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RESEARCH

The global, regional, and national burden of oral cancer, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021

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Abstract

Purpose This epidemiological study leverages data from the Global Burden of Disease (GBD) database spanning from 1990 to 2021 to analyze the global burden of oral cancer. The research aims to provide a comprehensive assessment of the age-standardized incidence rate (ASIR), age-standardized mortality rate (ASDR), and disability-adjusted life years (DALYs) for oral cancer, examining trends over three decades.

Methods The study used age standardized rate (ASRs) as an indicator of oral cancer epidemiological data. Trend analysis uses estimated annual percentage change (EAPC) to track changes in oral cancer indicators.

Results The study identifies a global increase in oral cancer incidence, mortality, and DALYs. From 1990 to 2021, the global incidence rate increased significantly from 3.26 (95% UI 3.14–3.41) to 5.34 (95% UI 4.94–5.70), the global mortality rate rose from 1.83 (95% UI 1.73–1.92) to 2.64 (95% UI 2.42–2.84), and the global estimate of DALYs increased from 55.05 (95% UI 52.38–57.97) to 74.44 (95% UI 67.50–80.44). High-risk regions include Palau and certain areas in Asia. Middle SDI regions show the most significant growth, while economically underdeveloped areas like parts of Africa show less significant trends.

Conclusion The research underscores the need for heightened awareness, surveillance, and prevention efforts, especially in regions with high oral cancer incidence. Policymakers are urged to implement screening programs and public health education to combat the disease.

Keywords Oral cancer · Epidemiology · Global Burden of Disease · Age-standardized rate · Estimated annual percent change

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Background

Oral cancer is one of the most common malignant tumors in the head and neck region (Peres et al. 2019). By definition, oral cancer refers to any malignant tumor occurring in the lips (vermilion border and the oral aspect) and within the oral cavity (including the anterior two-thirds of the tongue, buccal mucosa, gingiva, hard palate, retromolar pad, and floor of the mouth), primarily manifesting as squamous cell carcinoma (Scully and Bedi 2000; Pereira et al. 2007). According to the Global Cancer Statistics Database (GLOBOCAN) from the World Health Organization's International Agency for Research on Cancer (WHO/IARC) for the year 2022, oral cancer ranks 15th in global average mortality, causing 188,438 deaths, with 130,808 deaths in males and 57,630 in females (World Health Organization 2024). The five-year survival rate for patients with oral cancer is approximately 40%−50%, and many survivors may experience a significant reduction in quality of life (Torre et al. 2015). Studies have indicated that the occurrence of oral cancer is associated with a variety of risk factors, including smoking, alcohol consumption, and betel quid chewing (D'Souza and Addepalli 2018; Johnson et al. 2020), as well as human papillomavirus (HPV) infection (Marur et al. 2010). In recent years, the incidence of oral cancer has shown a significant upward trend, highlighting its urgency as a global public health issue.

Despite the significant impact of oral cancer on global health, there is currently a lack of comprehensive research on the epidemiological trends of oral cancer across various regions worldwide, particularly in developing countries and economically disadvantaged areas. The Global Burden of Disease (GBD) database for the year 2021, which utilizes the most recent data and a variety of statistical models, provides a comprehensive assessment of the disease burden and health loss in 204 countries and territories, offering a valuable data resource for epidemiological research on oral cancer (GBD 2021 Diseases and Injuries Collaborators 2024).

This study is based on data from the Global Burden of Disease (GBD) database spanning from 1990 to 2021, utilizing the 10th Revision of the International Classification of Diseases (ICD-10) for disease categorization, with a particular focus on oral cancer, including cancer of the lip (coded C00-C07, C08-C08.9). The study aims to estimate the age-standardized incidence and mortality rates, as well as disability-adjusted life years (DALYs), for oral cancer on a global scale. Additionally, this research analyzes the trends in these indicators at the global, regional, and national levels over the past three decades. The findings of this study help to fill the gaps in existing disease statistics, deepen the understanding of the epidemiological trends of oral cancer, and provide a scientific basis for guiding public health and medical decision-making.

Methods

Data Sources

This study utilized the most recent version of the GBD 2021 database for a global epidemiological analysis of oral cancer. Data on oral cancer from 1990 to 2021, stratified by sex, region, and country, were collected through the Global Health Data Exchange (GHDx) platform. Incidence, deaths, and DALYs, as well as the corresponding age-standardized rates (ASRs), were extracted for all age groups. The study encompassed data from 204 countries and territories, which were categorized into five tiers based on the Socio-demographic Index (SDI): low, low-middle, middle, high-middle, and high SDI (Table 1). Additionally, these countries and territories were further divided into 21 distinct geographical regions (Table S2). The data collection, processing, and statistical methods of the GBD 2021 database have been described in detail in previous studies, and this study adheres to these established methodological frameworks (GBD 2021 Diseases and Injuries Collaborators 2024).

