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Association between tooth loss and depression mediated by lifestyle and Inflammation- a cross-sectional investigation

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Abstract

Background Depression and tooth loss are associated with the occurrence of systemic disease or the progression of multi-factorial disease, and both are considered important public health issues by World Health Organization (WHO). Previous research just suggested that tooth loss can generate psychological stress, low self-esteem, anxiety and other emotional disturbances. However, the precise correlation and underlying mechanisms between depression and tooth loss remains poorly understood. Consequently, we aim to explore the association between depression and tooth loss through a cross-sectional study, as well as investigate potential pathways of influence.

Methods We analyzed data from the National Health and Nutrition Examination Survey (NHANES). Logistic regression models were employed to examine the relationship between depression and tooth loss, as well as the associations among healthy lifestyle, systemic immune-inflammation index (SII), depression and tooth loss. Through the mediating effect analysis by bootstrapping analysis, we evaluated the mediating effects of healthy lifestyle and SII between depression and tooth loss.

Results Depressed patients were more likely to be toothless, and at the same time showed a tendency to have more missing teeth, with odds ratio (OR) = 1.305 (1.098, 1.551), $p = 0.003$ for 1–7 missing teeth, OR = 1.557 (1.166, 2.079), $p = 0.003$ for 8–14 missing teeth, and OR = 1.960 (1.476, 2.603), $p < 0.001$ for 15–28 missing teeth. Lower healthy lifestyle scores and higher SII were both associated with more tooth loss. Healthy lifestyle and SII played a partial mediating role in this relationship, with a mediating effect ratio of 41.691% and 3.289%, respectively.

Conclusions Depression was positively associated with more severe tooth loss, which was partly mediated by lifestyle and SII. Therefore, attention should also be paid to the effects of depression as a mental disorder on physical health, such as depression and tooth loss. Adopting a healthier lifestyle and controlling systemic inflammation may be potential ways to reduce the impact of depression and tooth loss.

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Keywords Depression, Tooth loss, Healthy lifestyle, Systemic immune-inflammation index, HEI-2015 score, NHANES

Introduction

Depression, a common mental disorder, is characterized by persistent feelings of sadness, fatigue, and a diminished interest in activities. As a leading contributor to the Global Burden of Disease [1, 2], the etiology of depression involves intricate interplay among social, psychological, and biological factors. At the same time, depression can exacerbate stress, dysfunction, and negatively affect an individual's social, psychological and physical well-being. Numerous studies have established a significant association between depression and various chronic physical disorders, such as arthritis, asthma, cancer, cardiovascular disease, diabetes, obesity, hypertension, cognitive impairment, chronic respiratory disorders, chronic pain conditions, and dementia [3]. These studies shed light on the bidirectional relationship between depression and physical disorders, as well as the influence of shared antecedents impacting both mental and physical health.

Tooth loss often arises as a consequence of advanced dental caries and severe periodontitis, which are prevalent oral diseases. The World Health Organization estimates that globally, approximately 23% of individuals aged 60 years or older experience complete tooth loss. Tooth loss has been linked to increased overall mortality and a higher risk of death from stroke, heart disease, and upper gastrointestinal cancer [4, 5]. Furthermore, studies have shown that tooth loss is more prevalent among individuals with chronic diseases or overall worse health compared to those without these conditions. Additionally, research suggests that tooth loss is associated with accelerated aging, insulin resistance and an increased incidence of hypertension [6, 7]. Complete dentition plays a crucial role in social functions, including speech, smiling, and emotional expression. The absence of teeth can negatively impact facial appearance and pronunciation, thereby reducing confidence, limiting social activities, and potential contributing to mental pressure and depression [8]. However, the influence of depression on the condition of tooth loss remains unclear, and the underlying mechanisms are still largely unexplored.

In this study, we utilize cross-sectional data from the National Health and Nutrition Examination Surveys (NHANES) to investigate the relationship between depression and tooth loss in American adults. Moreover, according to modern research, both depression and tooth loss are thought to be linked to inflammation and diet. Therefore, we will consider the potential mediating role of lifestyle factors and inflammation, which will be tested by a mediating effect analysis. By delving into these mechanisms, our study seeks to enhance our understanding of the complex association between depression and oral health. The study will not only fill a gap in the field of research on whether and how depression affects tooth loss, but also provide new ideas for blocking or reducing the link.

