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Global, Regional and National Burden of Edentulism and Periodontal Diseases from 1990 to 2021: Analysis of Risk Factors and Prediction of Trends in 2050

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Abstract

Background/Aim: Periodontal diseases and edentulism remain a prevalent and disabling oral health condition worldwide, with significant regional disparities. This study systematically evaluated the burden of periodontal disease and edentulism at global, regional, and national levels from 1990 to 2021, using the Global Burden of Disease (GBD) 2021 framework.

Patients and Methods: We analyzed trends in incidence, prevalence, and years lived with disability (YLD), exploring their associations with the socio-demographic index (SDI) and other risk factors.

Results: The findings reveal considerable variations across SDI regions, with low and low-middle SDI regions experiencing the highest burden. In 2021, the global prevalence of periodontal diseases reached approximately 1.07 billion cases, and the age-standardized incidence and prevalence rates varied significantly by SDI levels. The burden of periodontal disease showed an increasing trend among middle-aged and elderly populations. While sex differences were present in both edentulism and periodontal diseases, they were relatively minor. ARIMA model projections indicate that the burden of edentulism will fluctuate by 2050, while the burden of periodontal diseases will remain stable.

Conclusion: This study underscores the need for targeted public health interventions, particularly in resource-limited regions, to improve access to oral healthcare and integrate preventive strategies into broader health initiatives.

Keywords: Periodontal disease, edentulism, Global Burden of Disease, Socio-Demographic Index, ARIMA model, public health, oral health disparities.

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Introduction

Periodontal disease is a common and highly disabling oral condition, primarily encompassing gingivitis periodontitis. It is characterized by chronic inflammation and progressive destruction of the supporting structures of the teeth, including the gingiva, alveolar bone, and periodontal ligament (1). If left untreated, periodontal disease can progress to severe periodontitis, ultimately leading to tooth loss, edentulism, impaired masticatory function, malnutrition, speech difficulties, and decreased self-esteem, significantly reducing patients' quality of life (2). Studies have shown that periodontal disease is not only related to local oral factors but is also significantly associated with various systemic conditions, such as diabetes, cardiovascular diseases, obesity, Alzheimer's disease, and chronic obstructive pulmonary disease (3). Therefore, the prevention and management of periodontal disease are crucial for improving overall health outcomes (4).

Periodontitis is widely regarded as one of the leading causes of tooth loss in adults, affecting approximately 11.2% of adults worldwide (5). With the aging global population, lifestyle changes, and increasing rates of tooth retention, the prevalence of periodontal disease has shown a sustained upward trend (6). It is estimated that severe periodontitis results in an annual productivity loss of up to \$54 billion, reflecting its severe impact on the global economy (7). Furthermore, the annual direct treatment costs of periodontitis are estimated at \$3.49 billion in the United States and €2.52 billion in Europe, underscoring its considerable socioeconomic burden (8).

The widespread prevalence and severe health consequences of periodontal disease make it a critical public health issue. However, despite the substantial burden of periodontal disease, oral health prevention and treatment are still not prioritized in public health agendas in many lowand middle-income countries (9). In these resource-limited settings, patients often lack access to timely and effective treatment, exacerbating the burden of disease and creating a vicious cycle. Thus, a comprehensive of periodontal disease is essential for providing evidence-based guidance to

governments, enabling the development of effective policies, and enhancing public awareness of this health issue.

This study aims to systematically assess the burden of periodontal disease at global, regional, and national levels based on the GBD framework, and to explore its temporal trends and associations with the socio-demographic index (SDI) and other risk factors. By analyzing the epidemiological characteristics of periodontal disease across different sexes, age groups, and geographic regions, this study seeks to provide evidence-based guidance for policymakers to optimize the allocation of limited healthcare resources, develop rational public health policies, and address the challenges posed by periodontal disease to global health through multi-level and multi-dimensional strategies.