Statistical Analysis

This study employs age-standardized rate (ASR) to examine the incidence and mortality of oral cancer, aiming to eliminate the impact of age structure, gender, population growth, and other factors on the overall data. This approach allows for comparisons of disease burden across different years and regions. The reference formula is as follows:

$$ASR = \frac{\sum_{i=1^{a_i w_i}}^{A}}{\sum_{i=1^{w_i}}^{A}} \times 100{,}000$$

In the given formula, a_i represents the age-specific rate of the selected reference standard population, w_i denotes the number of people in the same age subgroup. The 95% uncertainty interval (UI) represents the 25th and 95th values among all 100 draws. Analyzing the ASR allows for a better understanding of the burden of oral cancer and additional assessment of the efficiency of its prevention and treatment (Shiels et al. 2017).

Further utilize the estimated annual percent change (EAPC) to conduct a trend analysis of age-standardized rates in oral cancer models, with the reference formula as follows:

$$EAPC = 100 \times [\exp(\beta) - 1]$$

To calculate the 95% confidence interval (95% CI), fit a regression line to the natural

Table 1 Trends of death, incidence, prevalence, DALYs of lip and oral cavity cancer from 1990 to 2021 by SDI quintiles

	Global		High SDI		High-middle SDI	
	1990	2021	1990	2021	1990	2021
Death						
Rate per 100,000	1.83 (1.73–1.92)	2.64 (2.42–2.84)	2.37 (2.27–2.43)	2.90 (2.65–3.06)	1.83 (1.76–1.91)	2.39 (2.18–2.60)
EAPC of death	1.15 (1.06–1.24)		0.69 (0.61–0.78)		0.74 (0.65–0.83)	
Incidence						
Rate per 100,000	3.26 (3.14–3.41)	5.34 (4.94–5.70)	6.62 (6.38–6.78)	9.59 (8.94–10.02)	3.45 (3.31–3.58)	5.78 (5.27–6.26)
EAPC of incidence	1.60(1.50–1.70)		1.28 (1.23–1.34)		1.64 (1.51–1.77)	
Prevalence						
Rate per 100,000	11.01 (10.67–11.35)	19.49 (18.18–20.71)	30.20 (29.21–30.88)	45.52 (43.18–47.29)	11.22 (10.81–11.62)	22.34 (20.42–24.23)
EAPC of prevalence	1.92 (1.84–2.00)		1.47 (1.40–1.53)		2.30 (2.19–2.41)	
DALYs						
Rate per 100,000	55.05 (52.38–57.97)	74.44 (67.50–80.44)	64.48 (62.51–66.24)	67.57 (63.87–70.65)	54.06 (51.92–56.38)	64.02 (58.63–69.49)
EAPC of DALYs	0.93 (0.86–1.00)		0.17 (0.13–0.21)		0.40 (0.33–0.48)	
	Middle SDI		Low-middle SDI		Low SDI	
	1990	2021	1990	2021	1990	2021
Death						
Rate per 100,000	1.34 (1.25–1.43)	2.47 (2.24–2.71)	2.30 (2.06–2.55)	3.51 (3.11–3.88)	1.45 (1.26–1.65)	1.55 (1.33–1.78)
EAPC of Death	1.99 (1.90–2.08)		1.34 (1.25–1.43)		0.04 (−0.08–0.17)	
Incidence						
Rate per 100,000	1.97 (1.85–2.10)	4.65 (4.20–5.12)	3.06 (2.75–3.39)	5.31 (4.69–5.89)	1.90 (1.64–2.16)	2.25 (1.92–2.59)
EAPC of Incidence	2.83 (2.69–2.98)		1.76 (1.62–1.90)		0.36 (0.18–0.53)	
Prevalence						
Rate per 100,000	5.50 (5.17–5.83)	16.04 (14.46–17.75)	7.35 (6.67–8.13)	14.95 (13.10–16.67)	4.37 (3.75–5.00)	6.05 (5.11–7.09)
EAPC of Prevalence	3.59 (3.43–3.75)		2.30 (2.11–2.48)		0.88 (0.65–1.10)	
DALYs						
Rate per 100,000	41.36 (38.66–44.19)	69.91 (62.89–76.69)	72.92 (65.40–80.99)	106.26 (92.32–118.36)	46.16 (40.01–52.54)	48.52 (41.04–56.22)
EAPC of DALYs	1.71 (1.64–1.79)		1.20 (1.11–1.28)		−0.03 (−0.15–0.09)	

Parentheses for GBD estimates denote 95% confidence interval

GBD Global Burden of Diseases, *SDI* sociodemographic index

logarithm of the ASR, $y = \alpha + \beta x + \varepsilon$. Here, $y = \ln(ASR)$ and $x =$ the Gregorian calendar year. When the calculated EAPC value and its 95% confidence interval are greater than 0, it indicates that the age-standardized rate increases over time; when the calculated EAPC value and its 95% confidence interval are less than 0, it indicates that the trend decreases over time (Liu et al. 2019).

In this study, we determined the incidence and mortality rates of oral cancer in different populations based on the age-standardized incidence rate (ASIR) and age-standardized death rate (ASDR). The socio-demographic index (SDI) is a composite indicator assessed from data such as the total fertility rate of women under the age of 25, the average educational attainment of women aged 15 and above, and per capita income. It ranges from 0 to 1, with higher levels indicating a more advanced socio-economic status (‘Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021’ 2024). Disability-adjusted life years

(DALYs) for a disease or health condition is the sum of the years of life lost (YLLs) due to premature mortality and the years lived with disability (YLDs) in the population due to the prevalence of the disease or health condition (Deng et al. 2020; Safiri et al. 2020).

