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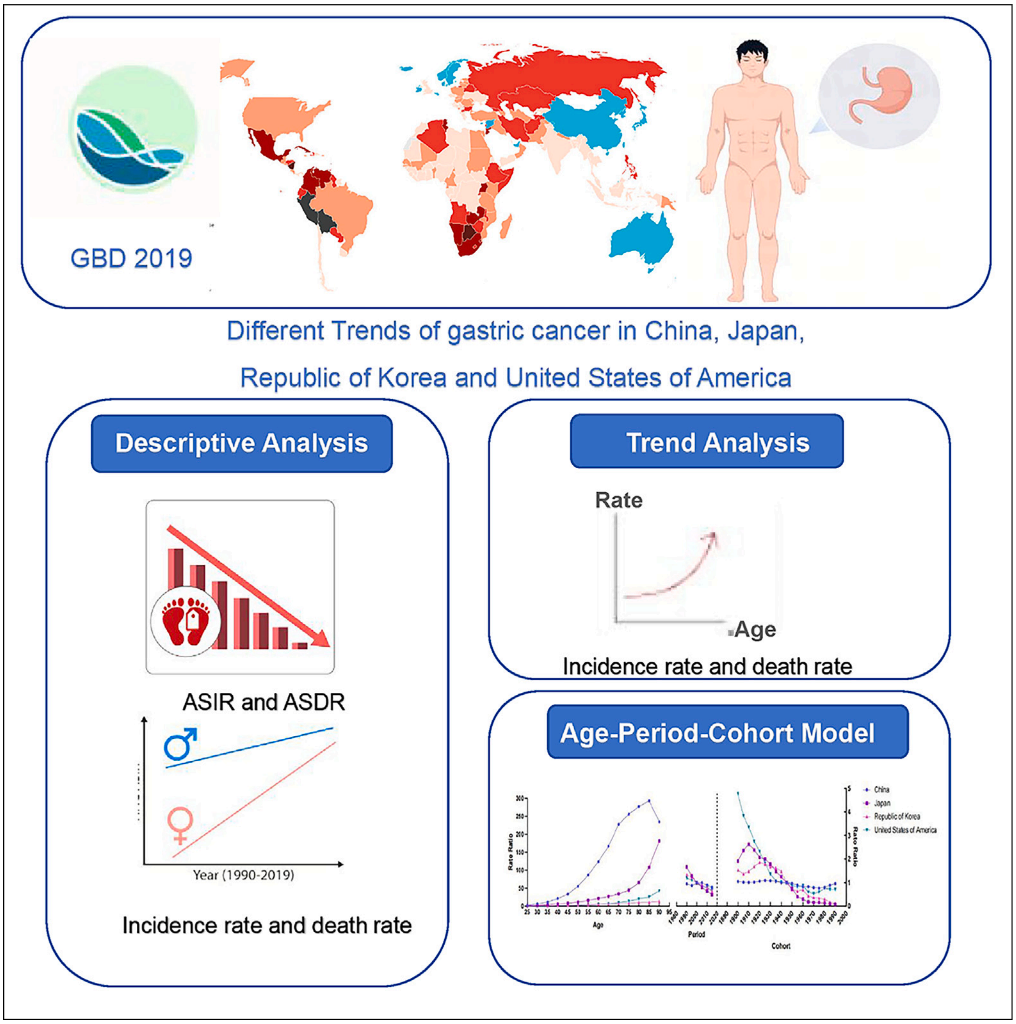

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Highlights

Gastric cancer exhibits large geographic heterogeneity in its epidemiology

The absolute number of new cases and deaths from GC has increased

The ASIR and ASDR of GC have declined in recent years

The study assesses the burden of GC and makes comprasions between four countries

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Different trends of gastric cancer in China, Japan, Republic of Korea and United States of America

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SUMMARY

Gastric cancer exerts a significant healthcare burden worldwide and is highly geographically heterogeneous. This study investigates the burden of gastric cancer in China from 1990 to 2019 and compares it with Japan, South Korea, and the United States. The results indicated a declining trend in ASIR and ASDR in four countries. However, the incidence and death rates in China remain disproportionately high. Significant gender disparities exist in the incidence and death rates, with males experiencing significantly higher rates than females. Incidence and death rates were found to increase with age in all studied countries. In China, a transient upward trend was observed in the period effect, whereas the cohort effect has been declining. In contrast, the remaining countries showed decreasing patterns in both period and cohort effects. The burden of disease remains high in China, therefore, broaden the scope of gastroscopy screening and concentrate on high-risk groups is vital.

INTRODUCTION

Gastric cancer is categorized into cardia and non-cardia tumors based on the proximity of the tumor to the gastroesophageal junction (cardia).[1] Non-cardia tumors are often associated with Helicobacter pylori infection.[2] It is estimated that most adults will contract a Helicobacter pylori infection at some point in their lives,[3] contributing to non-cardia gastric cancer. Studies suggest that an improved socioeconomic status, better hygiene practices, and widespread antibiotic use may be linked to declining Helicobacter pylori infection rates.[4] Additionally, the consumption of salt and salt-cured foods may enhance the risk of gastric cancer.[5]

Gastric cancer, one of the world's most prevalent cancers, is diagnosed in over a million patients globally each year.[6] While the absolute number of new cases and deaths from gastric cancer has increased in recent years,[7] its Age-Standardized Rate (ASR), including incidence and deaths, has declined.[8]

Besides, based on data from GLOBCAN and GBD 2019, only a few countries showed an increased trend in the incidence of gastric cancer in adolescents and young adults, while the mortality decreased in nearly all countries.[9,10] Korea has the highest proportion of young patients with gastric cancer, with 15% diagnosed before the age of 45.[11] Other studies suggest that the incidence of gastric cancer is also increasing among the young population in the United States.[12,13] Early-onset gastric cancer (diagnosed under 40 years of age) significantly differs from traditional late-onset gastric cancer (diagnosed over 40 years of age) in terms of genetics, proteomics, and clinical features,[14–16] exhibiting more diffuse, metastatic, and invasive histologic features, molecular heterogeneity, and poorer prognosis.[16]

Despite the improvement in the survival rate of gastric cancer in the past decades, the prognosis remains poor, with a 5-year survival rate of approximately 20%.[17] Nevertheless, Japan[18] and Korea[19] have relatively high survival rates of 65% and 71.5%, respectively, which may be due to early screening.[20]

The geographic distribution of gastric cancer is highly heterogeneous, and there can be a 5- to 10-fold difference in incidence between high- and low-risk countries.[21] China, the country with the largest population base, has a significantly higher number of new cases than the rest of the world,[22] accounting for nearly half of the global cases.[7] Gastric cancer also imposes the most significant burden among digestive tract cancers in China. Furthermore, China is currently facing unprecedented population aging, which poses a considerable challenge to digestive tract cancer prevention.[23]

In light of the low survival and high burden of gastric cancer, this study assesses the burden of gastric cancer in China using data from the Global Burden of Disease (GBD) 2019, describing trends from 1990 to 2019, and comparing these trends with Japan, the United States, and South Korea. This information can help inform global and local interventions, potentially curbing the increasing number of incidence and death cases.