Methods

Study design and participants

This study used data from NHANES, a publicly available database that collects comprehensive information on health, diet, and lifestyle through interviews, physical examinations, and laboratory tests. The study population comprised 11,552 individuals selected from NHANES 2007–2020 after excluding incomplete data (Fig. 1).

Depression

Depression was assessed using the Patient Health Questionnaire (PHQ-9), a self-reported tool that measures the severity of depressive symptoms. Since its development, researchers have confirmed the effectiveness and reliability of PHQ-9 in various contexts, making it a useful tool for assessing depression [9–11]. As shown in Table S1, the PHQ-9 consists of nine questions that assess the frequency of depressive symptoms experienced over the past two weeks. Healthcare professionals commonly use the PHQ-9 to screen, diagnose, and monitor depression in patients. Each question is scored on a scale from 0 to 3, and the total score ranges from 0 to 27, with higher scores indicating more severe depressive symptoms. A PHQ-9 score $\geq$10 is considered indicative of depression, with a sensitivity of 88% and specificity of 88% [12]. In this study, individuals with PHQ-9 scores $\geq$10 were defined as depression group, while those with scores below 10 were classified into the non-depressed group.

Tooth loss

Tooth loss was assessed by counting the number of all the missing teeth (meaning that there is no natural tooth or any form of restoration in that part) in the mouth. Only the third molar was excluded from the count, and a complete dentition was defined as having 28 teeth. Specific examination data were obtained from the "Oral Health-Dentition" section. Based on the number of tooth loss, individuals were divided into four groups (A1-A4): A1 had no missing tooth, A2 had 1–7 missing teeth, A3 had 8–14 missing teeth, and A4 had 15 or more missing teeth.

Healthy lifestyle

A healthy lifestyle score was calculated to evaluate an individual's overall adherence to a healthy lifestyle. This score encompassed six factors: diet, physical activity,

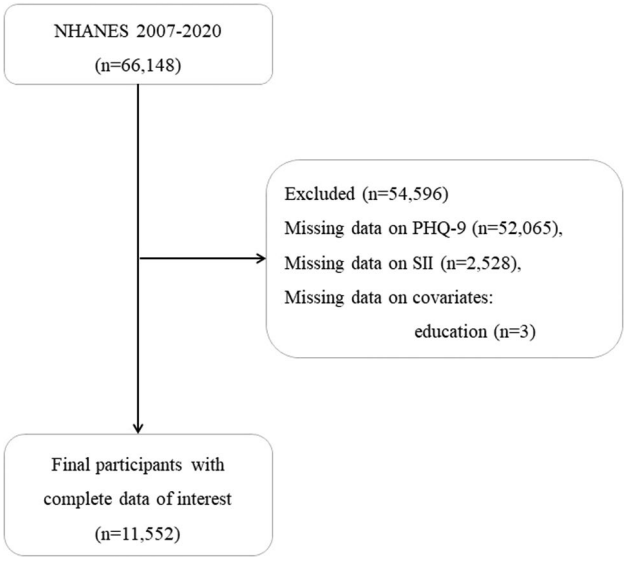

Fig. 1 Flow chart of recruitment procedure of study subjects. NHANES: National Health and Nutrition Examination Surveys; PHQ-9: Patient Health Questionnaire; SII: Systemic Immune-Inflammation Index

body weight, sleep habit, alcohol intake, and tobacco consumption, as shown in Table S2. These factors were selected based on previous studies highlighting their significant impact on physical and psychological health [13]. Firstly, a healthy diet referred to the top two fifths of diet quality scores based on the Healthy Eating Index-2015 (HEI-2015) [14]. The HEI-2015 score ranges from 0 to 100, with a higher HEI-2015 score indicating better diet quality [15]. The Day 1 Total Nutrient Intake (DR1TOT) was used to calculate the 13 components (9 adequate food components and 4 moderate food components) of the HEI-2015 score. Secondly, a healthy physical activity level was defined as engaging in at least 150 min of moderate activity, at least 75 min of vigorous activity per week, or an equivalent combination [16]. Thirdly, a healthy body weight was classified as a normal body mass index (BMI) between 18.5 and 24.9. Fourthly, a healthy sleep habit was defined as getting 7 to 8 h of sleep per day [16]. Fifthly, healthy alcohol intake was considered moderate intake, which meant consuming less than one drink per day for females and less than two drinks for males [14]. One drink typically contains about 14 g of pure alcohol and can be equivalent to 12 ounces of regular beer, 5 ounces of wine, or 1.5 ounces of distilled spirits. Lastly, healthy tobacco consumption was defined as being a non-smoker having smoked fewer than 100 cigarettes in their lifetime [17]. Each component was assigned a score of 1 if healthy and 0 if not, and the scores were summed to obtain a healthy lifestyle score ranging from 0 to 6, with a higher score indicating a healthier lifestyle.