Results

Incidence Rates

From 1990 to 2021, the global incidence rate increased significantly from 3.26 (95% UI 3.14–3.41) to 5.34 (95% UI 4.94–5.70), indicating a notable upward trend. During this period, EAPC in the global incidence rate was 1.60 (95% CI 1.50–1.70), demonstrating a positive growth trend (Table S2, Fig. 1). Globally, in 2021, the highest incidence rate was observed in Palau (32.32, 95% UI 24.64–41.33). The country with the lowest incidence rate was Sao Tome and Principe (0.07, 95% UI 0.06–0.11) (Table S1). Data for other countries and regions are presented in the supplementary document (Table S1).

In various Socio-demographic Index (SDI) regions, the Estimated Annual Percent Change (EAPC) for low SDI areas is 0.36 (95% CI 0.18–0.53), which is close to no significant change. In contrast, the middle SDI areas exhibit the highest EAPC at 2.83 (95% CI 2.69–2.98), indicating a significant increasing trend (Table 1). Analyzing the incidence rates in correlation with SDI indices, it is evident that, overall, the incidence of oral cancer is positively correlated with the level of SDI; the higher the SDI index of an area, the higher the incidence rate. Furthermore, in many regions with moderate development levels, the development patterns from 1990 to 2021 have shown different trends, with some areas still significantly below expected levels, while others are well above expected levels (Fig. 2).

Among the 21 regions classified based on economic levels, all regions show an increasing trend in incidence rates. East Asia has the highest increase, with an EAPC of 4.26 (95% CI 4.05–4.46), while Eastern Sub-Saharan Africa has the lowest increase, with an EAPC of 0.15 (95% CI −0.07–0.36) (Table S2). In the vast majority of regions, the incidence rate among males is significantly higher than among females, with the exception of Western Sub-Saharan Africa and Andean Latin America, where the incidence rate among females is higher than among males (Fig. 3).

Mortality rates

In 1990, the global mortality rate was 1.83 (95% UI 1.73–1.92), and by 2021, it had risen to 2.64 (95% UI 2.42–2.84). The mortality rate has increased compared to 1990. EAPC in global mortality rates between 1990 and 2021 was 1.15 (95% CI 1.06–1.24), indicating an upward trend (Table S2, Fig. 4). Among all countries and regions worldwide, the highest mortality rate was observed in Palau (17.62, 95% UI 13.37–22.83), while the lowest mortality rate was found in Sao Tome and Principe (0.05, 95% UI 0.04–0.07). Data for other countries and regions are presented in the supplementary document (Table S1).

Among all SDI regions, the Low SDI region shows little change, with a nearly flat trend, and the EAPC for mortality is the smallest at 0.04 (95% CI −0.08–0.17). The Middle SDI region exhibits the largest change, with an EAPC for mortality of 1.99 (95% CI 1.90–2.08), indicating a significant increasing trend (Table 1). In the analysis of the correlation between mortality rates and SDI, overall, the mortality rate of oral cancer is positively correlated with the level of SDI; the higher the SDI index of the region, the higher the mortality rate. However, in regions with higher SDI levels, the mortality rate tends to be lower than expected (Fig. 2).

Among the 21 regions classified by economic status, the most significant increase in mortality rates is observed in the High-income Asia Pacific region, with an EAPC of 3.05 (95% CI 2.69–3.41). The only region showing a decreasing trend is Eastern Sub-Saharan Africa, with an EAPC of −0.14 (95% CI −0.30–0.03) (Table S2). In the majority of regions, male mortality rates are significantly higher than female rates, with the exception of Western Sub-Saharan Africa and Andean Latin America, where female mortality rates are slightly higher than male rates (Fig. 3).

Disability-adjusted life years (DALYs)

In 2021, the global estimate of Disability-Adjusted Life Years (DALYs) was 74.44 (95% UI 67.50–80.44), marking a significant increase from the 1990 figure of 55.05 (95% UI 52.38–57.97). EAPC in global DALYs was 0.93 (95% CI 0.96–1.00), indicating a consistent upward trend (Table S2, Fig. 4). Among all countries and regions worldwide, Palau had the highest DALYs at 558.99 (95% UI 420.48–735.74), while Sao Tome and Principe had the lowest DALYs at 1.38 (95% UI 1.01–1.84) (Table S1). Data for other countries and regions can be found in the supplementary document (Table S1).

In the stratification by socio-demographic index (SDI), EAPC for low SDI regions is −0.03 (95% CI −0.15−0.09), indicating a slight decreasing trend. In contrast, the middle SDI regions exhibit the highest EAPC at 1.71 (95% CI 1.64–1.79), demonstrating a significant increase (Table 1). In the analysis of the correlation between DALYs and SDI indices, overall, there is a positive correlation between the DALYs of oral cancer and the level of SDI; the higher the SDI index of the region, the higher the DALYs. However, in regions with higher levels of SDI, DALYs tend to be lower than expected levels (Fig. 2).

