Epidemiological Characteristics of Pancreatic Cancer in China From 1990 to 2019

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Abstract

Background: Pancreatic cancer is an aggressive cancer and is predicted to become the second leading cause of cancer-related deaths in China. To understand the epidemic trend of pancreatic cancer and formulate targeted preventive measures, it is important to analyze the incidence and mortality of pancreatic cancer.

Methods: The incidence and mortality data of pancreatic cancer in China were obtained from Global Burden of Disease (GBD) data. We used joinpoint regression analysis to calculate the magnitude and direction of trends, and the age-period-cohort method to analyze the effects of chronological age, time period, and birth cohort.

Results: The age-standardized rates (ASRs) for both incidence and mortality of pancreatic cancer increased from 1990 to 2019, and were higher in males than females. The incidence and mortality rates have increased year by year in the age group above 25 years. The most common age group was 55–79 years, accounting for approximately 50% of all incident cases. In terms of incidence and mortality rates, the overall net drifts were above 0. The local drifts in all age groups were above 0 in both sexes and males, while the local drifts in the 15–39 age groups were below 0 in females. The longitudinal age curves increased with age, with higher incidence and mortality rates, mainly in older age groups. The period rate ratios increased by year. The cohort rate ratios showed an upward trend before 1970 and fluctuated after 1975.

Conclusions: The burden of pancreatic cancer is still very high in China, and attention should be paid to the key population that is, males and older people. The results of our study can be used by policy makers to allocate resources efficiently to improve early diagnosis and treatment, improving the awareness of self-protection, and advocating a healthy lifestyle to prevent pancreatic cancer.

Keywords

epidemiology, pancreatic cancer, age-period-cohort analysis, prevention, China

Introduction

According to GLOBOCAN 2020, pancreatic cancer is the 11th leading cause of cancer death in both men and women, and about 495 733 new cases of pancreatic cancer will be diagnosed and 466 003 deaths will occur due to this disease per year in the world.[1] Patients with pancreatic cancer have very poor survival, with a relative 5-year survival rate of only

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Table 1. The APC in the ASRs for Pancreatic Cancer for Both Sexes/by Sex in China from 1990 to 2019.

