37% -52,12% -51,25% -25,18%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           8         Liver cancer	Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Drain and central nervous system can Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma	Change -66.32% -39.26% -42.71% -77.72% cer -11.78% -56.37% -59.33% -59.14%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchws, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer	Leu Brai Coli Non Trai Cer Mal	Cancer type vikemia vikemia vikemia vikemia entral nervous system cancer vikemia entral nervous system cancer vikemia vikemia si kinemia si kinemia vikemia vikemi	-37,71% -32,70% -14,39% 9,37% -52,12% -51,25% -51,25% -22,37%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and ractum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain do central nervous system cancer	Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system can Tracheal, bronchus, and lung cancer Cervical cancer	Change -66.32% -39.26% -42.71% -77.72% -77.72% -711.78% -56.37% -5.93%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma	Leu Bra Colo Non Tra Cere Mal	Cancer type vast cancer ikemia in and central nervous system cancer in and rectum cancer n-todgkin lymphoma cheal, bronchus, and lung cancer rvical cancer lipant skin melanoma mach cancer or	-37,71% -32,70% -14,39% 9,37% -52,12% -51,25% -25,18%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancreatic cancer	Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Drain and central nervous system can Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Pancreatic cancer	Change -66.32% -39.28% -42.71% -77.72% -56.37% -5.93% -59.14% -42.03% -59.89% -39.78%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchws, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer	Leu Bra Col Non Tra Cer Mal Stor Ova Hod	Cancer type of ixemia in and central nervous system cancer in and rectum cancer of index of the cancer of the ca	-37,71% -32,70% -14,39% 9,37% -52,12% -51,25% -25,18% -22,37% -13,38% -25,87% -57,47%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and ractum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and cantral nervous system cancer           8         Liver cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancreatic cancer           12         Testicular cancer	Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Drain and central nervous system can Tracheal, bronchus, and lung cancer Carvical cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Pancreatic cancer Lip and oral cavity cancer	Change -66.32% -39.28% -42.21% -77.72% -56.37% -59.14% -42.03% -59.14% -59.39% -42.03% -59.48% -41.60%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central narvous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer           12         Testicular cancer	Brain Store	Cancer type Q sast cancer ukemia in and central nervous system thouse system thouse the system thouse the system thouse the system typant skin melanoma mach cancer dyskin tymphoma corcestic cancer	-37,71% -32,70% -14,39% 9,37% -52,12% -51,25% -25,18% -25,18% -32,37% -13,38% -25,87% -57,47% -1,41%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancreatic cancer	Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Drain and central nervous system can Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Pancreatic cancer	Change -66.32% -39.28% -42.71% -77.72% -56.37% -5.93% -59.14% -42.03% -59.89% -39.78%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchws, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer	Leu Bra Coll Nor Tra Cer Mal Stor Ova Hoo Ova Hoo	Cancer type vast cancer vast cancer vast and central nervous system cancer on and rectum cancer nor and rectum cancer vical cancer ignant skin melanoma mach cancer dgkin lymphoma reatin cancer dgkin lymphoma Cancer Cance	-37,71% -32,70% -14,39% 9,37% -52,12% -51,25% -25,18% -22,37% -13,38% -25,87% -57,47%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           9         Ovarian cancer           10         Cervical cancer           11         Panoreatic cancer           12         Testicular cancer           13         Galtbladder and billary tract cancer           14         Lip and orail cavity cancer           15         Kidney cancer	Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system can Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Lurer cancer Pancreatic cancer Lup and oral cavity cancer Testicular cancer Kidney cancer Uterine cancer	Change -66.32% -39.28% -42.71% -77.72% -56.37% -59.14% -59.94% -59.98% -39.78% -100% -66.88% -23.47% 13.22%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchws, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer           12         Testicular cancer           13         Pancreatic cancer           14         Kidney cancer           15         Liver cancer	Leu Bra Coli Non Tra Cer Mai Sto Ova Hod Ova Hod Pan Live Tes Kidi	Cancer type O sast cancer of the system in and central nervous system cancer on and rectum cancer of the system incheal, bronchus, and lung caper richeal, bronchus, and lung caper invical cancer of the system lignant skin melanoma mach cancer of the system dgkin lymphoma corceatic cancer of the system er cancer of the system sitcular cancer of the system sitcular cancer of the system sitcular cancer of the system sitcular cancer of the system system system sitcular cancer of the system system system system sitcular cancer of the system system system system system sitcular cancer of the system syst	-37,71% -32,70% -14.39% 9.37% -52,12% -51,12% -25,18% -25,18% -32,37% -13,98% -28,87% -7,47% 1,41% 28,11% -28,11% -28,11% -28,11%
Rank         Cancer type           1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           9         Darain and central nervous system cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancealic cancer           12         Testicular cancer           13         Gallbladder and biliary tract cancer           14         Lip and oral cavity cancer           15         Kichey cancer           16         Malignant skin melanoma	Cancer type Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system can Tracheal, bronchus, and lung cancer Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Luver cancer Pancreatic cancer Up and oral cavity cancer Testicular cancer Kidney cancer Ustar cancer Caliblaider and biliary tract cancer	Change -66.32% -39.26% -42.71% -7.72% -7.72% -56.37% -59.14% -42.03% -59.89% -9.98% -39.76% -56.88% -39.76% -56.88% -32.47% 13.22%	Rank         Cancer type           1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin hymphoma           5         Tracheal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer           12         Testicular cancer           13         Pancreatic cancer           14         Kidney cancer           15         Liver cancer           16         Liper cancer           17         Jand oral cavity cancer	Leu Brai Coll Nor Trai Cer Mal Stor Ova Hoo Pan Live Tes Kidd	Cancer type O sast cancer wast cancer wast cancer in and central nervous system cancer lon and rectum cancer n-hodgkin lymphoma acheal, bronchus, and lung cober rycal cancer March cancer arian cancer dgkin lymphoma arian cancer er cancer stoular cancer istoular cancer istoular cancer phaacel acncer	-37,71% -32,70% -32,70% 9,37% -52,12% -51,25% -25,18% -22,18% -23,37% -23,37% -23,88% -25,87% -57,47% 1,41% -24,96% -5,19% -7,17%
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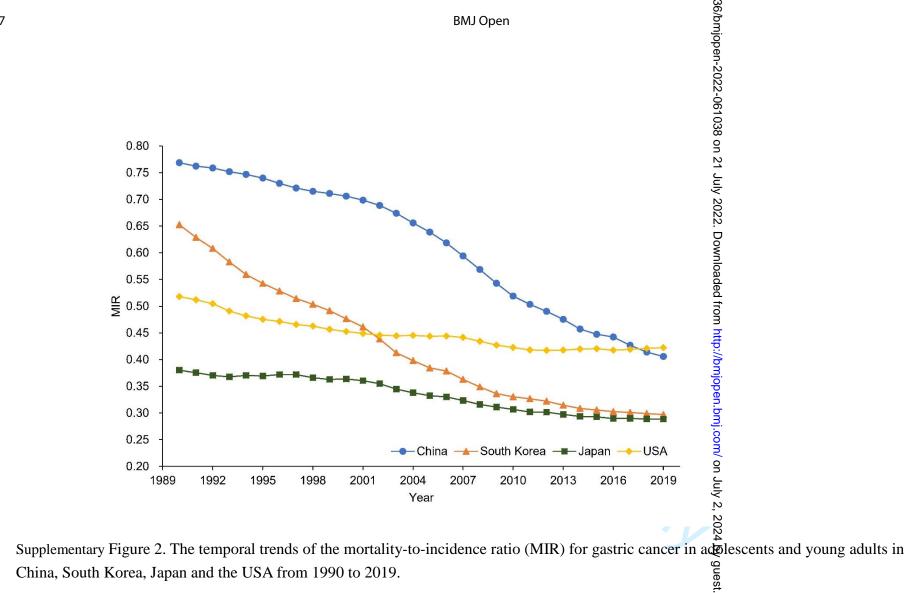
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Supplementary Figure 2. The temporal trends of the mortality-to-incidence ratio (MIR) for gastric cancer in adolescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019.

## Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below. Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation. Upload your completed checklist as an extra file when you submit to a journal. In your methods section, say that you used the STROBE cross sectional reporting guidelines, and cite them as: von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Page Reporting Item Number Title and abstract Title #1a Indicate the study's design with a commonly used term in the title or the abstract Abstract #1b Provide in the abstract an informative and balanced summary 2.3