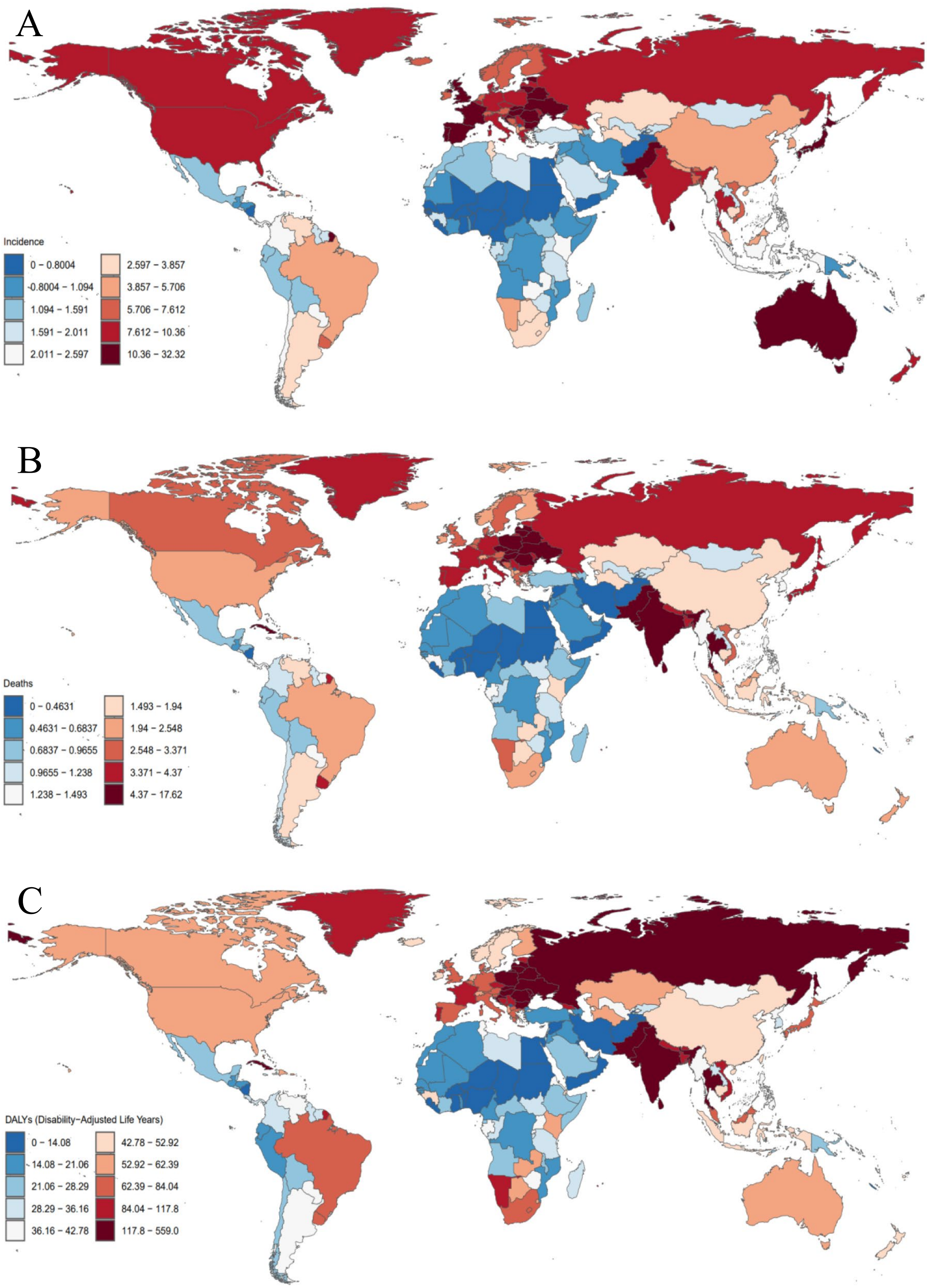

Fig. 1 Incident, death, and DALYs rates of lip and oral cavity cancer in 204 countries and territories in 2021. **A** ASIR: age-standardized incidence rate; **B**, ASDR: age-standardized death rate; **C** disability-adjusted life-years (DALYs) rate