	Incidence			Mortality		
	Both	Male	Female	Both	Male	Female
	APC (95%CI)	APC (95%CI)	APC (95%CI)	APC (95%CI)	APC (95%CI)	APC (95%CI)
15 to 19	−.6 (−.9, −.3)*	−.3 (−.7, .0)	−1.2 (−1.4, −1.0)*	−.7 (−1.0, −.4)*	−.4 (−.8, −.1)*	−1.4 (−1.6, −1.1)*
20 to 24	.0 (-.3, .3)	.8 (.5, 1.1)*	−1.2 (-1.7, −.6)*	−.1 (−.5, .2)	.7 (.4, 1.0)*	−1.3 (−1.9, −.8)*
25 to 29	.6 (.1, 1.0)*	1.9 (1.6, 2.2)*	−1.3 (−2.1, −.5)*	.5 (.0, .9)*	1.8 (1.5, 2.2)*	−1.5 (−2.2, −.7)*
30 to 34	1.2 (.8, 1.5)*	2.3 (2.0, 2.6)*	−1.0 (−1.7, −.3)*	1.1 (.8, 1.4)*	2.2 (1.9, 2.5)*	−1.2 (−1.9, −.5)*
35 to 39	1.4 (1.2, 1.5)*	2.0 (1.8, 2.2)*	−.2 (−.4, .1)	1.3 (1.1, 1.4)*	1.9 (1.7, 2.1)*	−.3 (−.6, −.1)*
40 to 44	2.3 (2.1, 2.4)*	3.0 (2.7, 3.2)*	.8 (.6, .9)*	2.2 (2.0, 2.3)*	2.9 (2.6, 3.1)*	.6 (.5, .8)*
45 to 49	2.0 (1.8, 2.2)*	2.9 (2.5, 3.3)*	.3 (.0, .6)*	1.9 (1.7, 2.2)*	2.9 (2.5, 3.3)*	.2 (−.1, .5)
50 to 54	1.3 (1.1, 1.6)*	1.9 (1.5, 2.0)*	.5 (.3, .7)*	1.3 (1.0, 1.6)*	1.8 (1.5, 2.2)*	.4 (.2, .6)*
55 to 59	1.5 (1.3, 1.8)*	1.8 (1.5, 2.0)*	1.2 (.9, 1.6)*	1.5 (1.2, 1.7)*	1.7 (1.5, 1.9)*	1.1 (.8, 1.5)*
60 to 64	2.1 (1.9, 2.3)*	2.5 (2.2, 2.8)*	1.5 (1.3, 1.7)*	2.0 (1.8, 2.2)*	2.5 (2.2, 2.7)*	1.4 (1.3, 1.6)*
65 to 69	2.4 (2.2, 2.6)*	2.6 (2.4, 2.9)*	2.1 (1.8, 2.3)*	2.3 (2.1, 2.6)*	2.6 (2.3, 2.8)*	2.0 (1.8, 2.2)*
70 to 74	2.5 (2.3, 2.8)*	2.7 (2.4, 2.9)*	2.3 (2.0, 2.5)*	2.4 (2.2, 2.7)*	2.6 (2.3, 2.8)*	2.2 (1.9, 2.5)*
75 to 79	2.8 (2.5, 3.1)*	2.9 (2.6, 3.2)*	2.6 (2.3, 2.9)*	2.7 (2.3, 3.0)*	2.7 (2.4, 3.1)*	2.5 (2.1, 2.8)*
80 to 84	3.3 (3.0, 3.6)*	3.1 (2.9, 3.3)*	3.3 (3.0, 3.7)*	3.0 (2.7, 3.3)*	2.7 (2.5, 3.0)*	3.0 (2.7, 3.4)*
85 to 89	3.2 (3.0, 3.3)*	3.4 (3.2, 3.7)*	2.8 (2.6, 3.0)*	2.9 (2.8, 3.1)*	3.1 (2.9, 3.4)*	2.6 (2.4, 2.7)*
90 to 94	2.7 (2.6, 2.9)*	3.9 (3.5, 4.3)*	2.4 (2.3, 2.6)*	2.3 (2.2, 2.4)*	3.4 (3.0, 3.8)*	2.1 (1.9, 2.2)*
Total	2.3 (2.1, 2.5)*	2.6 (2.4, 2.9)*	1.9 (1.7, 2.1)*	2.3 (2.1, 2.4)*	2.5 (2.3, 2.8)*	1.9 (1.7, 2.0)*

Abbreviations. ASR: age-standardized rate; APC: annual percentage change.
* represents P < .05.

10%, and approximately 80–85% of patients have diseases that cannot be resected or metastasized.[2] The close parallelism between the incidence and mortality of pancreatic cancer reflects the nature of the fatal malignancy. Several modifiable risk factors, including obesity, type 2 diabetes, and tobacco use have been identified in pancreatic cancer.[3-5] Due to the low rates of early detection and poor prognosis, pancreatic cancer is a tremendous public health burden worldwide.

The incidence and mortality of pancreatic cancer vary across different regions, and the incidence of pancreatic cancer is 3- to 4-fold higher in developed countries.[6] Pancreatic cancer is projected to become the second leading cause of cancer death in the USA and the third leading cause of cancer death in the European Union.[7] In China, there were 116 291 newly diagnosed new cases and 110 390 deaths, both of which accounted for approximately 1 in 4 pancreatic cancer cases, and the number of new cases and deaths in China ranked first in the world.[7] Pancreatic cancer puts a heavy burden on the family and society, so there is an urgent need for comprehensive understanding of the epidemic trend of pancreatic cancer in China.

We conducted this study to investigate and characterize the temporal trends over 30 years based on Global Burden of Disease (GBD) 2019, and performed an age-period-cohort model (APCM) with an intrinsic estimator (IE) algorithm to analyze the independent effects of chronological age, time period, and birth cohort, to provide the data for medical policies and opinions in the future.

