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Burden of gastrointestinal cancers in Asia, 1990–2019



Chengwei Xia^{1†}, Yini Liu^{2†} and Xin Qing^{2*}

Abstract

Objectives Gastrointestinal (GI) cancers are a major cause of morbidity and mortality worldwide. However, there has been no comprehensive assessment of GI cancers in Asia.

Study design This was an epidemiological study.

Methods The study calculated the incidence and deaths of six common GI cancers in Asia between 1990 and 2019 using data from the Global Burden of Disease study. The data are presented by sex, age, year, location, and risk factors, and are shown as counts and rates.

Results In 2019, the age-standardized incidence rates (ASIR) for colorectal, esophageal, gallbladder and biliary tract (GBTC), liver, pancreatic, and stomach cancers were 23.88, 8.24, 2.77, 7.97, 5.41, and 19.77, respectively. The agestandardized death rates (ASDR) for colorectal, esophageal, GBTC, liver, pancreatic, and stomach cancers were 12.49, 7.73, 2.53, 7.22, 5.47, and 14.67, respectively. From 1990 to 2019, there was an increasing trend in incidence and deaths for esophageal, liver, and stomach cancer, while a decreasing trend was observed in colorectal, GBTC, and pancreatic cancer. The burden of GI cancer increased successively in older generations and was higher in males than in females. Furthermore, this burden varied significantly across Asian subregions and countries. Dietary risks, smoking, alcohol use, and high BMI contribute to GI cancer mortality.

Conclusions GI cancers continue to be the primary contributor to the tumor burden in Asia, with increasing absolute numbers but varying age-standardized measures over the past three decades.

Keywords Gastrointestinal cancer, Global burden of disease study, Incidence, Death, Asia

Introduction

Cancer is the leading cause of death and a major challenge to improving the quality of life worldwide [1]. The cancer burden is increasing as the population grows and ages, and gastrointestinal (GI) cancers are no exception

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[2–4]. GI cancer is a term for the group of cancers originating from the digestive organs, including colon and rectum cancer (CRC), esophageal cancer (EC), gallbladder and biliary tract cancer (GBBTC), liver cancer (LC), pancreatic cancer (PC), and stomach cancer (SC). According to GLOBOCAN 2020, GI cancers represent 26.7% of the global cancer incidence and 36.5% of all cancer-related deaths [5]. It is urgent to identify the burden of GI cancers to organize health services and alleviate public stress.

Asia, as the most populous continent, is significantly affected by the burden of GI cancers due to their aggressive nature and poor survival probability [6, 7]. As demographic and epidemiological transitions continue, the



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distribution of GI cancers in Asia is changing [8, 9]. However, evidence on the prevalence and burden associated with GI cancers is limited, and only several studies have reported the burden of individual diseases and local areas. For example, China has nearly half of the global cases of liver cancer, but its incidence and mortality are showing a downward trend with socioeconomic development [10]. A comprehensive analysis of the Asian burden on GI cancers could help understand their specific patterns and temporal trends to guide personalized treatment in Asian populations.

The Global Burden of Disease (GBD) study assessed the GI cancer burden in 49 countries and territories in Asia, and facilitated understanding the evolution landscape of GI cancers [11]. In this study, we collected epidemiological data on GI cancers from GBD 2019 and further analyzed variations based on subtype, age, gender, and location groups.

Methods

Data source

The GBD 2019 database is a global database with epidemiological data on 369 diseases from 1990 to 2019 [12]. The estimation methodology of the GBD 2019 study employed the Cause of Death Ensemble model (CODEm)-a machine learning ensemble tool capable of integrating multiple data sources and selecting the best predictive model for mortality analysis; it also utilized the Spatio-Temporal Gaussian Process Regression (ST-GPR)-a Bayesian hierarchical framework designed to smooth and interpolate data gaps across geography and time; and DisMod-MR-a Bayesian meta-regression tool aimed at internally adjusting epidemiological parameters (such as incidence, prevalence, and mortality rates) while also adjusting based on covariates [13]. These tools were chosen to address key challenges in global health estimation: CODEm mitigates model selection bias through algorithmic integration, ST-GPR accounts for spatiotemporal autocorrelation in regions with sparse data, and DisMod-MR ensures internal consistency of disease metrics through systematic evidence synthesis. Since data from the GBD database is publicly available, informed consent from patients or institutions was not required for this study. In this study, the estimates and 95% uncertainty interval (UI) for age-standardized rate (ASR) of incidence and deaths were extracted from GBD 2019 at Asia, and national (48 countries and territories) levels.

Case definition

The GBD 2019 study employed the International Classification of Diseases, Tenth Revision (ICD-10) disease-coding system provided by the World Health Organization (WHO), thus contributing to the facilitation of disease statistics and analysis worldwide [14]. To obtain comprehensive evaluations for the burden of GI cancers, we first collected the data of these GI cancers based on ICD-10 codes, including the Colon and rectum cancer (C18-C21.9, D01.0-D01.3, D12-D12.9, D37.3-D37.5), Esophageal cancer (C15-C15.9, D00.1, D13.0), Gallbladder and biliary tract cancer (C23-C24.9, D13.5), Liver cancer (C22-C22.8, D13.4), Pancreatic cancer (C25-C25.9, D13.6-D13.7), and Stomach cancer (C16-C16.9, D00.2, D13.1, D37.1).

