Burden of pancreatitis and associated risk factors in China, 1990 to 2019: a systematic analysis for the Global Burden of Disease Study 2019

Ke Han[1], Shimin Chen[2], Yang Song[2], Chen Du[1], Fei Gao[1], Shaohua Liu[2], Yao He[2], Ningli Chai[1], Enqiang Linghu[1], Miao Liu[3]

[1]Department of Gastroenterology, First Medical Center of Chinese PLA General Hospital and Chinese PLA Medical School, Beijing 100853, China;
[2]Institute of Geriatrics, Beijing Key Laboratory of Aging and Geriatrics, National Clinical Research Center for Geriatric Disease, Second Medical Center of Chinese PLA General Hospital and Chinese PLA Medical School, Beijing 100853, China;
[3]Graduate School, Chinese PLA General Hospital and Chinese PLA Medical School, Beijing 100853, China.

Abstract

Background: Pancreatitis is a common disease of the digestive system. Acute pancreatitis is one of the most common reasons for gastrointestinal hospital admission, and chronic pancreatitis significantly reduces quality of life. However, national epidemiological data on pancreatitis in China are lacking. This study aimed to quantify the disease burden of pancreatitis in China from 1990 to 2019.

Methods: This study was based on the Global Burden of Disease Study 2019 dataset. Age-standardized rates of incidence (ASIR), prevalence (ASPR), mortality (ASMR), and disability-adjusted life years (DALYs) were used to describe the disease burden of pancreatitis, and estimated annual percentage change (EAPC) was used to indicate the average change in age-standardized rates. We also described the trend of pancreatitis-related mortality and DALYs, which are attributable to alcohol use by age and sex.

Results: From 1990 to 2019, the ASIR, ASPR, ASMR, and age-standardized DALYs of pancreatitis in China decreased by 10.90, 1.50, 0.49, and 15.54 per 100,000, respectively, with EAPCs of −1.35 (95% uncertainty interval [UI]: −1.67, −1.02) and −0.37 (95% UI: −0.43, −0.31), −2.01 (95% UI: −2.07, −1.94) and −2.32 (95% UI: −2.37, −2.28), respectively. Recently, the numbers of incident and prevalent cases have risen, with estimates of 380,018 (95% UI: 308,669–462,767) and 493,765 (95% UI: 416,705–578,675), respectively, in 2019. Among men, the disease burden of pancreatitis was more severe than among women, and with variances in the distribution among different age groups. Age-standardized DALYs caused by alcohol-related pancreatitis have gradually worsened in the past decade, accounting for 34.09% of the total in 2019.

Conclusions: The disease burden of pancreatitis in China has declined in the past 30 years, but the exacerbation of population aging poses a challenge to prevention and control of pancreatitis. Alcohol use has gradually become an important factor in the disease burden of pancreatitis in recent years.

Keywords: Alcohol use; Global disease burden; Incidence; Mortality; DALYs; Pancreatitis; China

Introduction

Pancreatitis is an inflammatory injury of the pancreas with a variety of causes, and is classified as acute pancreatitis (AP) and chronic pancreatitis (CP). AP is one of the most common gastrointestinal disorders leading to hospital admission and causes huge medical expenses.[1] Its annual incidence varies from 13 to 45/100,000 in different regions.[2,3] The incidence of CP is relatively low, but the long-term existence of CP significantly reduces the quality of life of patients and increases the burden of disease, with a prevalence of 41.76/100,000.[4] The latest reported worldwide incidence and mortality rates of pancreatitis are 34.8/100,000 and 1.4/100,000, respectively.[5] The incidence and mortality of pancreatitis in China are moderate compared to worldwide numbers.[5,6] The clinical course of most patients with AP is self-limiting, but 20% to 30% of patients have experienced dangerous clinical conditions, and the overall case fatality rate is 5% to 10%. To date, no studies have reported the annual

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000002164

Ke Han and Shimin Chen contributed equally to the work.

Correspondence to: Miao Liu, Graduate School, Chinese PLA General Hospital and Chinese PLA Medical School, No. 28, Fuxing Road, Haidian District, Beijing 100853, China
E-Mail: liumiaolmbxb@163.com;
Enqiang Linghu, Department of Gastroenterology, First Medical Center, Chinese PLA General Hospital and Chinese PLA Medical School, No. 28, Fuxing Road, Haidian District, Beijing 100853, China
E-Mail: linghuenqiang@vip.sina.com

Chinese Medical Journal 2022;135(11)
Received: 15-03-2022; **Online:** 13-07-2022 **Edited by:** Jing Ni

trends in the prevalence, incidence, mortality, and disability-adjusted life years (DALYs) of pancreatitis in China at the national level.

Alcohol consumption is a common risk factor for pancreatitis.[7] Alcoholic pancreatitis usually shows with a chronic course, and it can also act as an acute episode if many alcoholic drinks are consumed in a short period. In most Western countries, the incidence of alcoholic pancreatitis ranks first among all types of pancreatitis.[3] The incidence in northern Europe is 8.2/100,000, and the overall prevalence is 27.4/100,000.[8] In China, the incidence of alcoholic pancreatitis is significantly higher than that of 10 years ago, ranking first to third among all types of pancreatitis according to different reports.[9,10] Understanding the status and trends of the disease burden of pancreatitis attributed to alcohol is of great significance for disease control and health promotion.

Hence, in this study, we focused on the current status and secular trends over the past 30 years in the disease burden of pancreatitis and alcohol-related pancreatitis by sex and age in China. This study aimed to evaluate the current prevention and therapeutic strategies and provide information and guidance for formulating public health policy.

Methods

Data source

In this study, the analysis was based on the 1990 to 2019 dataset of Global Burden of Disease Study (GBD), which is publicly available in the Global Health Data Exchange query tool (http://ghdx.healthdata.org/gbd-results-tool). GBD is an international collaborative study that was developed and maintained by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington, and aims to provide rigorous and comparable measurements for important global health issues. GBD 2019 estimated statistical data on 369 diseases and 87 risk factors from 1990 to 2019 in 204 countries and territories. A detailed description of the data collection and modeling of the GBD 2019 has been outlined in previous reports.[11,12]

This study extracted publicly accessible data from GBD 2019, which contains de-identified data rather than individual data. Therefore, the institutional review board waived the requirement for ethical approval and informed consent.

