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Incidence and mortality trends in oral and oropharyngeal cancers in China, 2005–2013

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ABSTRACT

Background: Oral and oropharyngeal cancers are among the most common cancers globally. This study aimed to assess the incidence and mortality trends of oral and oropharyngeal cancers in China between 2005 and 2013.
Methods: Estimates of national trends of oral and oropharyngeal cancers were based on the data from Chinese Cancer Registry Annual Reports. The crude incidence rates of oral and oropharyngeal cancers between 2015 and 2035 were evaluated. The age-standardized rate was based on the world standard population.
Results: It was estimated that 285,857 new cases and 132,698 deaths were related to oral and oropharyngeal cancers in China between 2005 and 2013, with mouth and tongue cancers being the most frequently diagnosed and the leading causes of death among all oral and oropharyngeal cancers. The incidence rates of oral and oropharyngeal cancer fluctuated from 1.69 to 1.89 per 100,000 person-years, and the mortality rate showed an increasing trend, ranging from 0.77 and 0.84 per 100,000 person-years. Males were more susceptible than females to oral and oropharyngeal cancers. The incidence and mortality rates of oral and oropharyngeal cancers were significantly higher in urban regions. The crude incidence rates of oral cancers are projected to increase from 2.26 to 3.21 per 100,000 person-years over the next 20 years in China.
Conclusion: The incidence of oral and oropharyngeal cancers fluctuated, whereas the mortality rate showed an upward trend from 2005 to 2013. A heavier burden from oral and oropharyngeal cancers is predicted in the next two decades in China.

1. Introduction

Oral and oropharyngeal cancers represent a global public health issue with a significant socioeconomic impact, yet they are frequently neglected in public health policies. Tobacco (both smoked and smokeless), areca nut, alcohol, and human papillomavirus (HPV) infection are major risk factors for oral and oropharyngeal cancers [1–4]. Squamous-cell carcinomas (SCCs) make up over 90% of the malignancies affecting the oral cavity and oropharyngeal regions. Surgical treatment followed by radiotherapy or chemotherapy remain the standard therapies for SCC [5,6]. SCCs are frequently progressive; lymph-node density is a significant prognostic predictor for patients with oral cancer [7]. The 5-year survival rate varies from 40% to 50% due to recurrences and secondary metastases to the cervical lymph nodes [8].

An estimated 442,760 new cases and 241,458 deaths from oral and oropharyngeal cancers occurred globally in 2012, accounting for 3.1% and 3.0% of all new cancer cases and deaths [9]. GLOBOCAN estimated that the region with the highest incidence of oral and oropharyngeal cancers was Melanesia, followed by South-Central Asia and Western Europe, with incidences > 10 per 100,000 person-years. In contrast, Eastern Asia and Western Africa had the lowest incidences of oral and oropharyngeal cancers: about 2 per 100,000 person-years [9].

Asia is the region most severely affected by oral and oropharyngeal cancers. In South Asia, Bangladesh is the country with the highest incidence and mortality rates of oral and oropharyngeal cancers [9]. In India, over 100,000 cases are registered annually, and estimates are

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predicting 182,697 cases by 2030 [9]. Taken together, nearly two thirds of the burden of oral and oropharyngeal cancers is borne by less-developed countries [10].

Comparatively, oral and oropharyngeal cancer cases accounted for about 1.2% of all new cancer cases in China, indicating a lower oral and oropharyngeal cancer burden [11]. Nevertheless, due to the large number of people addicted to tobacco and alcohol in China, the incidence and mortality rates of oral and oropharyngeal cancers might be increasing. Thus it is important to evaluate epidemiological trends of oral and oropharyngeal cancers in China over a prolonged period. By comparing the incidence and mortality rates of oral and oropharyngeal cancers by gender, age group and geographic area, we aimed to provide basic information on the risk factors for oral and oropharyngeal cancers and to implement strategies for cancer prevention in China.