Model selection

Age-standardization was performed using the world standard population to allow for meaningful comparisons across different regions and time periods. By calculating the annual percentage change (APC) in a dataset, these APCs are then weighted to give a single value that represents the estimated change rate across the time interval. First, the ASR and their estimated annual percentage change (EAPC) were used to explore major trends in GI cancers [15, 16]. EAPC is a widely used statistical indicator derived from a log-linear regression model. It provides a comprehensive measure of the average rate of change in ASIR (Age-Standardized Incidence Rate) or ASDR (Age-Standardized Death Rate) over a specific period. EAPC can signify the percentage change (increase, decrease, or no change) from year to year. A positive EAPC value indicates an upward trend in ASR (Age-Standardized Rate), while a negative EAPC signifies a downward trend. If the 95% confidence interval of EAPC does not include zero, the trend is considered statistically significant. Meanwhile, regional and national trends were also reported. The same BAPC methodology was used for all statistical analyses. Population attributable fraction (PAF) of risk factors for GI cancers was obtained from the GBD 2019 database. The PAF represents the proportion of disease cases (such as gastrointestinal cancers) that could theoretically be prevented if a specific risk factor were eliminated from the population. We utilized PAF estimates to quantify the contribution of modifiable risk factors (such as smoking, unhealthy diet, alcohol consumption, and obesity) to the burden of gastrointestinal cancers in Asia, assuming a causal relationship between these exposures and the outcomes. A software tool (R version 4.2.3) was used for data analysis and presentation of results. The stats software package was utilized to calculate the Estimated Annual Percentage Change (EAPC). A linear regression model was fitted to the natural logarithm of the Age-Standardized Rate (ASIR/ASMR) against calendar year using the lm function. The ggplot2 software package was employed to generate time trend graphs. The significance of the regression coefficient was evaluated using a two-sided test, with p < 0.05 considered statistically significant.

Results

Overall burden of gastrointestinal cancers in Asia

Globally, new cases of GI cancers accounted for 23% of all cancer incidences in 2019, with more than half of the cases occurring in Asia. The incidence of GI cancers in Asia accounted for 35.9% of all cancers, led by gastric cancer and colorectal cancer (sFigure 1A-B). In both 1990 and 2019, the ASIR and ASMR of gastric and colorectal cancer in Asia were always among the top five (Fig. 1). The ASIRs of liver cancer and esophageal cancer were also among the top five in 1990, but both declined in 2019 to rank 7th and 8th respectively (Fig. 1A). Nevertheless, their ASMRs were among the top 5 in the ranking of all cancer mortality in both 1990 and 2019 (Fig. 1B). And pancreatic cancer incidence and mortality are increasing. In 2019, GI cancer-related deaths in Asia accounted for 43% of all cancer-related deaths, with gastric cancer remaining the most lethal GI cancer (sFigure 1C-D).

Further information on the metrics for gastrointestinal cancers in Asia can be found in Table 1. From 1990 to 2019, the number of incidences and deaths from such gastrointestinal cancers rose significantly in Asia, excluding liver cancer (Fig. 2A-2B). The burden of liver cancer fluctuated notably during 1990–2019, displaying a trend of rising-falling-rising. Colorectal cancer has now become the most commonly occurring gastrointestinal cancer in Asia, taking over from stomach

