ORIGINAL RESEARCH

Burden of Gastrointestinal Tumors in Asian Countries, 1990–2021: An Analysis for the Global Burden of Disease Study 2021

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Background: Gastrointestinal tumors represent a significant component of the cancer burden in Asia. This study aims to evaluate the burden of gastrointestinal tumors in Asia from 1990 to 2021 using data from the Global Burden of Disease Study 2021 (GBD 2021).
Methods: The absolute incidence, mortality, and disability adjusted life years (DALYs) number and rate of six gastrointestinal tumors (colon and rectum cancer (CRC), stomach cancer (SC), pancreatic cancer (PC), esophageal cancer (EC), liver cancer (LC) and gallbladder and biliary tract cancer (GBTC)) in 48 Asian countries were extracted from GBD 2021. Differences were analyzed based on gender, age, year, location and socio-demographic index (SDI).
Results: In 2021, SC accounted for the highest disease burden in Asia (DALYs=16.41million [95% *UI*: 13.70, 19.62]). From 1990 to 2021, the age-standardized incidence rates of EC, LC, and SC in Asia declined, while the incidence rates of CRC and PC increased significantly, with CRC showing the largest rise (AAPC=1.08 [95% *CI*: 1.02 to 1.12]). Gastrointestinal tumors DALY rates peaked at age 70 and above, with males generally exhibiting higher rates than females. Furthermore, East Asia bears a higher burden compared to other Asian subregions. A higher SDI correlates with increased DALY rates for PC, but no linear relationship was observed for other gastrointestinal tumors.
Conclusion: The burden of gastrointestinal tumors in Asia remains high and may continue to increase. Therefore, effective prevention and treatment measures are essential to address the challenge posed by gastrointestinal tumors.
Keywords: Asia, gastrointestinal tumors, burden, trends

Introduction

Gastrointestinal tumors, including colon and rectum cancer (CRC), stomach cancer (SC), pancreatic cancer (PC), esophageal cancer (EC), liver cancer (LC), and gallbladder and biliary tract cancer (GBTC), pose significant global challenges due to their high incidence and mortality rates. These tumors account for more than a quarter of all tumour cases worldwide and over a third of related deaths.[1] According to GBD 2019 data, five of the top ten cancers ranked by Disability Adjusted Life Year (DALY) in 2019 are gastrointestinal tumors, including CRC, SC, LC, EC, and PC.[2] In 2020, over half of the global cancer cases and 58.3% of deaths occurred in Asia, home to approximately 60% of the world's population. Over the past three decades, there has been a significant increase in the incidence of gastrointestinal tumors in Asia, with cases of CRC, GBTC, and PC more than doubling.[3] Remarkably, over three-quarters of SC and EC patients worldwide are located in Asia.[4]

The diverse ethnic background, a wide range of exposure variables, and rapid changes in personal habits (such as smoking, diet, and physical activity) in Asia have led to epidemiological shifts in gastrointestinal tumors in this region.[5]

For SC, *Helicobacter pylori* infection is a crucial risk factor, with infection rate around 90% in Asian countries and 60% in Western countries.[6–9] EC ranks as the seventh most common cancer globally, with China contributing to over half of global EC cases.[10] Studies suggest that this prevalence is strongly associated with Chinese dietary habits, including preferences for pickled vegetables and strong alcohol consumption.[11,12] In summary, various factors contribute to the heightened risk of gastrointestinal tumors among Asians, making them a significant public health threat in this region.

Recent studies have reported trends in specific gastrointestinal tumors globally or within individual Asian countries over the past three decades, but there is a lack of comprehensive studies on the overall burden of gastrointestinal tumors across all 48 Asian countries.[13,14] Our study aims to examine the burden of six gastrointestinal tumors across 48 Asian countries and regions from 1990 to 2021. Utilizing GBD 2021 data,[15] we assessed the current burden of gastrointestinal tumors through estimates of incidence, mortality, and DALYs. Differences based on gender, age, year, location, and socio-demographic index (SDI) were also analyzed. This comprehensive study is the first of its kind on the epidemiology of gastrointestinal tumors across all 48 Asian countries. Our research encompasses not only the analysis of specific gastrointestinal tumors but also a comprehensive assessment of the overall burden of these tumors. This study extends previous research and provides valuable insights for policymakers to assess the overall burden of gastrointestinal tumors and progress compared to other Asian countries at varying levels of development. This, in turn, will facilitate the formulation of targeted prevention strategies and the allocation of public health resources.

Method
Data Sources
The data for this study were sourced from the GBD 2021 study.[15] The retrieval of data was facilitated through the GBD results tool (https://vizhub.healthdata.org/gbd-results/). GBD 2021 provides estimates of incidence, prevalence, years of life lost (YLL), years lived with disability (YLD), DALYs, and health life expectancy (HALE) across time, region, gender, age group, and SDI, to evaluate the health losses caused by 371 diseases and injuries in 204 countries and regions, encompassing 811 locations from 1990 to 2021.

According to the definition of GBD, the cancer codes for the six types of gastrointestinal tumors are delineated as follows: C18-C21.9, D01.0-D01.3, D12-D12.9, D37.3-d37.5 for Colon and rectum cancer; C22-C22.9, D13.4 for liver cancer; C16-C16.9, D00.2, D13.1, D37.1 for stomach cancer; C15-C15.9, D00.1, D13.0 for esophageal cancer; C25-C25. 9, D13.6-D13.7 for pancreatic cancer; C23-C24.9, D13.5 for gallbladder and biliary tract cancer.

The 48 countries and regions in Asia were classified into five geographical subregions according to United Nations standards: East Asia, South-eastern Asia, Central Asia, Southern Asia, and Western Asia. Among these, Central Asia and East Asia comprise five countries each, Southern Asia has nine, South-Eastern Asia eleven, and Western Asia eighteen.

The Socio-demographic Index (SDI), a composite metric measuring per capita income distribution, average education level, and total fertility rate of the population under 25 years old, ranged from 0 to 1. Asian countries were categorized into five groups based on their 2021 SDI values: low SDI (<0.455), low-middle SDI ($\geq$ 0.455 and <0.608), middle SDI ($\geq$ 0.608 and <0.690), high-middle SDI ($\geq$ 0.690 and <0.805), and high SDI ($\geq$ 0.805).