Disease classification and coding

The International Classification of Diseases ninth (ICD-9) and tenth edition (ICD-10) were used to encode the cause of death data, which were reclassified and mapped to the GBD cause of death classification after the garbage code was redistributed. In this study, the coding range for pancreatitis was 577 to 577.9 ICD-9 and K85 to K86.9 ICD-10.

Risk factors

GBD 2019 uses a comparative risk assessment framework to estimate the mortality and DALYs attributable to 87 risk factors and risk factor combinations at the global level and in different countries and regions. Risk factors are divided into three categories—behavioral, environmental and occupational, and metabolic. Among the 87 risk factors assessed by GBD 2019, only one risk factor for pancreatitis (use of alcohol) has been identified.[12]

Disease burden

Prevalence, incidence, mortality, and DALYs were described in this study to evaluate the disease burden of pancreatitis. The non-fatal disease burden was modeled using DisMod-MR 2.1, a Bayesian meta-regression tool that allows the evaluation of all available data on disease incidence, prevalence, and remission to achieve consistency among epidemiological parameters.[11] Data were derived primarily from hospital inpatient data, national surveys, published studies, and the cause of death reporting system of the Chinese Center for Disease Control and Prevention. These data inform etiological models primarily by providing estimates of incidence and prevalence adjusted for a combination of factors including readmission, non-primary diagnosis, and outpatient utilization. The pancreatitis mortality rate was generated by the cause of death ensemble model, which is a systematic tool that can run different modeling methods for mortality rates or death cause fractions with varying choices of covariates and select the model set that best reflects all available input data.[13]

DALYs refer to the total healthy life years lost from morbidity to death, including years of life lost due to premature death (YLL) and years lost due to disability (YLD). The calculation formula of YLL is $YLL = N \times L$, where N represents the number of deaths and L represents the standard life expectancy at the age of death in years. The calculation formula of YLD is $YLD = I \times DW \times L$, where I is the number of incident cases, DW is the disability weight, and L is the average duration of disability years. Disability weight represents the severity of health loss associated with a single health condition.[14]

Analysis

In all analyses, prevalence, incidence, mortality, and DALYs were presented as an age-standardized rate (ASR) of 100,000 persons. ASRs were calculated using the following formula:[15]

$$\text{Age-standardized rate} = \frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} w_i} \times 100,000$$

The GBD Population Estimates from 1950 to 2019 were considered the standardized population.[16] Age-standardized rates of incidence (ASIR), prevalence (ASPR), mortality (ASMR), and DALYs in 1990 and 2019 were stratified by sex. In the GBD, the uncertainty interval (UI) was used to describe the possible heterogeneity of sampling error and non-sampling variance. The 95% UI was calculated by taking out 1000 samples from the post-distribution of each step in the modeling process, and reported as the 2.5th and 97.5th values of each estimated

value. Estimated annual percentage changes (EAPC) were used to indicate the average change in ASRs.[15] In the calculation of EAPC, we assumed that the annual change was constant and stable, with year as the independent variable, and after the natural logarithmic transformation of ASRs, linear fitting was used as the dependent variable, namely: $Y = a+bX+\varepsilon$, where $Y = Ln(ASR)$ and X is the year. Subsequently, $EAPC = 100 \times (\exp(\beta) - 1)$, where β is the estimated value of slope b. Then hypothesis testing was performed on EAPC and the 95% confidence interval (CI) was calculated, where the standard error was obtained from the fitted regression line.[17] When both the estimated value of EAPC and the upper limit of its 95% CI were less than 0, the ASR was considered to have a downward trend. If the estimated value of EAPC and the lower limit of its 95% CI are both > 0, it was considered that ASR is rising. Otherwise, ASR was considered stable.

To observe the year-on-year trend of the burden of pancreatitis from 1990 to 2019, we used a biaxial graph to stratify cases and ASRs by sex and year. Then, we divided the age into groups of 5-year intervals, and described the distribution of ASRs in the cross-section in 2019 according to age and sex.

The ASRs and fractions of pancreatitis-related mortality and DALYs attributable to alcohol use are shown by age groups in different sexes. And we further described the secular trend of them by sex from 1990 to 2019.

All statistical analyses and data visualizations were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA) and the R package ggplot2 (https://ggplot2.tidyverse.org).

Results

Burden of pancreatitis in 1990 and 2019

The numbers and ASRs of incidence, prevalence, mortality and DALYs of pancreatitis in 1990 and 2019 are presented in Table 1. At the national level, the number of incident cases of pancreatitis was 380,018 (95% UI: 308,669–462,767) and 493,765 (95% UI: 416,705–578,675) in 1990 and 2019, respectively. From 1990 to 2019, the total number of new cases, prevalence, and deaths due to pancreatitis has increased, while the number of DALYs has declined from 320,705 (95% UI: 254,956–320,705) to 301,310 (95% UI: 237,110–363,324). The ASIR, ASPR, ASMR, and age-standardized DALYs of pancreatitis in 2019 were 26.76 (95% UI: 22.76, 31.25), 15.06 (95% UI: 13.13, 17.03), 0.59 (95% UI: 0.46, 0.7), and 16.09 (95% UI: 12.73, 19.36), respectively. All ASRs showed a significant decline from 1990 to 2019. The EAPC of ASIR, ASPR, ASMR, and age-standardized DALYs are −1.35 (95% UI: −1.67, −1.02), −0.37 (95% UI: −0.43, −0.31), −2.01 (95% UI: −2.07, −1.94), and −2.32 (95% UI: −2.37, −2.28), respectively.

The numbers and ASIR, ASPR, ASMR, and DALYs of men were higher than those of women in both 1990 and 2019. All the numbers among men and women increased during the study period, while all the ASRs in both sexes

Table 1: The cases and rates of pancreatitis burden in 1990 and 2019 in China.

