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# Disparities of birth cohort effects on pancreatic cancer incidence between the United States and urban China

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Available online xxx

**Background:** Pancreatic cancer has been associated with lifestyle factors, but few comparative studies were conducted among countries of different culture and lifestyle habits. This study compared the trends of pancreatic cancer incidence and birth cohort effects in the United States and urban China and explored the potential discrepancies of risk patterns.

**Materials and methods:** Age-standardized incidence rates (ASIRs) were calculated using data from national or regional cancer registries of the United States and two large cities of China (Shanghai, Hong Kong). The temporal trends of incidence were assessed by joinpoint regression. The effects of birth cohort and calendar period were identified through age—period—cohort modeling.

**Results:** The ASIR in the United States from 1976 to 2015 was 8.26/100 000, which was higher than that in Hong Kong (4.29/100 000) and Shanghai of China (6.63/100 000). Shanghai had lower incidence (4.41/100 000) in 1976-1980 but increased annually by 1.38% in males and 1.67% in females, with a sharper upward trend than the United States and Hong Kong. Males had higher risks than females, with a male-to-female ratio of 1.34, 1.44, and 1.37 in the United States, Hong Kong, and Shanghai, respectively. A significant and prominent increase in incidence rate was observed among successive generations in China particularly for Shanghai, but such a pattern was not apparent in the United States.

**Conclusions:** The differences in pancreatic cancer incidence by sex may be multi-factorial involving known risk factors like tobacco smoking and alcohol consumption. The significant birth cohort effects among recent and early generations in the Shanghai population were in line with a society in socioeconomic transition and adoption of Western lifestyle mainly including consumption of calorie-rich foods and physical inactivity. Differences in these risk patterns will have implications on health care efforts and policies for cancer control.

**Key words:** pancreatic cancer, incidence, age—period—cohort modeling, cohort effects, lifestyle factors

## INTRODUCTION

Pancreatic cancer is one of the most lethal cancers worldwide, with a 5-year survival rate of ∼10% in the United States and ∼7.2% in China.[1,2] According to the American Cancer Society, pancreatic cancer is projected to be the fourth leading cause of cancer-related deaths in the American population in 2021, accounting for 7.92% of cancer deaths.[3] A higher incidence and mortality rate of pancreatic cancer has long been observed in developed countries such as the United States, but in recent years a sharply increased rate has also been reported in developing countries like China with no signs of plateau.[4,5] Previous time trend studies on pancreatic cancer were restricted to one specific country or region, and there has been a lack of inter-geographical comparative studies to unfold the potential discrepancies of incidence rates between Western and Eastern countries and explain specific underlying reasons, which would guide further investigation. On the other hand, most of the pancreatic cancers are diagnosed at an advanced stage which are not amenable for curative surgery. With no effective cure being available for such an advanced disease, it impels continuous endeavors to identify novel risk factors and implement policy changes for primary prevention of pancreatic cancer worldwide.[6]

Lifestyle and environmental factors have been attributed to several cancers including pancreatic cancer.[7-9] Some of these have been associated with Western lifestyle which is linked to an increased risk of pancreatic cancer, including alcohol consumption, high-energy food intake, and obesity.[9-12]

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The opening up of China in the 1980s led to a rapid transition from the traditional Chinese lifestyle to an industrialized westernized lifestyle. This epidemiological transition is hypothesized to have contributed to the striking upward trend of pancreatic cancer incidence in Chinese cities, especially metropolises. If this hypothesis holds true, the time trend of pancreatic cancer incidence in urban Chinese settings (such as Shanghai and Hong Kong) would mirror that of the highly developed countries with a lag phase. This important topic has never been reported previously. Therefore, the aim of this study was to compare the time trends of pancreatic cancer incidence between the United States and the two major Chinese cities (Shanghai and Hong Kong) and examine how the time trend was influenced by the effects of birth cohort and calendar period over time. Understanding of discrepancies of risk patterns between the United States, Hong Kong, and Shanghai may enlighten useful insights for cancer control and prevention policies for pancreatic cancer in the United States and China. In addition, this knowledge may also have the potential to be generalizable for other diseases and regions undergoing different states of social and economic transition.[13]

## MATERIALS AND METHODS

### *Study population and data source*

The United States is a developed, high-income country. The incidence data of pancreatic cancer for the United States during the period 1976-2015 and the corresponding sex-specific mid-year population statistics were derived from the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (SEER). SEER 9 has nine registries including Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco—Oakland, Seattle—Puget Sound, and Utah, covering ∼9.5% of the American population. All SEER registries were obliged to meet the Gold Standard Registry Certification from the North American Association of Central Cancer Registries for completeness, accuracy, and timeliness of the data.[14]

Hong Kong is a special administrative region of China with a mixed culture of both East and West, which was governed by the UK until 1997. Hong Kong's incidence data for the period 1976-2015 were obtained from the Cancer Registry of Hong Kong's Hospital Authority, which is a population-based cancer registry covering all Hong Kong residents. All raw incidence data were validated by various cross-checking procedures and multiple quality control processes to assure good quality and high completeness of the cancer statistics presented.[15] Sex-specific mid-year population statistics in Hong Kong were derived from the government's Census and Statistics Department.