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RESULTS

Incidence and mortality of gastric cancer in China, Japan, United States of America, and Republic of Korea

In China, the incidence of gastric cancer surged from 31.73/10000 in 1990 to 61.28/10000 in 2019. Gastric cancer primarily occurred in men, with a male-to-female ratio of 1.89 in 1990, rising to 2.80 in 2019. However, the age-standardized incidence rate (ASIR) dropped from 37.6/10000 in 1990 to 30.6/10000 in 2019, with an EAPC of −0.41 (−0.75–0.08). The ASIRs in Japan and Korea were comparable, but the number of new cases varied significantly. In 1990, there were approximately 10.34/10000 new cases in Japan (male-to-female ratio: 1.82) and 1.97/10000in Korea (male-to-female ratio: 1.81); in 2019, these figures stood at 10.22/10000 (male-to-female ratio: 1.91) in Japan and 2.51/10000 in Korea (male-to-female ratio: 1.92). The lowest ASIR was recorded in the United States (1990: 8.3/10000; 2019: 5.9/10000), with 2.69/10000 new cases in 1990 (male-to-female ratio: 2.09) and 3.21/10000 new cases in 2019 (male-to-female ratio: 1.59). Although all countries showed a decreasing trend in new gastric cancer cases, male patients in China displayed a stabilizing trend (EAPC: 0.14 (−0.19–0.48)). Moreover, the male-to-female incidence ratio increased in China, Japan, and Korea, with the exception of the United States, where it declined. (Table 1) (Figures 1, 2, and 3).

The number of deaths from gastric cancer in China rose from 30.55/10000 (male-to-female ratio: 1.82) in 1990 to 42.15/10000 (male-to-female ratio: 2.43) in 2019. Meanwhile, the age-standardized death rate (ASDR) decreased from 37.7/10000 in 1990 to 21.7/10000 in 2019, with an EPAC of −1.68 (-2.07–1.28). The number of deaths in Japan, Korea, and the United States remained relatively stable, with their ASDRs demonstrating a decreasing trend. Specifically, Japan's ASDR decreased from 32.2/10000 in 1990 to 14.1/10000 in 2019 (EPAC: −2.94 (−2.98–2.89)), while Korea's ASDR plummeted from 52.3/10000 in 1990 to 14.1/10000 in 2019 (EPAC: −5.26 (−5.49–5.04)). The ASDRs of Japan and Korea in 2019 were comparable. The US recorded the lowest ASDR (5.8/10000 in 1990 and 3.4/10000 in 2019), with an EPAC of −2.02 (−2.13–1.9). A decreasing trend was evident in gastric cancer deaths, with the most rapid decline seen in Korea. Furthermore, the proportion of males increased in all countries (Japan: 1.68 to 1.71; Korea: 1.74 to1.77; USA: 1.36 to 1.45). (Table 1) (Figures 1, 2, and 3).

Joinpoint Trends of Gastric Cancer ASRs by Sex in China, Japan, United States of America, and Republic of Korea

During the same period, significant heterogeneity in temporal trends of gastric cancer incidence emerged among China, Japan, Korea, and the United States. In China, the trends of ASIR and ASDR paralleled each other, initially sharply decreasing from 1990 to 1998, with an APC of −1.57(-1.73–1.45) ($p < 0.001$) and −2.02 (−2.32–1.72) ($p < 0.001$), respectively. Then, they showed an upward trend from 1998 to 2004, with APC values of 4.02 (3.33–4.72) ($p < 0.001$) and 3.01 (2.48–3.53) ($p < 0.001$). (Table 2) Subsequently, a decrease has been observed since 2004. Similar trend changes were evident in both male and female patients. Conversely, the ASIR and ASDR in Japan and the United States have consistently decreased regardless of gender. In Korea, the ASIR began to gradually decline from 1995 onwards. And the ASDR has consistently been showing a decreasing trend. (Table 2; Tables S1 and S2) (Figures S1 and S2).

Age-Period-Cohort Analyses for Gastric Cancer

Net Drift and Local Drift in Different Age Groups

Table 3 delineates the local and net drift in incidence rates for the four countries. The net drifts significantly differed among the countries. China showed a minimal decline between 1990 and 2019 (−0.4396 (−0.559 to −0.32)), whereas the largest decline was observed in Japan (−4.6574 (−4.7772 to −4.5375)). The declines in Korea were similar to those in the United States (−2.8681 (−3.0615 to −2.6743); −2.2945 (−2.3687 to −2.2201)). The downward trend of localized drift in gastric cancer incidence in China was weak, with the most substantial decline in the 45–49 age group (−0.975 (−1.1917 to −0.7578)), followed by the 50–54 age group, which was similar to Japan. Japan demonstrated a decreasing trend in all age groups, with the absolute value of localized drift greater than 1, except for the 90–94 age group. In contrast, Korea showed the most pronounced decrease in the younger age groups, particularly the 25–29 years old (−4.8144 (−6.4721 to −3.1272)) and 30–34 years old (−4.5296 (−5.4272 to −3.6235)), with a slight upward trend in the 85–89 age group (0.962 (0.1684–1.7619)). In the United States, there was a trend toward younger incidence rates, especially among the 25–29 years old, with a local drift of 1.1289 (0.4877–1.7742). However, there is a significant decrease in localized drift (absolute value > 3) in the older age group over 70 years, most noticeable in the 80–84 age group (−4.5202 (−4.6146 to −4.4257)). (Table 3).

In Japan and Korea, the net drift of mortality rates declined significantly, −5.150 (−5.311 to −4.988) and −5.295 (−5.496 to −5.094), respectively. In China and the United States, the net drift of mortality was −2.035 (−2.153 to −1.916) and −2.933 (−3.037 to −2.827), respectively. The localized drift is less than 0 for all age groups in all countries except for the United States. In China, the absolute value of localized drift less than 1 was concentrated in the age group of 80 years and above, while in Japan, it was dominated by the 90–94 age group, and in South Korea, it was dominated by the 85 years and older group. On the other hand, in the United States, it was dominated by the younger group, specifically the 25–34 years age group. (Table 3).

Age-Period-Cohort Effects on Gastric Cancer

In general, the incidence rate of stomach cancer escalates with age across all countries under review. This increase is most pronounced in China, with a surge from 2.766 to 292.871 per 100,000, closely followed by Japan, which reports an increase from 1.299 to 181.886 per 100,000 annually. Korea has also exhibited an increase, albeit at a comparatively steady pace. Predominantly, the high prevalence age in China falls between 85 and 89 years, whereas in the other three countries, it's primarily between 90 and 94 years.

