Stomach cancer epidemic in Chinese mainland: Current trends and future predictions

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Abstract

Background: China is one of the countries with the highest burdens of stomach cancer. The objective of this study was to analyze long-term trends in the incidence and mortality of stomach cancer in Chinese mainland from 1990 to 2019 and to make projections until 2030.

Methods: Data on stomach cancer were extracted from the Global Burden of Diseases Study 2019. Population data were extracted from the Global Burden of Diseases Study 2019 and World Population Prospects 2019. An age–period–cohort framework and decomposition analysis were used in this study.

Results: The net drift for the incidence of stomach cancer was 0.2% (95% confidence interval [CI]: 0, 0.4%) per year for men and –1.8% (95% CI: –2.0%, –1.6%) for women. The net drift for mortality was –1.6% (95% CI: –1.8%, –1.3%) per year for men and –3.3% (95% CI: –3.5%, –3.1%) for women. In the last 10–15 years, the risk of stomach cancer occurrence and death has continued to decline for both sexes. Regarding birth cohorts, although the risk of stomach cancer death decreased in general among women and men born after 1920, the risk of occurrence increased in recent birth cohorts (men born after 1970 and women born after 1985). It is expected that the age-standardized incidence will increase among men and decrease among women, and age-standardized mortality will decrease for both sexes. The largest contributor to the projected increase in incident cases and deaths is population aging, and elderly individuals are projected to have an increased proportion of occurrence and death.

Conclusions: In the past three decades, the incidence of stomach cancer among men has increased in Chinese mainland, and this trend is projected to continue. Aging will be the main contributor to future increased stomach cancer occurrence and deaths. To reduce the health impact of stomach cancer, more efforts are needed.

Keywords: Stomach cancer; Incidence; Mortality; Stomach neoplasms; Gastric cancer; Health burden

Introduction

Over the last few decades, the incidence and mortality rate of stomach cancer have declined in most populations.[1,2] As the country with the largest number of incident cases and deaths of stomach cancer worldwide (nearly half of the global incident cases of stomach cancer in 2017),[2] the decline in the incidence of stomach cancer in China has been relatively low compared to other regions of the world in recent decades.[2]

Previous studies evaluated the long-term trend of stomach cancer mortality in China before 2015, and they also conducted comparative analysis on the incidence of stomach cancer in urban and rural areas,[3,4] which provided important information to understand the health burden of stomach cancer in China. Considering existing evidence that stomach cancer incidence increased among young adults in some countries and may reverse the overall decline in stomach cancer incidence,[5,6] a detailed analysis of the potential effects in the long-term trend (such as age, period, and cohort effects) and further prediction of the future burden after considering these effects are needed.

To assess the long-term trend of stomach cancer in Chinese mainland and analyze the potential effects in the trend, age–period–cohort (APC) framework was used in this study. To better understand the disease burden, the future incidence and mortality of stomach cancer and the contributors (population growth, population aging,

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and changes in the epidemic) to these changes were predicted.

Methods

Ethical approval

The Global Burden of Disease (GBD) study uses identified, aggregated data. Therefore, a waiver of informed consent was reviewed and approved by the University of Washington Institutional Review Board.

Data sources

Stomach cancer incidence and death information was extracted from the GBD Study 2019.[7] GBD 2019 used all available up-to-date sources of epidemiological data to provide a comparative assessment of 369 diseases and injuries by sex and age group for 204 countries and territories.[7] Four data sources were used to assess the burden of stomach cancer in Chinese mainland: the disease registry (China Cancer Registry Annual Report), national survey (China Health and Retirement Longitudinal Study), the scientific literature, and vital records. A detailed description of these data sources can be found in Supplementary Table 1, http://links.lww.com/CM9/B867. In China, cancer diagnoses are reported to local cancer registries from multiple sources, including local hospitals, community health centers, the New Rural Cooperative Medical Scheme, and the Urban Resident Basic Medical Insurance program. The quality of the data submitted to each local registry is checked and evaluated by the National Central Cancer Registry of China.[8] The cancer registry covered 598 million people in 2020.[9] The China Health and Retirement Longitudinal Study is a nationally representative longitudinal survey[10] that provides further insight into the burden of stomach cancer in China. The GBD cause of death ensemble modeling tool was used to estimate cause-specific mortality, and the Bayesian meta-regression method was used to assess the incidence of nonfatal outcomes.[11] For this study, stomach cancer was defined as invasive neoplasms of the stomach (International Classification of Diseases 10th revision codes: C16-C16.9, D00.2, D13.1, and D37.1).[12] The GBD 2019 age-standardized population[13] was used to age-standardize the incidence and mortality of stomach cancer [Supplementary Table 2, http://links.lww.com/CM9/B867].