The indicators used in this study to quantify disease burden include incidence, mortality, and DALYs. The incidence estimates were generated using the Disease Modeling Meta Regression; version 2.1 (DisMod-MR 2.1) from the Global Burden of Disease Study. DisMod MR 2.1 is a Bayesian disease modeling meta regression tool.[16] The Cause of Death Ensemble model(CODEm) is a modeling tool developed by GBD to estimate cause-specific deaths rates. This model assesses the out-of-sample predictive validity of various statistical models and covariate arrangements, combining these results to generate cause-specific deaths estimates. DALYs is the sum of YLD and YLL, which quantifies the health loss caused by specific diseases.[16] YLDs were calculated by multiplying cause-age-sex-location-year-specific prevalence of sequelae by their respective disability weights, for each disease and injury. YLLs were calculated by multiplying cause-age-sex-location-year-specific deaths by the standard life expectancy at the age that death occurred.[17]

The age-standardized rate is a weighted average of age-specific rates per 100,000 population, where the weighting is based on the proportions of the population in the corresponding age groups in the WHO standardized population. Age-standardized rates adjust for differences in the age distribution across population by applying these rates to the

standardized population.[16] The percentage change is defined as (VALUES2021-VALUES1990)/VALUES1990×100%, showing the changes between 1990 and 2021. In the GBD study, all estimates were reported with a 95% uncertainty interval (*UI*), defined as the 25th and 975th values of the 1000 ordinal values.[16] The *UI* accounts for variance in parameter estimates as well as uncertainties from data collection, model selection, and parameter estimation processes.

Statistical Analyses

The absolute numbers and age-standardized rates of gastrointestinal tumor incidence, mortality, and DALYs were extracted, stratified by gender and 14 age groups (ranging from 30 to 95+ years in five-year intervals), annually from 1990 to 2021. To assess the temporal trends of gastrointestinal tumor burden in Asia from 1990 to 2021, we utilized joinpoint regression analysis (version 5.0). This method enables segmented regression modeling based on the temporal distribution characteristics of diseases. The study period was divided into distinct intervals using multiple joinpoints, facilitating trend fitting and optimization for each interval. This approach provided a comprehensive evaluation of disease dynamics across different time segments within the global timeframe.[18] The joinpoint model was applied to compute the average annual percentage change (AAPC), annual percentage change (APC), and corresponding 95% confidence interval (95% *CI*) for this study. APC was employed to detect linear trends during specific stages, whereas AAPC estimated the average APC across the entire period. Additionally, R software (version 4.3.1) was utilized for data analysis and visualization. Statistical significance was set at *P*<0.05.

Results

Burden of Gastrointestinal Tumors in Asia, 2021

In 2021, the absolute number of incidence, deaths and DALYs of gastrointestinal tumors in Asia significantly higher than those in Europe, the Americas and Africa. Asia reported the highest rates of incidence, deaths, and DALYs for EC, GBTC and SC, ranking third for CRC and PC. Additionally, LC displayed the highest incidence rate and the second highest mortality and DALY rates (Figure 1). Table 1 provides a comprehensive summary of gastrointestinal tumor indicators for 2021, highlighting that DALYs for gastrointestinal tumors in Asia were primarily attributed to SC (16.41 million, 95% *UI* 13.70–19.62), followed by CRC (13.37 million, 95% *UI* 11.82–15.05), EC (9.52 million, 95% *UI* 8.09–11.11), LC (8.87 million, 95% *UI* 7.73–10.32), PC (5.40 million, 95% *UI* 4.69–6.14), and GBTC (2.52 million, 95% *UI* 1.94–3.06). CRC (1.15 million, 95% *UI* 1.01–1.30 and SC (0.68 million, 95% *UI* 0.56–0.81) emerged as the primary contributors to the incidence and mortality burden of gastrointestinal tumors, respectively.

Time Trends in the Burden of Gastrointestinal Tumors in Asia, 1990-2021

From 1990 to 2021, the absolute number of gastrointestinal tumors in the Asian population showed a consistent increase. However, the decreasing age-standardized DALY rates for CRC, EC, GBTC, LC, and SC indicated a reduction in their burdens. Conversely, the increasing age-standardized rates for PC suggested a rising burden. Among these, PC, CRC, and GBTC experienced the fastest growth in absolute numbers. CRC showed the fastest increase in age-standardized incidence rate (AAPC=1.08 [95% *CI*: 1.02, 1.12]). PC displayed the most rapid increases in age-standardized mortality rate (AAPC=0.64 [95% *CI*: 0.61, 0.67]) and DALY rate(AAPC=0.38 [95% *CI*: 0.35, 0.41]). Conversely, SC showed the fastest declines in age-standardized incidence rate(AAPC=−1.78 [95% *CI*: −1.81, −1.74]), mortality rate (AAPC=−2.26 [95% *CI*: −2.29, −2.23]), and DALY rate(AAPC=−2.59 [95% *CI*: −2.61, −2.56]) (Table 1).