System immune-inflammation index

The systemic immune-inflammation index (SII), developed by Hu et al. in 2014, is a derived index that represents an individual's overall immune response and inflammatory status [18]. Many researchers consider it to be an efficient, stable, simple metric that is relevant to many diseases, such as tumors, cardiovascular diseases, insulin resistance, etc [7, 19, 20]. It combines three inflammatory cell types, namely, platelets, neutrophils, and lymphocytes. The SII is calculated using the following formula: SII = Platelet counts × Neutrophil counts / Lymphocyte counts.

Covariates

Five covariates were included in this study: gender, age, race, education level and ratio of family income to poverty [6, 7]. Gender was categorized as male and female. Race was classified as non-Hispanic white, non-Hispanic black, Mexican American, and other races. Education level was classified as less than a high school diploma, high school graduate/general educational development, some college/associate degree, and college graduate or higher. The ratio of family income to poverty was categorized as ≤100%, 100–300%, and >300%.

Statistical analyses

Confounding was evaluated using prior knowledge and descriptive statistics using a directed acyclic graph (DAG). Referring to Fig. S1 for details, we finally consider the following covariates as inclusions: age (continuous), sex (female and male), race and ethnicity (non-Hispanic white, non-Hispanic black, Mexican, American and other), education level (less than high school, high school or equivalent, and college or above), and ratio of family income to poverty (0–1.0, 1.0–3.0, and >3.0). In the following analysis of demographic characters of participants, descriptive statistics were used to present continuous variables as means (±standard error, SE) and categorical variables as counts (percentages, %). Participants were divided into four groups based on the grouping of the number of tooth. One-way analysis of variance (ANOVA) was employed to compare continuous variables between groups, while the chi-squared test was used to compare categorical characteristics. Regression models were utilized to investigate the associations between tooth loss and depression, healthy lifestyle and tooth loss and depression, and SII and tooth loss and depression, with odds ratio (OR) and 95% confidence interval (CI) computed in comparison to the non-depressed group. Mediation analysis using bootstrapping was conducted to examine the mediating effects of SII and healthy lifestyle between tooth loss and depression. Regression models are divided into two types depending on whether they are adjusted for covariates or not.

Table 1 Baseline demographic characters of 11,552 participants from NHANES 2007–2020 according to the number of tooth loss

Characteristics	Total	Number of tooth loss				*p*-value[c]
		0	1–7	8–14	15–28	
Age (year)[a]	46.17 (0.15)	37.98 (0.20)	48.95 (0.22)	58.48 (0.43)	62.91 (0.39)	**< 0.001**
Sex[b]						**< 0.001**
Female	5148 (44.56)	2175 (42.25)	2261 (43.92)	357 (6.93)	355 (6.90)	
Male	6404 (55.44)	2679 (41.83)	2660 (41.54)	485 (7.57)	580 (9.06)	
Race and ethnicity[b]						**< 0.001**
Non-Hispanic White	5530 (47.87)	2441 (44.14)	2264 (40.94)	320 (5.79)	505 (9.13)	
Non-Hispanic Black	2369 (20.51)	768 (32.42)	1056 (44.58)	288 (12.16)	257 (10.85)	
Mexican American	1393 (12.06)	617 (44.29)	649 (46.59)	76 (5.46)	51 (3.66)	
Other	2260 (19.56)	1028 (45.49)	952 (42.12)	158 (6.99)	122 (5.40)	
Education level[b]						**< 0.001**
Less than high school	1742 (15.08)	480 (27.55)	792 (45.46)	197 (11.31)	273 (15.67)	
High school or equivalent	2476 (21.43)	828 (33.44)	1090 (44.02)	262 (10.58)	296 (11.95)	
College or above	7334 (63.49)	3546 (48.35)	3039 (41.11)	383 (5.22)	366 (4.99)	
Ratio of family income to poverty[b]						**< 0.001**
0–1.0 (including 1.0)	1974 (17.09)	729 (36.93)	831 (42.10)	186 (9.42)	228 (11.55)	
1.0–3.0 (including 3.0)	4287 (37.11)	1585 (36.97)	1846 (43.06)	392 (9.41)	464 (10.82)	
>3.0	5291 (45.80)	2540 (48.10)	2244 (42.41)	264 (4.99)	243 (4.59)	

[a] Represents mean with standard error for continuous variables

[b] Represents counts with percentages for categorical variables

[c] *P*-values represent statistical measurement of comparing individuals among different number of missing teeth, which one-way analysis of variance (ANOVA) was employed to compare continuous variables between groups, while the chi-squared test was used to compare categorical characteristics

Mediation analyses were adjusted for all covariates. The HEI-2015 score was calculated using SAS 9.4, while other data were collated and analyzed using SPSS 18.0. Statistical significance was established as a two-tailed p-value < 0.05.