Burden metrics	1990		2019		EAPC (95% CI)
	N (95% UI)	ASR (95% UI), per 100,000	*N* (95% UI)	ASR (95% UI), per 100,000	
Total					
Incidence	380,018 (308,669, 462,767)	37.66 (30.77, 45.11)	493,765 (416,705, 578,675)	26.76 (22.76, 31.25)	−1.35 (−1.67, −1.02)
Prevalence	164,822 (143,291, 185,609)	16.56 (14.44, 18.70)	294,837 (255,299, 337,195)	15.06 (13.13, 17.03)	−0.37 (−0.43, −0.31)
Mortality	8976 (7191, 12,084)	1.08 (0.87, 1.46)	10,664 (8196, 12,810)	0.59 (0.46, 0.70)	−2.01 (−2.07, −1.94)
DALYs	320,705 (254,956, 320,705)	31.63 (25.47, 41.56)	301,310 (237,110, 363,324)	16.09 (12.73, 19.36)	−2.32 (−2.37, −2.28)
Male					
Incidence	224,570 (180,212, 275,554)	43.05 (34.91, 51.65)	280,913 (235,648, 330,689)	31.12 (26.30, 36.51)	−1.27 (−1.62, −0.93)
Prevalence	88,549 (77,077, 99,975)	17.43 (15.29, 19.62)	167,250 (144,878, 190,879)	17.33 (15.17, 19.50)	−0.04 (−0.09, 0.01)
Mortality	4818 (3565, 6884)	1.19 (0.87, 1.77)	6359 (4654, 8133)	0.77 (0.57, 0.96)	−1.30 (−1.39, −1.20)
DALYs	183,810 (138,398, 256,902)	35.43 (26.68, 49.89)	191,988 (142,573, 243,679)	20.99 (15.70, 26.47)	−1.65 (−1.73, −1.56)
Female					
Incidence	155,448 (127,568, 187,510)	31.92 (26.29, 38.03)	212,852 (178,910, 250,742)	22.41 (19.13, 26.15)	−1.40 (−1.70, −1.09)
Prevalence	76,273 (66,091, 86,555)	15.57 (13.46, 17.69)	127,587 (109,827, 146,695)	12.84 (11.15, 14.61)	−0.73 (−0.81, −0.65)
Mortality	4158 (2990, 6004)	0.98 (0.73, 1.42)	4305 (2886, 5515)	0.45 (0.30, 0.57)	−2.81 (−2.89, −2.74)
DALYs	136,895 (95,956, 194,346)	27.69 (19.86, 39.37)	109,322 (76,079, 139,529)	11.39 (7.93, 14.50)	−3.26 (−3.35, −3.17)

ASRs: Age-standardized rates; CI: Confidence interval; DALYs: Disability-adjusted life-years; EAPC: Estimated annual percentage change; UI: Uncertainty interval.

decreased. The EAPC of ASIR, ASPR, ASMR, and age-standard DALYs among females are −1.40 (95% UI: −1.70, −1.09), −0.73 (95% UI: −0.81, −0.65), −2.81 (95% UI: −2.89, −2.74), −3.26 (95% UI: −3.35, −3.17), respectively, which is higher than that among men.

The distribution of the pancreatitis disease burden at different ages in 2019 is shown in Figure 1. The incidence of pancreatitis in people aged 0 to 19 was low, and increased with age, especially after entering old age, when the incidence of pancreatitis was high [Figure 1A]. The ASPR peaked at 80 to 84 years with age (male: 75.86/100,000; female: 67.28/100,000) and then began to show a downward trend [Figure 1B]. When we explored the distribution of ASMR, we found an increase in older age groups, with the ≥95 age group having the highest mortality of 22.87/100,000 in men and 16.85/100,000 in women [Figure 1C]. As for age-standardized DALYs, values for women increased with age, reaching the highest value of 92.9/100,000 in the ≥95 age group; among men, the highest value of 138.15/100,000 was observed in the 85 to 89-year-old group [Figure 1D].

Trends in pancreatitis burdens, 1990 to 2019

From 1990 to 2019, the ASIR, ASPR, ASMR, and age-standardized DALYs of pancreatitis in China decreased by 10.90, 1.50, 0.49, and 15.54, per 100,000, respectively [Table 1]. Figure 2 shows the year-on-year trend of the numbers and ASRs of incidence, prevalence, mortality, and DALYs for pancreatitis from 1990 to 2019 by sex. The ASIR of pancreatitis remained stable at first, but then experienced a rapid decline from 1997 to 2000 (from 41.41/100,000 to 31.50/100,000), followed by a stable trend. The number of pancreatitis patients generally showed a steady increasing trend, with ASPR remaining stable in men and decreasing year by year in women. The age-standardized mortality and DALYs continued to decline during the study period, but in the last 20 years, the decline in women was greater than that in men.

Deaths and DALYs of pancreatitis attributable to alcohol use

In 2019, the estimated number of deaths caused by alcohol-related pancreatitis in China was 3327.29, accounting for 31.20% of the total deaths due to pancreatitis. The proportion was 43.96% in men, compared to 11.83% in women. The age-standardized DALYs attributable to alcohol were 102702.10, which accounted for 34.09% of the total pancreatitis DALYs. Upon further observation in different age groups, we found that the disease burden caused by alcohol use was most serious among young and middle-aged male, reaching the highest value in the age group of 35 to 54, where the attributable fractions of ASMR and age-standardized DALYs were over 40%. [Figure 3A]. This was mainly due to the distribution among men, because the proportion of the disease burden attributable to alcohol use among women was relatively low and did not change significantly with age. Among men, more than half of the ASMR and age-standardized DALYs in the 35 to 65 age group can be attributed to alcohol-related pancreatitis

