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Article

# Oral Health-Related Quality of Life and Oral Health Status Are Associated with the Development of Depression: A Longitudinal Study

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## Abstract

**Background/Objectives** Oral health-related quality of life (OHRQoL) may influence mental health outcomes, yet longitudinal evidence on its association with depression remains limited. This study aimed to examine whether oral health status and OHRQoL are associated with the development of depression among adults in Japan. **Methods** We analyzed data from the Japan COVID-19 and Society Internet Survey (JACSIS), conducted in 2022 and 2023. A total of 15,068 participants aged  $\geq 20$  years without depression at baseline were included. Depression onset was identified by self-reported measures between the two survey waves. Logistic regression models estimated odds ratios (ORs) and 95% confidence intervals (CIs) for depression development in relation to OHRQoL and oral health status, adjusting for sociodemographic and behavioral factors. **Results** During follow-up, 218 participants (1.45%) developed depression. Poorer OHRQoL was significantly associated with development of depression (OR: 1.018; 95% CI: 1.001–1.036;  $p = 0.039$ ). Additional risk factors included younger age (OR: 0.974; 95% CI: 0.964–0.985), participation in hobbies and cultural activities (OR: 2.224; 95% CI: 1.498–3.302), habitual use of sleeping pills or anxiolytics (current use OR: 3.512; 95% CI: 2.267–5.442), increased loneliness (OR: 1.217; 95% CI: 1.140–1.299), lower life satisfaction (OR: 0.900; 95% CI: 0.836–0.969), and poor self-rated health (OR: 2.921; 95% CI: 1.810–4.715). **Conclusions** Impaired OHRQoL was associated with depression development, potentially through psychosocial mechanisms. Maintaining good oral health and OHRQoL may help prevent depression, highlighting the need for integrated oral and mental health strategies in clinical practice.

**Keywords:** oral health-related quality of life; depression; longitudinal study

## 1. Introduction

Depressive disorders are recognized as a major cause of adverse health effects from early adulthood to old age [1], with over 330 million people affected worldwide [2]. In recent years, there has been increasing global concern regarding mental health issues such as depression, anxiety, and stress. According to the disability-adjusted life years metric developed by the World Health Organization, depression ranked third in 2004, is projected to rise to second by 2020, and to become the leading cause of adverse health effects by 2030 [3]. This indicates that diseases and disabilities that rank higher impose a greater socioeconomic burden on society.

The etiology of depression is complex, involving a myriad of factors ranging from biological to lifestyle-related, which poses challenges for primary prevention strategies [4]. According to de Sousa et al. [5], in their review of longitudinal study, “the course of depression varies among individuals and is influenced by factors such as age and gender [6–9], social isolation [6,7,10], socioeconomic factors including childhood and current economic status [11], educational level [10–14], employment [9,13,15], chronic conditions and comorbidities [7,8,13,16,17] such as arthritis/rheumatism, asthma, stroke, coronary heart disease, mental health issues, and having more than three chronic diseases), health behaviors [18,19] such as sedentary lifestyles and smoking, self-rated health [7], and family support [20]. Additionally, factors such as participation in extracurricular activities [21], the use of sleeping medications [22], spousal loss [23], social networks [21,24], event participation, decreased life satisfaction [25], and health-related quality of life (HRQOL) [26,27] have also been reported to be associated with depression.

There have also been reports of an association between depression and oral health status. Factors such as tooth loss [26,28–31], oral pain [32,33], periodontal disease [34–36], dental caries [37], deterioration of oral function [30], worsening oral hygiene [38], dental anxiety [39], dental visits within the past year [40], and oral health-related quality of life (OHRQOL) [41,42] have been linked to depressive symptoms. In their review, Karimi et al. [30] suggested a strong correlation between oral health habits, general health practices, and unhealthy lifestyles. These factors are considered potential causes of depression [43,44]. Therefore, they discussed the possibility not only that depression affects oral health, but also that oral health may impact depression. However, most studies have been cross-sectional, leaving many questions unanswered about how oral health impacts the development of depression.

Therefore, we hypothesized that OHRQOL and oral health status are associated with the development of depression. The aim of this longitudinal study was to investigate the association between oral health status, OHRQOL, and the development of depression.

