Cancer Investigation

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/icnv20

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To cite this article: Liping Yang, Haifeng Sun, Yan Bai, Shengzhi Sun, Xiaoming Wu, Zhenhai Gan, Jianqiang Du & Jianfei Du (2023) Trends and Projections of Stomach Cancer Incidence in Hong Kong: A Population-Based Study, Cancer Investigation, 41:4, 319-329, DOI: 10.1080/07357907.2022.2126982

To link to this article: https://doi.org/10.1080/07357907.2022.2126982

CANCER INVESTIGATION
2023, VOL. 41, NO. 4, 319–329
https://doi.org/10.1080/07357907.2022.2126982

Trends and Projections of Stomach Cancer Incidence in Hong Kong: A Population-Based Study

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ABSTRACT

Objectives: The burden of stomach cancer remains high in Hong Kong. We sought to evaluate the associations of age, period, and birth cohort with the changing trend in the incidence of stomach cancer and to provide projections through 2030.

Materials and Methods: We performed an age-period-cohort analysis and projections up to 2030 using data from the Hong Kong Cancer Registry. Additionally, we used a population decomposition algorithm to assess the drivers in the number of incident cases of stomach cancer in Hong Kong.

Results: Among the 26,813 stomach cancer patients, from 1994 to 2018, the age-standardized incidence rate of stomach cancer decreased for both sexes. The incidence increased with age and was highest for those aged 85 years or older. Period relative risk (RR) showed a monotonic decreasing pattern throughout the study period for both sexes before 2010. Cohort RR for males was monotonically decreasing but changed little after the 1967–1971 birth cohort. In contrast, cohort RR for females declined in the pre-1927–1931 birth cohort but slowed down since. It is projected that there will be 906 male patients and 954 female patients in 2030. Decomposition analysis suggested that population growth and aging were associated with substantial changes in the number of incident cases of stomach cancer in Hong Kong.

Conclusions: Both period and cohort risk of developing stomach cancer in Hong Kong have slowed down or plateaued. Our study demonstrates that population aging and growth are the main drivers of the increased number of incident cases of stomach cancer in Hong Kong.

ARTICLE HISTORY
Received 10 November 2021
Revised 1 June 2022
Accepted 17 September 2022

KEYWORDS
Stomach cancer; age-period-cohort analysis; projection; decomposition

Introduction

Stomach cancer is the fifth most common neoplasm and the fourth most deadly cancer worldwide in 2020 (1). East Asia is one of the regions with the highest incidence of stomach cancer globally. In Hong Kong, stomach cancer is the sixth most commonly diagnosed cancer (3.8% of total cases) and the cause of cancer death (4.7% of total cancer deaths) according to the Hong Kong Cancer Registry (HKCaR) in 2018 (2). Although the incidence of stomach cancer in Hong Kong showed a steady decline in the past decades, in line with the global trend, the number of incident cases and incidence rate remained relatively stable in recent years (2). However, the continuing trend of increasing new cases, especially among females, reflects both aging and population growth as well as changes in the prevalence and distribution of risk factors for stomach cancer (1,3). As Hong Kong's population will still grow and age, the burden of stomach cancer in Hong Kong is likely to increase.

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Supplemental data for this article is available online at https://doi.org/10.1080/07357907.2022.2126982

Chronic infection with *Helicobacter pylori* (*H. pylori*) is the most important cause of stomach cancer (4,5). Other risk factors for stomach cancer include high salt intake, smoking, obesity, and low consumption of fruits and vegetables, most of which are associated with low socioeconomic status (6–9). The prevalence of *H. pylori* and exposure to other risk factors vary across birth cohorts (10). Therefore, the risk of developing stomach cancer in birth cohorts may be strongly related to the prevalence of *H. pylori* and exposure to behavior risks. Temporal variations in the birth cohort and period effects on the incidence of stomach cancer can be isolated and analyzed by age-period-cohort (APC) models, which are better suited than traditional cross-sectional models to elucidate the possible determinants of temporal trends (11–13).

Therefore, to quantitatively explore the temporal trend of stomach cancer incidence in Hong Kong and better interpret the causes, we conducted a population-based analysis using APC analysis. In addition, using a model that includes age, period, and cohort effects, we projected the incidence of stomach cancer in Hong Kong by 2030. Finally, using a validated algorithm, we attributed the net change in stomach cancer cases in Hong Kong to population growth, population aging, and epidemiological changes.

Material and methods

Study data

We obtained data on stomach cancer incidence in Hong Kong by sex, age group, and calendar year from 1994 to 2018 from the HKCaR (2). HKCaR is a population-based cancer registry in the Hong Kong Special Administrative Region of the People's Republic of China and a member of the International Association of Cancer Registries (IARC). The data in HKCaR have reached the highest standards for developed countries as portrayed by the World Health Organization (WHO) International Agency for Research on Cancer. Considering the slightly lower quality of the data from the earlier stage and the requirements of APC analysis, we only selected data from 1994 onward. Stomach cancer was classified according to the International Classification of Diseases 9th/10th revision (151/C16). We excluded age groups younger than 30 years due to the low incidence in these groups. We obtained Hong Kong population data by sex, age group, and calendar year from the 2019 Revision of World Population Prospects of the Union Nations Population Division (based on the UN medium-fertility variant) (14). We used the WHO standard population for age standardization.

