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Epidemiological trends in gastrointestinal cancers and risk factors across U.S. states from 2000 to 2021: a systematic analysis for the global burden of disease study 2021

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Abstract

Introduction Gastrointestinal (GI) cancers account for over a quarter of all cancer-related deaths in the United States; however, the latest trends in their prevalence remain unclear.

Methods Data on GI cancers were obtained from the Global Burden of Disease Study 2021. Age-standardized incidence rates (ASIR) and age-standardized mortality rates (ASMR) were estimated across various states, sexes, ages, and risk factors, and annual percentage changes were calculated.

Results From 2000 to 2021, liver cancer exhibited the greatest increase in both the ASIR and the ASMR, followed by pancreatic cancer. In contrast, stomach cancer showed the greatest decline, followed by colorectal cancer, esophageal cancer, and biliary tract cancer. Most GI cancers predominantly affect men and tend toward a younger age of onset. Geographic disparities exist in the burden of GI cancers and their risk factors. For esophageal, stomach, and colorectal cancers, mortality rates linked to diet and smoking decreased, whereas alcohol-related mortality increased in several states, especially West Virginia. Hepatitis C remains the leading cause of liver cancer, with intravenous drug use as the primary risk factor. Non-alcoholic steatohepatitis (NASH) is the fastest-growing cause of liver cancer, followed by excessive alcohol use. Mortality rates for pancreatic cancer due to high body-mass index and high fasting plasma glucose have increased across states and age groups.

Discussion The epidemiological trends of GI cancers in the U.S. have shifted substantially. States need to implement targeted policies that address specific populations and risk factors for each cancer type.

Keywords Gastrointestinal cancers, Global burden of disease, Risk factors, Incidence

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Introduction

Gastrointestinal (GI) cancers represent one of the predominant types of malignant tumors in the United States and account for more than a quarter of all cancer-related deaths [1]. These cancers are characterized by delayed diagnosis, poor prognosis, and high mortality rates, and primarily include esophageal, gastric, colorectal, liver, biliary, and pancreatic cancers [2]. Factors such as an aging population, population growth, geographic disparities, and shifts in risk factors, including alcohol consumption, smoking, obesity, and unhealthy diets, contribute to the evolving epidemiological patterns of GI cancers in the United States [3–5]. Notably, the increasing incidence of early-onset GI cancers has attracted considerable attention.

Previous epidemiological studies on GI cancers have largely focused on a global perspective or on the East Asian region, leading to a notable deficiency in comprehensive systematic analyses regarding trends in GI cancers specific to the United States [6–9]. This study aims to provide an updated assessment of the burden of six major GI cancers in the U.S., utilizing the latest data from the Global Burden of Disease (GBD) Study 2021. Additionally, it analyzes trends from 2000 to 2021 across various states, genders, ages, and risk factors, offering valuable insights for the development of prevention and management strategies for GI cancers in the United States.

Methods

Data source

The data for this study are derived from the Global Burden of Disease Study 2021, which includes an epidemiological analysis of 371 diseases and injuries across 204 countries and regions [10]. This research extracted data on the incidence, mortality, and disability-adjusted life years (DALYs) of common gastrointestinal cancers from the GBD 2021. Specifically, primary liver cancer can be categorized by etiology into the following groups: hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol, non-alcoholic steatohepatitis (NASH), and other causes. The analysis of risk factors revealed risks related to gastrointestinal cancers identified in the GBD 2021, including dietary risk, excessive alcohol use, tobacco use, drug use, high body mass index, low physical activity, and high fasting plasma glucose.

Evaluation methodology

The general assessment metrics and methods of the GBD study have been previously detailed [10–12]. The indicators for incidence, mortality, and DALYs include total case numbers, crude rates, and age-standardized rates (ASR). The evaluation of risk factors is based on the percentage of attributable risk factors in relation to total mortality, alongside the ASMR [13, 14]. The number is expressed as the total number of cases or deaths for that year, accompanied by the 95% uncertainty interval (UI); the rate is quantified as the number of cases per 100,000 people, along with the corresponding 95% UI. Definitions of cancers and more detailed estimation methods are provided in the Supplementary Methods.

Future projection

The Bayesian age-period-cohort (BAPC) model was employed to predict the expected values of age-standardized incidence rates for gastrointestinal cancers in the United States over the next 15 years [15–17].

Statistical analysis

The annual percentage change was calculated via the joinpoint regression program developed by the National Cancer Institute (NCI), version 5.1.0.0, to assess the average temporal trend of ASR [18, 19]. An APC and its 95% confidence interval greater than or less than zero indicate an increasing or decreasing trend in the ASR, respectively; if the interval includes zero, the results are not statistically significant. Furthermore, all the statistical analyses and visualizations in this study were conducted using R (version 4.4.0), along with the following packages: data.table (version 1.15.4), ggplot2 (version 3.5.1), ComplexHeatmap (version 2.20.0), and BAPC (version 0.0.36).

Results

Temporal trends in gastrointestinal cancers in the United States

In 2021, there were 372,511 new cases and 199,978 deaths from gastrointestinal cancer in the United States. From 2000 to 2021, the incidence number of gastrointestinal cancers among all malignant tumors in the United States decreased from 9.58 to 5.71%, whereas the proportion of deaths due to these cancers increased from 25.54 to 28.36% (Fig. S1). During the study period, the incidence of six major types of GI cancer increased. Except for a slight decrease in gastric cancer mortality, the mortality of the other cancers increased (Table 1).

In 2021, the ASIR for GI cancers was highest for colorectal cancer at 38.17 per 100,000 people (95% UI: 35.56 to 39.98), followed by pancreatic cancer (10.33, 95% UI: 9.53 to 10.80), liver cancer (5.58, 95% UI: 5.20 to 5.79), gastric cancer (5.07, 95% UI: 4.74 to 5.30), esophageal cancer (4.20, 95% UI: 3.95 to 4.36), and biliary tract cancer (2.19, 95% UI: 2.01 to 2.30) (Table 1).

During the period from 2000 to 2021, liver cancer exhibited the fastest growth in ASIR (APC: 2.18%, 95% CI: 1.99 to 2.37), followed by pancreatic cancer (APC: 0.23%, 95% CI: 0.17 to 0.30). Additionally, the increase in

Table 1 Number, ASR, and changes in incidence, death, and DALYs for gastrointestinal cancers in the United States, 2000–2021