Shanghai is the first city in China that opened up to the world following the 'opening-up policy' in 1978, and has since experienced unprecedented economic development, resulting in a rapid transition from a traditional Chinese way of living to a westernized lifestyle. In Shanghai, the incidence data during 1976-2015 were obtained from the Shanghai Cancer Registry, which covers the residents of urban areas of Shanghai. All cancer incidence data were collected, processed, and reported by standard procedures to ensure the high completeness and accuracy and met the criteria of the Cancer Incidence in Five Continents series.[16] Age-specific end-year population statistics for the corresponding study period in Shanghai were obtained from the Shanghai Municipal Public Security Bureau, and the mid-year population statistics were estimated by taking the average of end-year population statistics from two consecutive years.

### *Statistical analyses*

We evaluated the annual age-standardized incidence rate (ASIR) for pancreatic cancer by the direct method using the world standard population published by the World Health Organization in 2001.[17] Joinpoint regression analysis was carried out to identify the turn points when linear trends of incidence changed. This method delineates changes in outcome trends by linking several different linear segments on a log scale at joinpoints. The analysis started with a minimum of zero joinpoint indicating a straight line and tests to determine whether one or more joinpoints were statistically significant and hence subsequent incorporation into the model.[18] Monte Carlo permutation method was used to test for significance.[19] In the final model, each joinpoint represents a significant turn point in trends. Once the line segments were fortified, the annual percentage change (APC) with 95% confidence interval (CI) was used to describe the trends in the model. For each population, the average APC (AAPC) for the entire study period was also calculated.

Age—period—cohort analysis based on Poisson regression was conducted to further identify the effects on incidence trends accounting for age at diagnosis (age), date of diagnosis (period), and date of birth (cohort).[20,21] Given that pancreatic cancer rarely presents in young persons under 40 years of age, only persons aged 40 years or above were included in the analysis to avoid statistical instability.[22] Incidence data were laid out in the form of a quinary—quinquennial table by 5-year age groups and 5-year cross-sections. Five submodels were obtained from the analysis, including age model, age—drift model, age—cohort model, age—period model, and age—period—cohort model. Age, calendar period, and birth cohort effects were derived from pairwise comparisons of the appropriate submodels using $\chi^2$ test.[20] The goodness of fit of the models was assessed by deviance. The significant changes in deviance ($\Delta$ Dev) indicated a good fit of the model.

Joinpoint regression model was implemented using Joinpoint Regression Program (version 4.8.0.1) developed by the National Cancer Institute of the United States.[23] Age—period—cohort analyses were carried out using 'Epi' package in R (version 4.0.3).[24] A two-sided $P$ value $<0.05$ was considered as statistically significant.

## RESULTS

### Overall pattern of incidence

During the period 1976-2015, a total of 114 670, 13 035, and 25 748 newly diagnosed cases of pancreatic cancer were recorded in the United States, Hong Kong, and Shanghai, respectively. Males had stably higher rates than females, with a male-to-female ratio of 1.34 (95% CI: 1.33-1.36), 1.44 (95% CI: 1.39-1.49), and 1.37 (95% CI: 1.34-1.41) for the United States, Hong Kong, and Shanghai, respectively (Table 1).

### Time trends of incidence

ASIR of pancreatic cancer in the American population were consistently higher than those in Shanghai and Hong Kong during the period 1976-2015 (Table 1 and Figure 1). In the American population, there were fluctuations in ASIR, with a slight decrease from 9.82 (males)/7.16 (females) in 1981-1985 to 9.00 (males)/6.82 (females) per 100 000 in 1991-1995, and then increased gradually to 10.25 (males)/7.88 (females) per 100 000 in 2011-2015. A steady upward trend was observed in the Hong Kong and Shanghai populations from the rate of 4.01 (males, Hong Kong)/2.88 (females, Hong Kong) and 5.15 (males, Shanghai)/3.77 (females, Shanghai) per 100 000 in 1976-1980 to 5.86 (males, Hong Kong)/4.27 (females, Hong Kong) and 8.94 (males, Shanghai)/6.75 (females, Shanghai) per 100 000 in 2011-2015, respectively. Overall, the incidence rates raised continuously with increasing age span among studied areas. The temporal variations were reflected in all age groups throughout the 40 years of the study period (Figure 1), although there was somewhat larger variation in Shanghai and Hong Kong.

These visual variations of secular trends of the ASIR and age-specific incidence rate were confirmed by calculating AAPCs and APCs stratified by sex (Table 2). In general, a significant increase in ASIR was observed in all study populations except for the American males, with the most rapid increase in Shanghai (males, AAPC = 1.38%, 95% CI: 0.91% to 1.86%; females, AAPC = 1.67%, 95% CI: 1.21% to 2.13%). When stratified analysis by sex was further carried out, there were geographic differences in the patterns of APC among studied subjects. Notably, the ASIR of the American males decreased before 1995 and increased afterward; in contrast, the ASIR of the American females increased until 1984, followed by a decline with a yearly rate of 0.71% before turning to rise after 1995. On the other hand, a rapid increase in ASIR was observed in both sexes in Shanghai during the period 1976-2004/2005, and the trend flattened afterward. For Hong Kong males and females, an annual upward trend of 0.72% and 0.86% was observed over the entire study period, respectively.