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	1990 Rank	ASIR		2019 Rank	ASIR	Change
	1 Stomach cancer	28.09 (25.97-30.21)		1 Lung cancer	27.82 (24.56-30.95)	23.34%
	2 Lung cancer	22.56 (20.73-24.61)		2 Colorectal cancer	23.88 (21.54-26.4)	70.85%
	3 Liver cancer	14.07 (12.44-15.92)		3 Stomach cancer	19.77 (17.54-22.28)	-29.63%
	4 Colorectal cancer	13.98 (13.18-14.85)	× /	4 Breast cancer	18.48 (16.46-20.66)	70.82%
	5 Esophageal cancer	11.65 (8.56-13.08)	N.	5 Skin cancer	11.34 (10.04-12.7)	50.86%
	6 Breast cancer	10.82 (10.01-11.66)		6 Prostate cancer		63.15%
	7 Leukemia	8.79 (6.82-10.54)	$ / \lambda$	7 Esophageal cancer	8.24 (6.96-9.43)	-29.31%
	8 Skin cancer	7.52 (6.68-8.48)	1 %. Y	8 Liver cancer	7.97 (7.15-8.93)	-43.33%
	9 Cervical cancer	6.33 (5.28-8.42)	-/ ``	9 Leukemia		-19.04%
	10 Prostate cancer	5.12 (4.31-5.92)		10 Cervical cancer	5.88 (4.72-6.79)	-7.14%
	11 Lip oral cavity cancer	3.98 (3.62-4.36)	/	11 Pancreatic cancer	5.41 (4.83-5.94)	58.44%
	12 Bladder cancer	3.52 (3.25-3.8)		12 Lip oral cavity cancer	4.9 (4.34-5.45)	23.19%
	13 Pancreatic cancer	3.42 (3.18-3.65)	1.	13 Lymphoma	4.65 (4.19-5.16)	72.45%
	14 Brain cancer	3.3 (2.67-4.49)	/	14 Bladder cancer	4.57 (4.12-5.04)	29.76%
	15 Gallbladder cancer	2.73 (2.45-3.32)	-/	15 Brain cancer	4.04 (3.04-4.58)	22.49%
	16 Lymphoma	2.7 (2.49-2.96)	/ ***.			
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В	1990 Rank	ASDR		2019 Rank	ASDR	Change
	1 Stomach cancer	25.65 (23.63-27.81)		1 Lung cancer	25.76 (22.79-28.72)	13.6%
	2 Lung cancer	22.67 (20.8-24.78)		2 Stomach cancer	14.67 (13.04-16.23)	-42.82%
	3 Liver cancer	14.08 (12.54-15.93)	. /	3 Colorectal cancer	12.49 (11.25-13.58)	23.49%
	4 Esophageal cancer	12.04 (8.7-13.54)	· · · ·	4 Esophageal cancer	7.73 (6.57-8.8)	-35.83%
	5 Colorectal cancer	10.11 (9.4-10.86)		5 Liver cancer	7.22 (6.5-7.94)	-48.74%
	6 Breast cancer	6.32 (5.8-6.84)	<u> </u>	6 Breast cancer	7.08 (6.35-7.86)	12.01%
	7 Leukemia	5.32 (4.54-6.1)		7 Pancreatic cancer	5.47 (4.91-5.98)	57.2%
	8 Cervical cancer	3.96 (3.33-5.28)	1.1	8 Prostate cancer	3.87 (3.28-4.63)	-2%
	9 Prostate cancer	3.94 (3.29-4.63)	7.	9 Leukemia	3.67 (3.26-4.11)	-31.01%
	10 Pancreatic cancer	3.48 (3.22-3.72)		10 Cervical cancer	2.97 (2.42-3.46)	-24.8%
	11 Lip oral cavity cancer	2.76 (2.49-3.04)		11 Lip oral cavity cancer	2.93 (2.6-3.29)	5.89%
	12 Brain cancer	2.75 (2.21-3.69)		12 Brain cancer	2.74 (2.05-3.1)	-0.45%
	13 Gallbladder cancer	2.6 (2.32-3.22)	· /	13 Lymphoma	2.73 (2.49-2.98)	22.4%
	14 Bladder cancer	2.43 (2.2-2.64)	1	14 Gallbladder cancer		-2.76%
	15 Lymphoma	2.23 (2.08-2.4)		15 Bladder cancer	2.21 (1.99-2.41)	-9.04%

Fig. 1 The relative rank of incidence (A) and mortality (B) for gastrointestinal cancers in site-specific cancers in Asia

 Table 1
 Age-Standardized Rate and Absolute Number of Incidence, Prevalence, DALYs, and Deaths for Gastrointestinal Cancers in Asia, 1990–2019