Cancer	Measure	Number, No.×10^4 (95% UI)		ASR per 100 000, No. (95% UI)		APC of ASR
		2000	2021	2000	2021	2000 to 2021
Esophageal cancer	Incidence	1.71 (1.62, 1.76)	2.43 (2.28, 2.53)	4.71 (4.49, 4.84)	4.2 (3.95, 4.36)	−0.69 (−0.77, −0.60)
	Deaths	1.51 (1.43, 1.56)	2.13 (1.99, 2.22)	4.11 (3.91, 4.23)	3.62 (3.4, 3.76)	−0.75 (−0.83, −0.68)
	DALYs	35.65 (34.44, 36.45)	47.95 (45.79, 49.54)	101.91 (98.75, 104.11)	86.55 (82.92, 89.36)	−0.91 (−0.99, −0.84)
Gastric cancer	Incidence	2.68 (2.49, 2.78)	2.85 (2.64, 2.99)	7.15 (6.7, 7.4)	5.07 (4.74, 5.3)	−1.66 (−1.75, −1.56)
	Deaths	1.66 (1.53, 1.73)	1.64 (1.5, 1.74)	4.33 (4.02, 4.5)	2.84 (2.62, 2.98)	−2.04 (−2.18, −1.89)
	DALYs	36.06 (34.25, 37.21)	36.31 (34.21, 37.79)	100.35 (95.89, 103.32)	69.16 (65.84, 71.77)	−1.74 (−1.87, −1.61)
Colorectal cancer	Incidence	18.27 (16.91, 19.01)	21.41 (19.79, 22.52)	48.99 (45.78, 50.82)	38.17 (35.56, 39.98)	−1.28 (−1.38, −1.19)
	Deaths	7.11 (6.44, 7.45)	7.51 (6.81, 7.97)	18.42 (16.87, 19.24)	12.79 (11.72, 13.51)	−1.83 (−1.96 to −1.69)
	DALYs	153.42 (143.74, 160.04)	169.24 (158.62, 177.63)	423.69 (399.67, 440.76)	315.59 (298.11, 330.02)	−1.41 (−1.55 to −1.28)
Liver cancer	Incidence	1.31 (1.24, 1.35)	3.15 (2.92, 3.27)	3.65 (3.49, 3.75)	5.58 (5.2, 5.79)	2.18 (1.99, 2.37)
	Deaths	1.05 (0.99, 1.08)	2.48 (2.29, 2.58)	2.86 (2.71, 2.94)	4.24 (3.94, 4.42)	2.08 (1.94, 2.21)
	DALYs	25.92 (24.97, 26.54)	57.69 (54.62, 59.76)	74.94 (72.45, 76.61)	106.24 (101.12, 110)	1.88 (1.70, 2.07)
Biliary tract cancer	Incidence	0.93 (0.85, 0.96)	1.28 (1.17, 1.35)	2.43 (2.25, 2.52)	2.19 (2.01, 2.3)	−0.37 (−0.51, −0.24)
	Deaths	0.43 (0.39, 0.45)	0.52 (0.47, 0.55)	1.1 (1.01, 1.15)	0.87 (0.79, 0.91)	−0.97 (−1.16, −0.78)
	DALYs	8.66 (8.15, 8.97)	10.86 (10.16, 11.35)	23.67 (22.44, 24.45)	19.23 (18.12, 20.02)	−0.80 (−1.00, −0.60)
Pancreatic cancer	Incidence	3.69 (3.44, 3.84)	6.13 (5.62, 6.43)	9.84 (9.22, 10.19)	10.33 (9.53, 10.8)	0.23 (0.17, 0.30)
	Deaths	3.48 (3.23, 3.62)	5.71 (5.22, 5.99)	9.18 (8.59, 9.51)	9.5 (8.74, 9.95)	0.17 (0.11, 0.22)
	DALYs	74.3 (70.61, 76.39)	119.24 (112.48, 123.8)	207.58 (198.1, 212.98)	210.01 (199.54, 217.4)	0.05 (−0.00, 0.10)

ASR age-standardized rate, *DALYs* disability-adjusted life years, *APC* annual percent change, *UI* uncertainty interval

the ASMR was smaller than that of the ASIR. Conversely, gastric cancer experienced the largest decrease in the ASIR (APC: −1.66%, 95% CI: −1.75 to −1.56), followed by colorectal cancer (APC: −1.28%, 95% CI: −1.38 to −1.19), esophageal cancer (APC: −0.69%, 95% CI: −0.77 to −0.60), and biliary tract cancer (APC: −0.37%, 95% CI: −0.51 to −0.24), with a greater decrease in ASMR than in the ASIR (Fig. 1; Table 1).

Differences in prevalence across states

In 2021, there were significant differences in the ASIR and ASMR of GI cancers at the state level in the United States (Fig. 2A and S2A). The states with the highest ASIR were as follows: for esophageal cancer, District of Columbia (5.73); for gastric cancer, Hawaii (7.88); for colorectal cancer, Kentucky (49.91); for liver cancer, Hawaii (8.98); for biliary tract cancer, Minnesota (2.71); and for pancreatic cancer, Louisiana (12.93).

From 2000 to 2021, the ASIR and ASMR for gastric and colorectal cancers showed a downward trend across states; conversely, there was a notable increase in liver cancer rates (Fig. 2B and S2B). Additionally, the ASIR and ASMR for esophageal cancer generally decline, with exceptions in a few states where rates either increased or remained stable, whereas the opposite trend was observed for pancreatic cancer. Notably, although only 31 states reported a decrease in biliary tract cancer incidence, mortality rates declined in all states. Table S1 presents relevant data for each state and the District of Columbia.

Age and gender differences

In 2021, GI cancers in the U.S. exhibited a marked male predominance in both incidence and mortality, with the exception of biliary tract cancer (Fig. 3A and S3A). Among all age groups, the incidence of esophageal cancer was greater in men than in women. The incidence of gastric cancer in males exceeded that in females until the age of 95. Furthermore, the age thresholds for colorectal cancer, liver cancer, and pancreatic cancer were 80 years, 95 years, and 80 years, respectively (Fig. 3A).

From 2000 to 2021, the incidence and mortality rates of esophageal cancer, gastric cancer, colorectal cancer, and biliary tract cancer generally decreased in most age groups (Fig. 3B and S3B). However, a concerning trend emerged, with the incidence of esophageal cancer, colorectal cancer, and biliary tract cancer increasing among younger age groups (Fig. 3B). The incidence of liver cancer significantly increased, particularly among males aged 60–64 years and females aged 50–59 years. The overall incidence of pancreatic cancer increased slightly but without a notable age-related trend (Fig. 3B). The APCs for incidence and mortality rates across different sexes and age groups are listed in Table S2.