Table 1. Incidence, mortality, corresponding age-standardized rates, and rate changes for gastric cancer in China, Japan, United States of America, and Republic of Korea, 1990-2019

		Incidence					Deaths				
Country	Sex	Num_1990 (/10000)	ASR_1990 (95%UI)	Num_2019 (/10000)	ASR_2019 (95%UI)	EAPC_CI (95%UI)	Num_1990 (/10000)	ASR_1990 (95%UI)	Num_2019 (/10000)	ASR_2019 (95%UI)	EAPC_CI (95%UI)
China	Both	31.73	37.6 (33.1–42.3)	61.28	30.6 (25.8–36.1)	−0.41 (−0.75–0.08)	30.55	37.7 (33.2–42.4)	42.15	21.7 (18.3–25.3)	−1.68 (−2.07–1.28)
	Male	20.75	51.1 (43–59.9)	45.13	47.3 (38–57.9)	0.14 (−0.19–0.48)	19.71	51.4 (43–59.9)	29.85	33.1 (26.7–39.9)	−1.17 (−1.56–0.79)
	Female	10.98	25.6 (21.5–29.6)	16.15	15.8 (12.8–19.4)	−1.6 (−1.93–1.26)	10.84	26.2 (21.9–30.4)	12.3	12.2 (9.9–14.9)	−2.59 (−2.99–2.19)
Japan	Both	10.34	61.2 (58.8–62.7)	10.22	28.3 (23.7–33.3)	−2.73 (−2.79–2.68)	5.33	32.2 (30.5–33)	5.72	14.1 (12.5–15)	−2.94 (−2.98–2.89)
	Male	6.67	90.6 (87.4–93)	6.72	42.2 (34.1–51.6)	−2.69 (−2.75–2.63)	3.34	47.8 (45.8–48.8)	3.61	21.3 (19.3–22.6)	−2.85 (−2.91–2.8)
	Female	3.67	39.1 (37–40.5)	3.51	16.9 (13.3–20.5)	−3.02 (−3.1–2.94)	1.99	21.2 (19.7–21.9)	2.11	8.4 (7–9.2)	−3.33 (−3.41–3.24)
Republic of Korea	Both	1.97	61.6 (58.7–64.5)	2.51	28.7 (23.7–34.2)	−3.24 (−3.51–2.97)	1.59	52.3 (50–55)	1.22	14.1 (12.6–15.6)	−5.26 (−5.49–5.04)
	Male	1.27	93.4 (87.6–99.7)	1.65	42.1 (34.6–50.5)	−3.32 (−3.63–3)	1.01	80.1 (75.3–85.9)	0.78	21.2 (18.9–23.8)	−5.27 (−5.5–5.04)
	Female	0.70	39.3 (37.2–41.4)	0.86	18.1 (14.9–21.6)	−3.35 (−3.59–3.11)	0.58	33.9 (32–35.8)	0.44	8.9 (7.7–10.2)	−5.43 (−5.71–5.16)
United States of America	Both	2.69	8.3 (8–8.5)	3.21	5.9 (5.1–6.9)	−1.4 (−1.49–1.32)	1.89	5.8 (5.5–6)	1.92	3.4 (3.2–3.5)	−2.02 (−2.13–1.9)
	Male	1.60	11.9 (11.5–12.2)	1.97	8 (6.5–9.7)	−1.63 (−1.73–1.54)	1.09	8.3 (7.9–8.5)	1.13	4.5 (4.3–4.7)	−2.27 (−2.41–2.13)
	Female	1.10	5.7 (5.3–5.9)	1.24	4.1 (3.4–5)	−1.28 (−1.36–1.2)	0.80	4.1 (3.8–4.2)	0.78	2.5 (2.3–2.6)	−1.88 (−1.97–1.79)

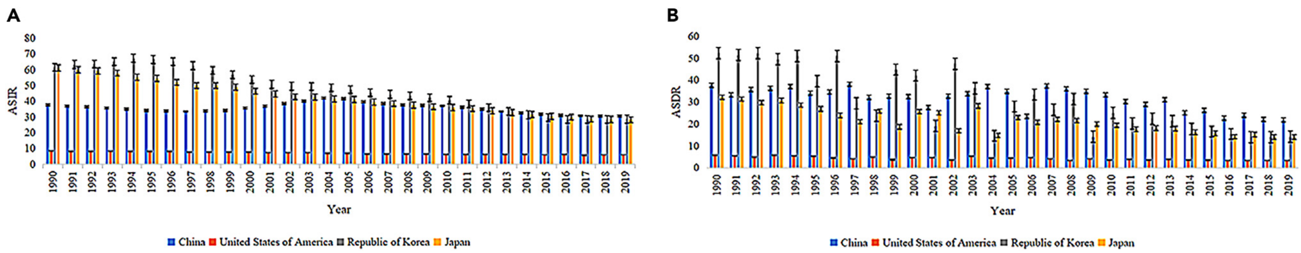

Figure 1. Age-standardized disease burden of gastric cancer among China, Japan, Republic of Korea, and United States of America from 1990 to 2019
(A) ASIR of gastric cancer among four countries from 1990 to 2019.
(B) ASDR of gastric cancer among four countries from 1990-201. ASIR, age-standardized incidence rate; ASDR, age-standardized death rate.

Excluding China, the period effects in the other countries have, on the whole, demonstrated a decrease over time. This decrease is most noteworthy in Japan, trailed by Korea and the United States. Conversely, China displayed a downward trend until 1999, had a brief surge during the 2005–2009 period, and has since been demonstrating a slow but steady decline. The cohort effect was found to positively influence the incidence of gastric cancer, the most substantial decline being observed in the United States (from 4.764 in 1900 to 0.713 in 1990), followed by Japan (from 1.911 in 1900 to 0.072 in 1990), and China, exhibiting a moderation trend (from 1.048 in 1900 to 0.958 in 1990) (Refer to Table 4; Figure 4).

In line with the incidence trend, death rates due to gastric cancer also amplified with age across all countries, most notably in China, where the high prevalence age group remains 85–89 years. This is followed by Japan, while the upward trend in Korea is comparatively moderate. The period effect diminished over time in all nations, most drastically in Korea, followed by Japan, while the downward trend was weakest in China. The cohort effect continued to have a positive impact on gastric cancer mortality rates, displaying the steepest decline in the United States (from 6.088 in 1900 to 0.521 in 1990), followed by Korea (from 3.791 in 1900 to 0.032 in 1990), and China, exhibiting a moderated decline (from 1.657 in 1900 to 0.344 in 1990). However, improvements in the cohort effect among younger generations appear to have slowed, if not stagnated (Refer to Table 4; Figure 5).

DISCUSSION

This study was designed to discern long-term trends in the incidence and death rates of gastric cancer in China, explore the potential age, period, and cohort influences on these trends, and draw comparisons with select developing and developed countries. Over the past three decades, new cases and deaths from gastric cancer in China have seen an increase, which may be associated with the rapid aging of the population.[24] The elderly, due to the deterioration of bodily functions, frail physical conditions, and the presence of underlying diseases, are susceptible to complications from various diseases, thereby facing a higher risk of death. Moreover, the high incidence of gastric cancer in Korea and Japan is closely associated with their dietary patterns. High salt diets can stimulate the gastric mucosa, resulting in atrophic gastritis, increased DNA synthesis and cell proliferation, thereby raising the risk of gastric cancer.[25]

Despite this, both the Age-Standardized Incidence Rates (ASIR) and Age-Standardized Death Rates (ASDR) exhibited an overall downward trend in China, Japan, Korea, and the United States. This trend may be linked to several factors: Infection rates of Helicobacter pylori have been decreasing, which can be attributed to improvements in socioeconomic conditions, health literacy, population screening, and vaccine development.[25–27] The degree of reduction, however, varies across different countries.