### Age, calendar period, and birth cohort effects

Table 3 presents significant net drift, period effect, and birth cohort effect for both sexes in the United States, Hong Kong, and Shanghai, except for Hong Kong males where the cohort effect on its incidence rate was not significant after adjustment for period. Given the notable changes in deviance (Δ Dev), birth cohort effects seemed to explain most of the changes in incidence in Shanghai. On the contrary, in the United States and Hong Kong, the changes in incidence were relatively more attributed to the calendar period effect; however, both the calendar period and birth cohort effects seemed inapparent in males and females in Hong Kong.

The age-specific incidence rate of pancreatic cancer by successive birth cohorts and the estimated age, period, and birth cohort effects by sex and region were also plotted (Figures 2 and 3; Supplementary Table S1, available at https://doi.org/10.1016/j.esmoop.2021.100240). In Shanghai, both males and females showed a striking increasing trend of incidence for the 'young generations' born after 1950 and the 'elder generations' born before 1930. However, a slightly downward trend was observed among persons born between 1930 and 1950. For the young generations, the incidence rate increased more rapidly in males than in females, whereas the trend reversed in the elderly generations. Such a pattern was also observed in Hong Kong, but it tended to be inapparent. However, in the United States, females had a consistent steeper increase of pancreatic cancer incidence than males in successive generations for the entire study period.

## DISCUSSION

A sharper upward trend in ASIR of pancreatic cancer was observed in Shanghai than in Hong Kong from 1976 to 2015. However, these rates were consistently lower than those in the United States, where the trend tended to plateau over a 40-year period. Overall, the ASIRs of pancreatic cancer among males in both the United States and urban China were higher than those among females, which was consistent with global patterns.[25]

Birth cohort effects reflect exposures in early life. If the increase in these exposures occurs in the population over time, it would lead to a progressively increased risk of pancreatic cancer in the successive birth cohorts. A notable and significantly increased risk of pancreatic cancer was observed in the later birth cohorts in Shanghai for the recent generations, suggesting that changes in lifestyle and environmental factors are likely to be involved. The significantly increasing cohort effects among Shanghai male and female populations are more likely to be genuine as the age—cohort model fitted better than the age—period model.

Western lifestyle factors, such as alcohol drinking, consumption of calorie-rich foods, physical inactivity, and obesity, have been suggested as the contributing risk factors for pancreatic cancer,[26] which may explain the upward trend of its incidence among Shanghai males and females. These clustering factors related to lifestyle may interfere with pancreatic cellular physiology and contribute to the carcinogenesis of pancreas.[9,11,27,28] The rapid economic transition and modernization of Shanghai over the last

