Global assessment and prediction of the disease burden of gastrointestinal cancer in women of childbearing age using the data from GBD Study 2021

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Abstract

Background & aims: This study aims to analyze the incidence and the disability-adjusted life years (DALYs) for five major gastrointestinal (GI) cancers (lip and oral cavity, stomach, colon and rectum, liver, and pancreatic cancers) in women of childbearing age (WCBA) globally from 1990 to 2021, explore the trends, address the health inequalities, and predict future trends.

Methods: Trends were evaluated using age-standardized rates and estimated annual percentage change (EAPC). The association between the burden and the sociodemographic index (SDI) was assessed using Spearman’s correlation analysis. Joinpoint regression was employed to identify inflection points. Health inequalities were assessed using both absolute (slope index of inequality, SII) and relative (concentration index, COI) measures. Finally, a Bayesian age-period-cohort (BAPC) model was used to predict future trends.

Results: In 2021, WCBA experienced approximately 183,000 new GI cancer cases and 4.635 million DALYs. From 1990 to 2021, the DALYs for stomach and colorectal cancers declined, while those for lip and oral cavity and pancreatic cancers increased; liver cancer remained stable. Incidence rose the fastest in low (EAPC = 2.28) and low-middle (EAPC = 2.49) SDI regions, while the DALYs declined in high SDI regions (EAPC = –1.04), despite a slight incidence increase (EAPC = 0.28). Joinpoint regression showed significant declines in the incidence of lip and oral cavity cancer in high SDI regions during the periods of 1997–2004 (EAPC = –0.29, 95% confidence interval (CI): –0.52, –0.07) and 2016–2021 (EAPC = –0.95, 95% CI: –1.37, –0.53). Furthermore, the pancreatic cancer burden shifted from high to low SDI regions (SII: 0.79 → 0.71; COI: –0.13 → –0.10), reflecting growing absolute but decreasing relative inequality. The BAPC model predicted noticeable increases in lip and oral cavity and pancreatic cancers, with 77% and 12% in 45-49, respectively.

Conclusions: Our findings reveal that lip and oral cavity cancer and pancreatic cancer are showing an upward trend in WCBA, while the burden of stomach cancer and colon and rectum cancer are improving. The disease burden of certain GI cancers (pancreatic cancer and lip and oral cavity cancer) is shifting from high-SDI regions to low-SDI regions, with the disease burden in low-SDI regions gradually worsening. This highlights the urgent need for global health initiatives to adjust their focus and strengthen cancer prevention, early detection, and treatment infrastructure in resource-poor regions to avoid an escalating crisis.

Keywords: Gastrointestinal cancers; Women of childbearing age; Joinpoint regression model; Health inequalities; Bayesian-age-period-cohort model

1. Introduction

Gastrointestinal (GI) cancers, which encompass malignancies of the digestive system, represent a major global health challenge and are one of the leading causes of cancer-related morbidity and mortality worldwide[1][2]. According to GLOBOCAN 2022 data (http://gco.iarc.fr/today), several GI cancers dominate the global oncology landscape. Specifically, colon and rectum cancer (1,926,000 cases), stomach cancer (969,000 cases), and liver cancer (866,000 cases) are the third, fifth, and sixth most commonly diagnosed cancers, respectively. In terms of mortality, they are the second, fourth, and third leading causes of cancer death. Furthermore, pancreatic cancer is notorious for its high mortality rate, and the incidence of lip and oral cavity cancer continues to rise.

Although the cancer burden is the highest in the elderly, an alarming trend of increasing incidence in younger adults has been observed for several GI cancers. The health of women of childbearing age (WCBA), as a core group of society and family, is of significant importance, yet this demographic is often overlooked in cancer epidemiology research. To date, few studies have systematically focused on the burden of GI cancers in this specific population[3].

The epidemiological landscape of GI cancers exhibits significant variations across countries and regions[4][5][6]. These differences may be attributed to a confluence of factors including genetic susceptibility, lifestyle changes, environmental exposures, infections such as helicobacter pylori or hepatitis viruses, psychological factors and the level of economic development[7][8][9][10]. This complex interplay of risk factors shapes the complex epidemiological profile of GI cancers globally.

Therefore, using the data from the Global Burden of Disease (GBD) Study 2021 (GBD 2021), this study systematically assesses the incidence, disability-adjusted life years (DALYs), and temporal trends of five GI cancers among WCBA globally and in different sociodemographic index (SDI) regions from 1990 to 2021. We also analyze the association between these trends and the SDI, and predict future trends until 2050. Our overarching goal is to provide robust quantitative evidence to inform the development of precise prevention and control strategies, optimize resource allocation, and ultimately strengthen public health interventions for this vital population.

2. Methods

2.1. Data sources

This study utilized the data primarily from the GBD 2021, which contains the data on women aged 15-49 years of childbearing age with five types of GI cancers, namely lip and oral cavity, stomach, colon and rectum, liver, and pancreatic cancers, from all countries in all regions of the world [11]. The complete list of data sources can be explored via the GBD 2021 Data Input Sources Tool (https://ghdx.healthdata.org/gbd-2021/sources) on the website of the Institute for Health Metrics and Evaluation (IHME), USA. To predict the future burden of disease, global population data for WCBA from

1991 to 2050 were also obtained from the Population Division database of the United Nations Department of Economic and Social Affairs (UNDESA).

2.2. Disease burden metrics and SDI

This study uses incidence and disability-adjusted life years (DALYs) to evaluate the burden of GI cancers, which were analyzed using both the counts and the rates, including age-standardized rate (ASR). The SDI, a composite measure reflecting a region's development level and strongly correlated with health outcomes, is derived from the geometric mean of the 0–1 indices of fertility under age 25, mean years of schooling (15+), and lag-distributed per capita income.

2.3. Statistical analysis of trends

The ASR per 100,000 WCBA was calculated using Formula (1):

$$ASR = \frac{\sum_{i=1}^{N} \alpha_i W_i}{\sum_{i=1}^{N} W_i} \quad (1)$$

where α_i represents the age-specific rate for the ith age group, W_i denotes the number of the individuals in the corresponding age group from the GBD 2021 standard population, and N is the total number of age groups.