The results of the joinpoint analysis further reveal that the changes in ASIR and ASDR in China significantly differ from those in Japan, Korea, and the United States. Both ASIR and ASDR in China experienced a sequence of decreasing, increasing, and again decreasing trends. The incidence of gastric cancer in China increased from 1998 to 2004, but has resumed a downward trend since 2005. This is closely tied to the initiation of early screening programs for gastric cancer in 2005.[28] Improvements in living conditions and the widespread use of refrigeration have significantly improved food storage, reducing carcinogens in food. Furthermore, the "Salt Reduction Campaign" and "Healthy Lifestyle

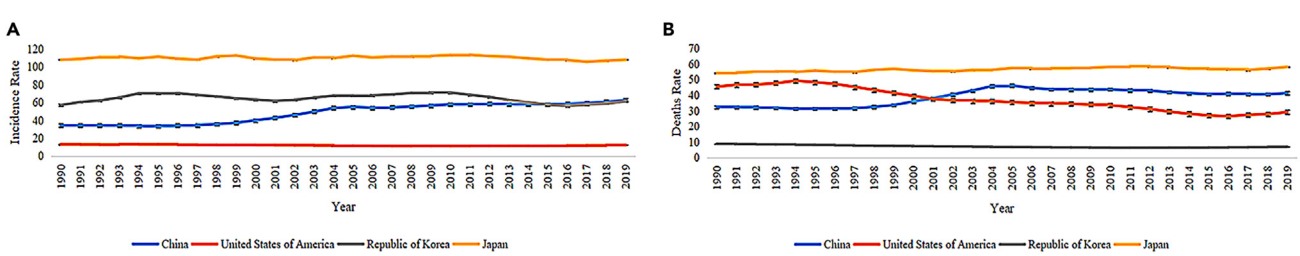

Figure 2. Trends in disease burden of gastric cancer across different countries in male patients from 1990 to 2019
(A) Trends in the incidence rate of gastric cancer in male patients from 1990 to 2019.
(B) Trends in the mortality rate of gastric cancer in male patients from 1990 to 2019.

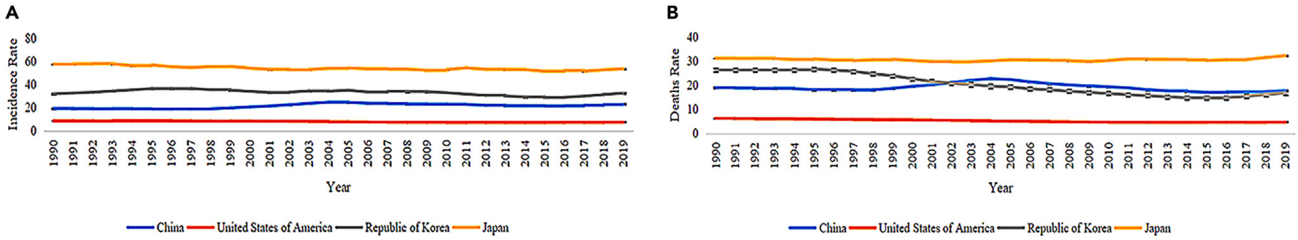

Figure 3. Trends in the disease burden of gastric cancer across different countries in female patients from 1990 to 2019

(A) Trends in the incidence rate of gastric cancer in female patients from 1990 to 2019.

(B) Trends in the mortality rate of gastric cancer in female patients from 1990 to 2019.

for All People" launched in China in 2007, continuous promotion of smoking cessation and alcohol restriction, and improvement of dietary patterns have all been instrumental in the decline of gastric cancer incidence rates.[29] In Korea, ASIR initially increased followed by a subsequent decrease, while ASDR has consistently shown a declining trend. Notably, in Korea, the implementation of nationwide gastric cancer screening was initiated in 1999 as an integral component of the National Cancer Screening Program (NCSP). Japan and the United States have shown a rapid downward trend in both ASIR and ASDR. This is mainly due to changes in lifestyle and diet, as well as advancements in early screening and treatment. The screening program was launched in Japan in 1960,[30] with the only recommended method being fluorescent photography (after a barium meal). Since February 2013, reimbursement for Helicobacter pylori eradication has been available in Japan. Excluding China, the Annual Average Percent Changes (AAPCs) of the other three countries were all below 0, indicating a downward trend. The AAPCs of Korea and Japan were notably higher than those of China and the United States, demonstrating more effective prevention and control measures.[31] In fact, this is closely related to the screening programs implemented by various countries. In Japan, a screening program was first introduced in 1983, which included radiation-based screenings for all adults over the age of 40 and endoscopic examinations for individuals with abnormal results from the radiation tests. In 2016, Japan revised this program to allow endoscopic or radiographic examinations every two years for adults over the age of 50.[32] Korea initiated a biennial screening program in 2002 that involved endoscopic or radiographic examinations for adults over the age of 40, with endoscopy being the primary method.[33]

Age and cohort demographics significantly influence the incidence trend of gastric cancer. The risk of gastric cancer incidence and death escalates with age in both China and Japan, as well as in Korea and the United States, which aligns with the findings of previous studies.[34] Moreover, there is a discernible shift in the incidence of gastric cancer toward younger age groups. With the advancement of social and economic levels, an increasing number of young people consume alcohol, smoke, and have irregular and unhealthy eating habits that include fried, hot, and spicy foods.[35,36] The decrease in the cohort effect of gastric cancer deaths in China may be associated with the implementation of an effective gastric cancer screening program, prevention and treatment strategies for Helicobacter pylori, and targeted attention toward high-risk individuals.[37] The declining cohort effect on death rates is also observed in Japan, Korea, and the United States, linked closely to improvements in economic status,[38] medical conditions,[39] and hygiene practices.[40]

The period effect may also influence the trend of gastric cancer. In China, the incidence of gastric cancer increased and then decreased, peaking around 2005, the year China commenced a cancer screening program.[9] However, the other three countries have already initiated screening programs. Especially Japan initiated a national cancer screening program as early as 1983,[41] 22 years prior to China. Furthermore, there was an overall downward trend in the period effect of the risk of death from gastric cancer in all countries, which may be attributed to the prevalence of gastroscopy, increased health awareness among the general public, and focused attention on high-risk groups.[42] Apart from national cancer control policies, other time-period effects may contribute to differences in cancer trends among countries. For instance, economic development spurred by China's reform and opening up had a positive impact on reducing gastric cancer incidence and death rates.[9] Changes in Japanese dietary habits toward plant-based foods and fish,[43] also had a positive impact on lowering the risk of gastric cancer. However, rapid urbanization and industrialization in China, which led to deteriorating air quality and increased social stress, negatively influenced the risk of gastric cancer.[44]

Besides, there is a significant gender discrepancy in the incidence and death rates of gastric cancer, with rates for female patients being lower than males. This discrepancy may be related to the protective effect of estrogen on gastric cancer.[45] Differences in behaviors such as smoking and alcohol consumption may also contribute to the differential incidence of gastric cancer between men and women. Among the male population, the rates of alcohol consumption and smoking are significantly higher than those of females.[46] Additionally, the trend of gastric cancer incidence is skewing toward younger ages. Therefore, young males should undergo regular health check-ups and screenings. In addition, it is necessary to widely promote a scientifically balanced diet structure and advocate for a healthy lifestyle.