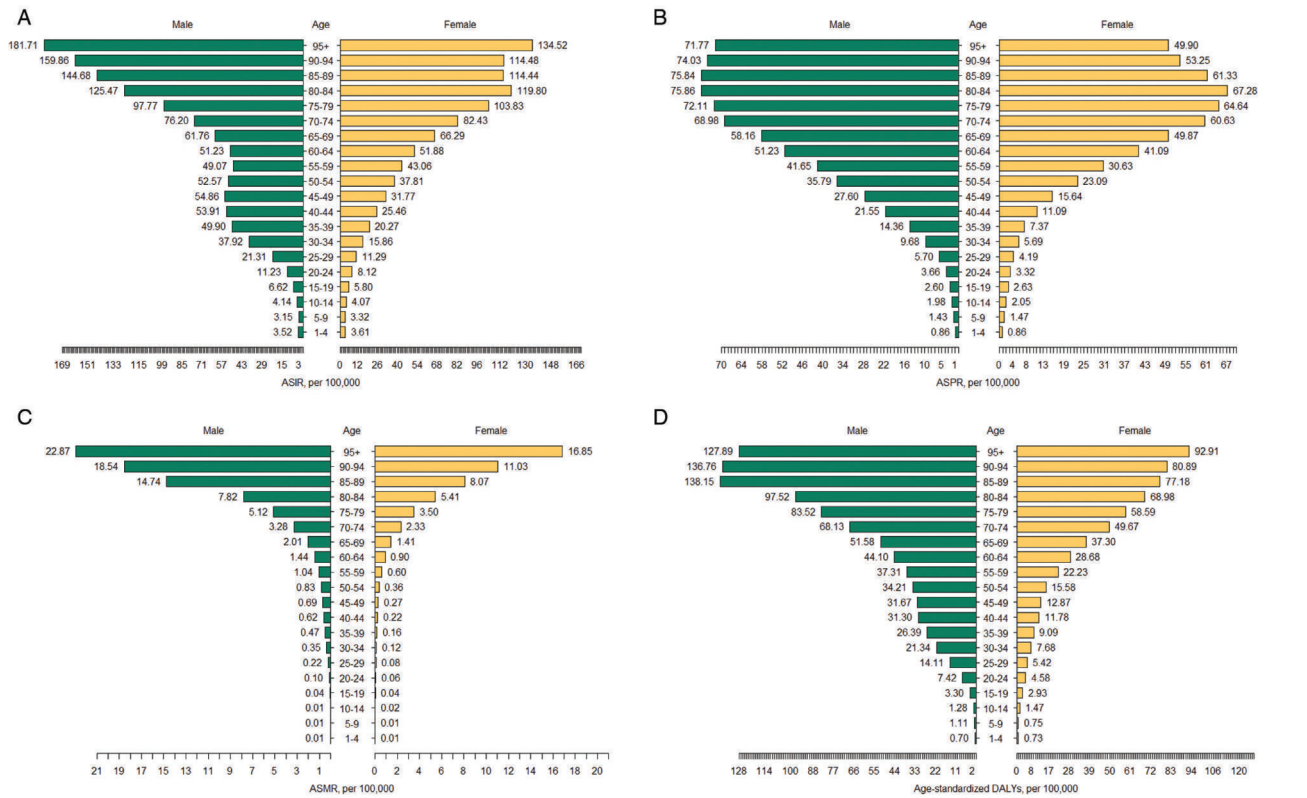

Figure 1: The age-standardized rates of (A) incidence, (B) prevalence, (C) mortality, and (D) DALYs due to pancreatitis by age and sex, 2019. ASIR: Age-standardized incidence rate; ASMR: Age-standardized mortality rate; ASPR: Age-standardized prevalence rate; DALYs: Disability-adjusted life-years.