Population data were extracted from two resources. To analyze the potential age, period, and cohort effects, the population in Chinese mainland estimated by GBD was used. For projection of the future burden of stomach cancer, the population estimated and predicted by the United Nations World Population Prospects 2019 was used.

Statistical analysis

We used an APC model to assess the temporal trends of stomach cancer incidence and mortality. APC analysis can help understand time-varying elements in epidemiology and discerns three types of time-varying phenomena: age, period, and cohort effects. The following functions were estimated by using the APC model: net drift, which represents the annual percent change in the expected age-adjusted incidence and mortality rate of stomach cancer over time; local drift, which represents the annual percent change in the expected age-specific incidence and mortality rate of stomach cancer over time; the longitudinal age curve, which indicates the expected age-specific stomach cancer incidence and mortality rate in a reference cohort adjusted for period effects; and the period (or cohort) rate ratios (RRs), which represent the period (or cohort) effect and reflect the risk of incidence and deaths of stomach cancer at a specific period (or in a specific cohort) to the reference period (or cohort).[14] Details about this model can be found in the supplementary text, http://links.lww.com/CM9/B867.

To conduct APC analysis, we arranged the incidence data, death data, and population data into consecutive 5-year periods from 1990–1994 to 2015–2019. This included 14 consecutive 5-year age intervals from 20–24 years to 85–89 years. We classified 19 consecutive birth cohorts, including those born from 1905–1909 to 1995–1999. The median age group, period, and birth cohort were used as references. The American National Cancer Institute APC web tool (Biostatistics Branch, National Cancer Institute, Bethesda, MD, USA)[15] was used to fit the APC model. Wald chi-square tests were used to determine the significance of estimable parameters. When the *P*-value was less than 0.05, the difference was statistically significant.

We used Bayesian APC methods to predict the future incidence and mortality of stomach cancer. Bayesian APC models are particularly useful to project future cancer burden, as they involve no parametric assumptions.[16] In this study, age-standardized incidence and mortality were projected to reflect the future burden of stomach cancer. To prepare for the decomposition analysis, we also projected age-specific incident cases and deaths in the future. To conduct Bayesian APC analysis, incident cases and deaths from 15–19 years to 90–94 years according to the age interval of 5 years from 1990 to 2019 were extracted. Population data were extracted from similar consecutive five-year age groups from 1990 to 2030. The R (Version 4.2.2; R Foundation for Statistical Computing, Vienna, Austria) package "BAPC" was used to fit the Bayesian APC model.[16] Details about Bayesian APC models can be found in the supplementary text, http://links.lww.com/CM9/B867.

To help understand the factors associated with the changes in the absolute number of incidents and deaths of stomach cancer in the future, we conducted a decomposition analysis.[17] Projected data from Bayesian APC models from 2019 and 2030 were extracted for the fitting decomposition method. This decomposition analysis decomposes differences in the total number of incidents or deaths into three components: population size, age structure of the population, and age-specific incidence/mortality rate change.[17,18] Details about the decomposition analysis can be found in Supplementary Text, http://links.lww.com/CM9/B867.

Results

Annual percent changes in stomach cancer incidence and mortality

Net drift represents the annual percent change in the expected age-adjusted rates over time. The net drift values for stomach cancer incidence were 0.2% (95% confidence interval [CI]: 0, 0.4%) for men and –1.8% (95% CI: –2.0%, –1.6%) for women. The local drift represents the annual percent change in the expected age-adjusted rates over time for each age group. The local drift values were higher than 0 for men aged 20–34 years and 80–89 years (significant P <0.05), indicating an increase in the incidence of stomach cancer in these age groups over the past 30 years. The local drift values were lower than 0 for men aged 45–59 years and women aged 25–84 years [Figure 1A and Supplementary Table 3, http://links.lww.com/CM9/B867], showing a decrease in the incidence of stomach cancer in these age groups over the past 30 years.

The net drift for stomach cancer mortality was –1.6% (95% CI: –1.8%, –1.3%) for men and –3.3% (95% CI: –3.5%, –3.1%) for women. The local drift values for men aged 30–84 years and women aged 20–89 years were lower than 0 (P <0.05), indicating a decrease in mortality in these age groups over the past 30 years [Figure 1B and Supplementary Table 3, http://links.lww.com/CM9/B867].

