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RESEARCH

# Southeast Asia burden and trend of Gastrointestinal tract cancers from 1990 to 2021 and its prediction to 2050: findings from the Global Burden of Disease Study 2021

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**Abstract**

**Background** The burden of disease associated with gastrointestinal (GI) tract cancer in Southeast Asia has changed significantly in recent years. This study analyzes data from the Global Burden of Disease Study (GBD)-2021 to examine trends in the burden of GI tract cancers in Southeast Asia from 1990 to 2021, identifies key risk factors, and predicts future trends.
**Method** First, this study obtained data on GI tract cancer by age, sex, etiology, incidence, prevalence, deaths, disability-adjusted life years (DALYs), and risk factor from the GBD-2021 study focused on Southeast Asia data from 1990 to 2021. Secondly, the study also examined the temporal trend of subtype-specific GI tract cancer disease burden in Southeast Asia from 1990 to 2021 using linear regression modeling to calculate estimated annual percentage change (EAPC) values. The autoregressive integrated moving average (ARIMA) model was also used to project the future disease burden from 2022 to 2050. Finally, risk factors for GI tract cancer of different etiologies were also analyzed.
**Results** In 2021, the number of deaths, DALYs, incidence, and prevalence cases of GI tract cancers in Southeast Asia were about 216,074, 5,955,050, 258,629, and 686,835, respectively, with colorectal cancer (CRC) associated with the most severe burden of disease. Between 1990 and 2021, the number of deaths and DALYs associated with CRC and pancreatic cancer (PC) and the corresponding age-standardized rates (ASRs) showed a significant upward trend, with the fastest growth being in PC. The total number of esophageal (EC), gastric (GC), liver (LC), and gallbladder and biliary tract (GBTC) cancer-related deaths and DALYs increased, but the age-standardized rates declined significantly. Predictive data suggest that age-standardized death rate (ASDR), ASR of DALYs, age-standardized incidence rate (ASIR), and age-standardized prevalence rate (ASPR) will continue to decline in EC, GC, and LC, with the most pronounced declines, especially in GC. Overall, ASRs will continue to rise in the cases of CRC, PC, and GBTC cancers. ASDRs associated with GI tract cancers are greatest among those over 90 years of age. The burden of disease is significantly greater in men than in women, and this gender-induced difference is most pronounced in LC.
**Conclusion** While the disease burden of various types of gastrointestinal (GI) cancers in Southeast Asia is experiencing both increases and declines, the overall burden remains significant, with the total number of cases expected to rise in the coming years. To alleviate the impact of severe GI cancers, public health professionals and policymakers must proactively develop and adapt prevention and control strategies, ensuring they are aligned with the shifting disease trends and the evolving risk factors associated with each type of GI tumor.

**Keywords** Southeast Asia · Gastrointestinal tract tumors · GBD · ASDR · DALYs · ASIR · ASPR

## Introduction

The disease burden of digestive tract cancers, which are malignant tumors occurring in the alimentary canal and the digestive system, including the esophagus, stomach, colorectum, liver, pancreas, and gallbladder, represents a significant public health challenge. Digestive tract cancers account for approximately 25% of global cancer incidence and one-third of cancer-related deaths [1]. In 2022, cancers of the digestive tract (such as colorectal, stomach, and liver cancers) ranked among the top 10 newly diagnosed cancers worldwide [2]. A global lifetime risk assessment of gastrointestinal (GI) cancers conducted by Wang et al. showed that

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1 in 12 people develop GI cancer in their lifetime and 1 in 16 die of GI cancers. Colorectal cancer (CRC) represents the highest risk, followed by GI, hepatic (LC), esophageal (EC), pancreatic (PC), and gallbladder and biliary tract (GBTC) cancers [3]. Although the global incidence of GI cancer is projected to decline overall, the incidence is expected to rise among individuals under 50 years of age. Furthermore, there is an increasing trend toward earlier onset of GI cancers, particularly CRC, PC, and GBTC, among younger populations [4]. Since young people are a vital part of the workforce and contribute significantly to social and economic development, the rising incidence of GI cancers in this demographic poses potential challenges to both public health and economic stability.

There are notable regional variations in the risk of digestive tract cancers worldwide. East Asia has the highest lifetime risk of stomach, liver, esophageal, and GBT carcinomas, while Western Europe experiences the highest risk of PC. In Southeast Asia, the incidence of CRC has been steadily increasing [2]. Over the past few decades, the epidemiology of GI cancers has evolved dynamically, influenced by economic globalization, environmental changes, and shifts in dietary patterns. Southeast Asian countries, in particular, are undergoing a significant dietary and lifestyle transition, with diets increasingly centered on animal-based foods and sedentary lifestyles becoming more common, which is heightening the risk of GI cancers [5, 6].

The incidence of LC has historically had the highest incidence in Southeast and East Asia. However, its etiology is undergoing a shift from decreasing rates of hepatitis B and C virus (HBV and HCV) infections and reduced aflatoxin exposure to an increase in the prevalence of obesity, alcoholic liver disease (ALD), nonalcoholic fatty liver disease (NAFLD), and metabolic syndrome, contributing to the changing landscape of LC risks [7]. GI tumors are largely preventable, and their incidence could be reduced through the elimination of established risk factors, such as smoking, alcohol consumption, obesity, *Helicobacter pylori* (*H. pylori*) infection, and viral hepatitis [8, 9]. Timely updates on the changing epidemiology of GI cancers in Southeast Asia, along with a close examination of shifting risk factors, are crucial for developing effective prevention strategies and reducing the associated disease burden.

Previous studies have reported global trends in specific GI tumors globally and examined trends in individual Asian countries from 1990 to 2019 [10, 11]. A more recent study extended this analysis to six types of GI tumors in 48 Asian countries and territories from 1990 to 2021 [12]. However, these studies have not thoroughly explored the changing trends of GI tumors in Southeast Asia or predicted future trends in the region. To address these gaps, our study comprehensively examines the burden of disease related to various GI cancers in Southeast Asia from 1990 to 2021, using the latest Global Burden of Disease (GBD)−2021 data to project future trends. Additionally, we provide an in-depth analysis of the evolving risk factors for these cancers, aiming to inform the assessment of existing prevention and control measures in Southeast Asia.

## Materials and methods

### Data source

The GBD-2021 study evaluated 371 health conditions, injuries, and impairments, along with 88 risk factors across 204 countries and regions using epidemiological data and standardized methodologies. Data were accessed via the Global Health Data Exchange (GHDx) (http://ghdx.healthdata.org/gbd-results-tool), divided into 27 geographic sectors.

GI tract cancer data, including incidence, mortality, prevalence, DALYs, and 95% uncertainty intervals, were retrieved for Southeast Asia using the following cancer codes: C18-C21.9, D01.0-D01.3, D12-D12.9, and D37.3-D37.5 for CRC; C22-C22.9 and D13.4 for LC; C16-C16.9, D00.2, D13.1, and D37.1 for gastric cancer; C15-C15.9, D00.1, and D13.0 for esophageal cancer; C25-C25.9 and D13.6-D13.7 for PC; and C23-C24.9 and D13.5 for GBTC [12].

Age-standardized rates (ASR) and estimated annual percentage changes (EAPC) were used to assess GI tract cancer prevalence and mortality. ASRs guided prevention strategies, while EAPC summarized ASR changes over time.

DisMod-MR 2.1 software estimated disease incidence through a cascade process, with adjustments for non-specific age and sex data and a meta-regression-Bayesian, regularized, trimmed (MR-BRT) approach [13]. Secondary and tertiary risk factors, selected based on World Cancer Research Fund guidelines, were analyzed using a comparative risk assessment model [14].

### Statistical analysis

The study first presents the number of deaths and DALYs from GI tract cancers for 2021, along with their ASRs and subtypes, categorized by age group and sex. Additionally, temporal trends from 1990 to 2021 were analyzed using EAPC values from linear regression. Spearman correlation analysis assessed EAPC-ASR relationships. For predicting future trends in the prevalence and incidence of GI tract cancer, we applied the autoregressive integrated moving average (ARIMA) model. This model requires transforming the time series data into a stationary form through differencing before analysis. The ARIMA model is defined by three key parameters: $p$ (autoregressive order), $d$ (differencing order), and $q$ (moving average order), which were determined through the autocorrelation function (ACF) and the partial autocorrelation function (PACF) analyses. Forecasting was performed using the forecast and tseries packages in R, which enabled both predictions and graphical representations of the results. To ensure the robustness and accuracy of our forecasts, several validation techniques were applied: we tested the independence of forecast errors using the Ljung-Box *Q*-test, confirmed the normal distribution of residuals with a mean of zero using the Shapiro–Wilk test, and assessed the homoscedasticity of residuals through visual inspection and the Breusch-Pagan test. Statistical significance was set at a *P* value of less than 0.05. All data organization and analysis were performed using R software (version 4.3.2).