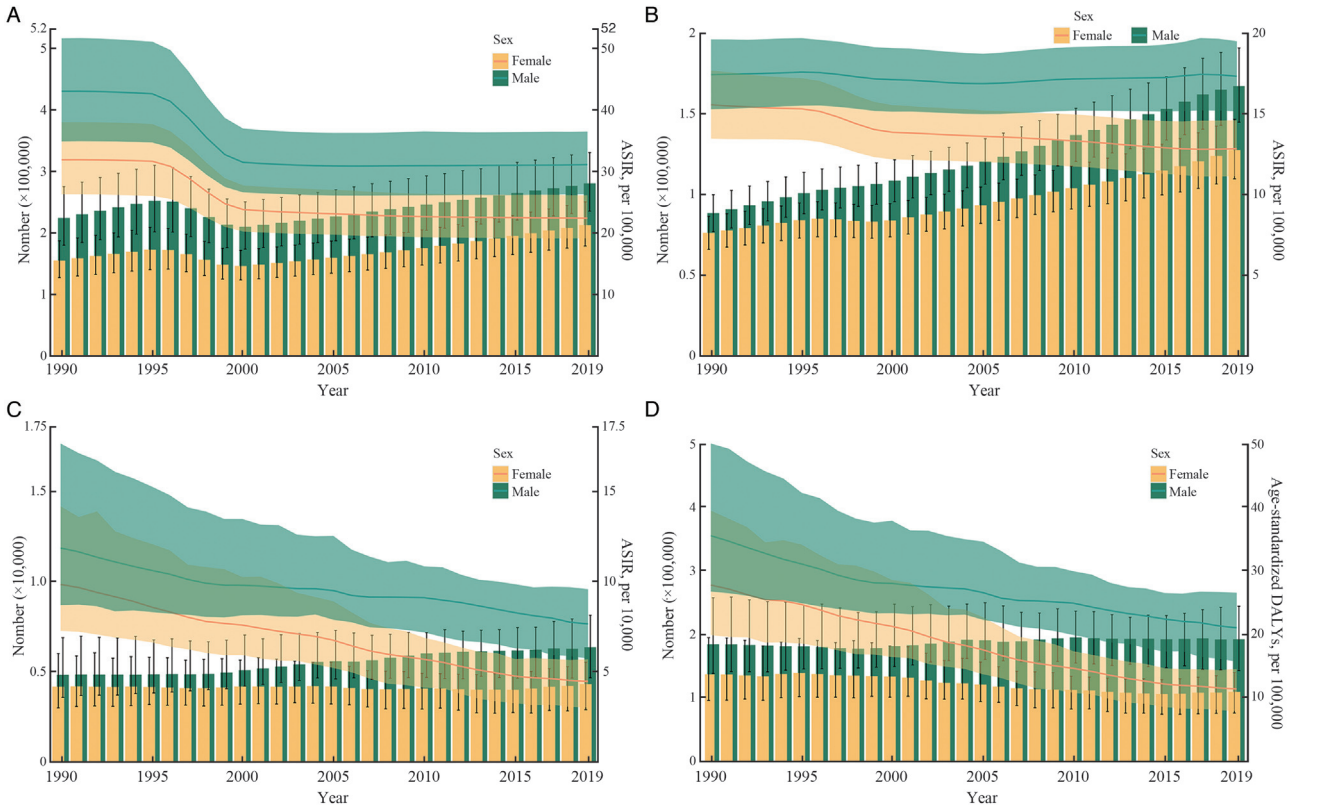

Figure 2: Trends in cases and age-standardized rates of (A) incidence, (B) prevalence, (C) mortality, and (D) DALYs of pancreatitis in China, from 1990 to 2019. The bar indicates the cases, and the line indicates the rates. Solid lines denote the estimated values, and shading indicates the upper and lower limits of the 95% UIs. ASIR: Age-standardized incidence rate; ASMR: Age-standardized mortality rate; ASPR: Age-standardized prevalence rate; DALYs: Disability-adjusted life-years; UIs: Uncertainty intervals.

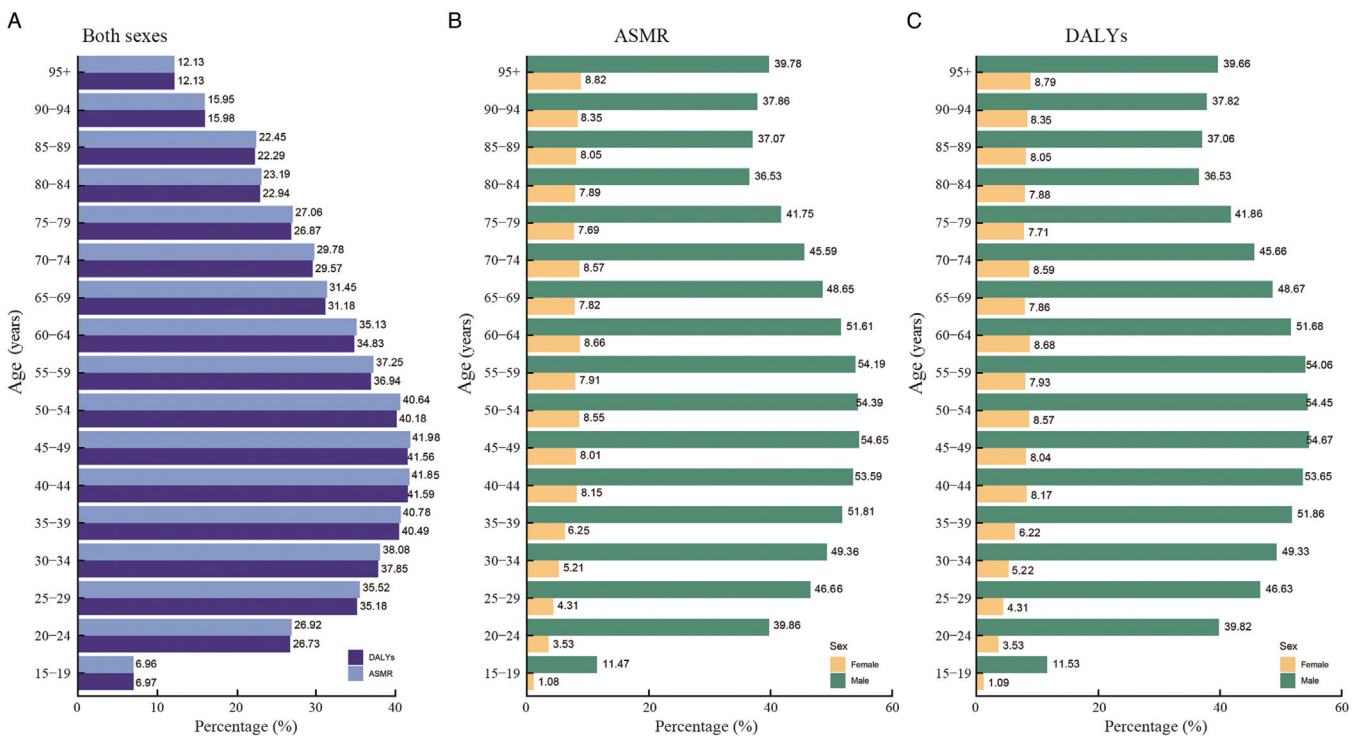

Figure 3: The fractions of pancreatitis ASMR and DALYs attributable to alcohol use, 2019. ASMR: Age-standardized mortality rate; DALYs: Disability-adjusted life-years.