Age-period-cohort analysis

To perform APC analysis, we tabulated incidence and population data into 12 five-year age groups from 30–34 years to 85+ years, and 5 five-year calendar periods from 1994–1998 to 2014–2018. The output estimates of the APC analysis mainly include longitudinal age-specific rates, period and cohort rate ratios, and local drifts with net drift. The longitudinal age curve indicates the expected age-specific rate in a reference cohort adjusted for period effects. Period effects are changes that affect all age groups simultaneously and may be caused by changes in the social, cultural, or economic environment. Cohort effects are associated with differences between groups of individuals with the same birth year. We calculated the cohort rate ratio (RR) using the central birth cohort (1947–1951) as the reference, as well as the period RR using the central calendar period (2004–2006) as the reference. Net drift indicates the overall annual percentage change in the expected age-adjusted rate, and local drifts represent the estimated annual percentage change over time specific to age groups. We performed the analyzes using the APC Web Tool (Biostatistics Branch, National Cancer Institute, Bethesda, USA) (15). The Wald chi-square test was used to evaluate the significance of the APC model. All statistical tests were two-sided, and a p-value of less than 0.05 was considered statistically significant.

Projection

Using the Bayesian age-period-cohort analysis with integrated nested Laplace approximations (16), we projected stomach cancer incidence in

Hong Kong from 2019 to 2030. The model was implemented in the R package BAPC (version 0.0.34) and has shown better coverage and accuracy than other statistical approaches (16,17).

Decomposition

Furthermore, to assess the contribution of demographic versus epidemiological changes, we decomposed the increase in stomach cancer cases in Hong Kong from 1995 to 2030 into three components: population aging, population growth, and change in age-specific incidence rates using 1994 as the reference year. Changes in age-specific incidence rates represent epidemiological changes, including differences in the number of incident cases that cannot be explained by population growth and aging (18). We performed the decomposition using a validated algorithm (19,20) robust to the order of decomposition and the reference selection. All statistical analyzes were performed with the statistical software environment R, version 3.6.3.

Results

Trends in the incidence of stomach cancer

A total of 26,813 patients (16,535 male patients [61.67%] and 10,278 female patients [38.33%]) were included in our analysis. From 1994 to 2018, the number of incident stomach cancer cases in Hong Kong increased from 604 and 350