The estimated annual percentage change (EAPC) [12] in ASR was computed to assess the average trend over a specific time interval. The natural logarithm of ASR was used to fit the following linear regression model:

$$\ln(ASR) = \alpha + \beta x + \varepsilon \quad (2)$$

where x is the calendar year. The EAPC and its 95% confidence interval (CI) were obtained as follows:

$$EAPC_{95\%\ CI} = 100 \times [\exp(\beta) - 1] \quad (3)$$

A statistically significant increasing or decreasing trend in ASR was identified when the 95% CI of the EAPC did not include 0. If the 95% CI included 0, the ASR change was considered non-significant.

All statistical analyses and graphical representations were performed using R version 4.2.2 (http://www.r-project.org).

2.4. Joinpoint regression analysis

The joinpoint regression model avoids the subjective bias of traditional linear trend-based analyses by estimating the pattern of change in disease rates through the least squares method[13]. In this study, we used Joinpoint version 5.3.0 to analyze the trends in incidence rates and DALYs among WCBA in five SDI regions from 1990 to 2021[14]. Trend turning points were identified by solving the sum of squares of the residuals between the estimated and actual values. The fluctuating trends at different stages were analyzed for statistical significance by calculating the average annual percentage change (AAPC) compared with 0[15]. The fluctuation trend was considered statistically significant if the p-value was < 0.05.

Joinpoint regression analyses allowed for the identification of turning points in the disease burden trend and divided the overall trend into several segments, and the formulas for calculating the annual percentage change (APC) and AAPC for each segment [16] were as follows:

$$APC = [\exp(\beta) - 1] \times 100\% \tag{4}$$

$$AAPC = \left[\exp\left(\frac{\sum \omega_i \beta_i}{\sum \omega_i}\right) - 1\right] \times 100\% \tag{5}$$

where ω_i is the width of the interval for each segmented function, and β_i is the regression coefficient corresponding to each interval.

2.5. Health inequality analysis

Socioeconomic health inequalities were quantified using two standard metrics. Slope index of inequality (SII)[17] is an absolute indicator, reflecting the linear relationship between health indicators in the distribution of socioeconomic status. The larger the value of the SII, the more serious the health inequality between countries. The concentration index (COI)[18], a relative indicator, measures the degree to which a health outcome is concentrated across the socioeconomic distribution. The COI ranges from -1 to 1. The value closer to 0 represents that health inequality is less severe, otherwise it means that health inequality is more severe. A positive value indicates that health status is worse in higher-SDI (richer) countries. In contrary, a negative value means that health status is worse in lower-SDI (poorer) countries.

2.6. Bayesian-age-period-cohort model

The age-period-cohort model (APCM) is widely used to explain demographic changes over time. However, due to the inherent covariance among age, period, and cohort effects, parameter estimation is challenging. This study applies the Bayesian age-period-cohort (BAPC) model[19], which incorporates Bayesian inference to estimate posterior distributions using prior knowledge and sample data. To improve efficiency and avoid the convergence issues of traditional Markov Chain Monte Carlo (MCMC) methods, the integrated nested Laplace approximation (INLA) was adopted. Compared to the standard APCM, the BAPC model with INLA offers better adaptability in handling covariance. We divided the age of WCBA into seven age groups for prediction: 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, and 45-49 years. Using the BAPC-INLA package in R (version 4.3.3), this study predicts incidence and DALYs trends for five GI cancers among WCBA globally from 2022 to 2050.

3. Results

3.1. Overall global burden and key trends of GI cancers (1990-2021)

In 2021, the global burden of GI cancers among WCBA was substantial (Table 1). An estimated 183,188 new GI cancer cases were diagnosed worldwide among WCBA (ASR = 40.7/100,000), with total DALYs of 4,634,723 (ASR = 622.7/100,000). From 1990 to 2021, age-standardized DALY rates significantly declined for colon and rectum cancers (21.4 to 20.2/100,000; EAPC = −0.29, 95% CI: −0.33 to −0.25); stomach cancer (16.6 to 8.6/100,000; EAPC = −2.24, 95% CI: −2.31 to −2.18) while significantly increasing for pancreatic cancer (4.7 to 5.0/100,000; EAPC = 0.25, 95% CI: 0.23–0.28); lip and oral cavity cancer (2.6 to 3.3/100,000; EAPC = 0.69, 95% CI: 0.61–0.77). Liver cancer DALYs remained stable (3.5 to 3.6/100,000; EAPC = 0.05, 95% CI: −0.03–0.14).

3.2. Geospatial and socioeconomic disparities in GI cancer burden

In 2021, the global burden of GI cancers demonstrated significant regional heterogeneity across 204 countries and 21 GBD regions (see Figures 1 and 2, respectively). The highest age-standardized DALY rates were concentrated in East Asia (particularly China), South Asia, and Eastern Europe, whereas the lowest burdens were observed in Western Europe, Australasia, and high-income North America. This spatial disparity was pronounced in specific metrics: the high-income Asia-Pacific region recorded the highest GI cancer DALY rate (ASR: 65.1/100,000), while Central Sub-Saharan Africa had the lowest (21.3/100,000). Regarding incidence burden, South Asia (872.6/100,000) and Andean Latin America (867/100,000) ranked highest. This contrasted sharply with lower rates in Central Sub-Saharan Africa (524.8/100,000) and Western Sub-Saharan Africa (518.9/100,000). At the national level, the United Arab Emirates (106.2/100,000) and Mongolia (100.3/100,000) exhibited extreme incidence peaks, while Algeria (12.2/100,000) and the Maldives (13.1/100,000) showed minimal rates.

Analyzing longitudinal trends from 1990 to 2021 reveals distinct patterns linked to the SDI. Low and low-middle SDI regions experienced the most rapid growth in incidence (EAPC=2.28 and 2.49, respectively) with corresponding increases in DALYs. In contrast, middle SDI regions showed moderate incidence increases (EAPC=0.97) but slight DALY reductions (EAPC=-0.33). High-middle and high SDI regions demonstrated the most successful public health outcomes; the former had marginal incidence growth (EAPC=0.35) with significant DALY declines (EAPC=-1.34), while the latter maintained nearly stable incidence (EAPC=0.28) alongside sustained DALY reductions (EAPC=-1.04). Over this period, the burden accelerated most rapidly in specific regions, with North Africa/Middle East (EAPC=3.15) leading in incidence growth, and Central Sub-Saharan Africa (EAPC=2.42) and Oceania (2.40) seeing the sharpest DALY increases. At a national level, Bahrain (EAPC=5.98) and Libya (EAPC=5.71) saw the largest surges in incidence, while Latvia (EAPC=−2.69), Estonia (EAPC=−2.42), and Japan (EAPC=−1.92) achieved significant declines.