Longitudinal age curves of stomach cancer incidence and mortality

The longitudinal age curve shows the expected age-specific incidence [Figure 2A] and mortality [Figure 2B] in the reference cohort after adjusting for period effects. In the same birth cohort, the incidence of stomach cancer was the lowest in the age group of 20–24 years and increased rapidly with age. The incidence was higher among men than among women in the same age group (P <0.05) and increased more rapidly with age among men than among women [Figure 2A and Supplementary Table 4, http://links.lww.com/CM9/B867].

The longitudinal age curve trend for mortality is similar to that for incidence. In the same birth cohort, the mortality of stomach cancer was the lowest in the age group of 20–24 years and increased monotonously with age for both sexes. In the same age group, the mortality rate of stomach cancer was higher among men than among women (P <0.05) [Figure 2B and Supplementary Table 4, http://links.lww.com/CM9/B867].

Period and cohort effect of stomach cancer incidence and mortality

As shown in Supplementary Table 5, http://links.lww.com/CM9/B867, period RRs were statistically significant for both sexes (P <0.05). Figure 3 and Supplementary Table 6, http://links.lww.com/CM9/B867 show the period RRs of stomach cancer occurrence among women and men. For incidence, the period RRs of stomach cancer continued to decline in the most recent periods (2005–2009 to 2015–2019 for men and 2000–2004 to 2015–2019 for women) [Figure 3A]. For mortality, a downward trend in period RRs was observed in recent periods (2000–2004 to 2015–2019 for men and women) [Figure 3B].

According to the results of the Wald test, cohort RRs were statistically significant (P <0.05) [Supplementary Table 6, http://links.lww.com/CM9/B867]. Figure 4 and

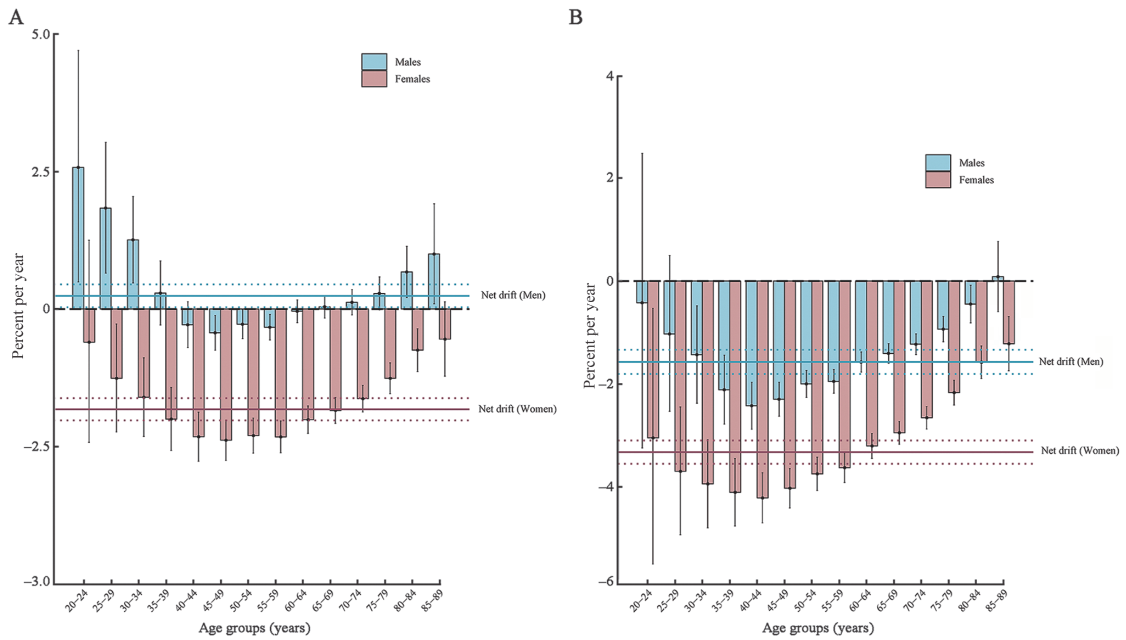

Figure 1: Net drift and local drift values for stomach cancer incidence (A) and mortality (B) in Chinese mainland. Net drift, annual percent change in the expected age-adjusted stomach cancer incidence and mortality over time. Local drift, age group-specific annual percent change in stomach cancer incidence and mortality. The long horizontal solid line indicates the net drift value, and the dashed line indicates its corresponding 95% CI. Vertical error bars indicate the corresponding 95% CI for local drift. Values below 0 indicate reductions in age-adjusted stomach cancer incidence and mortality during the study period. CI: Confidence interval.