Despite the decreasing trend in the incidence and death rates of gastric cancer in China, the absolute number remains high compared to other countries.[47] This high rate correlates closely with China's large population base. Consequently, the burden of gastric cancer in China remains substantial, necessitating the implementation of health education, the optimization of screening techniques and processes, targeted control of high-risk patients and factors, and the acceleration of scientific research on treatment. Yet, China's cancer control program is still in its nascent stages and is far from being as comprehensive and standardized as in other countries.[9]

In fact, various measures can be taken, including raising public health awareness and education, strengthening basic healthcare infrastructure, promoting disease prevention measures, enhancing medical and healthcare services, as well as implementing health promotion

Table 2. Joinpoint analysis for ASIR and ASMR of gastric cancer by age in China, Japan, United States of America and Republic of Korea between 1990 and 2019, without distinguishing by gender

		Trend 1		Trend 2		Trend 3		Trend 4		
Measure	Country	Year	APC (95%UL), *P*	Year	APC (95%UL), *P*	Year	APC (95%UL), *P*	Year	APC (95%UL), *P*	AAPC (95%UL), *P*
ASIR	China	1990–1998	−1.573 (−1.963–1.181), <0.001	1998–2004	4.021 (3.331–4.716),<0.001	2004–2019	−2.297 (−2.458–2.136),<0.001			−0.820 (−1.004–0.637),<0.001
	Japan	1990–2019	−2.762 (−2.827–2.697), <0.001							−2.762 (−2.827–2.697),<0.001
	Republic of Korea	1990–1995	1.934 (0.941–2.937), 0.001	1995–2001	−4.491 (−5.494–3.476),<0.001	2001–2009	−2.441 (−3.179–1.697),<0.001	2009–2019	−5.233 (−5.89–4.57),<0.001	−3.106 (−3.488–2.723),<0.001
	United States of America	1990–2012	−2.306 (−2.353–2.259),<0.001	2012–2002	−0.446 (−0.758–0.134), 0.007	2002–2007	−2.396 (−3.127–1.66),<0.001	2007–2019	−0.999 (−1.194–0.803),<0.001	−1.259 (−1.444–1.074),<0.001
ASMR	China	1990–1998	−2.022 (−2.32–1.724),<0.001	1998–2004	3.005 (2.484–3.528),<0.001	2004–2016	−4.092 (−4.258–3.926),<0.001	2016–2019	−2.277 (−4.159–0.359), 0.023	−1.900 (−2.131–1.668),<0.001
	Japan	1990–2019	−2.953 (-3–2.906), <0.001							−2.953 (-3–2.906), <0.001
	Republic of Korea	1990–1996	−1.428 (−1.828–1.026),<0.001	1996–2002	−7.013 (−7.53–6.493),<0.001	2002–2016	−5.559 (−5.728–5.391),<0.001	2016–2019	−0.19 (−2.765–2.453), 0.88	−4.480 (−4.763–4.195),<0.001
	United States of America	1990–2012	−2.306 (−2.353–2.259),<0.001	2012–2019	−0.446 (−0.758–0.134), 0.007					−1.860 (−1.939–1.782),<0.001

Table 3. Incidence and mortality of the local drifts and net drifts for China, Japan, Republic of Korea, and United States of America. (%)

Age	China		Japan		Republic of Korea		United States of America	
	Incidence							
Age	China		Japan		Republic of Korea		United States of America	
Local Drifts (95%CI)								
25–29	0.643 (−0.187 to 1.481)		−3.511 (−4.879 to −2.124)		−4.814 (−6.472 to −3.127)		1.129 (0.488–1.774)	
30–34	0.159 (−0.352 to 0.672)		−3.812 (−4.570 to −3.049)		−4.530 (−5.427 to −3.624)		−0.129 (−0.510 to 0.258)	
35–39	−0.465 (−0.846 to −0.083)		−4.358 (−4.845 to −3.869)		−3.448 (−4.040 to −2.852)		−0.927 (−1.206 to −0.647)	
40–44	−0.869 (−1.148 to −0.590)		−6.264 (−6.592 to −5.934)		−3.288 (−3.736 to −2.839)		−1.997 (−2.209 to −1.784)	
45–49	−0.975 (−1.192 to −0.758)		−7.639 (−7.888 to −7.389)		−3.571 (−3.933 to −3.208)		−2.364 (−2.531 to −2.196)	
50–54	−0.907 (−1.089 to −0.725)		−7.692 (−7.891 to −7.494)		−4.111 (−4.413 to −3.808)		−1.783 (−1.920 to −1.646)	
55–59	−0.908 (−1.070 to −0.747)		−6.454 (−6.611 to −6.296)		−4.000 (−4.264 to −3.735)		−0.993 (−1.110 to −0.877)	
60–64	−0.664 (−0.807 to −0.521)		−5.376 (−5.501 to −5.251)		−4.338 (−4.588 to −4.087)		−1.774 (−1.876 to −1.6714)	
65–69	−0.514 (−0.653 to −0.374)		−3.827 (−3.934 to −3.720)		−3.541 (−3.789 to −3.292)		−2.617 (−2.708 to −2.526)	
70–74	−0.340 (−0.492 to −0.188)		−2.954 (−3.059 to −2.848)		−2.090 (−2.348 to −1.832)		−3.464 (−3.550 to −3.379)	
75–79	−0.083 (−0.272 to 0.107)		−2.461 (−2.570 to −2.353)		−0.623 (−0.930 to −0.316)		−4.225 (−4.31 to −4.140)	
80–84	0.255 (−0.020 to 0.530)		−2.130 (−2.254 to −2.006)		0.241 (−0.203 to 0.687)		−4.520 (−4.615 to −4.426)	
85–89	0.340 (−0.139 to 0.821)		−1.324 (−1.504 to −1.143)		0.962 (0.168–1.762)		−4.022 (−4.151 to −3.893)	
90–94	0.200 (−1.017 to 1.432)		−0.154 (−0.534 to 0.228)		1.041 (−0.652 to 2.763)		−3.641 (−3.863 to −3.418)	
Net Drift (95%CI)								
	−0.440 (−0.559 to −0.320)	$p < 0.001$	−4.657 (−4.778 to −4.538)	$p < 0.001$	−2.868 (−3.062 to −2.674)	$p < 0.001$	−2.295 (−2.369 to −2.220)	$p < 0.001$
	Deaths							
Age	China		Japan		Republic of Korea		United States of America	
Local Drifts (95%CI)								
25–29	−2.102 (−3.167 to −1.026)		−4.90 (−6.865 to −2.897)		−7.764 (−9.921 to −5.556)		0.421 (−0.594 to 1.446)	
30–34	−2.463 (−3.084 to −1.839)		−4.907 (−5.967 to −3.836)		−7.386 (−8.510 to −6.249)		−0.817 (−1.406 to −0.224)	
35–39	−2.810 (−3.248 to −2.370)		−5.220 (−5.895 to −4.541)		−6.300 (−7.010 to −5.585)		−1.606 (−2.017 to −1.193)	