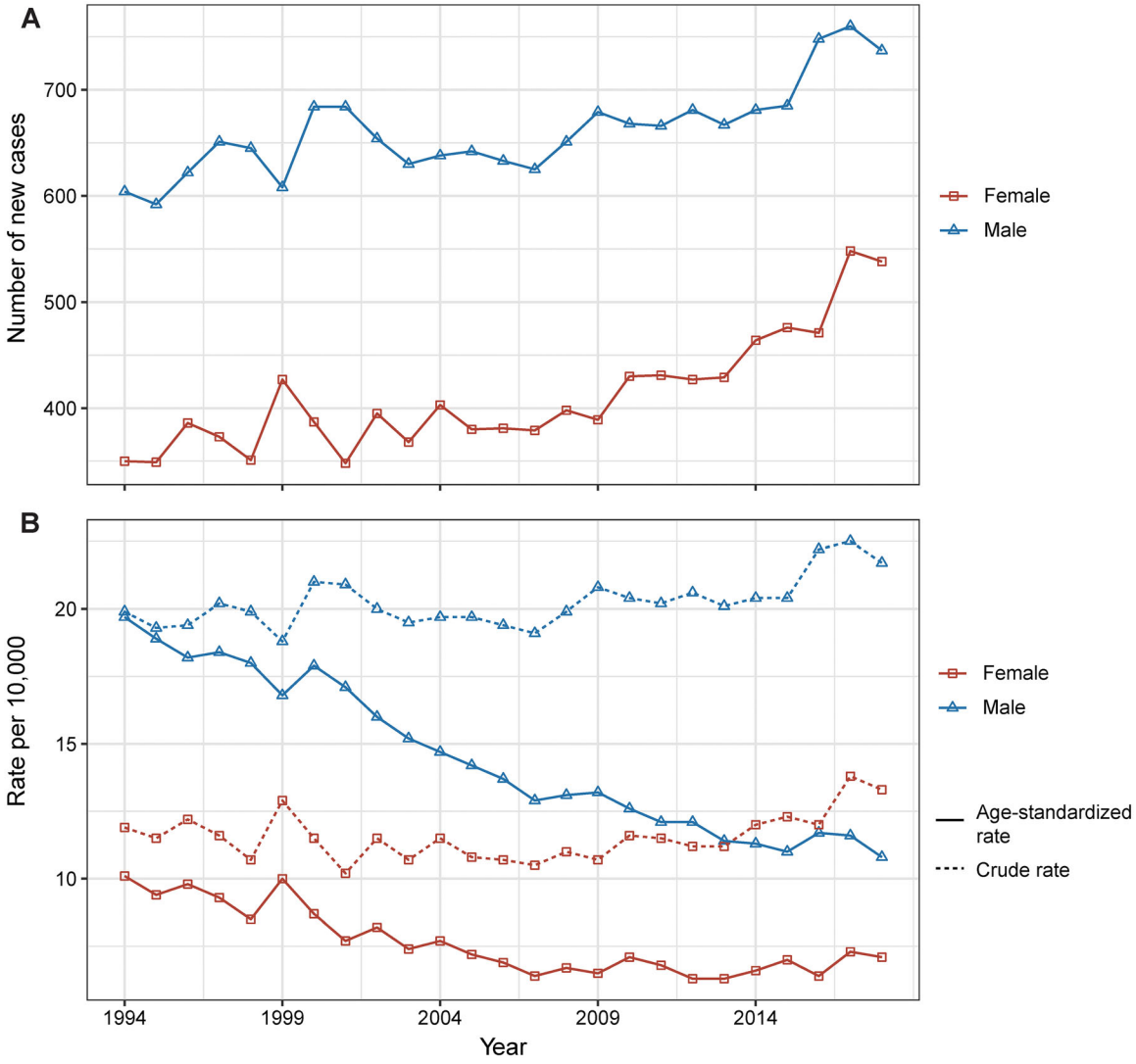

Figure 1. Changes in incidence rate and number of cases of stomach cancer for males and females in Hong Kong, 1994–2018. (A) Number of cases for males and females. (B) Age-standardized incidence rate and crude incidence rate for males and females.

to 737 and 538 for males and females, respectively (Figure 1(A)). The crude incidence rate of stomach cancer for both sexes fluctuated slightly. In contrast, the age-standardized incidence rate decreased markedly in both sexes during the same period, with a greater decline for males. The age-standardized incidence rate of stomach cancer decreased from 19.7 and 10.1 per 100,000 persons in 1994 to 10.8 and 7.1 per 100,000 persons in 2018 for males and females, respectively (Figure 1(B)).

Age-period-cohort analysis

Net drift, i.e., the overall annual percentage change in the expected age-adjusted rates over time, showed a statistically significant downward trend in stomach cancer incidence during the entire period by −2.74% (95% confidence interval [CI]: −3.11 to −2.36) per year for males and −1.47% (95% CI: −1.93 to −1.01) per year for females (Figure 2). However, local drifts, reflecting additional age-specific changes in incidence trends, were less than zero in all age groups, indicating a decrease in the incidence of stomach cancer for both sexes in all age groups. For females, the decline was less in the middle age groups and much higher in the younger and older age groups, but 95% CIs were wide. The deviation of local drifts was not statistically significant for males (Figure 2, Table S1).

The incidence of stomach cancer increased with age after adjusting for period deviations (Figure 3) and was much higher for males than for females, with the gap increasing with age. We performed a curve estimation of the longitudinal age curve and found that the logarithm of the incidence rate and patient age could be fitted by second-order