	Age-Standardized Rate (per 100,000) (95%UI)			Absolute Number (1,000s) (95%UI)		
	1990	2019	Percentage change	1990	2019	Percentage change
Colon and re	ctum cancer					
Incidence	13.98 (13.18–14.85)	23.88 (21.54–26.40)	0.71	270.85 (254.55–288.32)	1,113.66 (1,013.54–1,242.69)	3.15
Prevalence	59.78 (56.69–63.05)	122.75 (110.97–135.87)	1.05	1,226.63 (1,162.15–1,294.57)	5,951.85 (5,376.73-6,610.10)	3.85
DALYs	231.82 (214.81–249.09)	257.48 (249.63–299.40)	0.19	5,027.06 (4,462.05–5,414.46)	13,366,57 (12,116.85– 14,566.75)	1.66
Deaths	10.11 (9.36–10.86)	12.49 (11.25–13.58)	0.23	183.25 (169.87–196.78)	560.43 (504.63–609.81)	2.06
Esophageal o	ancer					
Incidence	11.65 (8.56–13.08)	8.24 (6.96–9.43)	-0.29	231.48 (169.64–261.09)	391.20 (332.57–449.27)	0.69
Prevalence	16.77 (12.38–18.87)	14.65 (12.37–16.77)	-0.13	352.13 (257.91–397.17)	713.82 (604.88–818.49)	1.03
DALYs	280.68 (199.75–317.89)	170.51 (145.87–194.85)	-0.39	5,996.46 (4,224.94–6,812.44)	8,409.03 (7,201.26-9,643.91)	0.40
Deaths	12.04 (8.70–13.54)	7.73 (6.57–8.80)	-0.36	232.78 (165.26–261.98)	361.12 (307.59–411.84)	0.56
Gallbladder a	and biliary tract cancer					
Incidence	2.73 (2.45–3.32)	2.77 (2.12–3.10)	0.02	48.60 (43.76–60.05)	124.22 (96.00–137.97)	1.56
Prevalence	3.05 (2.73–3.63)	3.31 (2.54–3.70)	0.09	57.01 (51.48–69.10)	151.91 (117.20–168.91)	1.66
DALYs	53.14 (47.47–67.25)	49.66 (39.30–54.91)	-0.07	1,079.71 (961.06–1,379.02)	2,383.12 (1,897.58–2,639.68)	1.21
Deaths	2.60 (2.32–3.22)	2.53 (1.94–2.80)	-0.03	44.82 (40.09–56.56)	111.34 (86.74–123.33)	1.48
Liver cancer						
Incidence	14.07 (12.44–15.92)	7.97 (7.15–8.93)	-0.43	307.99 (270.39–350.75)	381.91 (342.39–429.65)	0.24
Prevalence	15.82 (14.00–17.91)	11.28 (10.09–12.64)	-0.29	359.76 (316.46–409.60)	546.63 (487.43–614.23)	0.52
DALYs	400.95 (352.21–459.22)	182.81 (163.25–203.81)	-0.54	9,554.51 (8,350.29– 10,986.78)	9,071.13 (8,083.15– 10,145.70)	-0.05
Deaths	14.08 (12.54–15.93)	7.22 (6.50–7.94)	-0.49	299.35 (263.97–341.52)	340.60 (305.24–376.94)	0.14
Pancreatic ca	ncer					
Incidence	3.42 (3.18–3.65)	5.41 (4.83–5.94)	0.58	64.44 (59.82–69.27)	249.96 (224.07–274.32)	2.88
Prevalence	2.72 (2.53–2.91)	4.45 (3.96–4.89)	0.64	53.46 (49.69–57.49)	208.39 (186.11-229.31)	2.90
DALYs	77.56 (71.46–84.02)	116.55 (105.46–128.03)	0.50	1,645.69 (1,508.33-1,792.46)	5,692.19 (5,152.41-6,267.21)	2.46
Deaths	3.48 (3.22–3.72)	5.47 (4.91–5.98)	0.57	63.92 (59.02–68.93)	249.80 (226.02–273.32)	2.91
Stomach can	cer					
Incidence	28.09 (25.97–30.21)	19.77 (17.54–22.28)	-0.30	559.12 (514.30-602.07)	930.10 (821.90–1,052.24)	0.66
Prevalence	45.92 (42.94–48.90)	42.98 (37.64–48.97)	-0.06	970.15 (905.63–1,034.74)	2,089.18 (1,823.37-2,391.04)	1.15
DALYs	610.50 (560.86–663.77)	324.66 (288.65–360.64)	-0.47	13,363.30 (12,230.26– 14,582.12)	15,889.63 (14,119.89– 17,684.44)	0.19
Deaths	25.65 (23.63–27.81)	14.67 (13.04–16.23)	-0.43	491.46 (450.83–535.07)	672.83 (596.99–746.92)	0.37

Abbreviations: DALYs Disability-adjusted life-years, UI Uncertainty interval

cancer. Stomach cancer continues to be the primary cause of death among gastrointestinal cancers in Asia. However, this trend is also being overtaken by colorectal cancer. Over the last three decades, there have been notable discrepancies in the age-standardized incidence and mortality patterns of these gastrointestinal cancers in Asia (Fig. 2C-2D). The ASIR of colorectal cancer, pancreatic cancer, and gallbladder and cholangiocarcinoma in 2019 was 23.88, 5.41, and 2.77 per 100,000 population, respectively. The EAPC implied a substantial increase, reaching 2 for colorectal cancer, 1.73 for pancreatic cancer, and 0.23 for gallbladder and cholangiocarcinoma. The ASIR of esophageal, liver, and stomach cancer exhibited a noteworthy decline, with respective EAPCs of -1.36, -3.03, and -1.09. Moreover, a comparable decrease in the ASDR for esophageal, liver, and stomach cancer was identified, with corresponding EAPCs of -1.71, -3.38, and -1.84. The EAPC for colorectal cancer, pancreatic cancer, and gallbladder and cholangiocarcinoma in the ASDR exhibited an upward tendency, with respective values of 0.81, 0.05, and 1.68. Moreover, the evolution in the incidence and mortality

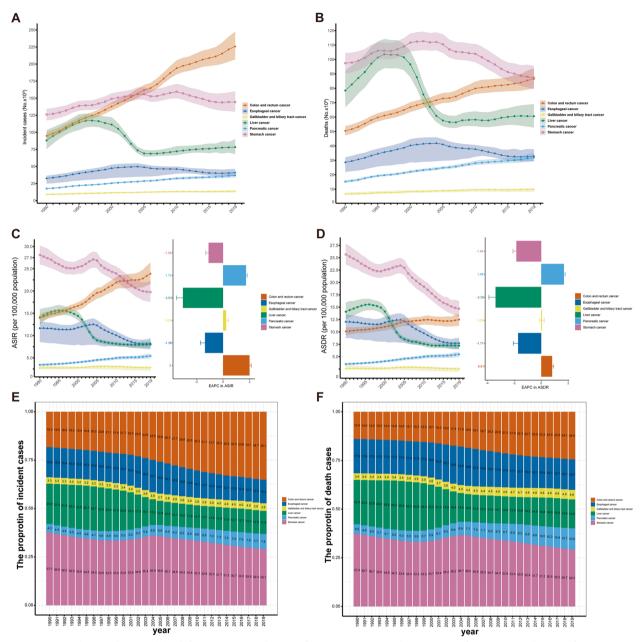


Fig. 2 Asia trends in incidence and death for gastrointestinal cancers from 1990 to 2019. **A** The new cases of gastrointestinal cancers from 1990 to 2019. **B** The number of deaths due to gastrointestinal cancers from 1990 to 2019. **C** ASIR and EAPC in gastrointestinal cancers over the last 30 years. **D** ASDR and EAPC in gastrointestinal cancers from 1990 to 2019. **F** The proportion of deaths of gastrointestinal cancers from 1990 to 2019. ASIR age-standardized incidence rate, ASDR age-standardized death rate, EAPC estimated annual percentage change