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1 2			of what was done and what was found	
3 4 5	Introduction			
6 7 8	Background /	<u>#2</u>	Explain the scientific background and rationale for the	4
9 10	rationale		investigation being reported	
11 12 13	Objectives	<u>#3</u>	State specific objectives, including any prespecified	4,5
14 15 16			hypotheses	
17 18 19	Methods			
20 21 22	Study design	<u>#4</u>	Present key elements of study design early in the paper	5
23 24 25	Setting	<u>#5</u>	Describe the setting, locations, and relevant dates, including	5
26 27 28			periods of recruitment, exposure, follow-up, and data collection	
28 29 30	Eligibility criteria	<u>#6a</u>	Give the eligibility criteria, and the sources and methods of	5
31 32 33			selection of participants.	
34 35		<u>#7</u>	Clearly define all outcomes, exposures, predictors, potential	5
36 37 38			confounders, and effect modifiers. Give diagnostic criteria, if	
39 40			applicable	
41 42 43	Data sources /	<u>#8</u>	For each variable of interest give sources of data and details of	5
44 45	measurement		methods of assessment (measurement). Describe	
46 47			comparability of assessment methods if there is more than one	
48 49 50			group. Give information separately for for exposed and	
51 52 53			unexposed groups if applicable.	
53 54 55 56	Bias	<u>#9</u>	Describe any efforts to address potential sources of bias	n/a
57 58	Study size	<u>#10</u>	Explain how the study size was arrived at	n/a
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1 2	Quantitative	<u>#11</u>	Explain how quantitative variables were handled in the	5
3 4	variables		analyses. If applicable, describe which groupings were chosen,	
5 6 7			and why	
8 9 10	Statistical	<u>#12a</u>	Describe all statistical methods, including those used to control	6
11 12 13	methods		for confounding	
14 15	Statistical	<u>#12b</u>	Describe any methods used to examine subgroups and	6
16 17 18	methods		interactions	
19 20	Statistical	<u>#12c</u>	Explain how missing data were addressed	n/a
21 22 23 24	methods			
24 25 26	Statistical	<u>#12d</u>	If applicable, describe analytical methods taking account of	6
27 28 29	methods		sampling strategy	
30 31	Statistical	<u>#12e</u>	Describe any sensitivity analyses	n/a
32 33 34	methods			
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39 40	Participants	<u>#13a</u>	Report numbers of individuals at each stage of study—eg	6,7
41 42			numbers potentially eligible, examined for eligibility, confirmed	
43 44			eligible, included in the study, completing follow-up, and	
45 46			analysed. Give information separately for for exposed and	
47 48 49			unexposed groups if applicable.	
50 51 52	Participants	<u>#13b</u>	Give reasons for non-participation at each stage	n/a
53 54 55	Participants	<u>#13c</u>	Consider use of a flow diagram	n/a
56 57 58	Descriptive data	<u>#14a</u>	Give characteristics of study participants (eg demographic,	6,7
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1 2			clinical, social) and information on exposures and potential	
3 4			confounders. Give information separately for exposed and	
5 6 7			unexposed groups if applicable.	
7 8 9	Descriptive data	<u>#14b</u>	Indicate number of participants with missing data for each	n/a
10 11 12			variable of interest	
13 14	Outcome data	<u>#15</u>	Report numbers of outcome events or summary measures.	6-10
15 16 17			Give information separately for exposed and unexposed	
17 18 19			groups if applicable.	
20 21	Main results	<u>#16a</u>	Give unadjusted estimates and, if applicable, confounder-	n/a
22 23 24			adjusted estimates and their precision (eg, 95% confidence	
25 26			interval). Make clear which confounders were adjusted for and	
27 28 29			why they were included	
30 31 32	Main results	<u>#16b</u>	Report category boundaries when continuous variables were	6-10
33 34 35			categorized	
36 37	Main results	<u>#16c</u>	If relevant, consider translating estimates of relative risk into	n/a
38 39 40			absolute risk for a meaningful time period	
41 42	Other analyses	<u>#17</u>	Report other analyses done—e.g., analyses of subgroups and	6-10
43 44 45			interactions, and sensitivity analyses	
46 47	Discussion			
48 49				
50 51 52	Key results	<u>#18</u>	Summarise key results with reference to study objectives	10
53 54	Limitations	<u>#19</u>	Discuss limitations of the study, taking into account sources of	14,15
55 56 57			potential bias or imprecision. Discuss both direction and	
57 58			magnitude of any potential bias.	
59 60		For pe	er review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

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1 2	Interpretation	<u>#20</u>	Give a cautious overall interpretation considering objectives,	10-15
3 4			limitations, multiplicity of analyses, results from similar studies,	
5 6 7			and other relevant evidence.	
8 9 10	Generalisability	<u>#21</u>	Discuss the generalisability (external validity) of the study	15
11 12 13			results	
14 15	Other Information			
16 17				
18	Funding	<u>#22</u>	Give the source of funding and the role of the funders for the	15,16
19 20 21			present study and, if applicable, for the original study on which	
22 23			the present article is based	
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## Gastric cancer incidence, mortality, and burden in adolescents and young adults: A time-trend analysis and comparison among China, South Korea, Japan and the USA

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#### **Original research**

Gastric cancer incidence, mortality, and burden in adolescents and young adults: A time-trend analysis and comparison among China, South Korea, Japan and the USA Silin Wu<sup>1</sup>, Yao Zhang<sup>2</sup>, Yi Fu<sup>2</sup>, Jian Li<sup>2</sup>, Jisheng Wang<sup>3</sup>

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## Abstract

**Objectives** To evaluate and compare the burden of gastric cancer in adolescents and young adults (GCAYA) among China, South Korea, Japan and the USA, four countries with similar or different rates of GC incidence, development levels, and cancer control strategies. **Design** This population-based observational study collected the epidemiologic data of GCAYA from the Global Burden of Diseases Study 2019. The trend magnitude and directions over time for incidence and mortality of GCAYA were analyzed and compared among four countries.

Main outcomes and measures Outcomes included new cases, deaths, mortality-to-incidence ratios (MIRs), disability-adjusted life-years (DALYs), and their age-standardized rates and estimated annual percentage changes (AAPCs).

**Results** There were 49 008 new cases and 27 895 deaths from GCAYA in 2019, nearly half of which occurred in China. The AAPCs for the age-standardized incidence and mortality rate were 0.3 (-0.1, 0.7), -3.6 (-3.7, -3.4), -3.2 (-3.8, -2.6), -0.1 (-0.6, 0.5) and -2.0 (-2.3, -1.6), -5.6 (-6.2, -5.0), -4.4 (-4.7, -4.1), -0.7 (-1.0, -0.3) in China, South Korea, Japan and the USA, respectively. The incidence rate for females in the USA rose by 0.4% annually. GC ranks fifth, first, fourth and ninth in China, South Korea, Japan and the USA regarding burdens caused by cancer in adolescents and young adults. The MIRs declined constantly in South Korea and China, and the MIR in the USA became the highest in 2019.

**Conclusions** Although not covered by prevention and screening programs, variations in disease burden and time trends may reflect variations in risk factors, cancer control strategies and treatment accessibility of GC among the four countries. Investigating the reasons behind

the varying disease burden and changing trends of GCAYA across countries will inform recommendations for prevention measures and timely diagnosis specific to this underserved population to further decrease the GC burden.

Key words gastric cancer; adolescents; young adults; disease burden; time trend

## Strengths and limitations of this study

- We provided a comprehensive description of variations in the incidence and mortality of gastric cancer in adolescents and young adults (GCAYA) among China, South Korea, Japan and the USA.
- Our study uses the average annual percentage change (AAPC) and the annual percentage change (APC) to quantify and compare secular trends in the incidence and mortality of GCAYA.
- This study analyses the mortality-to-incidence ratios (MIRs) of GCAYA and their changing trends among China, South Korea, Japan and the USA.
- We were unable to analyze cardia and noncardia gastric cancer separately, two subtypes that have different risk factors and temporal incidence trends.
- The incidence and mortality were low and volatile, especially in the USA, which means that even the smallest change could lead to a significant analytical outcome.

#### INTRODUCTION

Gastric cancer (GC) has long been a major disease burden caused by neoplasms worldwide.<sup>1</sup> Recent evidence suggests that the incidence and mortality of GC in the general population has fallen substantially,<sup>2</sup> primarily resulting from the prevention and nationwide screening programs.<sup>34</sup> On the contrary, a possible rising incidence of early-onset GC has been reported in the USA.<sup>56</sup> However, the incidence and disease burden caused by GC in the USA were relatively smaller than those caused by other cancer types. In addition, there are no nationwide screening programs for GC in the USA. In Japan and South Korea, and in recent years in China, population screening has been performed widely, although none of them covered people younger than 40 years old.<sup>78</sup> The trends of GC incidence in youth populations have also been reported in Asian countries. In Japan, no marked changes in the incidence of GC were noted for individuals aged 30-39.9 The results from the South Korean study showed a falling trend in the 20-39 age group.<sup>10</sup> However, the end time of the analysis period in these studies was 10-30 years ago or before the implementation of nationwide screening programs. Hence, trends in recent years and whether prevention and screening programs also influence the incidence and mortality of GC in adolescents and young adults (GCAYA), are unknown.

Given that adolescents and young adults represent the main proportion of people who contribute substantially to the economy and have an important role in caring for their families, GCAYA carries a disproportionate burden than GC among older patients due to its greater impact on life expectancy.<sup>11 12</sup> Variations in cancer incidence among different populations may reflect differences in the prevalence of risk factors and screening strategies. Variations in mortality reflect variations not only in incidence but also in case fatality, which can be

affected by differences in early diagnosis and accessibility to treatment.<sup>13</sup> Therefore, we conducted a comprehensive analysis of the rates and trends of incidence, mortality, and disability-adjusted life years (DALYs) for GCAYA in China, South Korea, Japan, and the USA, four countries with similar or different rates of GC incidence, development levels, and cancer control strategies. We collected all data from the Global Burden of Diseases, Injuries, and Risk Factors Study 2019 (GBD 2019). By investigating the differences in the burden and changing trends of GCAYA among the four countries, we hope that our findings can serve as a reference for the establishment of GCAYA control measures and help to reduce the disease burden caused by this neglected cancer type.