## Results

### GI tract cancer disease burden in Southeast Asia in 2021

In 2021, the total number of deaths from GI tract cancers in Southeast Asia was approximately 216,074, with 5,955,050 cases of DALYs, 258,629 new incidence cases, and 686,835 prevalent cases. Among these, CRC had the highest burden, with 79,420 deaths cases (95% UI: 68,450–89,290) and 2,166,650 DALYs cases (95% UI: 1,868,880–2,456,350). This cancer type had the largest ASRs. EC, with 15,830 deaths (95% UI: 13,725–18,154) and 437,488 DALYs (95% UI: 374,888–504,001), had an ASDR of 2.44 (95% UI: 2.13–2.78) per 100,000 and an ASR of DALYs of 61.71 (95% UI: 53.19–70.79) per 100,000 (Tables 1, 2, 3, and 4). Age-specific trends revealed that the highest number of deaths from EC and LC occurred in the 60–64 age group, while the highest number of deaths from GC, CRC, PC, and GBTC occurred in the 65–69 age group. The 90–94 age group showed the highest ASDRs for EC, LC, and PC, while the 95 + age group had the largest ASDRs for GC, CRC, and GBTC (Fig. 1A–F). Gender differences were notable across all GI cancers, with the disease burden significantly higher in men. The gender gap was most pronounced for LC (Fig. 2D), followed by EC (Fig. 2A) and GC (Fig. 2B) types. The smallest gender disparity was observed for PC (Fig. 2E).

### Changing trends in the disease burden of gastrointestinal tract cancer in Southeast Asia, 1990–2021

From 1990 to 2021, the burden of GI tract cancers in Southeast Asia—measured by deaths, DALYs, incidence, and prevalence—showed significant increases. PC displayed the largest rise in both deaths and DALYs, with a 2.87-fold increase in deaths and a 2.62-fold increase in DALYs from 1990. CRC followed closely in terms of growth. Conversely, the slowest growth was observed for GC, which observed only a 0.58-fold increase in deaths and a 0.45-fold increase in DALYs. ASRs indicate a general decline in the disease burden for EC, GC, LC, and GBTC types in Southeast Asia (Fig. 3A, B, D, F), with GC showing the most pronounced decreasing trend, while the disease burden of CRC and PC has been increasing (Fig. 3C, E).

Age-specific trends revealed that the largest increase in the number of deaths was observed in the 60–69 age group, while the 55–64 age group presented the most significant rise in DALYs. Although EC showed an overall decline, the burden continued to rise in the 95 + age group, as did the burden of CRC, LC, and PC in this age group (Fig. 4A). For GC, the decline in disease burden was most pronounced among individuals over 50 years of age (Fig. 4B). In CRC, the burden of disease increases significantly in people over 64 years of age (Fig. 4C). LC experienced a decreasing trend in the 65–74 age group, with an increase in the 80 + age group (Fig. 4D). In PC, the trend of increasing disease burden was most obvious in the age group of 50 years or older (Fig. 4E). GBTC experienced the greatest increase in deaths in the 65–74 age group (Fig. 4F).

At the gender level, both deaths, DALYs, incidence, and prevalence of GI cancers increased significantly in both sexes from 1990 to 2021 in Southeast Asia, with a more pronounced rise in men. In EC, ASRs remained stable in men, while they showed a marked decrease in women (Fig. 5A). This suggests that much of the decline in the overall burden of EC is driven by reduced disease burden in women. In GC and LC, the decreasing trend in disease burden was nearly identical in both sexes (Fig. 5B, D). In CRC and PC, the trend of increasing disease burden was more pronounced in males than in females (Fig. 5C, E). In GBTC, ASRs showed a significant increasing trend in males, while the opposite trend was observed in females. During 1990–2000, the disease burden of GBTC was significantly greater in females than in males in Southeast Asia, but by 2000, the trend reversed, with men now bearing a larger burden (Fig. 5F).

### Forecasting future trends in GI tract cancer disease burden in Southeast Asia

Based on projections from the ARIMA model, the disease burden of GI cancers in Southeast Asia is expected to continue rising over the next 25 years. By 2050, the number of deaths from EC, GC, CRC, LC, PC, and GBTC is projected to reach 2050 to be 27,586, 676,97, 157,659, 72,670, 48,569, and 23,028 (Table S1). The ASDR, ASR of DALYs, ASIR, and ASPR for EC, GC, and LC will continue to decline (Fig. 6A, B, and D), with GC showing the most significant decreases. In contrast, the overall ASRs for CRC, PC, and GBTC will rise (Fig. 6C, E, F).

**Table 1** Number of deaths and age-standardized deaths rates due to gastrointestinal (GI) cancer in 1990 and 2021 and trends in Southeast Asia from 1990 to 2021

| Characteristics | Number of deaths cases (95% uncertainty intervals (UI)) in 1990 | The age-standardized deaths rate/100,000 (95% UI) in 1990 | Number of deaths cases (95% UI) in 2021 | The age-standardized deaths rate/100,000 (95% UI) in 2021 | Estimated annual percentage change (EAPC) (95% confidence intervals (CI)) |
|---|---|---|---|---|---|
| Esophageal cancer (EC) | 7108 (5964–8306) | 2.83 (2.39–3.3) | 15,830 (13,725–18,154) | 2.44 (2.13–2.78) | − 0.55 (− 0.6 to − 0.51) |
| Female | 2795 (2028–3365) | 2.12 (1.56–2.55) | 4696 (3784–5821) | 1.4 (1.13–1.73) | − 1.48 (− 1.57 to − 1.39) |
| Male | 4314 (3586–5353) | 3.64 (3.04–4.49) | 11,134 (9568–12,711) | 3.65 (3.17–4.16) | − 0.02 (− 0.06 to 0.01) |
| Gastric cancer (GC) | 27,448 (22,187–31,331) | 10.92 (8.91–12.54) | 43,303 (37,510–51,160) | 6.83 (5.94–8.16) | − 1.7 (− 1.77 to − 1.63) |
| Female | 11,319 (9354–13,082) | 8.37 (6.88–9.71) | 16,544 (14,016–19,224) | 4.9 (4.16–5.66) | − 1.96 (− 2.05 to − 1.86) |
| Male | 16,129 (12,167–19,450) | 13.96 (10.51–16.85) | 26,758 (21,845–34,113) | 9.17 (7.46–11.79) | − 1.51 (− 1.56 to − 1.45) |
| Colorectal cancer (CRC) | 24,777 (20,969–28,065) | 10.11 (8.66–11.38) | 79,420 (68,450–89,290) | 12.74 (11.12–14.26) | 0.74 (0.67–0.8) |
| Female | 12,155 (9575–14,330) | 9.23 (7.33–10.85) | 34,102 (29,329–39,344) | 10.18 (8.72–11.71) | 0.27 (0.18–0.36) |
| Male | 12,622 (10,638–14,359) | 11.19 (9.37–12.75) | 45,317 (37,937–52,808) | 15.87 (13.42–18.39) | 1.15 (1.1–1.2) |
| Liver cancer (LC) | 19,338 (16,985–22,163) | 7.27 (6.36–8.28) | 43,943 (34,597–56,935) | 6.66 (5.23–8.57) | − 0.39 (− 0.48 to − 0.3) |
| Female | 5754 (4812–6589) | 4.27 (3.54–4.88) | 12,636 (8414–16,234) | 3.75 (2.51–4.81) | − 0.48 (− 0.59 to − 0.37) |
| Male | 13,584 (11,525–16,021) | 10.63 (9.06–12.59) | 31,307 (24,978–42,490) | 9.98 (8.03–13.41) | − 0.33 (− 0.42 to − 0.24) |
| Pancreatic cancer (PC) | 5791 (4995–6651) | 2.35 (2.03–2.7) | 22,414 (19,335–26,001) | 3.53 (3.04–4.1) | 1.27 (1.22–1.33) |
| Female | 2738 (2228–3296) | 2.12 (1.74–2.55) | 10,621 (8588–12,884) | 3.14 (2.54–3.78) | 1.21 (1.12–1.29) |
| Male | 3053 (2684–3476) | 2.6 (2.29–2.94) | 11,792 (10,060–13,807) | 3.95 (3.38–4.59) | 1.33 (1.3–1.36) |
| Gallbladder and biliary tract cancer (GBTC) | 4183 (3055–5271) | 1.78 (1.3–2.26) | 11,164 (8220–14,176) | 1.85 (1.37–2.35) | − 0.07 (− 0.14 to 0) |
| Female | 2210 (1573–3003) | 1.75 (1.25–2.39) | 4984 (3794–7647) | 1.52 (1.15–2.32) | − 0.75 (− 0.85 to − 0.65) |
| Male | 1972 (1180–2572) | 1.82 (1.1–2.36) | 6180 (3207–8327) | 2.26 (1.19–3.03) | 0.63 (0.54–0.72) |

*GI*, gastrointestinal; *UI*, uncertainty intervals; *EAPC*, estimated annual percentage change; *CI*, confidence intervals; *EC*, esophageal cancer; *GC*, gastric cancer; *CRC*, colorectal cancer; *LC*, liver cancer; *PC*, pancreatic cancer; *GBTC*, gallbladder and biliary tract cancer

## Analysis of risk factors for gastrointestinal tract cancer in Southeast Asia

We also examined the contribution of various risk factors to deaths from GI cancers in 2021. The primary risk factor for EC was smoking, followed by low vegetable intake and alcohol use (Fig. 7A). For GC, smoking and high-sodium diets were the dominant risk factors, with smoking declining and high-sodium diets increasing between 1990 and 2021 (Fig. 7B). CRC had the most complex risk factor profile, with a diet low in calcium being the most significant risk, followed by diets low in milk, low in whole grains, and high in red meat (Fig. 7C). For LC, alcohol use was the leading risk factor (Fig. 7D). In PC, high BMI was the predominant risk factor and high fasting plasma glucose has overtaken smoking as the second most significant risk factor in the last 30 years (Fig. 7E). For GBTC, high BMI was the most important risk factor (Fig. 7F).