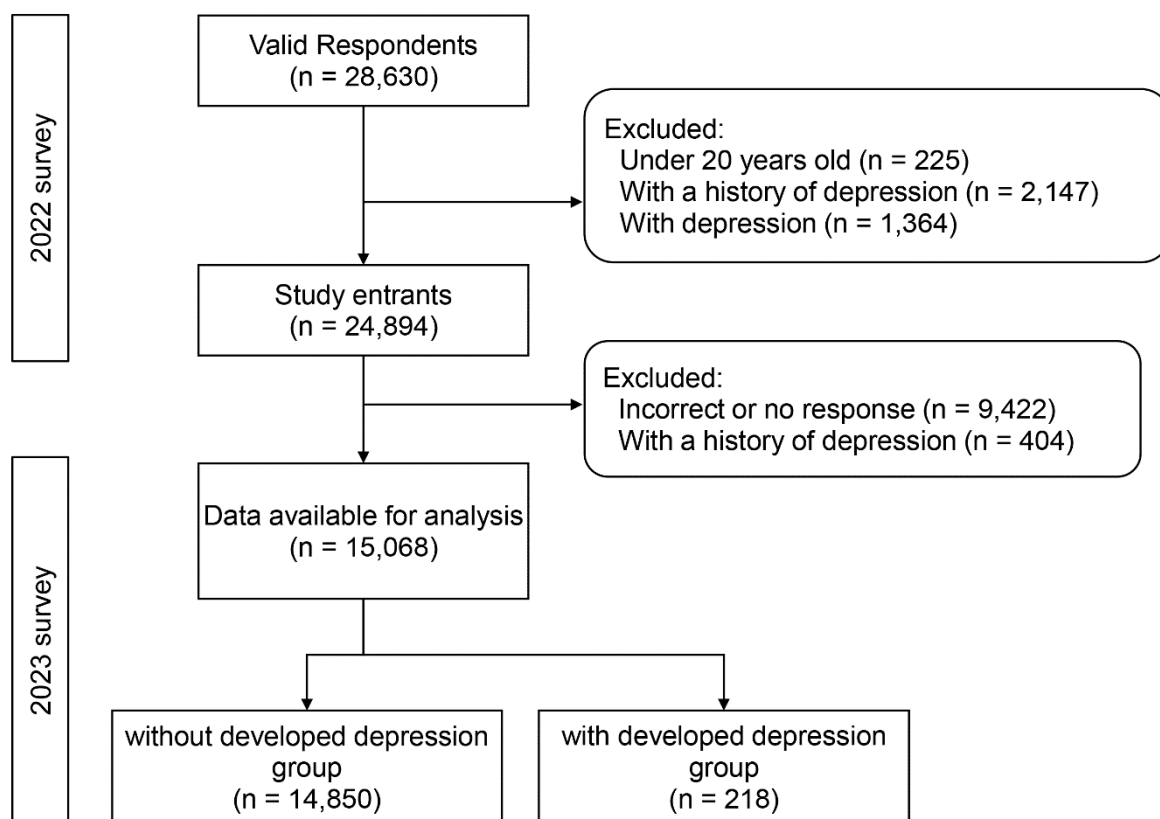
## 2. Materials and Methods

### 2.1. Participants

This longitudinal study utilized data from the Japan COVID-19 and Society Internet Survey (JACSIS) [45] conducted in 2022 and 2023, which surveyed 31,000 individuals aged 16–81 years. Sex was self-reported as male or female; gender identity was not assessed. Random sampling was performed based on sex, age, and prefecture, and then panel members were invited to participate in an online survey that included various questions on lifestyle, health, social interactions, and economic activities, as well as questions related to COVID-19. Participants provided web-based informed consent before answering the online survey and could withdraw consent at any time.

The survey for FY2022 started on September 12, 2022 and ended on October 19, 2022. The survey for FY2023 started on September 25, 2023 and concluded on November 17, 2023. The inclusion criteria were reporting no diagnosis of depression at baseline in 2022, age 20 years or older, and providing valid responses to all question items. The exclusion criteria were having been diagnosed with depression presently or in the past, taking less than 15 minutes to respond, answering “yes” to all drug use items, answering “yes” to all systemic disease items, age less than 20 years, and having missing data. Sex was included as a covariate in all statistical analyses. The study protocol was

approved by the Osaka International Cancer Institute Research Ethics Committee (approved on June 19, 2020; approval No. 20084) as well as the Ethics Review Board of Okayama University (approval Nos.: 2403-044, 2408-009).



**Figure 1.** Flowchart of the study. Flowchart illustrating the participant selection process for the study conducted in 2022 and 2023. The diagram shows inclusion and exclusion criteria applied to respondents from the 2022 survey (n = 28,630) and the subsequent 2023 follow-up. Participants under 20 years old, those with a history of depression, or those with depression at baseline were excluded, resulting in 24,894 entrants. Further exclusions for incorrect or missing responses and history of depression during follow-up yielded 15,068 participants for analysis. These were categorized into two groups: without developed depression (n = 14,850) and with developed depression (n = 218). Abbreviations: n = number of participants.

## 2.2. Measures

### 2.2.1. Depression

We asked the participants, “Do you currently have depression?”, to which they were instructed to respond with one of the following options: “Never had it”, “Not currently depressed but have had it in the past”, “Currently have depression (under treatment with medication)”, “Currently have depression (under treatment without medication)”, or “Currently have depression (not under treatment)”. Responses indicating “Currently have depression (under treatment with medication)”, “Currently have depression (under treatment without medication)”, or “Currently have depression (not under treatment)” were classified as “depression present”.

