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Impact of high body mass index on gallbladder and biliary tract cancer burden in China: a comprehensive analysis of trends from 1990 to 2021

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Abstract

Background Gallbladder and biliary tract cancer (GBTC) is a significant health burden in China, exacerbated by the rising prevalence of high body mass index (BMI). Understanding the trends and factors contributing to mortality and disability associated with GBTC is crucial for targeted public health interventions.

Methods We utilized data from the Global Burden of Disease (GBD) Study to assess the burden of GBTC attributable to high BMI in China from 1990 to 2021. Age-standardized rates of deaths, disability-adjusted life years (DALYs), years lived with disability (YLDs), and years of life lost (YLLs) were analyzed. Joinpoint regression and decomposition analyses were conducted to evaluate trends and identify contributing factors, including aging, population growth, and epidemiological changes. Gender-specific differences were also assessed.

Results In 2021, GBTC deaths attributable to high BMI in China reached 4,053, with males experiencing a higher overall burden than females, particularly in older age groups. While females showed a higher mortality and overall burden in the 60 to 79 age range, this trend reversed in older age brackets, with males experiencing steeper increases in mortality and disability-related indicators beyond age 80. The age-standardized DALYs rate mirrored this pattern, with higher rates in males in advanced age groups. From 1990 to 2021, China saw a steady increase in GBTC burden attributable to high BMI, contrasting with a global decline. Joinpoint analysis indicated marked rises in mortality and DALYs rates after 2005, especially in males. Decomposition analysis identified population growth and aging as major drivers of increased deaths, while epidemiological changes primarily contributed to rising DALYs, with a stronger impact observed in males.

Conclusions The burden of GBTC attributable to high BMI in China has increased substantially over the last three decades, driven by population growth, aging, and epidemiological shifts. The trends highlight a growing gender disparity, with males experiencing a greater rise in mortality and disability. Public health strategies targeting obesity and metabolic risk factors are critical to mitigating the increasing GBTC burden.

Keywords Gallbladder and biliary tract cancer, High body mass index, China, Global Burden of Disease, Epidemiological change

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Introduction

Gallbladder and biliary tract cancer (GBTC) is a relatively rare but highly fatal malignancy, accounting for a significant portion of gastrointestinal cancer deaths worldwide [1, 2]. In recent decades, an increasing number of studies have linked the rising prevalence of obesity and metabolic disorders, including high body mass index (BMI), to various cancers, including GBTC [3–5]. High BMI, now considered a major global health challenge, is strongly associated with chronic inflammation, insulin resistance, and altered hormone regulation, all of which contribute to cancer development [6–8]. Recent epidemiological studies have demonstrated a significant increase in cancers attributable to high BMI globally, with cancer-related deaths and disability-adjusted life-years rising by 35% and 34%, respectively, between 2010 and 2019 [9]. High BMI is a major risk factor for cancer, accounting for 5.1% of the attributable disability-adjusted life years (DALYs), as reported in the research on the burden of cancers and their attributable risk factors among Iranian adults aged 70 and above from 1990 to 2019 [10]. Additionally, early-onset biliary tract cancer (EOBTC) has emerged as a significant concern, accounting for nearly 7% of all BTC cases worldwide. Notably, the age-standardized rate (ASR) of EOBTC-related deaths and disability linked to high body mass index has increased in most regions [11]. As the rates of obesity continue to rise, particularly in developing countries like China, understanding the role of high BMI in GBTC incidence and mortality is essential for shaping public health policies and preventive strategies [12, 13].

China has witnessed a rapid epidemiological transition, with increasing rates of obesity and related non-communicable diseases over the last three decades [14]. This trend parallels a growing burden of obesity-associated cancers, including GBTC. Several studies have demonstrated that GBTC incidence is rising in China, a trend attributed largely to increasing BMI levels and metabolic risk factors [15, 16]. Unlike global trends, where GBTC mortality has remained relatively stable or even declined, China has seen a sharp rise in both incidence and mortality attributable to high BMI [17]. This pattern is particularly concerning in the context of China's aging population, where older adults with high BMI are at greater risk for developing GBTC [18]. Population aging, which is accelerating worldwide, particularly in countries like China, adds another layer of complexity to cancer burden trends. The growing proportion of older adults in the population, as highlighted in recent research [19], poses additional challenges for managing non-communicable diseases such as GBTC, as older individuals face a heightened risk due to age-related physiological changes and increased exposure to risk factors such as obesity [19].

Despite advances in diagnostic and therapeutic technologies, the prognosis for GBTC remains poor, with survival rates typically lower than other gastrointestinal cancers [20, 21]. The pathophysiological mechanisms linking high BMI to GBTC are complex, involving metabolic dysregulation, increased adiposity, and chronic inflammation, which promote carcinogenesis [22]. Furthermore, the geographic variation in GBTC incidence, particularly the higher rates in East Asia, underscores the need for region-specific epidemiological studies to better understand the interplay between genetic, environmental, and lifestyle factors [23]. This study aims to assess the trends in mortality and disease burden of GBTC attributable to high BMI in China, providing insights into potential public health interventions to address this growing challenge.

Methods

Study design and data sources

This study utilized data from the Global Burden of Disease (GBD) 2021 Study to assess the burden of GBTC attributable to high BMI in China from 1990 to 2021. The GBD study leverages diverse data sources, including vital statistics, national health surveys, disease registries, and other relevant health-related datasets. These sources provide robust estimates of disease burden using standardized methodologies across regions and time periods [24]. The GBD study applies the Cause of Death Ensemble modeling (CODEm) approach, a statistical framework used to estimate disease burden when data quality or availability is inconsistent [25]. Specifically, the GBD database includes metrics such as deaths, DALYs, years of life lost (YLLs), and years lived with disability (YLDs), which were extracted for GBTC and high BMI using the Global Health Data Exchange (GHDx) tool (http://ghdx.healthdata.org/gbd-results-tool). The analysis included ASRs and age-specific data for both genders across multiple age groups, ensuring comprehensive coverage for trend analysis. These data were modeled to assess temporal changes and their contributing factors.

Definitions

In the GBD study, GBTC are identified using the International Classification of Diseases 10th revision (ICD-10) codes C23 for gallbladder cancer and C24-C24.9 for biliary tract cancers. The burden of these cancers is analyzed in relation to high BMI, a known risk factor. For adults aged 20 and older, high BMI is defined as a BMI greater than 20-23kg/m^2, depending on country-specific thresholds. For children aged 2–19, high BMI is classified as being overweight or obese, according to the standards set by the International Obesity Task Force [26]. These definitions are crucial for standardized global

comparisons, particularly when analyzing risk factor-related cancer burdens over time.

Modeling techniques and assumptions

The GBD study uses DisMod-MR 2.1, a Bayesian meta-regression tool, to estimate disease incidence, prevalence, and duration in the absence of complete data [24]. The DisMod-MR 2.1 model is employed to pool data from different sources, using covariates such as sex, age, and healthcare access and quality indices. To estimate mortality-to-incidence ratios (MIRs), cancer registries were matched by sex, age, year, and region, and then modeled using cause-specific logistic regressions. These MIRs were subsequently pooled with cancer-specific mortality data to generate estimates of incidence and prevalence, along with 95% uncertainty intervals (UIs) [25]. The mortality-to-incidence ratio is a crucial parameter, reflecting both diagnosis accuracy and cancer progression.

To ensure the robustness of the models, the GBD study applies the Spatiotemporal Gaussian Process Regression (ST-GPR) framework to smooth out noise and estimate burden trends over time and space [24]. The GBD methodology assumes uniformity in disability weights across all regions, and cancer-related disability is modeled using the Global Health Estimates from the World Health Organization (WHO). This modeling strategy allowed for the decomposition of GBTC burden into four phases: diagnosis and primary therapy, controlled, metastatic, and terminal stages. Each phase was assigned specific disability weights, enabling a comprehensive assessment of YLDs and DALYs.

Joinpoint regression analysis

Joinpoint regression was applied to identify significant changes in trends over time. The joinpoint model estimates inflection points where trends change direction or magnitude, allowing for the calculation of annual percent change (APC) and average annual percent change (AAPC). Joinpoint regression models were fitted using Joinpoint software (version 5.2.0; National Cancer Institute, USA), and the statistical significance of each joinpoint was tested at a 95% confidence interval [27, 28]. The model fits an initial linear trend, followed by permutations of the data to detect potential inflection points, after which the AAPC is computed as a weighted average of the APCs from each segment.