2. Materials and methods

2.1. Classification of anatomical sites

According to the coding of the World Health Organization International Statistical Classification of Diseases and Related Health Problems 10th revision (ICD-10), oral cancers can be classified into cancers of the lip (C00), other and unspecified parts of the tongue (C02, excluding C02.4), gums (C03), floor of mouth (C04), hard palate (C05.0), other and unspecified parts of the mouth (C06). Oropharyngeal cancers include cancers of the base of the tongue (C01), soft palate (C05.1), lingual tonsil (C02.4), tonsil (C09), oropharynx (C10), pyriform sinus (C12), hypopharynx (C13), and unspecified pharynx (C14) [12]. Cancers of the salivary glands (C07–08) and nasopharynx (C11) were excluded from all analyses.

2.2. Data source

Cancer incidence and mortality data from January 1, 2005 to December 31, 2013 were obtained from the Chinese Cancer Registry Annual Reports published by the National Central Cancer Registry (NCCR) of China [13–21]. The NCCR compiles cancer incidence and mortality data from population-based, region-specific cancer registries in China. GLOBOCAN 2012 produced by the International Agency for Research on Cancer (IARC) provides estimates of cancer incidence, mortality, and prevalence worldwide, as well as individually for most countries and regions [9].

2.3. Quality control

The quality of submitted data from each local registry was evaluated by the NCCR based on the Guidelines for Chinese Cancer Registration and the International Agency for Research on Cancer/International Association of Cancer Registries (IARC/IACR) data quality criteria [22]. Data classified as category A or B were deemed acceptable for inclusion in the national data analysis.

2.4. Statistical analyses

The numbers of qualified registries in urban and rural areas and the proportion of the national population covered were recorded by the NCCR. The demographic information was based on the Sixth National Population Census (2010), which was provided by the National Statistics Bureau of China. By combining the population numbers and the incidence or mortality rates of oral and oropharyngeal cancers in each age group, we calculated the number of oral and oropharyngeal cancer cases and deaths therefrom in every group, and further estimated the new cases of oral and oropharyngeal cancers and consequent deaths nationwide. For national trends analysis, we stratified the population by area (urban/rural), gender (male/female) and age group (birth–14, 15–39, 40–59, 60–84, and ≥85 years). Additionally, we chose four representative cities in northern/southern China (north: Harbin and Beijing; south; Shanghai and Guangzhou), and one city in Hunan Province (Zhuzhou) which is one of the regions in China where betel quid and other forms of areca nut chewing are most popular. We extracted the incidence and mortality data of the five cities and compared them with the national data to explore the regional differences in the epidemiological characteristics in China.

The age-standardized rate (ASR) was based on the world standard population. The crude incidence rates of oral and oropharyngeal cancers in China from 2015 to 2035 were calculated by combining the estimates of new cancer cases [9] and the population projection from the United Nations (http://esa.un.org/unpd/wpp/DataQuery/). GraphPad 5.0 (GraphPad Inc., San Diego, CA) was used for data processing and analysis.

3. Results

The number of qualified registries has increased from 34 to 255 during the study years. Likewise, the proportion of the whole population of China covered by all eligible cancer registries rose from 5.31% to 21.11% from 2005 to 2013. Generally, our following interpretations—based on the original data from annual reports—are of high quality and reliability.

3.1. Incidence between 2005 and 2013

Overall, it was estimated that 285,857 new oral and oropharyngeal cancer cases occurred in China between 2005 and 2013. The ASR for all oral and oropharyngeal cancers combined fluctuated within the range 1.69–1.89 per 100,000 person-years, with a notable peak in 2007. Cancers of the tongue (C01–C02) and mouth (C03–C06) were the top two most common cancers among the included sites. In total 250,110 patients suffered from cancers of the mouth and tongue, accounting for 63.9% of all oral and oropharyngeal cancer cases (Table 1, Fig. 1A,B).