Materials and Methods

Data Source

The data on incident cases, deaths, incidence, and mortality were obtained from GBD 2019. Data are available at the GBD Data Tool repository and can be accessed at http://ghdx.healthdata.org/gbd-results-tool. Under the "single" tag, according to the research purpose, we can select indicators such as location, age, sex, year, and measure. The extracted data were downloaded and saved in "CSV" format. Data sorting and processing methods have been described in detail in previous studies.[8,9]

Statistical Analyses

The age-standardized rate (ASR) was used to estimate the trends. The ASR (per 100 000 population) is calculated by the direct method, which is the sum of the age-specific rates (ai, where i denotes the ith age class) and the number of persons (or weight) (wi) in the same age subgroup i of the chosen reference standard population, divided by the sum of standard population weights, that is

$$\text{ASR} = \frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} w_i} \times 100,000$$

We performed joinpoint regression analysis to calculate the annual percentage change (APC) and corresponding
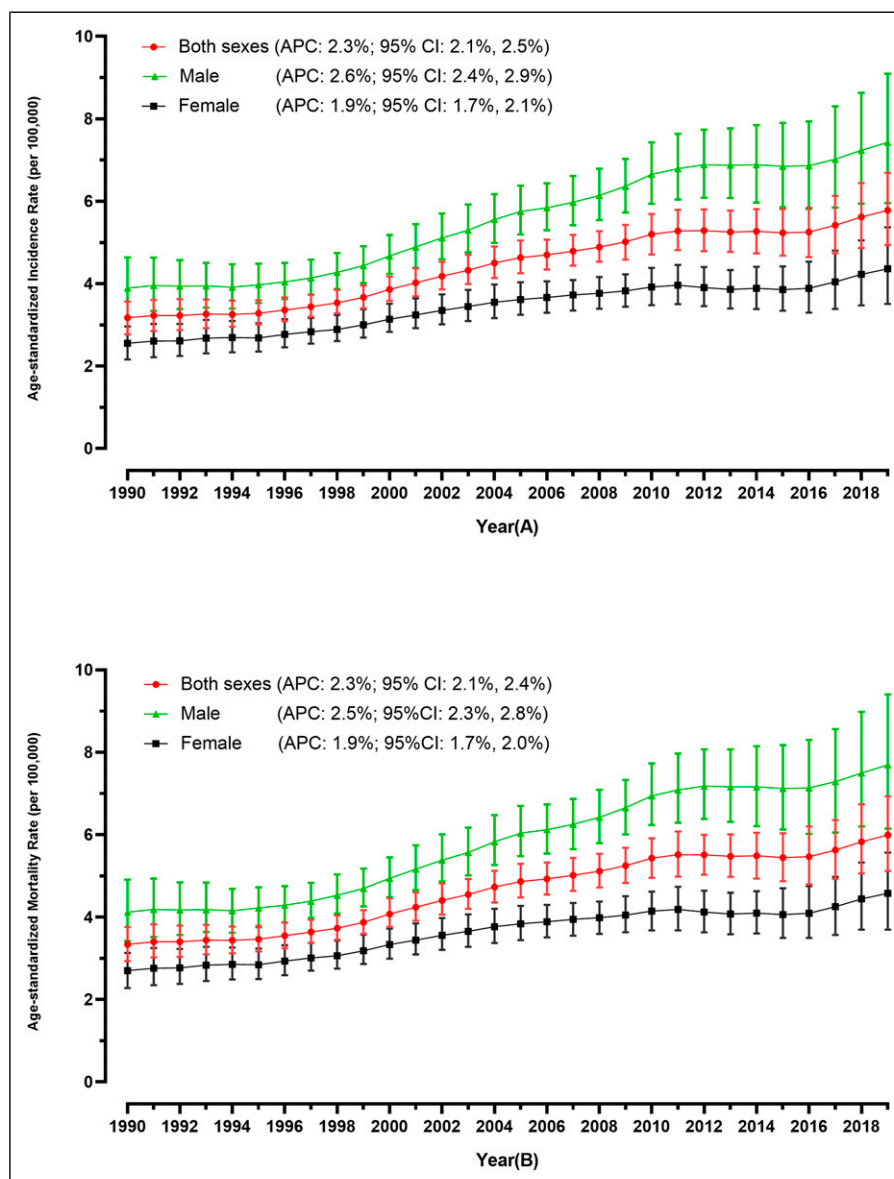
Figure 1. The APC in the ASRs for pancreatic cancer in China from 1990 to 2019. Note: APC: annual percentage change; ASR: age-standardized rate.