**Table 2** Number of disability-adjusted life years (DALYs) and age-standardized DALYs rates due to gastrointestinal (GI) cancer in 1990 and 2021 and trends in Southeast Asia from 1990 to 2021

| Characteristics | Number of DALYs cases (95% uncertainty intervals (UI)) in 1990 | The age-standardized DALYs rate/100,000 (95% UI) in 1990 | Number of DALYs cases (95% UI) in 2021 | The age-standardized DALYs rate/100,000 (95% UI) in 2021 | Estimated annual percentage change (EAPC) (95% confidence intervals (CI)) |
|---|---|---|---|---|---|
| Esophageal cancer (EC) | 206,568 (172,765–242,795) | 73.65 (61.86–86.17) | 437,488 (374,888–504,001) | 61.71 (53.19–70.79) | − 0.63 (− 0.68 to − 0.58) |
| Female | 79,908 (56,925–96,446) | 54.04 (38.88–64.99) | 119,585 (95,919–149,688) | 32.98 (26.54–41.11) | − 1.74 (− 1.84 to − 1.64) |
| Male | 126,660 (105,635–158,025) | 95.5 (79.39–118.59) | 317,903 (272,933–368,842) | 93.74 (80.64–107.49) | − 0.07 (− 0.11 to − 0.04) |
| Gastric cancer (GC) | 820,413 (659,024–941,613) | 285.4 (229.89–326.55) | 1,193,413 (1,021,566–1,404,696) | 170.78 (146.62–201.09) | − 1.83 (− 1.9 to − 1.76) |
| Female | 343,530 (283,630–396,670) | 223.08 (184.6–258.54) | 440,747 (374,882–522,987) | 120.92 (102.92–142.68) | − 2.2 (− 2.3 to − 2.1) |
| Male | 476,883 (355,385–574,751) | 356.64 (268.23–430.68) | 752,666 (603,730–942,409) | 227.61 (184.47–287.71) | − 1.59 (− 1.65 to − 1.54) |
| Colorectal cancer (CRC) | 735,822 (612,422–841,712) | 257.93 (218.13–292.17) | 2,166,650 (1,868,880–2,456,350) | 313.37 (270.75–353.54) | 0.61 (0.55–0.67) |
| Female | 358,744 (277,769–428,837) | 237.84 (186.4–281.4) | 896,766 (768,380–1,051,300) | 247.02 (212.19–288.06) | 0.06 (− 0.02 to 0.15) |
| Male | 377,078 (312,979–429,759) | 281.35 (235.57–319.88) | 1,269,885 (1,048,304–1,488,163) | 389.31 (323.46–454.02) | 1.07 (1.02–1.12) |
| Liver cancer (LC) | 631,450 (558,091–719,439) | 206.84 (182.35–236.94) | 1,287,277 (1,007,129–1,686,531) | 179.67 (141.22–234.26) | − 0.58 (− 0.67 to − 0.49) |
| Female | 175,832 (145,966–203,670) | 112.84 (94.46–129.81) | 329,883 (216,738–428,024) | 91.37 (60.46–118) | − 0.77 (− 0.86 to − 0.67) |
| Male | 455,618 (388,183–532,761) | 309.36 (263.39–364.38) | 957,394 (763,959–1,305,358) | 275.82 (220.49–376.31) | − 0.52 (− 0.61 to − 0.43) |
| Pancreatic cancer (PC) | 165,074 (142,221–189,673) | 59.32 (51.06–68.04) | 597,956 (515,407–697,938) | 85.92 (73.82–99.74) | 1.15 (1.09–1.21) |
| Female | 74,202 (59,609–89,951) | 51.63 (41.8–62.3) | 265,184 (213,813–325,558) | 73.14 (59.36–89.52) | 1.06 (0.97–1.14) |
| Male | 90,872 (79,626–103,307) | 67.6 (59.37–76.82) | 332,772 (281,816–392,263) | 99.55 (84.75–116.71) | 1.22 (1.18–1.26) |
| Gallbladder and biliary tract cancer (GBTC) | 111,514 (80,437–139,489) | 41.94 (30.48–52.65) | 272,266 (200,970–343,850) | 40.73 (30.05–51.36) | − 0.27 (− 0.34 to − 0.21) |
| Female | 57,923 (40,686–78,998) | 41.18 (29.43–56.31) | 115,854 (88,165–180,209) | 32.72 (24.99–50.62) | − 1.05 (− 1.16 to − 0.93) |
| Male | 53,592 (31,614–69,558) | 42.8 (25.49–55.58) | 156,412 (80,334–209,342) | 50.01 (25.88–67.13) | 0.45 (0.39–0.52) |

*DALYs*, disability-adjusted life years; *GI*, gastrointestinal; *UI*, uncertainty intervals; *EAPC*, estimated annual percentage change; *CI*, confidence intervals; *EC*, esophageal cancer; *GC*, gastric cancer; *CRC*, colorectal cancer; *LC*, liver cancer; *PC*, pancreatic cancer; *GBTC*, gallbladder and biliary tract cancer

## Discussion

In this study, we used the GBD-2021 database to comprehensively analyze the temporal trends of six GI tract tumor types and associated risk factors in Southeast Asia from 1990 to 2021, with projections for future trends. Our findings revealed that in 2021, CRC was the leading contributor to the GI cancer burden in Southeast Asia, while GBTC contributed the least. Overall, the disease burden for men was higher than for women, with the most significant gender difference observed in LC. CRC and PC experienced substantial increases in disease burden from 1990 to 2021,

**Table 3** Number of incidence and age-standardized incidence rates due to gastrointestinal (GI) cancer in 1990 and 2021 and trends in Southeast Asia from 1990 to 2021

| Characteristics | Number of incidence cases (95% uncertainty intervals (UI)) in 1990 | The age-standardized incidence rate/100,000 (95% UI) in 1990 | Number of incidence cases (95% UI) in 2021 | The age-standardized incidence rate/100,000 (95% UI) in 2021 | Estimated annual percentage change (EAPC) (95% confidence intervals (CI)) |
|---|---|---|---|---|---|
| Esophageal cancer (EC) | 6956 (5838–8146) | 2.69 (2.26–3.14) | 16,164 (13,984–18,580) | 2.42 (2.11–2.76) | − 0.4 (− 0.44 to − 0.36) |
| Female | 2725 (1944–3287) | 2 (1.46–2.41) | 4724 (3807–5822) | 1.37 (1.11–1.68) | − 1.35 (− 1.44 to − 1.27) |
| Male | 4232 (3504–5269) | 3.46 (2.88–4.28) | 11,440 (9826–13,077) | 3.62 (3.14–4.13) | 0.13 (0.09–0.16) |
| Gastric cancer (GC) | 28,024 (22,597–32,063) | 10.72 (8.69–12.28) | 47,761 (41,101–56,374) | 7.27 (6.28–8.69) | − 1.45 (− 1.52 to − 1.38) |
| Female | 11,442 (9449–13,206) | 8.17 (6.74–9.45) | 17,749 (15,061–20,738) | 5.12 (4.36–5.94) | − 1.75 (− 1.85 to − 1.65) |
| Male | 16,582 (12,462–19,955) | 13.71 (10.33–16.55) | 30,012 (24,308–38,002) | 9.81 (7.9–12.51) | − 1.24 (− 1.3 to − 1.18) |
| Colorectal cancer (CRC) | 29,321 (24,900–33,179) | 11.28 (9.64–12.72) | 116,942 (101,260–132,256) | 17.7 (15.41–19.89) | 1.45 (1.4–1.5) |
| Female | 14,345 (11,331–16,845) | 10.36 (8.26–12.16) | 49,302 (42,176–57,043) | 14.06 (12.02–16.21) | 0.94 (0.86–1.01) |
| Male | 14,976 (12,481–17,037) | 12.37 (10.41–14.09) | 67,639 (55,683–79,391) | 21.97 (18.27–25.56) | 1.89 (1.85–1.93) |
| Liver cancer (LC) | 19,103 (16,752–21,837) | 6.94 (6.07–7.91) | 44,025 (34,719–56,944) | 6.5 (5.13–8.36) | − 0.33 (− 0.42 to − 0.24) |
| Female | 5595 (4658–6435) | 4.01 (3.31–4.58) | 12,427 (8300–15,933) | 3.6 (2.42–4.62) | − 0.42 (− 0.52 to − 0.31) |
| Male | 13,508 (11,449–15,935) | 10.2 (8.66–12.1) | 31,598 (25,211–42,619) | 9.76 (7.83–13.1) | − 0.29 (− 0.38 to − 0.2) |
| Pancreatic cancer (PC) | 5584 (4808–6413) | 2.2 (1.9–2.52) | 21,702 (18,694–25,154) | 3.33 (2.88–3.87) | 1.31 (1.25–1.37) |
| Female | 2611 (2118–3147) | 1.97 (1.61–2.37) | 10,152 (8256–12,326) | 2.95 (2.4–3.56) | 1.24 (1.16–1.33) |
| Male | 2973 (2610–3370) | 2.44 (2.16–2.76) | 11,550 (9836–13,561) | 3.75 (3.22–4.38) | 1.37 (1.33–1.4) |
| Gallbladder and biliary tract cancer (GBTC) | 4093 (2956–5132) | 1.68 (1.22–2.12) | 12,035 (8763–15,157) | 1.93 (1.41–2.43) | 0.28 (0.21–0.35) |
| Female | 2147 (1523–2912) | 1.65 (1.18–2.23) | 5207 (3925–7871) | 1.55 (1.15–2.34) | − 0.48 (− 0.58 to − 0.39) |
| Male | 1946 (1161–2542) | 1.72 (1.03–2.25) | 6828 (3442–9189) | 2.39 (1.22–3.2) | 1.04 (0.94–1.13) |

*GI*, gastrointestinal; *UI*, uncertainty intervals; *EAPC*, estimated annual percentage change; *CI*, confidence intervals; *EC*, esophageal cancer; *GC*, gastric cancer; *CRC*, colorectal cancer; *LC*, liver cancer; *PC*, pancreatic cancer; *GBTC*, gallbladder and biliary tract cancer

whereas GC showed a notable decline. Additionally, the risk factors for these cancers have evolved over time.