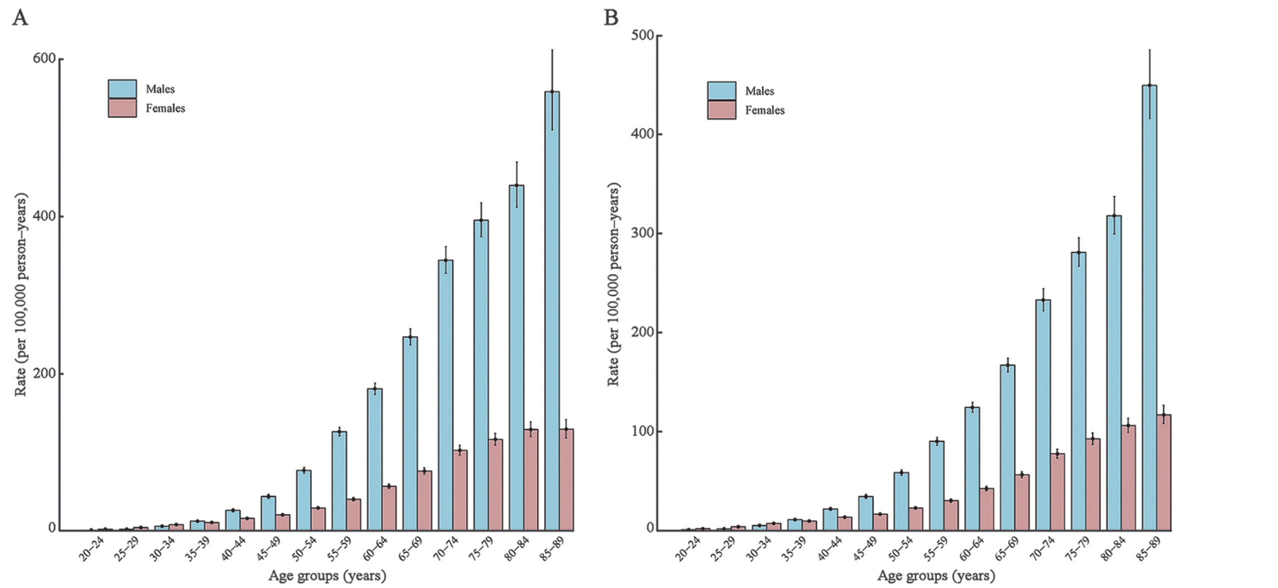

Figure 2: Longitudinal age curves of stomach cancer incidence (A) and mortality (B) in Chinese mainland. Fitted longitudinal age-specific rates of stomach cancer incidence/mortality (per 100,000 person-years) and the corresponding 95% CIs (some of them were too narrow to show in the figure). CI: Confidence interval.