Males were more likely than females to develop oral and oropharyngeal cancers, with an M:F ratio of 2.12:1. The incidence rate per 100,000 person-years in males (ranging from 2.24 to 2.55) was significantly higher than that in females (ranging from 1.02 to 1.27). Oral

Table 1
No. of the oral and oropharyngeal cancer cases in China, 2005-2013.

Anatomic cancer	2005	2006	2007	2008	2009	2010	2011	2012	2013
Lip (C00)	1059	1584	1329	1284	1748	1680	1747	1696	1540
Tongue (C01-C02)	8418	8719	9884	9151	9729	7940	8546	8582	8136
Mouth (C03-C06)	9837	10429	12912	12337	12598	11461	11497	11219	11376
Tonsil (C09)	1297	1513	1396	1522	1683	1567	1641	1476	1455
Other Oropharynx (C10)	2068	2433	2393	2302	2341	2361	2594	2481	2427
Hypopharynx (C12-C13)	3188	3406	4066	3394	3625	3682	4704	4451	5440
Pharynx Unspecified (C14)	1900	2385	1784	1713	2087	2189	1963	2198	2294
Total	27767	30469	33764	31703	33811	30880	32692	32103	32668

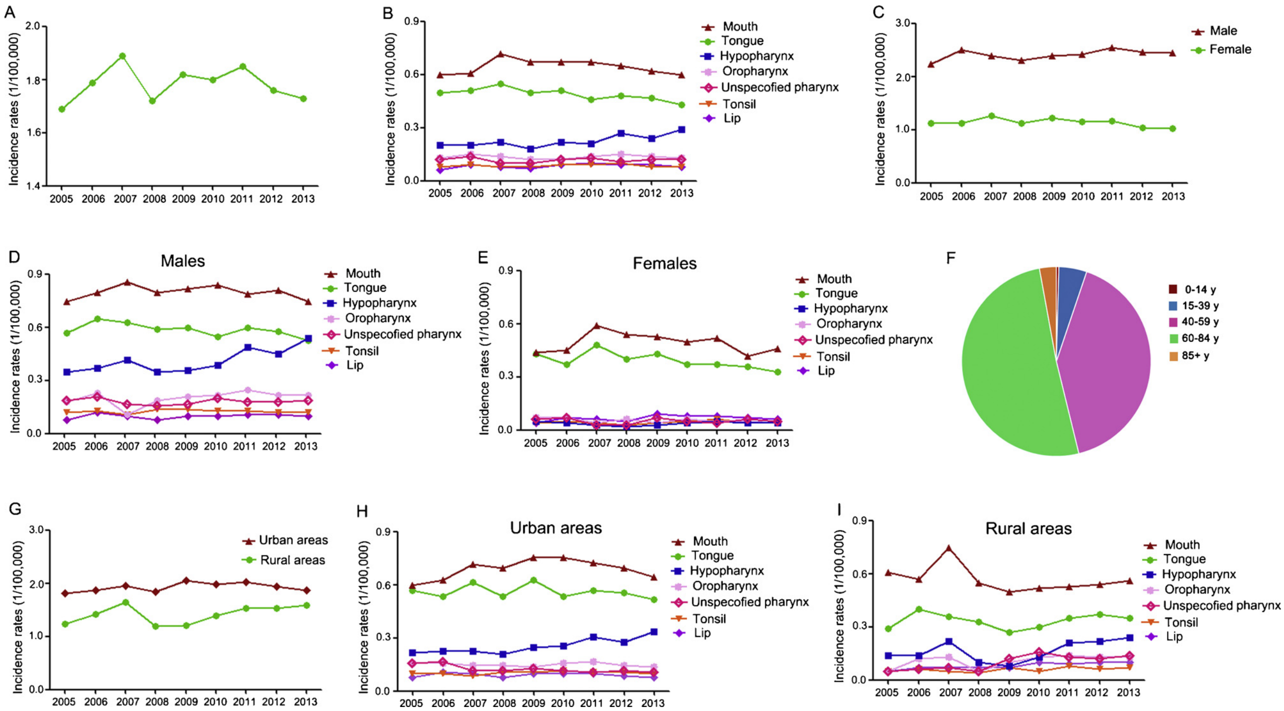

Fig. 1. Incidence of oral and oropharyngeal cancers in China, 2005 to 2013. **(A)** Age-standardized incidence rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers in China. **(B)** Age-standardized incidence rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers arising in different anatomical sites in China. **(C)** Age-standardized incidence rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers in males and females. **(D)** Age-standardized incidence rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers risen in different anatomical sites in males and **(E)** in females. **(F)** Pie chart of the percentage of oral and oropharyngeal cancer patients in different age groups. **(G)** Age-standardized incidence rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers in urban and rural areas. **(H)** Age-standardized incidence rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers arising in different anatomical sites in urban regions and **(I)** in rural regions.

cancers of the mouth and tongue showed the highest incidence in both genders, accounting for 57.1% of the male and 77.8% of the female cancer cases (Tables S1,S2, Fig. 1C–E).

The incidence of oral and oropharyngeal cancers also varied by age group. The incidence rate was highest in those aged ≥85 years and lowest in those aged 0–14 years. Notably, the incidence in those ≥85 years of age began to decrease from 2008 and approached that in 60–84-year-olds. The total number of cases was highest in the age groups 40–59 and 60–84 years (Fig. 1F, Fig. S1A).