Age-Period-Cohort (APC) analysis

An APC analysis was conducted to explore the effects of age, period, and birth cohort on the burden of GBTC attributable to high BMI. The APC analysis helps to disentangle the complex interplay between these factors by isolating the independent effects of each. The method was implemented using an APC model, which adjusts for the confounding effects of age, period, and cohort to assess trends more accurately. The age effect reflects the biological changes related to aging, the period effect captures temporal changes due to interventions or exposures, and the cohort effect reflects the impact of different risk exposures at different life stages [29]. APC analysis was conducted using R software, with the results providing insight into the distinct impacts of aging, birth cohorts, and period-specific factors on GBTC burden [30].

Decomposition analysis

Decomposition analysis was performed to identify the contributions of aging, population growth, and epidemiological changes to the trends observed in deaths and DALYs. The analysis decomposed the total change in these indicators into the effects of each factor using standard demographic techniques. Population aging was calculated by examining changes in the age structure, while epidemiological change was defined as shifts in the rates of GBTC attributable to high BMI independent of population dynamics. Population growth was determined by changes in the overall size of the population. This approach allows for the disentanglement of demographic and epidemiological contributions to the rising burden of GBTC in China.

Ethical considerations

This study utilized publicly available data from the GBD Study, and thus did not require ethical approval. All methods were carried out in accordance with relevant guidelines and regulations.

Results

Burden of GBTC attributable to high BMI in China in 2021

The 2021 data on the burden of GBTC attributable to high BMI in China demonstrate notable age- and sex-specific patterns across deaths, DALYs, YLDs, and YLLs. In younger age groups, females generally show lower values for these indicators. However, from the age group of 60–69 and beyond, females exhibit higher counts than males across deaths, DALYs, YLDs, and YLLs (Table 1, Fig. 1). In terms of overall deaths due to GBTC attributable to high BMI, females surpass males in older age groups, reversing the pattern seen in earlier ages. This age-related shift becomes evident at 60 years and continues in older age groups, where female values remain higher. For DALYs, a similar trend is observed, with lower values in younger females but a clear reversal beginning at 60–64 years, where females consistently display higher burdens. YLDs and YLLs also follow this age and sex-specific trend. In younger

Table 1 All-age cases and age-standardized deaths, DALYs, YLDs, and YLLs rates in 2021 for GBTC attributable to high BMI in China

Measure	All-ages cases			Age-standardized rates per 100,000 people		
	Total	Male	Female	Total	Male	Female
Deaths	4053 (2279, 6034)	1896 (1005, 3058)	2158 (1202, 3372)	0.2 (0.11, 0.29)	0.2 (0.11, 0.31)	0.19 (0.11, 0.3)
DALYs	95576 (53908, 142812)	46,733 (24,213, 76628)	48,843 (26,995, 75912)	4.45 (2.51, 6.66)	4.57 (2.39, 7.4)	4.36 (2.41, 6.78)
YLDs	1461 (824, 2384)	731 (375, 1262)	730 (375, 1255)	0.07 (0.04, 0.11)	0.07 (0.04, 0.12)	0.07 (0.03, 0.11)
YLLs	94,115 (53,089, 140713)	46,002 (23,868, 75306)	48,113 (26,575, 74645)	4.38 (2.48, 6.57)	4.5 (2.35, 7.27)	4.29 (2.37, 6.66)

DALYs Disability-adjusted life-years, *YLDs* Years lived with disability, *YLLs* Years of life lost, *GBTC* Gallbladder and biliary tract cancer, *BMI* Body mass index

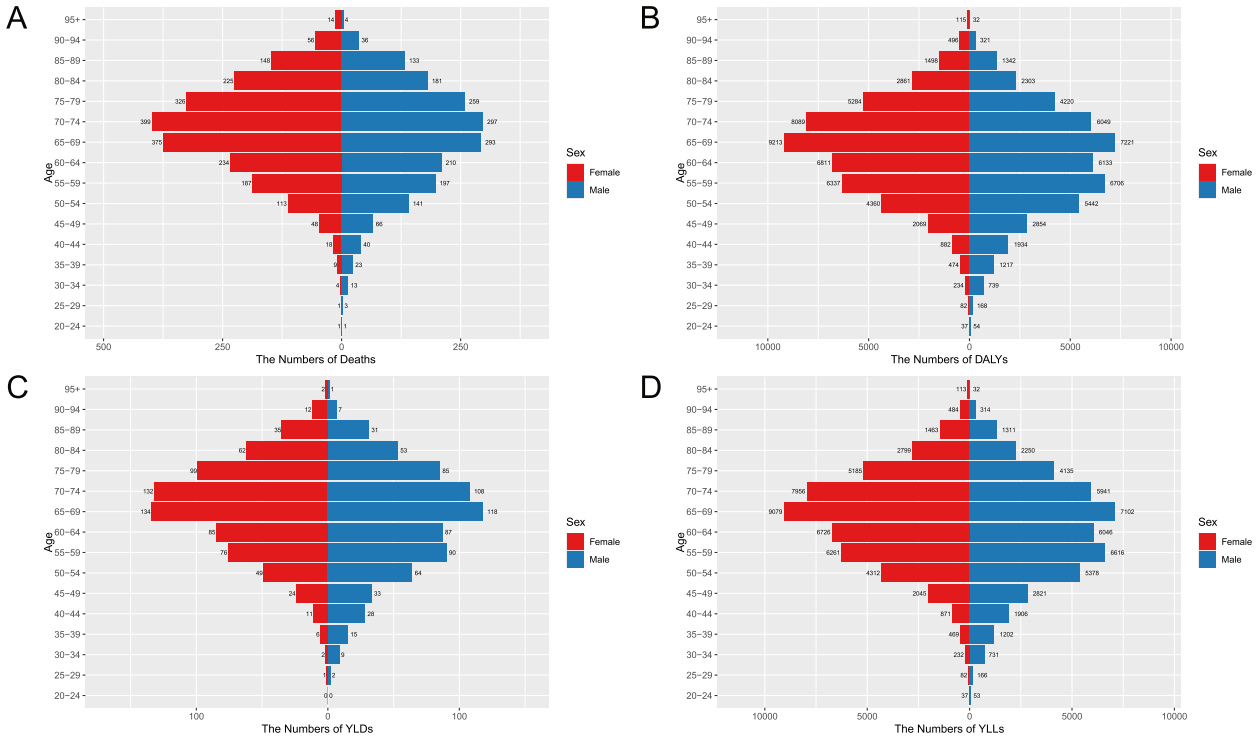

Fig. 1 Distribution of deaths, DALYs, YLDs, and YLLs attributable to high BMI in GBTC in China in 2021 by age and sex. **A** The number of deaths. **B** The number of DALYs. **C** The number of YLDs. **D** The number of YLLs. DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost; BMI, body mass index; GBTC, gallbladder and biliary tract cancer

age brackets, males and females show relatively similar YLD values, yet as age increases, particularly from 65 years onward, female YLLs dominate, reflecting a higher burden among older females. This change highlights the transition point at which female GBTC burden surpasses that of males, especially in mortality-related outcomes like YLLs, underlining the substantial impact of high BMI on GBTC among older female populations (Table 1, Fig. 1). In 2021 in China, colon and rectum cancer had the largest proportion among high BMI-related gastrointestinal cancers, followed by liver cancer and GBTC, with pancreatic cancer having the smallest proportion (Supplementary Fig. 1).