#### **METHODS**

#### **Study Population and Data Sources**

In this study, the research subjects were adolescents and young adults (AYAs) diagnosed with GC. AYA were defined as individuals aged 15-39. We obtained all data analyzed in this study from GBD 2019, which aims to analyze health trends over time, compare variability among countries, and help establish disease control strategies globally.<sup>14</sup> We collected data from the Global Health Data Exchange (GHDx) (<u>http://ghdx.healthdata.org/</u>) via the freely available GBD Results Tools repository. The search parameters were "stomach cancer" for cause; "incidence, deaths, DALYs" for measurements; "China, Republic of Korea, Japan, United States of America" for location; "1990-2019" for years; "number and rate" for metrics; "male, female and both" for sex; and "15 to 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.<sup>15</sup>

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## Definitions

The definition of GCAYA is not always consistent across studies, yet most authors adopted 40 years as the upper limit to categorize patients as having early-onset GC.<sup>12</sup> Therefore, in this study, we defined GCAYA as patients diagnosed between the ages of 15 and 39 years. The rationale for using this age range relates to biological and physiological maturity and relative stability; these individuals have not yet experienced the effects of hormonal and immune response decline or chronic medical conditions that can influence oncologic decision-making as it would in the care of older patients.<sup>16</sup> The DALY is a summary measure that quantifies the overall burden of disease, which represents the sum of years of life lost due to premature death and years lived with disability. One DALY can be regarded as the loss of 1 year in full health.

## Patient and public involvement

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

#### **Statistical Analysis**

Detailed estimation methods for incidence, mortality, and DALYs have been reported in previous studies by GBD Collaborators.<sup>14 17</sup> We computed the age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) using the crude rates of 5-year bands from 15-39, and the GBD 2019 standard population via the direct method, expressed as the rate per 100 000 person-years. We analyzed incidence, mortality, and DALYs descriptively by gender, country and year, and we calculated the change rates between 1990 and 2019. We also calculated the mortality-to-incidence ratio (MIR)—which has previously been employed

as a proxy for the 5-year survival rate across different neoplasias—as the ratio of death counts to new cases.<sup>18-20</sup> We plotted the temporal trends of these measures from 1990 to 2019. To compare the changing trends of GCAYA among the four countries, we utilized Joinpoint software (Version 4.9.0.0) to determine the average annual percentage change (AAPC) and the annual percentage change (APC) for each period, with a maximum of 2 joinpoints using a generalized linear regression model for the natural logarithm of the ASIR and ASMR. We established the statistical significance of the variation trend by their 95% confidential intervals (CIs). We considered AAPCs or APCs with a 95% CI of > 0 to represent a significant rising trend, while we deemed those with a 95% CI of < 0 to represent a significant falling trend; otherwise, they represented a stable ASIR or ASMR.<sup>21 22</sup>

## RESULTS

#### New Cases of GCAYA and Its Change Rates between 2019 and 1990

In 2019, there were an estimated 1 269 806 new GC cases globally, 49 008 (3.86%) of which were diagnosed between 15 and 39 years old. China accounted for 42.55% (20 855) of GCAYA cases. As shown in table 1, in South Korea and Japan, new cases of GCAYA were common in females, while in China and the USA, GCAYA was much more frequently diagnosed in males. Compared with that in 1990, the new cases of GCAYA declined by 58.51% in South Korea and 70.99% in Japan, and the degrees of reduction were similar in males and females. However, new cases in China and the USA have risen by 15.07% and 5.18%, respectively. The increased number of new cases in China contributed to male cases, while in the USA it contributed to female cases.

#### GCAYA-related Deaths and Their Change Rates between 2019 and 1990

In 2019, the number of deaths caused by GC was 957 185 worldwide, and GCAYA accounted for only 2.91% (27 895). China contributed to 13 929 (49.93%) of the deaths caused by GCAYA. The sex distribution was similar to that of new cases; females predominated in China and the USA, while males predominated in South Korea and Japan. In contrast to new cases, the number of deaths between 2019 and 1990 declined in all four countries. The most obvious changes occurred in South Korea, reaching more than 80% for both sexes. The lowest decline was among females in the USA, which was only 4.52% (table 1).

### The Age-Standardized Rates and Time Trends of GCAYA Incidence

As shown in table 2 and figure 1, for both sexes, the ASIRs of GCAYA in 2019 in China, South Korea, Japan and the USA were 3.71, 3.99, 2.55 and 0.71 per 100 000 person-years, respectively. Consistent with the sex variations in new cases, the ASIRs were higher for females than for males in Japan and South Korea, while the opposite was true in the USA and China. The variability of ASIR was also found through time trend analysis among the four countries. Only in Japan did the ASIR exhibit a constant declining trend, with AAPC values of -3.6 (-3.7, -3.4) for both sexes. In South Korea, there was a decreasing trend for both males (AAPC -3.4, 95% CI: -4.5, -2.2) and females (AAPC -2.7, 95% CI: -2.9, -2.5), although the ASIR in males tended to remain stable after 2016. The shifting characteristics of ASIRs in China are much more complex. The changing trends were not significant from 1990 to 2019, with an AAPC of 0.3 (-0.1, 0.7), resulting from a considerably falling trend from 2004-2014 (APC -1.6, 95% CI: -2.3, -0.8) but a significantly rising trend from 2014 to 2019 (APC 2.4, 95% CI: 0.4-4.4). The ASIR of GCAYA in the USA was low and remained relatively stable in males; however, the ASIR in females rose by 0.4% annually from 1990 to 2019.

The Age-Standardized Rates and Time Trends of GCAYA Mortality In 2019, the ASMRs of GCAYA in China, South Korea, Japan and the USA were 1.50 (1.27-1.75), 1.18 (0.94-1.47), 0.73 (0.68-0.78) and 0.30 (0.27-0.33), respectively. A decreasing

trend of ASMR was observed from 1990 to 2019 in all four countries, and the annual decline rates were 2.0%, 5.6%, 4.4% and 0.7% in China, South Korea, Japan and the USA, respectively. The decrease started at approximately 2000 in China for females; before that time, it had been rising for ten years (APC 0.8, 95% CI: 0.0-1.6). For males in China, among the total falling trend, there was a stable period (1997-2003). The downward trend continued in China and the USA untill 2019, but stabilized in South Korea and Japan from 2016 (Table

3; Figure 2).

## DALYs Caused by GCAYA and Its Change Rates between 2019 and 1990

The GBD 2019 estimated that GCAYA resulted in 475 977, 13 267, 15 367 and 19 233 DALYs in China, South Korea, Japan and the USA, respectively. The corresponding agestandardized DALY rates (ASDR) were 84.68, 66.67, 41.67, and 16.85 per 100 000 personyears. Similar to incidence and mortality, female predominance was noted in South Korea and Japan, while male predominance was witnessed in China and the USA. Between 1990 and 2019, the ASDR declined in all four countries. The proportions of reduction were 38.97%, 81.44%, 77.71% and 13.98% in China, South Korea, Japan and the USA, respectively (online supplemental table 1). Compared with other malignancies in AYA, the relative burden of GCAYA in the four countries and their changes are ranked in online supplemental figure 1. In South Korea, both in 1990 and 2019, GC was the leading burden of cancer in AYA. In China, it declined from third in 1990 to fifth in 2019. GC was once the leading cause of cancer-

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related DALYs in AYA in Japan and dropped to fourth in 2019. The burden of GCAYA was relatively small in the USA, ranking tenth in 1990 and then slightly rising to ninth in 2019.

### The MIR of GCAYA and Its Changes

In 1990, the MIRs for GCAYA in China, South Korea, Japan and the USA were 0.77, 0.65, 0.38 and 0.52, respectively. From 1990 to 2019, the MIR declined constantly in South Korea, which had a higher MIR in 1990 but fell to 0.30, slightly higher than that in Japan (0.29). The MIR in China also exhibited a significant, decreasing trend, reaching 0.41 in 2019. The changing trend of MIR in the USA was not obvious; however, the MIR was 0.42 in 2019, becoming the first out of the four countries. Japan had the lowest MIR throughout the analyzed period, although the decreasing trend was slight (online supplemental figure 2).

## DISCUSSION

The majority of GC occurs in elderly individuals, with its peak incidence and mortality reached among the total population aged 85-89 in China.<sup>23</sup> In the USA, more than 95% of GC cases are diagnosed in individuals older than 40.<sup>24</sup> Only 3.86% of new cases and 2.91% of deaths affected AYA in 2019 worldwide. GCAYA has traditionally been ignored by patients, physicians and policy-makers. However, compared with older patients with GC, the burden caused by GCAYA was disproportionate, given their long life expectancy and serving as the main contributors to the economy and family care. Thus, reducing the incidence and mortality in this underserved subpopulation may benefit the development of society and the economy.

We found that nearly half of new cases and deaths of GCAYA occurred in China, which was attributed to it having the world's largest population and a higher incidence rate. The ASIR of GCAYA was much higher in the three East Asian countries, 3-5 times that in the

USA. These geographic variations were also reflected in temporal trends. In Asian countries, the incidence of GCAYA showed a markedly downward trend, especially in South Korea and Japan; both had a more than 3% decrease annually. In the USA, a stable incidence was observed in males, while the ASIR in females rose steadily, although by only 0.4% per year. This is consistent with the pattern in the general population, indicating that environmental risk factors may also influence AYA, as in the elderly population.<sup>25</sup> In Asian countries, the high incidence of GC is closely linked to the high prevalence of *H. pylori* infection, which mainly contributes to cancers in the distal stomach.<sup>26</sup> In these countries, GCAYA also showed a distal predominance.<sup>27-29</sup> Hence, with the implementation of screening and eradication programs for this bacterium, the incidence of GC has fallen gradually, which has been called the 'epidemiology of an unplanned triumph'.<sup>30</sup> The effectiveness of the eradication of *H. pylori* infection to decrease the incidence of GC was also validated in many recent well-designed interventional trials.<sup>31</sup> Although *H. pylori* infection is primarily considered a risk factor for the development of GC in older populations, the etiological role of *H. pylori* infection in GCAYA has also been elucidated.<sup>32 33</sup> Therefore, this 'unplanned triumph' has also been achieved in young adults.<sup>34</sup> In addition, modern practices of food preservation and refrigeration have increased the consumption of fresh fruits and vegetables, which are protective factors for GC.35 In contrast, the risk factors associated with GC in the USA were somewhat different from those in Asian countries. Some authors have suggested that increased salt intake and obesity may contribute to an increased incidence of GCAYA.636 These risk factors are mainly associated with proximal GC, which cannot be distinguished in this study; however, the increasing trend in GCAYA is consistent with the dramatic shift in