Patients and Methods

This study systematically evaluated the epidemiological characteristics and health burden of periodontal disease from 1990 to 2021, using the Global Burden of Disease (GBD) framework. The specific research methods are as follows:

Data sources. The data for this study were derived from the GBD 2021 database in the Global Health Data Exchange (GHDx) platform (http://ghdx.healthdata.org/gbd-resulttool), which includes epidemiological data on 369 diseases and injuries globally, covering incidence, prevalence, years lived with disability (YLD), and their temporal trends. We collected data on periodontal disease from 204 countries and regions between 1990 and 2021.

Case definition. The case definition of periodontal disease in this study was based on the Community Periodontal Index of Treatment Needs (CPITN):

Primary definition: CPITN Class IV (attachment loss >6 mm or gingival pocket depth >5 mm). It is caused by chronic bacterial infection around the teeth. Periodontal disease is classified in the International Classification of Diseases, 10th Revision (ICD-10) under codes K05.0-K05.6 (10).

Alternative definitions: CPITN Class III (attachment loss >5 mm) or CPITN Class II (attachment loss >4 mm), depending on specific data sources used. These classifications align with the methodology used in the Global Burden of Disease (GBD) 2019 Diseases and Injuries Study (11).

In this study, edentulism was defined as the total loss of all permanent teeth, typically resulting from tooth decay or gum disease and was assessed only in individuals aged older than 15 years (12-14).

Data processing and analysis methods. Mixed-effects models were employed to analyze trends in periodontal disease and its impact across regions with different levels of the SDI. SDI is a composite indicator based on per capita income, educational attainment, and total fertility rate under the age of 25, categorizing 204 countries and regions into five levels: low SDI (<0.46), low-middle SDI (0.46-0.60), middle SDI (0.61-0.69), high-middle SDI (0.70-0.81), and high SDI (>0.81).

Bayesian meta-regression using the DisMod-MR tool was applied to integrate heterogeneous data, and Monte Carlo simulation was used to estimate disease prevalence and uncertainty intervals (UI), with the UI calculated from the median values of 1,000 simulations between the $25^{\rm th}$ and $975^{\rm th}$ values.

The age-standardized rate (ASR) was used to evaluate the burden and differences in periodontal disease between countries and regions. Estimated Annual Percentage Change (EAPC) was used to calculate the average annual change rate for age-standardized prevalence, incidence, and disability-adjusted life years (DALYs) to assess the temporal trends in periodontal disease. The formula for the model is:

$$EAPC = (e^{\beta} - 1) \times 100\%$$
 [1]

where β is the slope of the regression line, which represents the change in the log of the age-standardized burdens over time (15).

Statistical analysis. R software (v4.3.3) was used for data analysis, with age-standardized incidence, prevalence and YLDs serving as the primary evaluation metrics. All statistical analyses followed the "Guidelines for Accurate and Transparent Health Estimates Reporting" (GATHER). This study used YLD as an indicator of the burden of oral diseases. In GBD studies, DALYs are commonly used to assess disease burden, which includes years of life lost (YLL) due to periodontal disease and YLD. Since oral diseases typically do not lead directly to death, the DALY estimates in this study were primarily based on YLDs.

The formula for calculating YLDs is as follows:

Prospective forecast. This study also utilized GBD 2021 data to examine global trends in incidence, prevalence, and YLDs of edentulism and periodontal disease from 1990 to 2021. Furthermore, an Autoregressive Integrated Moving Average (ARIMA) model was applied to predict future trends in these metrics from 2022 to 2050, based on the 1990-2021 data.

Ethical considerations. As this study used publicly available data, ethical approval from an institutional review board was not required. The study adhered strictly to GATHER guidelines to ensure transparency in methods description and research outcomes.

Results

Global and regional SDI distribution of edentulism and periodontal disease burden. This study analyzed the burden of edentulism and periodontal disease across global and different SDI regions from 1990 to 2021, based on incidence, prevalence, and YLD data. The results indicated significant regional differences in these disease burdens.

In 2021, the global number of incident cases of edentulism was 26,527,331 (95% UI=22,613,423 to 31,167,558), with an age-standardized incidence rate of

305.04 per 100,000 population (95% UI=261.19 to 356.58). Since 1990, the EAPC for the age-standardized incidence rate (ASIR) was 0.95% (95% UI=-10.05% to 13.31%). In 2021, the global number of prevalent cases of edentulism was 353,000,621 (95% UI=300,591,593 to 416,167,869), with an age-standardized prevalence rate (ASPR) of 4,109.24 per 100,000 population (95% UI=3,504.63 to 4,834.95). The EAPC for ASPR from 1990 onward was 1.05% (95% UI=-9.95% to 13.40%) (Table I).