Globally, in 2020, there were approximately 600,000 new cases and 540,000 deaths from EC. Nearly 79.7% (about 480,000) of new cases of EC and 79.6% (about 430,000) of deaths occurred in Asia, with the highest number of incidences and deaths occurring in East Asia, and lower in Southeast Asia, where the number of incidences was only 14,000 and the number of deaths was 12,000 [15, 16]. Our study aligned with this trend, showing a decrease in ASDR, DALYs, ASIR, and ASPR for EC in the region from 1990 to 2021, particularly among women. This decline may be attributed to reduced smoking and improvements in alcohol control policies, though challenges remain due to increasing alcohol consumption and changes in dietary patterns, such as a decline in vegetable intake. The rise in alcohol consumption in Southeast Asia, fueled by economic growth and advertising, presents a continued risk for EC, particularly among men. In Southeast Asia, SCC is the most dominant type of esophageal cancer, and the main risk factors for SCC are alcohol consumption, smoking, and red meat intake[17, 18]. Alcohol consumption in most countries in the Southeast Asia region has been on an increasing trend with economic development from 2010 to 2017; however, the average alcohol consumption in the region (4.5 L) is still lower than the global level (6.5 L) [19], which may be one of the reasons

**Table 4** Number of prevalence and age-standardized prevalence rates due to gastrointestinal (GI) cancer in 1990 and 2021 and trends in Southeast Asia from 1990 to 2021

| Characteristics | Number of prevalence cases (95% uncertainty intervals (UI)) in 1990 | The age-standardized prevalence rate/100,000 (95% UI) in 1990 | Number of prevalence cases (95% UI) in 2021 | The age-standardized prevalence rate/100,000 (95% UI) in 2021 | Estimated annual percentage change (EAPC) (95% confidence intervals (CI)) |
|---|---|---|---|---|---|
| Esophageal cancer (EC) | 10,666 (8935–12,540) | 3.81 (3.21–4.46) | 26,443 (22,689–30,604) | 3.74 (3.22–4.31) | − 0.1 (− 0.14 to − 0.06) |
| Female | 4201 (2994–5056) | 2.85 (2.04–3.43) | 7587 (6030–9265) | 2.1 (1.67–2.55) | − 1.11 (− 1.19 to − 1.03) |
| Male | 6466 (5383–8072) | 4.88 (4.04–6.07) | 18,856 (16,089–21,851) | 5.56 (4.75–6.42) | 0.43 (0.39–0.46) |
| Gastric cancer (GC) | 40,283 (32,292–46,230) | 14.1 (11.34–16.16) | 75,213 (63,996–87,890) | 10.79 (9.23–12.59) | − 1.06 (− 1.14 to − 0.98) |
| Female | 16,345 (13,581–18,852) | 10.73 (8.86–12.42) | 26,580 (22,653–31,388) | 7.32 (6.24–8.61) | − 1.47 (− 1.58 to − 1.37) |
| Male | 23,939 (17,835–28,831) | 17.95 (13.47–21.63) | 48,633 (38,651–59,961) | 14.71 (11.66–18.24) | − 0.81 (− 0.88 to − 0.75) |
| Colorectal cancer (CRC) | 104,516 (89,925–117,295) | 37.09 (32.27–41.31) | 499,194 (433,063–562,668) | 71.39 (62.36–80.56) | 2.15 (2.12–2.18) |
| Female | 51,182 (40,939–59,625) | 34.45 (27.9–39.81) | 210,468 (182,293–242,931) | 57.42 (49.81–65.86) | 1.62 (1.57–1.68) |
| Male | 53,334 (44,825–60,236) | 40.14 (33.9–45.14) | 288,725 (235,927–340,039) | 87.15 (71.83–102.23) | 2.6 (2.57–2.63) |
| Liver cancer (LC) | 26,447 (22,411–30,317) | 8.25 (7.18–9.38) | 53,638 (42,303–69,356) | 7.65 (6.03–9.84) | − 0.35 (− 0.42 to − 0.28) |
| Female | 7858 (6138–9530) | 4.74 (3.85–5.56) | 14,833 (9969–18,988) | 4.21 (2.84–5.38) | − 0.44 (− 0.52 to − 0.36) |
| Male | 18,589 (15,547–21,798) | 12.08 (10.28–14.2) | 38,804 (30,843–52,370) | 11.43 (9.17–15.46) | − 0.31 (− 0.38 to − 0.24) |
| Pancreatic cancer (PC) | 4686 (4031–5381) | 1.71 (1.47–1.96) | 17,948 (15,470–20,858) | 2.63 (2.27–3.05) | 1.35 (1.29–1.42) |
| Female | 2126 (1716–2575) | 1.5 (1.22–1.8) | 8106 (6614–9896) | 2.27 (1.86–2.76) | 1.28 (1.19–1.38) |
| Male | 2561 (2245–2901) | 1.93 (1.7–2.18) | 9842 (8347–11,567) | 3 (2.56–3.52) | 1.4 (1.36–1.44) |
| Gallbladder and biliary tract cancer (GBTC) | 4291 (3068–5362) | 1.68 (1.21–2.11) | 14,399 (10,121–18,341) | 2.22 (1.57–2.82) | 0.77 (0.7–0.84) |
| Female | 2226 (1563–3005) | 1.64 (1.16–2.2) | 5950 (4396–8760) | 1.72 (1.27–2.53) | − 0.12 (− 0.21 to − 0.03) |
| Male | 2064 (1222–2706) | 1.73 (1.03–2.26) | 8448 (4062–11,437) | 2.81 (1.36–3.8) | 1.6 (1.5–1.7) |

*GI*, gastrointestinal; *UI*, uncertainty intervals; *EAPC*, estimated annual percentage change; *CI*, confidence intervals; *EC*, esophageal cancer; *GC*, gastric cancer; *CRC*, colorectal cancer; *LC*, liver cancer; *PC*, pancreatic cancer; *GBTC*, gallbladder and biliary tract cancer

for the lower burden of EC in the Southeast Asian regions. Multinational alcohol companies have actively expanded their presence in the region through increased advertising, promotion, and sponsorship, which may have contributed to higher alcohol consumption and related health issues [20]. To address this, countries should consider adopting stricter regulations, such as regularly increasing alcohol taxes, which have proven effective in reducing consumption. The Southeast Asia region has one of the highest tobacco burdens in the WHO region, and smoking and alcohol consumption tend to be complementary, with higher rates of alcohol consumption among smokers [21]. Men, in particular, tend to consume higher levels of both alcohol and tobacco, which may partly explain the greater burden of EC among men compared to women in the region. However, the implementation of the World Health Organization's Framework Convention on Tobacco Control (FCTC) and stricter anti-smoking policies have led to a significant decline in tobacco use across Southeast Asia [22]. This reduction in smoking may be a contributing factor to the observed decline in the region's EC burden. In addition to smoking and alcohol, dietary factors are playing an increasingly important role in EC risk. A diet low in vegetables, linked to the westernization of eating habits in Southeast Asia, is emerging as a