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the location of GC that has occurred in the United States, with a marked increase in diffusetype GC of the proximal stomach.<sup>24 37 38</sup>

In addition to the differences in risk factors, different forms of screening and early detection programs among the four countries may explain the variations in incidence and its time trends. As early as the 1960s, Japan began to implement a mass GC screening, which was expanded for all residents older than 40 in 1983.<sup>7</sup> In South Korea, GC screening started in 1999 and expanded nationwide in 2002.8 GC screening programs were launched much later in China, and the objects were limited to selected individuals with high-risk factors.<sup>8</sup> In contrast, to date, there have been no nationwide GC screening programs in the USA. The effects of these programs on the incidence of GC are contradictory, and recently published welldesigned studies have shown that screening programs effectively decrease the GC incidence.<sup>39</sup> <sup>40</sup> Although these programs did not cover the AYA populations, the changing trends of the ASIR of GCAYA in the four countries may partially reflect the effects of these programs. Because of the early establishment of GC screening and early diagnosis programs, the incidence of GCAYA decreased steadily in South Korea and Japan during the analysis period. In China, the change among the entire period was not apparent, which may have resulted from the first increase after the implementation of screening programs, which in turn might detect more new cases. Next, the incidence began to decline due to the effects of these programs. How GC screening programs can decrease the incidence of GC is not clear, especially in AYA, which was not covered by these programs. This could be explained by the fact that the implementation of GC screening programs may increase the awareness of GC in the entire population. This would also encourage young people to undergo GC-specific examinations.

*H. pylori* infection can be diagnosed by these examinations, leading to the eradication of this bacterium and a decrease in *H. pylori*-related GCs. Furthermore, electronic endoscopy has been widely accepted as the first method for GC screening, which may detect more precancerous benign lesions or in situ neoplasms. Thus, in the USA without GC screening programs, the incidence of GCAYA showed a stable trend in both sexes combined and increased steadily in females at 0.4% annually.

With regard to the mortality of GCAYA, regardless of deaths or ASMR, both showed significant downward trends among the four countries. The changing patterns in mortality reflect shifting patterns not only in terms of incidence but also in case fatalities, which we represented with MIR in this study.<sup>13</sup> Thus, a great decline in mortality was observed in Japan and South Korea, in which there was an impressive decrease in incidence and MIR. Case fatality (MIR) was determined primarily by advancements in therapy and early detection. Under the current concept of multidisciplinary therapy for GC, modern treatment methods have significantly increased the cure rate of localized GC and prolonged the survival of advanced GC.<sup>41</sup> However, in this study, we found that the MIR in the USA in 1990 was lower than that of China and South Korea, but it ranked first among the four countries in 2019, despite its highly developed healthcare system. This may have stemmed from the advanced stages of GCAYA diagnosed in the USA, increasing incidence in females, and the striking health disparities observed in cancers,<sup>42</sup> which balanced the improvement of therapy strategies. In Japan, the MIR of GCAYA was continuously the lowest during the analysis period, while in South Korea, it was gradually close to that of Japan starting in 2008. This phenomenon indicates that the most effective strategy to decrease the mortality of GCAYA is

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screening and early diagnosis. Therefore, according to recent studies, the prevalence of early GC rose from 28.6% in 1995 to 58.0% in 2007 in South Korea, and a 57% GC mortality rate reduction was attributed to endoscopic screening in Japan.<sup>43 44</sup>

Despite the decline in incidence and mortality of GCAYA in South Korea and Japan throughout the analysis period, the mortality tended to be stable in 2016. This implies that the effects of current prevention and screening programs for GC have reached their limitations in AYA. In addition, distinctive etiological characteristics have been recognized in GCAYA. Approximately 10% of GC cases showed familial clustering, which was more notable in GCAYA.<sup>45 46</sup> Up to 3% of GC cases are related to inherited cancer predisposition syndromes, including hereditary diffuse gastric cancer (HDGC), familial adenomatous polyposis (FAP), and Lynch syndrome, all of which predispose younger populations to GC development.<sup>47 48</sup> HDGC is an autosomal dominant syndrome arising from germline mutations in the tumor suppressor gene CDH1 and is characterized by the development of gastric cancers, predominantly the diffuse type and occurs in females at a young age.<sup>47 49</sup> These characteristics are consistent with diffuse gastric cancer and female predominance, reflecting the hereditary factors may contribute to the carcinogenesis of GCAYA. These hereditary factors are irreversible with current technological capabilities, and the best way to decrease the deaths caused by GC in these patients is precursor lesion detection by endoscopic surveillance and prophylactic total gastrectomy.<sup>47 50</sup> However, these specific cancer types still account for a minority of the total burdens caused by GCAYA. Other relevant opportunities to further improve the outcomes of GCAYA are worthwhile. Because the incidence of GC was low in AYA, endoscopic screening was considered to be associated with a low yield rate and not

cost-effective.<sup>51</sup> However, the burdens caused by GC are not small in AYA. Despite the significant decrease, GC still ranked first, fourth and fifth among all cancer types in AYA in South Korea, Japan and China, respectively, with regard to DALYs. Although it was relatively small, the burden caused by GCAYA in the USA increased from tenth in 1990 to ninth in 2019. In addition, as mentioned above, the AYA population has a long life expectancy and contributes greatly to society and the economy. Hence, prevention and screening among AYA in regions with a higher incidence of GC is worthwhile, and research into screening programs specifically in AYA is needed to determine the benefits and potential risks.

Our findings allow for a comprehensive estimation and comparison of the GCAYA burden among China, South Korea, Japan and the USA; however, several limitations exist, which were also described in studies using data from GBD 2019 and in studies on cancer incidence in AYA.<sup>10 15 17</sup> First, although GBD 2019 used many strategies to improve the data quality and comparability, they were obtained from selected registries and might not be accurate in reflecting the overall burden in some countries, particularly for countries where data are not available or are of poor quality, which may affect the integrity and accuracy of the data that we analyzed. Second, we were unable to analyze cardia and noncardia GC separately, two subtypes that have different risk factors and temporal incidence trends.<sup>52 53</sup> Third, the incidence and mortality were low and volatile, especially in the USA, which means that even the smallest change could lead to a significant analytical outcome, especially when determined with a very short duration. Despite these limitations, our study involved data retrieved from the GBD 2019, the best data currently available for a long time period. Our

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findings highlight the health burden of GCAYA and the effects of prevention and screening programs among GCAYA, as well as the need to increase awareness and resources for this neglected subpopulation.

Overall, we have offered a comprehensive analysis and comparison of the burden and temporal trends of GCAYA in China, Korea, South Japan and the USA. In the past three decades, the incidence and mortality of GCAYA have been declining significantly in South Korea and Japan. A falling trend also appeared for females in China in recent years, while a steadily slowly rising trend has been observed for females in the USA. Although not covered by prevention and screening programs, these variations in incidence and mortality of GCAYA may reflect variations in risk factors, cancer control strategies and treatment accessibility of GC among the four countries. Although GC is much less frequently diagnosed in AYA than in older populations, its effects remain considerable due to the long life expectancy of these individuals. Investigating the reasons behind the varying disease burden and changing trends of GCAYA across countrieswill inform inform recommendations for prevention measures and timely diagnosis specific to this underserved population to further decrease the GC burden.

Author contributions Conceptualisation: LJ and W-JS. Data curation: W-SL, ZY and FY. Formal analysis: W-SL, ZY, FY and LJ. Methodology: W-SL, W-JS and LJ. Software: LJ. Supervision: W-JS and LJ. Roles/Writing-original draft: All authors. LJ is responsible for the overall content as the guarantor.

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manuscript; and decision to submit the manuscript for publication.

Competing interests None declared.

Patient consent for publication All data in this study were anonymous and retrieved from the GBD 2019 database; therefore, informed consent was waived.

Ethics approval This study was approved by the Academic Committee of the Third Hospital of Mianyang (20190307).

Data availability statement Data are available in a public, open access repository. The data used in our study are available at the online Global Health Data Exchange query tool Lien (http://ghdx.healthdata.org/gbd-results-tool)

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#### Figure legends

Figure 1. The temporal trends of the age-standardized incidence rate (ASIR) for gastric cancer in adolescents and young adults by sex in China, South Korea, Japan and the USA from 1990 to 2019.

Figure 2. The temporal trends of the age-standardized mortality rate (ASMR) for gastric cancer in adolescents and young adults by sex in China, South Korea, Japan and the USA from 1990 to 2019.