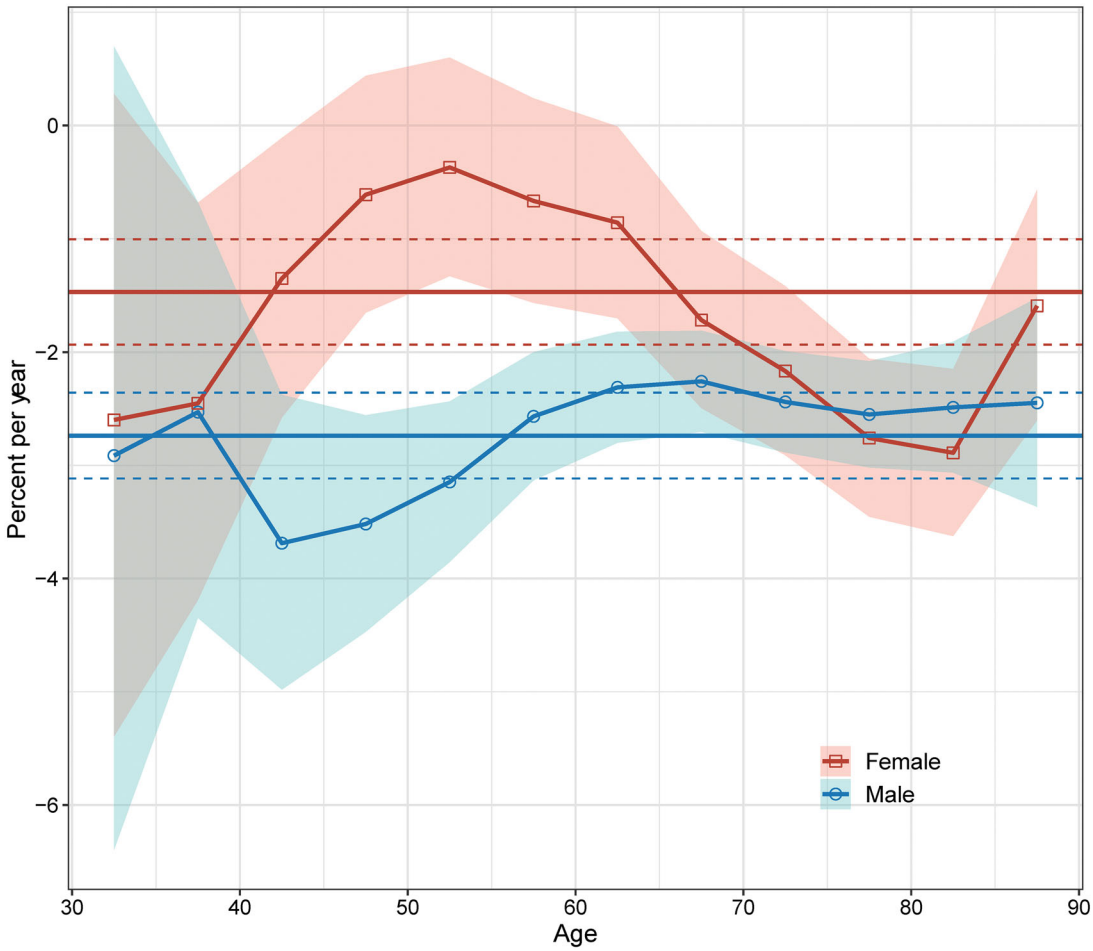

Figure 2. Local drifts with net drift values for males and females for stomach cancer incidence in Hong Kong from 1994 to 2018. Shaded areas indicate 95% confidence interval.

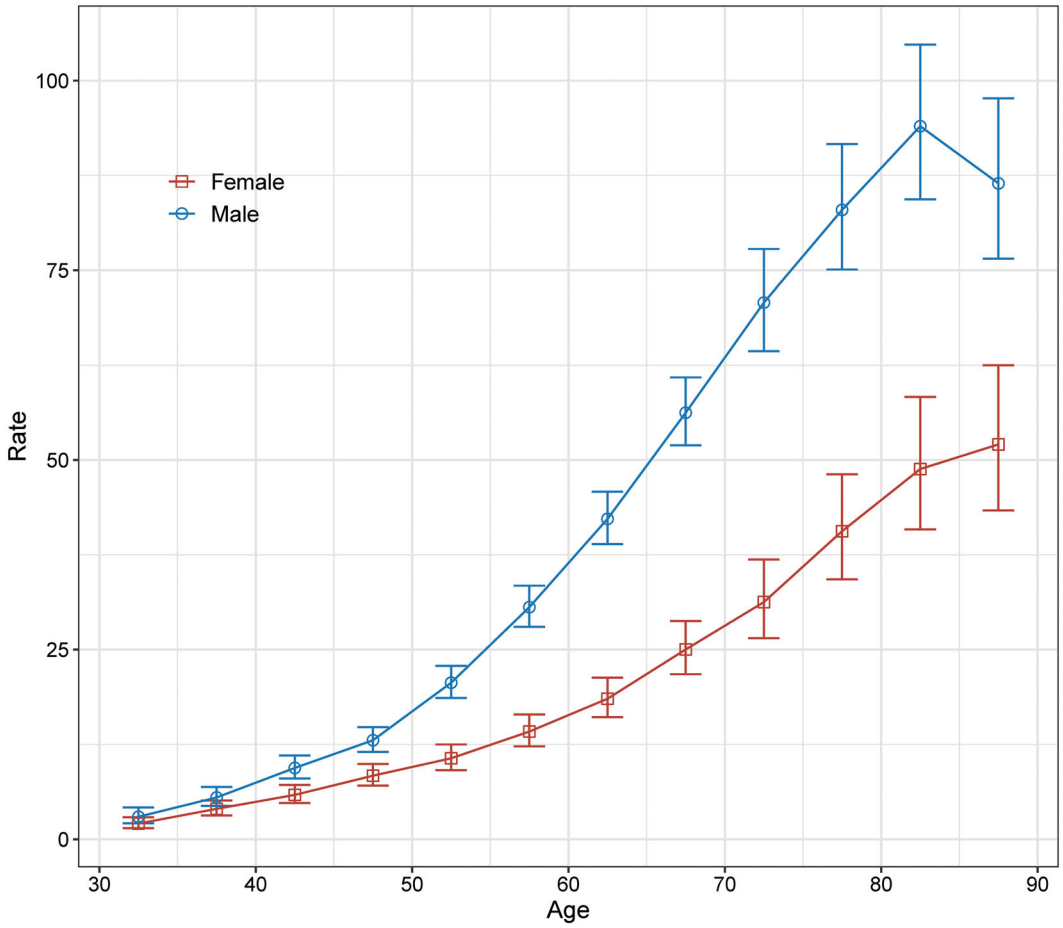

Figure 3. Fitted longitudinal age curves of stomach cancer incidence (per 100,000 person-years) and the corresponding 95% confidence interval for males and females in Hong Kong.

polynomial regression. The adjusted R-squared values were 0.998 for males and 0.994 for females, and the regression coefficients were significant at $p < 0.001$ level for both sexes.

Compared to the reference period (2004–2006), period RR showed a monotonic decreasing pattern throughout the study period for males and females before 2010, with a faster decrease for males. However, after the reference period, the period effect was absent for females (Figure 4). Cohort RR for males was monotonically decreasing but changed little after the 1967–1971 birth cohort. In contrast, cohort RR for females has been declining in the pre-1927–1931 birth cohort, but has been almost nonexistent thereafter (Figure 5). Wald tests showed that the main estimable functions were statistically significant for both sexes ($p < 0.05$), except for local drift for males ($p = 0.70$, Table S1).

Projection

We next performed a projection analysis to estimate the future incidence of stomach cancer in Hong Kong. Stomach cancer cases in Hong Kong will continue to increase, with 906 male patients and 954 female patients by 2030 (Tables S2, S3). The age-standardized incidence rate will continue to decline for males and may increase slightly for females (Figures S1, S2). The highest incidence increases were expected in the female population over 60 years of age and the male population over 70 years of age (Tables S2, S3).