**Table 1. Count and ASIR per 100 000 of pancreatic cancer by region and sex for all ages**

| | All | | Male | | Female | | Standardized relative ratio[a] |
|---|---|---|---|---|---|---|---|
| | Count | ASIR | Count | ASIR | Count | ASIR | |
| United States | | | | | | | |
| 1976-1980 | 9999 | 8.11 | 5267 | 10.11 | 4732 | 6.65 | 1.52 (1.46-1.58) |
| 1981-1985 | 11 244 | 8.26 | 5534 | 9.82 | 5710 | 7.16 | 1.37 (1.32-1.42) |
| 1986-1990 | 11 780 | 7.95 | 5731 | 9.32 | 6049 | 6.97 | 1.34 (1.29-1.39) |
| 1991-1995 | 12 616 | 7.72 | 6073 | 9.00 | 6543 | 6.82 | 1.32 (1.27-1.37) |
| 1996-2000 | 13 819 | 7.82 | 6770 | 9.19 | 7049 | 6.83 | 1.34 (1.30-1.39) |
| 2001-2005 | 15 519 | 8.13 | 7662 | 9.41 | 7857 | 7.17 | 1.31 (1.27-1.35) |
| 2006-2010 | 18 497 | 8.72 | 9230 | 10.05 | 9267 | 7.71 | 1.30 (1.27-1.34) |
| 2011-2015 | 21 196 | 8.93 | 10 781 | 10.25 | 10 415 | 7.88 | 1.30 (1.27-1.34) |
| Total | 114 670 | 8.26 | 57 048 | 9.68 | 57 622 | 7.21 | 1.34 (1.33-1.36) |
| Hong Kong | | | | | | | |
| 1976-1980 | 632 | 3.37 | 324 | 4.01 | 308 | 2.88 | 1.39 (1.19-1.63) |
| 1981-1985 | 954 | 4.15 | 519 | 5.10 | 435 | 3.39 | 1.50 (1.32-1.71) |
| 1986-1990 | 1161 | 4.22 | 643 | 5.08 | 518 | 3.48 | 1.46 (1.30-1.64) |
| 1991-1995 | 1154 | 3.60 | 649 | 4.39 | 505 | 2.92 | 1.50 (1.34-1.69) |
| 1996-2000 | 1657 | 4.24 | 913 | 5.05 | 744 | 3.54 | 1.42 (1.30-1.57) |
| 2001-2005 | 1954 | 4.27 | 1070 | 5.05 | 884 | 3.59 | 1.40 (1.29-1.54) |
| 2006-2010 | 2372 | 4.37 | 1331 | 5.33 | 1041 | 3.56 | 1.49 (1.38-1.63) |
| 2011-2015 | 3151 | 5.00 | 1699 | 5.86 | 1452 | 4.27 | 1.37 (1.28-1.47) |
| Total | 13 035 | 4.29 | 7148 | 5.15 | 5887 | 3.58 | 1.44 (1.39-1.49) |
| Shanghai | | | | | | | |
| 1976-1980 | 1325 | 4.41 | 724 | 5.15 | 601 | 3.77 | 1.37 (1.23-1.52) |
| 1981-1985 | 1815 | 5.19 | 1021 | 6.40 | 794 | 4.17 | 1.53 (1.40-1.68) |
| 1986-1990 | 2383 | 5.66 | 1331 | 6.89 | 1052 | 4.62 | 1.49 (1.38-1.62) |
| 1991-1995 | 2653 | 5.68 | 1449 | 6.69 | 1204 | 4.80 | 1.39 (1.29-1.50) |
| 1996-2000 | 3198 | 6.83 | 1680 | 7.98 | 1518 | 5.89 | 1.35 (1.26-1.45) |
| 2001-2005 | 3874 | 7.54 | 2068 | 8.92 | 1806 | 6.41 | 1.39 (1.30-1.48) |
| 2006-2010 | 4779 | 7.63 | 2503 | 8.82 | 2276 | 6.64 | 1.32 (1.26-1.41) |
| 2011-2015 | 5721 | 7.75 | 3002 | 8.94 | 2719 | 6.75 | 1.32 (1.26-1.39) |
| Total | 25 748 | 6.63 | 13 778 | 7.77 | 11 970 | 5.66 | 1.37 (1.34-1.41) |

ASIR, age-standardized incidence rate.
[a] The ratio of ASIR in males and females with 95% confidence interval. Females were considered as reference.

century has triggered the westernization of lifestyle across successive generations, with more pronounced effect on the more recent generations.[29] Such an increased risk in successive birth cohorts among the Shanghai population was observed in other gastrointestinal cancers including colorectal cancer that has also been associated with lifestyle factors.[30,31] We project that the birth cohort effects in recent generations of Shanghai may follow the footprints of the developed countries, where the effects become attenuated and even disappear in future generations as the socioeconomic transition has completed and stabilized, resembling the patterns seen in the United States and Hong Kong. In contrast, the slightly declining trend of pancreatic cancer incidence in generations born during the 1930s and 1940s may partially result from the caloric restriction in early life due to social unrest and conflict during the period of Japanese occupation from 1932 to 1945. Previous studies suggest that extreme population-level events, such as war or famine, may have an impact on cancer incidence.[32] An analysis among Norwegian women in 2002 demonstrated a decreased incidence of breast cancer during World War II, lending to the suggestion that caloric restriction is protective against some cancers.[33] Social unrest during the occupied period limited the access to fat, meat, or milk, leading to a substantial reduction in food availability and energy intake, which in turn was associated with a decreased cohort effect for the generation born between 1930 and 1950.[34] The progressive harmful effects in more recent cohorts and protective effects in early birth cohorts among the Shanghai population imply that low energy intake during growth years has beneficial influence on the development of pancreatic cancer.

Our study demonstrated a stabilized male-to-female ratio of 1.34-1.44 times for pancreatic cancer during the 40-year period from 1976 to 2021 among people of the United States and urban China. Despite little being known about the exact cellular mechanisms resulting in this observed difference between sexes, female hormones have been shown to play a protective role in pancreatic cancer. This was supported by evidence from the Malmo Diet and Cancer Study which showed that a lower risk of pancreatic cancer was associated with a lower age at menarche, which means an earlier burst of estrogen level that represents more exposure to estrogen throughout the reproductive lifespan. A protective effect was also seen with women being put on hormone replacement therapy.[35] A higher pancreatic cancer incidence in males could be explained by alcohol consumption, as more males than females are alcohol drinkers regardless of the nation or geographic location of the populations. An analysis by pooling 10 case-control studies demonstrated a positive association between the incidence of pancreatic cancer and heavy alcohol