Table 1 Global trends in incidence and DALYs of GI cancers in WCBA in 1990 and 2021

Characteristic	Incidence					DALYs				
	Number of cases, 1990	**ASR per 100000 population, 1990**	**Number of cases, 2021**	**ASR per 100000 population, 2021**	**EAPC, 1990–2021**	**Number of cases, 1990**	**ASR per 100000 population, 1990**	**Number of cases, 2021**	**ASR per 100000 population, 2021**	**EAPC, 1990–2021**
Global	4482465.8	933.2	4634723.1	622.7	-0.06	132760	48.8	183188	40.7	0.96
	(3986727.8-5019564.1)	(855.2-1017.4)	(4174428.5-5136249.1)	(561.6-682.0)	(-0.17-0.04)	(120062.7-146562.7)	(44.7-52.4)	(165526.9-203624.1)	(36.0-44.7)	(0.87-1.05)
Cause										
stomach	2049462.3	373.6	1447832.8	165.6	-2.8	53702.9	16.6	43335.8	8.6	-2.24
	(1825832.8-2288280.2)	(340.1-411)	(1301321.2-1605517.4)	(148.1-185)	(-2.89--2.71)	(48307.5-59710.2)	(15.1-18.1)	(38787.7-48813)	(7.5-9.7)	(-2.31--2.18)
liver	525995.5	97.8	647956.1	85.1	-0.52	11385.9	3.5	15911.3	3.6	0.05
	(450723.3-605852.5)	(86.9-110.4)	(582242.9-722083.3)	(77.2-93.7)	(-0.59--0.44)	(9744.3-13129)	(3.1-3.9)	(14229.3-17833.5)	(3.2-4)	(-0.03-0.14)
cavity	265615.3	39.6	506379.2	42.6	0.1	12104.1	2.6	28356.6	3.3	0.69
	(245610.3-290257.3)	(36.5-42.7)	(434422.8-588812.8)	(38.6-46.8)	(0.01-0.19)	(11353.4-12954.9)	(2.4-2.7)	(25154.2-32365.8)	(3-3.5)	(0.61-0.77)
colon	1368663.9	316.5	1615410.1	224.3	-1.25	49209.7	21.4	85224.5	20.2	-0.29
	(1215858-1533020)	(292.9-340.4)	(1475902-1767273.1)	(203.2-242.7)	(-1.3--1.19)	(44835.5-53755.3)	(19.7-22.6)	(77873-93406.8)	(17.9-22)	(-0.33--0.25)
pancreatic	272728.7	105.7	417144.9	105.2	-0.02	6357.4	4.7	10359.9	5	0.25
	(248703.3-302154.1)	(98.8-112.9)	(380539.6-452562.6)	(94.3-113.8)	(-0.05-0)	(5822-7013.2)	(4.3-5)	(9482.8-11205)	(4.4-5.5)	(0.23-0.28)
SDI quintile										
High	749629.3	910.8	547800.8	613.5	-1.04	33272.9	64.1	35773.1	54.8	0.28
	(720329.8-777322.2)	(856.6-946.0)	(524760.6-573194.6)	(556.7-651.1)	(-1.11--0.97)	(32103.9-34339.5)	(59.5-66.7)	(34270.0-37333.6)	(48.5-58.5)	(0.13-0.43)
High-middle	1204714.4	1108.7	873547	695.3	-1.34	35187.1	53.3	41178.1	47.7	0.35
	(1050884.3-	(1010.6-	(748144.0-	(607.7-795.5)	(-1.60--1.07)	(30960.2-39915.2)	(48.9-57.9)	(35035.3-	(41.3-54.4)	(0.15-0.55)

	1381826.2)	1219.4)	1023385.1)					48396.1)		
Middle	1591320.3 (1347107.8-1888831.7)	968.2 (836.5-1121.4)	1511169.4 (1324947.6-1732959.9)	587.9 (509.9-677.8)	-0.33 (-0.43--0.24)	41141.4 (34819.5-48802.3)	40.4 (35.1-46.6)	56868.3 (49230.3-66384.7)	33.8 (28.9-39.5)	0.97 (0.89-1.05)
Low-middle	656994.8 (547196.4-762016.7)	570.5 (483.0-658.0)	1163585.9 (1000342.0-1347817.2)	533.4 (475.7-593.7)	1.86 (1.79-1.94)	16557.5 (13886.6-19217.4)	22.3 (18.9-25.8)	35397.6 (30251.0-41260.0)	23.8 (21.3-26.5)	2.49 (2.44-2.54)
Low	276271.9 (207058.8-344480.6)	682.8 (534.2-848.1)	534964.8 (428973.3-650546.2)	563.7 (472.8-659.4)	1.98 (1.89-2.07)	6494.2 (4884.4-8048.2)	25.7 (20.0-31.9)	13831.4 (11139.0-16838.5)	23.4 (19.8-27.1)	2.28 (2.16-2.40)