Decomposition

Finally, we conducted a decomposition to attribute changes in the number of incident cases of stomach cancer in Hong Kong to population growth, population aging, and epidemiological

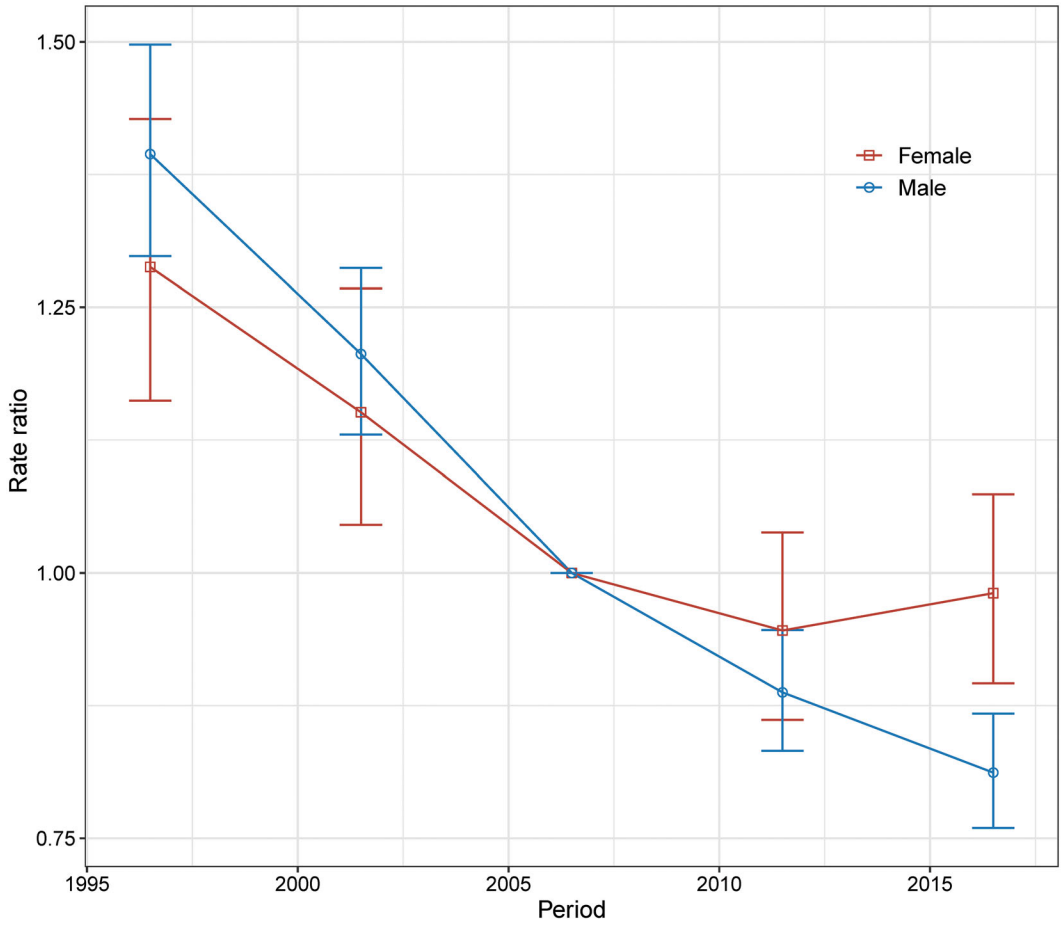

Figure 4. Relative risk of each period compared with the reference adjusted for age and nonlinear cohort effects and the corresponding 95% confidence interval for males and females.

changes between 1995 and each subsequent year from 1996 through 2030, using 1994 as the reference year. We found that population growth and aging were associated with substantial changes in the number of incident cases of stomach cancer in Hong Kong (Figures 6 and 7; Tables S4, S5).

Compared to 1994, the number of incident cases of stomach cancer in Hong Kong increased by 133 and 188 for males and females, or 22.0% and 53.7%, respectively, in 2018. In contrast, epidemiological changes resulted in a 65.6% and 41.4% decrease in cases for males and females during the same period. The drivers of the increase in incident cases of stomach cancer were population aging (52.3% and 26.8% increase for males and females, respectively, compared with 1994) and population growth (68.3% and 35.3% increase for males and females, respectively, compared with 1994) (Tables S4, S5).

Projection and decomposition analysis showed that the number of incident cases of stomach cancer in Hong Kong would be 50.0% and 172.6% more for males and females, respectively, by 2030 compared with 1994. For males and females, the contributions of population aging were 92.1% and 82.2%, and the contributions of population growth were 51.6% and 113.7%, while the contributions of epidemiological changes were −93.7% and −23.3%, respectively (Tables S4, S5).