proportions of these gastrointestinal cancers was illustrated. Stomach cancer represented the highest percentage of new cases of gastrointestinal cancers before 2012, accounting for more than one-third (Fig. 2E). However, it has since been surpassed by colorectal cancer. In contrast, the proportion of new esophageal and liver cancer cases has decreased. Meanwhile, new cases of gallbladder and pancreatic cancer have increased. The trends regarding new cases and deaths broadly corresponded, except for stomach cancer (Fig. 2F). Stomach cancer remained responsible for the largest portion of deaths over the past 30 years. Asia burden of gastrointestinal cancers by age and gender The age distribution of patients can reflect the health burden in different age groups, and thus provide evidence for primary prevention of these diseases. As presented in Fig. 3A-B, the age-stratified burden of gastrointestinal cancers measured in incidence and death was greatest in the 60+years age group in both 1990 and 2019. The age with the highest incidence and deaths from these six major gastrointestinal cancers was concentrated in the 65–74 age group (sFigure 2–3). Among all age groups, the highest incidence rates of CRC, EC, GBTTC, LC, PC, and SC were 95+, 85–89, 95+, 85–89, 95+, and

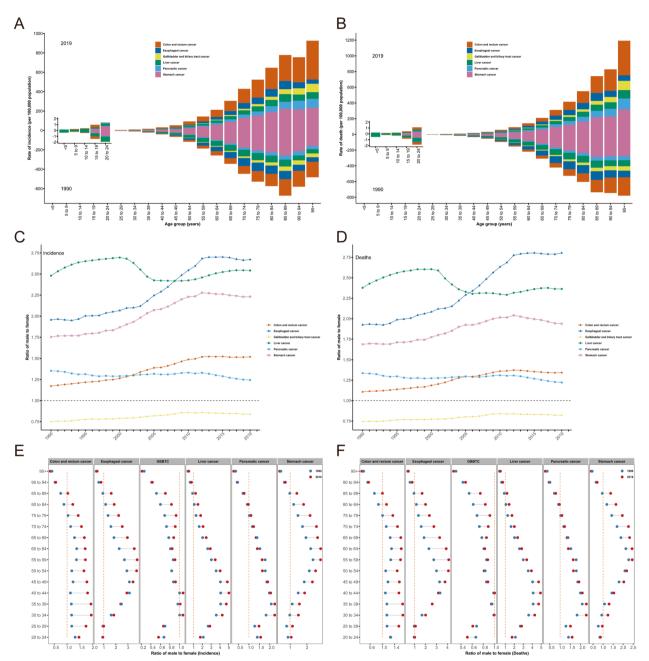


Fig. 3 Asia incidence and death of gastrointestinal cancers by age and sex. A Asia gastrointestinal cancers incidence rates by age for both sexes combined in 1990 and 2019. B Asia gastrointestinal cancers deaths by age for both sexes combined in 1990 and 2019. C The sex ratio of gastrointestinal cancers incident cases from 1990 to 2019 by specific causes. D The sex ratio of gastrointestinal cancers deaths from 1990 to 2019 by specific causes. D The sex ratio of gastrointestinal cancers deaths from 1990 to 2019 by specific causes. E The ratio of male to female in Asia gastrointestinal cancers incident cases by age in 1990 and 2019. F The ratio of male to female in Asia gastrointestinal cancers incident cases by age in 1990 and 2019.

95+groups, respectively, with rates of 411.12, 84.69, 86.72, 79.07, 92.2, and 234.13 per 100,000 population in 2019 (Fig. 3A, sFigure 4). The highest death rates of CRC, EC, GBTTC, LC, PC, and SC were 95+, 85-89, 95+, 95+, 95+, and 95+, with rates of 440.15, 100.65, 117.53, 106.2, 140.03, 317.58 per 100,000 population in 2019 (Fig. 3B, sFigure 5). The male-to-female ratio for CRC, EC, GBTTC, and SC continued to increase from 1990 to 2019, while those of LC and PC decreased (Fig. 3C-D). Except for gallbladder cancer, which is more common in women, all other gastrointestinal tumors are more common in men. Compared to females, males have more than twice the likelihood to develop EC, LC, and SC, have a modestly higher likelihood to develop CRC and PC, and have a lower likelihood to develop GBTTC in 2019 (sFigure 6-7). A similar pattern is seen in mortality levels among these gastrointestinal cancers (sFigure 8-9). We further showed the distribution of gastrointestinal tumors in different age groups and genders in 1990 and 2019 and found that not all age groups meet the above results (Fig. 3E-F). In the age group over 90 years, the proportion of women is significantly higher than that of men.