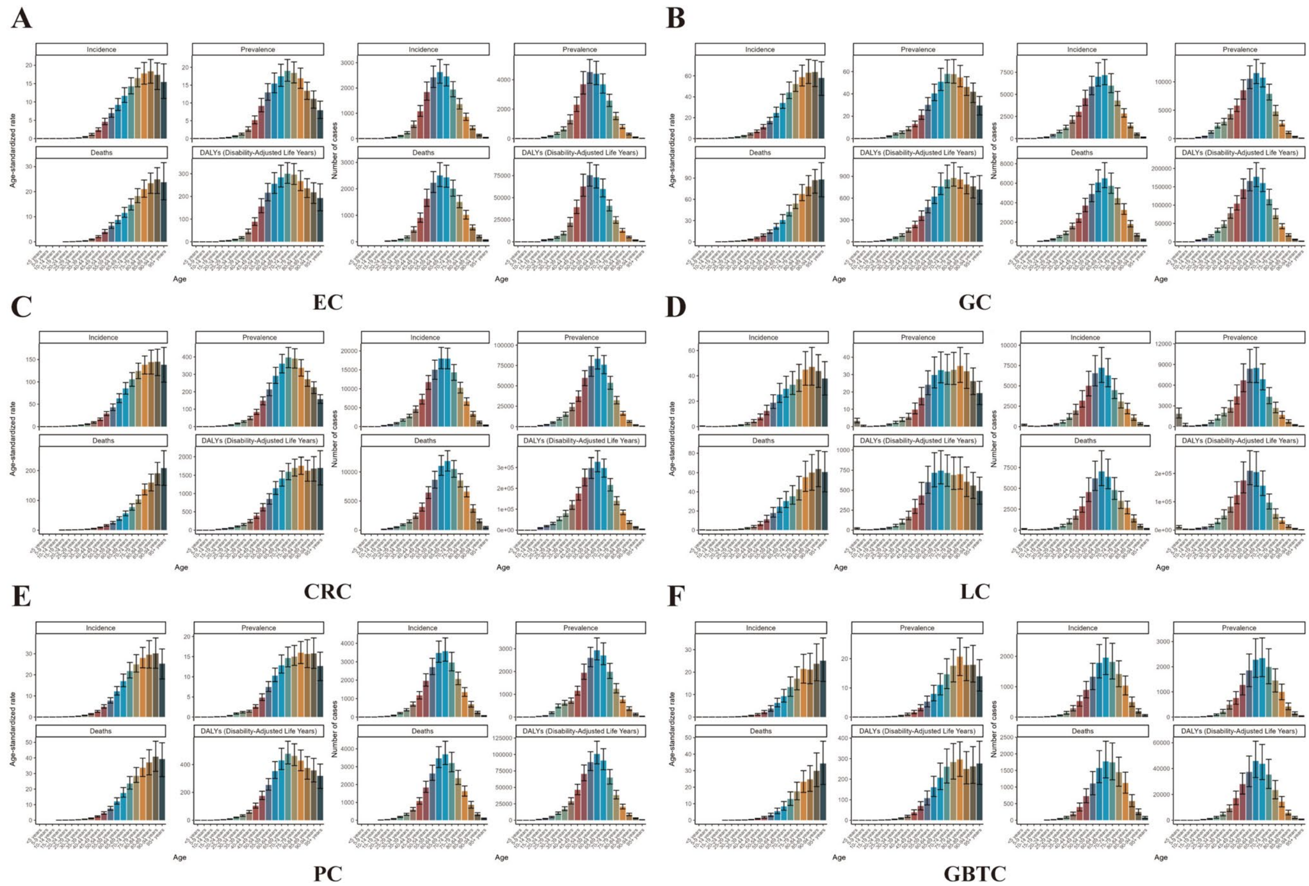


**Fig. 1** Disease burden of GI cancer in different age groups in Southeast Asia in 2021. **A** Esophageal cancer. **B** Gastric cancer. **C** Colorectal cancer. **D** Liver cancer. **E** Pancreatic cancer. **F** Gallbladder and biliary tract

prominent risk factor. This shift in dietary patterns, driven by globalization and economic changes, highlights the need for increased public health efforts to promote dietary adjustments, particularly encouraging higher vegetable intake, as part of future cancer prevention strategies.

In 2022, GC accounted for more than 968,000 new cases and nearly 660,000 deaths, making it the fifth most common cancer and the fifth leading cause of cancer mortality globally. It also has the highest ASDR and ASIR in Asia [23]. The mechanisms driving GC are multifactorial. Chronic *H. pylori* infection is the most significant cause of GC, accounting for approximately 90% of non-cardia cases [24]. Our study found a general decline in the GC disease burden in Southeast Asia from 1990 to 2021, which aligns with global trends. One major contributor to this decline is the reduction in *H. pylori* prevalence. Data from Yi-Chu Chen et al. indicated that the global prevalence of *H. pylori* infection in adults decreased from 52.6% before 1990 to 43.9% between 2015 and 2022 [25]. A comprehensive global systematic evaluation conducted in 2015 showed that the prevalence of *H. pylori* was 54.7% in Asia, and Southeast Asia accounted for 43.1% of the cases in Asia. With the improvement of infrastructure and environmental sanitation in Southeast Asia, as well as anti *H. pylori* treatment protocols have been further optimized, resulting in a significant increase in *H. pylori* eradication rates in the region [26]. However, the prevention and control of *H. pylori* in Southeast Asian countries still faces great challenges. On the one hand, the prevalence of *H. pylori* infection varies widely among different countries in the region, ranging from the lowest in Malaysia (20%) to the highest in Myanmar (68%), and also healthcare facilities for *H. pylori* management show a wide variation from country to country [27]. On the other hand, doctors in the region choose to select inappropriate regimens containing antibiotics with high resistance rates for the treatment of *H. pylori* infection based on their experiences, often leading to treatment failure [28], and negatively impacting the *H. pylori* infection reduction rate. Therefore, improving the *H. pylori* management system and updating the treatment guidelines promptly are important to reduce the disease burden of *H. pylori*–associated GC. Notably, high-sodium diets are gradually becoming a prominent risk factor for GC burden in Southeast Asia. High-sodium consumption has a synergistic effect with *H. pylori* infection, disrupting the

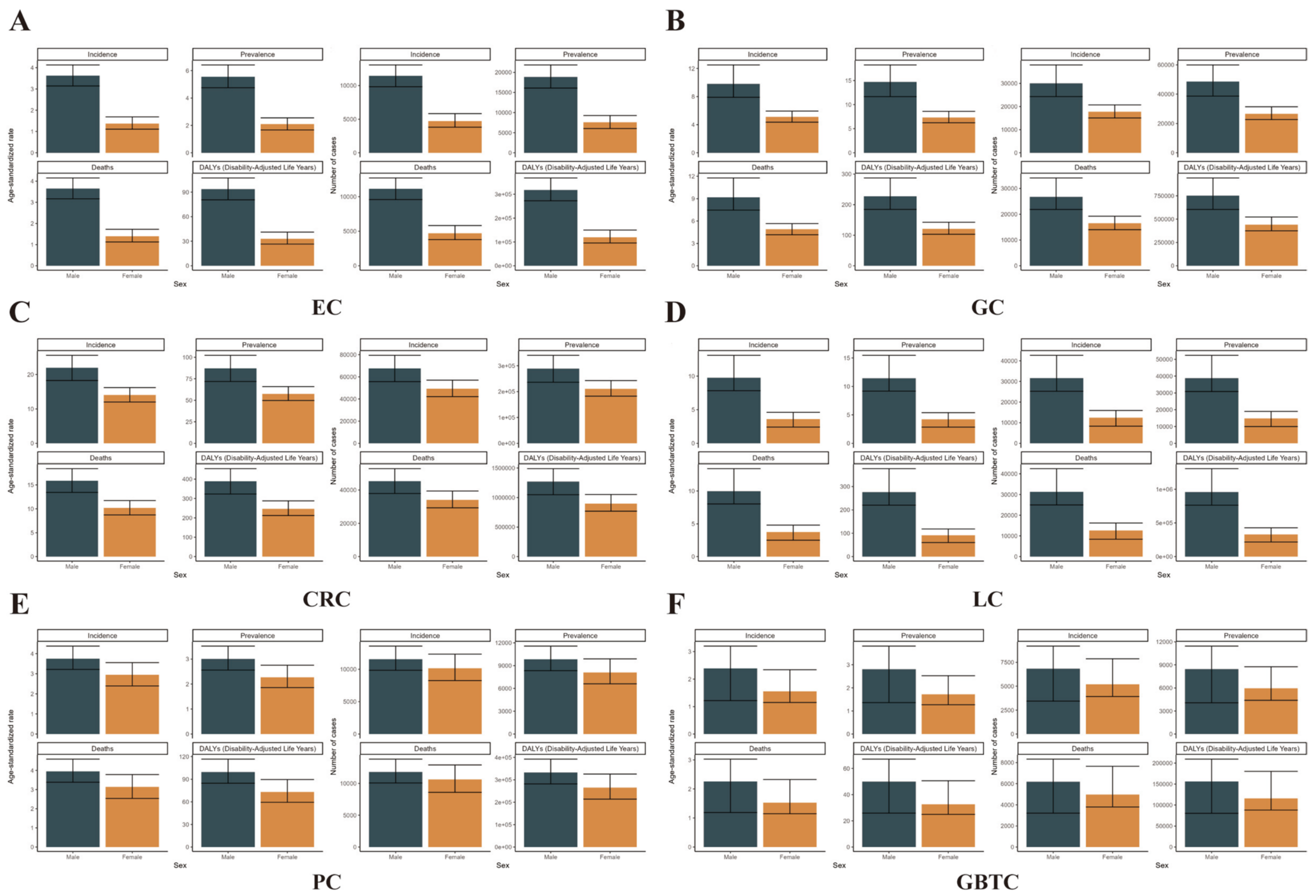


**Fig. 2** Disease burden of GI cancer in men and women in Southeast Asia, 2021. **A** Esophageal cancer. **B** Gastric cancer. **C** Colorectal cancer. **D** Liver cancer. **E** Pancreatic cancer. **F** Gallbladder and biliary tract

gastric mucosal barrier, damaging cellular integrity, and promoting oxidative stress and inflammation—processes that can accelerate gastric cancer development [29]. Therefore, controlling sodium intake is important to reduce the incidence of GC, especially in this region.