### 2.2.2. Oral Health-Related Quality of Life (OHRQOL)

Many studies have shown that OHRQOL is influenced by factors such as the number of teeth, the presence of dentures, the need for dental treatment, and the awareness of oral dryness [46–49]. Among the evaluation indicators for OHRQOL, the Oral Health Impact Profile (OHIP) and the General Oral Health Assessment Index (GOHAI) have been translated into Japanese and are

frequently used. However, while the GOHAI is affected by functional disabilities and pain, the OHIP is influenced by psychosocial factors [46,48]. Therefore, in this study, we used the Japanese version of the OHIP-14, a short version of the OHIP (see Table 1 for the English version), as a measure of OHRQOL.

**Table 1.** English version of the OHIP-14 questionnaire. The Oral Health Impact Profile (OHIP-14) assesses oral health-related quality of life across 14 items. Participants responded based on experiences during the past 7 days. Response options: 0 = Never, 1 = Hardly ever, 2 = Occasionally, 3 = Fairly often, 4 = Very often.

For the past 7 days, have you...
...had trouble pronouncing any words because of problems with your teeth or mouth?
...felt that your sense of taste has worsened because of problems with your teeth or mouth?
...had painful aching in your mouth?
...found it uncomfortable to eat any foods because of problems with your teeth or mouth?
...been self-conscious because of your teeth or mouth?
...felt tense because of problems with your teeth or mouth?
...had to interrupt meals because of problems with your teeth or mouth?
...found it difficult to relax because of problems with your teeth or mouth?
...been a bit embarrassed because of problems with your teeth or mouth?
...been a bit irritable with other people because of problems with your teeth or mouth?
...had difficulty doing your usual jobs because of problems with your teeth or mouth?
...felt that life in general was less satisfying because of problems with your teeth or mouth?
...been totally unable to function because of problems with your teeth or mouth?
Has been your diet been unsatisfactory because of problems with your teeth or mouth?

The OHIP-14 consists of 14 questions, each with five response options regarding experiences within the past month. The respondents were asked to select the option that best applied to them, with the scoring as follows: "Always" = 4, "Often" = 3, "Sometimes" = 2, "Rarely" = 1, and "Never" = 0. The OHIP-14 total score is calculated by summing the scores from each question, with a maximum possible score of 56. A higher score indicates poorer OHRQOL.

### 2.2.3. Oral Health Status

Oral health status was assessed for tooth loss, periodontal disease and oral pain.

#### Tooth Loss

We asked the participants, "Have you ever had permanent teeth extracted because of cavities or periodontal disease? If so, please specify the number of teeth extracted (excluding teeth extracted because of an external cause such as injury or orthodontic treatment)". They were instructed to respond with one of the following options: "0 teeth, 1 tooth, 2 teeth, 3 teeth, 4 teeth, 5 teeth, 6–9 teeth, 10–19 teeth, 20–27 teeth, or 28 teeth or more (edentulous)". Responses were categorized into three groups: 0–5 teeth, 6–9 teeth, and 10 or more teeth.

#### Periodontal Disease Screening

For the assessment of periodontal status, we used the periodontal screening index developed by Yamamoto et al. [50]. We asked the participants the following questions: "Do you experience bleeding from your gums (such as when brushing your teeth)?", "Do you feel that your gums have receded compared with before, making your teeth appear longer?", "Have you ever been told by a dental clinic that you need treatment for periodontal disease or gum issues?", and "Are you currently a smoker or have you smoked in the past?" Participants who answered "Yes" to three or more of these questions were classified as "having periodontal disease".

## Oral Pain

We asked the participants, "Have you experienced tooth pain because of cavities in the past 2 months?" and "Have you experienced gum pain because of periodontal disease in the past 2 months?" They were instructed to answer "Yes" or "No". Participants who answered "Yes" to one or more of these questions were classified as having "oral pain".

## Oral Health Behavior

We also asked the participants, "Have you visited a dentist in the past year?" They were instructed to respond with either "Yes" or "No".

### 2.2.4. Covariates

#### Developmental Factors

As developmental factors, we evaluated childhood socioeconomic status and experiences of abuse during childhood.

Regarding childhood socioeconomic status, we asked the participants, "Did you experience financial hardship before turning 18?" [51]. They were instructed to respond with "Yes" or "No".

Regarding childhood abuse, we asked the following questions [51]: "Have you ever been injured by being severely beaten by a parent before turning age 18?", "Have you ever lacked necessary care, such as meals or clothing, before turning age 18?", "Has a parent ever said hurtful or insulting things to you before turning age 18?", and "Did you feel suffocated because your opinions were never respected by your parents before turning age 18?". The participants were instructed to answer "Yes" or "No" to each question. Those who answered "Yes" to one or more questions were classified as having experienced abuse.

#### Sociodemographic and Relationship Characteristics

We also evaluated age, gender, years of education, and annual income. We classified annual income into the following categories: "Less than 3 million yen", "3 million yen to less than 6 million yen", "6 million yen to less than 9 million yen", and "9 million yen or more" [52].

We inquired about educational background (junior high school, high school, vocational school, junior college, university, and graduate school) and assigned the following years of education: "Junior high school" = 9 years, "High school" = 12 years, "Vocational school" = 13 years, "Junior college" = 14 years, "University" = 16 years, and "Graduate school" = 18 years [53]. Responses that fell outside these categories or were marked as "unknown" were excluded from the analysis.

