

# Estimate of Health Burden on Smoking-associated Oral Cancer in Shanghai and its Surrounding Areas

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**Objective:** To evaluate the temporal trend of inpatients with smoking-associated oral cancer in Shanghai and its surrounding areas and to forecast the public health burden in the next decade.

**Methods:** Data of inpatients with oral cancer were retrieved from Shanghai Ninth People's Hospital during a 15-year period. The annual numbers of inpatients were compared by Chi-test. The hospitalization expenditures were compared by Student's *t* test. The trend analysis and inpatient forecasting were performed by exponential smoothing, regression models, and the forecasting function in Excel software. The financial burden of smoking-associated oral cancer was calculated by polynomial equation.

**Results:** The annual number of inpatients with oral cancer increased during the study period. Most male patients were reported to have a smoking habit. Among the three estimation methods, polynomial regression model was most fitted to the existing data. By a conservative estimation, the public health burden of smoking-associated oral cancer patients will be 120 million RMB by the year 2026, not including the cost by prevalent patients and the patients' family members.

**Conclusion:** Smoking-associated oral cancer will cost a lot of public resource in the next decade. Efforts should be made to lower the amount of tobacco consumption.

**Key words:** forecast, health burden, oral cancer, smoking, trend  
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Oral cancer is common in the head and neck region. Worldwide, it represents the eighth most frequent among all malignancies<sup>1</sup>. Melanesia, in the Pacific

islands, was once reported to have the highest incidence of oral cancer in the world, with 22.9 per 100,000 in males and 16.0 per 100,000 in females<sup>2</sup>. In China, the incidence of oral cavity cancer was reported to be 2.16 per 100,000 in 2008. The national figures suggest that there has been a slight increase over the past 10 years<sup>3</sup>.

Without question, tobacco consumption is considered to be the greatest cause of oral cancer. This has been established since an epidemiological study confirmed the relationship between smoking and oral cancer incidence in the middle of 20th century<sup>4,5</sup>. Later, studies from not only South-Central Asia, where the rates were also high in men, but also European countries, the United States, and others revealed a higher proportion of smokers among oral cancer patients than in the rest of the population<sup>6,7</sup>. Furthermore, researchers from laboratories have also found carcinogens in tobacco that cause the normal oral mucosa to develop into dysplasia and malignancy<sup>8</sup>.

Despite warnings of the hazards, tobacco is still widely consumed throughout the world. In the Chinese

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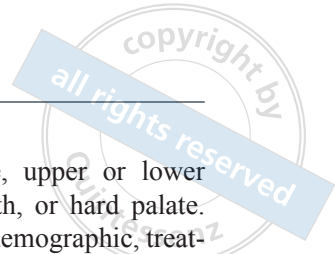
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Tobacco Development Report 2015, the tobacco industry remains a major component of the national economy and has been running at a high level for a long time. In 2014, national tobaccos sales figures were reported to be more than 1,400 billion RMB, with more than 50 million cartons of cigarettes sold<sup>9</sup>. In addition, tobacco companies continue to improve their marketing methods. They sponsor public welfare activities or grand entertainment programmes to improve their social influence, as well as their corporate image. They invented a filter at the end of cigarettes to reduce hazardous smoke. Fine cigarettes were also introduced to the market, which were much thinner than normal cigarettes. They claim that these methods mean lower tar and less harm. However, this is not true<sup>10,11</sup>.

In a nationwide survey on smoking behaviour in the Chinese population, about 60% of male adults were revealed to be current smokers and at least 10% were former smokers. The smoking habits of young people aged 15 to 24 have risen over the past 10 years<sup>12</sup>. Regarding this behaviour and the risk factor of oral cancer incidences, the number of current smokers and the increased number of young smokers also suggests a potential rise in the number of oral cancer patients in a few years.

Therefore, it is urgent to study the current status of oral cancer incidences related to smoking and forecast trends for the future. The aim of the present study is to estimate incidences of smoking-associated oral cancer on the social health burden and to provide the public health department with evidence-based clues for intervention policies.