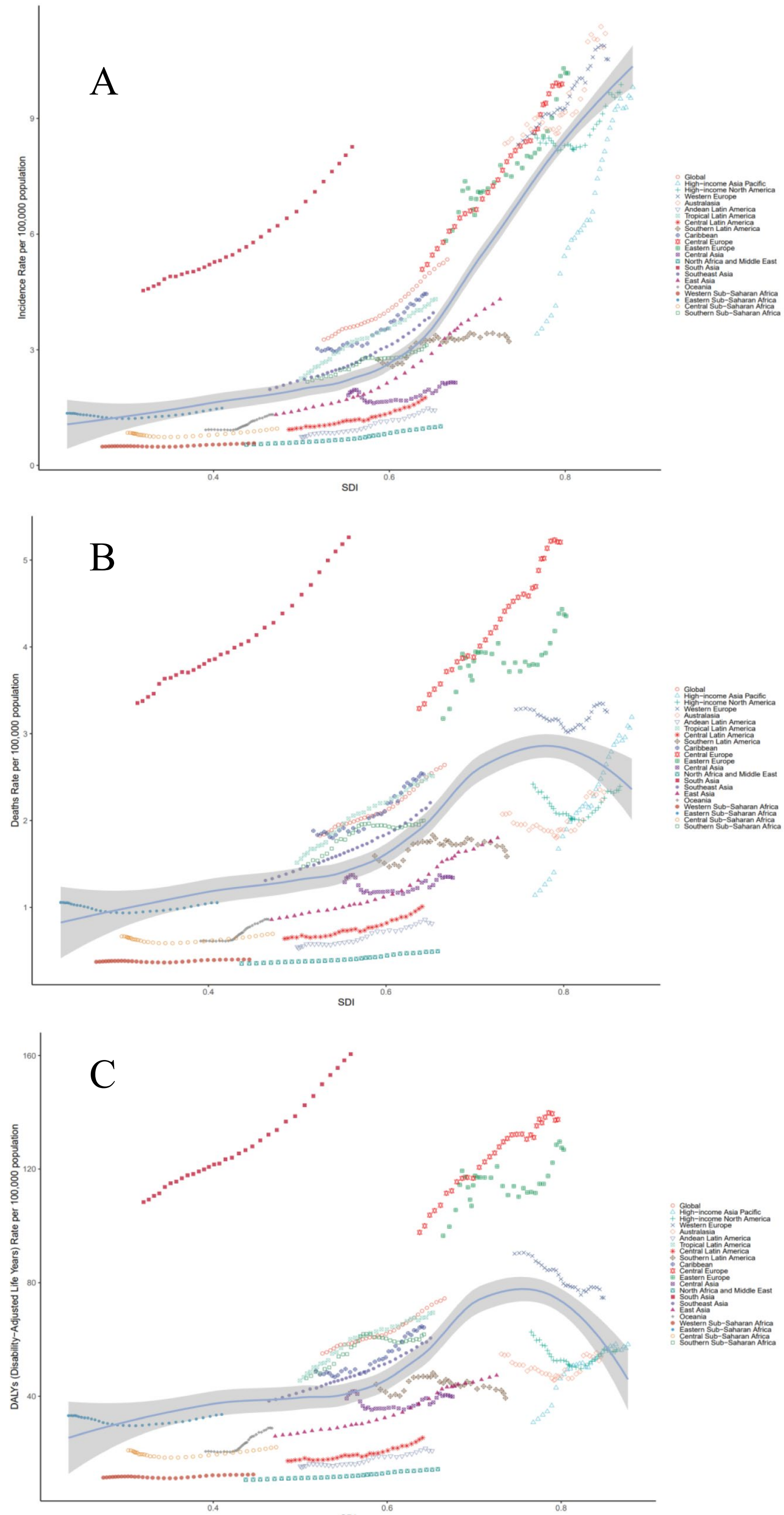

Fig. 2 The correlation between incident, death, and DALYs rates of lip and oral cavity cancer in 21 regions in 2021. **A** ASIR: age-standardized incidence rate; **B** ASDR: age-standardized death rate; **C** disability-adjusted life-years (DALYs) rate