Results

Demographic profiles

A total of 11, 552 subjects from NHANES 2007–2020 were included in this study. All covariables, including age, gender, race and ethnicity, education level, and ratio of family income to poverty, were found to be statistically significant. Among the study population, 7.4% of participants had depression, and 58% had missing teeth. Specifically, 4854 individuals were no tooth loss, 4921 individuals were missing 1–7 teeth, 842 individuals were missing 8–14 teeth, and 935 individuals were missing 15–28 teeth. Table 1 shows that as the number of tooth loss increased, the average age of individuals with tooth loss also increased. Additionally, individuals with higher education levels and higher household income-to-poverty ratios had fewer missing teeth, consistent with prior research.

Table 2 Multiple logistic regression analysis of the association between depression and tooth loss

Number of Tooth Loss	Model 1		Model 2	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
A1 (0)	Ref		Ref	
A2 (1–7)	1.379 (1.176, 1.616)	**<0.001**	1.305 (1.098, 1.551)	**0.003**
A3 (8–14)	1.719 (1.327, 2.227)	**<0.001**	1.557 (1.166, 2.079)	**0.003**
A4 (15–28)	2.000 (1.577, 2.535)	**<0.001**	1.960 (1.476, 2.603)	**<0.001**

Model 1: Multiple logistic regression model without adjustments;

Model 2: Multiple logistic regression model with covariate correction including age, sex, ethnicity, education level and family income/poverty ratio

OR: Odds ratio; CI: Confidence interval; Ref: The abbreviation of reference

Association between depression and tooth loss

Multiple logistic regression analysis was performed to explore association between depression and the number of tooth loss. In the depression group, the risk of missing more teeth progressively increased with higher PHQ-9 scores. In Model 1 of Table 2, without adjustments, the OR for groups A2 to A4 were 1.379 (95% CI=(1.176, 1.616), p<0.001), 1.719 (95% CI=(1.327, 2.227), p<0.001), and 2.000 (95% CI=(1.577, 2.535), p<0.001) compared to

A1 group. After adjusting for all covariates in Model 2 of Table 2, the OR for group A2 to A4 were1.305 (95% CI=(1.098, 1.551), p<0.01), 1.557 (95% CI=(1.166, 2.079), p<0.01), and 1.960 (95% CI=(1.476, 2.603), p<0.001), showing consistent yet attenuated results with unadjusted model.

Health lifestyle involvement in the association between depression and tooth loss

Using multifactor logistic regression, we found that there was a significant reduction in the risk of tooth loss in the 1st tertile (OR (95%CI)=1.570 (1.384,1.781), p<0.001) and 2nd tertile (OR (95%CI)=1.195 (1.061–1.346), p<0.01) at the time of missing teeth 1–7 referenced by the 3rd tertile without adjusting for covariates in Model 1 of Table 3. After adjusting for covariates, healthy life scores were measured in three tertiles, and the first tertile (T1) (OR (95%CI)=1.721 (1.494,1.983), p<0.001) and the second tertile (T2) (OR (95%CI)=1.293 (1.132,1.476), p<0.001) showed an increased risk of tooth loss for 1–7 missing teeth in Model 2 of Table 3, with the healthy lifestyle score decreased. Similar trends were observed for missing teeth 8–14 and 15–28, with the risk of tooth loss decreasing as the healthy lifestyle score increased. In other words, the lower the healthy lifestyle score, the greater the risk of missing teeth.