#### Lifestyle Factors

Regarding lifestyle factors, we evaluated participation in extracurricular activities, physical activity, sitting for more than 240 minutes per day, smoking history, and excessive alcohol intake.

We asked the participants about extracurricular activities and light exercise with the following questions: "Do you participate in hobby, learning, or educational groups or clubs?" and "Do you engage in walking or equivalent physical activity for more than 1 hour per day in your daily life?". The participants were instructed to respond with "Yes" or "No".

Regarding sitting for more than 240 minutes per day, we asked the participants, "What was your average sitting time per day in the past month?". Those who reported sitting for more than 240 minutes were classified as sitting for over 240 minutes per day.

Regarding smoking history, we asked the participants to respond with one of the following options: "Currently smoking", "I used to smoke but do not smoke now", or "I have never smoked".

Regarding excessive drinking, daily alcohol consumption was converted into sake, with the threshold set at more than 3 gou (a traditional Japanese measurement for sake) per day for men and more than 2 gou per day for women [54].

## Physical Health Status

We evaluated physical health status by assessing the number of diseases and the habitual use of sleeping pills and antianxiety medications.

We assessed the number of diseases by asking about the current prevalence of the following conditions: hypertension, diabetes, hyperlipidemia, pneumonia/bronchitis, asthma, heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, kidney disease, liver disease, immune disorders, and cancer/malignant tumors. The total number of diseases for which the participants answered “currently present” was classified as the number of diseases.

With regard to the habitual use of sleeping pills, the participants were asked whether they “currently use sleeping pills”, “never used them”, “used them at least once but not habitually”, “used them habitually but not anymore”, “used them occasionally some days”, or “used them almost every day”. Respondents who answered “never used them” or “used them at least once but not habitually” were defined as “never used them habitually”, and those who answered “used them occasionally on some days” or “used them almost every day” were defined as “used them habitually”.

## Psychosocial Factors

Regarding psychosocial factors, we assessed the following: loss of a spouse, family relationships, neighborhood, conversation with nonliving family members, frequency of eating alone (less than once a week, 1–5 times a week, 6–7 times a week), loneliness, social networks, risk of isolation, HRQOL, and life satisfaction.

We used social capital in terms of the family to describe familial relationships [55]. We asked the participants to respond to the following items: “I like my family”, “I enjoy spending time with my family”, “I go to someone in my family when I have a problem”, “I trust my family”, “My family goes on summer holidays and celebrates birthdays together”, “My family follows family rules”, and “We all help each other when someone in my family has a problem”. The participants were asked to rate each of these items as follows: “Strongly agree” (1 point), “Somewhat agree” (2 points), “Neither agree nor disagree” (3 points), “Disagree” (4 points) and “Strongly disagree” (5 points). The total score was used as the family social capital score.

The feeling of loneliness was assessed using the Japanese version of the UCLA Loneliness Scale Version 3, 3-item Short Form (UCLA-LS3-SF-3) [56,57]. The question items on the UCLA-LS3-SF-3 are each rated on a 4-point Likert-type scale, ranging from “Always” to “Never”, with scores assigned from 1 to 4. The total score is then calculated (range: 3–12 points), with higher scores indicating a greater sense of loneliness.

To evaluate social networks, we utilized the Japanese version of the Lubben Social Network Scale (LSNS-6) [58,59], a globally recognized screening tool for social isolation among older adults. The LSNS-6 measures the size of a participant’s active and intimate network with family and friends, assessing their ability to discuss issues with or seek help from others. Each item on the LSNS-6 is scored from 0 to 5 points. The total score is the evenly weighted sum of these six questions, with a range from 0 to 30 points. Higher scores indicate a larger social network. A score below 12 points is considered to indicate a greater risk of social isolation [60]. Therefore, a score below 12 points was categorized as an increased risk for social isolation.

The assessment of HRQOL utilized the HRQOL-4 developed by the Centers for Disease Control and Prevention (CDC; hereafter referred to as CDC HRQOL-4) [61,62]. The four items on the CDC HRQOL-4 assess the following: self-rated health; number of unhealthy days due to physical illness or an injury during the past 30 days; number of unhealthy days due to stress; depression, and problems with emotions during the past 30 days; and number of days with limitations in self-care, work, or recreation due to poor physical or mental health during the past 30 days. We dichotomized each CDC HRQOL-4 component variable as good vs. poor: general health into good (good or very good) vs. poor (poor or fair) [63], physical and mental health into good (<14 days/month) vs. poor (≥14 days/month), and activity limitations into good (<14 days/month) vs. poor (≥14 days/month) [63]. The number of “poor” values from four CDC HRQOL-4 components was summed, and then the

overall HRQOL variable was dichotomized into good (none) vs. poor (one or more). The four dichotomized variables were then summed (range 0–4) and further dichotomized as “good health” if scored from 0 to 2 and “poor health” if scored 3–4 [64].