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Table 3. *Continued*

Age	Deaths							
	China		Japan		Republic of Korea		United States of America	
40–44	−2.954 (−3.258 to −2.6495)		−6.893 (−7.342 to −6.441)		−6.048 (−6.562 to −5.5312)		−2.670 (−2.977 to −2.362)	
45–49	−2.801 (−3.027 to −2.5745)		−8.085 (−8.415 to −7.754)		−6.198 (−6.594 to −5.801)		−3.030 (−3.266 to −2.794)	
50–54	−2.586 (−2.770 to −2.402)		−8.023 (−8.279 to −7.767)		−6.619 (−6.938 to −6.298)		−2.452 (−2.640 to −2.264)	
55–59	−2.470 (−2.630 to −2.309)		−6.694 (−6.892 to −6.496)		−6.396 (−6.667 to −6.124)		−1.672 (−1.829 to −1.515)	
60–64	−2.127 (−2.264 to −1.989)		−5.566 (−5.718 to −5.413)		−6.642 (−6.891 to −6.392)		−2.450 (−2.586 to −2.315)	
65–69	−1.890 (−2.019 to −1.760)		−4.033 (−4.157 to −3.908)		−5.807 (−6.044 to −5.569)		−3.283 (−3.402 to −3.163)	
70–74	−1.615 (−1.750 to −1.481)		−3.235 (−3.352 to −3.118)		−4.360 (−4.592 to −4.127)		−4.098 (−4.208 to −3.988)	
75–79	−1.222 (−1.379 to −1.064)		−2.894 (−3.007 to −2.780)		−2.887 (−3.141 to −2.632)		−4.808 (−4.913 to −4.702)	
80–84	−0.774 (−0.991 to −0.5558)		−2.791 (−2.911 to −2.672)		−1.982 (−2.319 to −1.644)		−5.064 (−5.175to −4.953)	
85–89	−0.503(-0.8644 to −0.1403)		−2.070 (−2.229 to −1.911)		−0.988 (−1.538 to −0.436)		−4.502 (−4.642 to −4.363)	
90–94	−0.522 (−1.389 to 0.354)		−1.000 (−1.298 to −0.700)		−0.658 (−1.755 to 0.450)		−4.062 (−4.288 to −3.835)	
Net Drift (95%CI)								
	−2.035 (−2.153 to −1.916)	$p < 0.001$	−5.150 (−5.311 to −4.988)	$p < 0.001$	−5.295 (−5.496 to −5.094)	$p < 0.001$	−2.933 (−3.037 to −2.827)	$p < 0.001$

Table 4. Relative risks of incidence and deaths due to age, period, and cohort effects in China, Japan, Republic of Korea, and United States of America

	Incidence							
	China		Japan		Republic of Korea		United States of America	
	RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI
Age								
25–29	2.766	2.436 to 3.141	1.299	1.109 to 1.521	0.554	0.463 to 0.662	0.142	0.128 to 0.156
30–34	6.620	6.068 to 7.221	2.558	2.304 to 2.839	1.020	0.899 to 1.158	0.324	0.304 to 0.347
35–39	11.525	10.773 to 12.329	4.399	4.089 to 4.732	1.427	1.286 to 1.583	0.547	0.520 to 0.576
40–44	21.559	20.440 to 22.739	6.554	6.213 to 6.913	2.134	1.957 to 2.328	1.008	0.968 to 1.049
45–49	33.844	32.396 to 35.356	8.365	8.029 to 8.715	2.661	2.475 to 2.860	1.569	1.519 to 1.621
50–54	55.536	53.543 to 57.604	11.542	11.162 to 11.936	3.474	3.263 to 3.699	2.460	2.394 to 2.528
55–59	86.633	83.930 to 89.423	16.125	15.672 to 16.591	4.272	4.034 to 4.525	3.634	3.548 to 3.723
60–64	123.972	120.445 to 127.603	21.404	20.860 to 21.963	5.010	4.743 to 5.292	5.091	4.981 to 5.204
65–69	166.824	162.182 to 171.598	27.346	26.681 to 28.028	5.927	5.611 to 6.262	7.024	6.878 to 7.172
70–74	227.517	221.047 to 234.177	34.288	33.446 to 35.152	7.110	6.721 to 7.522	9.862	9.660 to 10.069
75–79	255.794	246.903 to 265.004	44.534	43.299 to 45.805	8.394	7.871 to 8.953	13.859	13.537 to 14.189
80–84	276.941	265.709 to 288.647	65.804	63.891 to 67.773	10.506	9.780 to 11.287	20.071	19.583 to 20.571
85–89	292.871	276.679 to 310.010	108.275	104.792 to 111.875	10.925	9.933 to 12.017	25.900	25.193 to 26.627
90–94	234.572	209.087 to 263.163	181.886	174.486 to 189.599	13.396	11.465 to 15.652	42.878	41.430 to 44.377
Period								
1990–1994	0.9584	0.929 to 0.988	1.670	1.632 to 1.710	1.346	1.282 to 1.414	1.202	1.180 to 1.224
1995–1999	0.8797	0.855 to 0.906	1.296	1.268 to 1.324	1.231	1.174 to 1.290	1.118	1.099 to 1.137
2000–2004	1.000	1.000 to 1.000	1.000	1.000 to 1.000	1.000	1.000 to 1.000	1.000	1.000 to 1.000
2005–2009	1.0054	0.980 to 1.032	0.808	0.791 to 0.825	0.923	0.881 to 0.967	0.865	0.851 to 0.880
2010–2014	0.9009	0.877 to 0.925	0.647	0.632 to 0.662	0.774	0.738 to 0.812	0.770	0.757 to 0.783
2015–2019	0.8089	0.787 to 0.832	0.498	0.486 to 0.511	0.653	0.621 to 0.686	0.687	0.675 to 0.699
Cohort								
1900–1904	1.048	0.693 to 1.584	1.911	1.680 to 2.174	1.536	0.873 to 2.701	4.764	4.413 to 5.142
1905–1909	1.016	0.868 to 1.188	2.364	2.224 to 2.514	1.367	1.053 to 1.776	3.839	3.671 to 4.015
1910–1914	1.003	0.918 to 1.096	2.627	2.518 to 2.741	1.484	1.282 to 1.718	3.351	3.243 to 3.463
1915–1919	1.017	0.957 to 1.080	2.384	2.301 to 2.471	1.682	1.522 to 1.860	2.756	2.680 to 2.835
1920–1924	1.060	1.013 to 1.109	2.067	2.003 to 2.134	1.862	1.722 to 2.013	2.315	2.257 to 2.375
1925–1929	1.092	1.051 to 1.135	2.001	1.945 to 2.059	1.788	1.671 to 1.914	1.832	1.789 to 1.877
1930–1934	1.078	1.042 to 1.115	1.797	1.749 to 1.846	1.675	1.574 to 1.782	1.358	1.326 to 1.390
1935–1939	1.052	1.019 to 1.087	1.475	1.437 to 1.514	1.632	1.540 to 1.729	1.064	1.040 to 1.089
1940–1944	0.995	0.964 to 1.027	1.247	1.214 to 1.281	1.482	1.401 to 1.569	1.030	1.006 to 1.054
1945–1949	1.000	1.000 to 1.000	1.000	1.000 to 1.000	1.000	1.000 to 1.000	1.000	1.000 to 1.000
1950–1954	0.965	0.934 to 0.996	0.751	0.729 to 0.773	0.703	0.660 to 0.750	0.876	0.854 to 0.898
1955–1959	0.898	0.867 to 0.931	0.407	0.392 to 0.423	0.636	0.594 to 0.681	0.821	0.798 to 0.843
1960–1964	0.819	0.783 to 0.856	0.296	0.282 to 0.311	0.697	0.647 to 0.751	0.883	0.855 to 0.911
1965–1969	0.827	0.787 to 0.869	0.178	0.167 to 0.189	0.432	0.395 to 0.472	0.599	0.576 to 0.623
1970–1974	0.793	0.745 to 0.844	0.157	0.145 to 0.170	0.368	0.331 to 0.410	0.536	0.510 to 0.563
1975–1979	0.7644	0.703 to 0.831	0.153	0.138 to 0.170	0.333	0.290 to 0.383	0.603	0.565 to 0.644
1980–1984	0.802	0.713 to 0.902	0.130	0.111 to 0.153	0.299	0.247 to 0.363	0.761	0.699 to 0.829