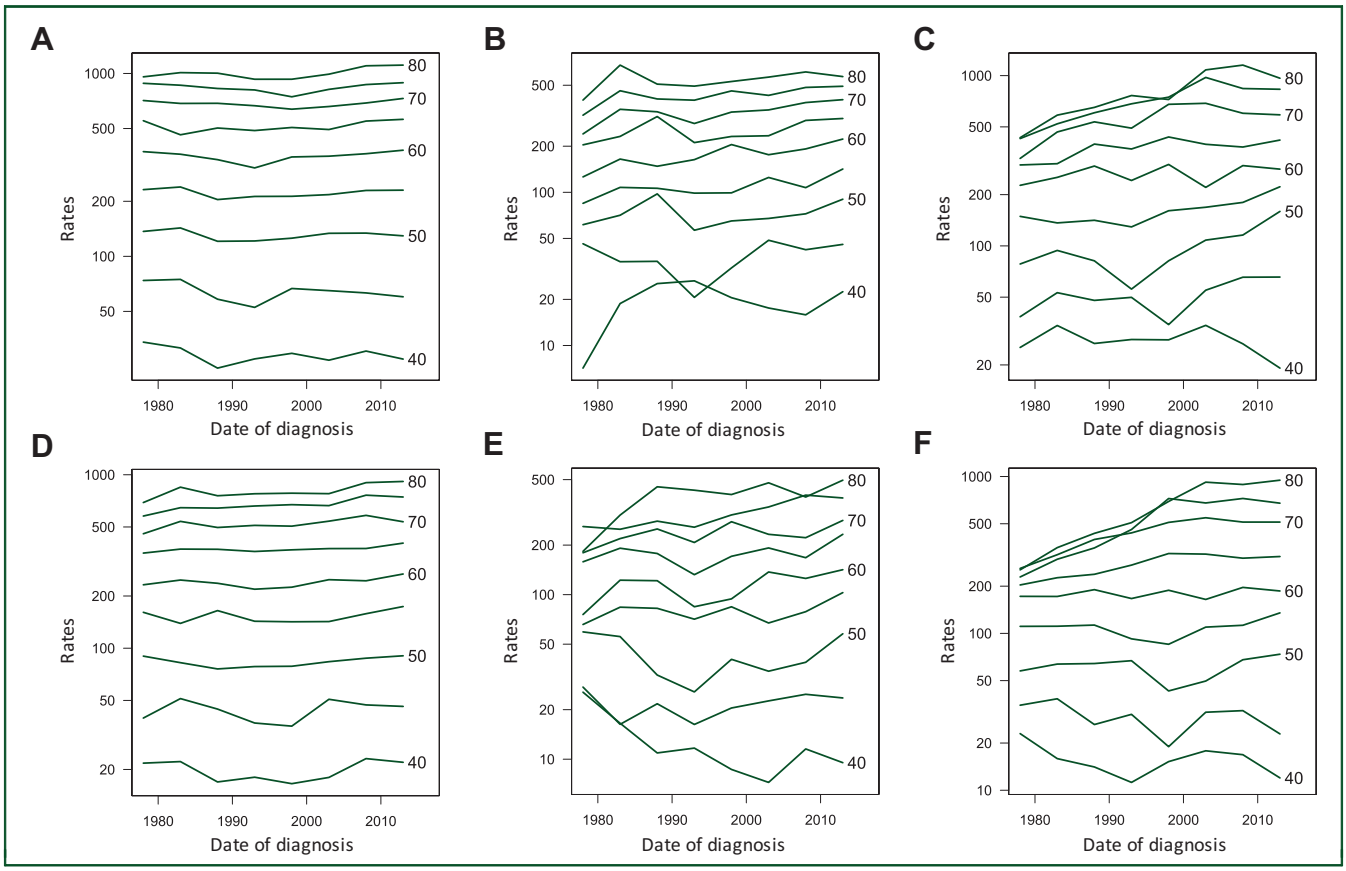


**Figure 1. Age-specific pancreatic cancer incidence rates (per 100 000) from 1976 to 2015 by region, sex, and calendar period.**
(A) Males in the United States. (B) Males in Hong Kong. (C) Males in Shanghai. (D) Females in the United States. (E) Females in Hong Kong. (F) Females in Shanghai.

**Table 2. APC and AAPC in pancreatic cancer incidence rates from 1976 to 2015 by region and sex for all ages**

| | Overall | Trend 1 | | Trend 2 | | Trend 3 | |
|---|---|---|---|---|---|---|---|
| | AAPC (95% CI), % | Period | AAPC (95% CI), % | Period | AAPC (95% CI), % | Period | AAPC (95% CI), % |
| United States | | | | | | | |
| Male | 0.05 (−0.09 to 0.19) | 1976-1995 | −0.75[a] (−0.98 to −0.52) | 1995-2015 | 0.81[a] (0.64 to 0.99) | — | — |
| Female | 0.56[a] (0.26 to 0.85) | 1976-1984 | 1.27[a] (0.23 to 2.33) | 1984-1995 | −0.71[a] (−1.39 to −0.03) | 1995-2015 | 0.97[a] (0.76 to 1.18) |
| Hong Kong | | | | | | | |
| Male | 0.72[a] (0.38 to 1.07) | 1976-2015 | 0.72[a] (0.38 to 1.07) | — | — | — | — |
| Female | 0.86[a] (0.50 to 1.23) | 1976-2015 | 0.86[a] (0.50 to 1.23) | — | — | — | — |
| Shanghai | | | | | | | |
| Male | 1.38[a] (0.91 to 1.86) | 1976-2004 | 1.95[a] (1.49 to 2.41) | 2004-2015 | −0.04 (−1.28 to 1.22) | — | — |
| Female | 1.67[a] (1.21 to 2.13) | 1976-2005 | 2.21[a] (1.79 to 2.63) | 2005-2015 | 0.11 (−1.26 to 1.51) | — | — |