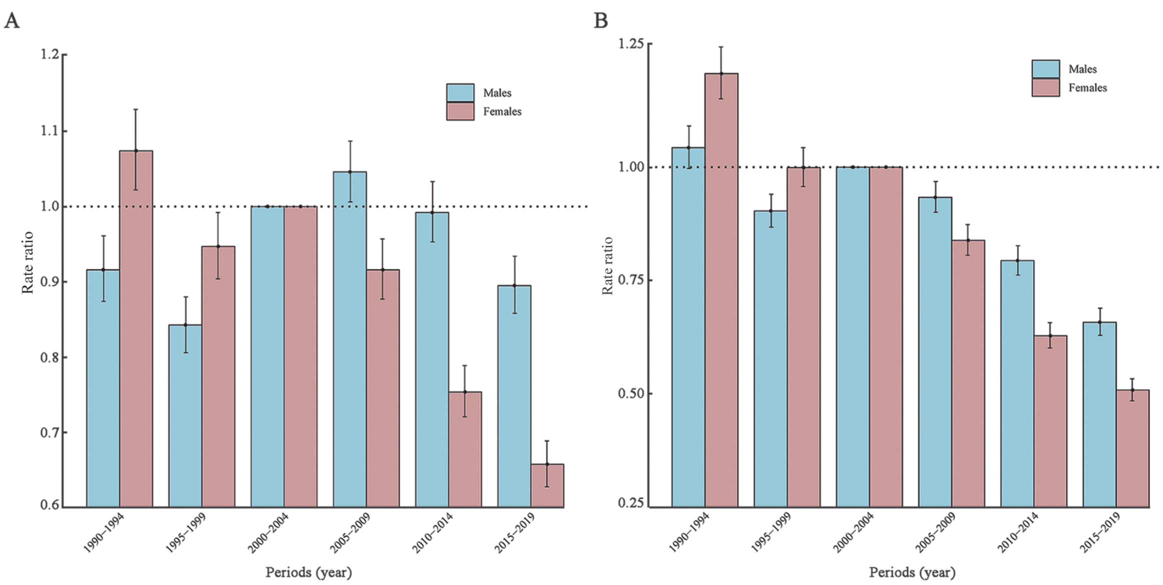

Figure 3: Period rate ratios of stomach cancer incidence (A) and mortality (B) by sex in Chinese mainland. Period rate ratios, which indicate the period effect, reflect the risk of incidence and deaths due to stomach cancer in a specific period. Period rate ratios were calculated as the ratio of age-specific rates in each period relative to the reference period (2000–2004). Vertical error bars indicate the corresponding 95% CIs. CI: Confidence interval.

Supplementary Table 7, http://links.lww.com/CM9/B867 show cohort RRs for stomach cancer for both sexes. Although the risk of stomach cancer death decreased in general among women and men born after 1920, the risk of occurrence increased in recent birth cohorts (men born after 1970 and women born after 1985) [Figure 4].

Projected future incidence of and mortality due to stomach cancer

Supplementary Figure 1, http://links.lww.com/CM9/B867 shows the prediction of the age-standardized incidence [Supplementary Figure 1A, http://links.lww.com/CM9/B867] and mortality [Supplementary Figure 1B, http://links.lww.com/CM9/B867] of stomach cancer in Chinese mainland (people aged 15–94 years). In 2019, the age-standardized incidence of stomach cancer was 50.4 (95% CI: 50.3, 50.9) per 100,000 people for men and 17.0 (95% CI: 16.9, 17.1) per 100,000 people for women. By 2030, it is expected that the age-standardized incidence will increase to 54.1 (95% CI: 11.8, 96.5) per 100,000 people (an increase of 7.4%) for men and decrease to 15.8 (95% CI: 7.6, 24.0) per 100,000 people (a decrease of 7.2%) for women [Supplementary Figure 1A, http://links.lww.com/CM9/B867].

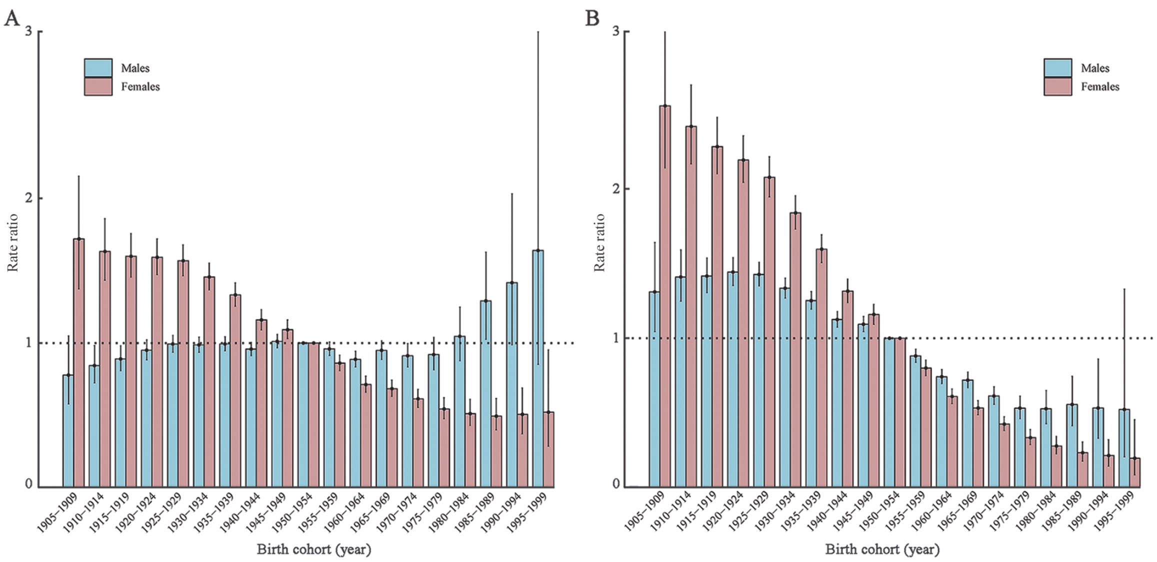

Figure 4: Cohort rate ratios of stomach cancer incidence (A) and mortality (B) by sex in Chinese mainland. The cohort rate ratios, which represent the cohort effect, reflect the risk of incidence and deaths due to stomach cancer in a specific cohort. Cohort rate ratios were calculated as the ratio of age-specific rates in each birth cohort relative to the reference cohort (birth cohort 1950–1954). Vertical error bars indicate the corresponding 95% CIs. CI: Confidence interval.