In recent years, global incidence and mortality rates for CRC have been increasing, and it is now the third most prevalent and second deadliest cancer in the world. Between 1990 and 2021, CRC incidence in Asia quadrupled, surpassing GC as the GI tumor with the highest disease burden [12]. In Europe, the total economic burden of CRC alone is equivalent to approximately 19 billion euros per year, which is ranked as the first of all digestive cancers [30]. As the number of CRC cases continues to increase, the associated direct and indirect healthcare costs are expected to rise accordingly. Our results show that in Southeast Asia, CRC ranks first among GI tumors in terms of incidence and deaths. The number of new CRC cases in the region is projected to reach 252,000 by 2050, posing a significant threat to public health. Addressing this growing burden will require urgent and comprehensive action. The risk factors for CRC are multifaceted, with unhealthy dietary habits being a primary contributor. Over the past 30 years, the disease burden associated with poor diet has significantly increased. In 2019, dietary risks were responsible for one-third of all CRC-related deaths [31]. Modifying dietary patterns is therefore crucial for reducing CRC incidence. Our study identified several major dietary risk factors, including low intake of calcium, milk, and whole grains, along with high consumption of red meat. Notably, from 1990 to 2021, the proportion of individuals consuming high amounts of red meat has increased, highlighting the need for dietary interventions in Southeast Asia.

Early screening for CRC has been shown to significantly reduce mortality and is considered a cost-effective strategy [32]. However, screening uptake remains suboptimal, particularly in low-income countries [33]. In the Philippines, colonoscopy screening is only available in urban areas and is often prohibitively expensive for the average citizen [34]. Although immunochemical fecal occult blood test (iFOBT) testing has been offered free of charge at the primary care clinics of the Malaysian Ministry of Health since 2014, the screening rate in Malaysia is only 2.29% [35]. A study in Thailand also showed that as the cost of CRC screening

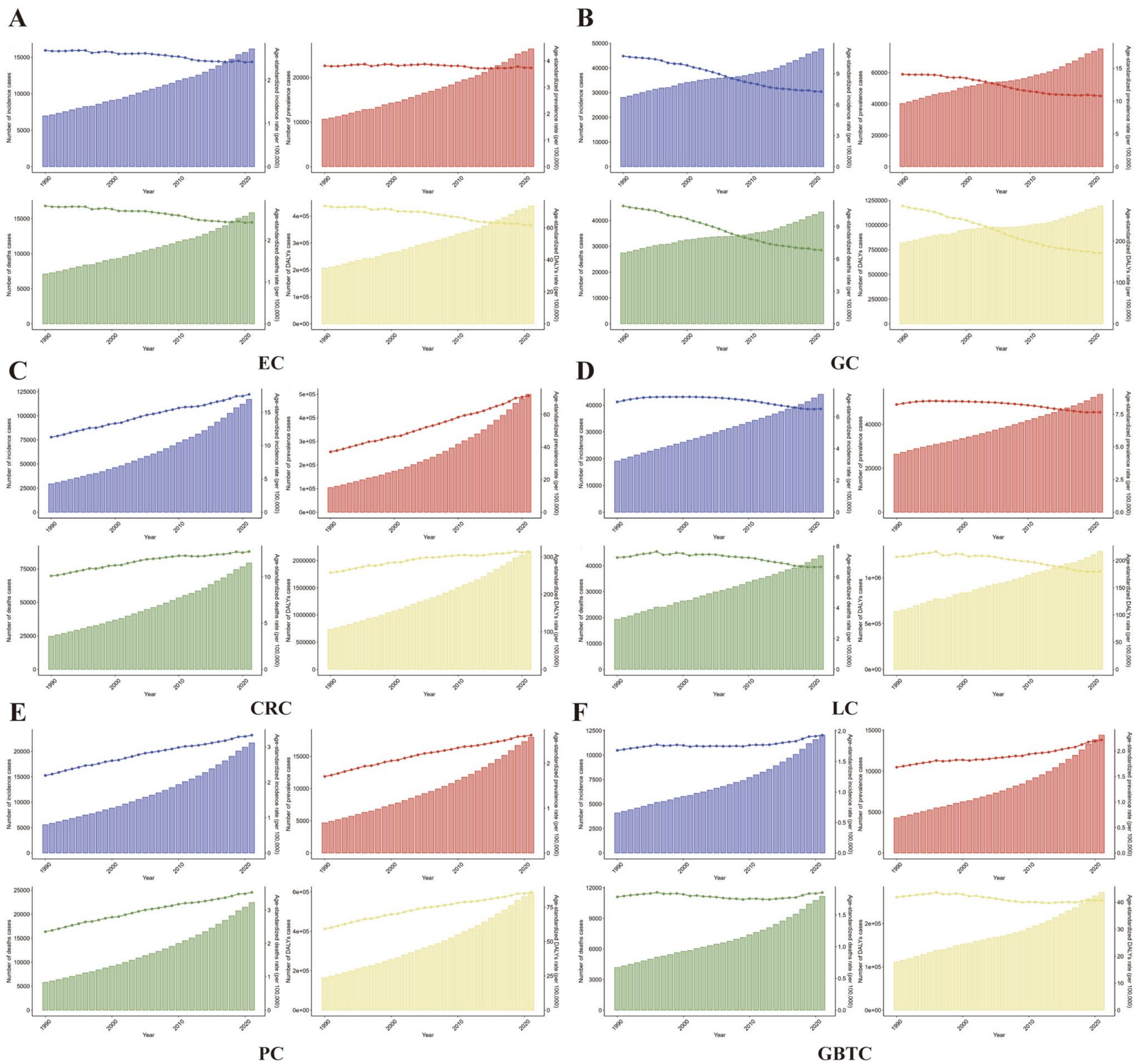


**Fig. 3** Overall trends in the disease burden of GI cancer in Southeast Asia, 1990–2021. **A** Esophageal cancer. **B** Gastric cancer. **C** Colorectal cancer. **D** Liver cancer. **E** Pancreatic cancer. **F** Gallbladder and biliary tract

increases, acceptance rates decrease [36]. The increasing burden of CRC in Southeast Asia over the past 30 years can partly be attributed to low screening rates. To combat this, it is critical for countries to integrate CRC prevention and early screening programs into national health policies, ensuring that screening is accessible, affordable, and widely implemented to facilitate early diagnosis.

Southeast Asia has long been a high-incidence region for LC, with ASIRs of 13.7 per 100,000 and ASDRs of 13.2 per 100,000, both significantly higher than the global averages of 9.5 per 100,000 and 8.7 per 100,000, respectively [37]. Our study found that the total number of LC incidences and deaths in Southeast Asia has been increasing from 1990 to 2021, but the corresponding ASRs have significantly decreased. This trend suggests that the region has made progress in controlling the burden of liver cancer, possibly due to a decline in the prevalence of HBV and HCV infections, as well as reduced exposure to aflatoxin. In 2016, the Southeast Asian Immunization Technical Advisory Group (SEAR TAG) set a regional goal for hepatitis B control, aiming for an HBsAg seropositivity rate of $\leq 1\%$ in children over 5 years of age by 2020. By 2019, the Hepatitis B Regional

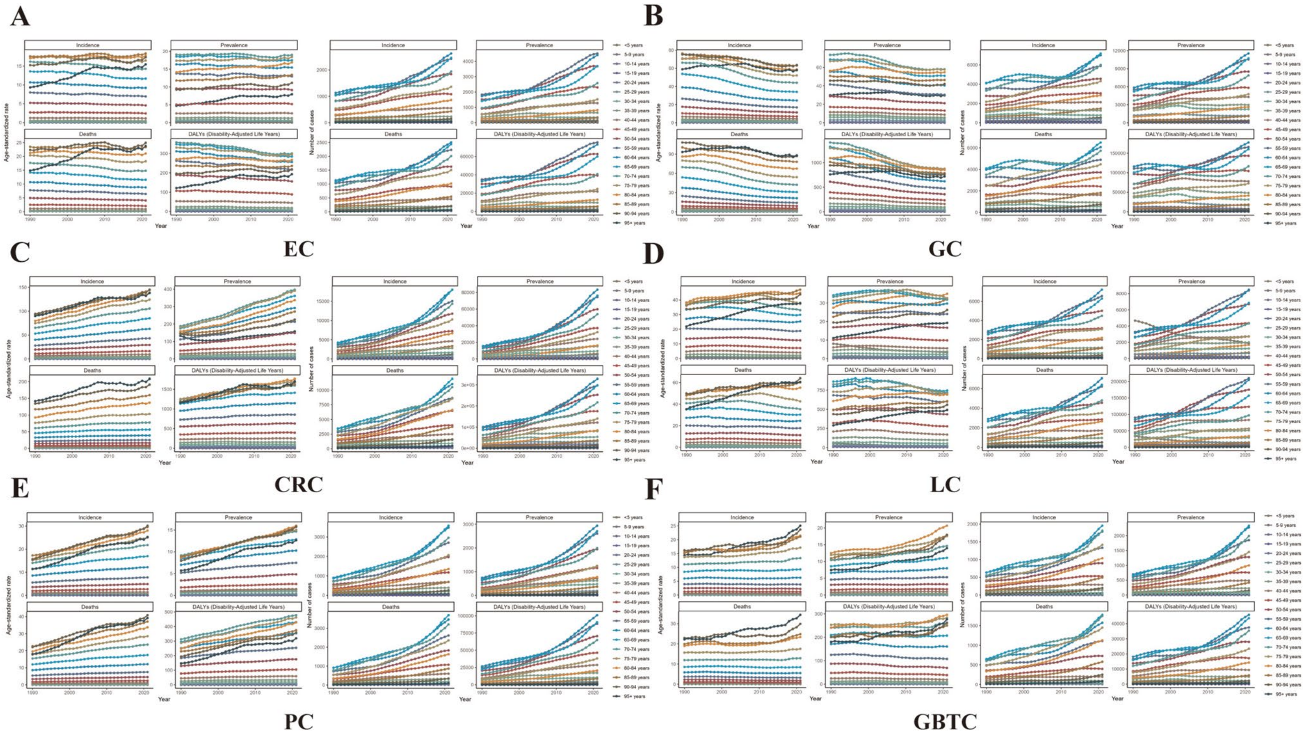


**Fig. 4** Trends in the burden of disease of GI cancer among different age groups in Southeast Asia, 1990–2021. **A** Esophageal cancer. **B** Gastric cancer. **C** Colorectal cancer. **D** Liver cancer. **E** Pancreatic cancer. **F** Gallbladder and biliary tract