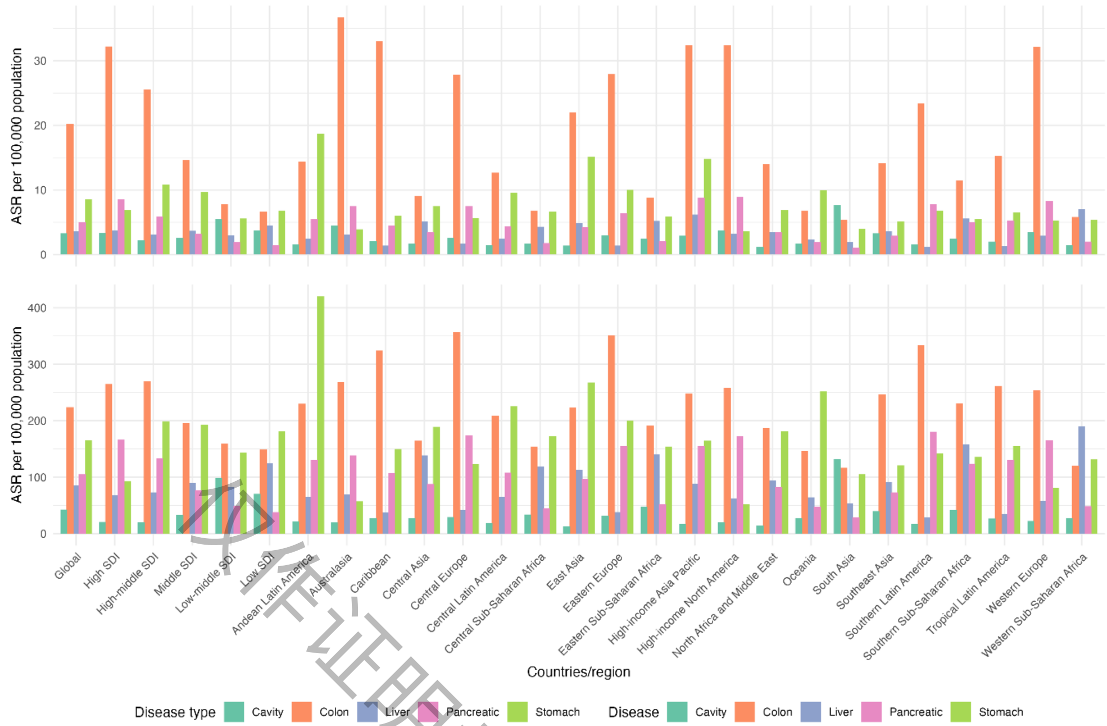

Figure 1 Age-standardized incidence and DALY rates in 2021

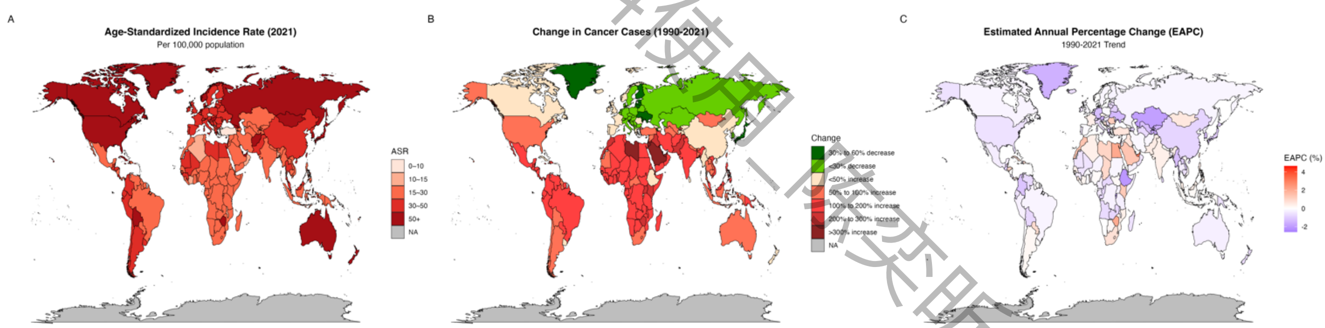

Figure 2 (A)Age-standardized incidence rates of GI in WCBA in 2021;(B) Changes in the number case and (C) EAPC distribution of GI incidence in WCBA 1990-2021; countries worldwide

3.3. Age group differences in burden of disease for five GI cancers

Globally, both the incidence and DALYs of GI cancer in WCBA increased with age, peaking in 45-49 age group (282.3 and 282.3/100,000, respectively). Among all cancer types, colon and rectum cancers accounted for the highest burden, followed by stomach, lip/oral cavity, liver, and pancreatic cancers. Trends specific to cancer type and age group revealed that the burden of stomach cancer declined across all age groups, while the burden of colon and rectum cancer showed an increasing trend among women aged 35–49. Notably, the burdens of lip and oral cavity and pancreatic cancers increased significantly among younger women (especially aged 15–29), while the burden of liver cancer remained stable across all ages.

3.4. Global association and regional differences in GI cancers burden and SDI in WCBA

From 1990 to 2021, the global burden of gastrointestinal cancers in women of childbearing age (WCBA) showed strong SDI-dependent gradients. Higher SDI levels correlated with increased incidence of colon/rectum cancers (peak ASIR=45.2/100,000 at SDI=0.75) and pancreatic cancer (+12.8%), but decreased stomach (-38%) and liver cancer incidence. Concurrently, while overall DALYs declined with rising SDI, cancer-specific burdens diverged: gastric and liver cancers concentrated in low-SDI regions (e.g., West Africa liver cancer DALYs=582.3/100,000), whereas colon and rectum and pancreatic cancers dominated medium-high-SDI regions (e.g., South Asia colon and rectum cancer DALYs=412.7/100,000).

Regionally, low-middle SDI countries exhibited rapid ASIR growth for colon/rectum (EAPC=2.1) and lip/oral cavity cancers (EAPC=1.9). In contrast, high-SDI regions achieved sharp stomach cancer DALY reductions (e.g., East Asia: -44%), yet faced rising pancreatic cancer burdens (e.g., Eastern Europe: 165.3/100,000). Liver cancer control remained stagnant in low-SDI settings.