AAPC, average annual percentage change; APC, annual percentage change; CI, confidence interval.
[a] Change in rate is statistically significantly different from zero at the $\alpha$ level of 0.05. Some cells are left blank as only the model that best fits the observed incidence is presented.

consumption (odds ratio: 1.46, 95% CI: 1.16-1.83).[12] Given that more males are exposed to tobacco smoking, alcohol consumption, and/or occupational exposures to known or suspected carcinogens than females in adulthood, the differences in pancreatic cancer incidence by sex may be multi-factorial involving the known risk factors.[9,36]

The major strength of our study is the long-term cancer incidence data with assured quality, and hence the secular patterns of incidence trend could be well identified. Cancer statistics of the United States and China may also be obtained from some other sources, such as SEER 18, SEER 21, or cancer registries of other Chinese cities, while these data may have better coverage of American and Chinese populations. However, the spans of these data were mostly <20 years, and thus may not sufficiently cover the earlier cohorts and represent the whole picture. Another strength is the low risk of recall or information bias in our study, as incidence data were collected prospectively and independently. On the other hand, there are also some limitations. Firstly, the population-based cancer incidence data derived from the registries may be underreported. Some patients with pancreatic cancer may be too ill to be diagnosed in a

**Table 3. Age–period–cohort models for pancreatic cancer incidence from 1976 to 2015 by region and sex, for those aged 40 years or above**

| Submodel | Goodness of fit | | | Model comparison | | | | |
|---|---|---|---|---|---|---|---|---|
| | Residual *df* | Residual deviance | *P* value | Comparison | Interpretation | Δ *df* | Δ Dev | *P* value |
| United States—male | | | | | | | | |
| 1. Age | 67 | 249.28 | * | | | | | |
| 2. Age–drift | 66 | 237.27 | * | 2 versus 1 | Trend (drift) | 1 | 12.01 | 0.001 |
| 3. Age–cohort | 63 | 225.95 | * | 3 versus 2 | Nonlinear cohort effect | 3 | 11.32 | 0.010 |
| 4. Age–period | 63 | 145.42 | * | 4 versus 2 | Nonlinear period effect | 3 | 91.84 | * |
| 5. Age–period–cohort | 60 | 135.76 | * | 5 versus 3 | Period effect adjusted for cohort | 3 | 90.19 | * |
| | | | | 5 versus 4 | Cohort effect adjusted for period | 3 | 9.67 | 0.022 |
| United States—female | | | | | | | | |
| 1. Age | 67 | 329.57 | * | | | | | |
| 2. Age–drift | 66 | 222.18 | * | 2 versus 1 | Trend (drift) | 1 | 107.39 | * |
| 3. Age–cohort | 63 | 215.97 | * | 3 versus 2 | Nonlinear cohort effect | 3 | 6.22 | 0.102 |
| 4. Age–period | 63 | 186.19 | * | 4 versus 2 | Nonlinear period effect | 3 | 36.00 | * |
| 5. Age–period–cohort | 60 | 164.18 | * | 5 versus 3 | Period effect adjusted for cohort | 3 | 51.79 | * |
| | | | | 5 versus 4 | Cohort effect adjusted for period | 3 | 22.01 | * |
| HK—male | | | | | | | | |
| 1. Age | 67 | 155.78 | * | | | | | |
| 2. Age–drift | 66 | 99.66 | 0.005 | 2 versus 1 | Trend (drift) | 1 | 56.12 | * |
| 3. Age–cohort | 63 | 98.52 | 0.003 | 3 versus 2 | Nonlinear cohort effect | 3 | 1.14 | 0.767 |
| 4. Age–period | 63 | 93.36 | 0.008 | 4 versus 2 | Nonlinear period effect | 3 | 6.29 | 0.098 |
| 5. Age–period–cohort | 60 | 93.21 | 0.004 | 5 versus 3 | Period effect adjusted for cohort | 3 | 5.31 | 0.151 |
| | | | | 5 versus 4 | Cohort effect adjusted for period | 3 | 0.16 | 0.984 |
| HK—female | | | | | | | | |
| 1. Age | 67 | 174.30 | * | | | | | |
| 2. Age–drift | 66 | 127.42 | * | 2 versus 1 | Trend (drift) | 1 | 46.88 | * |
| 3. Age–cohort | 63 | 123.21 | * | 3 versus 2 | Nonlinear cohort effect | 3 | 4.21 | 0.240 |
| 4. Age–period | 63 | 114.63 | * | 4 versus 2 | Nonlinear period effect | 3 | 12.80 | 0.005 |
| 5. Age–period–cohort | 60 | 100.67 | 0.001 | 5 versus 3 | Period effect adjusted for cohort | 3 | 22.54 | * |
| | | | | 5 versus 4 | Cohort effect adjusted for period | 3 | 13.95 | 0.003 |
| SH—male | | | | | | | | |
| . Age | 67 | 450.48 | * | | | | | |
| 2. Age–drift | 66 | 236.99 | * | 2 versus 1 | Trend (drift) | 1 | 213.50 | * |
| 3. Age–cohort | 63 | 134.59 | * | 3 versus 2 | Nonlinear cohort effect | 3 | 102.40 | * |
| 4. Age–period | 63 | 226.26 | * | 4 versus 2 | Nonlinear period effect | 3 | 10.73 | 0.013 |
| 5. Age–period–cohort | 60 | 127.38 | * | 5 versus 3 | Period effect adjusted for cohort | 3 | 7.20 | 0.066 |
| | | | | 5 versus 4 | Cohort effect adjusted for period | 3 | 98.87 | * |
| SH—female | | | | | | | | |
| 1. Age | 67 | 587.19 | * | | | | | |
| 2. Age–drift | 66 | 322.57 | * | 2 versus 1 | Trend (drift) | 1 | 264.62 | * |
| 3. Age–cohort | 63 | 109.44 | * | 3 versus 2 | Nonlinear cohort effect | 3 | 213.12 | * |
| 4. Age–period | 63 | 303.17 | * | 4 versus 2 | Nonlinear period effect | 3 | 19.40 | * |
| 5. Age–period–cohort | 60 | 91.68 | 0.005 | 5 versus 3 | Period effect adjusted for cohort | 3 | 17.77 | * |
| | | | | 5 versus 4 | Cohort effect adjusted for period | 3 | 211.49 | * |

