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Mortality and disease burden of oral cancer in China: a time-trend analysis on the China Death Surveillance Database from 2006 to 2021

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Abstract

Background Oral cancer is one of the most common cancers in China and seriously threaten life and health of Chinese people. We analysed the trends and disparities of oral cancer mortality rates and the disease burden of oral cancer in China from 2006 to 2021 to provide a reference for its prevention and control.

Methods Annual death data for oral cancer was gleaned from the China Death Surveillance Database. The age-standardized mortality rate (ASMR), annual percentage change (APC), and average APC (AAPC) were used to analyze the trend of mortality. Loss of life expectancy (LLE) and years of life lost (YLL) were adopted to assess disease burden.

Results From 2006 to 2021, the overall ASMR of oral cancer lightly declined (AAPC: − 0.97%; 95% CI: − 1.89%, − 0.04%), and the similar trend was observed among females (AAPC: − 1.22%; 95% CI: − 1.89%, − 0.55%). The ASMR of males was 2.31–3.16 times higher than that of females per year. The median of LLE for overall, males and females caused by oral cancer from 2006 to 2021 were 0.05, 0.06 and 0.03 years, respectively. There was a decrease of standardized YLL rate from 2006 to 2021 for overall (AAPC: − 1.31%, 95% CI: − 2.24% ~ − 0.37%) and for female (AAPC: − 1.63%, 95% CI: − 2.30% ~ − 0.95%). ASMR in urban areas was 1.02–1.28 times higher than that in rural areas from 2006 to 2011, but 0.85–0.97 times lower in urban areas than that in rural areas from 2018 to 2021. The disease burden was higher in urban areas than in rural areas in 2006, whereas the reverse was observed in 2021.

Conclusions There are severe health gaps and disparities in trends between sexes and different areas in China. Males and rural populations need to be focused on targeted interventions for the main influencing factors.

Keywords Oral cancer, Mortality, Loss of life expectancy, Years of life lost, China

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Background

As one of the most common cancers in the world, oral cancer is diagnosed with more than 300,000 cases each year, which is poor in prognosis and has become an important part of the global oral health problem [1, 2]. In 2020, cancer of the lip and oral cavity was estimated to rank 16th in incidence and mortality worldwide and was a common cause of cancer death in men across much of South and Southeast Asia and the Western Pacific [3]. Significant differences persist among countries, nearly two-thirds of cases occur in developing countries, half of them in South Asia [4]. Studies predicted that due to global demographic adjustment, the global incidence of oral cancer will increase by 62% to 856,000 cases by 2035 [5]. More than 90% of oral cancers are squamous cell carcinomas, which are easy to be ignored or misdiagnosed, so that many oral cancer patients are in the middle and advanced stages at the time of being diagnosed, resulting in a low 5-year survival rate [6].

As with systemic malignancies, the pathogenesis of oral malignancies has so far been considered a multifactorial problem. There are many studies on oral cancer, and risk factors are gradually discovered or verified, but its etiology and pathogenesis are still not fully understood. Current studies suggested that smoking, alcohol consumption, human papillomavirus (HPV) infection and betel nut chewing were recognized as etiologies or risk factors for oral cancer [7–10]. Where risk factors are prevalent, further analysis of mortality and disease burden due to oral cancer is needed.

In 2020, the number of new cases of oral cancer in China was more than 30,100, and the number of deaths was more than 14,700, which poses a serious threat to the life and health of Chinese residents [3]. In a study based on the Global Burden of Disease, the Age-Standardized Incidence Rate (ASIR) and ASMR of oral cancer in China increased from 1990 (1.40 and 0.92 per 100,000) to 2019 (2.25 and 1.16 per 100,000). In 2019, both ASIR and ASMR were higher in males (3.48 and 1.95 per 100,000) compared to females (1.16 and 0.50 per 100,000) [11]. Additionally, in 2011, the ASIR and ASMR were higher in urban areas (2.42 and 0.94 per 100,000) than in rural areas (1.88 and 0.84 per 100,000) [12]. The crude incidence rate of oral cancer in China was predicted to increase from 2.26 to 3.21 per 100,000 person-years over the next 20 years [13]. However, there is a lack of recent studies on mortality and disease burden trends of oral cancer in China. So further analysis of mortality and disease burden trends of oral cancer in China is needed to take measures to take a local, tailored approach to optimally reduce the burden of lip, oral and pharyngeal malignancies in the coming decades.