## Materials and methods

### *Data collection on oral cancer cases*

Data on oral cancer cases were collected from inpatients of the Shanghai Ninth People's Hospital from January 2002 to December 2016. The hospital's oral and maxillofacial department is renowned in the country. On average, the annual oral cancer patient admission numbers for the department is about 2,500. More than 90% of patients were from Shanghai and surrounding provinces. Thus, the data of oral cancer patients is considered to be representative of the local region.

Cases enrolled were patients whose diagnosis was pathologically confirmed to be oral squamous cell carcinoma and whom initially received treatment in this hospital. Recurrent and relapsed patients were not included. The lesion sites were confined to the oral

cavity, comprising the oral tongue, upper or lower gum, buccal mucosa, floor of mouth, or hard palate. Data collection included the patient demographic, treatment options, the cost of hospitalisation, and a detailed history of smoking habits. No information to identify individual cases was included and the informed consent was waived.

### *Trend analysis on historical data*

To compare trends in the annual number of oral cancer inpatients, the patients were divided into five different cohorts according to their dates of initial admission (cohort 1: 2002 to 2004 [n = 997]; cohort 2: 2005 to 2007 [n = 1360]; cohort 3: 2008 to 2010 [n = 2003]; cohort 4: 2011 to 2013 [n = 2187]; cohort 5: 2014 to 2016 [n = 2527]). The percentage comparison was calculated by  $\chi^2$  test. The medical costs of the different groups were compared by Student t test. Statistical significance was set to be  $P < 0.05$ . The analysis was performed using the statistical software package SPSS (version 19; IBM).

### *Forecasting with Microsoft Excel*

The Microsoft Excel is spreadsheet software written by Microsoft Corp's to handle various types of tables and data. Its forecast function is based on historical data to perform time series prediction. There are three main forecasting algorithms in Excel 2010: the exponential smoothing, the regression equation, and the forecasting function.

The exponential smoothing is suited to short-term prediction. It does not abandon the early data, but gives a gradually weakening impact on the previous values. For the earliest date, the weight of the numbers was converged to be zero. The principle of the method is that the exponential smooth value of any period is the weighted average of the actual value and the exponential smooth value of the previous period. By a series of exponentially decreasing smoothing values, the recent trend was extended to the future. In this study, the smoothing coefficient was originally set to be 0.2 in order to calculate the optimal damping coefficient on the basis of historical data to make the smallest deviation.

The method of regression model is to establish a regression equation by analysing the relationship between time and historical data. An estimate is then derived from the equation. The statistical significance of the relationship depended on the regression coefficient R-square. It was set as  $> 0.95$  for statistical significance in this study, which is similar to the  $P$  value in statistical hypothesis. There are three equations com-

**Table 1** Trend of the number of inpatients with oral cancer from 2002 to 2016

Oral cancer patients	No. (%)					$\chi^2$ - value	P value
	2002-2004	2005-2007	2008-2010	2011-2013	2014-2016		
Total <sup>1</sup>						36.69	0.001
	997 (29.6)	1360 (29.9)	2003 (32.1)	2187 (33.9)	2527 (33.6)		
Sex						9.57	0.048
Male	578 (58.0)	810 (59.6)	1175 (58.7)	1314 (60.1)	1578 (62.4)		
Female	419 (42.0)	550 (40.4)	828 (41.3)	873 (39.9)	949 (37.6)		
Smoking <sup>2,3</sup>						17.13	0.002
Never/former	108	133	189	190	198		
Current	461	674	976	1122	1374		
Tumour subsites						125.87	0.001
Tongue	419 (42.03)	539 (39.63)	808 (40.34)	872 (39.87)	994 (39.34)		
Cheek	225 (22.57)	250 (18.38)	531 (26.51)	477 (21.81)	537 (21.25)		
Gingiva	216 (21.66)	256 (18.82)	320 (15.98)	469 (21.44)	531 (21.01)		
Floor of mouth	80 (8.02)	252 (18.53)	208 (10.38)	236 (10.79)	319 (12.62)		
Palate	57 (5.72)	63 (4.63)	136 (6.79)	133 (6.08)	146 (5.78)		

<sup>1</sup> The percentage referred to oral cancer patients in the total number of inpatients at the same time.