In 2019, the age-standardized mortality rate of stomach cancer was 49.1 (95% CI: 48.9, 49.3) per 100,000 people for men and 18.5 (95% CI: 18.4, 18.6) per 100,000 people for women. By 2030, it is expected that the age-standardized mortality rate will decline to 41.3 (95% CI: 8.0, 74.6) per 100,000 people (a decrease of 16.0%) for men and 14.3 (95% CI: 6.3, 22.3) per 100,000 people (a decrease of 22.6%) for women [Supplementary Figure 1B, http://links.lww.com/CM9/B867].

The incident cases of stomach cancer and deaths will increase from 2019 to 2030, and the largest contributor to these increases is aging [Figure 5].

Figure 6 shows the trends in the age proportion of stomach cancer occurrence and death. This study showed that older adults will have an increasing proportion of stomach cancer occurrence [Figure 6A] and death [Figure 6B].

Discussion

This study analyzed the long-term trends of stomach cancer incidence and mortality in China and assessed the potential age, period, and cohort effects with these trends. Our results showed that the incidence of stomach cancer has increased among men and decreased among women in the past 30 years, and the mortality rates declined for both sexes. A favorable period effect was found in both stomach cancer incidence and mortality in recent periods (the risk of stomach cancer incidence and death decreased in the last 10–15 years). Regarding birth cohorts, although the risk of stomach cancer death decreased in general among women and men born after 1920, stomach cancer incidence increased in recent birth cohorts (men born after 1970 and women born after 1985). It is expected that mortality due to stomach cancer will continue to decrease for both sexes, and the incidence will decrease among women but increase among men. Population

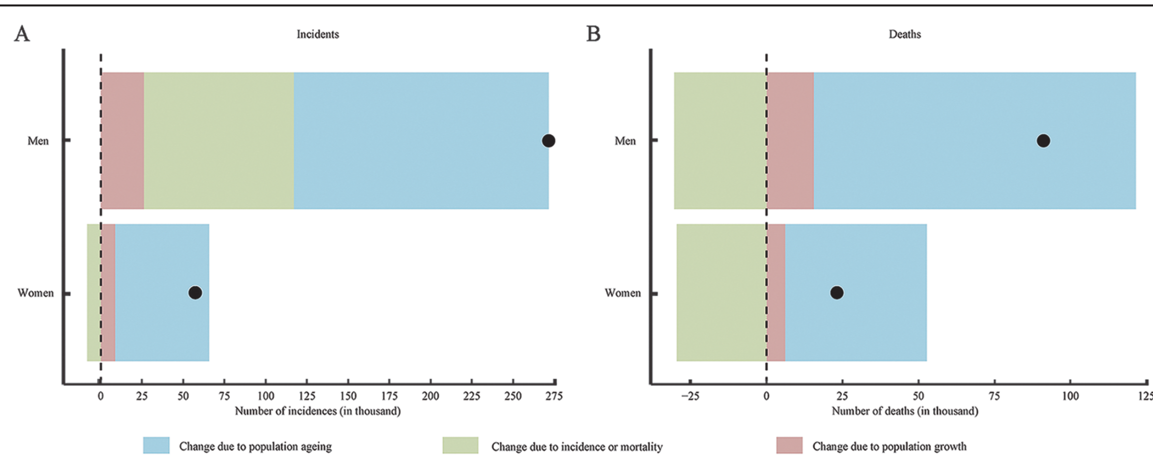

Figure 5: Changes in stomach cancer incidence (A) and deaths (B) associated with population aging, population growth, and incidence/mortality changes from 2019 to 2030. Decomposition was conducted using 2019 as the reference. The dark point indicates the changes in total incidence and deaths among people aged 15–94 years from 2019 to 2030.