As one of the most populous countries in the world, trends in resident mortality in China may serve as early indicators to support the progress of public health initiatives to reduce the burden of disease and improve the quality of life. In this study, we analysed the death data of lip, oral and pharyngeal malignancies based on sex and areas from the China Death Surveillance Database, aimed to evaluate the trends and disparities of mortality and disease burden of the major oral cancers from 2006 to 2021 in China. It will help identify high-risk groups of oral cancer, and provide basic data for prevention and health interventions.

Methods

Data source

This analysis based on data of mortality from the "China death cause surveillance dataset" (https://ncncd.china cdc.cn/jcysj/siyinjcx/syfxbg/), which is nationally representative and the data had been widely used to evaluate the disease burden in China. The database was collected by Death Surveillance Points system (DSPs), which was selected from 31 provinces in mainland China by using an iterative method involving multistage stratification [14, 15]. The content includes the number of overall, sex-specific and area-specific people in each age group in the monitoring areas and the number of deaths from 2006 to 2021 (see Additional file 1, Supplementary Table 1 and Supplementary Table 2). Causes of death were coded by International Classification of Diseases-Tenth Revision (ICD-10). Lip, oral and pharyngeal malignancies were coded as C00-C14 (see Additional file 1, Supplementary Table 3).

Statistical analysis

Age-standardized mortality rate (ASMR), annual percentage change (APC) and average APC (AAPC) were calculated to evaluate the trend of mortality by using Joinpoint 5.2.0 software. Joinpoint regression models were used to determine the periods for increases or decreases of ASMR and to calculate the APC with 95% confidence interval (CI). We employed the grid search method to select the grid point with the lowest mean as the segmentation function joinpoint. Monte Carlo permutation method [16] with 4499 randomly permuted data set was used and the overall asymptotic significance level was maintained through a Bonferroni correction. The default maximum number of connection points depends on the number of data points, and according to the algorithm recommendations provided by the Joinpoint Help System, the default value of 16 data points is 2. The AAPC with 95%CI were obtained from Joinpoint models to describe the average APCs. Loss of life expectancy (LLE), years of life lost (YLL), and YLL rates were

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used as indicators of disease burden [17]. The LLE and the proportion of expected life lost (PELL) were calculated by life table, and they were computed as e'_0-e_0 and $(e'_0-e_0)/e_0$ respectively, where e'_0 as the life expectancy at birth in the absence of lip, oral and pharyngeal malignancies and e_0 as the life expectancy at birth in the presence of lip, oral and pharyngeal malignancies. YLL was obtained by multiplying the corresponding standard life expectancy by the number of deaths in the age group [18]. Standardized YLL rate is the ratio of YLL to the number of monitored populations according to the age distribution of standard population. AAPC of standardized YLL rate were calculated by Joinpoint 5.2.0 software. Statistical significance among subpopulations was determined using the chi-square test and Mann–Whitney U Test in IBM SPSS Statistics 26.0. The World Health Organization's World Standard Population (2000–2025) was selected as the standard population [19]. The inspection level was set to $\alpha=0.05$.

Results

Mortality trends of lip, oral and pharyngeal malignancies during 2006–2021

The ASMR of overall oral cancer decreased from 2.12 per 100,000 in 2006 to 1.95 per 100,000 in 2021 (see Additional file 1, Supplementary Table 4). The trends of overall oral cancer ASMR were statistically significant from 2006 to 2021 (AAPC: −0.97%; 95% CI: −1.89, −0.04). There was a decrease from 2.12 in 2006 to 1.96 per 100 000 in 2013 (APC: −1.73%; 95% CI: −3.28, −0.15) and a decrease from 2.16 in 2018 to 1.95 per 100 000 in 2021 (APC: −3.44%; 95% CI: −6.00, −0.81) (Table 1).

The ASMR was 2.31–3.16 times higher for males than that for females per year (see Additional file 1, Supplementary Table 4). For males, the APC were not statistically significant from 2006 to 2021. For females, the AAPC decreased by −1.22% (95% CI: −1.89%, −0.55%) per year from 2006 to 2021 (Fig. 1a and Table 1).