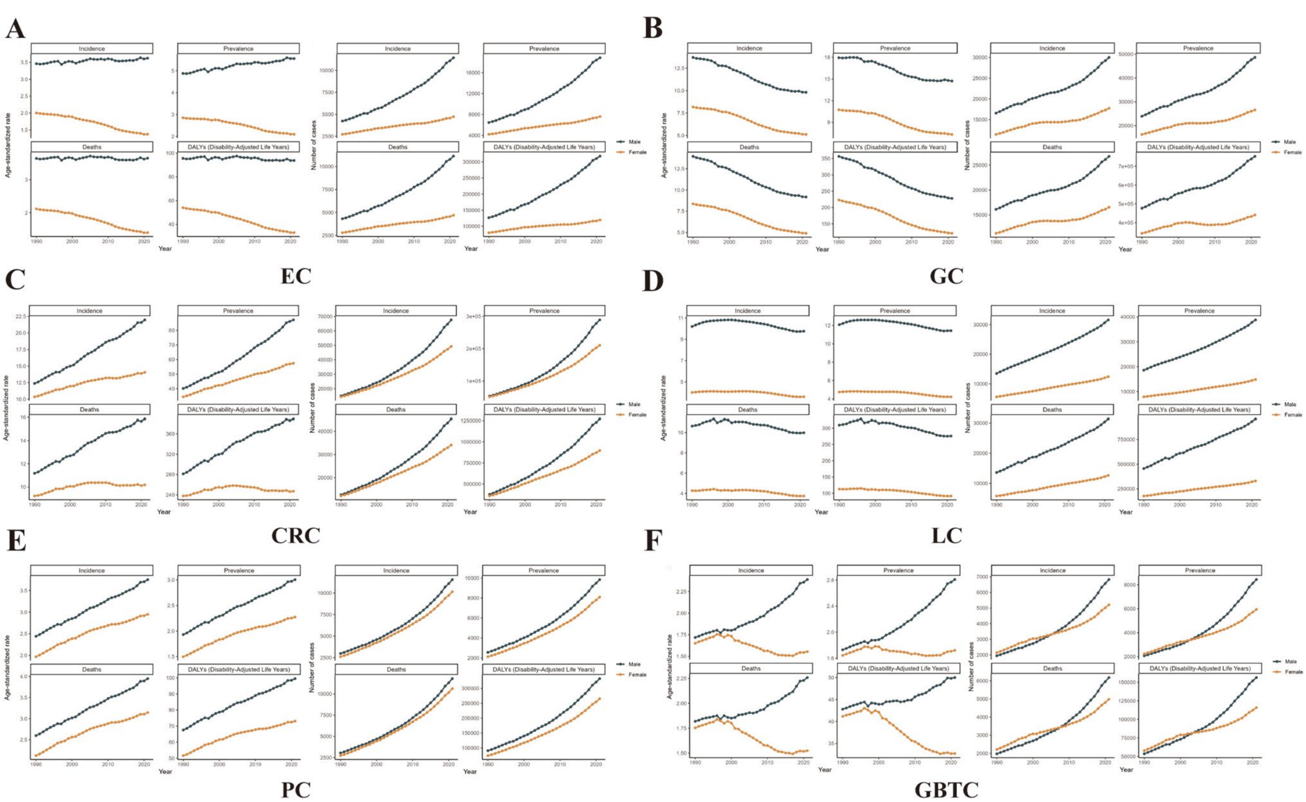


**Fig. 5** Trends in the burden of disease of GI cancer among men and women in Southeast Asia, 1990–2021. **A** Esophageal cancer. **B** Gastric cancer. **C** Colorectal cancer. **D** Liver cancer. **E** Pancreatic cancer. **F** Gallbladder and biliary tract

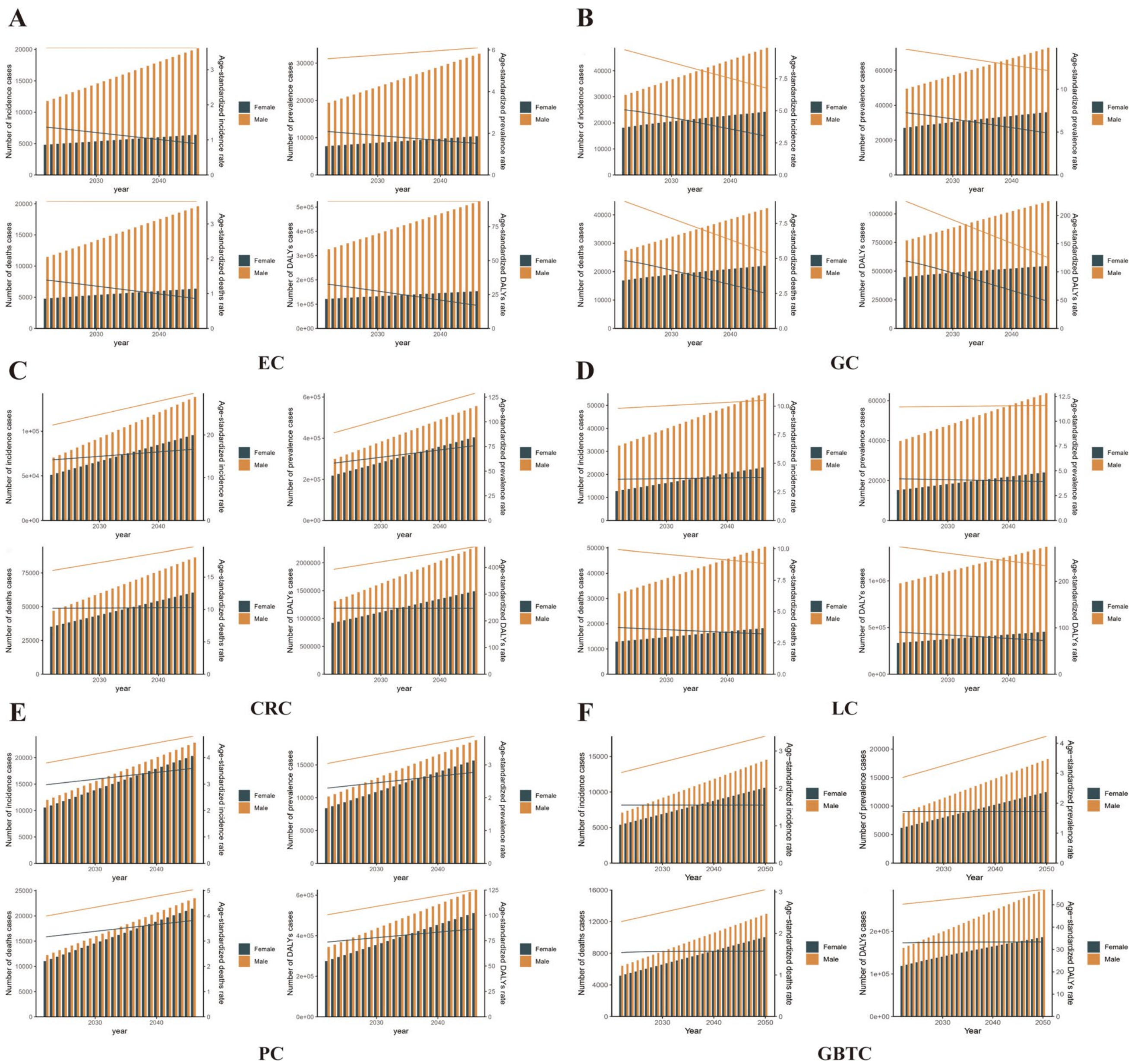


**Fig. 6** Projected trends in the overall burden of disease for GI cancer in Southeast Asia, 2022–2050. **A** Esophageal cancer. **B** Gastric cancer. **C** Colorectal cancer. **D** Liver cancer. **E** Pancreatic cancer. **F** Gallbladder and biliary tract

Expert Group (REG) reported significant progress: regional coverage for the three-dose hepatitis B vaccine (HepB3) increased from 89 to 91%, and the birth dose (HepB-BD) coverage rose from 34 to 54%. As of December 2019, four countries in the region had achieved the hepatitis B control target, and nine countries had achieved ≥ 90% HepB3 coverage [38]. Despite the lack of an effective vaccine for HCV, several direct-acting antiviral agents (DAAs) against HCV have been developed in recent years, and DAA-based therapeutic regimens have been highly effective in clearing HCV infections, significantly reducing HCV infections [39]. However, new risk factors, such as alcohol consumption and high BMI, are becoming increasingly important contributors to LC, highlighting the need for updated public health strategies that address these changing risk profiles. In our study, we also observed that among all GI tumors in Southeast Asia, LC showed the most pronounced difference between men and women, which might be because alcohol intake is most closely associated with LC, and men are more likely to consume a higher volume of alcohol than women. Perhaps controlling alcohol intake is another effective means of reducing the LC burden.