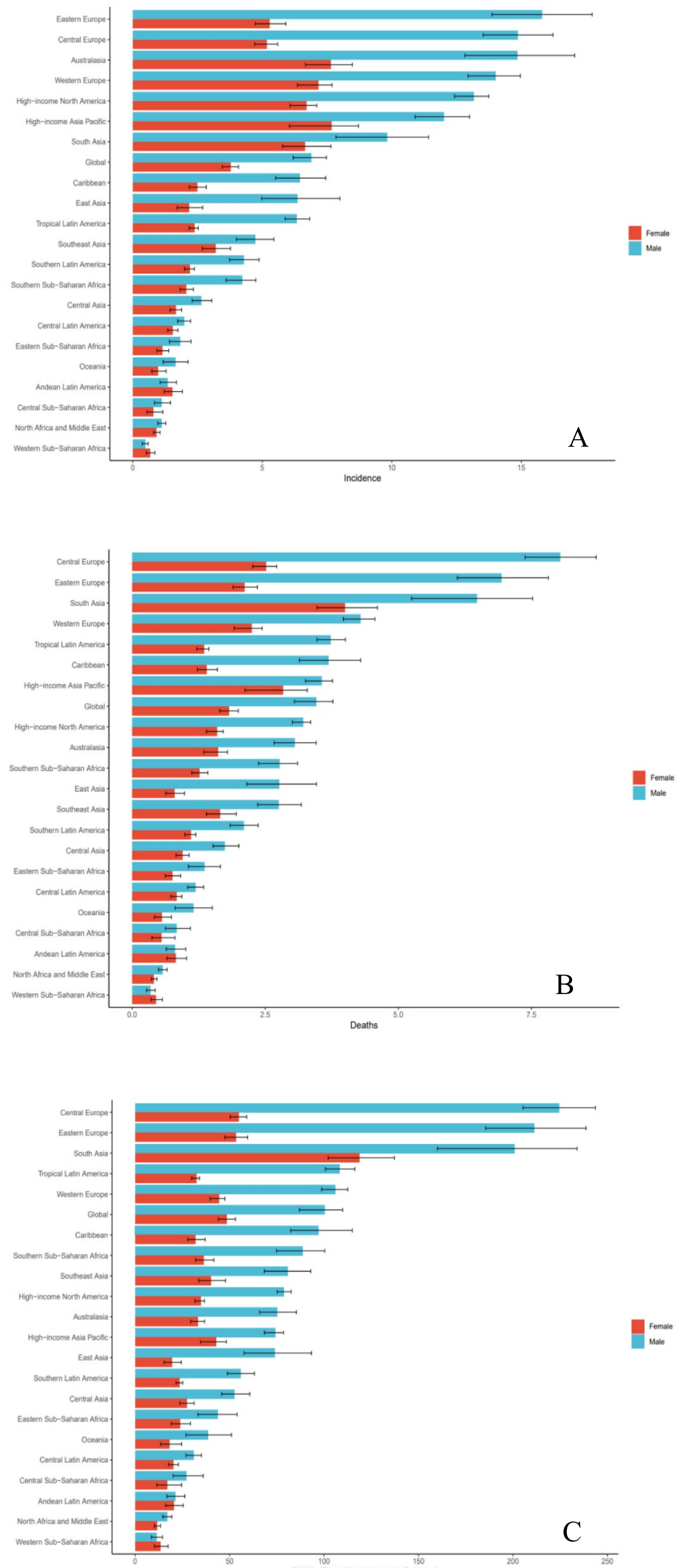

Fig. 3 Sex difference for incident, death, and DALYs rates of lip and oral cavity cancer in 21 regions in 2021. **A** ASIR: age-standardized incidence rate; **B** ASDR: age-standardized death rate; **C** disability-adjusted life-years (DALYs) rate

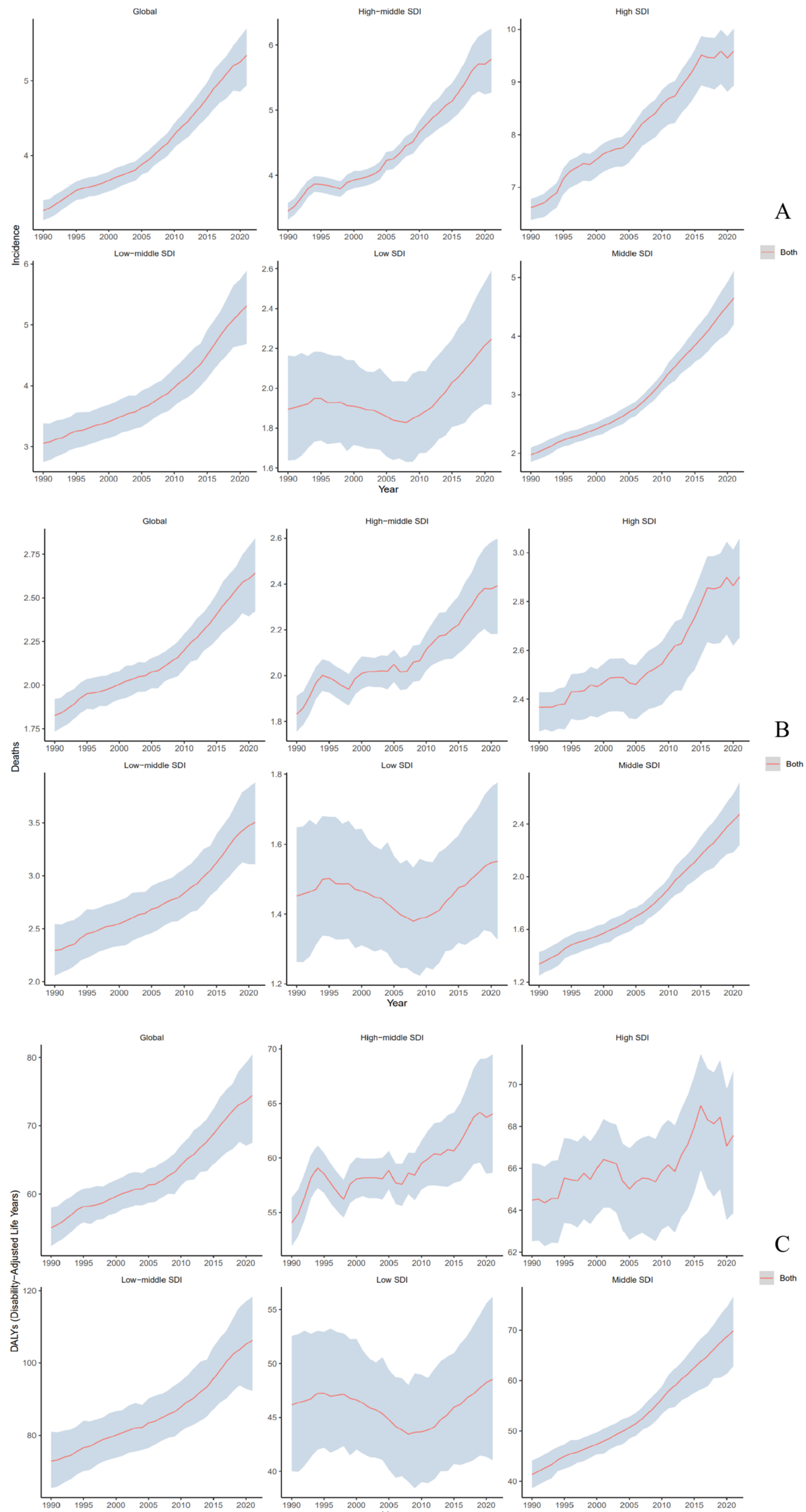

Fig. 4 Time trend for incident, death, and DALYs rates of lip and oral cavity cancer from 1990 to 2021 in 5 SDI regions. **A** ASIR: age-standardized incidence rate; **B** ASDR: age-standardized death rate; **C** disability-adjusted life-years (DALYs) rate