The ASMR was 1.02–1.28 times higher for urban areas than that for rural areas from 2006 to 2011, but it was 0.85–0.97 times lower for urban areas than that for rural areas from 2018 to 2021 (see Additional file 1, Supplementary Table 4). For urban areas, there was a decrease from 2.46 in 2006 to 1.90 per 100 000 in 2012 (APC: −2.98%; 95% CI: −5.83%, −0.05%) and a decrease from 2.12 in 2018 to 1.75 per 100 000 in 2021 (APC: −6.21%; 95% CI: −10.24%, −2.00%). For rural areas, the APC were not statistically significant from 2006 to 2021 (Fig. 1b and Table 1).

Disease burden of lip, oral and pharyngeal malignancies in China

The median of LLE for overall, males and females due to oral cancer from 2006 to 2021 were 0.05, 0.06 and 0.03 years, respectively (Fig. 2). Males had a higher LLE compared with that of females. The LLE of the urban areas was higher than those of the rural from 2006 to 2010, while it was not prominent from 2014 to 2021 (Table 2).

The overall standardized YLL rate of oral cancer in China ranged from $21.96/10^5$ to $27.46/10^5$, and there was a decrease from 2006 to 2021 (AAPC: −1.31%, 95% CI: −2.24 ~ −0.37%) (Table 3). The standardized YLL rate of females showed a downward trend (AAPC: −1.63%, 95% CI: −2.30 ~ −0.95%), while it did not change significantly for males. The standardized YLL rate was

Table 1 The APC and AAPC of lip, oral and pharyngeal malignancies ASMRs in China

Groups	Years	APC		AAPC	
		APC (95%CI)	P	APC (95%CI)	P
Overall	2006–2013	−1.73(−3.28, −0.15)	0.036	−0.97(−1.89, −0.04)	0.041
	2013–2018	1.63(−0.21, 3.50)	0.075		
	2018–2021	−3.44(−6.00, −0.81)	0.017		
Sex					
Male	2006–2013	−1.52(−3.43, 0.42)	0.108	−0.69(−1.81, 0.45)	0.234
	2013–2018	1.92(−0.31, 4.20)	0.082		
	2018–2021	−3.00(−6.08, 0.19)	0.062		
Female	2006–2021	−1.22(−1.89, −0.55)	0.002	−1.22(−1.89, −0.55)	0.002
Area					
Urban	2006–2012	−2.98(−5.83, −0.05)	0.047	−2.22(−3.62, −0.79)	0.002
	2012–2018	0.64(−1.48, 2.79)	0.510		
	2018–2021	−6.21(−10.24, −2.00)	0.010		
Rural	2006–2021	0.27(−0.29, 0.83)	0.316	0.27(−0.29, 0.83)	0.316

ASMR Age-standardized mortality rate, *APC* Annual percentage change, *AAPC* Average annual percentage change, *CI* Confidence intervals

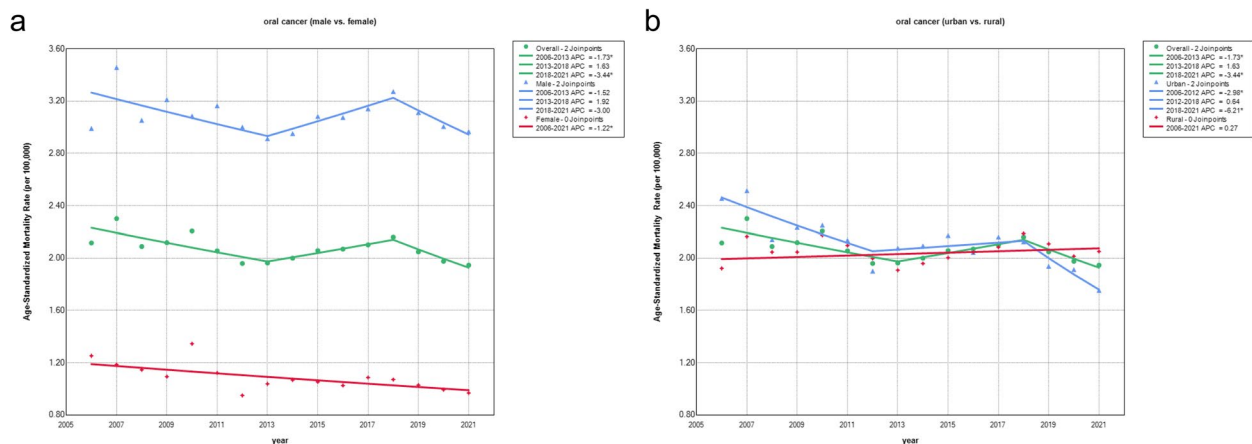Zhang *et al. BMC Oral Health* (2024) 24:938