Figure 2 and Table S1 present the Joinpoint analysis of various indicators of gastrointestinal tumors in Asia from 1990 to 2021. Joinpoint regression analysis revealed that SC, the most burdensome gastrointestinal tumor in Asia, exhibited a declining overall incidence and mortality rate, though its mortality and DALY rate remained significantly higher compared to other tumors, ranking first. Notably, CRC witnessed a rapid increase in incidence rate, becoming the highest among gastrointestinal tumors from 2013 to 2021. Its mortality and DALY rate remained relatively stable EC experienced the most significant decline in incidence rate(APC=−3.87 [95% *CI*: −4.14,-3.42]) and mortality rate (APC= −4.56 [95% *CI*: −4.90,-3.92]) between 2004 and 2007. LC demonstrated an upward trend in DALYs. The fastest growth DALYs was observed from 2012 to 2015 (APC=3.34 [95% *CI*: 2.40, 3.89]). Its DALY rate exhibited a downward trend.
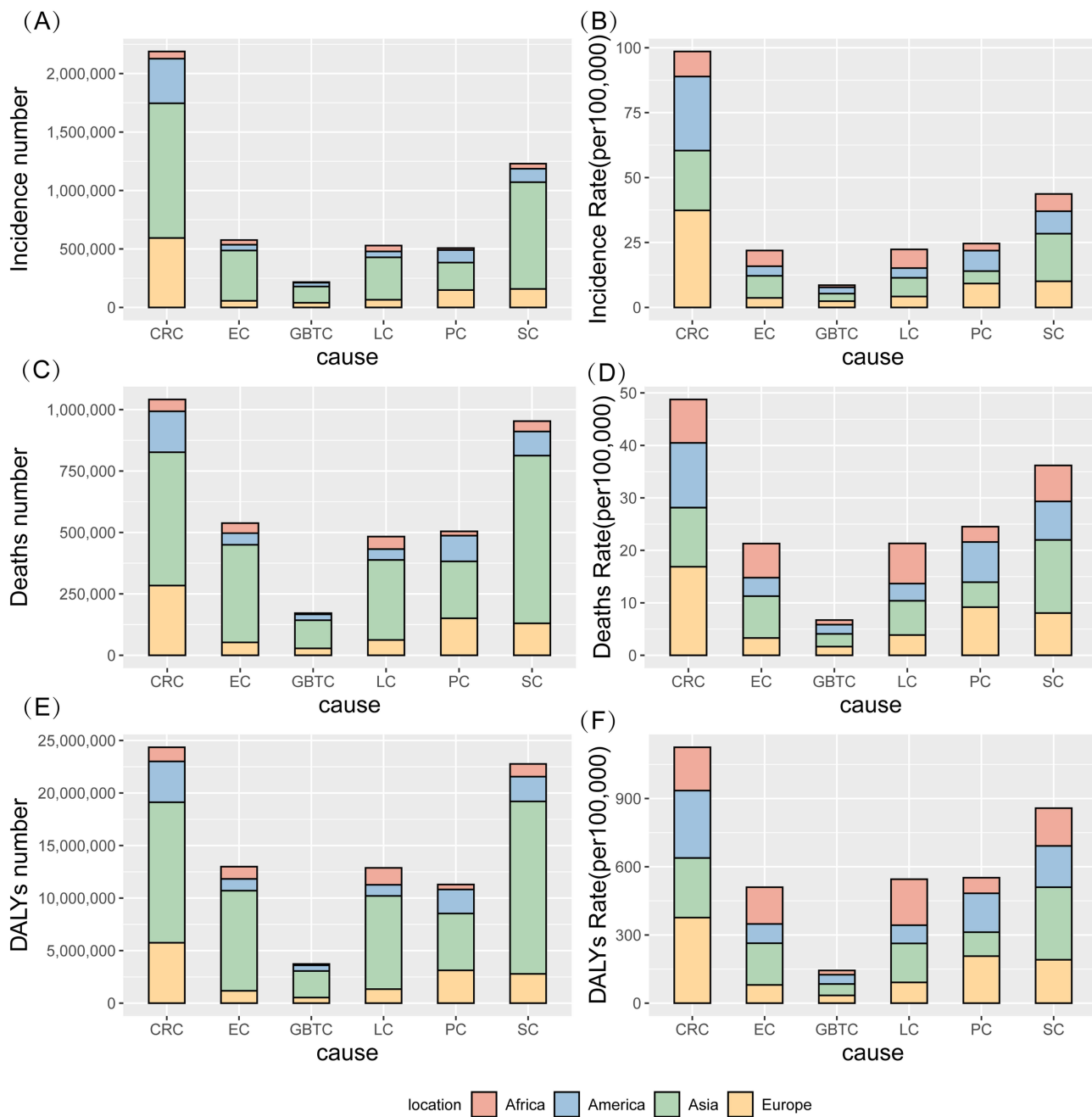
Figure 1 The burden of gastrointestinal tumors in four continents, 2021. (**A**) Incidence; (**B**) Age-standardized incidence rates(per 100,000); (**C**) Deaths; (**D**) Age-standardized deaths rates(per 100,000); (**E**) DALYs; (**F**) Age-standardized DALY rates(per 100,000).

The largest decrease was noted from 2000 to 2005 (APC=−3.19 [95% *CI*: −4.39,-2.50]). GBTC saw a continuous decrease in DALY rate over the study period. The most substantial decrease was observed from 2005 to 2015 (APC= −1.02 [95% *CI*: −1.12,-0.96]). From 1990 to 2021, despite an overall upward trend in DALY rate, PC experienced a slight decrease between 2011 and 2014 (APC=−0.48 [95% *CI*: −0.72,-0.08]).

Sex and Age Diversities in the Burden of Gastrointestinal Tumors in Asia, 2021

Distinct gastrointestinal tumors exhibited varying age distributions and age-standardized DALY rates. Detailed distributions of DALYs and age-standardized DALY rates across age groups and genders in 2021 were illustrated in Figure S1. In Asian males, CRC was the predominant contributor to gastrointestinal tumor DALYs and age-standardized DALY rates in the 30–34 and 95+