The numbers of oral and oropharyngeal cancer cases in urban and rural areas were also assessed. The incidence rate of oral and oropharyngeal cancers was much higher in urban areas than in rural areas during the study period. However, the incidence rate in rural areas continued to rise after 2008 and approached that of urban areas. Mouth and tongue cancers were the most frequently diagnosed oral and oropharyngeal cancers in both areas, accounting for 63.3% and 64.2% of the total cases in urban and rural regions, respectively (Tables S3,S4; Fig. 1G–I).

3.2. Mortality between 2005 and 2013

It was estimated that 132,698 patients died of oral and oropharyngeal cancers in China between 2005 and 2013. The ASR showed an upward trend, ranging from 0.77 to 0.84 per 100,000 person-years. Mouth and tongue cancers were the leading causes of death among all cancers, accounting for 63.3% of all mortality cases during the 9-year period (Table 2, Fig. 2A,B).

The mortality rate for oral and oropharyngeal cancers was higher in males than in females, with an M:F ratio of 2.34:1. The mortality rate per 100,000 person-years in males (ranging from 1.13 to 1.27) was significantly higher than that in females (ranging from 0.42 to 0.5). Cancers of the mouth and tongue were the leading causes of death for both genders, accounting for 57.7% and 78.2% of the total male and female deaths, respectively (Tables S5,S6; Fig. 2C–E).

Mortality rate increased with age, especially after the age of 40 years, and reached a peak in those aged > 85 years. However, cases in the 40–59- and 60–84-year age groups accounted for 91.1% of all oral and oropharyngeal cancer deaths (Figs. 2F and S1B).

The mortality rates for oral and oropharyngeal cancers showed different trends in urban and rural regions. Generally, the mortality rate increased gradually in urban regions, with a notable peak in 2009. In contrast, in rural areas the mortality rate showed a decreasing trend from 2007 and increased slightly after 2009. Moreover, the mortality rate in urban regions exceeded that in rural regions due to the inverse trend from 2008 (Fig. 2G). In urban regions, mouth and tongue cancers were the most frequent types resulting in death, the mortality rates of which tended to be stable from 2008 to 2013. In contrast, in rural areas the mortality rates of mouth and tongue cancers decreased significantly until 2010 and increased slightly thereafter (Fig. 2H,I, Tables S7,S8).