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Fig. 1 Trends in major oral cancer ASMRs by sex and area in China from 2006 to 2021. **a** The ASMRs trends in different sexes. **b** The ASMRs trends in urban and rural areas. *, $P < 0.05$
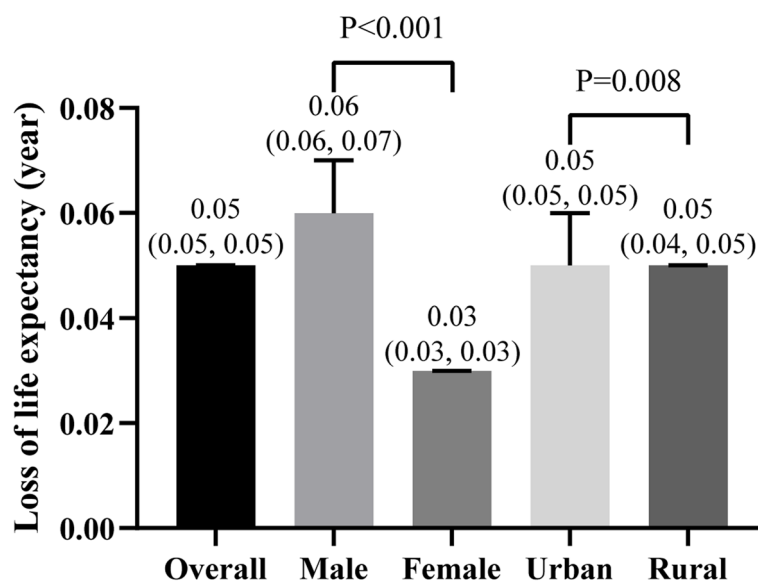

Fig. 2 LLE (years) in different sexes and areas in China due to lip, oral and pharyngeal malignancies mortality. LLE was represented by the median (P_{25}, P_{75})

2.61–3.36 times higher for males than that for females per year (Fig. 3a and Table 3). The standardized YLL rate of urban areas showed a downward trend (AAPC: −1.94%, 95% CI: −2.73% ∼ −1.16%), while the rural areas did not change significantly. In 2006, the YLL rate of urban areas was higher than that of rural areas, but the YLL rate of rural areas was higher than that of urban in 2021 (Fig. 3b and Table 3).

Discussion

In this nationally representative population-based study, the most recent current and spatial dynamics of major oral cancers were identified in different subpopulations in China. We found that overall ASMR and standardized YLL rates for oral cancer decreased from 2006 to 2021, with this trend also occurring in females and urban areas. The ASMR and standardized YLL rates of oral cancer in males were 2.31–3.16 times higher and 2.61–3.36 times higher than in females per year, respectively. Males had higher LLE than females due to oral cancer from 2006 to 2021. ASMR was 1.02–1.28 times higher in urban areas than in rural areas from 2006 to 2011, but 0.85–0.97 times lower from 2018 to 2021. The burden of disease also changed from higher in urban areas in 2006 to higher in rural areas in 2021.