Table S3 shows a statistically significant association between healthy lifestyle scores and depression (β (95%CI) = -0.067 (-0.072, -0.061), p<0.001). The multivariate logistic regression model indicates that depression significantly promote the occurrence of lower healthy lifestyle scores. Without adjusting for covariates, Model 1 in Table 4 shows that the OR values of the 1st tertile and 2nd tertile were 5.590 (95%CI = (3.964, 7.883), p<0.001) and 2.377 (95%CI = (1.677, 3.370), p<0.001) compared to 3rd tertile. After adjusting the covariates in Model 2 of Table 4, depression remains a risk factor for healthy lifestyle score, with OR of T1 and T2 compared to T3 being 4.108 (95%CI = (2.896, 5.827), p<0.001) and 2.061(95%CI = (1.449, 2.931), p<0.001) respectively in depression group.

SII involvement in the association between depression and tooth loss

Data analysis revealed a significant protective effect of lower SII on missing teeth compared to the highest SII in Q4, both in Model 1 with uncorrected covariates and in Model 2 with corrected covariates. Particularly, in Model 1 of Table 5, the OR values for Q1, Q2, and Q3 in the A4 group are statistically significant, with values of 0.668 (95% CI = (0.550, 0.812), p<0.001), 0.655 (95% CI = (0.541, 0.795), p<0.001), and 0.660 (95% CI = (0.544, 0.801), p<0.001), respectively. In Model 2 of Table 5, the OR values for Q1, Q2, and Q3 are 0.788 (95% CI = (0.629, 0.988), p<0.05), 0.792 (95% CI = (0.632, 0.992), p<0.05), and 0.779 (95% CI = (0.622, 0.975), p<0.05), respectively.

Table 3 Logistic regression analysis of the association between healthy lifestyle and tooth loss

Number of Tooth Loss	healthy lifestyle score	Model 1		Model 2	
		OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
A1 (0)	/	Ref		Ref	
A2 (1–7)	T1 (0–2)	1.570 (1.384, 1.781)	**<0.001**	1.721 (1.494, 1.983)	**<0.001**
	T2 (3–4)	1.195 (1.061, 1.346)	**0.003**	1.293 (1.132, 1.476)	**<0.001**
	T3 (5–6)	Ref		Ref	
A3 (8–14)	T1 (0–2)	3.108 (2.351, 4.108)	**<0.001**	4.015 (2.952, 5.460)	**<0.001**
	T2 (3–4)	1.867 (1.417, 2.459)	**<0.001**	2.216 (1.645, 2.985)	**<0.001**
	T3 (5–6)	Ref		Ref	
A4 (15–28)	T1 (0–2)	4.137 (3.091, 5.537)	**<0.001**	5.908 (4.237, 8.239)	**<0.001**
	T2 (3–4)	2.340 (1.752, 3.126)	**<0.001**	2.923 (2.116, 4.039)	**<0.001**
	T3 (5–6)	Ref		Ref	

Model 1: Multiple logistic regression model without covariate correction;

Model 2: Multiple logistic regression model with covariate correction including age, sex, ethnicity, education level and family income/poverty ratio;

T1: 1st tertile; T2: 2nd tertile; T3: 3rd tertile

OR: Odds ratio; CI: Confidence interval; Ref: The abbreviation of reference

Table 4 Logistic regression analysis of the association between depression and healthy lifestyle

healthy lifestyle score	Model 1		Model 2	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
T1 (0–2)	5.590 (3.964, 7.883)	**<0.001**	4.108 (2.896, 5.827)	**<0.001**
T2 (3–4)	2.377 (1.677, 3.370)	**<0.001**	2.061 (1.449, 2.931)	**<0.001**
T3 (5–6)	Ref		Ref	

Model 1: Multiple logistic regression model without covariate correction;

Model 2: Multiple logistic regression model with covariate correction including age, sex, ethnicity, education level and family income/poverty ratio;

T1: 1st tertile; T2: 2nd tertile; T3: 3rd tertile

OR: Odds ratio; CI: Confidence interval; Ref: The abbreviation of reference

According to the linear regression model in Table S4, the depression has a positive effect on SII (β (95% CI)=0.001 (0.000, 0.001), p<0.001). In Model 1 of Table 6, without covariate correction, the probability of Q1, Q2 and Q3 is relatively low compared to Q4 in the group of depression. The OR values for Q1 to Q3 are 0.659 (95% CI=(0.542, 0.802), p<0.001), 0.765 (95% CI=(0.633, 0.924), p<0.01), and 0.730 (95% CI=(0.603, 0.884), p<0.01). After the adjustments for covariates, depression is negatively correlated with the occurrence of Q1 (Model 2, Table 6, OR (95% CI)=0.715 (0.585, 0.873), p<0.01) and Q3 (Model 2, Table 6, OR (95% CI)=0.761 (0.626, 0.925),