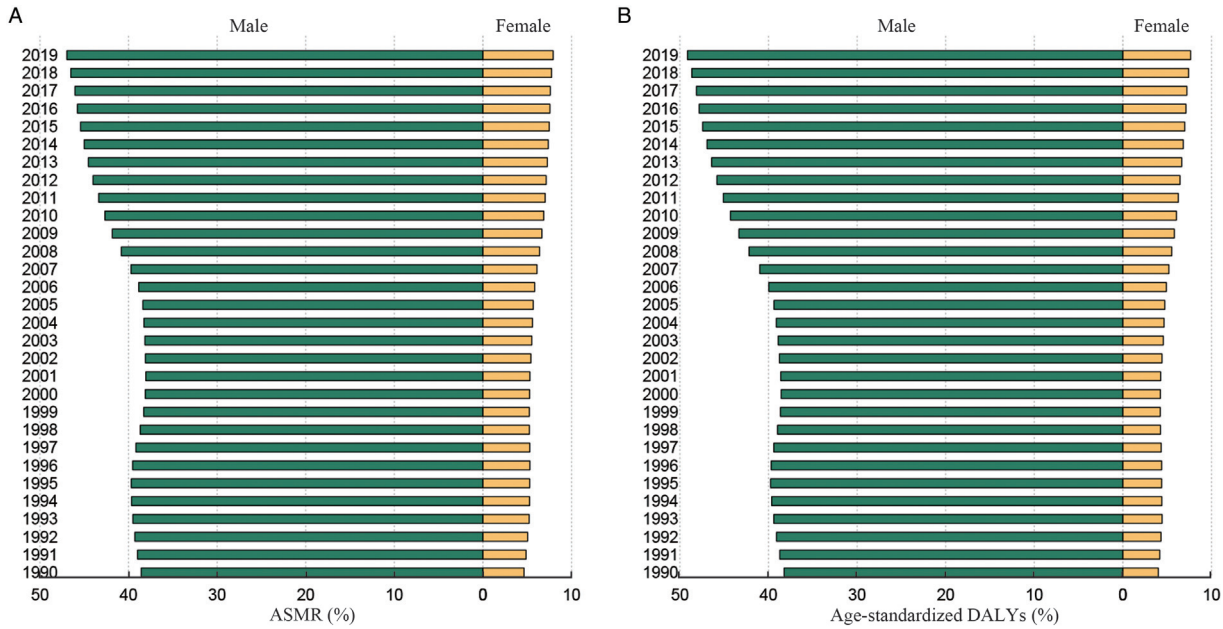

Figure 4: Trends in fractions of pancreatitis ASMR and DALYs attributable to alcohol use, from 1990 to 2019. ASMR: Age-standardized mortality rate; DALYs: Disability-adjusted life-years.

[Figure 3B and 3C]. Moreover, the ASMR of alcohol-related pancreatitis gradually increased with age, and age-standardized DALYs remained relatively stable in men >85 years of age [Supplementary Figure 1, http://links.lww.com/CM9/B76].

From 1990 to 2019, the ASMR and age-standardized DALYs of pancreatitis attributable to alcohol use showed an overall downward trend [Supplementary Figure 2, http://links.lww.com/CM9/B76]. However, the fractions of pancreatitis ASMR and DALYs attributable to alcohol use showed a general trend of first declining and then rising, and the fractions continued to rise after 2001 in both sexes [Figure 4].

Discussion

This study describes the secular trend of pancreatitis in the ASIR, ASPR, ASMR, and age-standardized DALYs in China at the national level for the first time, and provides the following key information. Nationally, we estimated that there were nearly 0.5 million incident cases, 0.3 million prevalent cases, 10.7 thousand deaths, and 0.3 million DALYs in 2019. The ASR of incidence, prevalence, deaths, and age-standardized DALYs were 26.76, 15.06, 0.59, and 16.09 per 100,000, respectively. From 1990 to 2019, the ASRs of pancreatitis declined in China, but the number of incident and prevalent cases has grown significantly. In addition, alcohol use has gradually become a more significant cause of death and DALYs caused by pancreatitis.

A meta-analysis of high-quality population-based cohort studies showed that the global incidence and mortality of AP were 33.74/100,000 and 1.60/100,000, respectively, and those of CP were 9.62/100,000, and 0.09/100,000.[18] In 2019, the estimated global incidence, mortality, and DALYs of pancreatitis were 34.8/100,000, 1.4/100,000, and 44.4/100,000, respectively.[5] Our results showed that the burden of pancreatitis in China is at a medium level from the perspective of ASRs. However, considering the huge population of China, the incidence and prevalence, mortality, and the morbidity rates are still a heavy burden. It is particularly important to note that the incidence and prevalence of pancreatitis in China have shown an upward trend in recent years. Studies have reported that the incidence and prevalence of CP are increasing.[19] CP is prone to recurrent episodes, and there is currently no curative treatment. The long-term existence of the disease will reduce patients' quality of life and shorten their life expectancy. Therefore, CP may be an important factor in the changes of pancreatitis DALYs.

The incidence and prevalence of pancreatitis in China have not declined significantly in the past 30 years, especially among men. Socioeconomic level plays an important role in the incidence and prevalence of pancreatitis. A positive correlation between the socio-demographic index (SDI) and the incidence and prevalence of pancreatitis has been reported in previous studies.[5,6] The GBD data showed that China's SDI has been on an upward trend, from 0.456 in 1990 to 0.707 in 2017. Since 2003, it has exceeded the global average and has increased by 55.04% in 28 years.[20] Therefore, while China's socioeconomic level is rapidly improving, the prevention of pancreatitis is worthy of attention. We also observed that the mortality rate of pancreatitis in China declined during the study period. In the past 10 years, the introduction of multidisciplinary and individualized treatments has greatly improved the prognosis of AP.[21] Advances in early diagnosis methods, application of minimally invasive endoscopy,[22] progress in the treatment of pancreas and peripancreatic necrosis,[23] and the improvement of critically ill patient management have greatly improved the prognosis of AP.[24] In addition, advances in the

diagnosis of pancreatitis may be part of the reason for the increase in annual incidence and the number of patients in addition to the increase in the total population during the 30 years.

According to the estimates of this study, the incidence and prevalence of pancreatitis among men were higher than those among women in China in 2019. It is commonly accepted that men and women have an equal proportion of AP,[6] but CP is more common in men.[25] The sex difference in the onset of pancreatitis may be related to the cause. Pancreatitis among women is more closely related to gallstones, autoimmune diseases or idiopathic pancreatitis, while alcohol-related pancreatitis is more common in men.[1,26] This may also explain the small increase in the incidence of pancreatitis in middle-aged men. Age is also a key factor in the occurrence, progression, and prognosis of pancreatitis. In general, the incidence and mortality rates significantly increased with age, and older adults were among the population with the highest burden of pancreatitis, especially the ≥85 age group. Considering that China is facing the world's largest population aging problem,[27] prevention and treatment of pancreatitis among older adults should receive more attention. Health education, nutritional support, surgical intervention, intensive care, and comorbidity management among older patients with pancreatitis are all areas that can be improved.

