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### **Title**

**Effect of lifestyle on 6-year periodontitis incidence or progression and tooth loss in older adults**

### **Running title**

Healthy lifestyle and oral diseases

**Key words:** aged; epidemiology; health behavior; life style; longitudinal studies; oral health; periodontal diseases; tooth loss

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The authors have no conflicts of interest to declare.

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### **Contributions**

Research concepts and study design: MI; data acquisition: MI, HO, TY, MS, KM, AY and HM; data analysis/interpretation: MI and WSB; statistical analysis: MI; supervision: TA and HM. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. MI takes responsibility for the fact that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

## **Clinical Relevance**

**Scientific rationale for the study:** Reduction of common, modifiable lifestyle risk factors is assumed to be effective for oral diseases, but their longitudinal combined effect on periodontitis and tooth loss remains unclear.

**Principal findings:** Significant linear decreases in the 6-year risk of incidence or progression of periodontitis and tooth loss was found in participants with the following four healthy baseline lifestyle factors: no smoking, good physical activity level, healthy body mass index, and high-quality diet.

**Practical implications:** Adherence to multiple healthy lifestyle factors may be effective in preventing periodontitis and tooth loss in older adults and should be encouraged.

## **Abstract**

**Aim:** To evaluate the longitudinal association of combined healthy lifestyle factors with incidence or progression of periodontitis and tooth loss in older adults.

**Materials and methods:** This 6-year study included 374 Japanese 70-year-olds with 7,157 teeth, from a source eligible baseline population of 554 individuals. Four lifestyle factors—cigarette smoking, physical activity, relative weight, and dietary quality—were scored as healthy (1 point) or unhealthy (0 point). Adding the individual scores generated the “healthy lifestyle score” (0–4 points). Multilevel mixed-effects logistic regression models were applied to evaluate tooth-specific associations between the baseline healthy lifestyle score and the incidence or progression of periodontitis (increase in clinical attachment loss  $\geq 3$  mm) and tooth loss.

**Results:** After 6 years, 19.0% of the teeth exhibited periodontitis incidence or progression and 8.2% were lost. Compared with a healthy lifestyle score of 0–1 (least healthy), the highest score (4 points) was associated with a significantly lower tooth-specific risk of periodontitis (adjusted odds ratio=0.32; 95% confidence interval: 0.16–0.62) and tooth loss (adjusted odds ratio=0.42; 95% confidence interval: 0.23–0.77).

**Conclusions:** Simultaneous adherence to multiple healthy lifestyle factors significantly lowers the risk of incidence or progression of periodontitis and tooth loss in older adults.

## Introduction

Even though tooth loss has decreased over the last several decades, both missing teeth (Kassebaum et al., 2014a, Kassebaum et al., 2014b) and periodontitis (Eke et al., 2015, Kassebaum et al., 2014a) remain common chronic conditions, particularly in older adults whose life expectancy increases and who keep their teeth longer (Eke et al., 2016). A national survey of dental disease conducted in 2011 in Japan showed that 57.3% of individuals aged  $\geq 70$  years exhibited periodontitis, defined as community periodontal index codes of 3 or 4, accompanied by a loss of 13.4 teeth on average (the Ministry of Health, Labour, and Welfare, 2011).

Oral disease, including periodontitis and tooth loss, is “*one of the most common public health issues worldwide*” (Jin et al., 2016) and poses significant health problems among older adults (Eke et al., 2016) that can have a major adverse impact on general health and quality of life (Griffin et al., 2012, Buset et al., 2016, Tan et al., 2016), as shown among older Japanese (Matsuyama et al., 2017). Furthermore, it has been suggested that poor oral health predicts declining function in older adults (Zhang et al., 2017) with tooth loss as a predictor of shortened longevity (Friedman and Lamster, 2016). Oral disease is also associated with increased healthcare costs among the elderly (Sato et al., 2016, Iwasaki et al., 2017). To decrease the burden of these oral diseases and establish more effective preventive strategies, it is necessary to investigate and understand the role of modifiable risk factors in detailed studies.