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Table 1 Age-Standardized Rates (per 100,000) and Absolute Number of Incidence, Deaths and DALYs by Gastrointestinal Tumors Category in Asia, 1990–2021
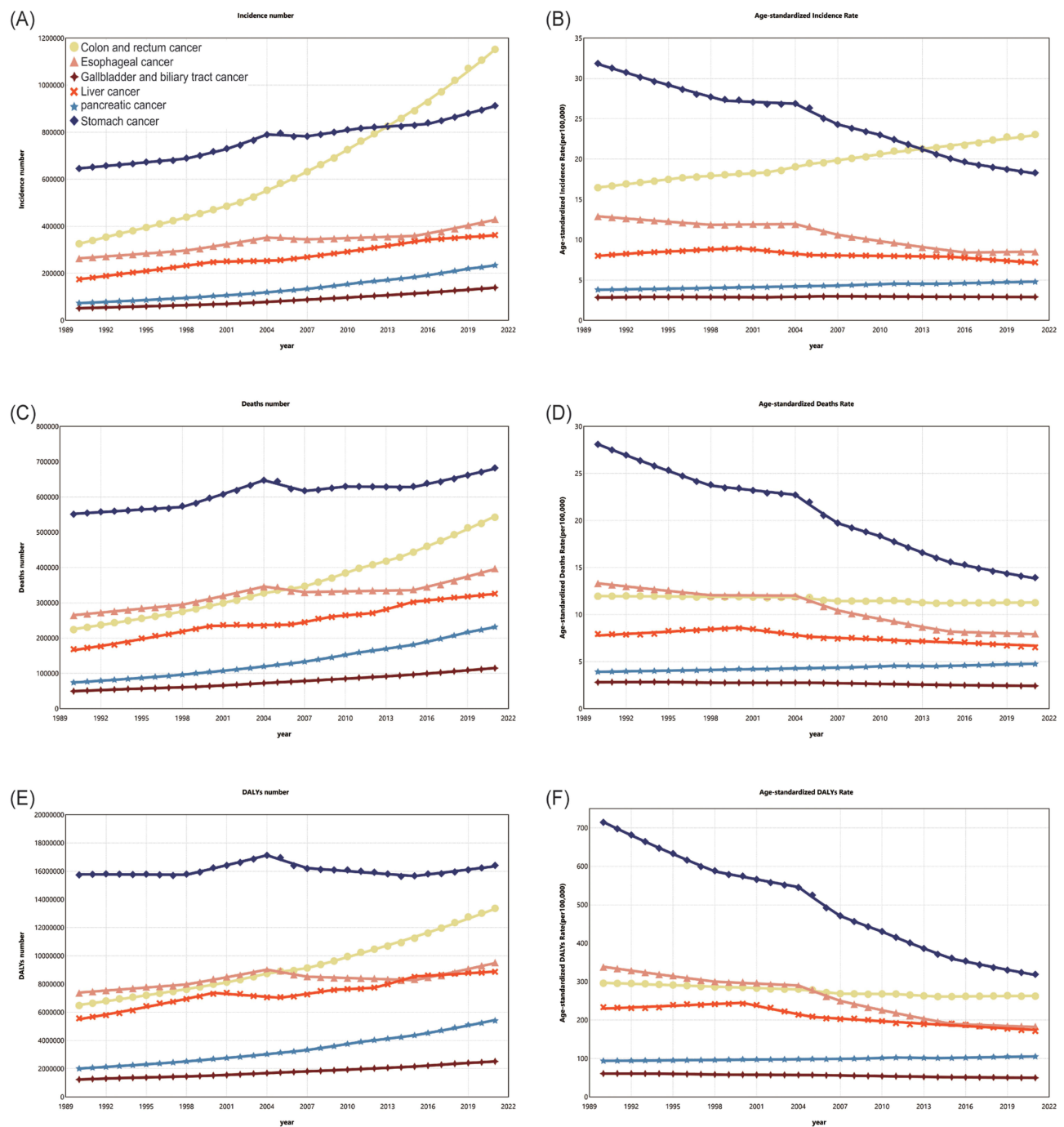
Gastrointestinal tumors	Absolute number (95% *UI*)			Age-standardized rate (per 100,000) (95% *UI*)		
	1990	2021	AAPC	1990	2021	AAPC
Colon and rectum cancer						
Incidence	325,782	1,152,347	4.16	16.46	23.06	1.08
	(296,880–354,365)	(1,007,126–1,299,533)	(4.11 to 4.20)	(15.01–17.87)	(20.10–25.98)	(1.02 to 1.12)
Deaths	224,181	542,560	2.89	11.95	11.26	−0.19
	(202,678–246,445)	(479,624–605,553)	(2.86 to 2.92)	(10.80–13.08)	(9.92–12.55)	(−0.22 to −0.16)
DALYs	6,481,032	13,371,934	2.34	295.96	262.34	−0.39
	(5,808,226–7,182,050)	(11,816,659–15,046,630)	(2.30 to 2.37)	(267.44–326.31)	(232.30–294.71)	(−0.42 to −0.36)
Esophageal cancer						
Incidence	263,115	429,890	1.57	12.90	8.50	−1.34
	(227,618–297,194)	(363,580–499,301)	(1.53 to 1.61)	(11.20–14.51)	(7.23–9.84)	(−1.38 to −1.30)
Deaths	264,537	397,324	1.30	13.31	7.98	−1.66
	(228,999–298,414)	(337,201–459,466)	(1.25 to 1.34)	(11.57–14.95)	(6.81–9.22)	(−1.71 to −1.62)
DALYs	7,366,387	9,523,437	0.81	338.13	183.21	−1.98
	(6,362,123–8,349,001)	(8,090,102–11,106,298)	(0.76 to 0.84)	(293.01–382.08)	(155.90–213.27)	(−2.03 to −1.95)
Gallbladder and biliary tract cancer						
Incidence	51,517	139,381	3.25	2.85	2.91	0.05
	(43,653–60,808)	(107,190–168,076)	(3.22 to 3.28)	(2.43–3.33)	(2.24–3.46)	(0.03 to 0.08)
Deaths	49,443	114,832	2.76	2.80	2.42	−0.48
	(41,691–59,255)	(89,031–137,721)	(2.73 to 2.79)	(2.40–3.33)	(1.87–2.85)	(−0.45 to −0.50)
DALYs	1,237,416	2,521,805	2.32	60.86	49.94	−0.64
	(1,008,638–1,478,176)	(1,936,539–3,061,532)	(2.29 to 2.35)	(50.73–72.79)	(38.65–60.40)	(−0.66 to −0.62)
Liver cancer						
Incidence	174,570	362,876	2.37	8.00	7.19	−0.36
	(157,322–191,617)	(319,312–418,350)	(2.33 to 2.41)	(7.25–8.78)	(6.33–8.28)	(−0.39 to −0.33)
Deaths	168,629	325,803	2.20	7.94	6.52	−0.48
	(151,464–185,189)	(287,401–375,776)	(2.12 to 2.26)	(7.19–8.74)	(5.74–7.52)	(−0.57 to −0.38)
DALYs	5,572,313	8,871,216	1.55	233.53	171.47	−0.89
	(4,970,859–6,151,703)	(7,734,221–10,317,636)	(1.47 to 1.62)	(208.97–256.87)	(150.05–198.86)	(−0.97 to −0.80)

(*Continued*)

Table 1 (Continued).