The burden of PC-related diseases is rapidly increasing in Southeast Asia. Our study found that, from 1990 to 2021,

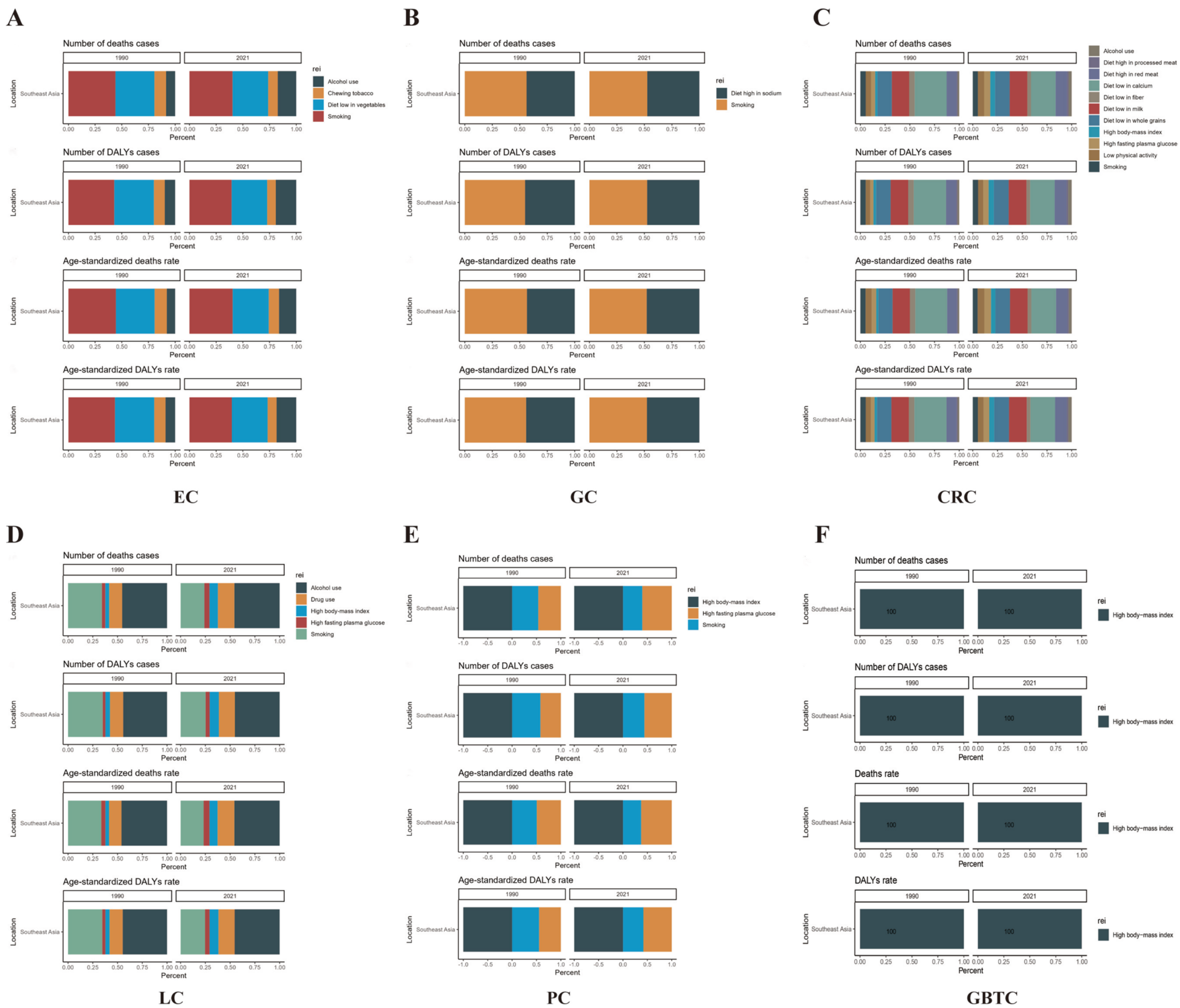


**Fig. 7** Risk factors for GI cancer disease burden in Southeast Asia. **A** Esophageal cancer. **B** Gastric cancer. **C** Colorectal cancer. **D** Liver cancer. **E** Pancreatic cancer. **F** Gallbladder and biliary tract

the number of PC-related deaths and DALYs more than tripled in the region, marking the highest growth rate among all GI cancers. This mirrors the global trend of rising PC incidence [40]. Despite its lower incidence compared to CRC, PC has a particularly poor prognosis and generates the second-highest indirect healthcare costs, highlighting the growing challenge it presents to the healthcare system [41]. Therefore, the challenges posed by PCs need to be given high priority. Age is a well-known risk factor for PC, and in Southeast Asia, shifting demographics combined with improved diagnostic capabilities may explain part of the increase in cases. In addition, there are other key modifiable risk factors for PC such as smoking, obesity, diabetes, and alcohol consumption. Our further analysis of risk factors for PC in Southeast Asia found the most significant risk factor to be obesity, followed by diabetes and smoking. In recent decades, South and Southeast Asia have experienced a period of rapid nutritional and lifestyle shifts, leading to a corresponding increase in the burden of obesity and diabetes, with the prevalence of obesity projected to double between 2010 and 2030 [42]. East and Southeast Asia has the highest burden of diabetes in the world, with approximately 247.6 million patients, accounting for 53% of the world's total diabetes population [43]. Despite the decline in smoking prevalence in Southeast Asia in recent years, the persistently high numbers of obesity and diabetes have been the main drivers contributing to the increasing burden of PC.

GBTC currently represents the smallest disease burden among all GI tumors in Southeast Asia. Over the past 30 years, while the ASDR and ASR of DALY have shown a gradual decline, both the ASIR and ASPR have remained significantly higher. A global study by Srineil Vuthaluru et al. found that of the 115,949 new cases of GBTC in 2020, Asia accounted for 82,137, or 71% of the global total. The age-standardized burden of GBTC is particularly high in Latin America (notably Bolivia and Chile) and Southeast Asia (especially Bangladesh and Nepal) [44]. This may be related to elevated levels of arsenic in groundwater in Nepal and Bangladesh, where arsenic is a significant risk factor for GBTC [45]. Improved diagnostic techniques have enabled earlier detection of GBTC, which, although leading to an increase in diagnosed cases, has resulted in better patient prognosis and a reduction in mortality. Additionally, advancements in surgical approaches and the introduction of combination therapies—including chemotherapy, radiotherapy, targeted therapy, and immunotherapy—have improved survival outcomes, contributing to a decline in ASDR and ASR of DALY. However, the rising ASIR and ASPR suggest that the overall disease burden of gallbladder cancer in Southeast Asia is still on the rise.

Interestingly, the disease burden of GBTC in Southeast Asia has been greater in women than in men until 2000; however, in recent years, the disease burden in men has continued to increase and has surpassed that of women, suggesting that we need to pay particular attention to the incidence characteristics of males when formulating public health strategies for the prevention and control of GBTC in the future. Our attribution analysis also identified obesity as an independent risk factor for GBTC, and with the increasing prevalence of obesity, the challenge of reducing the disease burden associated with GBTC is likely to intensify in the coming years.

Our study, based on GBD 2021 data, has several limitations. First, the accuracy of our disease burden estimates for GI tract tumors might have been influenced by the raw data's quality and completeness. During the 1990s, underdeveloped disease registry systems and limited internet access in low- and middle-income countries in Southeast Asia led to incomplete registrations and missing data, which may have resulted in an underestimation of the true number of case. In regions with missing data, estimates rely on modeling and historical trends, which could have introduced variability and discrepancies [46]. Second, our regional analysis lacks country-specific details, which may obscure important variations and regional differences. Lastly, the absence of genetic information in the GBD database limits our ability to conduct a comprehensive analysis that integrates both environmental and genetic factors. Despite these limitations, our study offers valuable insights into the trends of GI tract cancers across Southeast Asia.

## Conclusion

In conclusion, although the trends in disease burden for different GI cancers in Southeast Asia vary, the overall incidence, mortality, DALYs, and prevalence of GI tract cancers have all significantly increased and are projected to continue rising over the next 30 years. To reduce this burden, public health professionals and policymakers must take proactive steps to design and adapt prevention and control strategies that respond to the evolving trends in disease burden and the specific risk factors associated with each type of GI tract cancer.

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**Author contributions** Pengkhun Nov and Duanyu Wang designed the overall research, Duanyu Wang collected data and verified the accuracy of the data; Duanyu Wang prepared manuscript and images; Duanyu Wang and Minghao Tan analyzed and interpreted data; all authors contributed to revise manuscript. All authors read and approved the final manuscript.

**Data availability** No datasets were generated or analysed during the current study.

## Declarations

**Ethics approval and consent to participate** Not applicable.

**Consent for publication** Not applicable.

**Competing interests** The authors declare no competing interests.



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