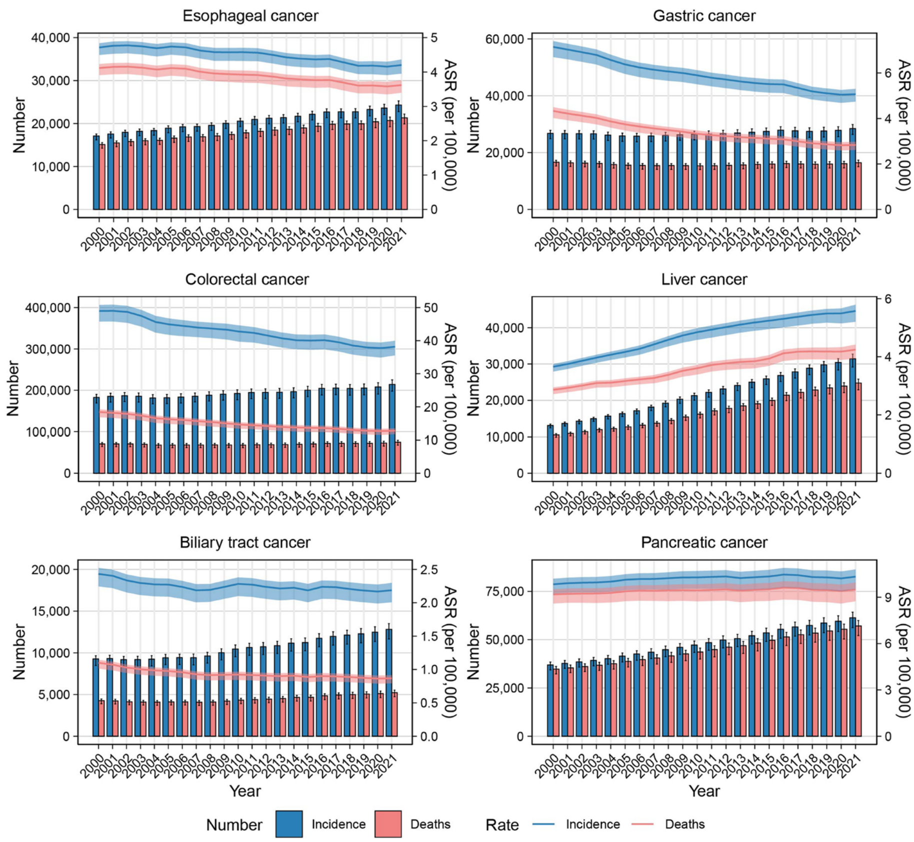

Fig. 1 Temporal trends in incidence and mortality of gastrointestinal cancers in the United States. The left Y-axis represents the number of incidences or deaths, whereas the right Y-axis indicates the ASR. ASR: age-standardized rate

Risk factor analysis

The GBD2021 data revealed that tobacco use accounted for the highest proportion of esophageal cancer deaths, accounting for 48.98% (95% UI 37.98 to 59.46) of the total deaths (Table 2). From 2000 to 2021, the mortality rate for tobacco-related esophageal cancer declined, with the most significant reduction observed for chewing tobacco (APC: −1.92%, 95% CI −2.06 to −1.78) (Table 2). Notably, although the overall mortality rate for esophageal cancer due to excessive alcohol use remained stable, rates increased in several states, particularly West Virginia (Fig. 4). Among individuals aged 25–34 years, mortality from esophageal cancer related to excessive alcohol use and insufficient vegetable intake increased (Fig. S4). For gastric cancer, mortality related to high sodium intake (APC: −1.91%, 95% CI >−2.02 to −1.79) and smoking (APC: −3.35%, 95% CI −3.45 to −3.25) declined across all states (Fig. 4).

In 2021, dietary risk was the leading cause of colorectal cancer death, contributing 40.28% (95% UI 8 to 63.38) of the total. These risks primarily involve low intake of whole grains, milk, calcium, and fiber, as well as excessive intake of red and processed meats. Over the study period, improved dietary practices and healthcare led to a decline in all GBD-associated colorectal cancer risk factors, particularly insufficient intake of fiber (APC: −2.81%, 95% CI −2.96 to −2.65) (Table 2). Regionally, alcohol-related colorectal cancer mortality increased in several states, notably Mississippi (Fig. 4). Among younger populations, various unhealthy dietary and behavioral risks contributed to an increase in colorectal cancer mortality, with low physical activity being the most significant (Fig. S4).

In 2021, intravenous drug use emerged as a leading risk factor for liver cancer deaths, especially among the 15–24 years age group, where the mortality rate due to drug use increased dramatically (Fig. S4). Throughout the study period, mortality from liver cancer due to all risk factors increased, with high fasting plasma glucose emerging as the fastest-growing contributor (APC: 3.57%, 95% CI 3.31 to 3.83) (Table 2). Additionally, high body mass index (BMI) -induced mortality slightly decreased overall in biliary tract cancer (APC: −0.25%, 95% CI −0.40 to −0.09), although significant geographical and age-related disparities were observed, with increasing trends among younger populations in certain states. Notably, high BMI and high fasting plasma glucose contributed to increased