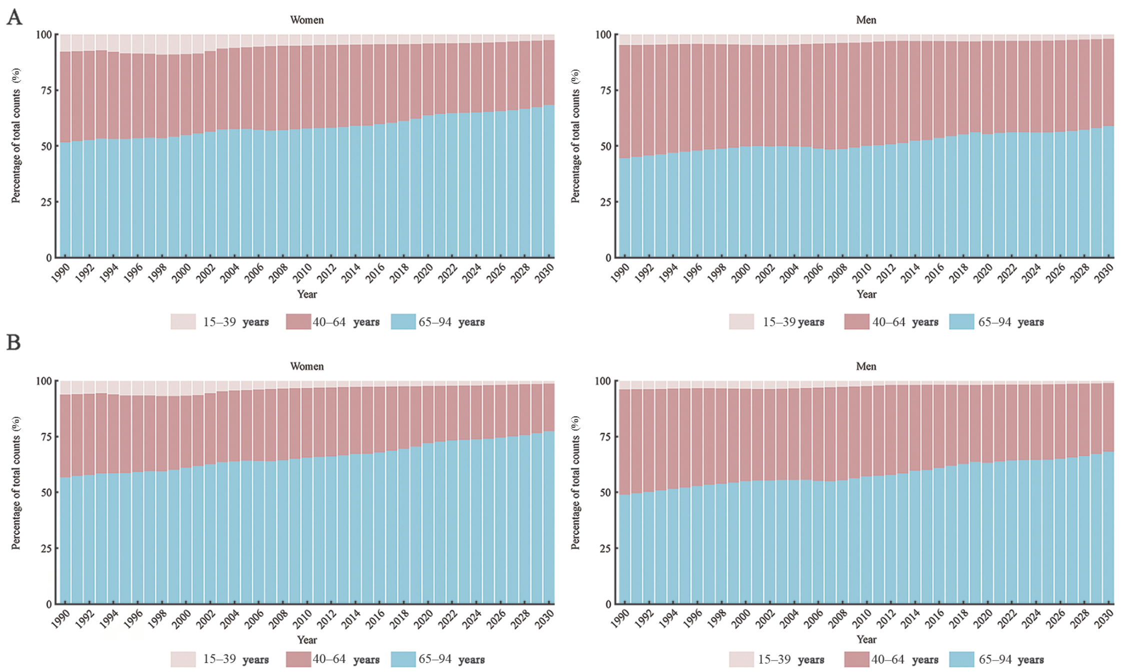

Figure 6: Percentage of modeled and projected stomach cancer incidence (A) and deaths (B) in three age groups (15–39, 40–64, and 65–94 years). The past and projected trends of stomach cancer incidence and deaths were extracted from the results from the Bayesian APC method. APC: Age–period–cohort.

aging will be the main contributor to future increases in stomach cancer incidence and deaths, and elderly people are projected to have an increased proportion of stomach cancer incidence and deaths.

In the past few decades, due to the decreasing prevalence of *Helicobacter pylori* and improvements in food preservation and storage, noncardia gastric cancer has declined in most populations.[2] As one of the most well-known causes of noncardia gastric cancer,[2] the infection rate of *H. pylori* in China dropped from 58.3% in 1983–1994 to approximately 40.0% in 2015–2019.[19] In addition, the increasing consumption of vegetables and fruits may also contribute to decreasing stomach cancer incidence in China.[20,21] Interestingly, after adjusting for age, the incidence of stomach cancer among men increased over the past 30 years. This may be related to more exposure to risk factors for stomach cancer among men, and these increasing exposures exceed the above-described benefits. For example, the proportion of harmful drinking behaviors and obesity prevalence all showed a significant increase among men over the past few decades.[22,23] Similar to global trends, the mortality of stomach cancer in China has decreased in the past 30 years. This decrease may be attributed to the rapid development of medical technologies such as detection and treatment. Early diagnosis and appropriate treatment of precancerous lesions of stomach cancer can reduce stomach cancer-related deaths.[24] The dietary risks (e.g., high-sodium diet) and behavioral risks (e.g., smoking) associated with stomach cancer have shown a general downward trend over the last three decades, as seen in Supplementary Figure 2, http://links.lww.com/CM9/B867. Notably, there are large geographic differences in the burden of stomach cancer in China. The province with the highest disability-adjusted life years rate of stomach cancer has a rate nearly three times that of the province with the lowest rate.[11] More effective measures may be needed in these areas.

Age is an important risk factor for stomach cancer.[5] In this study, we found that the incidence and mortality rate of stomach cancer showed an upward trend with age, which was consistent with previous studies.[4,5,25] There may be two main age-related factors for malignant tumorigenesis, including the accumulation of somatic mutations and changes in the tissue milieu (procarcinogenic tissue milieu).[26] In addition, the prognoses of stomach cancer are closely related to age. Although a previous study found that there was no difference between elderly and nonelderly patients in postoperative mortality, elderly patients were observed to have more hematogenous recurrence.[27] In addition, the complication rate after surgery increases with age,[28] which may partly contribute to higher stomach cancer mortality among elderly individuals. In this study, men had a higher incidence and mortality than women. Both stomach cancer-related environmental and genetic risk factors contributed to this difference.[29]