Table 5 Logistic regression analysis of the association between SII and tooth loss

Number of Tooth Loss	SII	Model 1		Model 2	
		OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
A1 (0)	/	Ref		Ref	
A2 (1–7)	Q1 (≤ 326.34)	0.941 (0.840, 1.053)	0.288	0.975 (0.862, 1.103)	0.690
	Q2 (326.35-451.92)	0.878 (0.784, 0.983)	**0.023**	0.928 (0.821, 1.049)	0.234
	Q3 (451.93-627.52)	0.922 (0.824, 1.032)	0.158	0.960 (0.850, 1.085)	0.512
	Q4 (≥ 627.53)	Ref		Ref	
A3 (8–14)	Q1 (≤ 326.34)	1.020 (0.834, 1.247)	0.848	1.090 (0.874, 1.360)	0.446
	Q2 (326.35-451.92)	0.816 (0.662, 1.005)	0.056	0.917 (0.730, 1.151)	0.456
	Q3 (451.93-627.52)	0.799 (0.648, 0.986)	**0.037**	0.888 (0.706, 1.117)	0.309
	Q4 (≥ 627.53)	Ref		Ref	
A4 (15–28)	Q1 (≤ 326.34)	0.668 (0.550, 0.812)	**<0.001**	0.788 (0.629, 0.988)	**0.039**
	Q2 (326.35-451.92)	0.655 (0.541, 0.795)	**<0.001**	0.792 (0.632, 0.992)	**0.042**
	Q3 (451.93-627.52)	0.660 (0.544, 0.801)	**<0.001**	0.779 (0.622, 0.975)	**0.030**
	Q4 (≥ 627.53)	Ref		Ref	

Model 1: Multiple logistic regression model without covariate correction;

Model 2: Multiple logistic regression model with covariate correction including age, sex, ethnicity, education level and family income/poverty ratio

Q1: 1st quartile; Q2: 2nd quartile; Q3: 3rd quartile; Q4: 4th quartile

OR: Odds ratio; CI: Confidence interval; Ref: The abbreviation of reference

Table 6 Logistic regression analysis of the association between SII and depression

SII	Model 1		Model 2	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Q1 (≤ 326.34)	0.659 (0.542, 0.802)	**<0.001**	0.715 (0.585, 0.873)	**0.001**
Q2 (326.35-451.92)	0.765 (0.633, 0.924)	**0.005**	0.839 (0.691, 1.017)	0.074
Q3 (451.93-627.52)	0.730 (0.603, 0.884)	**0.001**	0.761 (0.626, 0.925)	**0.006**
Q4 (≥ 627.53)	Ref		Ref	

Model 1: Multiple logistic regression model without covariate correction;

Model 2: Multiple logistic regression model with covariate correction including age, sex, ethnicity, education level and family income/poverty ratio

Q1: 1st quartile; Q2: 2nd quartile; Q3: 3rd quartile; Q4: 4th quartile

OR: Odds ratio; CI: Confidence interval; Ref: The abbreviation of reference

Table 7 Mediation analyses of healthy lifestyle and SII in the association between tooth loss and depression by bootstrap test

	Depression → Healthy lifestyle → Tooth loss	Depression → SII → Tooth loss
C (total effect)	0.057***	0.057***
c' (direct effect)	0.033*	0.055***
a	-0.052***	3.750***
b	-0.457***	0.0005**
a×b (indirect effect)	0.024	0.002
a×b (Boot SE)	0.003	0.001
a×b (95% Boot CI)	0.019, 0.029	0.000, 0.003
mediating effect ratio	41.691%	3.289%
Test conclusion	Partial mediation	Partial mediation

Note *: $p<0.05$;**: $p<0.01$; ***: $p<0.001$

SE: Standard error; CI: Confidence interval

$p<0.01$) compared with Q4, indicating that depression is more likely to lead to higher SII.

Mediating effects of healthy lifestyle and SII on the association between tooth loss and depression

Bootstrapping was used to test for mediation effects to further validate the influence of both SII and healthy lifestyle in the association between depression and tooth loss, as shown in Table 7. The direct relationship between depression and tooth loss as well as the indirect association mediated by healthy lifestyle and SII were further depicted in Fig. 2. Based on the analysis results, healthy lifestyle and SII were found to partially mediate the relationship between depression and tooth loss. The indirect effects of depression via healthy lifestyle or SII on tooth loss were 0.024 and 0.002, respectively, and the mediating effect ratios for the total effect values were 41.691% and 3.289%, both statistically significant.