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Table 2 LLE (years) and PELL (%) caused by lip, oral and pharyngeal malignancies mortality in different sexes and areas in China

Years	Overall	Sex		Area	
		Male	Female	Urban	Rural
2006	0.05(0.06)	0.06(0.08)	0.03(0.04)	0.06(0.07)	0.04(0.06)
2007	0.05(0.07)	0.06(0.09)	0.03(0.04)	0.06(0.07)	0.05(0.06)
2008	0.05(0.06)	0.06(0.08)	0.03(0.04)	0.05(0.07)	0.04(0.06)
2009	0.04(0.05)	0.05(0.07)	0.02(0.03)	0.05(0.06)	0.04(0.05)
2010	0.04(0.05)	0.05(0.07)	0.03(0.03)	0.05(0.06)	0.04(0.05)
2011	0.04(0.05)	0.05(0.07)	0.03(0.03)	0.04(0.05)	0.04(0.05)
2012	0.05(0.06)	0.06(0.08)	0.03(0.03)	0.05(0.06)	0.04(0.06)
2013	0.04(0.06)	0.06(0.08)	0.03(0.03)	0.05(0.06)	0.04(0.05)
2014	0.05(0.06)	0.06(0.08)	0.03(0.04)	0.05(0.06)	0.05(0.06)
2015	0.05(0.06)	0.06(0.08)	0.03(0.03)	0.05(0.06)	0.05(0.06)
2016	0.05(0.06)	0.06(0.08)	0.03(0.03)	0.05(0.06)	0.05(0.06)
2017	0.05(0.06)	0.07(0.09)	0.03(0.04)	0.05(0.06)	0.05(0.06)
2018	0.05(0.07)	0.07(0.09)	0.03(0.04)	0.05(0.06)	0.05(0.07)
2019	0.05(0.06)	0.06(0.08)	0.03(0.03)	0.05(0.06)	0.05(0.06)
2020	0.05(0.06)	0.07(0.08)	0.03(0.03)	0.05(0.06)	0.05(0.06)
2021	0.05(0.06)	0.07(0.09)	0.03(0.04)	0.05(0.06)	0.05(0.06)
Median (P_{25}, P_{75})	0.05(0.05, 0.05)	0.06(0.06, 0.07)	0.03(0.03, 0.03)	0.05(0.05, 0.05)	0.05(0.04, 0.05)
Mann–Whitney U Test		$P < 0.001$		$P = 0.008$	

LLE Loss of life expectancy, *PELL* Proportion of expected life lost

The overall ASMR and standardized YLL rates in China were generally stable and slightly declining, and they showed a downward trend in 2006–2013 and 2018–2021, which was consistent with the global trend [20]. The slight increase after 2013 may be related to the enhancement of China's cancer screening capacity, the formulation and implementation of cancer prevention and control policies, and the low 5-year survival rate of oral cancer. For example, it coincides with the release and implementation of policies such as the Outline of China Cancer Prevention and Control Plan (2004~2010) and the Project Management Measures for Early Diagnosis and Treatment of Urban Cancer (Trial). The decline of ASMR of overall oral cancer after 2018 may be related to the improvement of dietary patterns and structure, as well as other influencing factors such as ultraviolet radiation (UVR) and the reduction of high-risk human papillomavirus (HPV) infection [21–23]. HPV-based testing is a pivotal part for cervical cancer screening besides cytology-based tests. To restrict and standardize HPV testing market, China released guidelines for the clinical performance evaluation for HPV testing against clinical endpoints in 2015 [24]. China has launched five vaccines since 2016, including Cervarix, Gardasil, Gardasil-9, Cecolin and Walrinvax. In addition, HPV vaccines are only approved for females, with RCTs in males ongoing [25]. It

has been assessed that vaccination has effectively avoided a large number of cases and deaths [26]. In addition, some specific biomarkers are helpful to identify early oral cancer, make a better treatment plan for patients and improve the prognosis [27, 28].

ASMR and standardized YLL rates are significantly higher for males than that for females, indicating a sex difference in the burden of oral cancer disease, which is consistent with previous studies [29]. Other countries with similarly high ratios of male-to-female ASMR, including Brazil, Russia and the United States [30, 31]. This difference may be related to sex-specific lifestyles, occupational exposures, and physiological factors, with males being more exposed than females to risk factors such as smoking, alcohol and betel nut chewing [5, 32–35]. A study has shown that the risk of oral cancer is 123 times higher in the population who smoke, drink and chew betel nut than in the general population [36]. In China, smoking is much more prevalent among men than women, with rates of 47.2% and 2.7% respectively in 2013. The standardized smoking prevalence has remained consistently high: 26.0% in 2003, 24.9% in 2008, and 25.2% in 2013, with no statistically significant changes [37]. Alcohol consumption is significantly higher among Chinese men (55.6%) than women (15%) in 2007 [38]. In East Asia, including China, DPR Korea, and