3.3. Oral and oropharyngeal cancers in different regions of China

To analyze the association between geographic factors and the epidemiology of oral and oropharyngeal cancers in China, Harbin, Beijing, Shanghai, and Guangzhou were selected as representative cities. In addition, Zhuzhou was chosen as another representative city where use of betel quid and other forms of areca nut is quite prevalent. The epidemiological data of Harbin, Beijing, Shanghai and Guangzhou were available from 2006, whereas in Zhuzhou the data were available from 2010. In males, the incidence and mortality rates in Harbin, Beijing and Shanghai were all close to the national data, whereas data from Guangzhou and Zhuzhou were significantly higher than the national data (Fig. 3A,B). In females, the incidence rates of oral and oropharyngeal cancers in Beijing and Shanghai were close to the national

Table 2
No. of the oral and oropharyngeal cancer deaths in China, 2005-2013.

Anatomic cancer	2005	2006	2007	2008	2009	2010	2011	2012	2013
Lip (C00)	267	178	278	506	583	646	567	386	398
Tongue (C01-C02)	3716	3693	4509	3842	4056	3642	3781	3940	3640
Mouth (C03-C06)	5207	4964	5388	6186	5587	5053	5388	5577	5811
Tonsil (C09)	546	666	970	543	693	548	516	638	693
Other Oropharynx (C10)	1056	688	1182	933	878	983	1237	1356	1561
Hypopharynx (C12-C13)	1252	1573	1499	1790	1667	1595	2045	2250	2775
Pharynx Unspecified (C14)	1518	1358	1301	1256	1317	1614	1520	1440	1452
Total	13562	13120	15127	15056	14781	14081	15054	15587	16330

data. The data in Zhuzhou fluctuated but have been approaching the national data during recent years. Data from Guangzhou and Harbin were respectively higher and lower than the national data in females. Referring to the female mortality rates, the data from five cities were all close to the national data (Fig. 3C,D).

3.4. Projected future burden

China's population was 1.40 billion in 2016 and will reach 1.43 billion by 2035 according to the United Nations. The estimated 5-year crude incidence rates show a rising trend in the near future, ranging from 2.26 to 3.21 per 100,000 person-years (Table S9).

4. Discussion

Oral and oropharyngeal cancers are the third most common cancers in developing countries and the sixth most common cancers globally [23]. Their prevalence varies across different studies and geographic areas, with high incidences in South-Central and Southeast Asia [10,24]. GLOBOCAN 2012 estimated the incidence and mortality rates of oral and oropharyngeal cancer to be ranked 20th and 24th among all cancers in China in 2012 [9]. We present the population-based epidemiological trends of oral and oropharyngeal cancer in China from 2005 to 2013, providing basic information to give the public a deeper awareness of the urgency and importance of oral and oropharyngeal cancer prevention.

In this study, we combine oral and oropharyngeal cancers because it is impossible to separate them owing to the limitations of data derived from annual reports. Although the incidence and mortality rates of oral and oropharyngeal cancers in China are lower than those in high-risk regions, large numbers of patients are still suffering and dying from oral and oropharyngeal cancers due to China's large population and the low 5-year survival rate [25]. Thus, oral and oropharyngeal cancers should be a focus of attention in China.

Gender differences in oral and oropharyngeal cancers may be important. The results of this study are similar to those of the IARC which has reported that oral and oropharyngeal cancers are more prevalent in males than in females, with two thirds of oral cancer cases occurring in males worldwide [26].

Tobacco is a major risk factor for oral and oropharyngeal cancers.