Asia burden of gastrointestinal cancers by geographical variations

At the national level, the five most affected countries in both 1990 and 2019 were Mongolia, Japan, South Korea, Brunei, and China for the incidence of gastrointestinal cancers (Fig. 4A). Most Asian countries have lower age-standardized incidence rates than basic levels in Asia. The age-standardized death rates between 1990 and 2019 have remained relatively stable in most countries, and Mongolia is also the Asian country with

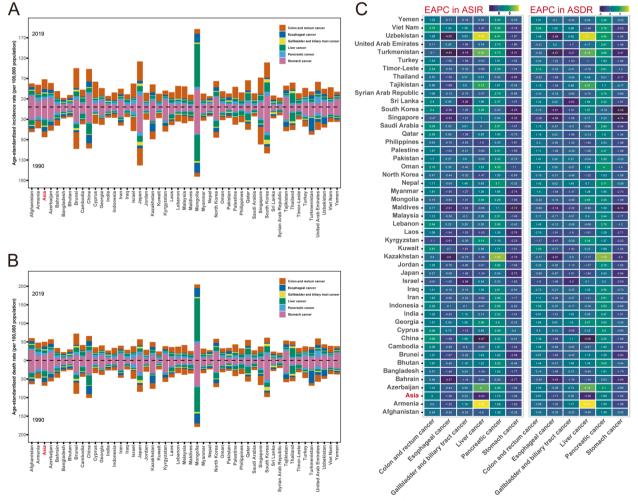


Fig. 4 The Asia trends in gastrointestinal cancers by five subtypes and regions. (A) The ASIR of gastrointestinal cancers at a regional level in 1990 and 2019. (B) The ASDR of gastrointestinal cancers at a regional level in 1990 and 2019. (C) The EAPC in ASIR and ASDR of gastrointestinal cancers from 1990 to 2019, by subtypes and by regions, for both sexes, combined

the highest age-standardized death rate (Fig. 4B). The age-standardized death rate of Mongolia in both 1990 and 2019 far exceeds that of other countries, and Mongolia is the only Asian country with an age-standardized death rate above 200 per 100,000 population in 2019. Although there are significant differences in age-standardized burden across countries, the overall distribution in Asia remains relatively stable. The changing trend of these gastrointestinal cancers in all Asian countries was further presented (Fig. 4C-D), and liver cancer is the best-controlled gastrointestinal cancer in Asia, with EAPCs of -3.03 in ASIR and -3.38 in ASDR. China and Uzbekistan were the countries with the most significant decrease and increase in the burden of liver cancer, respectively, with their EAPCs in ASIR being -4.67 and 9.46, while their EAPCs in ASDR were -5.06 and 9.56, respectively. The incidence and mortality of pancreatic cancer have simultaneously shown an increasing trend in all Asian countries over the past three decades, especially in Kazakhstan with the EAPC of 7.66 in ASIR and 7.52 in ASDR. Conversely, the ASDR of SC presented a significant downward trend in all Aisa countries, Meanwhile, Cyprus is the only Asia country where the ASIR for stomach cancer has shown an upward trend from 1990 to 2019. The EAPC in age-standardized rates for EC and GBTTC varied widely across Asian countries, and we observed that the extreme values of EAPCs existed in Turkmenistan and Sri Lanka. 45 of the 49 Asian countries showed an increase in age-standardized incidence rates, while 39 showed an increase in age-standardized death rates. The fastest increase in the burden of colorectal cancer was found in Vietnam. Detailed data for incidence, deaths, and age-standardized burden for all gastrointestinal cancers in Asian countries are available in sTables 4-9. When the EAPC was compared to the SDI in 2019, no clear associations were observed in these countries (sFigure 10–11).

Gastrointestinal cancer attributable to risk factors in Asia

We found that dietary risks were primarily responsible for CRC mortality, especially diets low in milk and calcium (Fig. 5A, sFigure 12A). CRC mortality due to diets low in calcium increased in both sexes from 1990 to 2019. Smoking is a common and major risk factor for GI cancers, particularly esophageal cancer. the proportion of deaths attributable to smoking and alcohol use was significantly higher among men than among women (Fig. 5, sFigure 12). High body mass index (BMI), a metabolic factor, has caused a gradual increase in GI cancer mortality in both sexes during 1990–2019, with the fastestgrowing rates in both sexes.

Discussion

GI cancers represent an important component of the cancer burden in Asia, with significant increases in new cases and deaths at these major sites (colorectal, esophageal, gallbladder and biliary tract, pancreatic, and stomach) over the past three decades [9, 17]. Although some significant progress has been made in battling GI cancers, such as the development of liver cancer being under control, many challenges remain in the fight against GI cancers [18].