It is generally believed that alcoholic pancreatitis occurs frequently in Europe [28] and North America,[29] but alcohol use is not the most important factor for pancreatitis in China.[9] However, our research found that it played an increasingly important role in the disease burden caused by pancreatitis in China in recent years. A study reported that the proportion of patients with AP attributable to alcohol use ranged from 19% to 32%, and those with CP increased from 55% to 70%.[3] In developing countries, approximately 35% of AP cases are related to alcohol abuse.[10] The majority of alcoholic pancreatitis manifests as AP, but alcoholic AP is more likely to progress to CP,[30-32] which is an important factor for its prevalence. Alcohol damages the pancreas through many mechanisms,[33,34] and genetic factors as well as ethnic background play an important role in alcohol-related pancreatitis.[35] Previous studies have shown that CP risk factors in the European population, such as CEL-HYB variants,[36] CTRB1-CTRB2 alleles,[37] do not affect the risk of CP in the Chinese population. In contrast, the high frequency of the ethanol dehydrogenase ADH2*2 allele in Asian populations increases susceptibility to alcoholic pancreatitis.[38] A review confirmed that there is a dose-response relationship between alcohol consumption and the risk of pancreatitis.[7] At the same time, the prevalence of alcohol consumption is also increasing with the rise of the socioeconomic level.[39] Therefore, as a potentially changeable risk factor, health education and public health strategies for alcohol control may be beneficial in relieving the disease burden of pancreatitis.

The limitations of this study need to be acknowledged. First, due to the limitations of GBD data, we were unable to conduct an analysis of the distribution of disease burden at the provincial level and between urban and rural areas. Further data are needed to provide more detailed information on the disease burden of pancreatitis in China. Second, risk factors such as gallstone and hypertriglyceridemia also play an important role in the pathogenesis of pancreatitis.[10,40] However, this wave of GBD data does not support our analysis of the burden of disease caused by these meaningful risk factors. Third, if all the estimates in this study can be presented in stratification based on AP and CP, it may provide more valuable and more targeted information for disease burden control.

Conclusions

In conclusion, this study described the latest disease burden and its secular trend of nearly 30 years of pancreatitis in China on indicators of ASIR, ASPR, ASMR, and age-standardized DALYs. From 1990 to 2019, the ASRs of pancreatitis in China have declined, but the incident cases and prevalent patients have increased constantly. In addition, in recent years, alcohol consumption has gradually become a more important factor in mortality and DALYs caused by pancreatitis. Therefore, further research and targeted public health initiatives are needed to discover better methods for the prevention, diagnosis and management of pancreatitis to relieve the disease burden.

Acknowledgements

The authors thank the GBD collaborators for sharing data in public, allowing relevant analysis and interpretations.

Funding

This study was supported by grants from the National Natural Science Foundation of China (Nos. 81773502, 82173589, and 82173590) and the National Key Research and Development Programs of China (Nos. 2016YFC1303601 and 2020YFC2002705). The views and opinions expressed in this paper are those of the authors and do not necessarily reflect the official position of the study sponsors.

Conflicts of interest

None.

References

1. Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology 2013;144:1252–1261. doi: 10.1053/j.gastro.2013.01.068.
2. Satoh K, Shimosegawa T, Masamune A, Hirota M, Kikuta K, Kihara Y, *et al*. Nationwide epidemiological survey of acute pancreatitis in Japan. Pancreas 2011;40:503–507. doi: 10.1097/MPA.0b013e318214812b.
3. Yadav D, Whitcomb DC. The role of alcohol and smoking in pancreatitis. Nat Rev Gastroenterol Hepatol 2010;7:131–145. doi: 10.1038/nrgastro.2010.6.
4. Yadav D, Timmons L, Benson JT, Dierkhising RA, Chari ST. Incidence, prevalence, and survival of chronic pancreatitis: a population-based study. Am J Gastroenterol 2011;106:2192–2199. doi: 10.1038/ajg.2011.328.
5. Li CL, Jiang M, Pan CQ, Li J, Xu LG. The global, regional, and national burden of acute pancreatitis in 204 countries and