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Table 4. *Continued*

	Incidence							
	China		Japan		Republic of Korea		United States of America	
	RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI
1985–1989	0.888	0.76 to 1.0377	0.092	0.072 to 0.118	0.175	0.129 to 0.237	0.714	0.635 to 0.803
1990–1994	0.958	0.736 to 1.247	0.072	0.046 to 0.115	0.123	0.069 to 0.219	0.713	0.583 to 0.873

	Deaths							
	China		Japan		Republic of Korea		United States of America	
	Rate	95%CI	RR	95%CI	RR	95%CI	RR	95%CI
Age								
25–29	2.957	2.569 to 3.402	0.564	0.460 to 0.693	0.555	0.458 to 0.671	0.071	0.061 to 0.083
30–34	6.719	6.125 to 7.369	1.034	0.902 to 1.185	0.885	0.773 to 1.012	0.166	0.151 to 0.184
35–39	11.505	10.736 to 12.330	1.646	1.495 to 1.812	1.144	1.027 to 1.275	0.310	0.288 to 0.333
40–44	19.788	18.751 to 20.882	2.337	2.179 to 2.507	1.434	1.308 to 1.571	0.541	0.512 to 0.573
45–49	29.138	27.892 to 30.439	3.255	3.090 to 3.428	1.703	1.583 to 1.832	0.868	0.830 to 0.907
50–54	45.967	44.335 to 47.658	4.590	4.403 to 4.785	2.082	1.955 to 2.217	1.388	1.337 to 1.440
55–59	67.490	65.416 to 69.630	6.534	6.310 to 6.766	2.330	2.198 to 2.469	2.013	1.948 to 2.079
60–64	93.609	90.987 to 96.308	8.998	8.723 to 9.281	2.534	2.395 to 2.680	2.781	2.699 to 2.864
65–69	124.186	120.784 to 127.684	12.189	11.838 to 12.550	2.794	2.641 to 2.956	3.757	3.652 to 3.865
70–74	170.012	165.288 to 174.870	16.546	16.074 to 17.031	3.196	3.019 to 3.383	5.270	5.126 to 5.419
75–79	201.088	194.526 to 207.870	23.638	22.890 to 24.410	3.777	3.546 to 4.024	7.792	7.554 to 8.038
80–84	222.890	214.652 to 231.443	36.863	35.656 to 38.111	4.480	4.181 to 4.801	11.236	10.881 to 11.604
85–89	261.174	248.941 to 274.007	69.698	67.277 to 72.206	5.462	5.027 to 5.936	18.318	17.700 to 18.959
90–94	226.372	207.269 to 247.236	147.603	141.734 to 153.715	6.957	6.149 to 7.871	33.121	31.817 to 34.478
Period								
1990–1994	1.076	1.046 to 1.107	1.744	1.696 to 1.793	1.834	1.752 to 1.920	1.346	1.315 to 1.379
1995–1999	0.937	0.913 to 0.962	1.321	1.290 to 1.353	1.449	1.387 to 1.514	1.167	1.142 to 1.193
2000–2004	1.000	1.000 to 1.000	1.000	1.000 to 1.000	1.000	1.000 to 1.000	1.000	1.000 to 1.000
2005–2009	0.914	0.892 to 0.936	0.782	0.764 to 0.801	0.771	0.736 to 0.807	0.846	0.828 to 0.864
2010–2014	0.739	0.721 to 0.759	0.609	0.592 to 0.625	0.593	0.565 to 0.623	0.729	0.713 to 0.746
2015–2019	0.615	0.598 to 0.632	0.458	0.444 to 0.473	0.492	0.467 to 0.518	0.651	0.636 to 0.667
Cohort								
1900–1904	1.657	1.233 to 2.226	2.476	2.235 to 2.744	3.791	2.621 to 5.483	6.088	5.624 to 6.589
1905–1909	1.545	1.371 to 1.740	2.884	2.725 to 3.052	3.115	2.590 to 3.747	4.822	4.587 to 5.070
1910–1914	1.508	1.405 to 1.620	3.164	3.031 to 3.302	3.270	2.915 to 3.667	4.156	3.993 to 4.325
1915–1919	1.466	1.393 to 1.542	2.699	2.598 to 2.803	3.349	3.074to 3.650	3.323	3.206 to 3.443
1920–1924	1.464	1.406 to 1.525	2.235	2.158 to 2.315	3.338	3.108 to 3.585	2.726	2.638 to 2.817
1925–1929	1.433	1.384 to 1.484	2.096	2.028 to 2.165	2.872	2.693 to 3.064	2.100	2.035 to 2.167
1930–1934	1.335	1.293 to 1.379	1.844	1.787 to 1.902	2.380	2.240 to 2.529	1.507	1.461 to 1.554
1935–1939	1.221	1.184 to 1.258	1.495	1.450 to 1.542	2.052	1.937 to 2.174	1.142	1.107 to 1.177
1940–1944	1.079	1.046 to 1.112	1.261	1.222 to 1.302	1.670	1.577 to 1.769	1.067	1.034 to 1.101
1945–1949	1.000	1.000 to 1.000	1.000	1.000 to 1.000	1.000	1.000 to 1.000	1.000	1.000 to 1.000
1950–1954	0.896	0.868 to 0.926	0.741	0.715 to 0.769	0.621	0.580 to 0.664	0.846	0.818 to 0.876
1955–1959	0.769	0.742 to 0.798	0.397	0.378 to 0.416	0.488	0.454 to 0.525	0.767	0.738 to 0.796
1960–1964	0.637	0.609 to 0.667	0.281	0.264 to 0.300	0.468	0.431 to 0.507	0.798	0.763 to 0.833

(*Continued on next page*)

Table 4. *Continued*

	Deaths							
	China		Japan		Republic of Korea		United States of America	
	Rate	95%CI	RR	95%CI	RR	95%CI	RR	95%CI
1965–1969	0.583	0.553 to 0.614	0.164	0.151 to 0.178	0.252	0.228 to 0.278	0.523	0.495 to 0.552
1970–1974	0.497	0.465 to 0.532	0.139	0.125 to 0.154	0.185	0.163 to 0.209	0.451	0.420 to 0.485
1975–1979	0.415	0.377 to 0.456	0.127	0.110 to 0.148	0.142	0.120 to 0.168	0.491	0.446 to 0.540
1980–1984	0.379	0.329 to 0.436	0.101	0.081 to 0.126	0.109	0.086 to 0.139	0.599	0.528 to 0.681
1985–1989	0.357	0.293 to 0.436	0.066	0.046 to 0.094	0.056	0.037 to 0.083	0.542	0.451 to 0.652
1990–1994	0.344	0.242 to 0.490	0.046	0.023 to 0.092	0.032	0.015 to 0.071	0.521	0.377 to 0.721

policies. Additionally, these measures should be tailored to the specific circumstances of different countries and regions. For countries with higher incidence rates, greater efforts should be made in health education, promoting healthy diets, and improving lifestyle habits.