In 2021, the country with the lowest the age-standardized rate of incidence for edentulism was Bangladesh, with 106.34 per 100,000 population (95% UI=83.92 to 133.25), followed by Nepal at 114.03 (95% UI=91 to 142.8) and Djibouti at 119.05 (95% UI=95.37 to 148.24). The highest was observed in Bolivia (Plurinational State of), with 658.02 per 100,000 population (95% UI=569.01 to 736.1), followed by Peru at 630.02 (95% UI=542.75 to 710.04), and Brazil at 598.99 (95% UI=529.47 to 657.95) (Supplementary Table I).

In 2021, the global number of incident cases of periodontal diseases was 89,613,534 (95% UI=79,069,091 to 101,005,642), with the age-standardized rate of incidence 1,069.44 per 100,000 population (95% UI=942.71 to 1,204.58). The EAPC for ASIR from 1990 onward was 0.85% (95% UI=-10.18% to 13.23%). The global number of prevalent cases of periodontal diseases was 1,066,953,744 (95% UI=896,546,186 to 1,234,839, 287), with the age-standardized rate of prevalence 12,498.3 per 100,000 population (95% UI=10,526.8 to 14,493.37). The EAPC for ASPR since 1990 was 1.04% (95% UI=-10.00% to 13.44%) (Table I).

The country with the lowest the age-standardized rate of incidence for periodontal diseases in 2021 was Kiribati, with 224.21 per 100,000 population (95% UI=167.35 to 310.61), followed by the Solomon Islands at 226.74 (95% UI=168.75 to 312.03) and Spain at 228.16 (95% UI=166.81 to 312.89). The highest was observed in Sierra Leone, with 1,578.93 per 100,000 population (95% UI=1,439.14 to 1,728.99), followed by Gambia at 1,529.52 (95% UI=1,324.17 to 1,676.61), and Cabo Verde at 1,510.84 (95% UI=1,283.37 to 1,662.22) (Supplementary Table II).

In 2021, among the different SDI regions, the agestandardized rate of incidence for edentulism was lowest in low SDI regions, at 208.12 per 100,000 population (95% UI=177.7 to 245.57), and highest in middle SDI regions, at 335.23 per 100,000 population (95% UI=289.54 to 388.97). Similarly, age-standardized rates of prevalence and YLD of edentulism were also lowest in low SDI regions and highest in middle SDI regions. The EAPC from 1990 to 2021 for the age-standardized incidence rate showed a declining trend across all regions, with the largest decrease observed in high SDI regions, while low and middle SDI regions showed the smallest declines. ASPR and age-standardized YLD rate (ASYR) exhibited similar trends, with an increasing trend observed in lowmiddle and low SDI regions, whereas other regions experienced a declining trend (Supplementary Table III).

In 2021, the age-standardized rate of incidence for periodontal diseases was highest in low-middle SDI regions, at 1,174.58 per 100,000 population (95% UI=1,030.71 to 1,314.31), and lowest in high SDI regions, at 927.32 per 100,000 population (95% UI=793.31 to 1,084.81). Age-standardized rates of prevalence and YLD in periodontal diseases were also highest in low-middle SDI regions and lowest in high SDI regions. From 1990 to 2021, the EAPC for ASIR, ASPR, and ASYR showed a similar trend, with an increasing trend in high-middle and middle SDI regions, while the other regions exhibited a declining trend (Supplementary Table III).

The impact of age and sex on the burden of periodontal diseases. Age distribution characteristics. The age distribution of global edentulism in 2021 is shown in Figure 1. From age 20 onwards, the incidence rate increased with age, peaking at ages 70-79, and then declined with advancing age. The prevalence and YLD rates exhibited a similar trend, generally increasing with age and stabilizing after age 85.