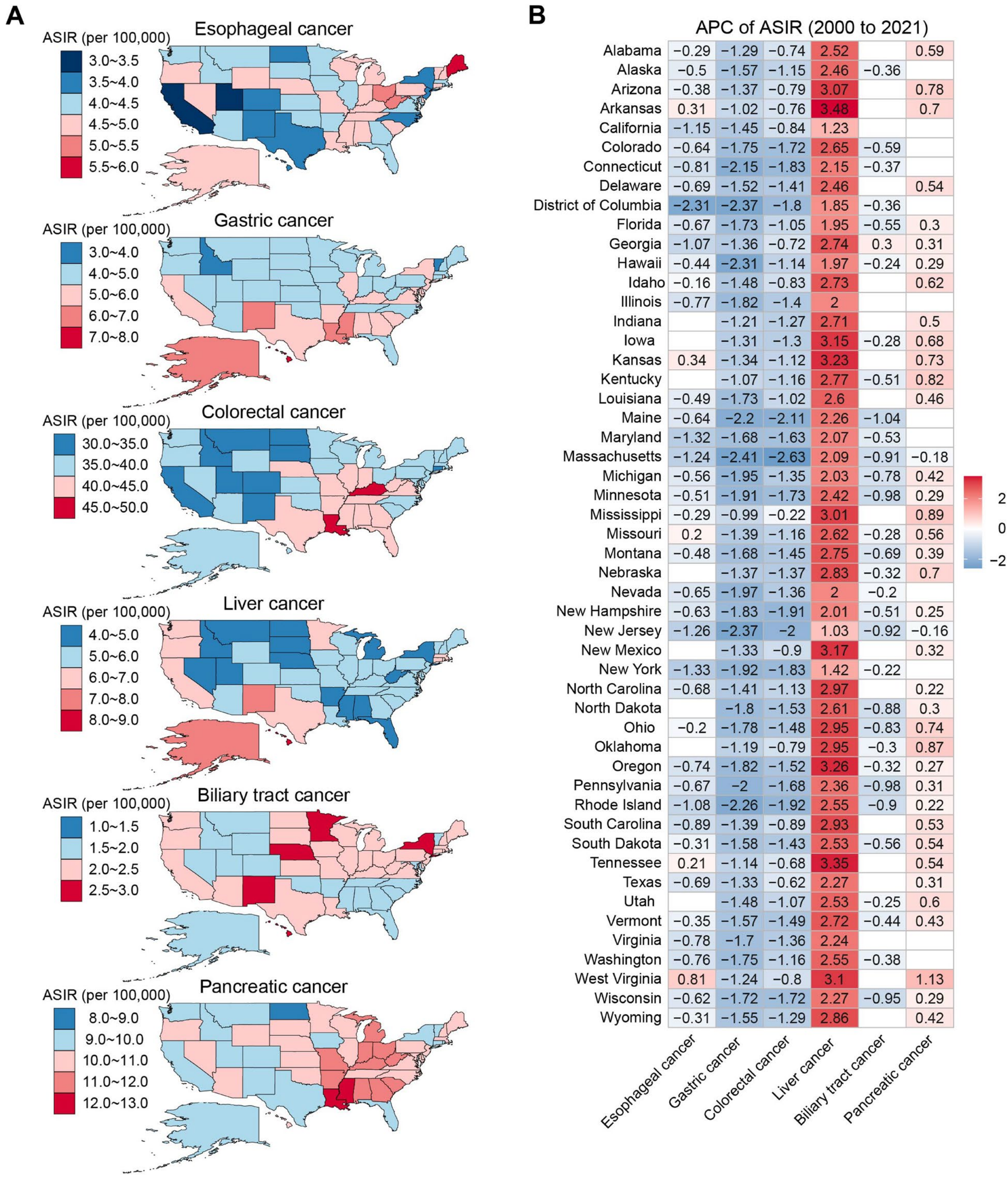

Fig. 2 Geographic variations in the incidence of gastrointestinal cancers in the United States. **A** ASIR of gastrointestinal cancers across U.S. states in 2021. **B** APCs in the ASIR of gastrointestinal cancers by state from 2000 to 2021. ASIR: age-standardized incidence rate; APC: annual percentage change

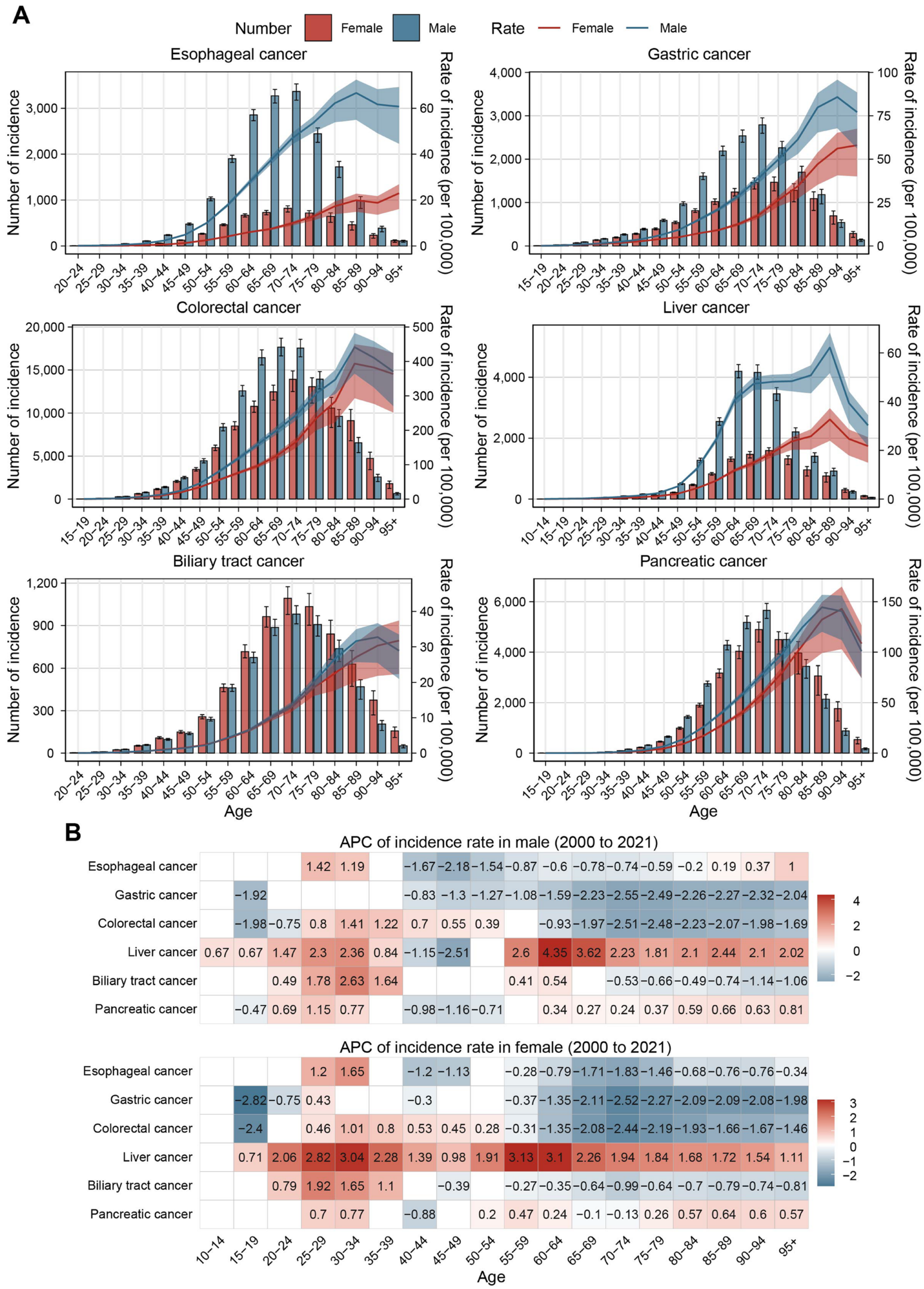

Fig. 3 Age and sex differences in gastrointestinal cancer incidence in the United States. **A** The number and incidence rates of gastrointestinal cancers by age and sex in 2021. **B** APC in incidence rates of gastrointestinal cancers by sex and age group from 2000 to 2021. APC: annual percentage change

Table 2 Percentage contribution of various risk factors to the number of all-age deaths in GI cancers, and age-standardized mortality rates for risk attribution, 2000–2021