Discussion

To our knowledge, our study is the first to examine the underlying reasons for the changing trends in the incidence of stomach cancer in Hong Kong using APC analysis. While age-standardized stomach cancer incidence rates decreased for both sexes, demographic shifts did not lead to a lower burden of stomach cancer on the health system. The number of incident cases of stomach cancer continued to increase. Furthermore, both

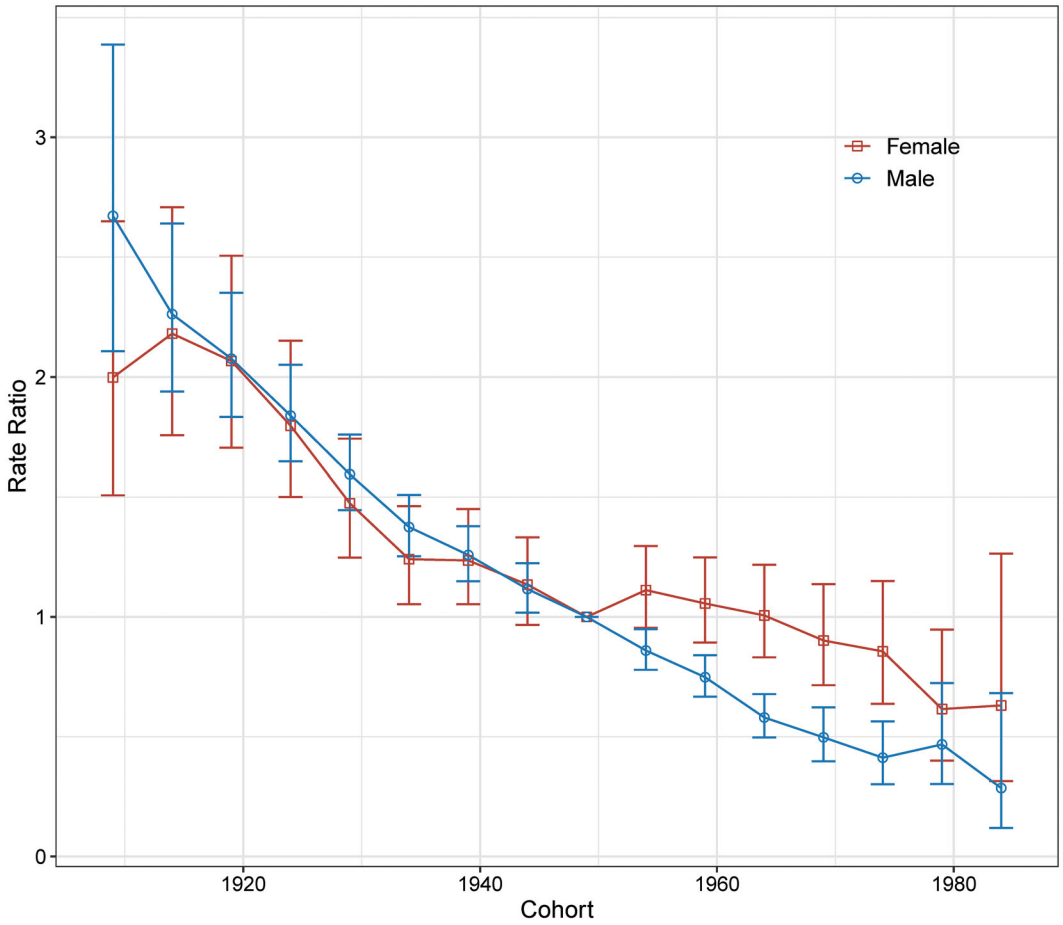

Figure 5. Relative risk of each cohort compared with the reference adjusted for age and nonlinear period effects and the corresponding 95% confidence interval for males and females.

period and cohort risk of developing stomach cancer showed a downward trend in the early stages but plateaued or absented in the later study period. Our study demonstrates that although Hong Kong has made substantial progress in preventing stomach cancer, this progress has been offset by an aging population and population growth, resulting in a continued rise in the number of incident case of stomach cancer. Therefore, continued epidemiological surveillance and clinical studies on this disease and ways to prevent it are needed.

Trends in stomach cancer incidence reflect differences in exposure to the major risk factors for stomach cancer over time and across birth cohorts. *H. pylori* infection is a crucial determinant of stomach cancer and may be a necessary cause (5). According to a large prospective case-cohort study (21), *H. pylori* infection is a significant risk factor for non-cardia and cardia stomach cancer in Chinese adults, accounting for 78.5% of non-cardia stomach cancers and 62.1% of cardia stomach cancers. In asymptomatic adults in Hong Kong, *H. pylori* infection was once as high as 60% (22). In contrast, the prevalence of *H. pylori* infection in symptomatic Hong Kong children decreased from 25.6% in 2005 to 12.8% in 2017 (23), comparable to that of developed countries (10). The change in prevalence of *H. pylori* infection may explain the cohort effect that we observed in the present study. Lifestyle factors play a crucial role in the burden of stomach cancer, especially the high-salt diet in East Asian populations and smoking among males (4,24). The sustained decline in period effect is likely attributable to reducing salt intake and smoking prevalence. However, it should be noted that in our study, we were unable to assess the role of *H. pylori* infection, high salt intake, and smoking in the burden of stomach cancer because these data were not included in the HKCaR.