Period effects reflected the risk of stomach cancer occurrence and death in a specific period. We found that the risk of stomach cancer occurrence and death decreased in the last 10–15 years. The decreasing risk of stomach cancer may partly reflect the achievement of stomach cancer prevention and control in China. In 2003, China launched The Outline of the Chinese Cancer Program (2004–2010), which heralded the inception of nationwide cancer prevention programs.[30] In 2005, early diagnosis and treatment for major cancers in rural areas were initiated, and two rural areas with high risk were selected for the stomach cancer screening program pilot. With more high-risk rural areas participating in this program, more than 2.6 million participants had undergone gastroendoscopy by 2021, and more than 70% of upper gastrointestinal cancers were detected in early stages.[30] In urban areas, the Cancer Screening Program in Urban China was launched in 2012, and 143,000 participants had undergone upper gastrointestinal endoscopic examinations by 2018.[30]

Cohort effects reflected the risk of stomach cancer occurrence and death in different birth cohorts. Our findings showed that the risk of occurrence was increased in recent birth cohorts (people born recently had a higher risk of stomach cancer occurrence). This may be attributed to a greater explosion in stomach cancer-related risk factors in new birth cohort populations. For example, younger birth cohorts have a higher mean consumption of alcohol and prevalence of heavy episodic drinking,[22] and child obesity increased tremendously.[31] However, these unfavorable cohort effects seem insufficient to affect the downward trends of stomach cancer among women. In our study, we projected that the stomach cancer incidence would continue to decrease among women. Among men, who had substantially increased cohort effects, stomach cancer incidence was projected to continue to increase in the future. As the birth cohort progressed, the risk of death from stomach cancer decreased among both men and women, and it is expected that mortality due to stomach cancer for both sexes will decrease in the future in China. It should be noted that aging will be the main contributor to future increases in stomach cancer incidence and deaths, and the proportion of stomach cancer cases and deaths will continue to increase among elderly individuals. Considering the continued aging of the Chinese population,[32] it seems necessary to increase stomach cancer screening specifically for elderly people in the future.

The results of this study are a further supplement to the existing evidence and provide certain references for comprehensively understanding the disease burden of stomach cancer in China and clues for further stomach cancer prevention. This study was subject to some limitations. First, although this study provided valuable supplementary information to help understand the long-term trend of the stomach cancer burden in China, this was an ecological study, which does not imply direct causal relationships, and so inferences cannot be made about individuals. Further studies based on individuals are needed to confirm these results. Second, the projection in this study was based on past trends, and fluctuations in past trends would increase the uncertainty of the predictions. In addition, unexpected events (e.g., stomach cancer prevention-related policies, new effective treatment measures, etc.) in the future may change the overall trends. Third, the prediction coverage of the Bayesian APC model was larger than that with other methods,[33] which may result in bias when using the projected results to fit new models because uncertainty in the projection is not considered. Fourth, we did not distinguish between cardia and noncardia forms of stomach cancer in this study. Because the definition of cardia cancer has evolved over time and some cardia tumors might be classified as lower esophageal adenocarcinomas, it is complex to assess the secular trends of cardia versus noncardia tumors.[5] Fifth, due to the purpose of this study, we did not make assumptions about how different levels of intervention methods could reduce the burden of stomach cancer. Future interventions may depend on these estimates to effectively reduce the burden of stomach cancer. Sixth, stomach cancer information was extracted from the GBD, which provided comparable information across different countries and territories. However, there were some minor limitations that may restrict the application of this information. For example, the GBD did not provide information on rural or urban areas. Considering the different burdens of stomach cancer in rural and urban areas,[34] expanding the scope of data collection and assessing trends in these areas is necessary.

In summary, although the age-standardized incidence of stomach cancer among women and mortality among women and men has decreased over the last 30 years, the incidence among men has increased. It was projected that these trends will continue in the next decade, with an increase in the stomach cancer age-standardized incidence among men. Measures to reduce the stomach cancer burden among men are needed. Aging will be the main contributor to the increase in future stomach cancer incidence and deaths, and the proportion of stomach cancer cases and deaths is expected to increase among elderly individuals. Considering the rapid aging of the Chinese population, stomach cancer may have a tremendous impact on the health of elderly individuals in China. More effective measures may be needed in addition to population-based screening and opportunistic screening for improved population coverage.[30]

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Conflicts of interest

None.

Data availability

The original anonymized GBD data have been made publicly available at the website of the Institute for Health Metrics and Evaluation and can be accessed online (http://ghdx.healthdata.org/gbd-2019).

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