95% CIs, which assessed the magnitude and direction of trends over time for the rate using JoinPoint software (Version 4.7.0.0). The natural logarithm of ASRs as dependent variable (y) and calendar year as independent variable (x) were used to calculate trend data, which were fitted to the linear model: $y = \alpha + \beta x + \varepsilon$, ($\alpha$: constant term, β: regression coefficient, and ε: random error term). Annual percentage change was estimated using a regression coefficient and expressed as percentage: APC = $100 \times (e^{\hat{\beta}} - 1)$. When APC and lower CI limit were above zero, ASR showed an upward trend; otherwise, ASR showed a downward trend. We used the APCM to assess new cases and death risks experienced by the population in a particular year and the accumulation of health risks

since birth. The APCM contained the long age curve, Period rate ratios (Period RRs), and Cohort rate ratios (Cohort RRs), which reflected the effects of chronological age, time period, and birth cohort. The longitudinal age curve represents fitted longitudinal age-specific rates in cohorts adjusted for period deviations. Period rate ratios represent the ratio of age-specific rates in a period relative to the reference period. Cohort rate ratios represent the ratio of age-specific rates in a cohort relative to the reference cohort. Local drifts represent the APC in the expected age-specific rates over time. Net drift represents the APC of the expected age-adjusted rates over time. A general linear model was used to analyze the slope of the period/cohort RRs. The "apc" packages was used to
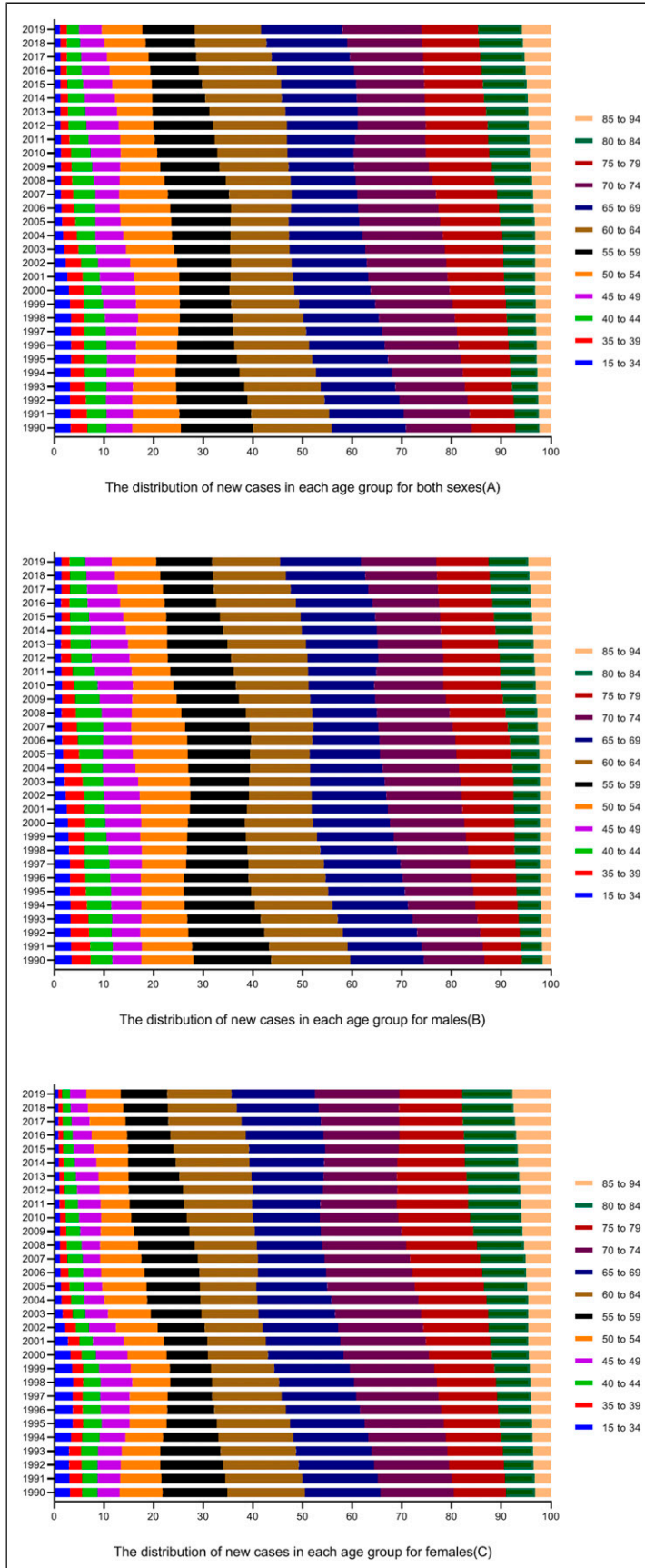
Figure 2. The proportion of incident cases of pancreatic cancer from 1990 to 2019.
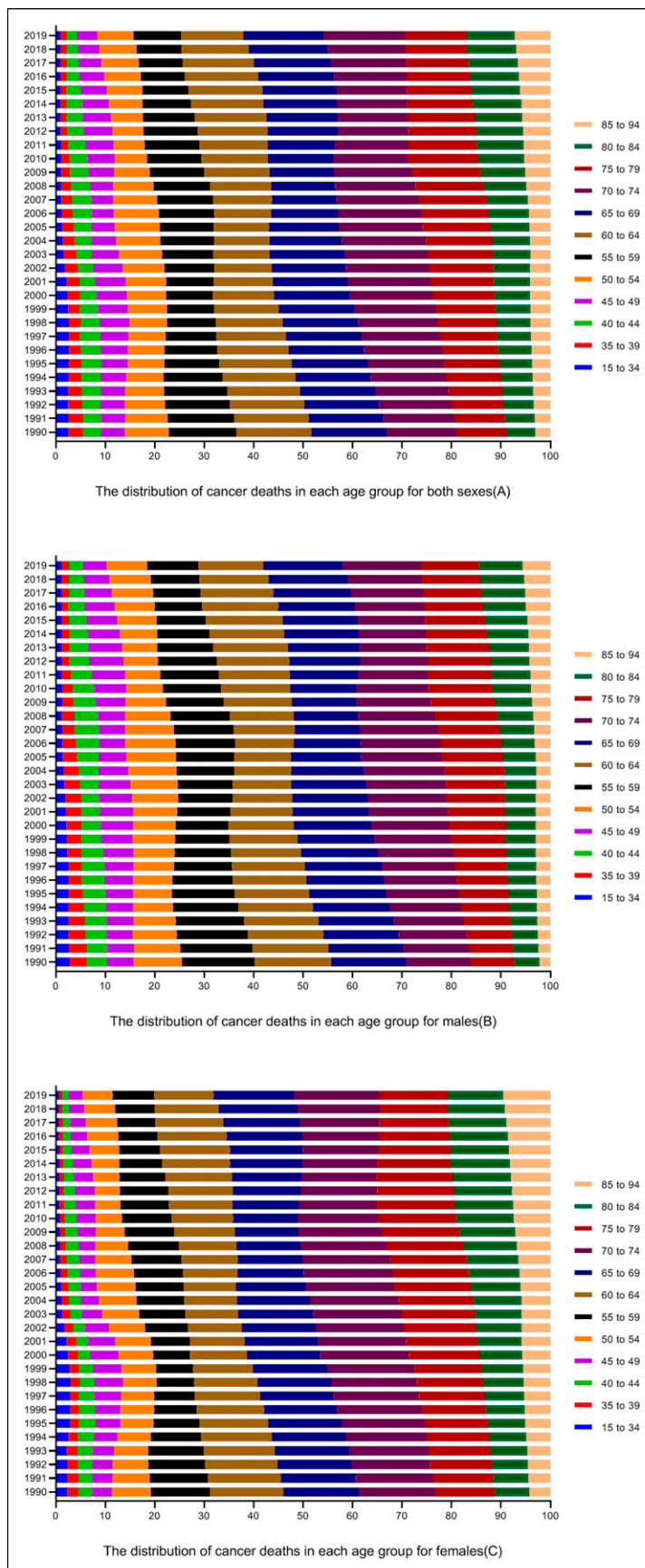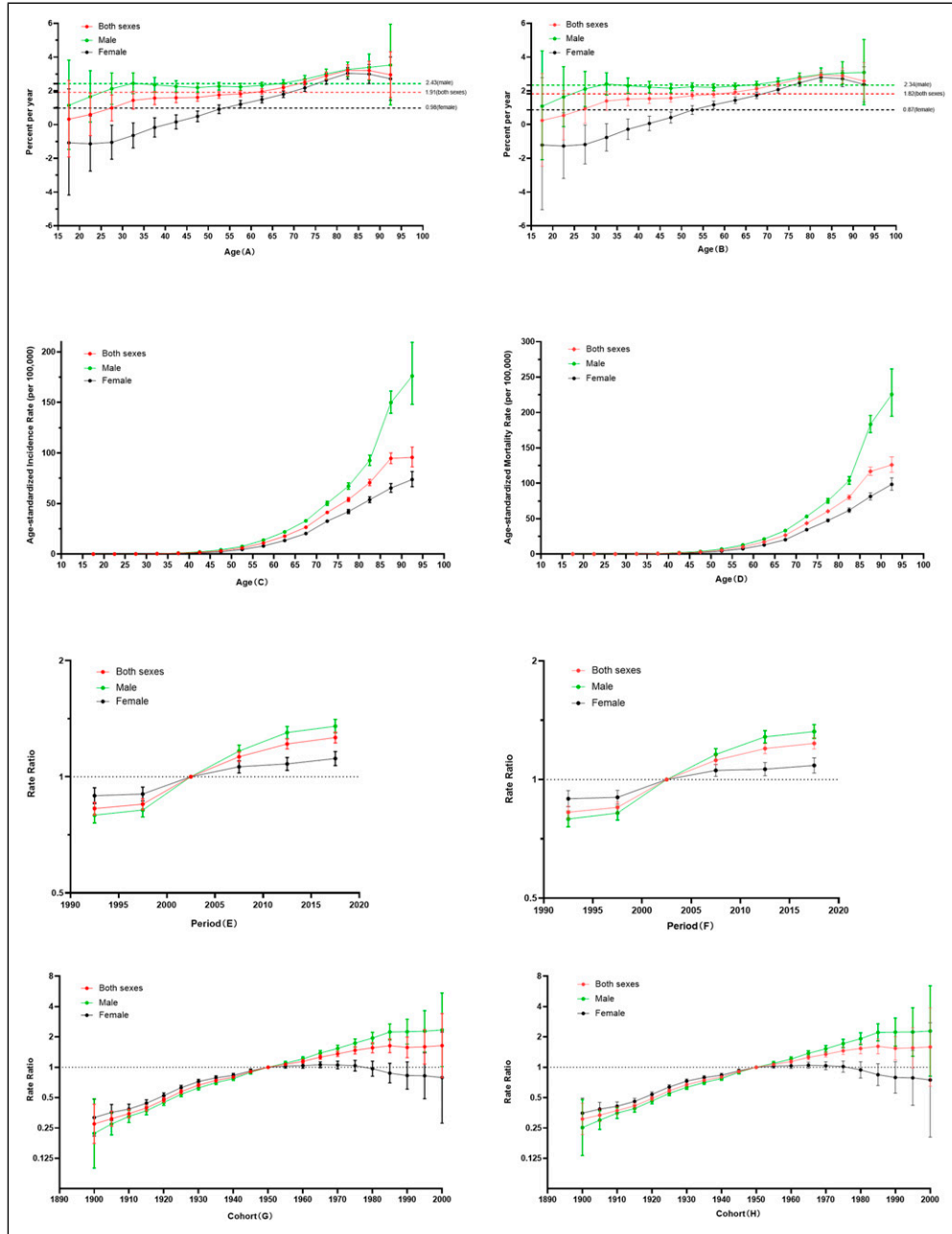
Figure 3. The proportion of cancer deaths of pancreatic cancer from 1990 to 2019.