Cancer	Risk factor	Percent, No.% (95% UI)		ASMR per 100 000, No. (95% UI)		APC of ASMR
		2000	2021	2000	2021	2000 to 2021
Esophageal cancer	Diet low in vegetables	18.36 (−3.98, 36.76)	18.41 (−4.01, 36.83)	0.75 (−0.16, 1.5)	0.66 (−0.14, 1.34)	−0.71 (−0.86, −0.57)
	High alcohol use	15.32 (9.8, 21.17)	18.51 (12.48, 24.89)	0.65 (0.43, 0.9)	0.69 (0.47, 0.9)	0.09 (−0.06, 0.23)
	Tobacco	56.75 (45.68, 66.84)	48.98 (37.98, 59.46)	2.36 (1.9, 2.8)	1.74 (1.35, 2.13)	−1.57 (−1.68, −1.47)
	Smoking	54.3 (42.97, 64.6)	46.73 (35.39, 57.19)	2.26 (1.79, 2.71)	1.66 (1.26, 2.07)	−1.60 (−1.70, −1.50)
	Chewing tobacco	5.68 (3.41, 8.39)	4.48 (2.48, 6.96)	0.23 (0.14, 0.34)	0.16 (0.09, 0.25)	−1.92 (−2.06, −1.78)
Gastric cancer	Diet high in sodium	7.42 (0, 39.1)	7.62 (0, 39.67)	0.32 (0, 1.69)	0.22 (0, 1.13)	−1.91 (−2.02, −1.79)
	Smoking	15.91 (12.63, 19.29)	12.55 (9.92, 15.44)	0.7 (0.55, 0.86)	0.35 (0.27, 0.43)	−3.35 (−3.45, −3.25)
Colorectal cancer	**Dietary risks**	40.01 (8.18, 62.94)	40.28 (8, 63.38)	7.38 (1.47, 11.63)	5.16 (1.02, 8.17)	−1.77 (−1.89, −1.65)
	High in processed meat	11.28 (−2.82, 22.94)	11.74 (−3.02, 23.79)	2.1 (−0.52, 4.26)	1.52 (−0.39, 3.08)	−1.64 (−1.72, −1.56)
	High in red meat	15.97 (−0.01, 31.84)	16.05 (−0.01, 31.97)	2.95 (0, 5.89)	2.06 (0, 4.1)	−1.80 (−1.93, −1.66)
	Low in calcium	3.45 (2.38, 4.57)	3.33 (2.35, 4.43)	0.61 (0.42, 0.83)	0.41 (0.28, 0.56)	−1.77(−1.89, −1.65)
	Low in fiber	1.55 (0.72, 2.36)	1.22 (0.56, 1.91)	0.27 (0.13, 0.43)	0.15 (0.07, 0.24)	−2.81 (−2.96, −2.65)
	Low in milk	8.9 (2.35, 15.37)	8.2 (2.16, 14.19)	1.63 (0.44, 2.83)	1.04 (0.28, 1.84)	−2.02 (−2.21, −1.84)
	Low in whole grains	17.93 (7.5, 26.64)	17.94 (7.5, 26.76)	3.3 (1.41, 4.95)	2.29 (0.98, 3.44)	−1.81 (−1.93, −1.68)
	High alcohol use	4.7 (3.17, 6.16)	6.24 (4.8, 7.74)	0.91 (0.63, 1.2)	0.84 (0.64, 1.04)	−0.40 (−0.46, −0.33)
	High body-mass index	12.7 (5.57, 19.95)	15.19 (6.86, 23.49)	2.38 (1.04, 3.82)	1.96 (0.88, 3.03)	−1.03 (−1.12, −0.93)
	High fasting plasma glucose	8.88 (4.57, 13.13)	11.71 (6.02, 17.29)	1.63 (0.84, 2.39)	1.45 (0.74, 2.18)	−0.76 (−0.85, −0.68)
	Low physical activity	6.35 (3.52, 9.2)	6.83 (4.1, 9.57)	1.09 (0.6, 1.59)	0.82 (0.48, 1.17)	−1.34 (−1.56, −1.11)
	Smoking	4.76 (2.95, 6.73)	4.15 (2.54, 5.92)	0.92 (0.56, 1.3)	0.55 (0.33, 0.78)	−2.49 (−2.62, −2.35)
Liver cancer	Drug use	31.17 (25.99, 36.13)	37.8 (31.9, 43.12)	0.92 (0.77, 1.06)	1.6 (1.35, 1.84)	2.82 (2.56, 3.08)
	High alcohol use	27.49 (25.27, 29.97)	29.9 (26.45, 33.91)	0.8 (0.72, 0.88)	1.26 (1.12, 1.43)	2.42 (2.31, 2.53)
	High body-mass index	16.9 (6.99, 28.39)	21.1 (9.12, 33.97)	0.49 (0.21, 0.83)	0.9 (0.39, 1.47)	2.99 (2.76, 3.22)
	High fasting plasma glucose	4.84 (0.57, 9.08)	6.89 (0.85, 12.31)	0.13 (0.02, 0.25)	0.28 (0.03, 0.51)	3.57 (3.31, 3.83)
	Smoking	11.97 (3.81, 20.56)	10.51 (3.29, 18.28)	0.35 (0.11, 0.6)	0.45 (0.14, 0.79)	1.30 (1.12, 1.47)
Biliary tract cancer	High body-mass index	16.77 (11.49, 22.5)	19.7 (13.41, 26.31)	0.19 (0.13, 0.26)	0.17 (0.12, 0.23)	−0.25 (−0.40, −0.09)
Pancreatic cancer	High body-mass index	3.19 (−0.23, 8.2)	4.69 (0, 10.74)	0.31 (−0.02, 0.77)	0.45 (0, 1.01)	1.74 (1.57, 1.91)
	High fasting plasma glucose	27.24 (3.39, 50.01)	35.78 (4.53, 64.32)	2.48 (0.31, 4.57)	3.33 (0.41, 5.98)	1.28 (1.08, 1.49)
	Smoking	16.45 (14.35, 18.74)	13.84 (11.83, 16.2)	1.57 (1.38, 1.79)	1.34 (1.14, 1.58)	−0.76 (−0.83, −0.69)

ASMR age-standardized mortality rate, *APC* annual percent change, *UI* uncertainty interval

liver cancer mortality across nearly all states and age groups (Fig. 4 and S4).

Epidemiological trends of liver cancer by etiology

Since liver cancer represents the gastrointestinal cancer with the largest increase in incidence rates in the United States, further analysis was conducted on different types of liver cancer. In 2021, the order of causes for liver cancer incidence was as follows: HCV, alcohol use, HBV, NASH, and other causes (Fig. 5A). At the state level, Hawaii had the highest ASIR for all types of liver cancer, except for liver cancer related to other causes (Fig. 5B).

From 2000 to 2021, all types of liver cancer exhibited varying degrees of growth across all states in the United States, except for the ASIR of HBV-related liver cancer in California, which showed no significant change (Fig. 5C). Notably, NASH-related liver cancer was the fastest-growing type of liver cancer nationwide (APC: 2.56%, 95% CI: 2.36 to 2.76), followed by alcohol-related liver cancer (APC: 2.49%, 95% CI: 2.32 to 2.65), HCV-related liver cancer (APC: 2.21%, 95% CI: 1.97 to 2.46), liver cancer related to other causes (APC: 1.71%, 95% CI: 1.54 to 1.87), and HBV-related liver cancer (APC: 1.42%, 95% CI: 1.20 to 1.65) (Fig. 5C). The APCs for ASIR of liver cancer by different causes across the United States and each state can be found in Table S3.

Future projection

By 2035, the absolute incidence of the six major GI cancers in the United States is projected to continue rising, with the most substantial increase anticipated for liver