Gastrointestinal tumors	Absolute number (95% UI)			Age-standardized rate (per 100,000) (95% UI)		
	1990	**2021**	**AAPC**	**1990**	**2021**	**AAPC**
Pancreatic cancer						
Incidence	73,435	234,559	3.80	3.81	4.78	0.77
	(66,358–81,421)	(205,778–264,948)	(3.77 to 3.84)	(3.45–4.20)	(4.19–5.39)	(0.74 to 0.80)
Deaths	74,009	231,770	3.74	3.92	4.75	0.64
	(66,873–82,214)	(203,197–261,662)	(3.70 to 3.78)	(3.54–4.33)	(4.17–5.34)	(0.61 to 0.67)
DALYs	2,010,590	5,404,922	3.26	93.87	105.26	0.38
	(1,809,748–2,243,943)	(4,693,887–6,135,548)	(3.23 to 3.29)	(84.72–104.39)	(91.81–119.10)	(0.35 to 0.41)
Stomach cancer						
Incidence	645,662	913,055	1.12	31.86	18.30	−1.78
	(559,936–727,668)	(751,620–1,089,660)	(1.09 to 1.14)	(28.02–36.01)	(15.05–21.65)	(−1.81 to −1.74)
Deaths	551,130	682,477	0.67	28.11	13.93	−2.26
	(475,566–630,497)	(561,131–809,426)	(0.65 to 0.70)	(24.60–32.27)	(11.47–16.44)	(−2.29 to −2.23)
DALYs	15,737,264	16,409,105	0.11	714.46	319.08	−2.59
	(13,322,575–17,823,025)	(13,701,719–19,619,475)	(0.08 to 0.14)	(610.59–812.06)	(266.18–379.89)	(−2.61 to −2.56)

Abbreviations: *UI*, uncertainty interval; AAPC, average annual percentage change; DALYs, disability adjusted life years.

Figure 2 Asian temporal trends in the burden of gastrointestinal tumors, 1990–2021. (**A**) Incidence number (**B**) Age-standardized incidence rate (**C**) Deaths number (**D**) Age-standardized deaths rate (**E**) DALYs number (**F**) Age-standardized DALYs rate.
Abbreviation: DALYs, disability adjusted life years.

age brackets. LC accounted for the highest DALYs and age-standardized DALY rates in males aged 35–39, followed by CRC and SC. SC was the leading cause of gastrointestinal tumor burden in males aged 40–94. For Asian females, SC led in DALYs and age-standardized DALY rates for the 30–44 and 65–79 age groups, while CRC was highest among aged 45–64 and 80+. Overall, the total number of DALYs in males significantly exceeded that in females across these tumors. The male burden was particularly higher than the female for CRC, EC, LC, PC, and SC (gender ratio ≥ 1.63) (Table 2, Figure 3). Contrarily, the DALY rate in females aged 30–69 in GBTC surpassed those in males, and the absolute number of DALYs was also higher in females

Table 2 Asian Age-Standardized DALY Rate(per 100,000) of Male and Female and the Male to Female Ratio by Gastrointestinal Tumors in 2021

Gastrointestinal Cancer	Male(95% UI)	Female(95% UI)	Male to Female Ratio
Colon and rectum cancer	330.42(281.41–389.89)	199.58(172.32–229.06)	1.66
Esophageal cancer	292.07(238.76–351.22)	81.94(63.17–98.48)	3.56
Gallbladder and biliary	50.38(33.39–62.14)	49.89(36.08–60.98)	1.01
Liver cancer	253.92(214.16–312.00)	91.21(79.78–104.74)	2.78
Pancreatic cancer	131.09(111.96–153.41)	80.44(68.10–93.47)	1.63
Stomach cancer	458.63(360.63–583.92)	190.28(162.71–222.34)	2.41

Abbreviation: *UI*, uncertainty interval.

aged 45–74 (Figure S1). Peak DALY numbers for CRC, EC, GBTC, PC, and SC occurred between ages 65 and 69 in both sexes. LC peaked at 55–59 years. Males and females peaked at ages 55–59 and 65–69, respectively. DALY rates of CRC, GBTC and PC escalated with age, peaking at 95+ years old, while those for LC and SC peaked at 90–94 years, and EC peaked at 75–79 years.

Diversities of Gastrointestinal Tumor Burden in Asian Countries, 2021

In 2021, substantial differences were noted in the age-standardized DALY rates for gastrointestinal tumors across Asian countries (Figure S2, Tables S2-S8). Mongolia recorded the highest age-standardized DALY rates for EC, LC, and SC among 48 Asian countries. The highest age-standardized DALY rates for CRC, GBTC, and PC were in Brunei Darussalam, Thailand, and Armenia, respectively. From 1990 to 2021, there was an increase in total DALYs associated with gastrointestinal tumors in 45 countries, while the rate of DALYs decreased in the same number of countries. Qatar saw the most significant rise in DALYs (percentage change=494.94%), whereas Pakistan and Republic of Korea experienced the most substantial growth and decline in DALY rates, respectively (8.44% and −63.39%).