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Discussion

This study identified the link between depression and tooth loss, as well as the mediating role of healthy lifestyle and SII, helpful to understand how depression affects tooth loss. Depression not only affects mental health but also has physical consequences. Our study revealed that depression correlates with elevated systemic immune-inflammation, lower healthy lifestyle scores, and ultimately more missing teeth. Healthy lifestyle contributed to mediating 41.691% of the association between depression and tooth loss, underscoring the importance of lifestyle interventions in mitigating the adverse physical effects caused by mental illness. On one hand, a healthy

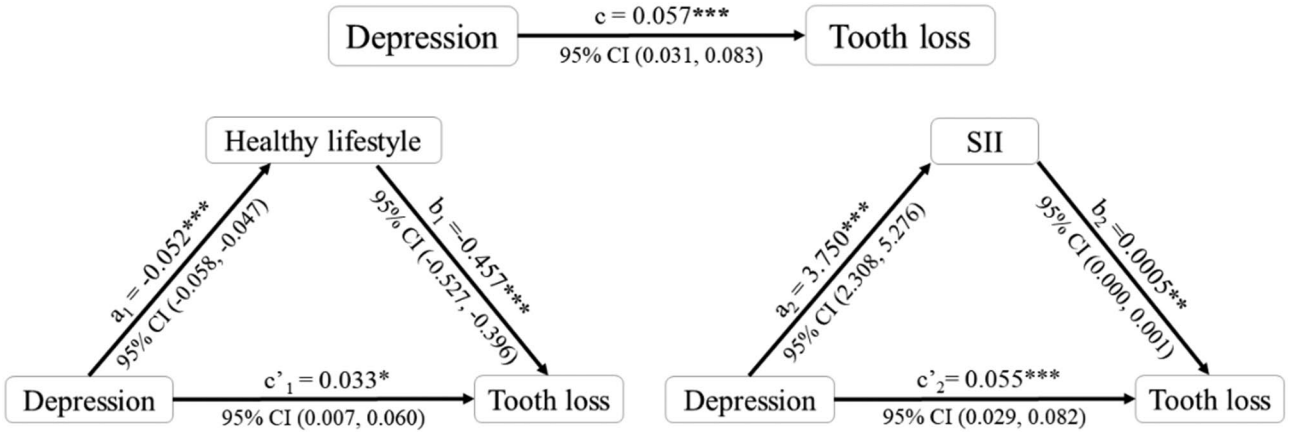

Fig. 2 Partial mediation of healthy lifestyle and SII in the association between depression and tooth loss. *: $p < 0.05$;**: $p < 0.01$; ***: $p < 0.001$. CI: Confidence interval

lifestyle can help mitigate the physical diseases caused by mental disorders, and on the other hand, it can also improve mental health. Additionally, system immune-inflammation, as indicated by SII, partially mediates the impact of depression on tooth loss, explaining 3.289% of the association. These findings highlight the importance of considering the role of inflammation in various diseases and the potential for using inflammatory markers for early diagnosis and prognosis.

Depression is a serious public health problem that requires widespread attention. At the same time, we should be aware that mental health significantly impacts physical health, as a positive mental state promotes physical well-being while a negative mental state disrupts the balance and can lead to various diseases [21]. Numerous meta-analyses of longitudinal studies have consistently shown that depression is a predictor of subsequent onset of coronary artery disease, stroke, diabetes, heart attacks, obesity, osteoporosis and certain types of cancer [22]. Several biologically plausible mechanisms, such as hypothalamic-pituitary-adrenal hyperactivity, autonomic dysregulation, and impaired immune function, have been proposed to explain the associations between depression and these disorders [23]. Persistent low-grade inflammation of surrounding tissues may be a common causative factor underlying depression and comorbidities. Research indicates that depression and inflammation interact to promote disease development [24]. Peripheral cytokine concentrations have been linked to brain function, wellbeing, and cognition [25]. The role of inflammation in the etiology and exacerbation of depression is further supported by evidence of increased interleukin 6 in childhood enhancing the risk of depression later in life and by findings of microglial activation and neuroinflammation in the brains of patients with depression examined post mortem [26]. These insights have prompted the investigation of non-steroidal anti-inflammatory drugs for the treatment of major depressive disorder [27]. In addition, a variety of unhealthy behaviors, such as smoking and excessive alcohol consumption [28], poor eating habits [29], unhealthy food intake [30], and low levels of physical activity [31], are known to increase the risk of developing depression. Previous research has suggested that several lifestyle factors are associated with depressed mood [32]. Moreover, a prospective cohort study demonstrated that high-risk lifestyle factors were associated with higher risk of transitioning from depression to dementia [33].