<sup>2</sup> Owing to the low smoking rate in women, analysis of smoking history only referred to male patients.

<sup>3</sup> Patients whose smoking history was not available were not included in the analysis.

monly used: two polynomial regression, exponential regression, and logarithmic regression. All were fitted to the historical data in this study to find the best one to estimate the financial burden of smoking-associated oral cancer.

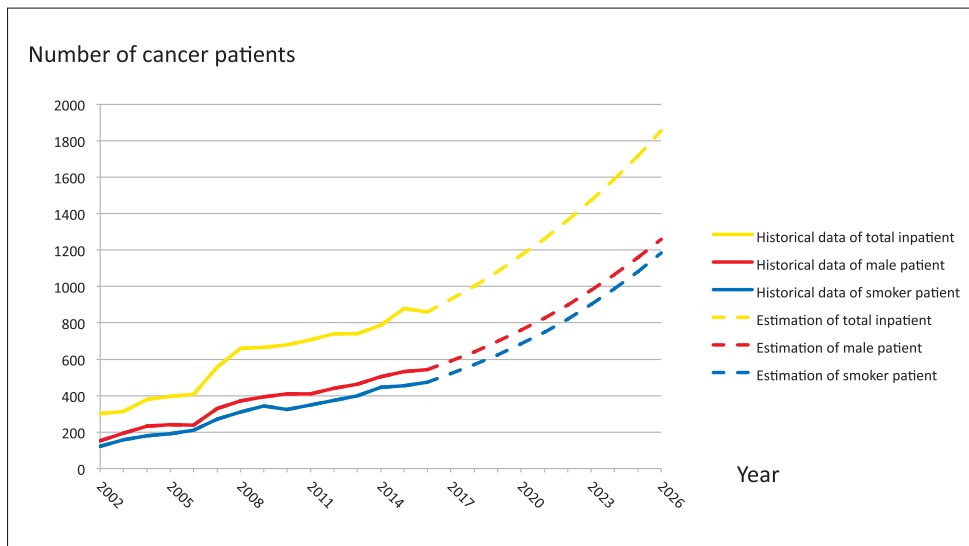
The forecasting function in the Excel software is based on linear regression. The linear regression is the first type of regression analysis model that has been strictly studied and widely used in practice. It can easily generate the statistical properties and fit the historical data better than other methods. Thus, it is simple, but basic in projection. Originally, the model was established by step-by-step summing of the square errors between hypothetical and actual figures. In Excel 2010, the function eliminates the complicated calculation and is modified to a friendly interface. The three forecasting methods were all used in this study for the optimal estimation of the public health burden from smoking-associated oral cancer for the next decade.

## Results

### *Temporal trend of historical data*

A total of 15 years' worth of data was collected, with 9074 cases enrolled. This included 5455 males and 3619 females. The median age at admission was 58.8 years, and ranged from 17 to 97 years. In this series, 84.5% of male patients reported to be current smokers.

The temporal trends of inpatient numbers with oral cancer from 2002 to 2016 are shown in Table 1. Annually, the total number of oral cancer patients has significantly increased ( $P < 0.001$ ), from 302 in 2002 to 859 in 2016. This amounts to a percentage increase from 29.6% to 33.6% during the study period. The figures of both male and female patients rose during the study period. Meanwhile, the percentages of the male inpatients increased more obviously ( $P = 0.048$ ). Owing to the low smoking rate in women, the smoking history analysis referred only to male patients. Compared with the number of non-smoking patients or



**Fig 1** Estimation of oral cancer patients and patients with smoking habits in the next decade by exponential smoothing in Excel.

former smokers, the number of patients with a smoking habit significantly increased over time ( $P = 0.002$ ). In the 15-year period, there were changes in tumour sub-site classification, with a small increase in the number of floor of mouth cancers treated and a reduction in cases of tongue cancer cases.