Age and sex differences in disease rates

The age-specific rates illustrated in Fig. 2 reveal pronounced sex and age-related differences across mortality, DALYs, YLDs, and YLLs for GBTC attributable to high BMI. Among individuals under 60, males and females generally exhibit comparable mortality rates. However, in populations over 60, mortality rates become notably higher in females than in males, particularly between

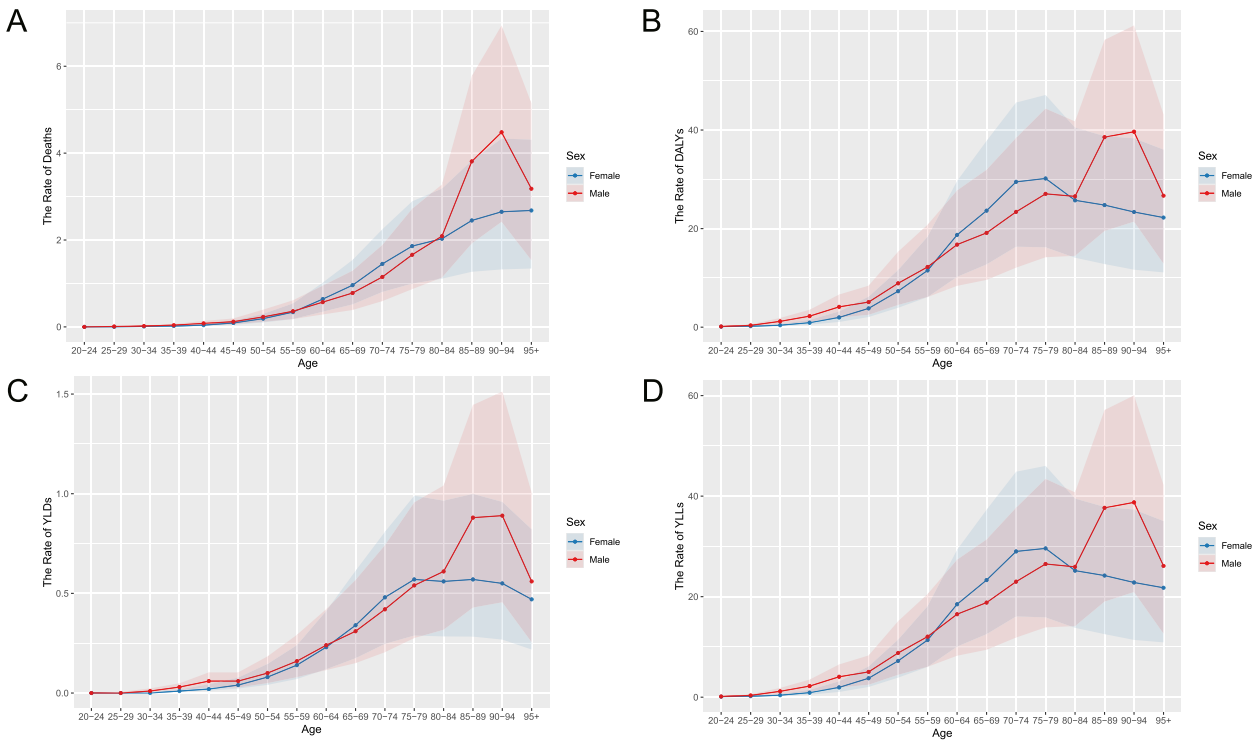

Fig. 2 Age-specific rates of deaths, DALYs, YLDs, and YLLs attributable to high BMI in GBTC in China in 2021, by sex. **A** The rate of deaths by age and sex. **B** The rate of DALYs. **C** The rate of YLDs. **D** The rate of YLLs. DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost; BMI, body mass index; GBTC, gallbladder and biliary tract cancer

ages 60 and 64, indicating a shift in the burden at this age group. As age advances, especially in the 80–84 age range, mortality rates among males experience a sharp increase, ultimately surpassing those of females in the oldest age groups. For DALYs, YLDs, and YLLs, the trends follow similar age-related patterns. There is minimal variation between sexes in the younger age groups, s, with males showing slightly higher values than females. At the 60–64 age bracket, females experience higher rates than males, marking a transition point. However, in the 80–84 age range, males again exhibit a marked rise, particularly for YLLs, which indicates an elevated burden of life lost due to GBTC in aging males. This age-specific increase underscores the growing impact of high BMI on GBTC-related mortality and disability in older males, while females experience a higher burden in earlier older age groups.

Trends in burden attributable to high BMI in GBTC from 1990 to 2021

Figure 3 shows a consistent year-on-year increase in the number of deaths, DALYs, YLDs, and YLLs attributable to high BMI in GBTC for both males and females from 1990 to 2021. While the overall number of cases for these indicators increased for both sexes, females tended to have higher numbers than males throughout much of the time period. However, when looking at the rates, females had higher ASRs for all four indicators during the earlier years of the analysis, particularly before 2006–2007. After this period, a turnaround occurred, with males showing higher ASRs for deaths, DALYs, YLDs, and YLLs compared to females. This shift highlights a growing burden on males in more recent years, while females had a more prominent burden in the earlier period (Fig. 3).

Comparison of GBTC burden attributable to high BMI between 1990 and 2021 by age group

Figure 4 demonstrates the increased burden of GBTC attributable to high BMI across different age groups in China from 1990 to 2021. The growth in crude rates of deaths, DALYs, YLDs, and YLLs is particularly evident beginning in the 60–64 age range, with the most substantial increases concentrated in the elderly population. In both deaths (Fig. 4A) and DALYs (Fig. 4B), the crude rates show accelerated growth starting at this age group, with older populations experiencing the highest rise. Although YLDs (Fig. 4C) are comparatively smaller in magnitude, they display a steady increase across age groups, reflecting a consistent rise in the burden of non-fatal health outcomes associated with high BMI. The YLLs (Fig. 4D) show the steepest increase among older

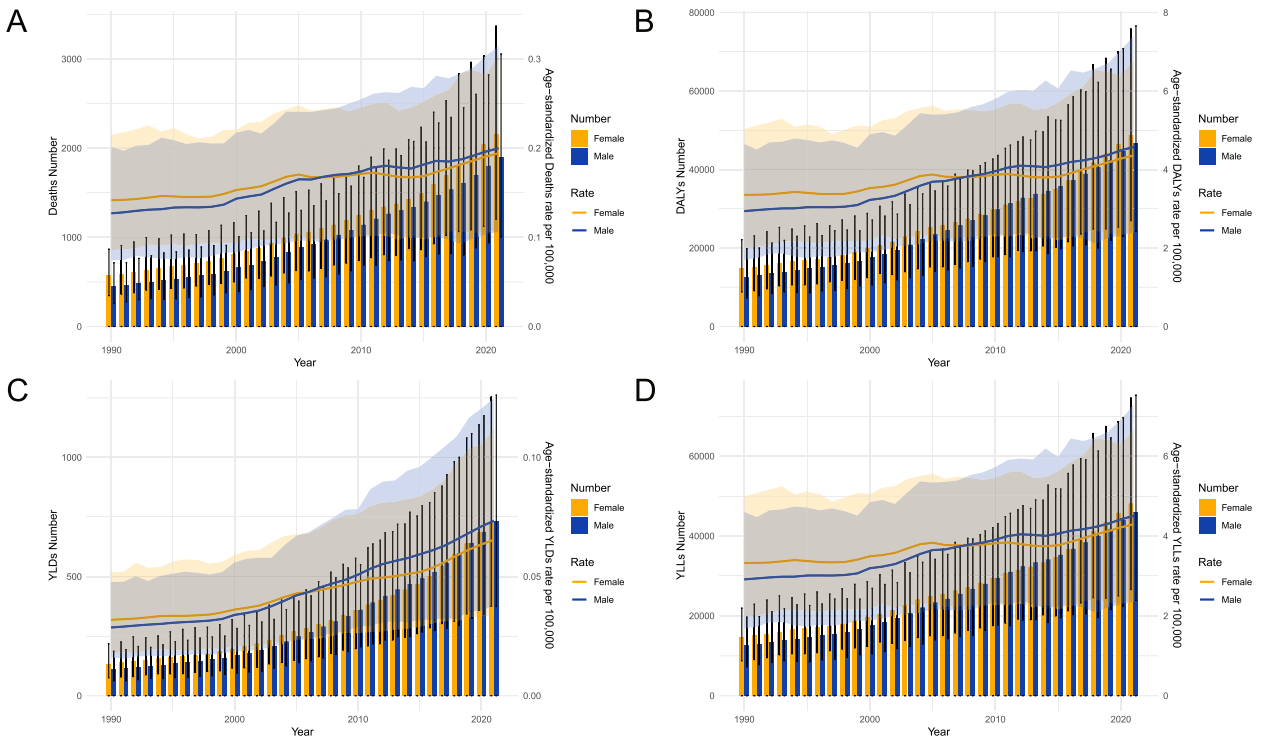

Fig. 3 Trends in the number and age-standardized rates of deaths, DALYs, YLDs, and YLLs attributable to high BMI in GBTC in China, 1990–2021, by sex. **A** The number of deaths and age-standardized death rates. **B** The number of DALYs and age-standardized DALY rates. **C** The number of YLLs and age-standardized YLL rates. **D** The number of YLDs and age-standardized YLD rates. DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost; BMI, body mass index; GBTC, gallbladder and biliary tract cancer

individuals, further emphasizing the growing impact of high BMI on premature mortality in the aging population. This age-specific trend highlights a notable shift in the disease burden, with older age groups disproportionately affected by the increased rates observed in 2021 compared to 1990.