Figure 4. The age-period-cohort results in the incidence and mortality of pancreatic cancer from 1990 to 2019.

perform the APCM in R statistical software (R version 3.5.1).

Results

1. The incident case/cancer death of pancreatic cancer and population coverage in China Between 1990 and 2019, there were 1 817 952 incident cases, including 1 103 184 males and 714 768 females. There were 1 854 761 cancer deaths, including 1 112 926 males and 741 835 females. The ratios of incident cases to

cancer deaths were 1.54 and 1.50, respectively. During the 30 years, the number of incident cases and cancer deaths increased by 329.40% and 333.05%, respectively. (Supplemental Material Table S1)

2. The trends of the incidence and mortality of pancreatic cancer from 1990 to 2019 As for the incidence rate, the age-standardized incidence rate (ASIR) of pancreatic cancer increased by 81.25% from 1990 to 2019 (APC: 2.3%; 95% CI: 2.1%, 2.5%), and the similar upward trend was observed

between males and females. Compared to females, the ASIR in men was higher, and the increment in men (APC: 2.6%; 95% CI: 2.4%, 2.9%) was also higher than that in women (APC: 1.9%; 95% CI: 1.7%, 2.1%). Compared to the incidence rate, a similar transition was observed in the mortality rate, the age-standardized mortality rate (ASMR) increased by 81.82% from 1990 to 2019 (APC: 2.3%; 95% CI: 2.1%, 2.4%), The detailed results are shown in Table 1 and Figure 1.