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Table 3 Standardized YLL rate of lip, oral and pharyngeal malignancies in different sexes and areas in China (1/10^5)

Years	Overall	Sex		Area	
		Male	Female	Urban	Rural
2006	24.78	35.90	13.33	27.47	23.15
2007	27.46	40.80	13.84	28.37	26.82
2008	25.33	36.71	13.74	25.45	25.12
2009	23.70	35.25	12.15	25.53	22.52
2010	24.19	34.91	13.36	24.71	23.79
2011	22.63	34.67	11.77	21.59	24.53
2012	22.82	35.05	10.47	21.00	23.99
2013	22.69	33.83	11.39	23.40	22.39
2014	23.07	34.11	11.87	23.27	23.07
2015	23.53	35.84	11.09	23.75	23.43
2016	24.26	36.01	11.03	21.77	24.64
2017	24.51	36.94	11.93	23.55	25.15
2018	24.94	37.99	11.70	22.98	26.08
2019	23.00	35.50	10.58	20.44	24.43
2020	22.55	34.64	10.54	20.77	23.61
2021	21.96	33.92	10.14	18.49	23.89
AAPC	−1.31	−0.85	−1.63	−1.94	−0.51
95%CI	−2.24, −0.37	−1.92, 0.23	−2.30, −0.95	−2.73, −1.16	−1.82, 0.82
t	−2.73	−1.54	−5.13	−5.26	−0.75
P	0.006	0.124	<0.001	<0.001	0.450

YLL Years of life lost, *AAPC* Average annual percentage change, *CI* Confidence intervals

Taiwan, per capita alcohol consumption rose from 4.4 L in 1990 to 7.3 L in 2017, projected to reach 10.0 L by 2030 [39]. Pakistan, India and Bangladesh had the highest rates of oral cancer mortality, with the highest tobacco chewing prevalence, revealing a strong relationship between tobacco chewing and oral cancer. Brazil has adopted measures control tobacco, and the burden of oral cancer has been reduced, which is worth learning. Tobacco control may be the most cost-effective solution to reduce the burden of oral cancer [29]. Notably, the combination of smoking and drinking shows a synergistic effect [40]. Occupational exposure is also a risk factor for oral cancer in modern society, with more time occupational exposure to chlorinated solvents, oxygenated solvents,
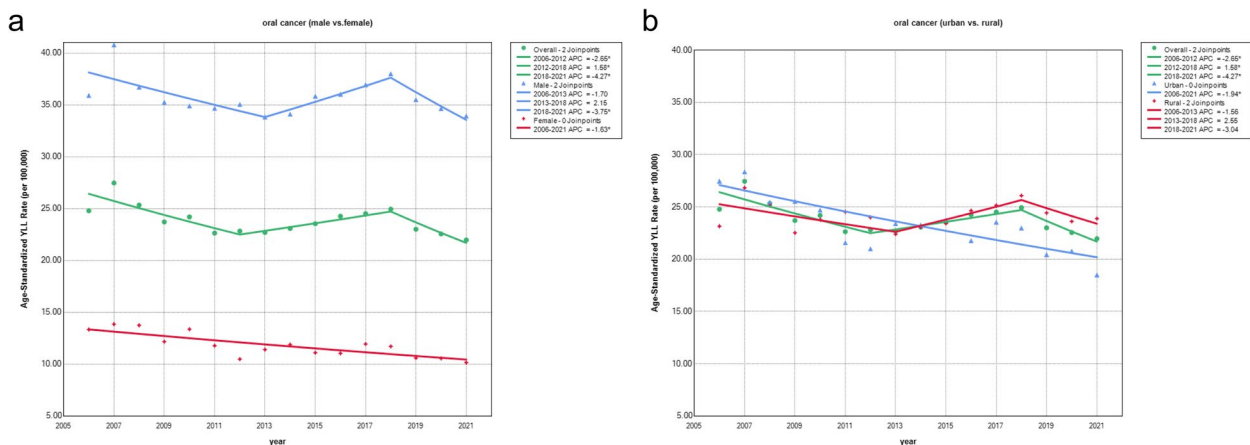

Fig. 3 Trends in major oral cancer standardized YLL rate by sex and area in China from 2006 to 2021. **a** The standardized YLLr trends in different sexes. **b** The standardized YLLr trends in urban and rural areas. *, *P* < 0.05

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welding and other environments [6, 41]. For the perspective of physiological factors, the female body secretes estrogen and benefits from the protection of endogenous estrogen, thereby improving its adaptability to the environment [42]. Therefore, the disease burden of oral cancer for males in China is higher than that for females, suggesting that males are the key population in reducing the disease burden and we should pay more attention to this high-risk groups.