Comparison of global, Asia and Chinese trends and burden in ASRs for GBTC attributable to high BMI between 1990 and 2021

In China, all indicators show marked increases over this period. The ASRs for deaths and DALYs both rise considerably, with deaths increasing from 0.13 to 0.2 per 100,000, and DALYs from 3.14 to 4.45 per 100,000. YLLs similarly display a rising trend, moving from 3.11 to 4.38 per 100,000. YLDs, although lower in magnitude, also exhibit a notable increase from 0.03 to 0.07 per 100,000, reflecting an upward trend in non-fatal disease burden. In contrast, global trends show a decline in ASRs for deaths, DALYs, and YLLs related to high BMI in GBTC over the same period. Death rates decrease from 0.26 to 0.24 per 100,000, and DALYs show a decline from 5.74 to 5.2 per 100,000. YLLs follow this downward trajectory globally, moving from 5.67 to 5.12 per 100,000. YLDs display a slight increase worldwide, rising from 0.07 to 0.08 per 100,000, but the growth remains modest compared to the increase observed in China. These contrasting trends underscore the ongoing rise in GBTC burden related to high BMI in China, while global rates have generally trended downward or stabilized over the past three decades (Fig. 5, Table 2). In 2021, China's high BMI-related GBTC accounted for approximately 21% of the global burden across key indicators, including deaths, DALYs, YLDs, and YLLs, as shown in Supplementary Fig. 2. Supplementary Fig. 3 illustrates that the age-standardized death rates for high BMI-related GBTC were highest in the Kingdom of Thailand, followed by the Republic of Korea and Mongolia, with China's rates falling around the median level among Asian countries. Similarly, Supplementary Fig. 4 shows that the age-standardized DALYs rates for high BMI-related GBTC were also highest in Thailand, with significant contributions from the Republic of Korea and Mongolia, while China again ranked near the middle compared to other countries in the region.

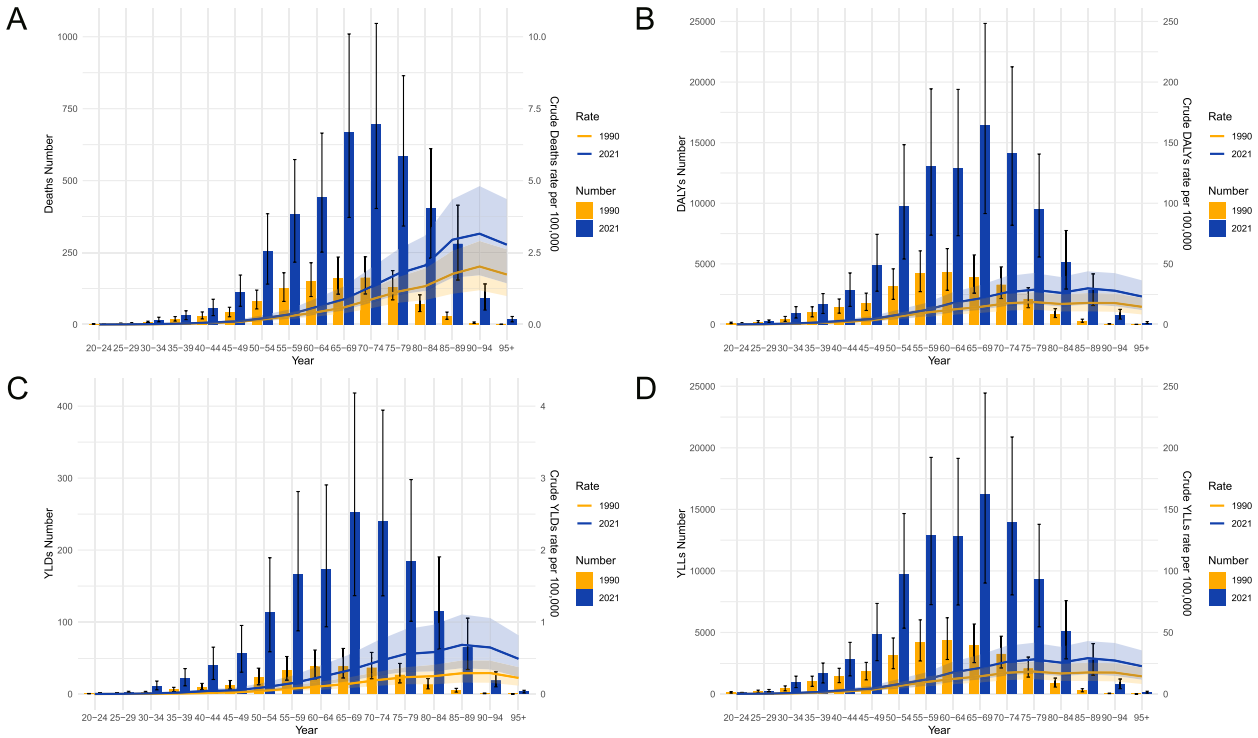

Fig. 4 Comparison of the number and crude rates of deaths, DALYs, YLDs, and YLLs attributable to high BMI in GBTC in China by age group for 1990 and 2021. **A** The number of deaths and crude death rates. **B** The number of DALYs and crude DALY rates. **C** The number of YLDs and crude YLD rates. **D** The number of YLLs and crude YLL rates. DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost; BMI, body mass index; GBTC, gallbladder and biliary tract cancer

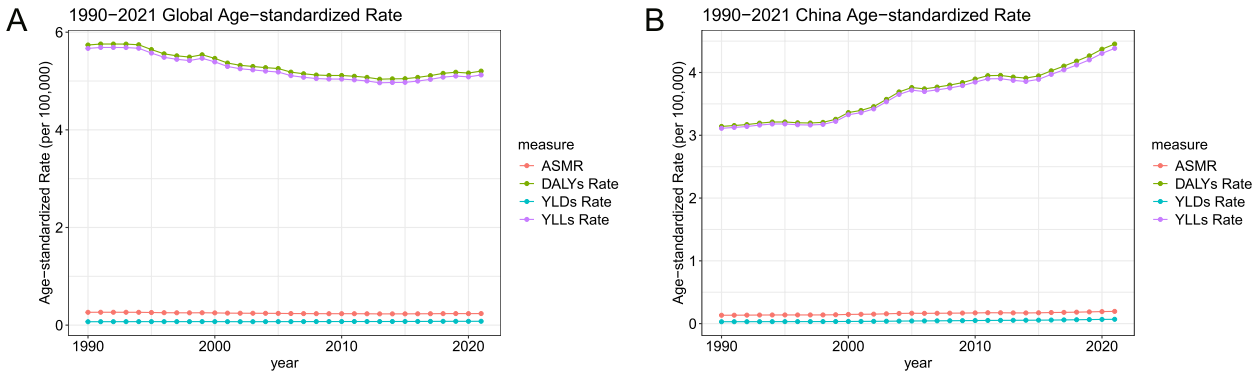

Fig. 5 Global and China trends in age-standardized rates of deaths, DALYs, YLDs, and YLLs attributable to high BMI in GBTC from 1990 to 2021. **A** The global trend of age-standardized rates. **B** The age-standardized trends for China. DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost; BMI, body mass index; GBTC, gallbladder and biliary tract cancer

Trends in ASRs for GBTC attributable to high BMI in China, 1990–2021

Figure 6 and Table 3 illustrate the trends in ASRs for deaths, DALYs, YLDs, and YLLs attributable to high BMI in GBTC in China, with a breakdown by gender and time periods. Overall, males experienced a more substantial increase across most indicators compared to females. The joinpoint analysis identifies critical periods of change, with significant accelerations in mortality and DALY rates, particularly among males following 2005. From 2015 onward, however, females exhibited a more pronounced increase in mortality rates compared to males, marking a shift in the gender-specific burden of GBTC. Table 3 further emphasizes these differences, showing

Table 2 Change of age-standardized rates in deaths, DALYs, YLDs, and YLLs for GBTC attributable to high BMI between 1990 and 2021 in China and Global level