Regarding life satisfaction, the participants were asked, “How satisfied are you with your overall life recently?”. Responses were given on a Likert scale ranging from 0 (not applicable at all) to 10 (completely applicable).

### 2.3. Statistical Analysis

Among individuals who reported no depression in the 2022 survey, those who reported having depression in the 2023 survey were classified as the “with developed depression” group, and those who reported no depression were classified as the “without developed depression” group. Correlations with covariates were analyzed using the chi-square test and the Mann–Whitney *U* test. Items with a *p*-value <0.1 were treated as independent variables, and the presence or absence of depression was treated as a dependent variable in a multivariate binary logistic regression analysis. Sex (male/female) was included as a covariate in all models. SPSS (ver. 26, IBM Japan, Tokyo, Japan) was used for all statistical analyses, with the level of significance set at 5%.

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## 3. Results

Table 2 shows the characteristics of the respondents, including sex distribution (male/female). The “with developed depression” group consisted of 218 individuals (1.5%). The results of the comparison between the with developed depression and without developed depression groups are presented in Table 3. The items that showed a significant correlation between the two groups (*p*<0.1) included: dental visits within the past year; OHIP-14 score; age; gender; income; smoking history; participation in hobbies, learning, and cultural activities; walking or equivalent physical activity for more than 1 hour a day; chatting with non-cohabiting family members; economic situation until age 18; abuse until age 18; frequency of eating alone; habitual use of sleeping pills or antianxiety medications; family social capital; UCLA-LS3-SF-3 score; risk of social isolation; life satisfaction; and CDC HRQOL-4 score.

**Table 2.** Characteristics of participants at baseline (n=15068). Baseline characteristics of study participants, including oral health-related variables (OHIP-14 score, oral health status), sociodemographic factors, and behavioral covariates. Continuous variables are presented as mean ± standard deviation (SD), and categorical variables as n (%). OHIP: Oral Health Impact Profile; UCLA: University of California, Los Angeles; CDC HRQOL-4: Centers for Disease Control and Prevention Health-Related Quality of Life.

Variables	Categories	n (%) /average ± SD
OHIP-14 score		3.8 ± 6.9*
<b>Oral health status</b>		
Number of tooth loss	None	7,553 (50.1) <sup>†</sup>
	1~5	6,903 (45.8)
	10 or more	612 (4.1)
Periodontal disease	None	13,346 (88.6)

	Yes	1,722 (11.4)
Oral pain	None	13,379 (88.8)
	Yes	1,689 (11.2)
Dental visits within 1 year	Yes	9,010 (59.8)
	None	6,058 (40.2)
<b>Covariates</b>		
Age (years)		51.9 ± 16.8
Gender	Male	7,715 (51.2)
	Female	7,353 (48.8)
Years of Education (years)		14.4 ± 2.0
Annual income	< 3 million yen	2,560 (21.0)
	3-6 million yen	4,819 (39.6)
	6-9 million yen	2,631 (21.6)
	>9 million yen	2,155 (17.7)
Smokin history	Never	9,439 (62.6)
	Past	3,058 (20.3)
	Currently	2,571 (17.1)
Excessive alcohol intake	None	13,795 (91.6)
	Yes	1,273 (8.4)
Number of diseases		0.6 ± 1.0
Participation in hobbies, study, and culture-related activities	Nonparticipation	13,112 (87.0)
	Participation	1,956 (13.0)
Walking ≥1 hour/day or equivalent physical activity	Yes	6,096 (40.5)
	No	8,972 (59.5)
Relationship with Neighbors	None	8,338 (55.3)
	Yes	6,730 (44.7)
Chatting/mingling with non-family members	None	2,962 (19.7)
	Yes	12,106 (80.3)
Sitting ≥240 minutes/day	Yes	5,639 (38.7)
	None	8,924 (61.3)
Loss of spouse	None	13,627 (90.4)
	Yes	1,441 (9.6)
Financial situation up to age 18	Not poor	11,852 (78.7)
	Poor	3,216 (21.3)
Abuse experience up to age 18	None	12,606 (83.7)
	Yes	2,462 (16.3)
Frequency of eating alone	<1 time/week	6,005 (39.9)
	1-5 times/week	4,768 (31.6)
	6-7 times/week	4,295 (28.5)
Habitual use of sleeping pills/anxiolytics	No	13,911 (92.3)
	Past use	354 (2.3)
	Current use	803 (5.3)
Family social capital		14.6 ± 6.1
UCLA Loneliness Scale (3-item)		5.4 ± 2.6
Risk of social isolation	None	8,686 (57.6)
	Yes	6,382 (42.4)
CDC HRQOL-4	Good	14,650 (97.2)
	Poor	418 (2.8)
Life satisfaction		7.4 ± 2.3

\*: average±SD, †: n(%).

**Table 3.** Comparison of depressed and healthy groups by each indicator. Baseline characteristics and oral health-related variables compared between participants who developed depression and those who did not during follow-up. Continuous variables are presented as mean  $\pm$  standard deviation (SD), and categorical variables as n (%). Statistical tests: Student's t-test for continuous variables ( $\dagger$ ) and Chi-square test for categorical variables ( $\S$ ).