Overall, the incidence rates increased annually in the above 25 age groups. Although the upward trend was similar between males and females, the incidence rates increased from 20 to 24 age group in males and 40 to 44 years in females. We also found a similar transition in the mortality rate. The detailed results are presented in Table 1.

In terms of incident cases, the most common age group was 55–79 years, accounting for ~50% of all incident cases. The proportion of incident cases showed a slight decrease in the 15–39 age group and increased in the older-than-70 age groups during 1990–2017. The proportion of new cases was mainly in the 50–79 age group in males, while 55–84 years in females. (Figure 2) Compared to the incident case, a similar transition was observed for cancer death. (Figure 3)

3. The APCM analysis in the incidence and mortality of pancreatic cancer from 1990 to 2019

Figure 4A and 4B show the net and local drifts for the incidence and mortality of pancreatic cancer. The overall net drifts per year were 1.91% (95% CI, 1.74% to 2.08%) in both sexes, 2.43% (95% CI, 2.22% to 2.64%) in males and .98% (95% CI, .75% to 1.21%) in females. The local drifts in all age groups were above 0 in both sexes and males, while the local drifts in the 15–39 age groups were below 0 in females. The overall net drifts per year were 1.82% (95% CI, 1.64% to 2.00%) in both sexes, 2.33% (95% CI, 2.11% to 2.56%) in males and .87% (95% CI, .62% to 1.12%) in females. The changes in local drifts of mortality were similar in incidence.

Figure 4C and 4D show the longitudinal age curves for the incidence and mortality of pancreatic cancer. In the same birth cohort, both the incidence and mortality rates increased gradually with age, reaching their highest values in the 90–94 age group. Before 49 years of age, the incidence and mortality rates were lower than $5/10^5$, and similar trends were observed in men and women. Figure 4E and 4F show the trend of the estimated period RRs in the incidence and mortality of pancreatic cancer. The period RRs increased from 1990 to 2019, regardless of gender. Before 2002, the period RRs in males were lower than those in females, but after 2002, the period RRs in males were higher than those in females. Figure 4G and 4H show the trend of the estimated cohort RRs in the incidence and mortality of pancreatic cancer. Regardless of gender, the cohort RRs showed an upward trend before 1970

and fluctuated from 1975 to 2000. Before 1950, the cohort RRs in males were lower than those in females, but after 1950, the cohort RRs in males were higher than those in females.

Discussion

Our study showed that from 1990 to 2019, there was an approximately 4.3 times increase in incident cases and deaths from pancreatic cancer in both sexes from 1990 to 2019. Both the ASIR and ASMR significantly increased, and compared to GLOBOCAN 2020, the ASIR and ASMR in China were higher than the average levels in the world.[1] The higher rates and their upward trend may be mainly attributed to the aging population and environmental and behavioral changes in China during the past 30 years.[10] As the common risk factors for pancreatic cancer, the prevalence of overweight and diabetes in China has risen to 28.1% and 11.2%, respectively, and 28.1% of adults in China ever smoked.[11-13] A meta-analysis of 35 prospective cohort studies found that current and former smokers had 70% and 20% increased risk of pancreatic cancer.[14] In a meta-analysis conducted by the World Cancer Research Fund (WCRF), overweight was positively associated with the risk of pancreatic cancer (RR 1.10, 1.07–1.14), and diabetes was associated with a 1.5-fold to 2.5-fold higher risk of pancreatic cancer.[15,16]

We also found that the increasing amplitude, curve shape, and age constituent ratio in the incidence and mortality of pancreatic cancer were similar. This is mainly due to the lack of an effective early diagnosis and treatment of pancreatic cancer.[17] No suitable early diagnosis technology for pancreatic cancer leads to the fact that pancreatic cancer is found in an advanced stage and older state.[18] In addition, patients with pancreatic cancer have a poor response to chemotherapy,[19,20] and the 5-year survival rate of pancreatic cancer has only increased from 3% in 1970 to 5% at present.[21] Therefore, more research efforts should be made in the early diagnosis and treatment of pancreatic cancer, and improving early diagnosis rate and the survival rate of pancreatic cancer.