The mortality rates were higher in urban areas than in rural areas from 2006 to 2017, and higher in rural areas than in urban areas from 2018 to 2021, and the gap between urban and rural areas gradually narrowed and then widened. Higher stress in fast-paced urban populations may explain the high mortality rates in urban areas. A study in India has shown a significantly increased risk of oral cancer in the sample of stress and current health problems [43]. Studies have shown that tooth trauma and bleeding gums are highly associated with oral cancer [44]. The mortality rate lower in urban areas than in rural areas in recent years, may be related to the fact that the urban medical system is more complete than the rural one, the oral health awareness is stronger, and it is easier to be diagnosed and treated early [45].

Therefore, Chinese need to avoid or delay oral cancer through a healthy diet, maintaining oral hygiene, quitting smoking and limiting alcohol, and timely examination and treatment of oral related diseases, especially males and people in rural areas. In addition, educational attainment and socioeconomic status also have an impact on the disease burden of oral cancer [46, 47]. A cross-sectional study from Latin America showed that greater inequality, higher health expenditure per capita and greater investment in research and development were associated with a higher mortality rate from oral cancer [48]. An ecological study from Brazil showed that greater Bolsa Família Program (BFP) coverage was associated with lower oral cancer mortality rates, suggesting that Egalitarian strategies such as BFP can reduce the risk of death from oral cancer [49]. Targeted poverty alleviation policies may helpful to reduce the oral cancer mortality rate in this regard in China.

The advantage of this study is to analyze the changing trend of oral cancer mortality and disease burden by sex and area based on the Chinese death surveillance database, identify high-risk groups, and then explore the favorable measures and unfavorable factors of high-risk groups of oral cancer death, so as to provide early prevention strategies for reducing oral cancer mortality and disease burden in China. However, some limitations in this study should be considered. As data are not available in the China Death Surveillance Database, we have not yet analysed the burden of disease in different subsites. Morbidity information, Disability Adjusted Life Year (DALY) as the other two indicators of disease burden were not calculated because the surveillance content was mainly death data. Additionally, the latest available surveillance data is currently 2021. Since ICD codes were used to assess the cause of death, there might be certain selection bias or tendency in determining the main causes of death in how reporting is carried out at the national/areal/level. As the Chinese population ages, the trend of mortality and burden of disease in different age groups should be included in future studies.

By China Death Surveillance Database (2006–2021), our study analysed the trend of mortality and disease burden of lip, oral and pharyngeal malignancies, founding that the changing trends and disease burden of the major oral cancer are related to sex and area, to help achieve accurate early screening and warning of high-risk groups, and to provide a scientific basis for the government to formulate policies and improve the health status of residents in China.

Conclusions

To summarize, our study shows that the disease burden of oral cancer ASMRs in China remains stable or declining. Despite this, China still bears a huge burden of oral cancer. Males are much higher than females in both mortality and disease burden, and the gap of mortality and disease burden remains between rural and urban areas. Males and rural populations need to be focused on targeted interventions for the main influencing factors.

Abbreviations
ASMR   Age-standardized Mortality Rates
APC   Annual Percent Changes
AAPC   Average Annual Percent Changes
CI   Confidence Interval
DSPs   Death Surveillance Points system
GBD   Global Burden of Disease
ICD   International Classification of Diseases
LLE   Loss of Life Expectancy
PELL   Proportion of Expected Life Lost
YLL   Years of Life Lost

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s12903-024-04717-5.

Additional file 1.

Authors' contributions
Peng Wang, Jicun Zhu and Xiaoyue Zhang conducted study design and study concepts. Weihong Xie, Hua Ye, Xiaoyue Zhang, Yaxin Zhang and Zhong Zheng conducted data acquisition and quality control of data and algorithms.

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Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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