OHIP: Oral Health Impact Profile; UCLA: University of California, Los Angeles; LSNS: Lubben Social Network Scale; CDC HRQOL-4: Centers for Disease Control and Prevention Health-Related Quality of Life.

		Without developed depression group (n=14850)	With developed depression group (n=218)	P value
OHIP-14 score		3.7 $\pm$ 6.9*	6.0 $\pm$ 9.0	<0.001 $\dagger$
<b>Oral health status</b>				
Number of tooth loss	None	7437 (50.1) $\dagger$	116 (53.2)	0.471 $\S$
	1~5	6807 (45.8)	96 (44.0)	
	10 or more	606 (4.1)	6 (2.8)	
Periodontal disease	None	13157 (88.6)	189 (86.7)	0.393
	Yes	1693 (11.4)	29 (13.3)	
Oral pain	None	13193 (88.8)	186 (85.3)	0.101
	Yes	1657 (11.2)	32 (14.7)	
Dental visits within 1 year	Yes	8894 (59.9)	116 (53.2)	0.051
	None	5956 (40.1)	102 (46.8)	
<b>Covariates</b>				
Age (years)		52.0 $\pm$ 16.8	43.9 $\pm$ 15.3	<0.001
Gender	Male	7590 (51.1)	125 (57.3)	0.076
	Female	7260 (48.9)	93 (42.7)	
Years of Education (years)		14.4 $\pm$ 2.0	14.2 $\pm$ 2.1	0.262
Annual income	< 3 million yen	2513 (21.0)	47 (26.6)	0.082
	3-6 million yen	4746 (39.6)	73 (41.2)	
	6-9 million yen	2605 (21.7)	26 (14.7)	
	>9 million yen	2124 (17.7)	31 (17.5)	
Smoking history	Never	9317 (62.7)	122 (56.0)	0.009
	Past	3016 (20.3)	42 (19.3)	
	Currently	2517 (16.9)	54 (24.8)	
Excessive alcohol intake	None	13597 (91.6)	198 (90.8)	0.724
	Yes	1253 (8.4)	20 (9.2)	
Number of diseases		0.6 $\pm$ 1.0	0.8 $\pm$ 1.6	0.960
Participation in hobbies, study, and culture-related activities	Nonparticipation	12943 (87.2)	169 (77.5)	<0.001
	Participation	1907 (12.8)	49 (22.5)	
Walking $\geq$ 1 hour/day or equivalent physical activity	Yes	6025 (40.6)	71 (32.6)	0.019
	No	8825 (59.4)	147 (67.4)	
Relationship with Neighbors	None	8205 (55.3)	133 (61.0)	0.100
	Yes	6645 (44.7)	85 (39.0)	
Chatting/mingling with non- family members	None	2902 (19.5)	60 (27.5)	0.004
	Yes	11948 (80.5)	158 (72.5)	
Sitting $\geq$ 240 minutes/day	Yes	5549 (38.7)	90 (43.3)	0.174
	None	8806 (61.3)	118 (56.7)	
Loss of spouse	None	13428 (90.4)	199 (91.3)	0.805
	Yes	1422 (9.6)	19 (8.7)	

Financial situation up to age 18	Not poor	11695 (78.8)	157 (72.0)	0.018
	Poor	3155 (21.2)	61 (28.0)	
Abuse experience up to age 18	None	12456 (83.9)	150 (68.6)	<0.001
	Yes	2394 (16.1)	68 (31.2)	
frequency of eating alone	<1 time/week	5949 (40.1)	56 (25.7)	<0.001
	1-5 times/week	4683 (31.5)	85 (39.0)	
	6-7 times/week	4218 (28.4)	77 (35.3)	
Habitual use of sleeping pills/anxiolytics	No	13749 (92.6)	162 (74.3)	<0.001
	Past use	340 (2.3)	14 (6.4)	
	Current use	761 (5.1)	42 (19.3)	
Family social capital		14.6 ± 6.1	17.3 ± 6.9	<0.001
UCLA Loneliness Scale (3-item)		5.4 ± 2.6	7.7 ± 3.0	<0.001
Risk of social isolation	None	6322 (42.6)	60 (27.5)	<0.001
	Yes	8528 (57.4)	158 (72.5)	
CDC HRQOL-4	Good	14468 (97.4)	162 (83.5)	<0.001
	Poor	382 (2.6)	36 (16.5)	
Life satisfaction		7.4 ± 2.3	5.6 ± 2.8	<0.001

\*: Mean ± SD; †: n (%); ‡: Student's t-test; §: Chi-square test.