Based on GBD 2019, we found that CRC was the fastest-growing cancer in terms of incidence and mortality in Asia. CRC places a heavy burden on the Asian population and is an emerging concern for medical services, confirming previous reports [19, 20]. A similar pattern was observed for PC, and CRC and PC became the major drivers of the growing threat of GI cancers in Asia [21, 22]. It is worth noting that this study demonstrates an increase in the age-standardized incidence rate (ASIR) of colorectal cancer (CRC) from 13.98 per 100,000 in 1990 to 23.88 per 100,000 in 2019, with an estimated annual percentage change (EAPC) of 2.00, indicating a continuous upward trend. Conversely, the ASIRs for stomach cancer (SC) and esophageal cancer (EC) have declined; however, the absolute number of cases and deaths continues to rise, reflecting the impact of population aging. Our findings are consistent with the GLOBOCAN 2020 data, and the burden of CRC and PC will continue to increase rapidly [5, 23].

Following a 30-year trend, EC and SC in Asia have shown a fluctuating decline in incidence and mortality, but a fluctuating increase in the number of new cases and deaths. These fluctuations may reflect varying progress made by different Asian sub-regions in controlling risk factors and implementing public health interventions. In the case of myocardial infarction, the decline in incidence is partly attributed to reduced smoking and alcohol consumption in high-risk areas such as China and Japan, coupled with improved dietary habits like increased intake of fresh fruits and vegetables, and decreased consumption of nitrite-rich pickled foods. However, Central Asia, particularly countries like Kazakhstan, remains a high-incidence area for myocardial infarction, possibly due to persistent smoking rates and socioeconomic disparities in access to endoscopic screening. In South Asia, the gradual decline in Helicobacter pylori infection rates aligns with successful H. pylori eradication programs and salt reduction campaigns in East Asia, such as in Japan and Korea. Fluctuations in mortality rates in South and Southeast Asia may stem from delayed diagnosis and limited endoscopic monitoring in resource-constrained environments. SC-related deaths remain the highest of all GI cancers. The Asian populations still face serious

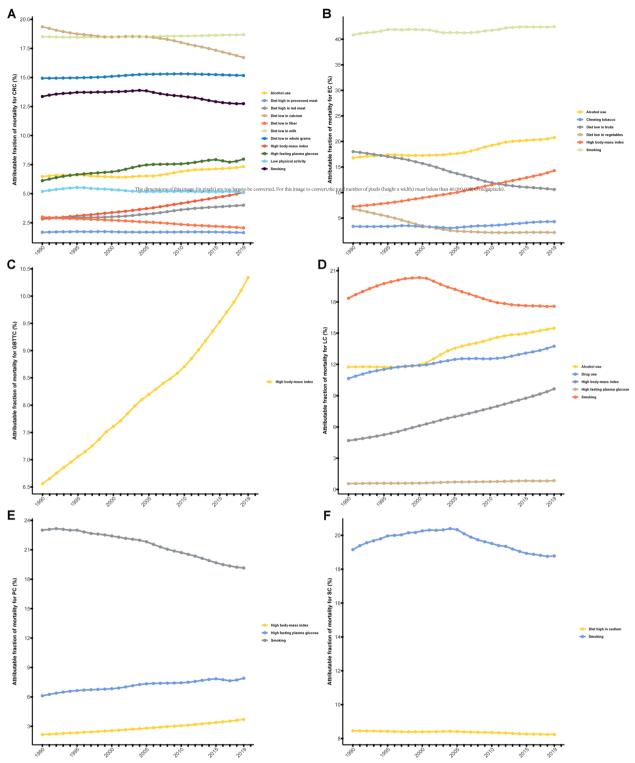


Fig. 5 Temporal trends of risk factor population attributable fractions for GI cancers in Asia, 1990–2019. A Colorectal cancer; (B) Esophageal cancer; (C) Gallbladder and biliary tract cancer; (D) Liver cancer; (E) Pancreatic cancer; (F) Stomach cancer

challenges in controlling EC and SC. Although the ASDR of SC decreased from 25.65 per 100,000 in 1990 to 14.67 per 100,000 in 2019 (EAPC=-0.43), it remains the leading cause of deaths related to gastrointestinal cancers in Asia, highlighting the need for continuous strategies for early detection and prevention. The ASIR and ASDR of LC have been gradually decreasing over the two decades, but have shown a worrying stagnation trend since 2014. Unlike Huang et al., we observed that the number of incident cases and deaths from LC will increase with the rebounding trend in recent years [9]. As a relatively rare GI cancer, GBBTC has received limited attention. Our findings on the relative stability of GBBTC incidence and mortality agree with those reported by Chen et al., who observed that GBBTC demonstrated decreasing trends in both its incidence and mortality since 2010 [17]. The temporal trends in incidence and mortality for GI cancers share some characteristics but are largely distinct in their descriptive epidemiological profiles.

In the broader epidemiological context of Asia, our research findings highlight distinct patterns among different sub-regions. Age and gender have a significant impact on both the incidence and mortality of GI cancers [24, 25]. The predominance of older people in GI cancers has been observed throughout Asia, consistent with global surveys [26, 27]. Several reports have found a positive association between advanced age and the risk of GI cancer [28-30], and GI cancer rejuvenation has also been observed in Asian populations. Our data indicates that individuals aged 65 and above account for over 60% of all gastrointestinal cancer cases, underscoring the increasingly heavy burden posed by gastrointestinal cancers among the aging population in Asia. Meanwhile, the results of this study showed that males had a greater risk of most GI cancers than females. This phenomenon may be related to various factors, including differences in genetic information and lifestyle. Notably, GBBTC is more common in women, a disparity that may be associated with hormones and gallbladder disease [31]. For example, estrogen promotes the development of cholelithiasis, thus increasing the risk of gallbladder cancer in women [32]. The gender differences in GI cancers also varied by age. For all GI cancers, the male-to-female ratios decreased from a certain age until women dominated, with different peak ages.