As depicted in Figure 4, disparities were evident in the rankings of gastrointestinal tumors by age-standardized DALY rates across Asian nations. SC was the predominant cause in most Central and Southern Asian countries, whereas CRC led in Southeast Asia, followed by SC and LC, except for Thailand, where LC and CRC were the leading causes. In Western Asia, CRC was most prevalent, followed by SC, with PC ranking second in four nations. GBTC was ranked
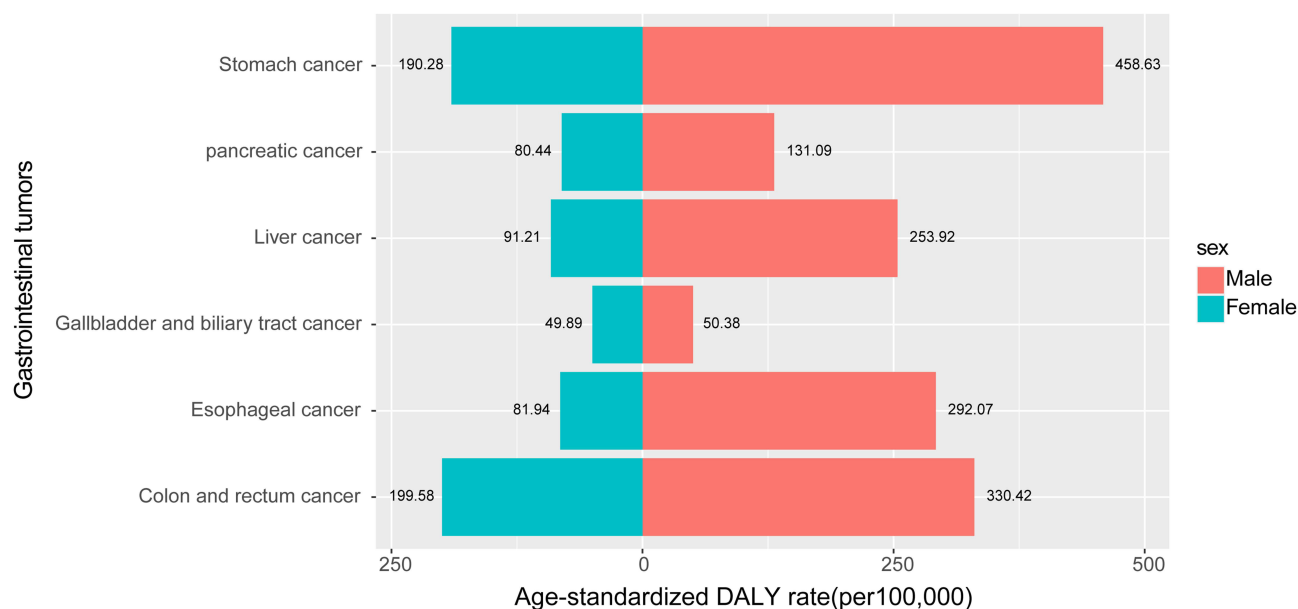
Figure 3 Asian age-standardized DALY rate(per 100,000) of male and female by gastrointestinal tumors in 2021.
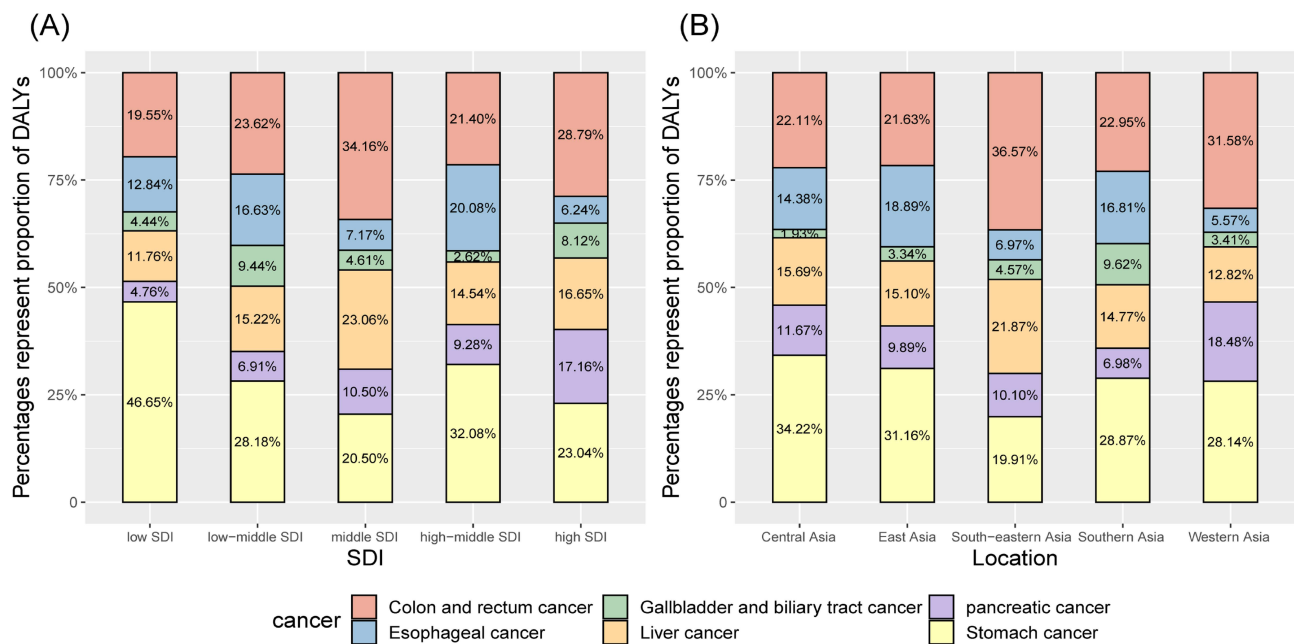**Abbreviation**: DALYs, disability adjusted life years.

Figure 4 Ranking of age-standardized DALY rates(per 100,000) for all gastrointestinal tumors by Asian countries, 2021.
Abbreviation: DALYs, disability adjusted life years.

sixth in 34 countries. Rankings of LC and EC varied significantly, with LC ranking first in nations like Republic of Korea and fifth in Sri Lanka and Iran, whereas EC ranked first in Pakistan and sixth in countries like the Republic of Korea.

Figure 5B highlighted the percentage contribution of each tumor to the overall burden of gastrointestinal tumors DALYs within various Asian subregions. Despite diverse age-standardized DALY rates across countries within the same region, Southeast Asian countries contributed notably more to the CRC burden (36.57%) compared to Central (22.11%) and East Asia (21.63%). Contributions from SC were higher in Central (34.22%) and East Asia (31.16%), but lower in Southeast Asia (19.91%). EC, GBTC, LC, and PC showed the highest contributions in East Asia (18.89%), Southern Asia (9.62%), Southeast Asia (21.87%), and Western Asia (18.48%), respectively.

Figure 5 Percentage contribution of DALYs burden to gastrointestinal tumors in Asia, 2021. (**A**) Different sub-regions; (**B**) Different SDI levels.
Abbreviations: SDI, socio-demographic index; DALYs, disability adjusted life years.