*Estimation of inpatients with oral cancer*

Based on the analysis of historical trends, the numbers of total oral cancer inpatients, male patients, and patients with a smoking history for the next decade were estimated separately.

Figure 1 shows the estimation by exponential smoothing method in Excel for the coming decade (2017 to 2026). By the year 2026, the number of oral cancer patients treated in our hospital is expected to reach 1855 per year, with 1260 male patients (93.9%)

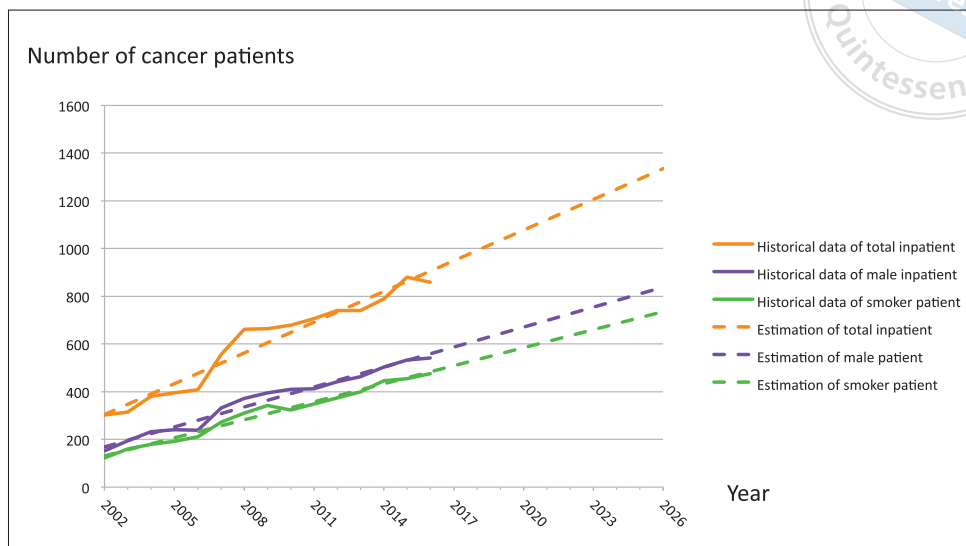
having a smoking habit. However, the standard number of errors between estimation and historical data were 100.2, 60.2, and 54.7 for total oral cancer inpatients, male patients, and smoking patients, respectively.

Table 2 shows the estimation of total inpatients with oral cancer, male patients, and smoking patients using three regression methods: two polynomial regression, exponential regression, and logarithmic regression. Among the regression functions, the two polynomial regressions had the biggest  $R^2$  value, so best fitted with the historical data of the study. According to the two polynomial, there will be 982 inpatients diagnosed with oral cancer by the year 2026 and 94% of male patients will report a smoking habit.

The estimation by forecast function in Excel is displayed in Figure 2. After modelling the historical data, the total number of inpatients with oral cancer will be 1335 in the year 2026, with 88% of male patients hav-

**Table 2** Estimation of oral cancer patients for the next 10 years by different regression models.

Year	Two polynomial regression			Exponential regression			Logarithmic regression		
	Total inpatients	Male patients	Current smoker	Total inpatients	Male patients	Current smoker	Total inpatients	Male patients	Current smoker
2017	889	563	495	1068	672	590	821	504	432
2020	944	616	554	1351	868	777	862	530	456
2023	975	660	607	1708	1120	1021	897	552	476
2026	982	695	655	2160	1446	1342	927	572	494
R <sup>2</sup> value	0.9616	0.9794	0.9822	0.9105	0.9254	0.9371	0.8836	0.8992	0.8892



**Fig 2** Historical data and estimation of oral cancer patients from 2002 to 2026 using the FORECAST function in Excel.

ing a smoking habit. The  $R^2$  values were 0.949, 0.974, and 0.980 for total inpatients, male patients, and smoking patients, respectively.