Globally in 2021, the incidence rate of periodontal diseases increased with age starting from age 15, reaching a peak at ages 45-49, and then remained relatively stable. The prevalence and YLD rates showed a similar trend, gradually increasing from ages 15, peaking at ages 55-59,

Table I. Incidence, prevalence, and years lived with disability (YLDs) of edentulism and periodontal disease by sex globally in 2021, along with the corresponding age-standardized data and estimated annual percentage change values.

	2021 Incidence	ASR (per 100,000		2021 Prevalence	
		E	Edentulism		
Both	26,527,330.87	305.04		353,000,621.3	
Female	(22,613,423.11 to 31,167,558.12) 14,742,192.94	(261.19 to 356.5) 325.06		(300,591,593.41 to 416,167,869.43) 205,082,137.29	
Male	(12,634,250.01 to 17,184,611.71) 11,785,137.93	(279.96 to 378.2) 284.91	, , , ,	(175,492,677.18 to 240,096,947.15) 147,918,484.01	
riaic	(9,959,671.14 to 13,974,345.87)	(241.98 to 335.6		(124,806,630.91 to 176,522,082.49)	
		Perio	dontal diseases		
Both	89,613,533.89	1069.44		1066,953,744.48	
Female	(79,069,090.86 to 101,005,641.52) 45,088,346.64	(942.71 to 1204.5 1062.84	, , , ,	(896,546,186.14 to 1,234,839,286.71) 531,001,797.44	
Male	(39,831,310.87 to 50,860,220.16) 44,525,187.25	(936.53 to 1197.3 1075.77		(446,954,541.78 to 614,316,075.63) 535,951,947.04	
Male	(39,166,860.14 to 50,155,804.18)	(947.93 to 1211.5		(450,707,883.88 to 620,330,206.6)	
	2021	EAPC 1990-2021			
	YLDs	ASR (per 100,000)	ASIR	ASPR	ASYR
		E	Edentulism		
Both	9,590,986.73	111.51	0.95%	1.05%	1.05%
Female	(6,202,443.69 to 13,470,473.18) 5,541,814.3	(72.25 to 156.83) 120.95	(-10.05% to 13.31%) 0.95%	(-9.95% to 13.40%) 1.04%	(-9.96% to 13.39%) 1.03%
	(3,599,911.92 to 7,753,058.49)	(78.38 to 169.51)	(-9.42% to 12.51%)	(-9.34% to 12.60%)	(-9.34% to 12.60%)
Male	4,049,172.43 (2,606,258.48 to 5,723,048.42)	101.03 (65.27 to 142.82)	0.96% (-9.37% to 12.47%)	1.07% (-9.25% to 12.56%)	1.07% (-9.25% to 12.56%)
		Perio	dontal diseases		
Both	6,903,283.68	80.89	0.85%	1.041.04%	1.04%
Female	(2,772,283.94 to 14,106,182.31) 3,414,153.62	(32.47 to 165.37) 78.88	(-10.18% to 13.23%) 0.89%	% (-10.00% to 13.44% 1.09%	%) (-10.01% to 13.44%) 1.08%
	(1,373,546.59 to 6,962,500.17) 3,489,130.06	(31.7 to 161.22) 83.02	(-9.49% to 12.47%) 0.80%	(-9.31% to 12.68%) 1.00%	(-9.32% to 12.67%)
Male	(1,398,737.35 to 7,146,187.82)	(33.28 to 169.77)	(-9.57% to 12.36%)	(-9.38% to 12.57%)	

The parentheses indicate the 95% uncertainty interval. ASIR, Age-standardized incidence rate; ASPR, age-standardized prevalence rate; ASYR, age-standardized years lived with disability (YLD) rate; ASR, age-standardized rate (per 100,000 population); EAPC, estimated annual percentage change.

and then gradually decreasing. At ages 85-89, the rate of decrease slowed, eventually becoming stable (Figure 2).

Sex differences. In 2021, the overall trend in the incidence of edentulism and periodontal diseases was similar for males and females globally (Figure 1). For edentulism, the incidence

rate among females was higher than that among males from ages 20 to 74. At ages 75-79, the incidence rates for females and males were identical, but after age 80, the decline in incidence was steeper for females compared to males. After age 20, the prevalence and YLD rates for edentulism were consistently higher among females compared to males.