territories, 1990–2019. BMC Gastroenterol 2021;21:332. doi: 10.1186/s12876-021-01906-2.
6. Ouyang G, Pan G, Liu Q, Wu Y, Liu Z, Lu W, *et al*. The global, regional, and national burden of pancreatitis in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. BMC Med 2020;18:388. doi: 10.1186/s12916-020-01859-5.
7. Irving HM, Samokhvalov AV, Rehm J. Alcohol as a risk factor for pancreatitis. A systematic review and meta-analysis. JOP 2009;10:387–392.
8. Schneider A, Singer MV. Alcoholic pancreatitis. Dig Dis 2005;23:222–231. doi: 10.1159/000090169.
9. Zhu Y, Pan X, Zeng H, He W, Xia L, Liu P, *et al*. A study on the etiology, severity, and mortality of 3260 patients with acute pancreatitis according to the revised Atlanta classification in Jiangxi, China over an 8-year period. Pancreas 2017;46:504–509. doi: 10.1097/MPA.0000000000000776.
10. Wang GJ, Gao CF, Wei D, Wang C, Ding SQ. Acute pancreatitis: etiology and common pathogenesis. World J Gastroenterol 2009;15:1427–1430. doi: 10.3748/wjg.15.1427.
11. Diseases GBD, Injuries C. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020;396:1204–1222. doi: 10.1016/S0140-6736(20)30925-9.
12. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, *et al*. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020;396:1223–1249. doi: 10.1016/s0140-6736(20)30752-2.
13. Collaborators GdaIIaP. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018;392:1789–1858. doi: 10.1016/s0140-6736(18)32279-7.
14. Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, *et al*. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob Health 2015;3:e712–e723. doi: 10.1016/S2214-109X(15)00069-8.
15. Hankey BF, Ries LA, Kosary CL, Feuer EJ, Merrill RM, Clegg LX, *et al*. Partitioning linear trends in age-adjusted rates. Cancer Causes Control 2000;11:31–35. doi: 10.1023/a:1008953201688.
16. Global Burden of Disease Study 2019 (GBD 2019) Population Estimates 1950-2019. [Internet]. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME). 2020. Available from: https://doi.org/10.6069/7EGY-0354. [Accessed on December 9, 2021].
17. de Vries E, Schouten LJ, Visser O, Eggermont AM, Coebergh JW. Rising trends in the incidence of and mortality from cutaneous melanoma in the Netherlands: a Northwest to Southeast gradient? Eur J Cancer 2003;39:1439–1446. doi: 10.1016/s0959-8049(03)00320-4.
18. Xiao AY, Tan ML, Wu LM, Asrani VM, Windsor JA, Yadav D, *et al*. Global incidence and mortality of pancreatic diseases: a systematic review, meta-analysis, and meta-regression of population-based cohort studies. Lancet Gastroenterol Hepatol 2016;1:45–55. doi: 10.1016/s2468-1253(16)30004-8.
19. Beyer G, Habtezion A, Werner J, Lerch MM, Mayerle J. Chronic pancreatitis. Lancet 2020;396:499–512. doi: 10.1016/s0140-6736(20)31318-0.
20. Yu C, Bai J. The concept of Socio-Demographic Index (SDI) and its application. J Public Health Prev Med 2020;31:5–10. doi: 10.3969/j.issn.1006-2483.2020.01.002.
21. Boxhoorn L, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA, *et al*. Acute pancreatitis. Lancet 2020;396:726–734. doi: 10.1016/s0140-6736(20)31310-6.
22. Bang JY, Arnoletti JP, Holt BA, Sutton B, Hasan MK, Navaneethan U, *et al*. An endoscopic transluminal approach, compared with minimally invasive surgery, reduces complications and costs for patients with necrotizing pancreatitis. Gastroenterology 2019;156:1027.e3–1040.e3. doi: 10.1053/j.gastro.2018.11.031.
23. Baron TH, DiMaio CJ, Wang AY, Morgan KA. American Gastroenterological Association clinical practice update: management of pancreatic necrosis. Gastroenterology 2020;158:67.e1–75.e1. doi: 10.1053/j.gastro.2019.07.064.
24. Nathens AB, Curtis JR, Beale RJ, Cook DJ, Moreno RP, Romand JA, *et al*. Management of the critically ill patient with severe acute pancreatitis. Crit Care Med 2004;32:2524–2536. doi: 10.1097/01.ccm.0000148222.09869.92.
25. Hirota M, Shimosegawa T, Masamune A, Kikuta K, Kume K, Hamada S, *et al*. The seventh nationwide epidemiological survey for chronic pancreatitis in Japan: clinical significance of smoking habit in Japanese patients. Pancreatology 2014;14:490–496. doi: 10.1016/j.pan.2014.08.008.
26. Kleeff J, Whitcomb DC, Shimosegawa T, Esposito I, Lerch MM, Gress T, *et al*. Chronic pancreatitis. Nat Rev Dis Primers 2017;3:17060. doi: 10.1038/nrdp.2017.60.
27. United Nations, Department of Economic and Social Affairs, Population Division (2015). World Population Prospects: The 2015 Revision, Key Findings and Advance Tables. Working Paper No. ESA/P/WP.241.
28. Karjula H, Saarela A, Ohtonen P, Ala-Kokko T, Mäkelä J, Liisanantti JH. Long-term outcome and causes of death for working-age patients hospitalized due to acute pancreatitis with a median follow-up of 10 years. Ann Surg 2019;269:932–936. doi: 10.1097/sla.0000000000002612.
29. Conwell DL, Banks PA, Sandhu BS, Sherman S, Al-Kaade S, Gardner TB, *et al*. Validation of demographics, etiology, and risk factors for chronic pancreatitis in the USA: a report of the North American Pancreas Study (NAPS) group. Dig Dis Sci 2017;62:2133–2140. doi: 10.1007/s10620-017-4621-z.
30. Lankisch PG, Assmus C, Maisonneuve P, Lowenfels AB. Epidemiology of pancreatic diseases in Lüneburg County. A study in a defined German population. Pancreatology 2002;2:469–477. doi: 10.1159/000064713.
31. Petrov MS, Yadav D. Global epidemiology and holistic prevention of pancreatitis. Nat Rev Gastroenterol Hepatol 2019;16:175–184. doi: 10.1038/s41575-018-0087-5.
32. Clemens DL, Mahan KJ. Alcoholic pancreatitis: lessons from the liver. World J Gastroenterol 2010;16:1314–1320. doi: 10.3748/wjg.v16.i11.1314.
33. Vonlaufen A, Wilson JS, Pirola RC, Apte MV. Role of alcohol metabolism in chronic pancreatitis. Alcohol Res Health 2007;30:48–54.
34. Gu H, Werner J, Bergmann F, Whitcomb DC, Büchler MW, Fortunato F. Necro-inflammatory response of pancreatic acinar cells in the pathogenesis of acute alcoholic pancreatitis. Cell Death Dis 2013;4:e816. doi: 10.1038/cddis.2013.354.
35. Takahashi T, Miao Y, Kang F, Dolai S, Gaisano HY. Susceptibility factors and cellular mechanisms underlying alcoholic pancreatitis. Alcohol Clin Exp Res 2020;44:777–789. doi: 10.1111/acer.14304.
36. Zou WB, Boulling A, Masamune A, Issarapu P, Masson E, Wu H, *et al*. No association between CEL-HYB hybrid allele and chronic pancreatitis in Asian populations. Gastroenterology 2016;150:1558.e5–1560.e5. doi: 10.1053/j.gastro.2016.02.071.
37. Tang XY, Zou WB, Masson E, Hu LH, Ferec C, Chen JM, *et al*. The CTRB1-CTRB2 risk allele for chronic pancreatitis discovered in European populations does not contribute to disease risk variation in the Chinese population due to near allele fixation. Gut 2018;67:1368–1369. doi: 10.1136/gutjnl-2017-315180.
38. Zhong Y, Cao J, Zou R, Peng M. Genetic polymorphisms in alcohol dehydrogenase, aldehyde dehydrogenase and alcoholic chronic pancreatitis susceptibility: a meta-analysis. Gastroenterol Hepatol 2015;38:417–425. doi: 10.1016/j.gastrohep.2014.11.009.
39. GBD 2016 Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2018;392:1015–1035. doi: 10.1016/s0140-6736(18)31310-2.
40. Yang AL, McNabb-Baltar J. Hypertriglyceridemia and acute pancreatitis. Pancreatology 2020;20:795–800. doi: 10.1016/j.pan.2020.06.005.

How to cite this article: Han K, Chen S, Song Y, Du C, Gao F, Liu S, He Y, Chai N, Linghu E, Liu M. Burden of pancreatitis and associated risk factors in China, 1990 to 2019: a systematic analysis for the Global Burden of Disease Study 2019. Chin Med J 2022;135:1340–1347. doi: 10.1097/CM9.0000000000002164