Combining the three methods, the number of oral cancer inpatients treated at our hospital will increase annually by 7.31% in the next 10 years. By the year 2026, about 92% of male oral cancer patients will be associated with a smoking habit.

#### *Estimating the financial burden of smoking-associated oral cancer*

The male patients were only referred when considering the estimation of the financial burden of smoking-associated oral cancer because the smoking habits of females were uncommon in the series. During the study period, the average cost of hospitalisation was 52,327 RMB per case. However, the expense for those

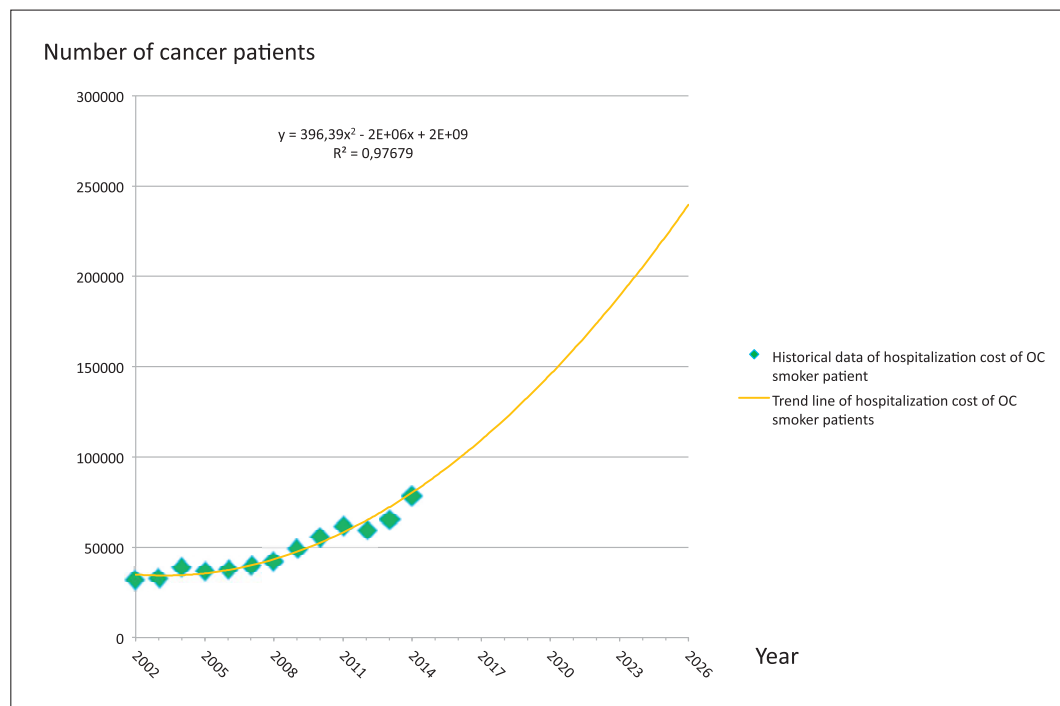
patients with a smoking history reached 56,522 RMB per capita ( $P < 0.05$ ). Table 3 shows the difference in the hospitalisation expenses between patients with and without a history of smoking, according to age groups during the years 2002 to 2016. For all age groups there was a significant difference in the cost for patients with a history of smoking and those without a smoking habit.

Figure 3 shows the growth curve of hospitalisation fees of patients with a history of smoking over the next decade. After modelling the historical data by regression model, this hospitalisation fee will reach 240,000 RMB per capita by the year 2026, which is equal to more than 120 million RMB on public health for smoking-associated oral cancers. This figure only refers to newly diagnosed cases.

**Table 3** Comparison of the hospitalisation expense per capita of oral cancer patients with a smoking history and patients without a smoking habit, according to age\*.