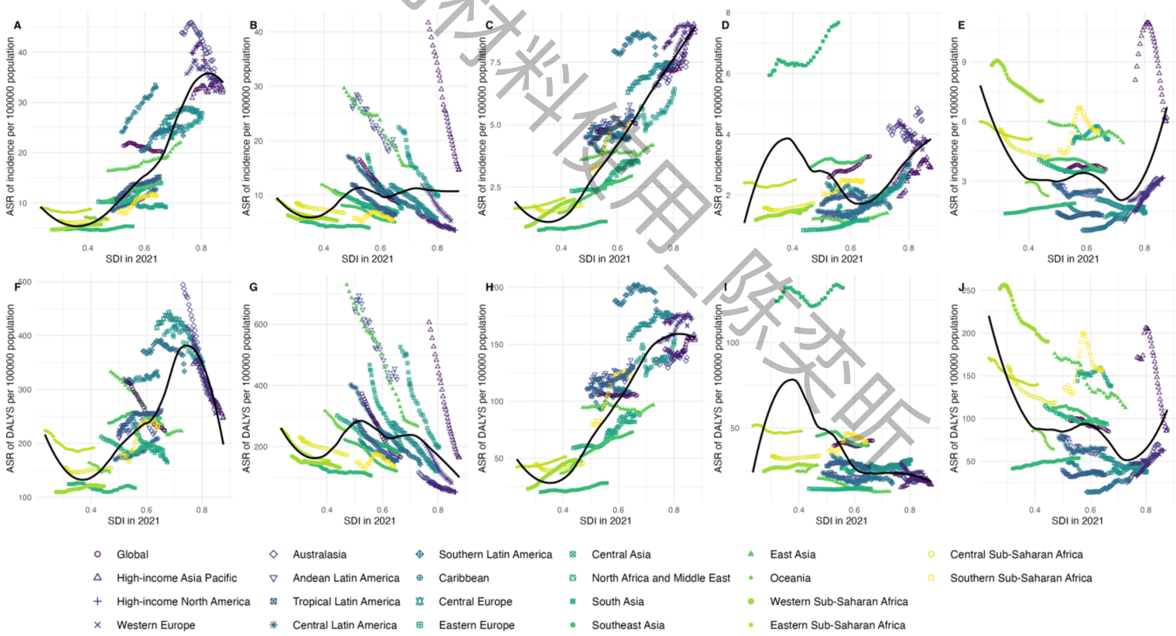

Figure **3** Age-standardized incidence rates and DALYs for each GI cancers by SDI (2021) globally and across 21 GBD regions. Panels display age-standardized incidence rates (A-E) and disability-adjusted life year (DALY) rates (F-J). The cancers shown are: (A, F) colon and rectum cancer, (B, G) stomach cancer, (C, H) pancreatic cancer, (D, I) lip and oral cavity cancer, and (E, J) liver cancer.

3.5. The result of Joinpoint regression model

Between 1990 and 2021, the incidence and DALYs burden of GI cancers for WCBA in the five SDI regions worldwide showed markedly differentiated trends.The overall incidence of cancers of the lips and oral cavity cancer increased, with decreases in the high SDI regions in 1997-2004 and 2016-2021; decreases were also seen in the low SDI regions in 2003-2008. GI cancers continue to decline in all regions. Colon and rectum cancer incidence rates rose in 1990-1995, followed by a gradual but still high decline in high SDI regions, and another rise in low SDI regions since 2011. The high SDI regions of liver cancer experienced the process of rising-declining-raising again, while the low-middle SDI region tended to stabilize or decline slightly. Pancreatic cancer is basically rising slowly in all regions, and only the high SDI region has a downward trend after 2018.

For detailed results, please refer to the appendix Figure 4-23.

3.6. Evolving patterns of health inequality (SII & CI analysis)

Health inequalities in five types of GI cancers exhibited complex trends in both absolute and relative terms, 1990-2021. SII of the gap in incidence for five major GI cancers among WCBA were respectively from 0.21, -0.29, 1.28, -1.99 and 0.79 in 1990 to -0.55, -1.71, 0.36, -2.75 and -0.71 in 2021, showing that the burden of lip and oral cavity cancer, colon and rectum cancer, pancreatic cancer and is shifting from high SDI regions to low SDI regions, with pancreatic cancer showing the most significant shift, becoming a typical example of absolute inequality increasing and relative inequality decreasing. In contrast, stomach cancer and liver cancer has still remained concentrated in low SDI regions, reflecting persistent severe health inequalities.

Meanwhile, CI reveals a more complex pattern of relative inequality, were respectively 0.1, 0.01, -0.12, 0.2 and -0.13 in 1990 and 0.2, 0.01, -0.14, 0.12, and -0.1 in 2021, showing that most cancers, such as lip and oral cavity cancer, stomach cancer, and liver cancer, maintain positive CI values, indicating that their burden remains relatively concentrated in high SDI regions. However, when combined with SII changes, this relative advantage fails to reflect the actual shift in absolute burden. Overall, pancreatic cancer, due to its dual transformation in SII and CI, reflects the redistribution of disease burden within global population structures and warrants particular attention. Figure **4** SII and CI for the incidence of five major GI cancers among WCBA, 1990 and 2021. The figure illustrates health inequality using the Slope Index of Inequality (SII), representing absolute inequality (left panels), and the Concentration Index (CI), representing relative inequality (right panels). The analysis covers the global incidence for the following cancers, in order: lip and oral cavity cancer, stomach cancer, colon and rectum cancer, liver cancer, and pancreatic cancer.