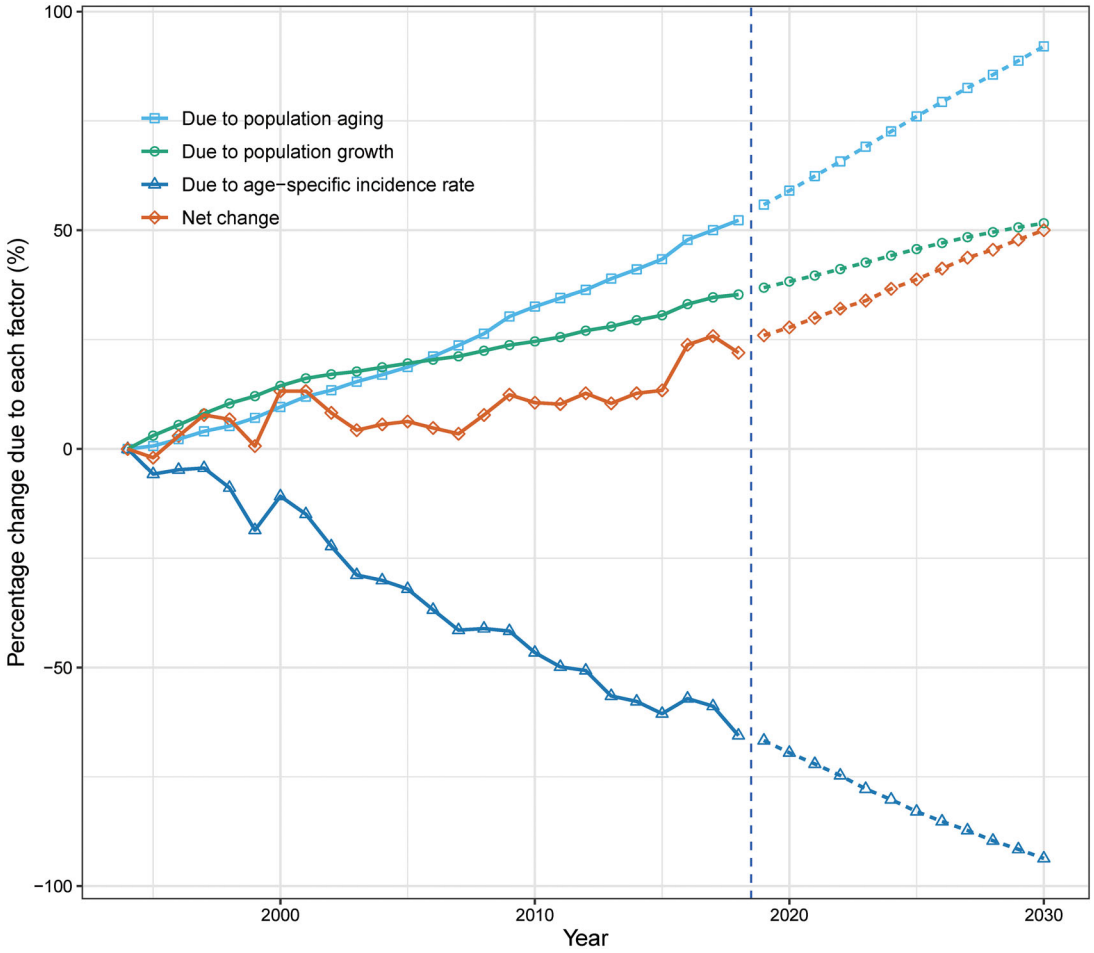

Figure 6. Contribution of changes in population aging, population growth, and age-specific incidence rate to changes in incident cases from 1995 to 2030 for Hong Kong males, using 1994 as the reference year. Data in the right of the blue dashed line were the decomposition based on the projected data.

We show a marked downward trend in the age-standardized incidence rate, suggesting that Hong Kong has made significant progress in preventing the disease. However, stomach cancer cases in Hong Kong continue to increase. This inconsistency reflects the crucial role of the demographic shift in the burden of stomach cancer. The demographic shift has offset the impact of epidemiological changes in stomach cancer. Our findings indicate that population growth and aging have become the main drivers of increasing stomach cancer cases in Hong Kong. Our projections demonstrate that the trend will continue as Hong Kong's population ages and continues to grow.

Our results are generally consistent with previous epidemiological studies on the incidence of stomach cancer (4,25). Although other studies have shown that the incidence of stomach cancer is age-related (4,26), after controlling for cohort and period effects, we found a second-order polynomial relationship between the incidence of stomach cancer and age. In addition, the prevalence of *H. pylori* infection in Hong Kong has declined to levels of developed countries (23). Therefore, to reduce the burden of stomach cancer, more emphasis needs to be placed on reducing high salt intake and smoking rate. Currently, the smoking rate in Hong Kong is already among the lowest in the world (27), while salt intake levels are still above the World Health Organization's recommended levels, and excessive salt intake is still not fully recognized (28). Therefore, it is necessary to continue existing smoking cessation measures and enhance the reduction of high-salt foods in the diet, which are cost-effective in preventing stomach cancer and other related diseases.