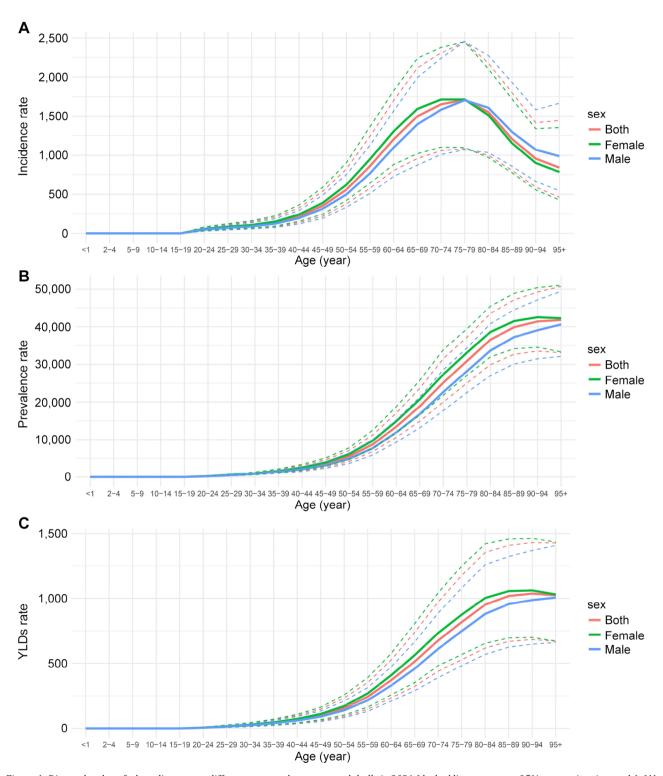


Figure 1. Disease burden of edentulism across different sexes and age groups globally in 2021 (dashed lines represent 95% uncertainty intervals). (A) Incidence rate, (B) Prevalence rate, and (C) years lived with disability (YLD) rate (per 100,000 population).

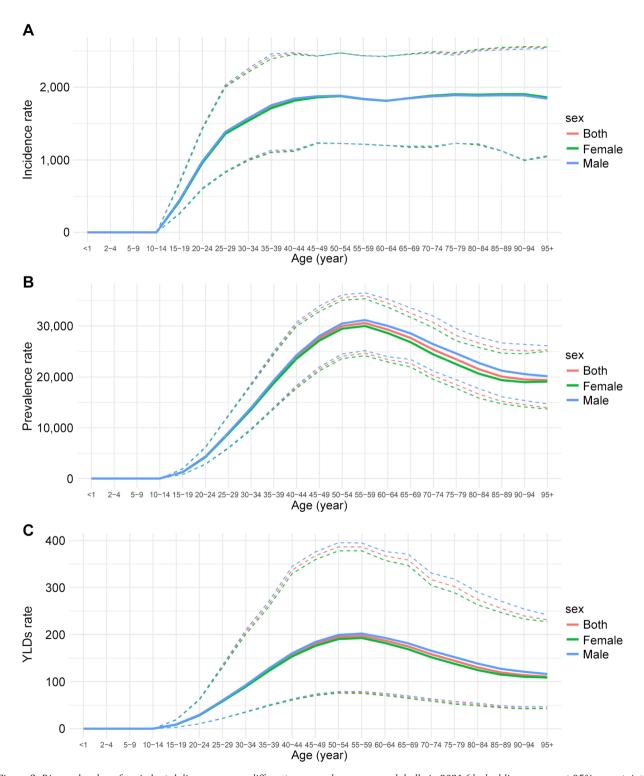
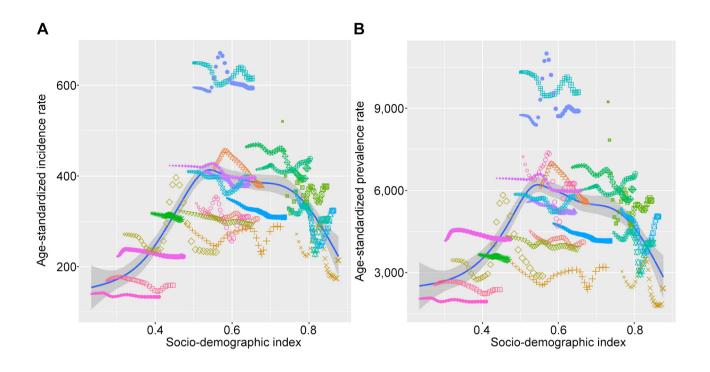