Tooth loss is primarily caused by dental caries and periodontitis. It can also trigger depression, especially when tooth loss is long-term, leading to anxiety and feelings of shame regarding one's appearance. Recent clinical studies have shown that periodontitis is a risk factor for neuroinflammatory and degenerative diseases, including depression, and is thought to induce systemic inflammation and contribute to the development of neurodegenerative diseases [34–36]. Meanwhile, a cross-sectional study showed that oral health affects perception and is associated with inflammatory markers [37, 38]. A population-cohort study with a 10-year follow-up demonstrated a significantly higher incidence of depression in the periodontitis group compared to the non-periodontitis group [39]. Periodontitis may increase the risk of depression through psychosocial influences such as bad breath or tooth loss, which can cause shame and embarrassment [40]. Additionally, neuroinflammation caused by systemic inflammation related to periodontitis or by periodontal pathogens and their inflammatory products directly invading the brain is associated with the occurrence and development of depression [41]. Furthermore, there is a link between tooth loss and a healthy lifestyle, as factors like smoking [42], excessive alcohol consumption [43], sleep insufficiency [44], high BMI [45], and lower diet quality [46] can increase the risk of tooth loss.

This study originally confirmed the relationship between depression and tooth loss, and explored the influence of depression on tooth loss through mediating effect analysis. Based on a vast body of previous research, it is likely that the causality between tooth loss and depression is bidirectional in most cases. Lifestyle and inflammation are key mediators, with systemic inflammation promoting both depression and tooth loss, while a healthy lifestyle helps prevent and reverse these conditions. However, the cross-sectional design of this study limits the ability to establish causality. Future longitudinal prospective studies are needed to establish causality between tooth loss and depression, and explore additional potential mediating mechanisms.

Strengths and limitations

To the best of our knowledge, this is the first study to explore the mediating role of healthy lifestyle and SII in the association between depression and tooth loss. Both depression and oral health are important public health issues highlighted by the World Health Organization and should not be ignored. This study focused on the association between depression and tooth loss, suggested possible mediators, and provided effective guidance for public health intervention strategies.

However, there are several limitations that we must acknowledge. First, the study was a cross-sectional design, which means that it is discouraging to inquire into a causal relationship between depression and tooth loss, and further work, such as high-quality cohort studies, is needed. Second, the mediating effect ratios for the total effect value of depression via healthy lifestyle or SII on tooth loss were 41.691% and 3.289%, respectively, suggesting the existence of other potential pathways between depression and tooth loss. Focusing on this, we need more observational and experimental studies to understand the mechanisms underlying the association between depression and tooth loss and to develop targeted interventions. Last, this study used data from NHANES, and all subjects included were United States populations, which may make conclusions unsuitable for populations in other countries.

Conclusion

This study established the relationship between depression and tooth loss, and highlighted the mediating role of healthy lifestyle and SII. It would provide new insights into how mental illnesses impact physical diseases, emphasizing the important regulatory role of lifestyle and systemic inflammation. These findings can suggest practical entry points for the prevention and treatment of related diseases.

Abbreviations

WHO	World Health Organization.
NHANES	National Health and Nutrition Examination Survey.
SII	Systemic immune-inflammation index.
OR	Odds ratio.
PHQ-9	Patient Health Questionnaire.
HEI-2015	Healthy Eating Index-2015.
DR1TOT	Day 1 Total Nutrient Intake.
BMI	Body mass index.
SE	Standard error.
ANOVA	One-way analysis of variance.
CI	Confidence interval.

Supplementary Information

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Supplementary Material 1

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Author contributions

Y.H. designed the study and drafted the manuscript. Y.H. and Z.Y. conducted the data analysis. Y. Z., S. L. and J. G. interpreted the data, and reviewed the manuscript. S. D. and L. N. proposed critical revisions to the manuscript. All authors read and approved the final manuscript.

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Data availability

All data used in this study are from the National Health and Nutrition Examination Survey (https://wwwn.cdc.gov/nchs/nhanes).

Declarations

Ethics approval and consent to participate

NHANES is conducted by the Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics (NCHS). And the NHANES study protocol was reviewed and approved by the NCHS Research Ethics Review Committee. All participants in NHANES provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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