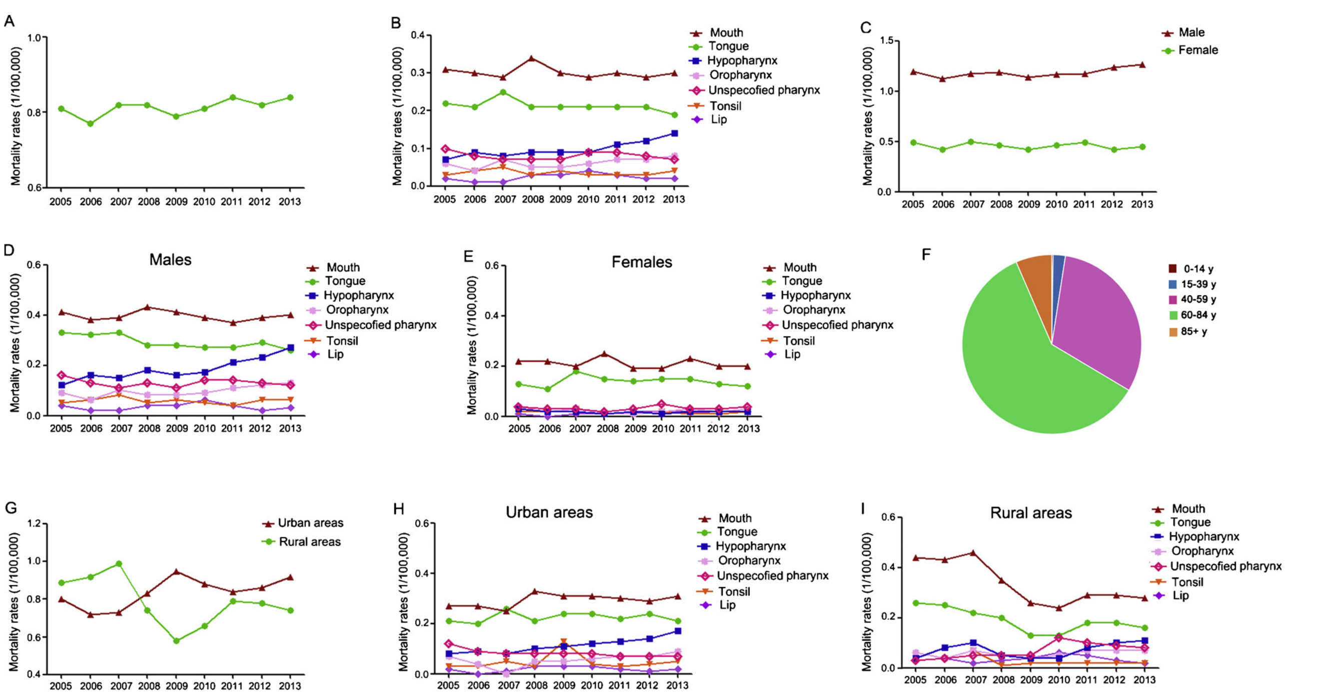

Fig. 2. Mortality of oral and oropharyngeal cancers in China, 2005 to 2013. **(A)** Age-standardized mortality rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers in China. **(B)** Age-standardized mortality rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers arising in different anatomical sites in China. **(C)** Age-standardized mortality rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers in males and females. **(D)** Age-standardized mortality rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers arising in different anatomical sites in males and **(E)** in females. **(F)** Pie chart of the percentage of oral and oropharyngeal cancers deaths in different age groups. **(G)** Age-standardized mortality rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers in urban and rural areas. **(H)** Age-standardized mortality rate (per 100,000 person-years) by world population of oral and oropharyngeal cancers arising in different anatomical sites in urban and **(I)** in rural regions.