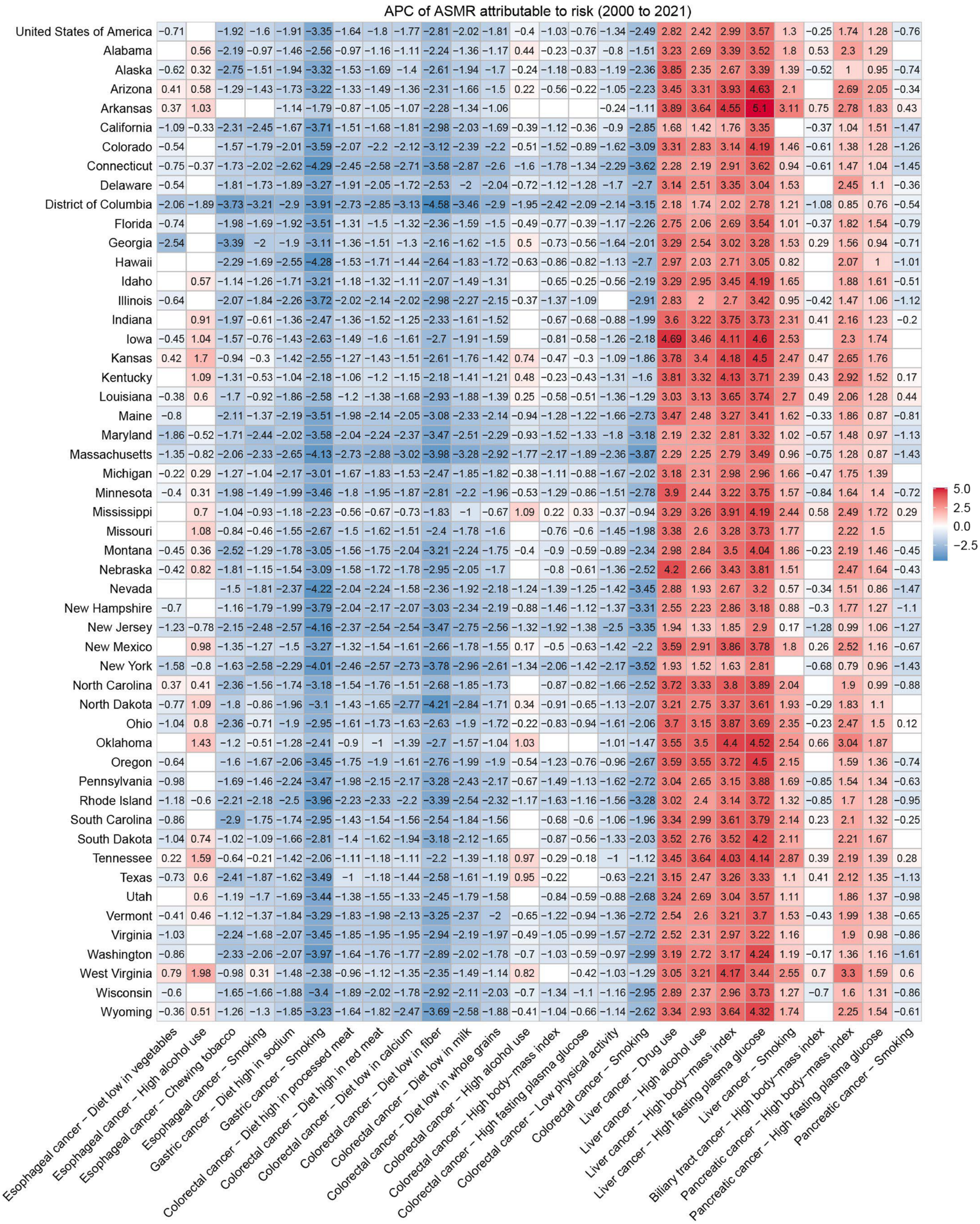

Fig. 4 Annual percentage change in the ASMR of attributable risk factors for GI cancer by state, from 2000 to 2021

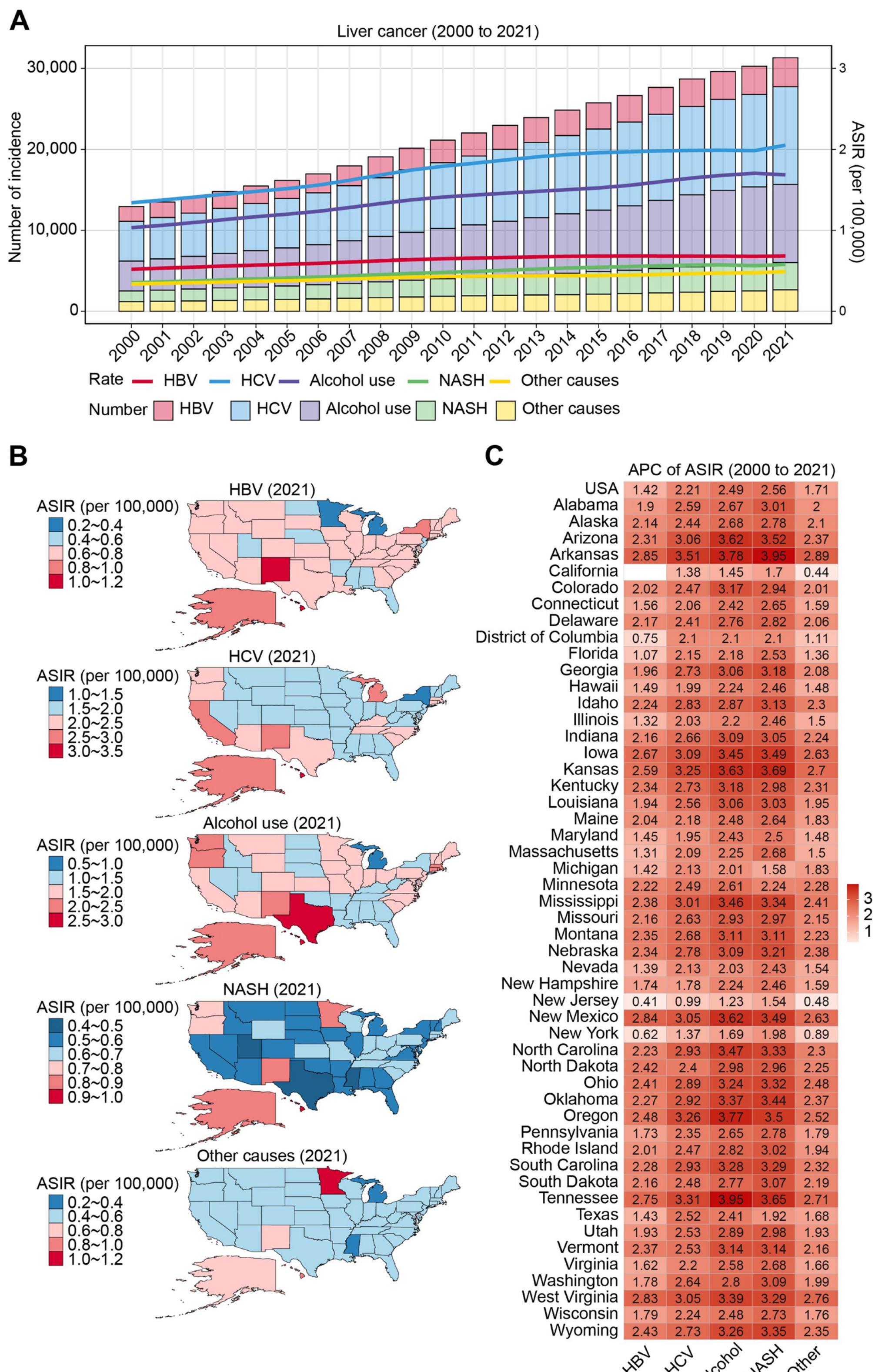

Fig. 5 Trends in the epidemiology of liver cancer by etiology in the United States.**A** Time trends of incidence numbers and ASIR for liver cancer by etiology. **B** Geographic distribution of ASIR for liver cancer by etiology in 2021. **C** Annual percentage change in the ASIR for liver cancer across states. ASIR: age-standardized incidence rate; APC: annual percentage change