During 1990–2019, Asian countries and territories experienced rapid epidemiologic transitions for the burden of GI cancers. However, due to public health challenges and uneven economic development, healthcare reforms have had different rates of success across the Asian region [33]. Our data are consistent with Huang's report, and East Asia is the area with the highest agestandardized burden of GI cancers, especially Mongolia [9]. The overall GI cancer burden in Asian countries has not improved significantly from 1990 to 2019, which may be associated with many people in developing countries inside Asia having no health insurance [34, 35].

With the development of diagnostic techniques and treatment modalities, the burden of GI cancer has been effectively controlled, but primary prevention remains a key strategy to reduce the burden. Numerous reports have identified the common risk factors for GI cancers, and there were some heterogeneities within Asia [24, 36]. For instance, Japan and Korea have successfully implemented nationwide gastric cancer screening programs, leading to a decline in ASIR, while other Asian countries with limited screening coverage continue to struggle with high mortality rates. Unreasonable dietary habits are major risks for CRC, and the increasingly westernized dietary patterns for Asian populations may be used to explain the increasing burden of colorectal cancers in Asia [37, 38]. Some lifestyles, such as smoking, lack of exercise, and unhealthy dietary patterns, are modifiable, and government investments, such as the Healthy China 2030 strategy are necessary [39, 40]. In terms of the European Community (EC), the persistent burden in Central Asia underscores the need to implement targeted tobacco control policies in arid regions and provide subsidies for access to fresh food; whereas in East Asia, stricter regulation of advertising is necessary to further reduce alcohol-related EC. Regarding stomach cancer (SC), promoting Helicobacter pylori screening and treatment in low-income countries-following Japan's successful model-could mitigate fluctuations in mortality rates.

Based on the GBD 2019 database, this study systematically analyzed the burden of gastrointestinal cancers in 49 countries and regions in Asia from 1990 to 2019, filling a gap in existing research that often focuses on single countries or short-term trends [9, 17]. Compared to previous studies, this research provides the first comprehensive assessment across regions, time periods, and cancer types, and untangles the long-term trends of different cancers through EAPC analysis [24, 37]. We further explored the influence of gender, age, and risk factors, and uncovered distinct patterns of disease burden in different sub-regions, such as Mongolia having the highest incidence of gastrointestinal cancers and a rapid rise in colorectal cancer in China. However, our study has some limitations. Firstly, the estimations from GBD 2019 rely on cancer registry data and modeling assumptions, which may introduce biases. For instance, in lowand middle-income Asian countries such as Afghanistan and Nepal, the scarcity or fragmentation of cancer registration systems could lead to underreporting or misclassification of gastrointestinal cancer cases, especially rare subtypes like GBBTC. Secondly, while the GBD methodology standardizes data from different regions, its reliance on the DisMod-MR 2.1 model may oversimplify temporal trends in epidemiologically rapid-transition countries like China, potentially masking subnational variations. Thirdly, the current estimates for gastrointestinal cancers do not incorporate the impact of COVID-19, which could have disrupted cancer diagnosis and treatment pathways in Asia after 2019. Finally, these findings require validation through external studies utilizing alternative methodologies or fine-grained subnational data.

Conclusion

In conclusion, GI cancers remain a serious public challenge in Asia, and while some effort has been made, they are still on the rise in many countries. The burden of GI cancers is generally higher in the elderly and males, and East Asia is an area that needs more attention. This study offers insights for estimating trends in the Asia burden of GI cancers, and it should incorporate how intercept interventions impact the incidence of new cases.

Abbreviations

Abbieviation	15
ASDR	Age-Standardized Death Rate
ASIR	Age-Standardized Incidence Rate
BMI	Body Mass Index
CODEm	Cause of Death Ensemble model
CRC	Colon and rectum cancer
DALYs	Disability-adjusted life-years
DisMod-MR	Disability-Adjusted Life Year Meta-Regression
EAPC	Estimated Annual Percentage Change
EC	Esophageal cancer
GBBTC	Gallbladder and biliary tract cancer
GBD	Global Burden of Disease
ICD-10	International Classification of Diseases, Tenth Revision
LC	Liver cancer
PAF	Population attributable fraction
PC	Pancreatic cancer
SC	Stomach cancer
SDI	Socio-demographic Index
ST-GPR	Spatio-Temporal Gaussian Process Regression
UI	Uncertainty interval
WHO	World Health Organization
	-

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

All authors contributed to the study's conception and design. XQ and CX performed data collection and analysis. XQ and YL wrote the manuscript. XQ, CX,

and YL polished and revised the manuscript. All authors commented on previous versions of the manuscript and read and approved the final manuscript.

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Data availability

All data were available from the GBD 2019 database (https://ghdx.healthdata. org/gbd-2019).

Declarations

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Consent for publication

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Competing interests

The authors declare no competing interests.

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