We performed APCM to analyze the independent effects of chronological age, time period, and birth cohort on the changes in the incidence and mortality of pancreatic cancer during the past 30 years. From the results of the overall net drifts and local drifts, we found that the burden of pancreatic cancer was still heavy in China and showed an upward trend in China. Local drifts in incidence and mortality rates increased with age. We also found that the longitudinal age curves increased with age in both the incidence and mortality rates. It reminded us that age is considered the most important risk factor in the development of pancreatic cancer.[22] This may be due to age-related decline in immunity and an increased risk of pancreatic cancer.[23]

With regards to sex, the local drifts of the incidence and mortality rates in males increased in each age group, while in females, it increased in the 40–94 age group. This demonstrates that pancreatic cancer is harmful to men regardless of

age. In the longitudinal age curves, the incidence and mortality rates in each age group were also higher in men than in women. Gender differences might be due to smoking, which has been identified as the main environmental risk factor of pancreatic cancer by the International Agency for Research on Cancer.[24] The prevalence of active smoking in males was 5 times higher than that in females, and active smoking contributed to 11–32% of all pancreatic cancer deaths.[15] As a social behavior, smoking among Chinese people is significant, especially in young and middle-aged male smokers. In China, the male smoking rates in all age groups were also higher than those in females.[12] Based on higher incidence and mortality rates in older groups and males, prevention and control strategies should focus on older age groups and males to achieve better control outcomes.

Since the 21st century, with the rapid progress of science and technology in China, the level of diagnosis and treatment of pancreatic cancer has improved, but the overall rising trend of incidence and mortality of pancreatic cancer has not changed; therefore, early diagnostic technology and good treatment technology are urgently needed to reduce the burden of pancreatic cancer.[25,26] From 1990 to 2019, the period RRs in the incidence and mortality consistently indicated an upward trend from 1990 to 2019, with no downward trend. The cohort RRs reflect variations in socioeconomic status or different risk factors in groups of individuals born in the same year or years. The cohort RRs in incidence and mortality showed an upward trend before 1975 and fluctuated after 1975. This stage was China's reform and opening up, and with the increase in people's income, health awareness had improved. A series of recommendations on healthy diet and regular exercise have been released, which will help reduce the burden of pancreatic cancer.[27-29] From the results of the period and cohort RRs, we should continue to strengthen health education for the population, increase the medical level, and improve early diagnosis and survival rate.

Our study has some limitations. First, the data extracted from the GBD 2019 were mainly from the Chinese surveillance data. Disease surveillance sites were set up under the social and economic conditions in each period, and the collected data were most likely to represent the incidence and mortality of cancer in China. The establishment and expansion of disease surveillance sites requires time to improve, which exists in any country or region. From 1990 to 2019, there were some changes in the quality and quantity of data collection, which might have had an impact on our results.[30] Global burden of disease collected data by the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement, which defines the best practices for synthesizing evidence from multiple sources to quantitatively describe past and current population health and its determinants.[31] These measures not only improved the quality of data collection but also made the data representative. Therefore, using GBD data is relatively objective and accurate for determining the trend of pancreatic cancer incidence and death in 30 years. Second,

the GBD database, which started in 1990, provided related data from 1990 to 2019, which was the largest time span in public data. The GBD database did not collect data before 1990, so we could not analyze the trend of pancreatic cancer before 1990. Third, some studies found that the incidence and mortality of pancreatic cancer in urban areas were higher than those in rural areas.[32,33] Unfortunately, the GBD database only provided the overall data of China, so we could not further analyze and compare the incidence and mortality of different regions in China.

In summary, there were significant increases in the incidence and mortality of pancreatic cancer in China between 1990 and 2019, and the incidence and mortality rates were higher in elderly and males. The disease burden of pancreatic cancer in China was still very serious. We hoped that our findings would provide a basis for future public health policies, which should continue to focus on the key population, improving health awareness, and improve early diagnosis and clinical treatment methods for reducing the disease burden of pancreatic cancer in China.

Supplemental material

Supplemental material for this article is available online.

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Supplementary Materials

Supplementary Material for the article is available online.

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