Measure	China			Global		
	1990	2021	Change	1990	2021	Change
Deaths	0.13 (0.09, 0.19)	0.2 (0.11, 0.29)	1.22 (0.89—1.54)*	0.26 (0.18, 0.36)	0.24 (0.16, 0.33)	-0.33 (-0.45—-0.21)*
DALYs	3.14 (2.08, 4.44)	4.45 (2.51, 6.66)	1.12 (0.97—1.27)*	5.74 (3.95, 7.83)	5.2 (3.56, 7.17)	-0.31 (-0.44—-0.19)*
YLDs	0.03 (0.02, 0.05)	0.07 (0.04, 0.11)	2.71 (2.52—2.91)*	0.07 (0.04, 0.1)	0.08 (0.05, 0.12)	0.40 (0.27—0.54)*
YLLs	3.11 (2.06, 4.4)	4.38 (2.48, 6.57)	1.10 (0.95—1.26)*	5.67 (3.9, 7.73)	5.12 (3.5, 7.05)	-0.32 (-0.45—-0.20)*

DALYs Disability-adjusted life-years, *YLDs* Years lived with disability, *YLLs* Years of life lost, *GBTC* Gallbladder and biliary tract cancer, *BMI* Body mass index

**P < 0.05*

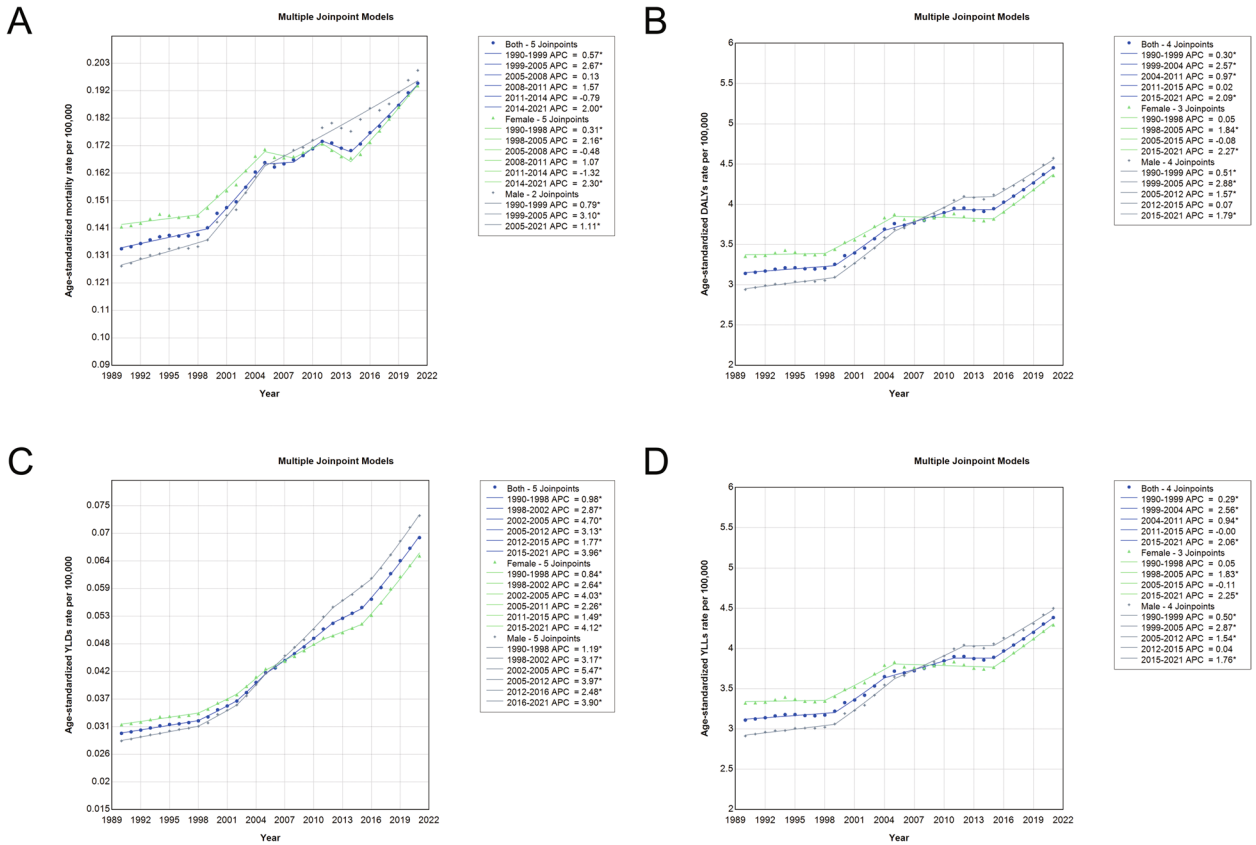

Fig. 6 Joinpoint analysis of age-standardized rates for deaths, DALYs, YLDs, and YLLs attributable to high BMI in GBTC in China from 1990 to 2021. **A** The trend in age-standardized death rates. **B** The trend in age-standardized DALYs rate. **C** The trend in YLDs rate. **D** The trend in YLLs rate. DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost; BMI, body mass index; GBTC, gallbladder and biliary tract cancer

that males had higher average annual percent changes (AAPC) in age-standardized mortality and DALY rates during earlier periods, particularly between 1999 and 2005, when the annual percent change (APC) for males peaked at 3.10% for mortality and 2.88% for DALYs. In contrast, females experienced slower increases or even declines during these earlier years, with minimal growth between 2005 and 2011. However, from 2015 onward, the trend reversed as females exhibited steeper rises in mortality rates compared to males, contributing to a marked increase in the overall burden of GBTC attributable to high BMI in China in recent years (Table 3, Fig. 6).

Trends in APC for death and DALYs rates attributable to high BMI in GBTC

Figures 7 and 8 illustrate the trends in annual percent changes (APC) for age-standardized death rates (Fig. 7) and DALYs rates (Fig. 8) attributable to high BMI in

Table 3 Trends in age-standardized mortality, DALY, YLD, and YLL rates (per 100,000 persons) among both sexes, males, and females from 1990 to 2021 for GBTC attributable to high BMI in China

	Age-standardized mortality rate			Age-standardized DALY rate			Age-standardized YLD rate			Age-standardized YLL rate		
Gender	**Period**	**APC (95% CI)**	**AAPC (95% CI)**	**Period**	**APC (95% CI)**	**AAPC (95% CI)**	**Period**	**APC (95% CI)**	**AAPC (95% CI)**	**Period**	**APC (95% CI)**	**AAPC (95% CI)**
Both	1990–1999	0.57 (0.40—0.74)*	1.22 (0.89—1.54)*	1990–1999	0.30 (0.16—0.44)*	1.12 (0.97—1.27)*	1990–1998	0.98 (0.84—1.13)*	2.71 (2.52—2.91)*	1990–1999	0.29 (0.15—0.43)*	1.10 (0.95—1.26)*
	1999–2005	2.67 (2.23—3.11)*		1999–2004	2.57 (2.07—3.08)*		1998–2002	2.87 (2.22—3.52)*		1999–2004	2.56 (2.05—3.07)*	
	2005–2008	0.13 (-1.81—2.11)		2004–2011	0.97 (0.70—1.24)*		2002–2005	4.70 (3.43—5.97)*		2004–2011	0.94 (0.67—1.21)*	
	2008–2011	1.57 (-0.40—3.58)		2011–2015	0.02 (-0.79—0.84)		2005–2012	3.13 (2.91—3.34)*		2011–2015	-0.00 (-0.82—0.82)	
	2011–2014	-0.79 (-2.77—1.23)		2015–2021	2.09 (1.78—2.39)*		2012–2015	1.77 (0.49—3.08)*		2015–2021	2.06 (1.75—2.36)*	
	2014–2021	2.00 (1.71—2.28)*					2015–2021	3.96 (3.72—4.20)*				
Female	1990–1998	0.31 (0.10—0.52)*	1.01 (0.70—1.32)*	1990–1998	0.05 (-0.18—0.29)	0.84 (0.70—0.98)*	1990–1998	0.84 (0.65—1.03)*	2.37 (2.13—2.60)*	1990–1998	0.05 (-0.19—0.29)	0.82 (0.69—0.96)*
	1998–2007	2.16 (1.83—2.48)*		1998–2005	1.84 (1.48—2.21)*		1998–2002	2.64 (1.78—3.51)*		1998–2005	1.83 (1.47—2.19)*	
	2007–2011	-0.48 (-2.36—1.44)		2005–2015	-0.08 (-0.28—0.11)		2002–2005	4.03 (2.29—5.80)*		2005–2015	-0.11 (-0.30—0.09)	
	2011–2014	1.07 (-0.79—2.96)		2015–2021	2.27 (1.86—2.69)*		2005–2011	2.26 (1.88—2.63)*		2015–2021	2.25 (1.84—2.67)*	
	2014–2019	-1.32 (-3.20—0.60)					2011–2015	1.49 (0.62—2.36)*				
	2019–2021	2.30 (2.01—2.59)*					2015–2021	4.12 (3.81—4.43)*				
Male	1990–1999	0.79 (0.50—1.09)*	1.40 (1.24—1.56)*	1990–1999	0.51 (0.35—0.67)*	1.41 (1.21—1.61)*	1990–1998	1.19 (1.03—1.34)*	3.08 (2.90—3.27)*	1990–1999	0.50 (0.34—0.66)*	1.39 (1.19—1.59)*
	1999–2005	3.10 (2.40—3.81)*		1999–2005	2.88 (2.49—3.28)*		1998–2002	3.17 (2.46—3.89)*		1999–2005	2.87 (2.47—3.26)*	
	2005–2021	1.11 (0.99—1.23)*		2005–2012	1.57 (1.29—1.85)*		2002–2005	5.47 (4.11—6.85)*		2005–2012	1.54 (1.26—1.82)*	
				2012–2015	0.07 (-1.67—1.84)		2005–2012	3.97 (3.74—4.21)*		2012–2015	0.04 (-1.70—1.81)	
				2015–2021	1.79 (1.46—2.12)*		2012–2016	2.48 (1.78—3.18)*		2015–2021	1.76 (1.43—2.09)*	
							2016–2021	3.90 (3.55—4.24)*				