Age (years)	Hospitalisation expense per capita (RMB)		t-value	P value
	Current smoker	Non-smoker		
45	52764	47729	2.755	0.003
45 ~ 65	58118	47762	9.852	< 0.001
≥ 65	55142	43220	9.242	< 0.001

\*Female patients and patients whose smoking history was not available were not included in the analysis.



**Fig 3** Estimation of the public health burden relating to smoking-associated oral cancer in the next decade.

## Discussion

Incidences of oral cancer remain high worldwide, especially in the Oceania islands, South Central Asia, and some central and eastern European countries. An increase in incidence has been reported recently in some developing countries<sup>13</sup>. In Shanghai (China), the incidence has slightly increased; the reported incidence was 3.02 per 100,000 inhabitants in 2003 vs 4.28 per 100,000 in 2012<sup>14</sup>. The main established etiological factor for oral cancer is smoking. Thus, one could hypothesise that the increase in oral cancer incidences is due to the increase in consumption of tobacco products. However, to our knowledge, there have been no reports that have analysed the smoking habits of patients with oral cancer over time and that forecast the future. In addition, national cancer registries do not collect data on smoking of patients with cancer. A careful analysis of tobacco consumption in oral cancer patients is important because smoking is a preventable factor for oral cancer. The aim of the study was to determine the trend of prevalence of tobacco use in patients with oral cancer in a single institution over a 15-year period and forecast the health burden on smoking-associated oral cancer over the next decade.

Our study showed that there has been a slight increase in the number of oral cancer patients treated in our hospital for the years 2002 to 2016. The demographic characteristics of the patients were similar

to most other literatures; that male patients were predominant and the median age was about 58 years old. However, the upward trend of annual inpatient numbers is more obvious in men than in women. Most male patients in the study were current smokers. The percentage of smokers out of the total number of inpatients also rose over the time. The average hospitalisation fee for smoking patients was higher than for non-smoking ones during the study period. Estimated by forecasting function in Excel, the annual number of inpatients with oral cancer will reach 1335 in our department by the year 2026. The public health burden of smoking-related oral cancer will be 120 million RMB in the Shanghai area by the end of the next decade.

Estimating future figures is useful for insight research. In this study, we used the Excel software to make these estimations. Among the three forecasting methods, exponential smoothing is the most aggressive in this study. Its estimation of total inpatients with oral cancer was twice as much as the estimation made by polynomial regression equation. The reason for this is that the exponential smoothing method weighed more heavily on latter data than the former ones<sup>15</sup>. In our series, the annual number of inpatients with oral cancer has rapidly risen since 2013. With heavily weighed on recent data that increased rapidly, the long-term trend forecasting may well be overestimate. Thus, the method was more suited for revealing short-term expectations<sup>16</sup>.

The regression analysis was also used to forecast smoking-associated oral cancer cases for the next decade. Among the three regression equations, the polynomial regression had the biggest R-squared value, which means the most fitness of the historical data with the smallest forecasting error. However, the estimation by the polynomial is the most conservative of the three methods. The figures it calculated were about half of those calculated by the exponential smoothing method and two-thirds of those by the forecasting function in Excel. The polynomial regression comes close to the observed values and provides a built-in conservative feature<sup>17</sup>. Thus, it will not be overestimated<sup>18</sup>. Although the other two regression models – exponential equation and logarithmic equation – are normally used in trend analysis, the forecast errors were high in the series after modelling the historical data. Thus, they are not suited in forecasting the number of smoking-associated oral cancer cases in this study.

The forecasting function in Excel 2010 is similar to the linear regression model. It is a widely used method for analysing the relationship between two variables and forecasting the dependent one in a certain time<sup>19</sup>. It uses a standard algorithm to calculate and gives an objective result<sup>20,21</sup>. However, the premise of using the method is that both the historical data and the estimated future conform to the linearity distribution. In this study, the number of oral cancer inpatients estimated by the forecasting function is in the middle of the three methods, but the R-square value was bigger than the polynomial regression model. The polynomial was able to recover enough to forecast the next decade with only small errors. Thus, we chose the polynomial regression equation to forecast the financial burden of smoking-associated oral cancer on public health in the next decade.