Figure 2. Disease burden of periodontal diseases across different sexes and age groups globally in 2021 (dashed lines represent 95% uncertainty intervals). (A) Incidence rate, (B) Prevalence rate, and (C) years lived with disability (YLD) rate (per 100,000 population).



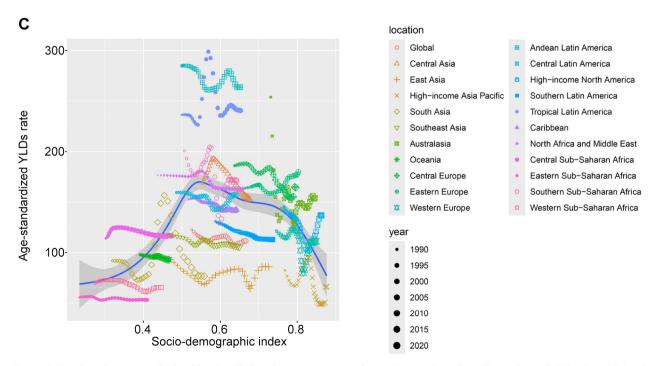
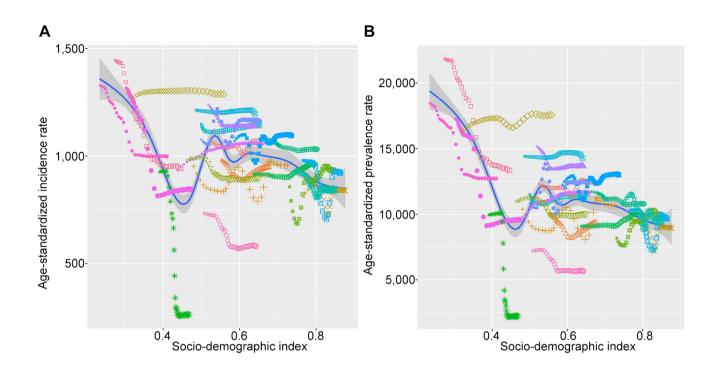


Figure 3. Trends in the age-standardized burden of edentulism across regions from 1990 to 2021 and its relationship with SDI values. (A) Incidence rate, (B) Prevalence rate, and (C) years lived with disability (YLD) rate (per 100,000 population).



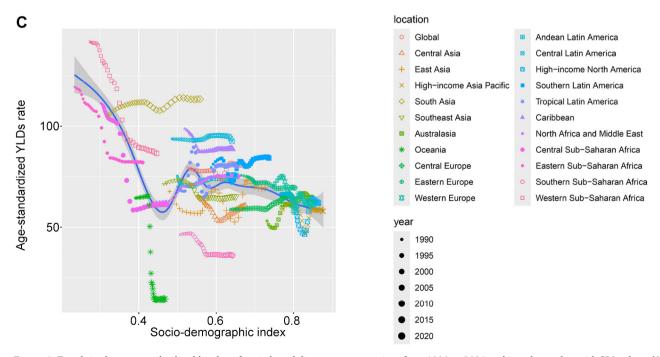


Figure 4. Trends in the age-standardized burden of periodontal diseases across regions from 1990 to 2021 and its relationship with SDI values. (A) Incidence rate, (B) Prevalence rate, and (C) years lived with disability (YLD) rate (per 100,000 population).

Globally, the incidence rates of periodontal diseases did not show significant differences between males and females across age groups (Figure 2). However, the prevalence and YLD rates for periodontal diseases were slightly higher in males, especially between ages 55 and 85, where the differences between males and females became more pronounced.