Correlations Between the SDI and Gastrointestinal Tumor Burden, 2021

The relationship between the burden of gastrointestinal tumors and SDI was analyzed in 2021, as illustrated in Figure S3. The age-standardized DALY rates of PC correlated positively with SDI, indicating an association between higher socioeconomic development and increased PC burden. Figure 5A presented the contribution of each tumor to the total gastrointestinal tumors burden across different SDI levels in Asian countries. SC showed the highest proportions of age-standardized DALY rates in low SDI nations (46.65%). LC and CRC were most significant in middle SDI nations (23.06% and 34.16%). GBTC and PC predominated in nations with high-middle SDI and high SDI, respectively.

Discussion

The study offered a comprehensive analysis of the epidemiology of six gastrointestinal tumors across 48 Asian countries from 1990 to 2021, including EC, SC, LC, PC, CEC and GBTC. During this period, Asia emerged as the region with the highest burden of gastrointestinal tumors compared to other continents. In 2021, SC was the primary contributor to DALYs in Asia for gastrointestinal tumors, followed by CRC, EC, LC, PC, and GBTC.

A notable finding is the significant increase in the incidence number of CRC across Asia during the study period. From 1990 to 2021, the incidence number of CRC quadrupled, surpassing SC as the gastrointestinal tumor with the highest incidence number and age-standardized incidence rate. In the 48 Asian countries studied, the age-standardized incidence rate of CRC increased in 36 nations. CRC predominantly contributes to the burden of gastrointestinal tumors in Asian nations with high and middle SDI. The rapid economic growth and industrialization in middle SDI countries post-21st led to changes in lifestyle, including adoption of Western dietary habits characterized by high fat and red meat intake, reduced physical activity, and rising obesity rates,[19,20] which are associated with heightened CRC risk.[21]

Conversely, SC exhibited the most significant decline in the burden among gastrointestinal tumors from 1990 to 2021, despite remaining the top contributor to DALYs. The incidence and mortality rates of SC in Asia decreased significantly, following global trends.[22] *Helicobacter pylori* infection, a major risk factor for SC, accounts for 90% of non-cardiac cases.[23] Recent decades have witnessed a reduction in *Helicobacter pylori* infection, paralleled by improvements in food safety and sanitation conditions, contributing to the decrease in SC incidence.[24] Our research also identified significantly higher incidence rates of SC in select East Asian countries, including Republic of Korea, Japan, Mongolia, China, and Democratic People's Republic of Korea. This disparity may be attributed to the elevated prevalence of East Asian type cagA strains, which confer a greater risk of SC compared to non-East Asian variants.[25,26] Lifestyle factors, particularly the high-sodium diet prevalent among East Asian populations, significantly influence the burden of SC.[27,28] Interventions to reduce dietary salt are essential in addressing SC in high-risk Asian countries.[29]

The geographic distribution of EC cases exhibits significant disparities. Nearly 80% of occurrences are observed in Asia.[30] The Asian Esophageal Cancer Belt, stretching from China to Iran along the Caspian Sea, consistently reports high incidence rates of EC since the 1970s, with over 90% of cases being esophageal squamous cell carcinoma.[31] Distinct from the global trend where tobacco and alcohol are primary risk factors for EC, this region faces unique challenges such as low intake of fresh fruits and vegetables, opium use, poor oral health, and indoor air pollution.[32–34] The negative correlation between the age-standardized DALY rate of EC and socio-economic status in Asia suggests that socio-economic improvements could influence EC incidence rates.[30]

LC ranks as the third leading cause of cancer-related deaths globally in 2020, following lung cancer and CRC.[35] Hepatocellular carcinoma (HCC) constitutes the predominant histological type of LC, accounting for 70% to 90% of LC cases.[36] Hepatitis B virus (HBV) and hepatitis C virus (HCV) remain the primary risk factors for LC.[37] Regional disparities in LC etiology reflect variations in risk factors. For instance, East and Southeast Asia reported the majority of LC cases in 2020, largely due to the high prevalence of HBV infection, which accounts for around three-quarters of global HBV carriers.[36] Our research findings reveal diverse trends in LC burden across the Asian population from 1990 to 2021. The incidence and mortality rates of LC have increased in Asian countries such as Nepal, India, Malaysia and Mongolia. Nepal has the highest incidence and mortality rates of LC. Nonetheless, most Asian countries witnessed declines in LC incidence and mortality rates, suggesting successful prevention and control efforts targeting risk factors such as viral hepatitis, alcohol consumption, and metabolic diseases. For example, the incidence and mortality rate of LC

in China decreased by 10.04% and 22.35% respectively, attributed to breakthroughs in HBV prevention and treatment, transitioning from a high to a moderate prevalence area.[38] Therefore, the prevention and treatment methods of LC should be adjusted accordingly according to the changes in the epidemiology of LC in Asia to address new challenges.

PC is the twelfth most common cancer globally but ranks seventh in mortality rates.[1] Its aggressive nature, high malignancy, and challenges in early detection make PC a grave public health concern.[39] From 1990 to 2021, Asia saw substantial increases in PC incidence, mortality, and DALY rates. Deaths nearly equaling the number of diagnosed cases. Our study found that PC burden was much higher in high SDI countries than in low SDI countries. One explanation for this observation is that diagnosis rates are higher in high SDI countries. In contrast, the lack of a well-developed health care system and advanced diagnostic modalities in poorer economic groups leads to under-diagnosis of PC potentially. Western dietary patterns, smoking, and diabetes are major contributors to PC development, with smoking and diabetes being particularly prevalent risk factors in Asia.[40] The age standardized DALY rate of PC in Kuwait, Cyprus, Israel and Bahrain ranks second among various gastrointestinal tumors. Previous studies identified smoking as a primary risk factor for PC, attributing a significantly elevated risk (odds ratio (OR)=1.77) to current smokers.[41] Of global smokers, 30% reside in Asia, particularly in China and India.[42] Moreover, diabetes emerges as an independent risk factor for PC. The association between diabetes and PC risk has been reported in many studies. Having diabetes increases the risk of PC by 1.8 times, especially among Hispanic men and Asians.[43,44] Unfortunately, Southeast Asia and the Western Pacific region harbor the largest populations of diabetes patients globally, constituting approximately 20% of cases worldwide.[45]