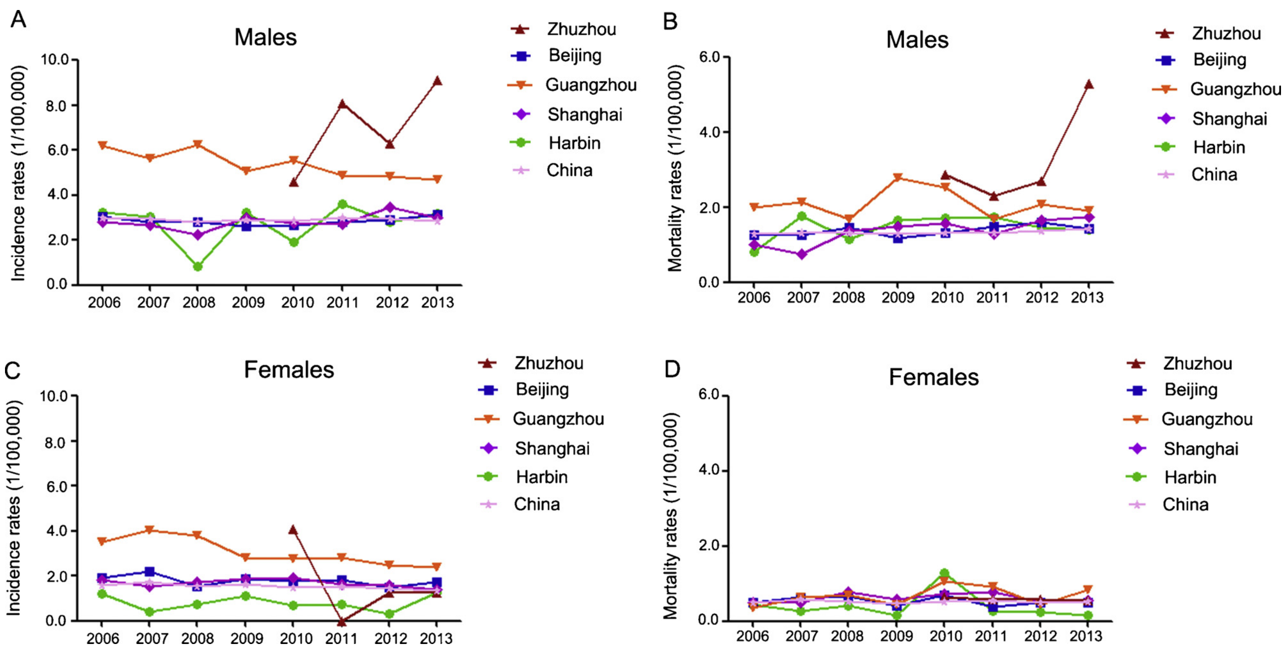

Fig. 3. Oral and oropharyngeal cancers in five representative cities and in the whole of China, 2005 to 2013. Age-standardized incidence and mortality rate (per 100,000 person-years) of oral and oropharyngeal cancers in males (**A, B**) and in females (**C, D**).

An estimated 301 million Chinese were current smokers in 2010, when 52.9% of males and 2.4% of females were considered to be addicted to tobacco [27]. The average number of cigarettes smoked per day was about 15 in males and ten in females. Among male smokers, 63% were 45–64 years of age, the high-risk age group for oral cancers [27]. Furthermore, it has been reported that the risk of oral and oropharyngeal cancers increases with the frequency and duration of tobacco consumption [28]. Thus, differences in smoking habits might be a reasonable explanation for the gender disparity in the incidence and mortality of oral and oropharyngeal cancers. However, the contradiction between high smoking rate and low incidence of oral and oropharyngeal cancer in China remains an elusive issue. Few studies have focused on this problem.

Age is also correlated positively with the incidence and mortality rates of oral and oropharyngeal cancers. Generally, most cases occur in the fifth to eighth decades of life, probably because of prolonged exposure to tobacco, alcohol, areca nut, poor oral hygiene, and complex systemic conditions. However, an alarming trend in the incidence of oral and oropharyngeal cancers in younger people has been reported in some countries [29–31]. The trend appears to be continuing due to HPV infections and heavy consumption of various forms of tobacco from an early age combined with alcohol intake [32]. In addition, the change in sexual behaviors could lead to oral HPV exposure, which might lead to the increase in oral and oropharyngeal cancer incidence among those < 60 years old [33]. Moreover, it has been reported that estrogen deficiency caused by the menopause or hysterectomy might contribute to the high rates of oral cancer reported among younger females [34].