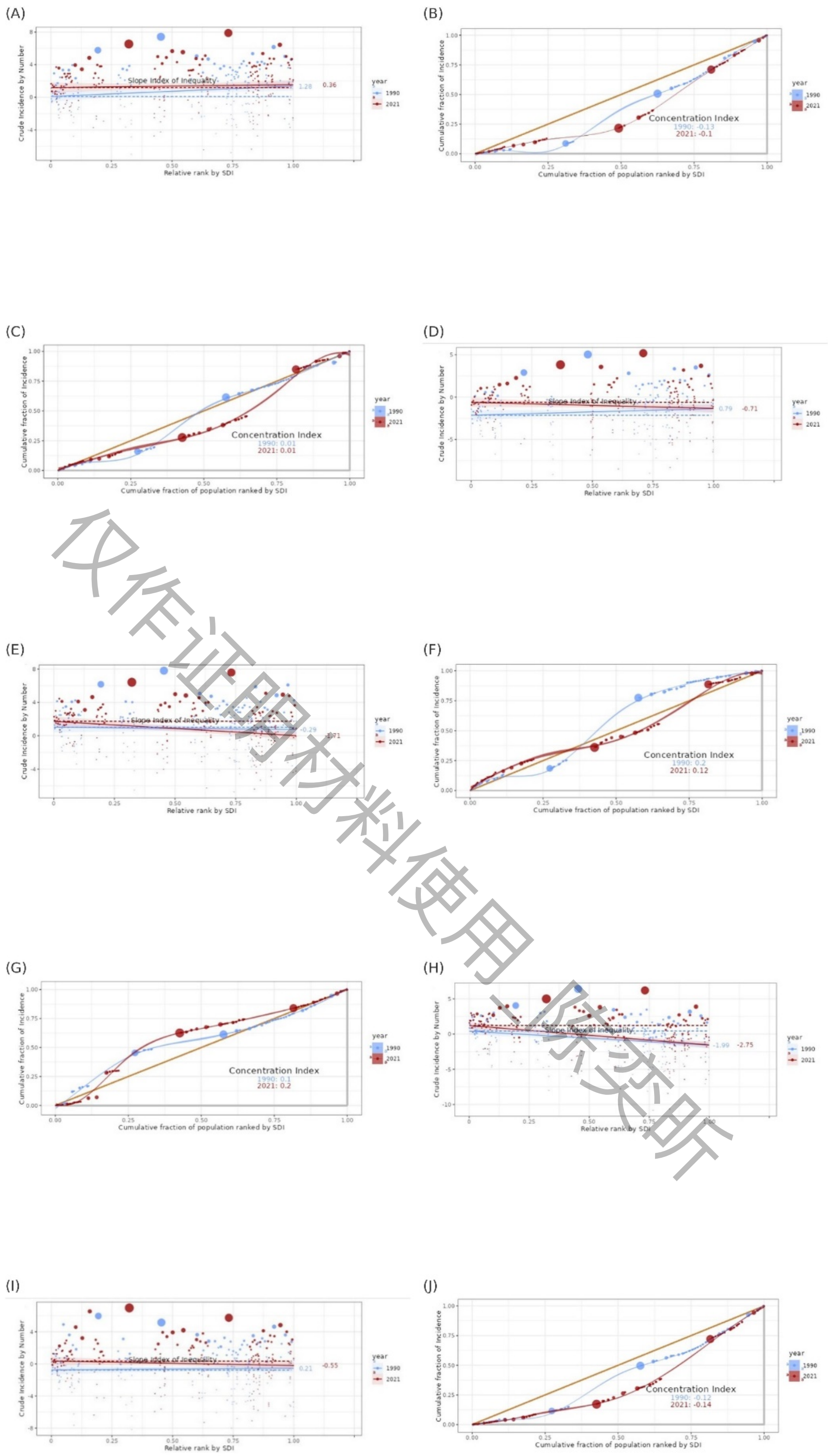

Figure **4** SII and CI for the incidence of five major GI cancers among WCBA, 1990 and 2021. The figure illustrates health inequality using the Slope Index of Inequality (SII), representing absolute inequality (left panels), and the Concentration Index (CI), representing relative inequality (right panels). The analysis covers the global incidence for the following cancers, in order: lip and oral cavity cancer, stomach cancer, colon and rectum cancer, liver cancer, and pancreatic cancer.

3.7. Prediction of Future Disease Burden (BAPC Model)

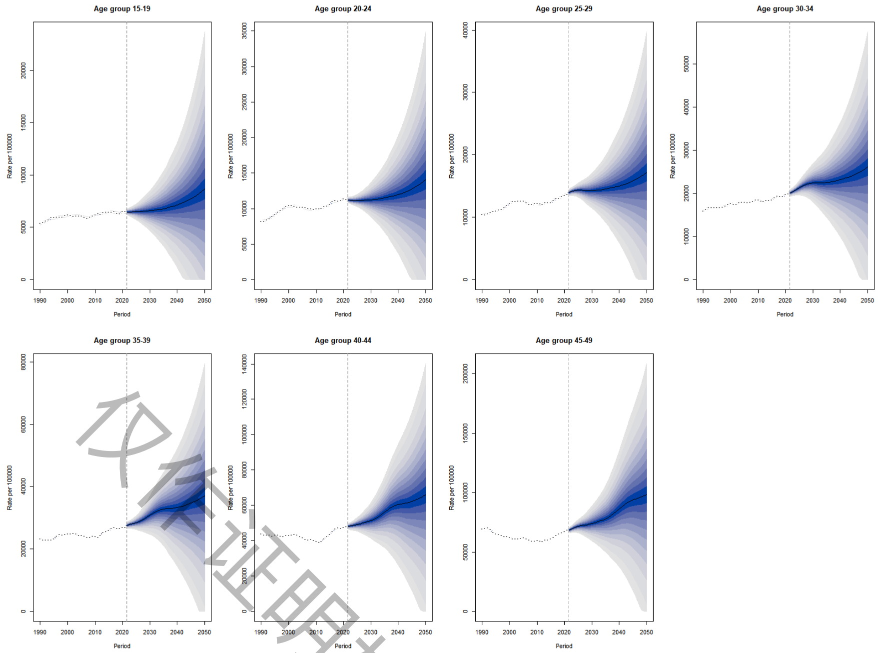

Figure **5** BAPC prediction of age groups' lip and oral cavity cancer DALYs in WCBA globally

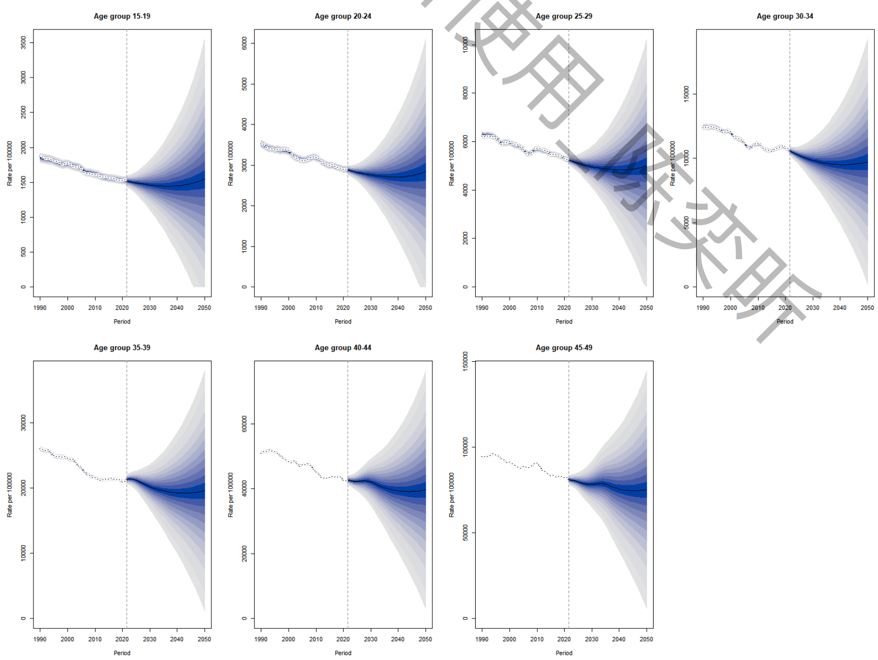

Figure **6** BAPC prediction of age groups' pancreatic cancer DALYs in WCBA globally