GBTC showed the lowest incidence and mortality rates among gastrointestinal tumors, and is the only tumor with more female than male patients in some age groups.[46] Our results indicated that the DALY rate in females aged 30–69 in GBTC was higher than that in males, and the absolute number of DALYs in females aged 45–74 was higher than those in males. This may be linked to biological factors such as sex hormones and pregnancies, which can increase the secretion of cholesterol in the bile, leading to the occurrence of gallstone mediated gallbladder cancer.[47,48] Previous studies have shown that the gallstone is the most important risk factor for GBTC, and other risk factors include diabetes, obesity, hepatitis B and hepatitis C infection.[49–51] In many developed nations, laparoscopic and endoscopic techniques are widely employed for gallstone treatment, effectively halting disease progression.[52] Moreover, early detection plays a crucial role in improving survival rates. Therefore, factors such as underdeveloped economies, high cholelithiasis incidence, and limited medical technology in low-middle SDI areas likely contribute to the rising incidence rates of GBTC.

In terms of time trends, the DALY rate and mortality rate of gastrointestinal tumors in Asia have generally declined (except for PC) over the past three decades, and the absolute numbers have increased significantly. These trends can be attributed to substantial advances in medical technology, including advances in cancer screening techniques and treatments. In addition, increased life expectancy, reduced premature mortality, and an aging population likely contribute to these findings. Notably, the significant and sustained increase in incidence, mortality, and DALY rates for PC far exceeds that of other gastrointestinal tumors, particularly among the elderly.[53] This suggests a unique trend for PC compared to other tumors. Experts predict that within the next decade, the number of deaths from PC will surpass colorectal cancer in the United States and breast cancer in Europe.[54,55] Smoking, hyperglycemia, and high BMI remain critical risk factors for PC globally. As mortality rates from PC continue to climb, the associated costs are also expected to rise. There is an urgent need for further research to identify additional high-risk populations and to expand diagnostic testing. Public health strategies that focus on reducing tobacco use and managing metabolic syndrome should be prioritized.

Significant gender disparities are evident in the burden of gastrointestinal tumors in Asia. In 2021, Asian males bore a considerably higher burden of gastrointestinal tumors compared to females (excluding GBTC). The gender ratios varied from 1.63 in PC to 3.56 in EC. This discrepancy may stem from higher tobacco and alcohol consumption among men, established as primary cancer risk factors. Additionally, hormonal differences between genders could also play a role. Matsuoka H et al[56] have demonstrated that the estrogen receptor ER beta in women can inhibit the growth of EC. Research on colon cancer cells has shown that ER beta receptors also suppress the proliferation of these cells.[57] Sukocheva et al reported that long-term exposure to high concentrations of estrogen makes Barrett's esophageal cells responsive to ER ligand therapy, inhibiting the growth and induces apoptosis in esophageal adenocarcinoma cells.[58] Similarly, a meta-analysis suggests that prolonged exposure to the ovaries or exogenous estrogenic may act as a protective factor against SC.[59] These findings underscore the necessity of

targeted tobacco control strategies, especially for males, such as increasing the legal age for tobacco sales.[60] Implementing these strategies could significantly reduce the burden of gastrointestinal tumors.

Our study underscores a progressive increase in the burden of various gastrointestinal tumors with advancing age. The peak age-standardized DALY rates for these tumors exceed 70 years, reflecting a heightened tumor burden among the elderly. This phenomenon could be attributed to cumulative exposure to risk factors, including unhealthy lifestyle habits (smoking, alcohol consumption), poor dietary choices (high fat, sodium, and sugar diets), and chronic inflammation.[61,62] Age-related physiological changes, such as diminished cell repair and immune function, likely increase cancer susceptibility in older adults.[63] Consequently, implementing tailored intervention measures, such as broader vaccination coverage for middle-aged and elderly populations, early screening for high-risk individuals, promoting healthy lifestyles, and leveraging advancements in medical technology, is crucial.

Several limitations of our study warrant acknowledged. First, the low data quality in less developed regions may significantly impact the overall quality of our study results. The lack of advanced health services, inadequate population coverage, under-diagnosis of diseases, and incomplete data collection in low SDI countries likely contribute to an underestimation of the cancer burden in these countries. Second, the absence of data stratification by cancer subtypes limits the precision of our findings. For example, SC includes both cardiac and non-cardiac types, and EC can be divided into esophageal squamous carcinoma and esophageal adenocarcinoma. These subgroups display distinct characteristics and trends in age-standardized incidence and mortality rates.

Conclusion

In summary, although age-standardized DALY rates for gastrointestinal tumors have shown a decline in most Asian countries over the past three decades, the number of incidence and deaths has witnessed significant increases due to population growth. Nowadays, gastrointestinal tumors remain a substantial contributor to the cancer burden in Asia and globally, presenting formidable challenges to public health advancement. Due to risk factors such as an aging population, tobacco and alcohol consumption, obesity, unhealthy lifestyles, and high rates of viral hepatitis infections, the future burden of gastrointestinal tumors may continue to rise. Variations in disease burden are notable across different countries and regions. Therefore, considering the serious consequences that gastrointestinal tumors can bring to patients and healthcare systems, it is necessary to develop targeted prevention strategies that are suitable for specific socio-economic development conditions and high-risk populations.

Acknowledgments

Ethic Statement

Our study was based on publicly available Global Burden of Disease Study 2021. In the Measures for Ethical Review of Research in Life Sciences and Medicine Involving Human Beings, Article 32 specifies that research in life sciences and medicine involving human beings that uses human information data or biological samples to conduct research in life sciences and medicine involving human beings under the following circumstances, which does not cause harm to human beings, or does not involve sensitive personal information or commercial interests, may be exempted from ethical review, so as to reduce the unnecessary burden on scientific researchers, and to Promote the conduct of life sciences and medical research involving human beings, and stipulates that ethical review can be exempted if research is conducted using legally obtained public data, or data generated by observation and not interfering with public behavior. Therefore, after consultation with the Zhengzhou University Life Sciences Ethics Review Committee, it was deemed that ethical approval was not required.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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The authors declare that there is no conflict of interest in this work.

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