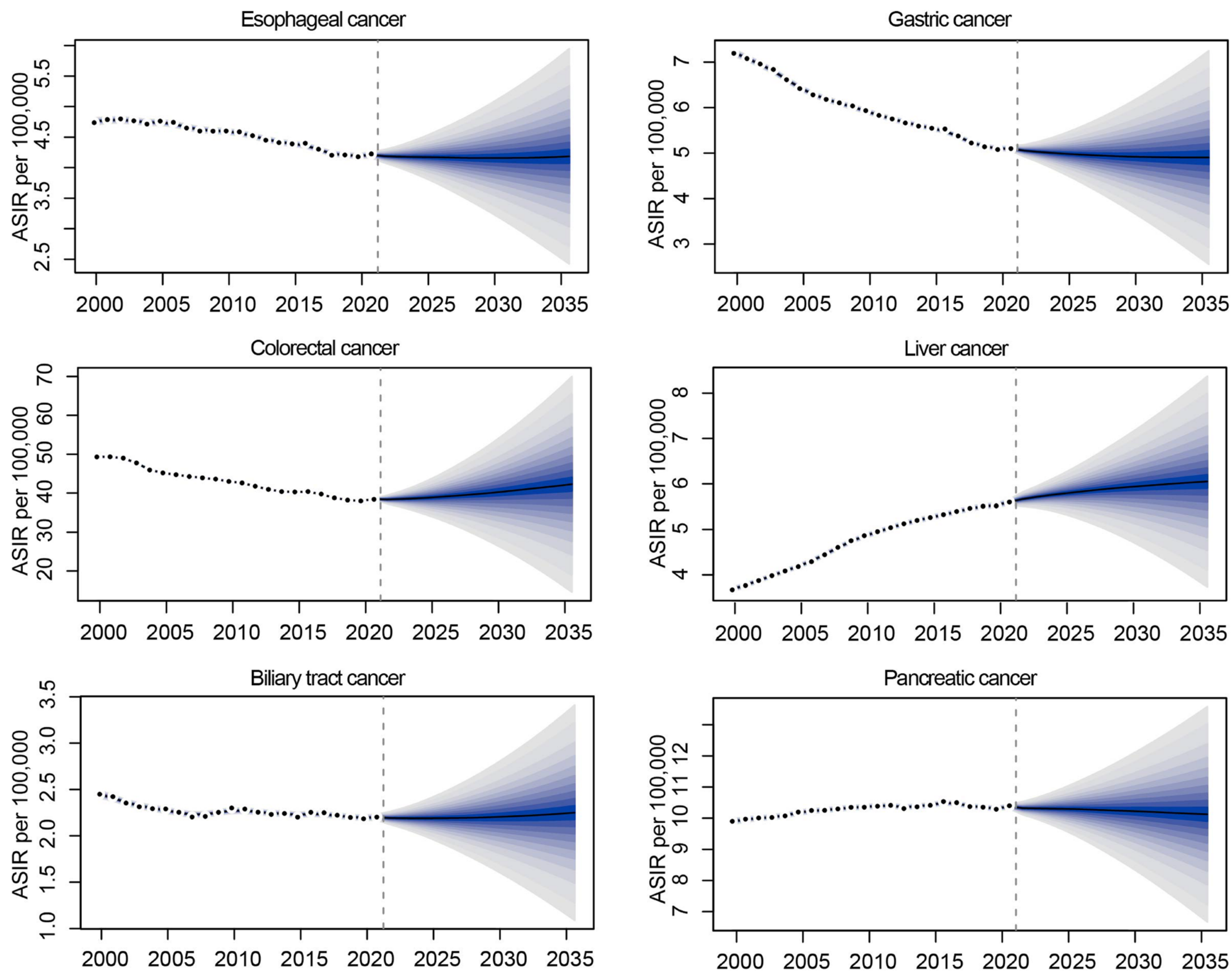

Fig. 6 Predicted age-standardized incidence rate of gastrointestinal cancers in the United States over the next 15 years

cancer (38.01%). The remaining increases are expected for colorectal cancer (34.5%), biliary tract cancer (33.28%), pancreatic cancer (30.04%), esophageal cancer (24.01%), and gastric cancer (20.89%) (Table S4).

By 2035, the ASIR for esophageal cancer is expected to remain stable, whereas the ASIR for stomach and pancreatic cancers are projected to slightly decline, reaching 4.9 cases and 10.14 cases per 100,000 people, respectively. In contrast, the ASIR for colorectal cancer, liver cancer, and biliary tract cancer is anticipated to increase, reaching 41.88 cases, 6.03 cases, and 2.24 cases per 100,000 people, respectively (Fig. 6 and Table S5). By 2035, all types of liver cancer, except for HBV-related liver cancer, are expected to see an increase in ASIR (Fig. S5 and Table S6).

Discussion

This study presents an analysis of the most recent trends of GI cancers and their attributable risk factors in the United States. From 2000 to 2021, significant shifts in the epidemiology of GI cancers occurred. Although the incidence and mortality rates of most gastrointestinal cancers have been declining, several challenges remain: the increasing incidence of early-onset cancers; changing patterns of risk factors (such as obesity, poor dietary habits, and drug use); and significant health disparities associated with race, ethnicity, geography, education level, and socioeconomic status [20].

According to GBD2021, the overall incidence and mortality rates of esophageal cancer in the U.S. have steadily decreased, particularly due to the impacts of poor diet and tobacco use. Previous studies have also reported a significant reduction in the incidence of esophageal cancer, primarily driven by a decrease in the incidence of esophageal squamous cell carcinoma, although the incidence of esophageal adenocarcinoma remained stable from 2006 to 2018 [21]. In certain regions, such as the district of Columbia, the high incidence of esophageal cancer is associated with excessive alcohol use [22]. The socioeconomic challenges and limited access to healthcare in states such as West Virginia and Arkansas have worsened the mortality rates in these areas. Our study also revealed a lower incidence of esophageal cancer among individuals aged 20–40 years, although this group showed an increasing trend. Studies have indicated an increase in the incidence of esophageal adenocarcinoma among those under 50 years of age, accompanied by a higher proportion of late-stage diagnoses, which is likely linked to increasing obesity rates in younger populations [23, 24]. We propose that the incidence of esophageal cancer will remain stable over the next 15 years, although other studies suggest that it could increase due to the increasing incidence of esophageal adenocarcinoma [25].

The incidence and mortality rates of gastric cancer in the U.S. have significantly decreased, particularly among individuals over 50, which is attributed to reduced *Helicobacter pylori* infections, changes in dietary habits, and decreased tobacco consumption [26, 27]. In regions with a high incidence of gastric cancer, such as Hawaii, the higher proportion of Asian populations and their consumption of preserved foods may contribute to these trends [28]. Research has shown that while the incidence of gastric adenocarcinoma, the most common type, has decreased, the incidence of gastric neuroendocrine tumors and gastrointestinal stromal tumors has increased [29]. Compared with non-Hispanic whites, non-Hispanic minorities, especially those from lower socioeconomic backgrounds, face a greater risk of non-cardia gastric cancer (associated with *H. pylori* infection) [30]. Targeted screening for *H. pylori* in underserved regions and high-risk populations could help reduce the incidence of gastric cancer and improve health equity [31, 32].