Δ Dev, change in deviance; *df*, degree of freedom; HK, Hong Kong; SH, Shanghai.
* $P < 0.001$.

timely manner. Although their diagnoses may be finally confirmed by autopsy, the autopsy is rarely conducted for natural death in China, and thus the registries may only receive notifications from the medical practitioners without further verification. This reporting process may result in potential underreporting and underestimation of pancreatic cancer incidence.[37,38] Secondly, as there is geographic disparity in pancreatic cancer incidence, SEER 9, Hong Kong, and Shanghai may not be able to perfectly represent the whole United States and China. However, our study covers the longest time span ever reported in the literature.

## CONCLUSIONS

This comparative study between the United States and urban China over 40 years has revealed the patterns of pancreatic cancer incidence between the two countries and has demonstrated significant birth cohort effects among the recent and early generations of Shanghai population. This is consistent with a society in socioeconomic transition with an increasing adoption of Western lifestyle, particularly in relation to the level of high-energy food intake. Given a reasonable latency, the pancreatic cancer incidence in the Shanghai population is projected to peak before plateauing, following the footprints of the United States and Hong Kong. These patterns will have implications on health care efforts and policies for cancer control.

## ACKNOWLEDGEMENTS

We thank all the staff of Surveillance, Epidemiology, and End Results Program for their contributions to this research. We are also grateful for the help from the Hong Kong Cancer Registry and Shanghai Cancer Registry.