Relationship between the burden of edentulism and periodontal diseases and SDI over different years. The relationship between edentulism and the SDI is shown in Figure 3. The age-standardized incidence, prevalence, and YLD rates in different regions followed similar patterns. According to the fitted curve, regions with an SDI value between 0.5 and 0.7 had a higher disease burden. Tropical Latin America and Andean Latin America had the highest disease burden, whereas Eastern Sub-Saharan Africa had the lowest age-standardized incidence rate, and the Highincome Asia Pacific region had the lowest age-standardized prevalence and YLD rates from 2013 to 2019.

Between 1990 and 2021, the burden of edentulism showed considerable fluctuations in most regions. Overall, the burden of edentulism in 2021 was lower than in 1990.

As shown in Figure 4, between 1990 and 2021, age-standardized incidence, prevalence, and YLD rates for periodontal diseases exhibited similar patterns across different regions. Overall, based on the fitted curve, the burden of periodontal diseases was relatively lower in regions with high SDI values and relatively higher in regions with low SDI values. Oceania had the lowest burden of periodontal diseases, whereas Western Sub-Saharan Africa had the highest.

From a temporal perspective, most regions showed a declining trend in the age-standardized burden of periodontal diseases. Additionally, in regions with lower SDI values, the decrease in age-standardized burden was more pronounced, whereas regions with higher SDI values experienced a smaller decline. This finding may indicate that there is greater potential for reducing the burden of periodontal diseases in low-SDI regions.

Future trend projections. This study used regression models to predict the incidence, prevalence, and YLD rates of the two oral diseases globally and across different SDI regions over the next 29 years (2022 to 2050).

Globally and across all SDI regions, age-standardized incidence, prevalence, and YLD rates for edentulism exhibited similar trends from 1990 to 2021 (Supplementary Figure 1). Except for high SDI and high-middle SDI regions, other SDI regions reached relatively high values in 2015. The burden of edentulism in low SDI regions remained below the global level throughout the period.

Between 1990 and 2021, the age-standardized burden of edentulism exhibited considerable fluctuations globally and across different SDI regions. According to the ARIMA model, age-standardized disease burdens at the global and regional levels are projected to continue fluctuating from 2022 to 2050.

For periodontal diseases, globally and across all SDI regions, the trends for age-standardized rates of incidence, prevalence, and YLD were similar. From 1990 to 2021, only low SDI regions showed a clear declining trend, while low-middle SDI regions experienced minimal change, and other SDI regions showed significant overall fluctuations (Supplementary Figure 2).

The burden of periodontal diseases in low and low-middle SDI regions consistently remained above the global level, whereas high-SDI and high-middle SDI regions consistently remained below the global level. All SDI regions reached a lower burden in 2010, followed by an increase until 2015, after which the burden stabilized.

According to the ARIMA model, all SDI regions are expected to show relatively stable trends from 2022 to 2050. The low SDI region exhibited the most significant changes from 1990 to 2021, leading to the widest confidence interval in the forecast curve. Conversely, the low-middle SDI region showed the smallest degree of change, resulting in the narrowest confidence interval for the forecast, lending greater credibility to the projections.

Discussion

This study systematically evaluated the epidemiology and burden of periodontal diseases and edentulism from 1990 to 2021 at global and regional levels, based on the GBD 2021 data. Despite progress in oral health care in some countries, the findings reveal that periodontal diseases and edentulism remain significant public health challenges worldwide, particularly in low and low-middle SDI regions.

Trends in the global burden of periodontal diseases and edentulism. From 1990 to 2021, there was a significant increase in the prevalence and incidence of periodontal disease globally, particularly in low and low-middle SDI regions. This trend can be attributed to factors such as global population aging, changes in lifestyle, and the inadequate accessibility of oral health services (16). In 2021, the number of periodontal disease cases worldwide reached approximately 1.07 billion, indicating that periodontal diseases remain a substantial issue affecting global public health. Despite showing a decline since 1990, the incidence rate of edentulism in 2021 still poses a significant burden, particularly in low-SDI regions.

The increasing trend in periodontal diseases was especially pronounced among middle-aged and elderly populations, with the peak incidence occurring between 45 and 59 years of age, while the incidence of edentulism peaked between 70 and 79 years. These results highlight the need for early prevention and intervention efforts targeting older populations, particularly in regions experiencing accelerated aging and insufficient health services (17).