Among the 21 regions classified by economic status, the region with the most significant increase in DALYs is East Asia, with an EAPC of 2.19 (95% CI 2.04–2.34). The region with the most pronounced decrease in DALYs is Western Europe, with an EAPC of −0.62 (95% CI −0.69 to −0.54) (Table S2). In the vast majority of regions, male DALYs are significantly higher than female DALYs, with the exception of Western Sub-Saharan Africa, where female DALYs are higher than male DALYs (Fig. 3).

Proportion of deaths attributable to risk factors

In the statistical analysis of GBD database from 1990 to 2021 regarding the risk factors for oral cancer, we identified high alcohol use and tobacco as the two most significant risk factors. Global trend analysis reveals that the risk factor of high alcohol consumption shows a decreasing trend, while the risk factor of tobacco use exhibits a more gradual decline. However, there are significant differences in the patterns of risk factors across different regions. Specifically, the risk factor of high alcohol consumption is on the rise in low- and middle-income regions, while it shows a decreasing trend in high SDI regions and high-middle SDI regions. Although the decline in the risk factor of tobacco is more pronounced in regions with higher socio-demographic index, the downward trend is less apparent in regions with lower income levels (Fig. 5).

Discussion

Since 1990, there has been a rising trend in the global burden of oral cancer. Given the increase in its medical and socio-economic costs, oral cancer has become an important issue in global public health. Considering the poor prognosis of the disease and its significant impact on patients' quality of life, there is an urgent need to intensify research and focus. This study, based on the 2021 Global Burden of Disease (GBD) data, systematically analyzes the global epidemiological trends of oral cancer over the past three decades, including incidence, mortality, and Disability-Adjusted Life Years (DALYs), taking into account the Socio-demographic Index, temporal trends, mortality risk factors, and gender differences. The findings aim to provide data support for epidemiological research on oral cancer and to offer a scientific basis for policy-making and clinical practice.

In this study, the global incidence, mortality, and DALYs of oral cancer have shown an upward trend, which is