According to the BAPC model projections of WCBA, by 2050, lip and oral cavity cancer, liver cancer, and pancreatic cancer will continue to rise globally, while stomach cancer and colon and rectum cancer will show a declining trend. Taking oral cancer as an example, the number of cases in 20 – 24 of oral cancer increased from 33,000 to 44,000, representing a 33% increase; the 45 – 49 age group will rise from approximately 161,000 to 285,000 cases, an increase of 77%. Liver cancer in the 30 – 34 age group will increase from 74,000 to 167,000 cases, a 125% increase; In the 45 – 49 age group, cases increased from 221,000 to 419,000, an increase of nearly 90%. Although pancreatic cancer has a smaller baseline, its growth is significant, with cases in the 45 – 49 age group increasing from 194,000 to 217,000. In contrast, the burden of colon and rectum cancer decreased slightly in several age groups, such as the 25 – 29 age group, which decreased from 85,000 to 67,000; Stomach cancer has generally decreased across all age groups, such as the 45 – 49 age group, which decreased from 474,000 to 384,000, a decrease of approximately 19%.

From a regional perspective, the burden of stomach cancer and colon and rectum cancer has significantly decreased across all age groups in high and high-middle SDI regions; In middle SDI regions, some age groups showed a trend of initial decline followed by an increase or fluctuations; In low and low-middle SDI regions, the burden of lip and oral cancer, liver cancer, and pancreatic cancer continued to increase. Country-level projections also reveal diverse trends. Egypt currently has low but rapidly increasing lip and oral cavity cancer incidence, while Germany has high but stable incidence; Stomach cancer is declining in China but rising in Zimbabwe. Detailed predicted values and trends are presented in the appendix tables and figures.

Discussion

This study provides a systematic analysis of the global GI cancer burden among WCBA over a three-decade period. Our analysis reveals several key findings. First, from 1990 to 2021, the global ASIR declined slightly due to decreases in colon and rectum and stomach cancers, while age-standardized DALYs rose, driven by lip and oral cavity and pancreatic cancers. Second, significant regional disparities persist: high SDI regions bear a greater burden of colon and rectum cancer, while stomach and liver cancer dominate in low-middle SDI regions. Third, as SDI increases, colon and rectum and pancreatic cancer incidence rises, while stomach and liver cancer burden declines. Notably, lip and oral cavity cancer is rising fastest among those aged 15–29. Fourth, a critical observation from 1990–2021 is that absolute inequality in DALYs increased for all five cancers, most acutely for liver cancer. While the burden of colon and rectum and pancreatic cancer shifted from high to low SDI regions, the burden of other cancers remained concentrated in low-SDI areas. Finally, the burden of colon and rectum cancer has decreased in high SDI regions but risen in low SDI regions, a pattern mirrored to varying degrees by other GI cancers, suggesting dynamic regional and national variations that may continue to evolve.

Regarding lip and oral cavity cancer, our results showed that from 1990-2021, the ASIR of WCBA showed an overall increasing trend in all SDI regions. In contrast, the standardized DALYs showed an alternating trend of increasing and then decreasing in all regions except for the high SDI regions which showed a decreasing trend from the outset. Crucially, the incidence rate of lip and oral cavity cancer increased most significantly in the younger age groups, with the low-middle SDI countries experiencing the fastest rise in ASIR. This finding is largely consistent with previous studies[22], which can be attributed to several factors. Firstly, we focus on behavioral factors, including smoking, alcohol consumption, betel quid chewing, oral hygiene habits, and dietary habits, among which betel quid chewing is a specific risk factor for lip and oral cavity cancer, with a high prevalence in South and Southeast Asia, as well as in China's Hunan and Taiwan Provinces. According to relevant studies, betel nut chewing can cause an increase in basal cell division activity of oral mucosal epithelium[23], thus increasing the risk of lip and oral cavity cancer. Secondly, microbiological factors are of concern, among which human papilloma virus (HPV) and human immunodeficiency virus (HIV) promote oral squamous cell carcinoma and Kaposi's sarcoma[24], respectively. Meanwhile, factors such as environmental pollution and occupational exposure are also associated with lip and oral cavity cancer.

Stomach cancer showed overall declines in age-specific incidence and DALYs, indicating improved global prevention, consistent with earlier research[25]. This decline is attributable to factors such as reduced H. pylori infection, better hygiene, low-salt dietary practices, and increased consumption of fruits and vegetables[26]. However, the burden remains high in countries like China, Japan, and Korea, likely due to greater intake of preserved foods. Some countries have implemented early screening programs—Japan and South Korea, for instance, have nationwide screening efforts, while Singapore has set up a stomach cancer consortium to promote early detection[27].

For colon and rectum cancer, we observed regionally variable ASIR trends: a fluctuating pattern of rising, falling, and rising again in high SDI areas, and overall increases elsewhere. DALYs peaked in the high-middle SDI region, particularly in the 45–49 age group, and were lowest in South Asia. While prior research indicates a global rise in incidence, our study found a declining trend among WCBA, implying that gender differences may have been overlooked[28]. Contributing factors include urbanization, sedentary lifestyles, and changes in processed meat and refined carbohydrate intake[29]. Rising obesity among WCBA in middle and high SDI regions is a key concern, as it drives carcinogenesis via insulin resistance and chronic inflammation[30].