The incidence rates of oral and oropharyngeal cancers were much lower in rural areas than in urban areas. This may be related to the better environment, less stress, a slower pace of life, and different dietary habits. Air pollutants are reportedly positively correlated with squamous cancer of the pharynx [35], while a diet rich in fruits and vegetables can prevent oral cancer [36,37]. However, the incidence rate began to decrease from 2009 in urban areas and increase from 2008 in rural areas. The causes might be various. On the one hand, with the popularity of cancer registries in China, increasing registries have been set up to collect the epidemiological data of rural areas which might have been missed during the earlier years. On the other hand, according to the data from National Bureau of Statistics of China, more and more rural young people have been moving to cities in recent years. The trend of a floating population might result in an increase in the proportion of elderly residents in rural areas who constitute a high-risk age group for oral cancer. In contrast, the mortality rate in rural areas was higher than that in urban areas before 2008 and decreased thereafter. The declining mortality in rural areas might be attributable to earlier diagnosis and improved treatment. With economic development in China, an increasing proportion of the rural population has access to better medical care.

Hundreds of millions of people worldwide are estimated to consume betel quid or areca nut. The consumption is especially prevalent in the Asia–Pacific region [38]. Hunan is one of the regions in China in which the use of areca nut is prevalent. Numbers of areca-nut-associated oral cancer patients are increasing rapidly in Hunan Province, where an estimated 75,162 new cases are projected by 2030 [39]. Areca nut has been classified by the IARC as carcinogenic to human beings (Group 1) and is associated with dependence in users [4,38]. Local governments must develop professional surveillance, clinical services, and policy considerations to control or even reverse the fast-growing trend in oral cancers associated with areca-nut products.

Infection with Epstein–Barr virus (EBV) and food structure diversity may be involved in the high incidence of oral and oropharyngeal cancer in Guangdong Province. EBV is closely associated with nasopharyngeal carcinoma (NPC), which is quite prevalent in Guangdong Province [40,41]. Genetic susceptibility and EBV reactivation by environmental or dietary factors may contribute to the high incidence of NPC in southern China [42,43]. Considering the possible association between EBV infection and oral cancers [40,44], we hypothesize that there might be some similarities between the high incidence of oral and oropharyngeal cancer and NPC in southern China. However, further research is needed to verify this hypothesis.

We estimate that the crude incidence rate of oral and oropharyngeal cancer will show an upward trend from 2015 to 2035. With a growing and aging population and the accompanying increasing socioeconomic burden, future attention should be focused on epidemiological aspects of oral and oropharyngeal cancer in China. It is generally advisable to encourage people to quit or decrease their consumption of tobacco and to seek regular oral health care to reduce the risk of oral and oropharyngeal cancer.

This study has some limitations. First, although the proportion of the population covered by eligible cancer registries is increasing, the majority of the population is not covered, and this may affect the assessment of the epidemiological trends in China. Second, because most cancer registries are located in east-central regions of China, epidemiological data for western areas were inadequate. Furthermore, the quality of information from rural registries is lower than that from urban registries, which could lead to bias. Third, because the estimates derived from GLOBOCAN 2012 may vary in the completeness and reliability of data from national/regional cancer registries, deviation between the global data from GLOBOCAN 2012 and the actual situation is inevitable.

5. Conclusion

Our preliminary investigation indicates that the incidence of oral and oropharyngeal cancers fluctuates, whereas the mortality rate shows a rising trend from 2005 to 2013. Although the prevalence of oral and oropharyngeal cancers is not high in China, these conditions deserve attention based on the terrible prognosis, especially among elderly males. Early diagnosis, early intervention, and regular follow-ups should be promoted to improve the prognosis of oral and oropharyngeal cancers and to reduce future incidence and mortality rates.

Author contributions

Li-Wei Zhang and Jin Li contributed to data acquisition and analysis, and drafted the manuscript; Xin Cong, Xiao-Sheng Hu, Dan Li and Li-Ling Wu contributed to data analysis and interpretation; Guang-Yan Yu, Hong Hua and Alexander Ross Kerr contributed to conception and design, and critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of the work

Conflict of interest

The authors declare no conflict of interests.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2018.10.014.

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