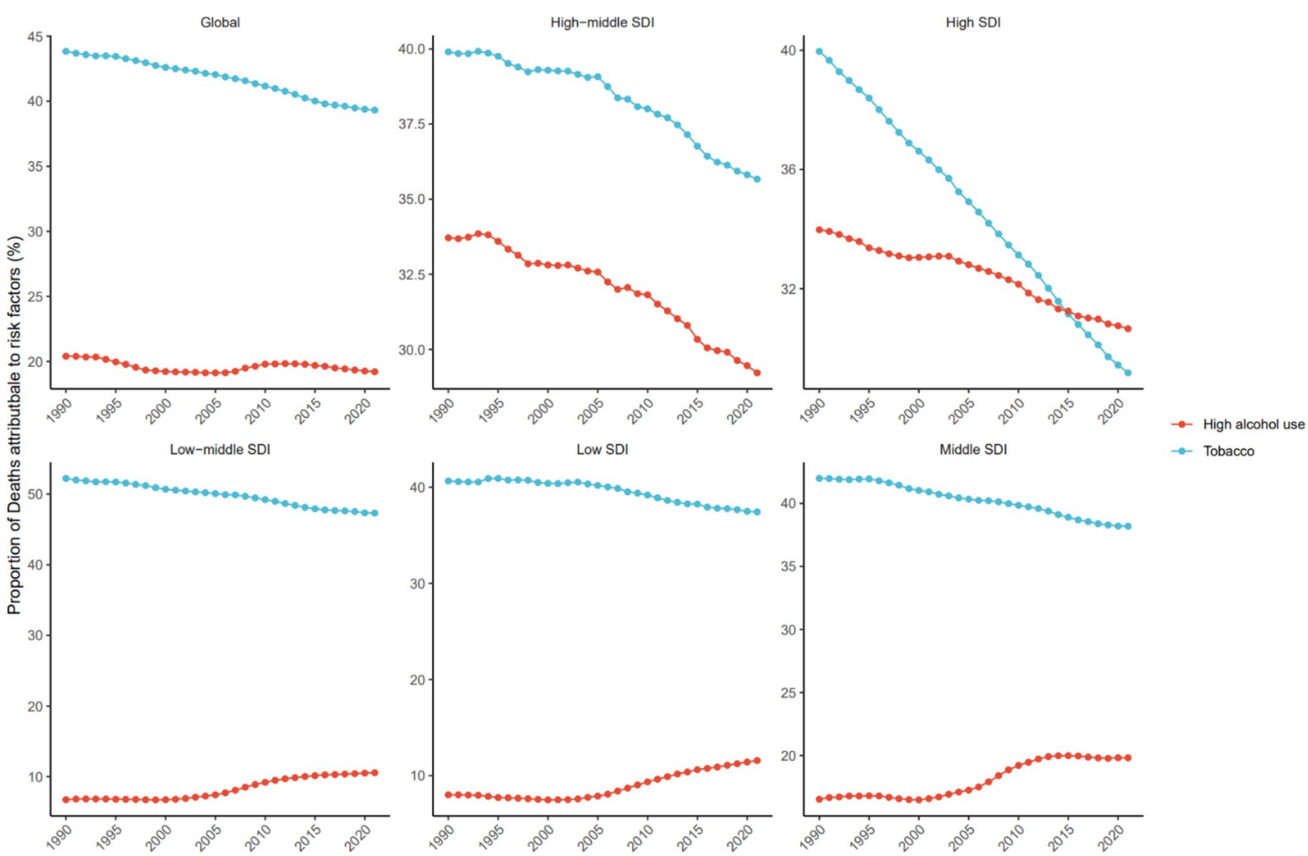

Fig. 5 The changing trend of the Proportion of Deaths attributable to risk factors in the five SDI regions from 1990 to 2021

consistent with previous research findings (Ren et al. 2020; Kocarnik et al. 2022). In the 2021 Global Burden of Disease (GBD) data, Palau ranks first in the world in terms of oral cancer incidence, mortality, and Disability-Adjusted Life Years (DALYs), a region with a long history of chewing tobacco (Rieth et al. 2023). Following closely are certain areas in Asia, which face a higher risk of oral cancer due to the long-term use of tobacco chewing products (Wang et al. 2018; Cheng et al. 2023). Tobacco chewing comes in various forms, such as gutkha (a combination of betel nut, lime, and sun-dried tobacco), pan masala (a combination of betel nut, lime, and sweeteners), and pan-tobacco (a combination of betel leaf, lime, areca nut, and sun-dried tobacco) (Shrestha et al. 2020). The alkaloids, reactive oxygen species, and nitrosamines in betel nut are all known oral carcinogens (Warnakulasuriya and Chen 2022). Additionally, the high incidence of oral cancer in Pakistan may also be related to its large population size (Ren et al. 2020). Economic constraints and a lack of oral health education may further exacerbate the disease burden of oral cancer in these regions.

In the analysis combined with SDI, we found that not only do the incidence, mortality, and DALYs of oral cancer show an upward trend in low- and middle-income countries, but they also rise in high-income countries and regions. Among them, the most significant change in growth is in the middle SDI regions, which may be related to the acceleration of urbanization and industrialization processes in middle-income countries in recent years, leading to changes in people's lifestyle (Petti 2009). In economically underdeveloped areas, especially in most regions of Africa, the increasing trend of oral cancer incidence, mortality, and DALYs is not significant. This phenomenon may be attributed to the lower level of economic development and the relatively backward medical care system in these areas, leading to limited diagnostic capabilities among healthcare professionals. In addition, the general health awareness of local residents is not high, which may hinder them from taking effective medical intervention measures (Herrera-Serna et al. 2019).

In the research analysis of the Proportion of Deaths attributable to risk factors, it was observed that in regions with High SDI and High-middle SDI, the risk factors of tobacco use and high alcohol consumption showed a significant downward trend. This phenomenon may be related to the increased awareness of oral health and the improved accessibility of oral health checks and preventive measures in middle- and high-income areas. However, in low- and middle-income regions, the risk of tobacco use is still on the rise, indicating that the prevention of oral cancer still requires long-term attention (Shoaee et al. 2024).

It is noteworthy that the initial signs of oral cancer often manifest as pain, swelling, or lumps in the mouth, white or red patches on the oral mucosa, and loose teeth without apparent dental problems, and asymptomatic oral cancers are often overlooked (Abati et al. 2020). Research indicates that early diagnosis and treatment of oral cancer are crucial for improving patient prognosis, survival rates, and quality of life (Seoane et al. 2012).Therefore, we emphasize the importance of raising awareness of oral cancer epidemiological trends and recommend that healthcare professionals enhance surveillance of the disease and public education. In areas with high incidence of oral cancer, policymakers should consider implementing organized screening programs and preventive measures to increase public disease awareness and prevention capabilities.

Limitations

This study has certain limitations. Firstly, although the GBD database used is the most recent version, the COVID-19 pandemic between 2020 and 2021 may have disrupted data collection and survey methods. Secondly, the raw data in the database does not cover all countries and regions worldwide, resulting in data gaps for some areas. Thirdly, resource-poor regions may lack the capacity for adequate clinical examination of oral cancer, which could lead to a systematic underrepresentation of data from these areas.

Conclusion

Over the past 30 years, the global incidence, mortality, and DALYs of oral cancer have all shown an upward trend, yet there are differences among various countries and regions. The study aims to provide a solid basis for public health decision-making and offer references for relevant departments to optimize the allocation of medical resources.

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Author contributions Junmeng Wu and Na An contributed to conception, design, data acquisition, analysis and interpretation, Junmeng Wu and Ruotong Yang performed all statistical analyses, Junmeng Wu drafted and Na An critically revised the manuscript. He Chen and Yingjun Liu contributed to oral cancer conception, data acquisition, analysis and critically revised the manuscript. All authors gave their final approval and agree to be accountable for all aspects of the work.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

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