Association between socio-demographic index and disease burden. The study revealed significant disparities in the burden of periodontal diseases and edentulism across SDI regions, with low and low-middle SDI regions showing the highest prevalence and incidence rates of periodontal diseases and edentulism. The high burden of these conditions in such regions may be linked to limited medical resources, poor living conditions, and insufficient awareness of oral health (6, 18).

Conversely, high SDI regions had relatively lower prevalence rates, likely due to more robust public health infrastructure, greater accessibility to healthcare, and heightened awareness of oral hygiene. However, even in high SDI regions, there remains room for improvement in preventive oral health care, especially considering the increasing demand from an aging population (17).

Impact of age and sex on disease burden. The findings also showed differences in the burden of periodontal diseases and edentulism between males and females. The prevalence of periodontal diseases was slightly higher in males than in females, particularly between the ages of 55 and 85 years. This disparity may be due to the higher rates of tobacco and alcohol use among males in this age group, both of which are known risk factors for periodontal diseases (19). Conversely, the incidence of edentulism was higher in females between 20 and 74 years of age, potentially linked to specific health issues faced by women, such as osteoporosis (20). Therefore, targeted and sex-specific preventive and therapeutic interventions could help effectively mitigate these health inequalities.

Systemic health implications of periodontal diseases. The study further highlights the systemic health implications of periodontal diseases. Previous literature has demonstrated significant associations between periodontitis and systemic diseases such as diabetes, cardiovascular diseases, and chronic obstructive pulmonary disease (21-23). These relationships are likely mediated through mechanisms involving chronic inflammation and altered immune responses. The findings of this study are consistent with these associations, emphasizing the need to integrate periodontal diseases management into broader chronic disease management strategies to mitigate its systemic health impacts (24).

Future projections and public health implications. Based on ARIMA model projections, the burden of periodontal diseases and edentulism is expected to is expected to show

relatively stable trends globally from 2022 to 2050. However, as the global population continues to grow, the number of periodontal disease cases is also expected to rise, posing a significant challenge to global health systems. To effectively address this burden, governments – especially those in low and low-middle SDI regions – should strengthen preventive measures and improve oral health service provision (25, 26). Specific actions should include increasing investments in public health resources, implementing preventive health education, and enhancing access to essential oral care services. Moreover, promoting collaboration between general practitioners and dental specialists could improve the early diagnosis and intervention of periodontal diseases (27).

Study limitations. Despite providing comprehensive assessments of the global burden of periodontal diseases and edentulism, this study has several limitations. First, the analysis relies on GBD data, and in certain low- and middle-income countries, data quality and coverage may be insufficient, leading to potential underestimation or overestimation of disease burden. Second, data heterogeneity may affect the accuracy of the findings, especially given the differences in case definitions and data collection methods across countries and regions. Future research should focus on improving data collection and standardization to ensure accurate burden estimation across different contexts. Additionally, the projections of the future burden in this paper are based only on trends over the past 30 years and do not consider the impact of future changes in population size and demographics.

In conclusion, this study reveals the significant public health burden of periodontal diseases and edentulism globally, with projections suggesting a continued increase in the coming decades. These findings provide important insights for policymakers to develop effective oral health interventions, particularly in low and low-middle SDI regions. Improving access to healthcare and implementing preventive strategies may significantly alleviate the global burden of periodontal diseases and edentulism.

Supplementary Material

Supplementary Tables I-III and Supplementary Figures 1 and 2 are available at: DOI: 10.6084/m9.figshare.28016939

Conflicts of Interest

The Authors declare no potential conflicts of interest concerning the authorship and/or publication of this article.

Authors' Contributions

YF: conceived the study, supervised the experiments and drafted the manuscript. LYX: conceived the study, supervised the experiments, and drafted the manuscript. LLF: data evaluation, manuscript preparation. MG, TV, US, RS, and RR: analyzed the data and revised the manuscript. REF and MY: conceived the study, performed the data evaluation, and prepared the manuscript.

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