Previous studies have demonstrated that modifiable lifestyle factors such as cigarette smoking, physical inactivity, obesity/underweight, and an unhealthy diet are associated with various chronic systemic diseases (Ford et al., 2009, Sasazuki et al., 2012, Kirkegaard et al., 2010, Jiao et al., 2009), as well as periodontitis (Borgnakke,

2016). Health effects of these individual risk factors have been studied (Saito et al., 1998, Al-Zahrani et al., 2005a, Johnson and Hill, 2004, Moynihan and Petersen, 2004, Bawadi et al., 2011, Merchant et al., 2003, Jenzsch et al., 2009). However, despite the underlying assumption that the identification of modifiable risk factors can lead to intervention and ultimately improved health, their combined effects on oral health remain unclear. In particular, data from longitudinal studies are limited, which prevents assessment of causality.

Therefore, we designed a longitudinal study to explore the association between lifestyle, measured as the combination of four healthy lifestyle factors, and the development of new periodontitis or its progression and tooth loss risks in older adults. To achieve our aim, we scored study participants at baseline according to their simultaneous adherence to the following four healthy lifestyle factors that were selected based on previous research investigating the effects of healthy lifestyle factors on chronic disease risk (Ford et al., 2009): not smoking, engaging in good physical activity levels, having a healthy body mass index (BMI), and taking in a high-quality diet. We hypothesized that a higher combined healthy lifestyle score would be associated with a lower risk for incidence or progression of periodontitis as well as for tooth loss.

## **Materials and Methods**

### **Study design, setting, and participants**

Data for the current investigation were sourced from the Niigata Study, a community-based cohort study investigating factors that affect oral health in older individuals. Details regarding sampling and data collection procedures have been described previously (Hirotoomi et al., 2006). Briefly, a random sample of men and



women aged 70 years was drawn from a database of the citizens of Niigata City, Japan.

In total, 600 individuals (306 men and 294 women) were enrolled for baseline examinations conducted in 1998, which comprised dental and medical examinations, anthropometric evaluations, and responding to questionnaires. Follow-up dental examinations were conducted after 6 years.

Because the primary analyses were performed at the person- and tooth-level, exclusion criteria were based on both levels. Accordingly, participants were excluded from our analysis if they were edentulous at baseline or did not have complete data. Teeth were excluded from our analyses if data on their clinical attachment loss (CAL) could not be obtained at both time points.

All participants provided informed consent prior to enrolment, and the study was approved by the Ethics Committee of the Faculty of Dentistry, Niigata University (Approval number: 12-R1-4-21). The STROBE statement was applied for reporting.

#### Data collection

Using sufficient artificial illumination, four trained dentists assessed tooth status (sound, decayed, or filled), type (anterior or posterior), and position (maxillary or mandibular jaw) as well as probing depth and recession (for calculation of CAL) at six sites for all natural teeth. Furthermore, use of each tooth as an abutment for a dental bridge or a removable denture was recorded (World Health Organization, 1997).

Ten patients at the Niigata University Medical & Dental Hospital volunteered for pre-study calibration. Cohen's kappa statistic (exact and within 1 mm of CAL) was used to assess inter-examiner reliability for each pair of examiners, which ranged from 0.79 to 0.93.

Data regarding oral health behaviour, income, education, living situation, cigarette smoking status, physical activity levels, dietary habits, and medical conditions were obtained using a self-administered questionnaire. Fasting blood samples were collected for albumin assessment. Weight and height were measured with the participant wearing light clothing, but no shoes.

The oral examination was repeated six years later by the same dentists.

*Principal exposure variable: “healthy lifestyle score”*

We selected the four baseline lifestyle factors—cigarette smoking, physical activity, healthy BMI, and dietary quality—based on a priori knowledge of risk factors for periodontitis and tooth loss (Johnson and Hill, 2004, Saito et al., 1998, Moynihan and Petersen, 2004, Al-Zahrani et al., 2005a, Merchant et al., 2003, Borgnakke, 2016).