Limitations of the study

This study does have some limitations. Firstly, the diagnostic criteria for gastric cancer is continuously being updated, introducing potential bias in the data on newly diagnosed cases across different years. Secondly, the accuracy of Global Burden of Disease (GBD) data is affected by each country's cancer registration and reporting system. For example, China's system only covers one-third of the population, and the cancer registry data are not detailed enough to determine whether cases originate from screening, whereas Japan's system covers about 70% of cancer cases.[48] Data quality issues such as inconsistent definitions, reporting errors, and methodological variations may also impact research accuracy and comparability. Finally, establishing causality in the age-period-cohort model is challenging, and only relevant assumptions can be made.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- RESOURCE AVAILABILITY
  - Lead contact
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- EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS
- METHOD DETAILS
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  - Variables
- QUANTIFICATION AND STATISTICAL ANALYSIS
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  - Trend analysis
  - Age-period-cohort model

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.isci.2024.110074.

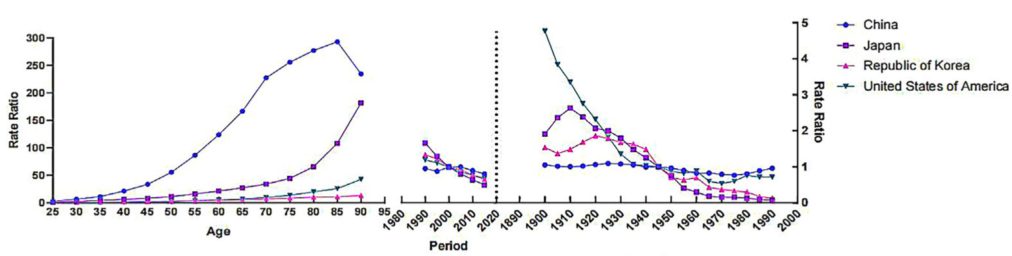

Figure 4. Age-Period-Cohort Model analysis of gastric cancer incidence among China, Japan, Republic of Korea, and United States of America

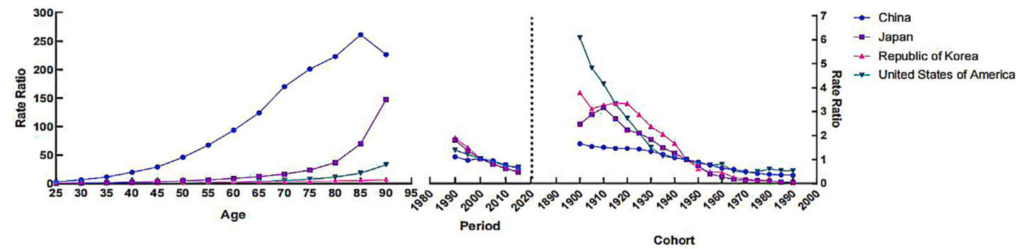

Figure 5. Age-Period-Cohort Model analysis of gastric cancer mortality among China, Japan, Republic of Korea, and United States of America

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DECLARATION OF INTERESTS

The authors declare no competing interests.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and algorithms		
R software 4.0.5	R Foundation, USA	https://www.r-project.org/
Microsoft Excel 2016	Microsoft Office	https://www.microsoft.com/zh-cn/
Joinpoint Regression software 4.8.0.1	NIH	https://surveillance.cancer.gov/joinpoint/
National Cancer Institute's online tool		https://analysistools.cancer.gov/apc/

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Xiangpan Li (E-mail: rm001227@whu.edu.cn).

Materials availability

This study did not generate new unique reagents.

Data and code availability

Data reported in this paper will be shared by the lead contact upon request.

This paper does not report original code.

Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

All data used in this study were obtained from the the Global Burden of Disease (GBD) database.

METHOD DETAILS

Data sources

The Global Burden of Disease (GBD) database49 provides statistics on incidence, deaths, and corresponding age-standardized rates (ASR) for 369 diseases across 204 countries or territories. The gastric cancer data necessary for this study were acquired from GBD 2019 via the online tool GHDx (https://ghdx.healthdata.org/).

We included patients diagnosed with gastric cancer from China, South Korea, the United States, and Japan within the period of 1990 to 2019. Here were the steps for filtering. GBD Estimate: cause of death or injury; Measure: Incidence and deaths; Cause: all causes; Location: China, Japan, United States of America, and Republic of Korea; Age: All ages, age-standardized, <20, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-55, 56-59, 60-64, 65-69,70-74,75-79,80-84,85-89,90-94,>95;Sex: Both, Male and Female; Year: 1990-2019.

Variables

The variables included in the study were age, sex, country, calendar year, incidence (number, ASR), and deaths (number, ASR).

QUANTIFICATION AND STATISTICAL ANALYSIS

Descriptive analysis

Data on overall, age-, and sex-specific new gastric cancer cases, deaths, and ASRs (95% uncertainty intervals (95% UI)) were extracted from the GBD 2019 database for the period 1990-2019 for China, Japan, Korea, and the United States. Rates were reported per 100,000 population. The natural logarithm of ASR was observed to linearly correlate with time. The Estimated Annual Percentage Change (EAPC) was used to describe the ASR trend over the specified time interval.[49] An increase in ASR was inferred if both the EAPC value and the lower limit of its 95% CI were positive. Conversely, if both the EAPC value and the upper limit of its 95% CI were negative, the ASR was deemed to be decreasing. Any other conditions led to the ASR being considered stable. Data visualization and statistics were performed using R software (version 4.0.5) and Microsoft Excel (version 2016).

The database from GBD 2019 employs internationally standardized population data to calculate age-standardized incidence and mortality rates. The calculation formula is as follows:

$$ASR = \frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} w_i} \times 100,000$$

The variable "i " represents the specific age group, while "aiwi" denotes the ratio of that particular age group. The symbol "wi" signifies the number of cases or weight assigned to each observation, and finally, "A" stands for the total number of age groups.

Trend analysis

The Joinpoint regression model,[50] which divides a long-term trend line into segments—each segment being described by a continuous line—was tested using the Z-test. To characterize trends in cancer incidence over time, we employed the best-fit log-linear regression model to calculate the annual percentage change (APC) and the corresponding 95% CI for each line segment, and to identify the joinpoints at which the APC significantly changed ($p < 0.05$). Joinpoint regression analyses were performed using NCI Joinpoint Regression software (version 4.8.0.1; Information Management Services Inc.), where the number of joinpoints and associated p-values were computed by the permutation test. The best model was selected based on the Bayesian Information Criterion (BIC). An increasing trend in the interval or overall was indicated when APC>0 and the average annual percentage change (AAPC)>0, while APC<0 and AAPC<0 indicated a decreasing trend in the interval or overall incidence.

Age-period-cohort model

This model accounts for the effects of age, period, and cohort as factors, and has been used to analyze statistical data on disease incidence or deaths. In the initial step, we categorized the data into 15 age groups (25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, and 95+ years). Following this, we divided them into 6 cohorts throughout the entire observation period (1990-1994, 1995-1999, 2000-2004, 2005-2009, 2010-2014, and 2015-2019). The Age-Period-Cohort model was computed using the Wald's chi-square test for functions and estimable parameters through the National Cancer Institute's online tool (https://analysistools.cancer.gov/apc/).[51] All statistical tests were two-sided, and P<0.05 was considered statistically significant.