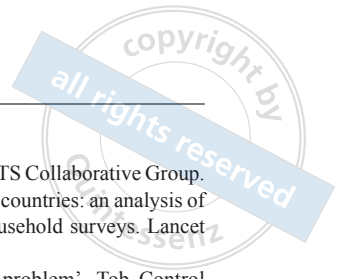
In this study, the projections of the future burden on smoking-associated oral cancer will reach 120 million RMB in the Shanghai area over the next decade. The calculation is based on the annual incidences reported by the official registration at the Shanghai Municipal Center for Disease Control and Prevention and the hospitalisation fee per capita estimated from inpatients' data at our hospital. The figure does not include the medical or social costs from the prevalence of patients and patients' family members. Thus, the actual expenditure should be far beyond the estimation.

Oral cancer is a serious problem owing to its poor prognosis, as well as the destruction of patients' chewing function and facial appearance. Smoking has long been established as a confirmed risk factor for oral cancer. In western countries, the prevalence of smoking habits

reached its peak after World War II when the number of oral cancer patients increased rapidly. The potential effect of tobacco consumption on oral cancer was then established<sup>5</sup>. In the literature the relationship between tobacco consumption and oral cancer incidence is unanimously identified, especially in male patients. The amount of daily smoking and the duration of smoking habits were both affected to the oral cancer incidence. On the other hand, smoking is the single most preventable cause of oral cancer. In the United States, the public health policy has been successful in achieving a decline in tobacco usage since the 1980s. Oral cancer incidence was also declined by the Surveillance, Epidemiology and End Results (SEER) database<sup>2</sup>. Giving up smoking is the most cost-effective strategy for not only reducing oral cancer incidence, but also its morbidity and mortality. Montero and his colleagues investigated smoking consumption trends in patients with oral cavity cancer over 25 years<sup>23</sup>. They concluded that there had been a progressive decrease in incidence and an improvement in the survival of patients with oral cancer. This was in parallel with the decline of tobacco consumption in the United States. The decline in use includes people who have never smoked, smokers who have quit the habit, and a decrease in smoking consumption.

There are some limitations in the study. Most of all, other risk factors were not referred to in the study, such as alcohol drinking, betel nut chewing and HPV infection. Because this is a single-factor predictive study, other factors will be analysed in another comprehensive questionnaire research. Also, female patients were not included in the study because the numbers in our series were small.

In summary, this study showed that oral cancer incidences from between 2002 and 2016. The increased trend was more obvious in men than in women, especially men with smoking habits. The estimation of smoking-associated oral cancer patients for the next decade was most fitted by polynomial regression equation, as this was the most conservative among Excel software's three forecasting methods. By the year 2026, the total number of oral cancer inpatients in our hospital will reach 982 per year, with 94% of male patients reporting a smoking habit. By a conservative estimation, the annual financial burden of smoking-associated oral cancer will be 120 million RMB in the Shanghai area in the next decade. This figure only referred to newly diagnosed cases, and does not include the cost paid for the prevalent patients and the patients' family members. Smoking is still the main etiological factor for oral cancer. Western countries have been successful in reducing incidence of oral cancer by smoking



cessation. This study provided an important guide to the development of public health policies on reducing incidences of smoking-associated oral cancer and improving the patients' prognosis.

### Conflicts of interest

The authors reported no conflicts of interest related to this study.

### Author contribution

Dr Jin Ye FU designed the study, collected and statistically analysed data, and prepared the manuscript; Dr. Chen Ping ZHANG designed the study, prepared and revised the manuscript; Drs Jing GAO and Jian Feng LUO statistically analysed data and prepared the manuscript; Dr Jiang LI collected data; Dr Jia Wei ZHENG designed the study and finally revised the manuscript.

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