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		New cases			Deaths		
		1990	2019	1990-2019 change (%)	1990	2019	1990-2019 change (% -39.25
China	Both	18 123	20 855	15.07	13 929	8 462	-39.25
	Male	9 803	14 005	42.86	7 464	5 508	
	Female	8 320	6 851	-17.66	6 465	2 955	-54.29
Korea	Both	1 921	797	-58.51	1 254	237	-81.10
	Male	904	352	-61.06	571	101	-82.31
	Female	1 017	445	-56.24	682	136	-80.06
Japan	Both	3 258	945	-70.99	1 239	273	-77.97
	Male	1 626	462	-71.59	538	131	-75.65
	Female	1 632	483	-70.40	700	142	-79.71
USA	Both	772	812	5.18	400	343	-14.25
	Male	450	441	-0.02	223	174	-21.97
	Female	322	370	14.91	177	169	-4.52
							-26.21 -54.29 -81.10 -82.31 -80.06 -77.97 -75.65 -79.71 -14.25 -21.97 -4.52

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Table 2. The temporal trend in the incidence rate of gastric of	cancer in adolescents and young adults fi	rom 1990-2019 in Ghina, South Korea, Japan and the
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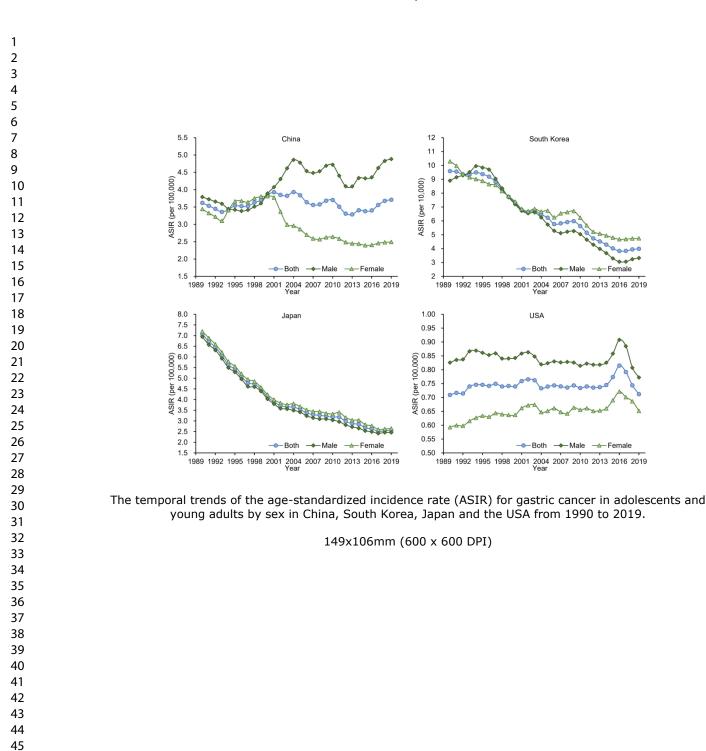
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Country	Sex	ASIR (pe	er 100 000)	Trends 1	1	Trends 2	1	Trends 3	July	1990-2019
		1990	2019	Years	APC (95% CI)	Years	APC (95% CI)	Years	ARC (95% CI)	AAPC (95% CI)
China	Both	3.62	3.71	1990-2004	0.9 (0.5, 1.3)	2004-2014	-1.6 (-2.3, -0.8)	2014-2019	2.4 (0.4-4.4)	0.3 (-0.1, 0.7)
	Male	3.79	4.88	1990-1997	-1.9 (-3.6, -0.1)	1997-2003	5.5 (2.3, 8.8)	2003-2019	-0ad (-0.6, 0.4)	0.6 (-0.2, 1.4)
	Female	3.44	2.49	1990-2000	1.8 (0.9, 2.6)	2000-2006	-6.1 (-8.3, -3.9)	2006-2019	-07 (-1.2, -0.1)	-1.0 (-1.6, -0.4)
Korea	Both	9.59	3.99	1990-1994	0.0 (-4.4, 4.5)	1994-2019	-3.7 (-4.0, -3.4)		n http:	-3.2 (-3.8, -2.6)
	Male	8.90	3.32	1990-1995	1.8 (-1.6, 5.3)	1995-2017	-5.0 (-5.4, -4.7)	2017-2019	2.5(-12.0, 19.3)	-3.4 (-4.5, -2.2)
	Female	10.29	4.74	1990-2019	-2.7 (-2.9, -2.5)	- CL			pen.bmj.cor	-2.7 (-2.9, -2.5)
Japan	Both	7.07	2.55	1990-2001	-5.3 (-5.7, -4.9)	2001-2019	-2.5 (-2.7, -2.3)		nj.con	-3.6 (-3.7, -3.4)
	Male	6.94	2.46	1990-2002	-5.2 (-5.5, -4.9)	2002-2017	-2.6 (-2.8, -2.4)	2017-2019	0.29(-4.6, 5.2)	-3.5 (-3.8, -3.2)
	Female	7.20	2.65	1990-2002	-5.1 (-5.4, -4.9)	2002-2011	-1.8 (-2.3, -1.2)	2011-2019	-3 <sup><u>L</u></sup> <sub>N</sub> (-3.6, -2.6)	-3.5 (-3.8, -3.3)
USA	Both	0.71	0.71	1990-2013	0.1 (-0.1, 0.2)	2013-2016	2.9 (-2.2, 8.2)	2016-2019	-4 <sup>N</sup> / <sub>4</sub> (-6.4, -3.4)	-0.1 (-0.6, 0.5)
	Male	0.83	0.77	1990-2013	-0.2 (-0.3, -0.1)	2013-2016	3.4 (-1.6, 8.6)	2016-2019	-5 (-7.3, -2.7)	-0.4 (-0.9, 0.2)
	Female	0.59	0.65	1990-2019	0.4 (0.3-0.5)				est. P	0.4 (0.3-0.5)

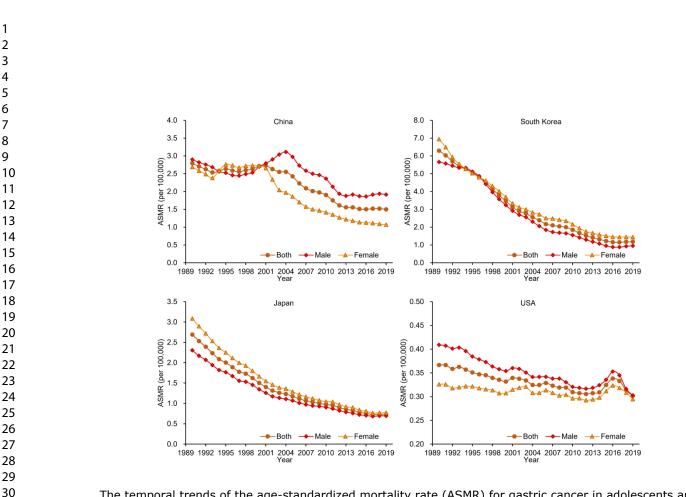
Abbreviations: AAPC, average annual percentage change; APC, annual percentage change; ASIR, age-standardized incidence rate of the py copyright.

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JSA. Country	Sex	ASMR (p	er 100 000)	Trends 1		Trends 2		Trends 3	n 21 July	1990-2019
		1990	2019	Years	APC (95% CI)	Years	APC (95% CI)	Years	NAPC (95% CI)	AAPC (95% C
China	Both	2.80	1.50	1990-2003	0.0 (-0.4, 0.3)	2003-2013	-5.1 (-5.7, -4.4)	2013-2019	<b>Q</b> 0.8 (-2.0, 0.5)	-2.0 (-2.3, -1.6)
	Male	2.90	1.91	1990-1997	-2.7 (-4.8, -0.5)	1997-2003	3.8 (0.0-7.8)	2003-2019	3.5 (-4.1, -2.9)	-1.8 (-2.7, -0.9)
	Female	2.69	1.07	1990-2000	0.8 (0.0-1.6)	2000-2007	-7.9 (-9.5, -6.3)	2007-2019	ਰ ਰੂੱ3.3 (-3.9, -2.8)	-3.1 (-3.6, -2.6)
Korea	Both	6.29	1.18	1990-1995	-4.6 (-6.7, -2.4)	1995-2016	-6.8 (-7.0, -6.5)	2016-2019	<b>3</b> .9 (-4.0, 6.1)	-5.6 (-6.2, -5.0)
	Male	5.66	0.95	1990-1994	-1.1 (-5.1, 3.0)	1994-2016	-7.8 (-8.1, -7.5)	2016-2019	<u>.</u> .9 (-4.5, 8.7)	-6.0 (-6.8, -5.2)
	Female	6.94	1.44	1990-2016	-5.8 (-6.0, -5.6)	2016-2019	0.5 (-4.3, 5.5)		pen.b	-5.2 (-5.7, -4.7)
Japan	Both	2.69	0.73	1990-2003	-5.6 (-5.8, -5.4)	2003-2017	-3.8 (-4.0, -3.6)	2017-2019	<u>3</u> . <u>6</u> 0.0 (-3.9, 3.9)	-4.4 (-4.7, -4.1)
	Male	2.30	0.69	1990-2003	-5.2 (-5.5, -5.0)	2003-2017	-3.6 (-3.8, -3.4)	2017-2019	g.0 (-3.3, 5.5)	-4.0 (-4.3, -3.7)
	Female	3.08	0.77	1990-2003	-5.9 (-6.1, -5.7)	2003-2017	-4.1 (-4.3, -3.9)	2017-2019	<u>u</u> ≤0.6 (-4.6, 3.6)	-4.7 (-4.9, -4.4)
USA	Both	0.37	0.30	1990-2013	-0.8 (-0.9, -0.7)	2013-2016	3.6 (0.3, 6.9)	2016-2019	No. 10, 10, 10, 10, 10, 10, 10, 10, 10, 10,	-0.7 (-1.0, -0.3)
	Male	0.41	0.30	1990-2013	-1.2 (-1.2, -1.1)	2013-2016	4.2 (0.0, 8.7)	2016-2019	g g 5.0 (-7.0, -3.0)	-1.0 (-1.5, -0.6)
	Female	0.33	0.29	1990-2013	-0.4 (-0.5, -0.3)	2013-2016	2.9 (-1.6, 7.6)	2016-2019	-2.7 (-4.8, -0.5)	-0.3 (-0.8, 0.2)

Abbreviations: AAPC, average annual percentage change; APC, annual percentage change; ASMR, age-standardized mortality rate





The temporal trends of the age-standardized mortality rate (ASMR) for gastric cancer in adolescents and young adults by sex in China, South Korea, Japan and the USA from 1990 to 2019.