Colorectal cancer remains the leading cause of gastrointestinal cancer burden in the U.S. Despite a significant decline in overall incidence and mortality, largely due to improvements in dietary conditions and expanded screening programs, the incidence of early-onset colorectal cancer (under 50 years) has notably increased [33, 34]. In response, the 2021 USPSTF guidelines lowered the recommended starting age for colorectal cancer screening in average-risk populations from 50 to 45 years [35, 36]. Various initiatives, such as expanded Medicaid coverage for uninsured low-income individuals, have reduced barriers to screening and narrowed health disparities [37]. Additionally, our study identified obesity-related behaviors, insulin resistance, and poor dietary habits as key risk factors contributing to rising mortality rates from colorectal cancer in younger populations, which may drive future increases in the incidence of colorectal cancer in the U.S [25].

The incidence of liver cancer in the U.S. has been steadily increasing, driven by worsening risk factors such as intravenous drug use, alcohol consumption, obesity, and insulin resistance. Research has suggested that the liver cancer mortality rate has started to decline [38]. However, data from the recent period of 2019 to 2021 indicate a continued increase, which may be influenced by the effects of COVID-19. HCV-related liver cancer remains the most prevalent form of liver cancer in the U.S. Deaths linked to HCV now exceed those from all other infectious diseases combined, with intravenous drug use being the primary risk factor for new HCV infections [39, 40]. Direct-acting antivirals (DAAs), with a cure rate exceeding 95%, have improved survival rates for HCV-related diseases [41]. The National Viral Hepatitis Strategic Plan aims to achieve viral elimination in more than 80% of HCV patients by 2030 [42]. Evidence suggests that people who inject drugs and are coinfected with HCV can benefit from DAAs, although specialized healthcare and treatment policies for this population remain essential [43]. Additionally, the expansion of the HBV vaccination program has led to a vaccination rate above 90% among U.S. infants [44]. However, coverage for adults aged 19 and over remains low, with only 30% vaccinated, highlighting the need for universal vaccination for adults aged 19–59 years [45]. NASH-related liver cancer is the fastest-growing type of liver cancer in the U.S., largely due to rising obesity rates and increasing insulin resistance. Projections suggest that the obesity rate among U.S. adults will reach an alarming 48.9% by 2030 [46]. Gaps in NASH prevention and treatment persist, such as the lack of effective non-invasive biomarkers and FDA-approved treatments [47, 48]. Furthermore, increasing excessive alcohol consumption may surpass HCV as the leading cause of liver cancer, underscoring the need for stricter alcohol policies, particularly in high-incidence states such as Hawaii, Texas, and the District of Columbia. If current trends continue, the incidence of liver cancer is expected to rise.

During the study period, the incidence of biliary tract cancer in the U.S. decreased, likely due to a reduction in gallbladder cancer incidence, which has been linked to the widespread use of cholecystectomy [49]. In contrast, the incidence of bile duct cancer has increased [50]. Notably, there was a trend toward younger age groups being affected by biliary tract cancer, which was correlated with high BMI. Regionally, bile duct cancer mortality rates related to high BMI have risen in several states, particularly Arkansas, and are projected to continue increasing.

The incidence and mortality rates of pancreatic cancer in the U.S. are increasing [51, 52]. Previous studies have revealed a rise in early-onset pancreatic cancer, particularly among non-Hispanic white women [52]. However, owing to the relatively low incidence and limited screening accuracy for pancreatic cancer, the harms of routine screening in asymptomatic populations outweigh the potential benefits [53]. Therefore, selective monitoring of high-risk groups is more likely to detect early-stage pancreatic cancer and reduce mortality. Moreover, this study revealed a decrease in pancreatic cancer deaths attributed to smoking but an increase in deaths linked to obesity and insulin resistance. Projections indicate a continued rise in the incidence of pancreatic cancer, highlighting the need for primary prevention efforts [25].

Study limitations

This study relies on GBD2021 data to assess the burden and trends of GI cancers in U.S. states. However, several limitations should be noted. First, the reliability of the study's conclusions depends on the quality of the GBD2021, which may differ from estimates provided by the American Cancer Society owing to variations in modeling approaches and estimation methods. Second, the risk factors included in GBD2021 are limited and do not encompass all cancer risk factors. Third, GBD data lack detailed pathological classifications for GI cancers and do not further subdivide biliary tract cancers by site. Finally, GBD2021 lacks data on U.S. racial and ethnic groups. Given the diverse racial compositions and high immigrant rates in the U.S., studies stratified by race and ethnicity are necessary, and further research is needed to address these gaps.

Conclusion

In conclusion, our study provides a comprehensive overview of the latest trends in GI cancers and their risk factors in U.S. states. Over the study period, liver and pancreatic cancer incidence and mortality rates have continued to rise, particularly for HCV, alcohol, and NASH-related liver cancers. While the burden of other cancers has declined, many are showing an emerging trend toward younger age groups. Strict tobacco control policies have significantly reduced smoking-related mortality, but the increasing risks associated with alcohol consumption, obesity, and intravenous drug use require urgent attention. Strengthening primary prevention efforts and expanding screening programs, particularly in lower socioeconomic regions, are essential strategies for reducing the burden of GI cancers and promoting health equity. Although our study lacks an analysis of racial/ethnic factors, it contributes to increasing awareness of the GI cancer burden in the U.S. and provides valuable insights to guide future prevention and treatment efforts.

Abbreviations

APC	Annual percentage change
ASIR	Age-standardized incidence rate
ASMR	Age-standardized mortality rate
ASR	Age-standardized rate
BAPC	Bayesian Age-Period-Cohort
BMI	Body-mass index
CI	Concentration index
COVID-19	Coronavirus disease 2019
DAAs	Direct-acting antivirals
DALYs	Disability-adjusted life years
GBD	Global Burden of Disease
GI cancers	Gastrointestinal cancers
HBV	Hepatitis B virus
HCV	Hepatitis C virus
NASH	Non-alcoholic steatohepatitis
NCI	National Cancer Institute

Supplementary Information

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Additional file 1.

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Informed Consent

N/A.

Registry and the registration No. of the study/trial

N/A.

Animal Studies

N/A.

Authors' contributions

JJH, XZQ: study design; JJH, XZQ, WQB: data acquisition and analysis; JJH, XZQ, WQB: data visualization; JJH, XZQ, WQB, WBK, HR, XWK: manuscript writing, review, and/or revision; Supervision: SCZ, CYJ.

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Data availability

The GBD2021 data are available from the online website (https://vizhub.healthdata.org/gbd-results/). Additionally, the analysis results related to this study are available upon request by contacting the corresponding author via email.

Declarations

Ethics approval and consent to participate

Ethical approval was waived as this study utilized data from publicly available databases.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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