Regarding liver cancer, we found that the global standardized incidence rate of liver cancer in WCBA showed a slight decreasing trend from 1990 to 2021, with significant differences in the trend of standardized incidence rate of liver cancer in women in different SDI regions. The DALYs showed a increasing trend followed by a decreasing trend except for those in the high-middle and high SDI regions, where others showed a decreasing trend followed by an increasing trend. DALYs for liver cancer were relatively stable in all age groups, and DALYs for liver cancer were higher in low SDI regions, mainly in regions such as Mongolia and West Africa, which is consistent with previous studies[31]. Hepatitis B and C, as risk factors for liver cancer, are more prevalent in western sub-Saharan Africa and Asia-Pacific, respectively. Aflatoxin likewise contributes to the increased incidence of liver cancer and it is common in Asia, parts of Africa and Latin America.

Finally, with regard to pancreatic cancer, our study showed that the global standardized incidence of pancreatic cancer in WCBA remained essentially stable, but there were large variations in the standardized incidence rates across the five SDI regions. The standardized DALYs showed a more uniform upward trend, except for the high, high-middle and middle SDI regions, which had large variations in ups and downs, with multiple increase-decrease-increase changes. Its incidence was positively correlated with SDI and concentrated in the over 40 age group. This is consistent with previous studies[32]. Pancreatic cancer, as a disease with low incidence and high mortality, requires our focused attention. Its etiology may be related to obesity and diabetes, with high BMI[33] and high fasting glucose[34] as risk factors for pancreatic cancer. It has been shown that the burden of pancreatic cancer associated with high BMI is higher in women than in men and tends to increase with age, whereas a high-energy diet leads to increased body weight and thus higher risk of the disease, while a high-sugar diet leads to increased fasting blood glucose, which in turn increases the risk of pancreatic cancer development.

All GI cancers share common risk factors such as smoking, alcohol use, diet, and psychological stress, along with non-modifiable genetic risks. These shared risks underscore the need for comprehensive prevention strategies that begin early, including healthy lifestyle adoption, risk factor avoidance, and vaccination. For high-risk groups, particularly middle-aged and older women, a focus on early screening and treatment is critical. Post-diagnosis, standardized treatment, adherence to care, and emotional support are vital to improving survival and quality of life.

From a policy perspective, countries should adopt tailored strategies based on their specific cancer burden trends. High SDI regions must emphasize lifestyle interventions for colon and pancreatic cancers; middle SDI regions should adapt policies to local conditions; and low SDI regions need investment in medical infrastructure, public health, and women’s healthcare systems.

It is crucial to interpret these trends in the context of healthcare capacity. The rise in colon and rectum cancer in high SDI areas is associated with universal access to screening (e.g., colonoscopy), which pushes up incidence by detecting early cases, whereas the growth in pancreatic cancer burden in low SDI areas lacks the corresponding diagnostic capacity, leading to late diagnosis and high mortality. These patterns call for targeted prevention strategies: lifestyle interventions (e.g., obesity control) need to be strengthened in high SDI areas, and vaccination (hepatitis B), dietary interventions (salt reduction), and low-cost screening (e.g.,faecal immunochemical testing for colon and rectum cancer) should be expanded in low SDI areas.

Our age-specific analysis reveals a critical demographic shift in the disease burden. For women aged 15-34 years, the burden of disease for most cancers has shown a downward trend, which may be attributed to the fact that modern society continues to pay attention to women's health education, vaccinations, and lifestyle improvements. Conversely, for women over 35 years of age, the burden of disease is rising rapidly, especially for colon and rectum, lip and oral cavity and pancreatic cancers. This highlights that the primary burden of GI cancers is shifting toward middle-aged women, underscoring age as a significant, non-modifiable risk factor.

This study analyses GI cancers in WCBA, which can provide some guidance for future prevention efforts among this population. It utilizes data from the GBD database, which is reliable, has a large sample size, and is statistically significant, thereby enhancing the reliability of the study's conclusions. However, this study only analyzes and predicts certain types of GI cancers, and a more comprehensive analysis of GI cancers could be conducted. Additionally, this study only considers the impact of regional, socioeconomic factors, and age on GI cancers, and further inclusion of risk factors could be explored to comprehensively investigate the causes of the disease.

Conclusions

This study reveals a critical and complex epidemiological transition of GI cancers among WCBA over the past three decades, characterized by starkly divergent trends. While the burdens of stomach and colorectal cancer are declining, particularly in high-SDI nations, the incidence of lip and oral cavity and pancreatic cancers is increasing globally. Crucially, the burden of pancreatic, lip and oral cavity, and colorectal cancers is progressively shifting towards low- and middle-SDI regions, while the high burdens of stomach and liver cancer remain entrenched in these same areas, creating a dual challenge of both emerging and persistent inequalities. This transition is further complicated by age-specific patterns, with an alarming rise in lip and oral cavity and pancreatic cancers among younger women, signaling future public health challenges. These multifaceted trends underscore the urgent need to move beyond one-size-fits-all public health policies. Therefore, it is essential to develop and implement tailored, region-specific, and age-appropriate strategies that not only address the persistent burden of stomach and liver cancer in low-SDI settings but also proactively build infrastructure for the prevention, early detection, and treatment of the rising threat from pancreatic and oral cancers to mitigate the future burden in this vulnerable population.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

This work was supported by the National Natural Science Foundation of China [grant number 82173619], the Guangdong Basic and Applied Basic Research Foundation [grant number 2023A1515011242], and Hainan Province Science and Technology Special Fund [grant number ZDYF2025SHFZ046].

CRediT authorship contribution statement

Jia-Hui Hu: Formal analysis, Software, Writing – original draft, Methodology. **???**: Resources, Investigation, Project administration, Methodology. **???**: Methodology, Validation, Software. **???**: Writing – review and editing, Validation. **???**: Data curation, Visualization. **Yuan-Sheng Li**: Conceptualization, Resources, Supervision, Project administration. **Ji-Yuan Zhou**: Writing – review and editing, Funding acquisition, Supervision, Data curation, Validation, Project administration.

Data availability

The National Health and Nutrition Examination Survey (NHANES) data are publicly available at **https://www.cdc.gov/nchs/nhanes/about/index.html**.

Acknowledgements

We appreciate the contribution of all the staffs and participants in the United States National Health and Nutrition Examination Survey (NHANES).

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