149x108mm (600 x 600 DPI)

# 36/bmjopen-2022-061038 on **Supplementary material** Gastric cancer incidence, mortality, and burden in adolescents and young adults: A time-trend analysis and comparison among China, South Korea, ıly 2022. Japan and the USA Supplementary Table 1. Disability-adjusted life years and its age-standardized rate of gastric cancer in adolescents and young adults, and percentage changes from 1990 to 2019 in China, South Korea, Japan and the USA. Supplementary Figure 1. Rank changes in disability-adjusted life years attributable to cancers in adolescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019. Supplementary Figure 2. The temporal trends of the mortality-to-incidence ratio (MIR) for gastric cancer in addlescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019. This supplementary material has been provided by the authors to give readers additional information about their work. en on .com/ on July 2, 2024 by guest. Protected by copyright

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ercentage ch	hanges				,e-stanuaru	nzed rate	of gastric cancer in adolescoents and young ad	Juits, and
		from 199 DALYs	0 to 2019 :	in China, South Korea	a, Japan and ASDR	1 the USA		
Country Sex		1990	2019	1990-2019 change (%)	1990	2019		
China Bot		779 909	475 977	-38.97	155.81	84.68	-45.65	
Mal		416 551	308 971	-25.83	160.93	107.71	-49.77 de	
		363 358	167 005	-50.04	150.31	60.78	1990-2019 change (%)       -45.65       -49.77       -59.56       -81.27       -83.08       -79.44       -72.37       -69.49       -74.55       -17.92       -25.35	
Korea Bot	oth	71 475	13 267	-81.44	355.99	66.67	-81.27	
Mal	ale	32 299	5 667	-82.45	317.60	53.75	-83.08	
Fen	emale	39 176	7 600	-80.60	395.55	81.26	-79.44	
Japan Bot	oth	68 962	15 367	-77.71	150.80	41.67	-72.37	
Mal	ale	30 060	7 399	-75.39	129.57	39.53	-69.49 P	
Fen	emale	38 903	7 969	-75.92	172.44	43.88	-74.55	
USA Bot	oth	22 359	19 233	-13.98	20.53	16.85	-17.92	
Mal	ale	12 413	9 778	-21.23	22.80	17.09	-25.35	
Fen	emale	9 946	9 455	-4.93	18.28	16.62		
obreviations: ASD	DR, age-st	andardized DA	LYs rate; DAL	Ys, disability-adjusted life years.			-9.08 Protected by copyright.	