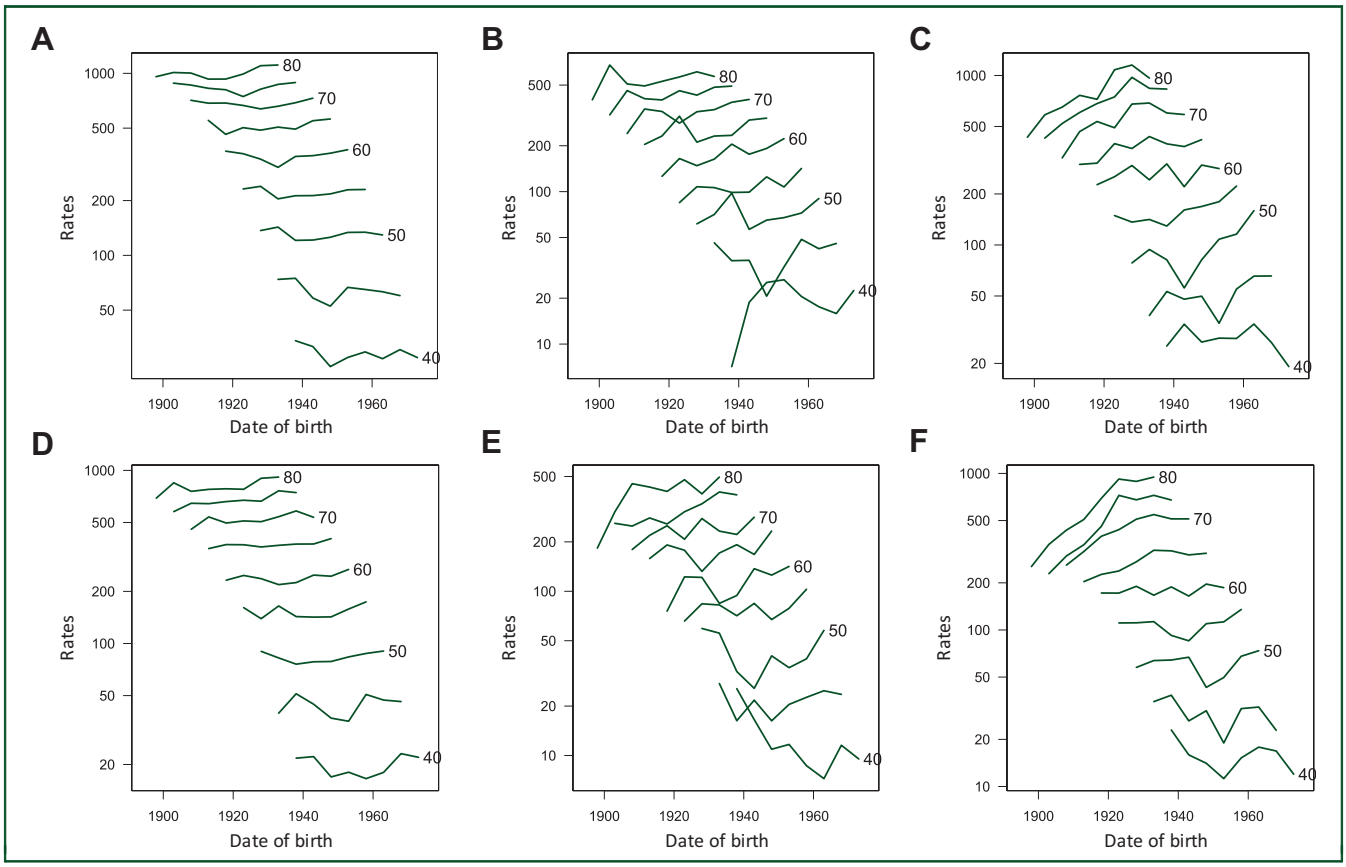


**Figure 2. Age-specific pancreatic cancer incidence rates (per 100 000) from 1976 to 2015 by region, sex, and birth cohort.**
(A) Males in the United States. (B) Males in Hong Kong. (C) Males in Shanghai. (D) Females in the United States. (E) Females in Hong Kong. (F) Females in Shanghai.

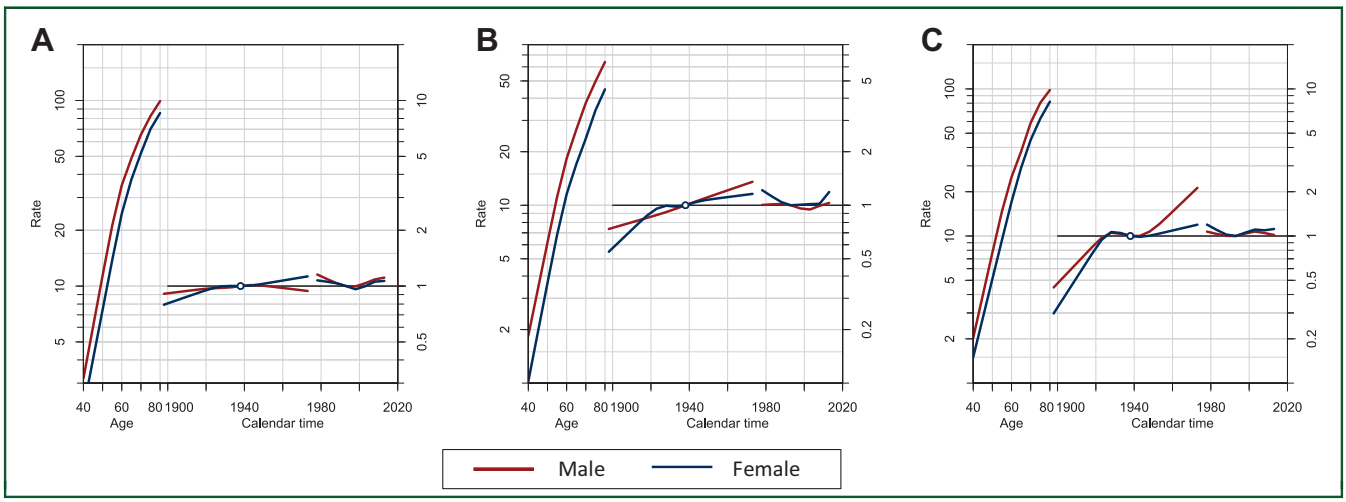


**Figure 3. Age, period, and cohort effects of pancreatic cancer incidence from 1976 to 2015 by region and sex.**
(A) United States. (B) Hong Kong. (C) Shanghai.

## FUNDING

None declared.

## DISCLOSURE

The authors have declared no conflicts of interest.

## DATA SHARING

The data of the United States underlying this article are available in Surveillance, Epidemiology, and End Results Program at https://seer.cancer.gov/, and can be accessed with SEER 9 Regs Custom Data, Nov 2019 Sub (1975-2017).

The data of Hong Kong underlying this article are available in Cancer Statistics Query Systems at https://www3.ha.org.hk/cancereg/allages.asp. The data of Shanghai underlying this article were provided by Shanghai Cancer Registry by permission. Data will be shared on a reasonable request to the corresponding author with permission of Shanghai Cancer Registry.

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