GBTC Gallbladder and biliary tract cancer, *BMI* Body mass index, *AAPC* Average annual percent change presented for full period, *APC* Annual percent change, *CI* Confidence interval

* $P < 0.05$

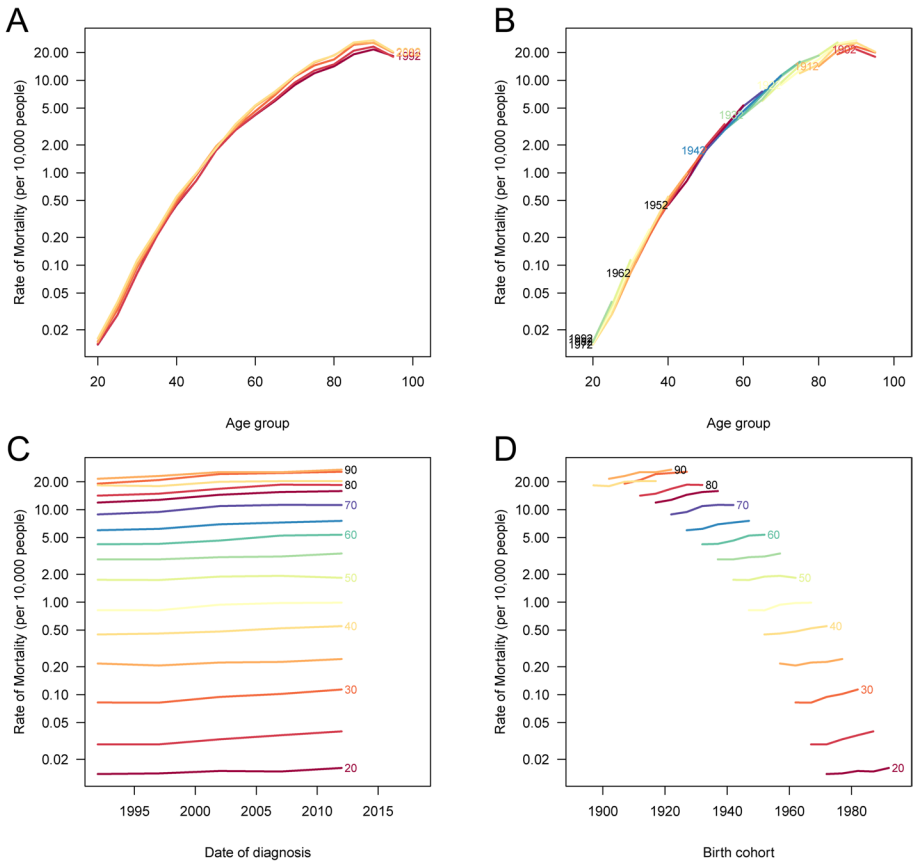

Fig. 7 Age-specific annual percent changes (APC) in age-standardized death rates attributable to high BMI in GBTC in China. **A** The age-specific APCs in death rates according to time periods; each line connects the age-specific APCs for a specific time period. **B** The age-specific APCs in death rates according to birth cohorts; each line connects the APCs for a specific birth cohort over time. **C** The period-specific APCs in death rates according to age groups; each line connects the APCs for a specific age group across different periods. **D** The birth cohort-specific APCs in death rates according to age groups; each line connects the cohort-specific APCs for a 5-year age group across different birth cohorts. This figure illustrates the varying trends in death rates due to high BMI by age, time period, and birth cohort. BMI, body mass index; GBTC, gallbladder and biliary tract cancer

GBTC in China, analyzed across different age groups, time periods, and birth cohorts. Both figures reveal distinct variations by age and time. In Fig. 7, the APCs for death rates show sharp increases during specific time periods, with particularly notable rises occurring after 2005. The increases are especially pronounced in older age groups, where the rate of change becomes steeper. Figure 8 displays similar trends for DALYs rates, where the APCs reflect a clear upward trend, particularly in older populations and more recent periods. The birth cohort analysis in both figures highlights that more recent cohorts have experienced steeper increases in both death and DALYs rates, indicating a growing burden of GBTC attributable to high BMI among these cohorts over time. These patterns emphasize the increasing impact of high BMI on both mortality and disability in GBTC across various demographic groups and time periods.

Decomposition of changes in deaths and DALYs attributable to high BMI in GBTC

Figure 9 shows the decomposition of factors contributing to changes in deaths and DALYs attributable to high BMI in GBTC in China from 1990 to 2021. For deaths, aging emerges as the most significant driver, followed by epidemiological changes and population growth. Aging has the greatest impact across both sexes, with a slightly more pronounced effect on males. Epidemiological change also plays a crucial role, particularly impacting males more than females, while population growth influences both sexes similarly. In terms of DALYs, epidemiological change is the dominant factor contributing to the overall increase, followed by population growth. Aging, however, exerts a diminishing effect on the increase in DALYs, thereby moderating the overall burden. This moderating effect of aging is evident in both males and females. However, the influence of epidemiological changes