36/bmjopen-2022-06103 South & Control & Contro

Rank         Cancer type           1         Liver cancer           2         Leukemia           3         Stomach cancer           4         Tracheal, bronchus, and lung cancer	Cancer type		South Korea 1990		en-2022-06103 the c	- 000 MWH-1001 (1
2 Leukemia 3 Stomach cancer	Leukemia	Change -43.35%	Rank Cancer type 1 Stemach cancer	Cancer ty Stomach cancer		-81.44%
	Liver cancer	-58.76%	2 Leukemia	Leukemia	N	-68.11%
	Tracheal, bronchus, and lung cance Colon and rectum cancer	r -11.12% 21.07%	3 Tracheal, bronchus, and lung cancer 4 Brain and central nervous system cancer	Liver cancer Breast cancer		-19.95% -14.50%
5 Brain and central nervous system cancer	Stomach cancer	-38.97%	5 Colon and rectum cancer	Colon and rectum cancer		-35.97%
6 Colon and rectum cancer	Brain and central nervous system ca	ancer -13.19%	6 Liver cancer	Brain and central nervous	system cancer	-44.26%
7 Breast cancer 8 Nasopharvnx cancer	Breast cancer Non-Hodgkin lymphoma	0.27% 9.66%	7 Breast cancer 8 Non-Hodgkin lymphoma	Tracheal, bronchus, and lu Non-Hodgkin lymphoma	ng qancer	-56.59% -48.67%
9 Non-Hodgkin lymphoma	Cervical cancer	-1.61%	9 Cervical cancer	Cervical cancer		-62.46%
10 Cervical cancer	Pancreatic cancer	59.32%	10 Pancreatic cancer	Pancreatic cancer		-36.88%
11 Esophageal cancer 12 Pancreatic cancer	Nasopharynx cancer Esophageal cancer	-48.79% -39.08%	11 Gallbladder and biliary tract cancer 12 Ovarian cancer	Ovarian cancer Gallbladder and biliary trac		-14.79% -62.64%
13 Hodgkin lymphoma	Ovariah cancer	1.36%	13 Uterine cancer	Kidney cancer		26.23%
14 Ovarian cancer	Kidney cancer	103.02%	14 Esophageal cancer	Thyroid cancer		93.90%
15 Uterine cancer 16 Bladder cancer	Lip and oral cavity cancer Gallbladder and biliary tract cancer	-8.01%	15 Lip and oral cavity cancer 16 Nasopharynx cancer	Lip and oral cavity cancer Malignant skin melanoma		-12.48% -7.60%
17 Lip and oral cavity cancer	Bladder cancer	-30.63%	17 Kidney cancer	Nasopharynx cancer	oao	-47.10%
18 Gallbladder and biliary tract cancer 19 Kidney cancer	Uterine cancer	-44.69%	18 Larynx cancer	Hodgkin lymphoma		-27.32%
20 Malignant skin melanoma	Multiple myeloma Malignant skin melanoma	82.61% -12.38%	19 Non-melanoma skin cancer 20 Malignant skin melanoma	Uterine cancer Esophageal cancer		-76.01% -76.20%
21 Larynx cancer	Testicular cancer	-2.82%	21 Hodgkin lymphoma	Testicular cancer	2	-22.69%
22 Testicular cancer 23 Thyroid cancer	Non-melanoma skin cancer	6.00%	22 Bladder cancer	Bladder cancer	m	-40.75%
23 Thyroid cancer 24 Non-melanoma skin cancer	Hodgkin lymphoma Thyroid cancer	-72.84%	23 Thyroid cancer 24 Testicular cancer	Multiple myeloma Non-melanoma skin cance		-2.87% -69.69%
25 Multiple myeloma	Larynx cancer	-45.66%	25 Multiple myeloma	Prostate cancer	<u> </u>	-18.80%
26 Other pharynx cancer 27 Prostate cancer	Mesothelioma Prostate cancer	6.49% -6.89%	26 Prostate cancer 27 Mesothelioma	Larynx cancer	0:/	-77.88%
28 Mesothelioma	Other pharynx cancer	-43.39%	27 Mesothelioma 28 Other pharynx cancer	Other pharynx cancer Mesothelioma	6	-0.22% -10.94%
Japan 1990	Japan 201		USA 1990		2229	
Rank Cancer type	100000-0000000000000000000000000000000	5				
	Cancor turo	Change		Capacette	ne 若 🗠	nange
1 Stomach cancer	Cancer type	Change -66.32%	Rank         Cancer type           1         Breast cancer	Breast cancer		-37.71%
1 Stomach cancer 2 Leukemia	Leukemia Breast cancer	-66.32% -39.26%	1 Breast cancer 2 Leukemia	Breast cancer Leukemia	en.	-37.71% -32.70%
1 Stomach cancer 2 Leukemia 3 Colon and rectum cancer	Leukemia Breast cancer Colon and rectum cancer	-66.32% -39.26% -42.71%	Breast cancer     Leukemia     Brain and central nervous system cancer	Breast cancer Leukemia Brain and central nervous s	en.	-37.71% -32.70% -14.39%
1 Stomach cancer 2 Leukemia 3 Colon and rectum cancer 4 Breast cancer 5 Tracheal, bronchus, and lung cancer	Leukemia Breast cancer	-66.32% -39.26% -42.71% -77.72% ancer -11.78%	Breast cancer     Leukemia     Brain and central nervous system cancer     Non-Hodgkin lymphoma     Tracheal, bronchus, and lung cancer	Breast cancer Leukemia Brain and central nervous s Colon and rectum cancer Non-Hodgkin lymphoma	encer	-37.71% -32.70% -14.39% 9.37% -52.12%
1 Stomach cancer 2 Leukernia 3 Colon and rectum cancer 4 Breaat cancer 5 Tracheal, bronchus, and lung cancer 6 Non-Hodgkin lymphoma	Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system ca Tracheal, bronchus, and lung cance	-66.32% -39.26% -42.71% -77.72% ancer -11.78% or -56.37%	I Breast cancer     Leukemia     Leukemia     Brein and central nervous system cancer     Non-Hodgkin lymphoma     Tracheal, bronchus, and lung cancer     Colon and rectum cancer	Breast cancer Leukenia Brain and central nervous s Colon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lu	ng cancer	-37.71% -32.70% -14.39% 9.37% -52.12% -51.25%
1 Stomach cancer 2 Leukemia 3 Colon and rectum cancer 4 Broast cancer 5 Tracheal, bronchus, and lung cancer 6 Non-Hodgkin lymphoma 7 Brain and central nervous system cancer	Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system ca Tracheal, bronchus, and lung cance Cervical cancer	-66.32% -39.26% -42.71% -77.72% ancer -11.78% m -56.37% -5.93%	Breast cancer     Leukemia     Brain and central nervous system cancer     Non-Hodgkin lymphoma     Tracheal, bronchus, and lung cancer	Breast cancer Leukemia Brain and central nervous i Colon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lu Cervical cancer	eystem cancer	-37.71% -32.7% -14.39% 9.37% -52.12% -51.25% -25.18%
Stomach cancer     Leukemia     Leukemia     Colon and rectum cancer     Breast cancer     Tracheal, bronchus, and lung cancer     Non-Hodgkin lymphoma     Brain and cantral nervous system cancer     Liver cancer     Ovarian cancer	Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system ca Tracheal, bronchus, and lung cance Cervical cancer Non-Hodgkin lymphoma Ovarian cancer	-66.32% -39.26% -42.71% -77.72% ancer -11.78% or -56.37% -59.34% -42.03%	Breast cancer           Leukemia           Brain and central nervous system cancer           Mon-Hodgkin lymphoma           Tracheal, bronchus, and lung cancer           Coho and rectum cancer           Malignant skin melanoma           Cervical cancer           Hodgkin lymphoma	Breast cancer Leukemia Brain and central nervous I Colon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and u Cervical cancer Malignant skin melanoma Stomach cancer	en ancer system cancer ng coocer	-37.71% -32.70% -14.39% -9.37% -52.12% -52.12% -25.18% -32.37% -13.98%
1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and cantral nervous system cancer           8         Liver cancer           9         Ovarian cancer           10         Cervical cancer	Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system ca Tracheal, bronchus, and lung cance Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer	-66.32% -39.26% -42.71% -77.72% ancer -11.78% or -56.37% -59.14% -29.03% -59.14%	1         Breast cancer           2         Lexkemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer	Breast cancer Leukemia Brain and central nervous s Colon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lu Cervical cancer Malignant skin melanoma Stomach cancer Ovarian cancer	en	37.71% -32.70% 9.37% -52.12% -51.25% -32.37% -32.37% -13.89% -25.87%
Stomach cancer     Leukemia     Leukemia     Colon and rectum cancer     Breast cancer     Tracheal, bronchus, and lung cancer     Non-Hodgkin lymphoma     Brain and cantral nervous system cancer     Liver cancer     Ovarian cancer	Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system ca Tracheal, bronchus, and lung cance Cervical cancer Non-Hodgkin lymphoma Ovarian cancer	-66.32% -39.26% -42.71% -77.72% ancer -11.78% or -56.37% -59.34% -42.03%	Breast cancer           Leukemia           Brain and central nervous system cancer           Mon-Hodgkin lymphoma           Tracheal, bronchus, and lung cancer           Coho and rectum cancer           Malignant skin melanoma           Cervical cancer           Hodgkin lymphoma	Breast cancer Leukemia Brain and central nervous I Colon and rectum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and u Cervical cancer Malignant skin melanoma Stomach cancer	vyster Cancer	-37.71% -32.70% -14.39% -9.37% -52.12% -52.12% -25.18% -32.37% -13.98%
1         Stomach cancer           2         Leukamia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           8         Liver cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancreatic cancer           12         Testicular cancer           13         Galtbadder and biling tract cancer	Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system ca Tracheal, bronchus, and lung cance Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Pancreatic cancer Lip and grai davity cancer Testicular cancer	-66.32% -39.26% -42.71% -77.72% ancer -11.78% or -56.37% -50.14% -42.03% -59.98% -39.78% -1.60%	1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Mailgnant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer           12         Testicular cancer           13         Pancreatic cancer           14         Poratice cancer	Breast cancer     Leukemia     Brain and central nervous 1     Colon and reckum cancer     Non-Hodgkin lymphoma     Tracheal, bronchus, and lu     Cervical cancer     Malignant skin melanoma     Stomach cancer     Hodgkin lymphoma     Pancreatic cancer     Liver cancer     Liver cancer	en. yystationcer ing com/on July	37.71% 32.70% 9.37% 52.12% 51.25% 52.518% 32.37% 13.98% 57.47% 1.41% 28.11%
1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breaat cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancreatic cancer           12         Testicular cancer           13         Galibladder and billary tract cancer           14         Lipa and onal cavity cancer	Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system ca Carvical cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Pancreatic cancer Up and roat cavity cancer Tasticular cancer Kidney cancer Kidney cancer	-66.32% -30.26% -42.71% -77.72% ancer -11.7.8% -56.37% -59.14% -42.03% -59.9% -59.8% -1.60% -1.60% -56.8%	1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracteal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer           12         Testicular cancer           13         Pancreatic cancer           14         Kiloney cancer	Breast cancer Leukemia Brain and central nervous r Colon and rectum cancer Non-Hodgkin lympioma Tracheal, bronchus, and lu Cervical cancer Malignant skin melanoma Stomach cancer Ovarian cancer Hodgkin lymphoma Pancreatic cancer Liver cancer Testicular cancer	en ng coor ng coor ny	37 71% 32 70% -14.39% 9.37% -52.12% -51.25% -25.18% -32.37% -13.98% -25.87% -57.47% 1.41% -28.11% -24.96%
1         Stomach cancer           2         Leukamia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           8         Liver cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancreatic cancer           12         Testicular cancer           13         Galtbadder and biling tract cancer	Leukemia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system ca Cervicel cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Parceatic cancer Lip and rait cavity cancer Testicular cancer Kidney cancer Uterine cancer	-66.32% -39.26% -42.71% -77.72% ancer -11.78% or -56.37% -50.14% -42.03% -59.98% -39.78% -1.60%	1         Breast cancer           2         Leukemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Mailgnant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer           12         Testicular cancer           13         Pancreatic cancer           14         Poratice cancer	Breast cancer Leukemia Brain and central nervous r Colon and reckum cancer Non-Hodgkin lymphoma Tracheal, bronchus, and lu Genvical cancer Malignant skin melanoma Stomach cancer Hodgkin lymphoma Pancreatic cancer Liver cancer	en and and and and and and and and and an	37.71% 32.70% 9.37% 52.12% 51.25% 52.51% 13.98% 57.47% 1.41% 28.11%
1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancreatic cancer           12         Testicular cancer           13         Galibladder and billary tract cancer           14         Lip and canl call y cancer           15         Kidney cancer           16         Mailgnant skin melanoma           16         Hodgkin lymphoma	Leukemia Breast cancer Colon and ractum cancer Stomach cancer Brain and central nervous system ca Carvicel cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Pancreatic cancer User cancer Pancreatic cancer Carviel cancer Handrower Handrower User cancer Carviel cancer Calibiadder and bilary tract cancer Malignant skin melanoma	-66.32% -30.26% -42.71% -77.72% ancer -11.78% w -56.37% -59.14% -59.3% -59.4% -42.03% -58.8% -39.78% -1.60% -56.88% -23.47% 13.22% -57.19% -84.33%	1         Breast cancer           2         Leakemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer           12         Testicular cancer           13         Pancreatic cancer           14         Kidney cancer           15         Liver cancer           16         Lip and oral cavity cancer           17         Esciphageal cancer	Breast cancer     Leukemia     Brain and central nervous 1     Colon and rectum cancer     Non-Hodgkin lymphoma     Tracheal, bronchus, and lu     Cervical cancer     Malignant skin melanoma     Stomach cancer     Ovarian cancer     Hodgkin lymphoma     Pancreatic cancer     Liver cancer     Testicular cancer     Kidney cancer     Espohageal cancer     Lip and orali cavity carcer	en ing @om/ on July 2, 20	37 71% 32.70% 9.37% 52.12% 51.25% 25.18% 32.37% 13.98% 25.87% 57.47% 1.41% 28.11% 24.96% -6.19% 7.17%
1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           8         Liver cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancreatic cancer           12         Testicular cancer           13         Galibladder and bilingy tract cancer           14         Lip and oral cavity cancer           15         Kidney cancer           16         Malignant skin melanoma           17         Hodgkin lymphoma           18         Esophageal cancer	Leukenia Breast cancer Colon and rectum cancer Stomach cancer Brain and central nervous system ca Tracheal, bronchus, and lung cance Cervical cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Encreatic cancer Lip and oral cavity cancer Tasticular cancer Kidney cancer Uterine cancer Gallbladder and biliary tract cancer Malignart skin melanoma Hodgkin lymphoma	-66.32% -39.26% -42.71% -77.72% arcet -11.78% or -56.37% -50.14% -42.03% -50.98% -30.78% -30.78% -30.78% -33.78% -33.78% -33.78% -33.78% -33.78% -33.74% -33.43% -35.14%	Ereast cancer           Leukemia           Brain and central nervous system cancer           Non-Hodgkin lymphoma           Tracheal, bronchus, and lung cancer           Colon and rectum cancer           Malignant skin melanoma           Cervical cancer           Hodgkin lymphoma           Colon and rectum cancer           Hodgkin lymphoma           Coraca cancer           Testicular cancer           Testicular cancer           Kidney cancer           Lip and oral cavity cancer           Lip and oral cavity cancer           Explagad cancer           Non-melanoma skin cancer	Breast cancer Leukemia Brain and central nervous 1 Colon and rectum cancer Non-Hodykin lymphoma Tracheal, bronchus, and lu Genvical cancer Malignant skin melanoma Stomach cancer Ovarian cancer Hodykin lymphoma Pancreatic cancer Liver cancer Testicular cancer Kidney cancer Esophageal cancer Lip and oral cavity cancer Lip and oral cavity cancer	en.aptancer ng gom/ on July 2, 202	37.71% 32.70% 9.37% 52.12% 51.25% 52.51% 53.23% 55.81% 57.47% 1.41% 28.11% -24.96% 4.19% 7.17% 7.17%
1         Stomach cancer           2         Leukemia           3         Colon and rectum cancer           4         Breast cancer           5         Tracheal, bronchus, and lung cancer           6         Non-Hodgkin lymphoma           7         Brain and central nervous system cancer           9         Ovarian cancer           10         Cervical cancer           11         Pancreatic cancer           12         Testicular cancer           13         Galibladder and billary tract cancer           14         Lip and canl call y cancer           15         Kidney cancer           16         Mailgnant skin melanoma           16         Hodgkin lymphoma	Leukemia Breast cancer Colon and ractum cancer Stomach cancer Brain and central nervous system ca Carvicel cancer Non-Hodgkin lymphoma Ovarian cancer Liver cancer Pancreatic cancer User cancer Pancreatic cancer Carviel cancer Handrower Handrower User cancer Carviel cancer Calibiadder and bilary tract cancer Malignant skin melanoma	-66.32% -30.26% -42.71% -77.72% ancer -11.78% r -56.37% -59.14% -42.03% -59.89% -59.89% -30.78% -16.0% -56.88% -23.47% -13.22% -57.19% -18.43% -35.14% -42.16%	1         Breast cancer           2         Leakemia           3         Brain and central nervous system cancer           4         Non-Hodgkin lymphoma           5         Tracheal, bronchus, and lung cancer           6         Colon and rectum cancer           7         Malignant skin melanoma           8         Cervical cancer           9         Hodgkin lymphoma           10         Stomach cancer           11         Ovarian cancer           12         Testicular cancer           13         Pancreatic cancer           14         Kidney cancer           15         Liver cancer           16         Lip and oral cavity cancer           17         Esciphageal cancer	Breast cancer     Leukemia     Brain and central nervous 1     Colon and rectum cancer     Non-Hodgkin lymphoma     Tracheal, bronchus, and lu     Cervical cancer     Malignant skin melanoma     Stomach cancer     Ovarian cancer     Hodgkin lymphoma     Pancreatic cancer     Liver cancer     Testicular cancer     Kidney cancer     Espohageal cancer     Lip and orali cavity carcer	en usite transmission on July 2, 2024	37 71% 32.70% 32.70% 9.37% 52.12% 51.25% 25.18% 32.37% 13.38% 25.87% 57.47% 14.1% 28.11% 24.96% -6.19% 7.17% -22.85%
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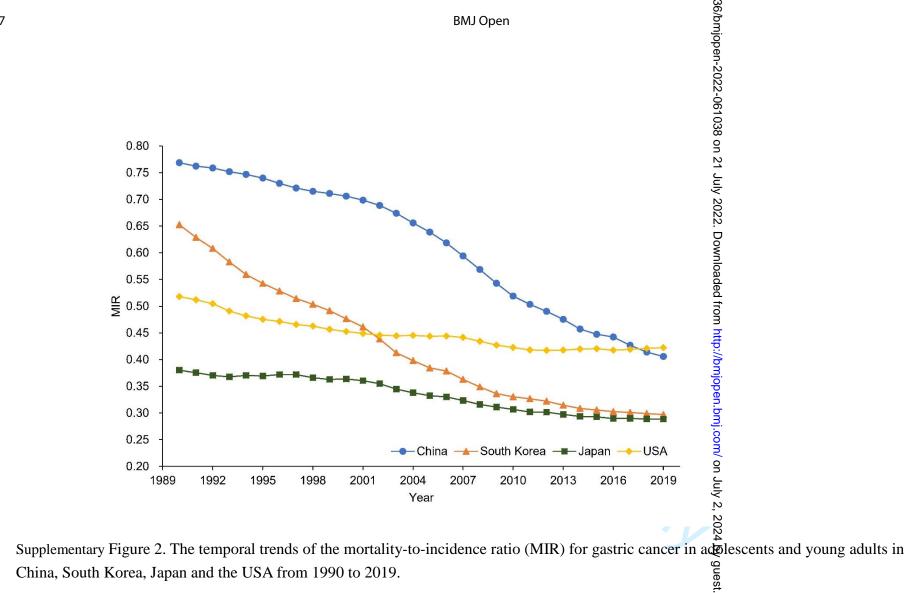
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Supplementary Figure 2. The temporal trends of the mortality-to-incidence ratio (MIR) for gastric cancer in adolescents and young adults in China, South Korea, Japan and the USA from 1990 to 2019.

## Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below. Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation. Upload your completed checklist as an extra file when you submit to a journal. In your methods section, say that you used the STROBE cross sectional reporting guidelines, and cite them as: von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Page Reporting Item Number Title and abstract Title #1a Indicate the study's design with a commonly used term in the title or the abstract Abstract #1b Provide in the abstract an informative and balanced summary 2.3

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1 2			of what was done and what was found	
3 4 5	Introduction			
6 7 8	Background /	<u>#2</u>	Explain the scientific background and rationale for the	4
9 10 11	rationale		investigation being reported	
11 12 13	Objectives	<u>#3</u>	State specific objectives, including any prespecified	4,5
14 15 16			hypotheses	
17 18 19	Methods			
20 21 22	Study design	<u>#4</u>	Present key elements of study design early in the paper	5
23 24 25	Setting	<u>#5</u>	Describe the setting, locations, and relevant dates, including	5
26 27			periods of recruitment, exposure, follow-up, and data collection	
28 29 30	Eligibility criteria	<u>#6a</u>	Give the eligibility criteria, and the sources and methods of	5
31 32 33			selection of participants.	
34 35		<u>#7</u>	Clearly define all outcomes, exposures, predictors, potential	5
36 37 38			confounders, and effect modifiers. Give diagnostic criteria, if	
39 40			applicable	
41 42 43	Data sources /	<u>#8</u>	For each variable of interest give sources of data and details of	5
44 45	measurement		methods of assessment (measurement). Describe	
46 47			comparability of assessment methods if there is more than one	
48 49 50			group. Give information separately for for exposed and	
51 52 53			unexposed groups if applicable.	
53 54 55 56	Bias	<u>#9</u>	Describe any efforts to address potential sources of bias	n/a
57 58	Study size	<u>#10</u>	Explain how the study size was arrived at	n/a
59 60		For pe	eer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

1 2	Quantitative	<u>#11</u>	Explain how quantitative variables were handled in the	5
3 4	variables		analyses. If applicable, describe which groupings were chosen,	
5 6 7			and why	
8 9 10	Statistical	<u>#12a</u>	Describe all statistical methods, including those used to control	6
11 12 13	methods		for confounding	
14 15	Statistical	<u>#12b</u>	Describe any methods used to examine subgroups and	6
16 17 18	methods		interactions	
19 20	Statistical	<u>#12c</u>	Explain how missing data were addressed	n/a
21 22 23 24	methods			
24 25 26	Statistical	<u>#12d</u>	If applicable, describe analytical methods taking account of	6
27 28 29	methods		sampling strategy	
30 31	Statistical	<u>#12e</u>	Describe any sensitivity analyses	n/a
32 33 34	methods			
35 36	Results			
37 38				07
39 40	Participants	<u>#13a</u>	Report numbers of individuals at each stage of study—eg	6,7
41 42			numbers potentially eligible, examined for eligibility, confirmed	
43 44			eligible, included in the study, completing follow-up, and	
45 46			analysed. Give information separately for for exposed and	
47 48 49			unexposed groups if applicable.	
50 51 52	Participants	<u>#13b</u>	Give reasons for non-participation at each stage	n/a
53 54 55	Participants	<u>#13c</u>	Consider use of a flow diagram	n/a
56 57 58	Descriptive data	<u>#14a</u>	Give characteristics of study participants (eg demographic,	6,7
59 60		For pe	er review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

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1 2			clinical, social) and information on exposures and potential	
3 4			confounders. Give information separately for exposed and	
5 6 7			unexposed groups if applicable.	
7 8 9	Descriptive data	<u>#14b</u>	Indicate number of participants with missing data for each	n/a
10 11 12			variable of interest	
13 14	Outcome data	<u>#15</u>	Report numbers of outcome events or summary measures.	6-10
15 16 17			Give information separately for exposed and unexposed	
17 18 19			groups if applicable.	
20 21	Main results	<u>#16a</u>	Give unadjusted estimates and, if applicable, confounder-	n/a
22 23 24			adjusted estimates and their precision (eg, 95% confidence	
25 26			interval). Make clear which confounders were adjusted for and	
27 28 29			why they were included	
30 31 32	Main results	<u>#16b</u>	Report category boundaries when continuous variables were	6-10
33 34 35			categorized	
36 37	Main results	<u>#16c</u>	If relevant, consider translating estimates of relative risk into	n/a
38 39 40			absolute risk for a meaningful time period	
41 42	Other analyses	<u>#17</u>	Report other analyses done—e.g., analyses of subgroups and	6-10
43 44 45			interactions, and sensitivity analyses	
46 47	Discussion			
48 49				
50 51 52	Key results	<u>#18</u>	Summarise key results with reference to study objectives	10
53 54	Limitations	<u>#19</u>	Discuss limitations of the study, taking into account sources of	14,15
55 56 57			potential bias or imprecision. Discuss both direction and	
57 58			magnitude of any potential bias.	
59 60		For pe	er review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

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1 2	Interpretation	<u>#20</u>	Give a cautious overall interpretation considering objectives,	10-15
3 4			limitations, multiplicity of analyses, results from similar studies,	
5 6 7			and other relevant evidence.	
8 9 10	Generalisability	<u>#21</u>	Discuss the generalisability (external validity) of the study	15
11 12 13			results	
13 14 15	Other Information			
16 17				
18 19	Funding	<u>#22</u>	Give the source of funding and the role of the funders for the	15,16
20 21			present study and, if applicable, for the original study on which	
22 23			the present article is based	
24 25 26 27 28	None The STROBE checklist is distributed under the terms of the Creative Commons Attribution			
	License CC-BY. This checklist can be completed online using <u>https://www.goodreports.org/</u> , a tool			
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