Table 4 shows the results of the multivariate binomial logistic regression analysis with these items as independent variables and with or without developed depression as the dependent variable. The items found to be associated with incident depression after adjusting for other items were: "OHIP-14: (odds ratio [OR]: 1.02, 95% confidence interval [CI]: 1.00–1.04, p=0.039)", "Age (OR: 0.97, 95%CI: 0.96–0.99, p<0.001)", "Participation in hobbies, learning, and cultural activities: Yes (OR: 2.22, 95%CI: 1.50–3.30, p<0.001)", "Habitual use of sleep or antianxiety medications: Ever (OR: 1.97, 95%CI: 1.06–3.68, p=0.033) and Currently (OR 3.51, 95%CI: 2.27–5.44, p<0.001)", "UCLA-LS3-SF-3 (OR: 1.22, 95%CI: 1.14–1.30, p<0.001)", "Life satisfaction (OR: 0.90, 95%CI: 0.84–0.97, p=0.005)", and "CDC HRQOL-4: Poor (OR: 2.92: 95%CI: 1.81–4.72, p<0.001)".

**Table 4.** Binomial logistic regression analysis with developed depression as dependent variable. Odds ratios (ORs) and 95% confidence intervals (CIs) for factors associated with the development of depression, adjusted for sociodemographic and behavioral covariates. OHIP = Oral Health Impact Profile; UCLA = University of California, Los Angeles; LSNS = Lubben Social Network Scale; CDC HRQOL-4 = Centers for Disease Control and Prevention Health-Related Quality of Life; Ref = Reference category.

Independent variable	Category	Odds Ratio	95% CI	p-value
OHIP-14 score	—	1.02	1.00-1.04	0.039
Dental visits within 1 year	Yes (Ref)	—		
	None	1.17	0.85-1.60	0.329
Age (years)	—	0.97	0.96-0.99	<0.001
Gender	Male (Ref)	—		
	Female	1.08	0.78-1.52	0.637
Annual income	>9 million yen (Ref)	—		
	6–9 million yen	0.64	0.38-1.10	0.106
	3–6 million yen	0.97	0.62-1.51	0.883
	<3 million yen	1.07	0.65-1.77	0.787
Smoking history	Never (Ref)	—		
	Past	1.28	0.83-1.96	0.268
	Current	1.28	0.86-1.92	0.221
Participation in hobbies, study, and culture-related activities	Nonparticipation (Ref)	—		
	Participation	2.22	1.50-3.30	<0.001

Walking $\geq$ 1 hour/day or equivalent physical activity	Yes (Ref)	—		
	No	0.96	0.69-1.32	0.783
Chatting/mingling with non-family members	None (Ref)	—		
	Yes	1.05	0.72-1.55	0.788
Financial situation up to age 18	Not poor (Ref)	—		
	Poor	0.97	0.67-1.41	0.864
Abuse experience up to age 18	None (Ref)	—		
	Yes	1.09	0.75-1.59	0.653
Frequency of eating alone	<1 time/week (Ref)	—		
	1–5 times/week	1.41	0.96-2.08	0.084
	6–7 times/week	0.87	0.56-1.34	0.518
Habitual use of sleeping pills/anxiolytics	No (Ref)	—		
	Past use	1.97	1.06-3.68	0.033
	Current use	3.51	2.27-5.44	<0.001
Family social capital	—	1.01	0.98-1.03	0.715
UCLA Loneliness Scale (3-item)	—	1.22	1.14-1.30	<0.001
Risk of social isolation	None (Ref)	—		
	Yes	1.17	0.81-1.68	0.408
CDC HRQOL-4	Good (Ref)	—		
	Poor	2.92	1.81-4.72	<0.001
Life satisfaction	—	0.90	0.84-0.97	0.005

OR = Odds Ratio; CI = Confidence Interval.

#### 4. Discussion

In this study, we investigated developed depression and associated factors among adults aged 20 years and older. The findings revealed that younger age, participation in hobbies, learning, and cultural activities, habitual use of sleeping pills and anxiolytics, lower scores on the UCLA-LS3-SF-3 (indicating feelings of loneliness), higher scores on the CDC HRQOL-4 (indicating poor self-rated health), lower life satisfaction scores (indicating low satisfaction), and higher scores on the OHIP-14 (indicating poor OHRQOL) were significantly associated with the development of depression. These results suggest that maintaining good OHRQOL may help prevent the development of depression.

In this study, a significant association was observed between OHRQOL and developed depression. The potential pathways from OHRQOL impairment to the onset of depressive symptoms may include the deterioration of social activities and psychosocial issues. Ohi et al. [26] investigated whether OHRQOL impairment at baseline was associated with the development of depressive symptoms 4 years later among participants without depressive symptoms by conducting a questionnaire survey on adults aged 55 years and older. They reported that baseline OHRQOL impairment was significantly associated with an increased risk of depressive symptoms, independent of potential confounding factors such as dental status and dental visits. Those findings suggest that a deterioration of social activities and psychosocial issues may be involved in the pathway from OHRQOL impairment to the development of depressive symptoms. In a cross-sectional study, Zhang et al. [65] reported that college students with inadequate OHRQOL are more likely to exhibit depressive symptoms. Their findings suggest that OHRQOL may influence the prevalence of depressive symptoms through a decrease in self-esteem and life satisfaction caused by barriers to interpersonal communication. These previous reports investigated the relationship between self-assessment depression scales and OHRQOL. By contrast, the present study, aiming to clarify the association with the development of depression more clearly, longitudinally examined the correlation between the presence or absence of a depression diagnosis and OHRQOL. In the present study, OHRQOL may also have influenced the development of depression through the deterioration

of social activities, psychosocial problems, impaired interpersonal communication, and decreased self-esteem and life satisfaction.