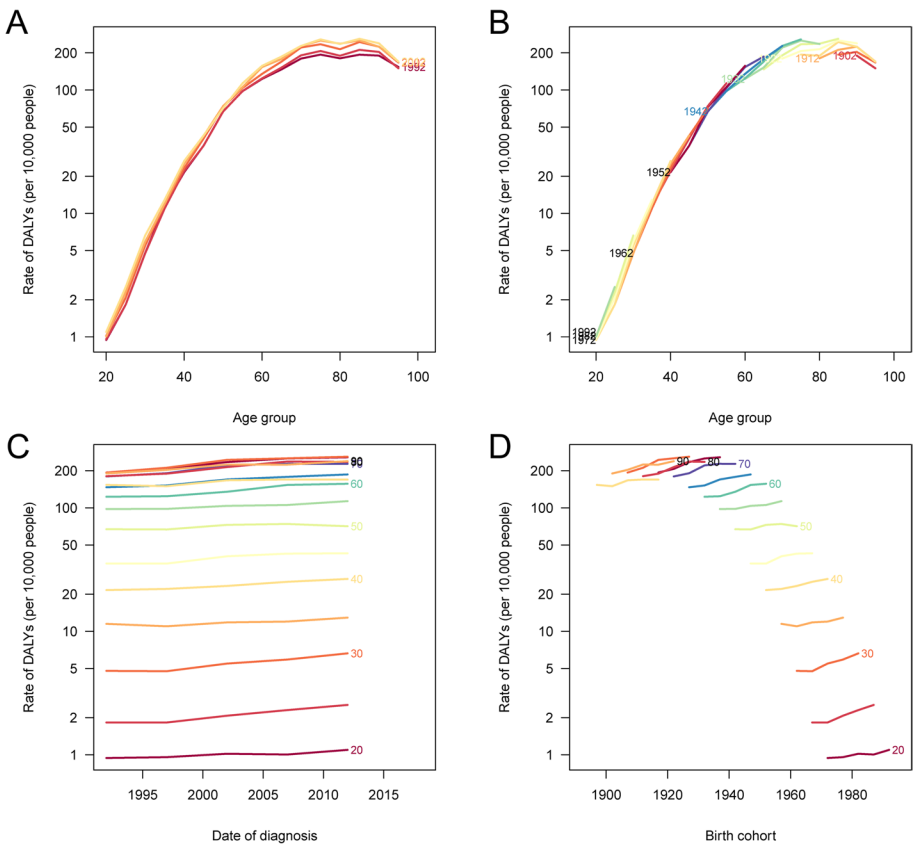

Fig. 8 Age-specific annual percent changes (APC) in age-standardized DALYs rates attributable to high BMI in GBTC in China. **A** The age-specific APCs in DALYs rates according to time periods; each line connects the age-specific APCs for a specific time period. **B** The age-specific APCs in DALYs rates according to birth cohorts; each line connects the APCs for a specific birth cohort over time. **C** The period-specific APCs in DALYs rates according to age groups; each line connects the APCs for a specific age group across different periods. **D** The birth cohort-specific APCs in DALYs rates according to age groups; each line connects the cohort-specific APCs for a 5-year age group across different birth cohorts. This figure highlights the trends in DALYs rates due to high BMI, showing variations by age, time period, and birth cohort. DALYs, disability-adjusted life years; BMI, body mass index; GBTC, gallbladder and biliary tract cancer

remains stronger in males compared to females. Population growth is also a substantial contributor to the rise in DALYs, with a slightly greater impact on males. The analysis highlights the complex interplay of aging, epidemiological shifts, and population growth in shaping the trends in GBTC burden due to high BMI.

Discussion

This study highlights the increasing burden of GBTC attributable to high BMI in China from 1990 to 2021, which mirrors global trends but at a more accelerated pace. Our findings show that both the number and ASRs of deaths and DALYs due to high BMI-related GBTC have risen significantly, with males experiencing a steeper increase compared to females, particularly after 2005. Joinpoint regression analysis revealed key inflection points where mortality and DALY rates accelerated, while decomposition analysis identified population growth and aging as primary drivers of the rising death rates, with epidemiological changes contributing more substantially to the rise in DALYs. Additionally, APC analysis demonstrated that younger birth cohorts are increasingly affected by high BMI, with recent cohorts showing a steeper increase in both mortality and DALYs. These findings underscore the growing public health impact of high BMI on GBTC in China, particularly in the context of an aging population and rising obesity rates.

Globally, high BMI is a well-established risk factor for several types of cancer, including GBTC, with studies reporting a strong correlation between rising obesity rates and increased cancer incidence and mortality [4]. Studies show that the cancer burden attributable to high BMI varies significantly by region, with higher impacts seen in developed and middle-to-high income countries due to both higher obesity rates and aging populations. In Brazil, for example, it's projected that cancer cases attributable to high BMI could nearly double by 2025 [31].

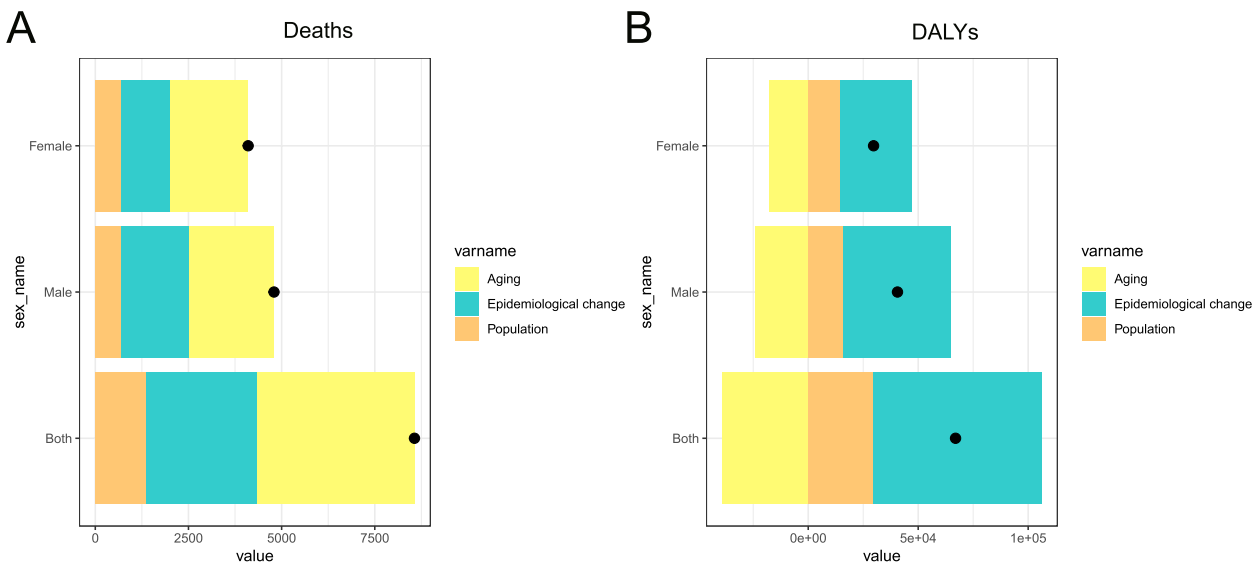

Fig. 9 Decomposition analysis of changes in deaths and DALYs attributable to high BMI in GBTC in China from 1990 to 2021, by aging (yellow), epidemiological changes (green), and population growth (orange). The black dots representing the sum of the effects of these factors. **A** Decomposition of changes in deaths for both sexes, males, and females. **B** Decomposition of changes in DALYs for both sexes, males, and females. DALYs, disability-adjusted life years; BMI, body mass index; GBTC, gallbladder and biliary tract cancer

Importantly, the increase in BMI from 1982 to 2012 was associated with a quarter of BMI-related cancer cases, underscoring the need for public health efforts to address the obesity epidemic as a cancer prevention strategy [32]. High BMI accounts for 5.1% of the cancer burden risk among Iranian adults aged 70 and above [10]. However, the burden in China has risen more sharply than in many other countries, as shown in our findings. This can be attributed to China's rapid economic development, leading to lifestyle changes that favor higher-calorie diets and reduced physical activity [13, 33]. The increase in the number and rate of deaths and DALYs related to high BMI in China highlights the growing public health challenge posed by obesity and its consequences. These trends are exacerbated by demographic factors such as population aging, which amplifies the burden of obesity-related cancers in the older population, and by changes in epidemiological patterns reflecting increased cancer risk among more recent cohorts [34, 35].

The underlying mechanisms linking high BMI to GBTC have been explored in several studies. Obesity promotes chronic inflammation, insulin resistance, and alterations in hormone levels, all of which contribute to carcinogenesis in the biliary tract [5, 36, 37]. Adipose tissue, particularly visceral fat, produces pro-inflammatory cytokines and adipokines that can create a tumor-promoting environment [38]. Furthermore, insulin resistance and hyperinsulinemia, common in individuals with high BMI, may increase the risk of cancer by stimulating cell proliferation and inhibiting apoptosis [8, 39]. Given these mechanisms, addressing high BMI through lifestyle interventions—such as dietary modification, increased physical activity, and weight management—should be prioritized as part of cancer prevention strategies. Public health policies promoting early screening, awareness campaigns, and behavioral interventions could reduce the incidence of GBTC in populations at risk.