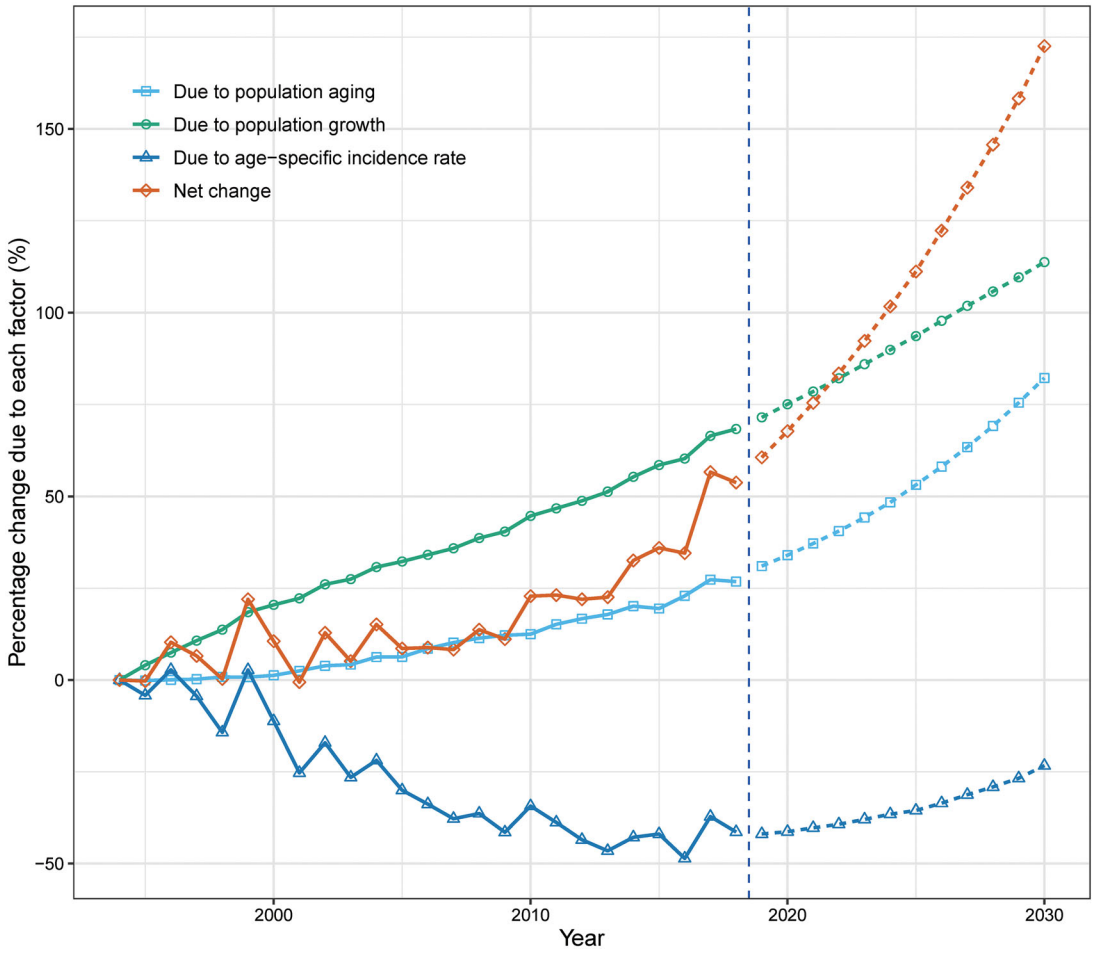

Figure 7. Contribution of changes in population aging, population growth, and age-specific incidence rate to changes in incident cases from 1995 to 2030 for Hong Kong females, using 1994 as the reference year. Data in the right of the blue dashed line were the decomposition based on the projected data.

Several limitations are evident in our study. First, although stomach cancer is often reported as one entity, it can usually be divided into two distinct topographical subsites, cardia and non-cardia (1,5), yet no distinction is made in the HKCaR. Non-cardia stomach cancer is mainly associated with *H pylori* infection and high salt intake, which may be the main reason for the global trend of stomach cancer. On the other hand, cardia stomach cancer is related to obesity and gastroesophageal reflux disease and accounts for about 12% of stomach cancers globally (29). However, a report showed that *H pylori* infection is a significant risk factor for both non-cardia and cardia cancer in Chinese adults (21). In addition, cardia stomach cancer is not easily distinguished from lower esophageal adenocarcinoma (29), which makes comparing long-term trends in the cardia and non-cardia stomach cancer more complicated even if we have the data. Second, HKCaR is limited because it lacks patient-specific data regarding *H. pylori* infection status, smoking habits, etc. Knowing these data will assist us in modifying our analysis. Third, the population structure and size of Hong Kong were derived from UN World Population Prospects, which may be subject to significant biases, adding to the uncertainty of the projections. Finally, we employed a variety of modeling approaches, which inevitably introduce a lot of uncertainty. Despite these limitations, we believe that our findings are the best estimate possible given the available data in Hong Kong.

In summary, the period and cohort risk of developing stomach cancer in Hong Kong have slowed down or disappeared. Population growth and aging have offset the effects of epidemiological changes, and therefore, the number of

incident cases of stomach cancer will continue to increase in Hong Kong. Further research and epidemiological assessment of this trend are needed.

Ethical approval

As the data were publicly available and data were aggregated and de-identifiable, institutional review board approval and informed consent were not needed.

Declaration of interest

The authors report no conflicts of interest.

Funding

This work was supported by the Huilan Public Welfare Fund Project under Grant No. HL-HS2020-45 and Beijing Xisike Clinical Oncology Research Foundation under Grant No.Y-QL202102-0175.

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Data availability statement

These data were derived from the following resources available in the public domain: https://www3.ha.org.hk/cancereg/default.asp.

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