No significant association was found between missing teeth and the development of depression. Kusama et al. [66] conducted a 3-year longitudinal study involving participants with an average age of 72.7 years to investigate the relationship between tooth loss and depressive symptoms. They found that having 19 or fewer teeth significantly increased the risk of depressive symptoms by 1.3 times. This relationship was notably mediated by difficulties in speaking, smiling, and chewing. Ohi et al. [26] examined the association between depressive symptoms and the number of teeth among Japanese older individuals aged 55 years and older. While a cross-sectional study revealed a correlation, a 4-year longitudinal study did not. Chu et al. [28] reported a connection between the number of teeth and the onset of depression in a 20-year cohort study with an average participant age of 58.8 years. They considered the potential involvement of nutritional status and social participation in this relationship. This may be because the study period was short and the study population did not comprise only older adults.

In the present study, no significant association was found between periodontal disease screening and the development of depression. In an 11-year cohort study, Hsu et al. [67] found that periodontitis (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] 523.4x and 523.5x) was associated with the onset of depression (ICD-9-CM 296.2x, 296.3x, 300.4x, and 311.xx). They considered that periodontitis leads to the release of proinflammatory cytokines such as interleukin (IL)-1 $\beta$ , IL-6, and tumor necrosis factor into systemic circulation, and that psychological stress in patients with periodontitis promotes disturbances in the hypothalamic–pituitary–adrenal (HPA) axis and related hypercortisolism. This, in turn, affects immune dysfunction and neuroinflammation, potentially leading to the development of depression. In the present study, the lack of an association may be due to the use of questionnaire-based screening indicators rather than oral examinations for periodontal disease. Additionally, the short follow-up period of 1 year may have contributed to the absence of observed associations.

In a systematic review, Anita et al. [33] suggested a correlation between oral-facial pain (e.g., temporomandibular joint pain, stomatitis) and depression. It is noted that oral-facial pain activates the HPA axis, which is involved in the release of cortisol hormones in patients with depressive symptoms. In this study, only the presence or absence of pain related to caries and periodontal disease was investigated, and temporomandibular joint pain was not included, which may explain the lack of observed associations.

In this study, no significant association was observed between regular dental visits and the onset of depression. In a cross-sectional survey, Peltzer et al. [40] reported a correlation between depression and regular dental visits. Although they did not discuss the mechanisms, it is generally considered that lower socioeconomic status can lead to poorer oral health behaviors. It has also been suggested that university students with lower socioeconomic status may be less likely to attend regular dental check-ups because of their inability to afford dental treatment [68]. In the present study, a significant association was found between income and the presence of regular dental visits (not shown), but neither income nor the presence of regular dental visits was associated with the onset of depression.

This study was based on a large web-based survey of residents in 47 prefectures throughout Japan, which is a strength in ensuring high generalizability. Furthermore, the large sample size from the JACSIS is a strength of this study.

The incidence of depression in this study was 1.45%. Büchtemann et al. [69] reported in a systematic review of elderly individuals aged 70 and older that the incidence of major depression ranged from 1.7% to 7.6%. Although the definitions of depression and the age groups of the subjects differ, it cannot be conclusively stated that the incidence of depression in this population is low.

### *Limitations*

This study has several limitations. First, it relied entirely on self-reporting and was not an objective survey. As a result, the actual outcomes may have been either underestimated or

overestimated. Second, there are confounding factors that could not be surveyed. Genetic factors and stress resilience have not been investigated. Third, due to limitations regarding the statistical analysis, binary variables were used for exposure, mediators, and outcomes, which may have led to an overestimation or underestimation of the results. Fourth, because this study depended on an online survey, there is a possibility that the sample was overrepresented by individuals with high Internet literacy [70]. This may have led to selection bias; however, it has been confirmed that this population is not disproportionate compared with census data. In future research, objective measurements such as oral examinations and the use of medical records should be used in addition to self-reported evaluations.

## 5. Conclusion

In a longitudinal study of participants who had not been diagnosed with depression, we investigated whether OHRQOL and oral health status were associated with the development of depression. The results indicated that OHRQOL is associated with incident depression, even after adjusting for other related factors.

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data used in the present study are not deposited in a public repository due to containing personally identifiable or potentially sensitive information. In accordance with ethical guidelines in Japan, dissemination of the data is restricted by the Research Ethics Committee of the Osaka International Cancer Institute. Any inquiries regarding data use should be directed to Dr. Takahiro Tabuchi (tabuchitak@gmail.com). More details of data availability can be found on the JACSIS website (<https://jacsis-study.jp/howtouse/>).

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