Gender differences in the burden of GBTC attributable to high BMI were evident, with males experiencing a higher overall burden than females, particularly in the older age groups. While females showed a higher mortality and overall burden in the 60 to 79 age range, this trend reversed in older age brackets, with males experiencing steeper increases in mortality and disability-related indicators beyond age 80. This discrepancy could be due to biological, behavioral, and social factors. Biologically, males tend to accumulate more visceral fat, which is more metabolically active and associated with an increased risk of inflammation and insulin resistance. These metabolic changes are known to elevate the risk of certain cancers, including GBTC. Visceral fat releases pro-inflammatory cytokines and other bioactive molecules that may contribute to a more aggressive cancer environment, contrasting with the subcutaneous fat more commonly accumulated in females, which is less metabolically active [40, 41]. Behavioral factors also play a significant role in these gender differences. Males generally have higher rates of smoking and alcohol consumption compared to females, both of which are established risk factors for GBTC. These behaviors

can compound the effects of obesity, potentially creating a more hostile environment for cancer development and progression. This may explain the steeper rise in the burden of GBTC observed in older men. Hormonal factors further influence these differences. In females, estrogen has a protective role, particularly in premenopausal women, potentially reducing the impact of obesity on cancer risk. Estrogen can modulate inflammatory responses and metabolism, which may contribute to a lower cancer risk. However, as women age and transition through menopause, the decrease in estrogen levels may increase their susceptibility to obesity-related cancers like GBTC, explaining the higher burden observed in the 60–69 age group before it tapers off compared to males [42]. These findings highlight the importance of tailored prevention strategies that address gender-specific risk factors.

The age-period-cohort analysis revealed that younger birth cohorts in China are experiencing a greater increase in GBTC burden due to high BMI compared to older cohorts. This trend reflects the increasing prevalence of obesity in younger generations, likely driven by lifestyle changes such as high-calorie diets and sedentary behavior [43, 44]. The younger cohorts are also exposed to these risk factors earlier in life, leading to a longer cumulative exposure to obesity-related carcinogenic processes. The period effects further suggest that recent social and environmental changes have contributed to the growing cancer burden, while the aging population compounds the problem by increasing the number of individuals at risk of developing GBTC. To mitigate the rising burden of GBTC attributable to high BMI, specific preventive and control measures are needed. Public health efforts should focus on reducing obesity rates through targeted interventions that encourage healthier diets, regular physical activity, and weight management, especially among high-risk populations. Additionally, implementing nationwide screening programs for early detection of GBTC, particularly in individuals with a high BMI, could significantly reduce mortality. Policies aimed at reducing the consumption of processed foods, promoting healthy food environments, and increasing public awareness about the risks of obesity are essential. For gender-specific strategies, efforts should address behavioral risk factors more prevalent among men, such as smoking cessation and alcohol reduction, while emphasizing the importance of weight management across all demographics. Given the trends observed in younger birth cohorts, early intervention in childhood and adolescence to prevent obesity is critical for reducing future cancer risks [45].

Despite the valuable findings, this study has several limitations that should be acknowledged. First, the reliance on the GBD database means the data is derived from population-level estimates, which may not fully capture regional variations or specific individual risk factors, such as lifestyle choices and genetic predispositions. This could lead to an underestimation or overestimation of the true burden in certain regions of China. Additionally, while the study provides an overview of the contributions of high BMI to the GBTC burden, it lacks detailed patient-level data, which limits the ability to explore specific biological mechanisms or interactions between high BMI and other risk factors like diet, physical inactivity, or metabolic disorders. Another limitation is that the study is observational in nature and, as such, cannot establish causality between high BMI and GBTC risk or progression. Furthermore, the decomposition analysis does not account for the potential effects of healthcare access or improvements in cancer treatment, which may have influenced the outcomes observed. Future studies should aim to address these limitations by incorporating more detailed, individual-level data that accounts for lifestyle factors, healthcare access, and genetic variability. Prospective cohort studies with long-term follow-up could provide more robust evidence on the causal relationships between high BMI and GBTC. Additionally, integrating molecular and genomic data with epidemiological findings would enhance the understanding of how obesity contributes to cancer development and progression, particularly in genetically susceptible populations. Lastly, further research should explore the effectiveness of public health interventions focused on reducing obesity rates and their potential to mitigate the burden of GBTC.

Conclusions

This study underscores the increasing burden of GBTC attributable to high BMI in China, driven by demographic changes and rising obesity rates. The findings highlight the need for urgent public health strategies focused on reducing BMI-related risk factors. Prevention efforts should emphasize weight management, early screening, and lifestyle interventions tailored to high-risk populations. Future research should aim to incorporate individual-level data, including genetic and molecular markers, to deepen the understanding of the mechanisms linking high BMI to GBTC development. Additionally, exploring the effectiveness of public health interventions in reducing obesity rates and their potential impact on GBTC incidence will be crucial. Longitudinal studies with robust cohort data could also provide greater clarity on the causal pathways and help refine cancer prevention and control strategies, especially in rapidly aging populations.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12957-024-03582-4.

Supplementary Material 1: Supplementary Figure 1. Proportion of high BMI-related gastrointestinal cancers in China in 2021. (A) Proportion of deaths due to high BMI-related gastrointestinal cancers, including liver cancer, colon and rectum cancer, GBTC, and pancreatic cancer. (B) Proportion of DALYs attributable to high BMI among these cancers. (C) Proportion of YLDs for high BMI-related gastrointestinal cancers. (D) Proportion of YLLs for high BMI-related gastrointestinal cancers. BMI, body mass index; GBTC, gallbladder and biliary tract cancer; DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost.

Supplementary Material 2: Supplementary Figure 2. Proportion of China's high BMI-related GBTC burden compared to the global total in 2021. (A) Proportion of deaths from high BMI-related GBTC in China as a percentage of the global total. (B) Proportion of DALYs attributable to high BMI-related GBTC in China compared to the global burden. (C) Proportion of YLDs for high BMI-related GBTC in China relative to global values. (D) Proportion of YLLs for high BMI-related GBTC in China against global data. BMI, body mass index; GBTC, gallbladder and biliary tract cancer; DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost.

Supplementary Material 3: Supplementary Figure 3. Age-standardized death rates for GBTC attributable to high BMI across Asian countries in 2021. The figure compares age-standardized death rates for high BMI-related GBTC among various Asian countries, including China, Thailand, Republic of Korea, and Mongolia. Thailand exhibits the highest death rates, followed by the Republic of Korea and Mongolia, while China's rates are approximately at the median level among the analyzed countries. GBTC, gallbladder and biliary tract cancer; BMI, body mass index.

Supplementary Material 4: Supplementary Figure 4. Age-standardized DALYs rates for GBTC attributable to high BMI across Asian countries in 2021. This figure presents a comparison of age-standardized DALYs rates for high BMI-related GBTC among Asian countries, highlighting the variations in the burden across the region. The Kingdom of Thailand shows the highest DALYs rates, followed by the Republic of Korea and Mongolia, whereas China's burden is near the middle of the range compared to other countries. DALYs, disability-adjusted life years; GBTC, gallbladder and biliary tract cancer; BMI, body mass index.

Authors' contributions

Author Contributions Conceptualization: All authors contributed to formulating the research ideas and overall framework. Data curation: Zhouwei Zhan, Xiamei Chen, Shaohua Xu, Qifei Li, Jiami Yu, Zengqing Guo, and Bijuan Chen jointly curated and organized the data. Formal analysis: The group of authors carried out in-depth formal analysis to draw meaningful conclusions. Funding acquisition: Zhouwei Zhan took the lead in securing the necessary funds for the research. Investigation: All authors actively participated in the investigative process to explore the research topic. Methodology: Together, they developed appropriate research methodologies. Project administration: Bijuan Chen oversaw the management and progress of the project. Resources: Each author contributed to gathering relevant resources for the research. Software: As required, all authors contributed to software usage and adaptation. Supervision: Bijuan Chen provided guidance and supervision throughout. Visualization: All worked on presenting the research findings visually. Writing – original draft: All had a hand in drafting the initial manuscript. Writing – review & editing: The entire team participated in reviewing and editing the manuscript to ensure its quality.

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Data availability

The data used in this study were obtained from the GBD 2021 database, which is publicly available through the Institute for Health Metrics and Evaluation (IHME) website. All data analyzed during this study are accessible at the GBD Results Tool (http://ghdx.healthdata.org/gbd-results-tool) and can be requested for research purposes in accordance with IHME's data-sharing policies. No additional data were generated or analyzed in this study.

Declarations

Ethics approval and consent to participate

This study utilized publicly available, de-identified data from the GBD database. As such, it did not involve direct contact with human participants or the collection of personal health information. Therefore, no ethical approval or informed consent was required. The research adhered to the principles outlined in the Declaration of Helsinki, ensuring ethical conduct in the use of secondary data for public health research.

Competing interests

The authors declare no competing interests.

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