Using a self-administered questionnaire, participants provided information on smoking status and physical activity levels based on the average time spent per day performing three types of physical activity: heavy physical work or strenuous exercise, standing or walking, and sitting. The metabolic equivalent (MET)-hours/week was estimated by multiplying the time spent per week on each activity by the MET intensity level of that activity (Sasazuki et al., 2012). MET has been validated for use in physical activity assessments (Aadahl and Jorgensen, 2003). The Japanese Ministry of Health, Labour and Welfare recommends  $\geq 10$  MET-h/week of physical activity for individuals aged  $\geq 65$  years (the Ministry of Health, Labour, and Welfare, 2013). The BMI was computed by dividing the weight in kilograms by the squared height in meters. A global consensus is lacking regarding a lower, evidence-based BMI threshold to define being overweight among Japanese seniors due to suggested generational, genetic, metabolic,

ethnic, and environmental factors among Asians (2017, Kubota et al., 2015). Thus, we used the generally applied BMI cut-off value of  $25 \text{ kg/m}^2$  for overweight (World Health Organization, 2017). Based on the values reported by previous studies (Murayama et al. 2015, Nagai et al. 2010), a BMI cut-off value of  $18.5 \text{ kg/m}^2$  was used for underweight. Dietary quality was measured with the dietary variety score (DVS) (Kumagai et al., 2003) previously used in epidemiological studies among older adults (Kwon et al., 2006). Participants completed a food frequency questionnaire covering the 10 main food groups: meat, fish and shellfish, eggs, milk, soybean products, potatoes, green/yellow vegetables, fruits, seaweed, and fat and oils. For each food group, a score of 1 was assigned if consumed daily or 0 if not consumed daily. Adding the scores for each food group, the total score ranged from 0 to 10, with higher scores indicating greater dietary variety.

Each participant was allocated 1 point for being a non-smoker (never smoked or quit smoking) (Kirkegaard et al., 2010), 1 point for a good physical activity level ( $\geq 10$  MET-h/week) (the Ministry of Health, Labour, and Welfare, 2013), 1 point for a healthy BMI ( $18.5\text{--}25 \text{ kg/m}^2$ ) (the Ministry of Health, Labour, and Welfare, 2012), and 1 point for a diverse, high-quality diet (greater than the group median DVS of 6). Scores of 0 were assigned for these factors if the participants did not meet the above specifications (Table 1).

The principal exposure variable —“healthy lifestyle score”— was generated by adding the points for each of the four factors and hence ranged from 0 (least healthy) to 4 (most healthy). Participants were categorized into four groups according to their healthy lifestyle score of 0–1, 2, 3, and 4. Combining participants with scores of 0 and 1 into the same group was performed to achieved sufficient numbers of participants in

each group.

#### Outcome variables

The primary outcome variable was defined as tooth-specific progression of CAL ( $\geq 1$  site exhibiting a  $\geq 3$  mm increase in CAL) at 6 years after baseline (Zhan et al. 2014, Hirotsuki et al. 2010). We have considered this variable to include a) “periodontitis incidence,” that is, development of periodontitis involving a tooth without any sites qualifying for a periodontitis case definition (CAL  $\geq 3$  mm) at baseline, but with  $\geq 1$  sites with CAL  $\geq 3$  mm at follow-up, as well as b) “periodontitis progression,” which indicates a tooth that already had  $\geq 1$  site with CAL  $\geq 3$  mm at baseline and exhibited an additional increase in CAL of  $\geq 3$  mm at follow-up. We combined both into one main outcome variable, “tooth-specific incidence or progression of periodontitis.” The secondary outcome was tooth-specific incidence of tooth loss.

#### Covariates

The description of covariates is included in the online Supplementary Material.

#### Statistical analyses

Baseline tooth- and person-based factors were compared among the different groups based on the healthy lifestyle score using analysis of variance, Kruskal–Wallis tests, or Chi-square tests, as appropriate. Associations among the four healthy lifestyle factors were studied using the Chi-square test.

Multilevel mixed-effects logistic regression models were used to calculate (sex-combined and sex-stratified) odds ratios (ORs) for the tooth-specific incidence or

progression of periodontitis and tooth loss. Because our analyses were performed at the tooth level (the tooth was the unit of analysis), multilevel models were used to account for correlations between teeth in the same participant. First, we evaluated the association between individual healthy lifestyle factors and the tooth-specific risk of periodontitis incidence or progression and tooth loss, respectively. Second, we evaluated the same risk by comparing the combined healthy lifestyle scores to the least healthy group (score 0–1). A p-value for the linear trend was further calculated using the model in which the healthy lifestyle score was included as a continuous variable. The multivariable models were adjusted for tooth-based (tooth status, tooth type, tooth location, use as an abutment, and greatest CAL) and person-based (sex [in sex-combined model], regular dental check-ups, brushing frequency, use of interdental cleaning devices, income, education level, living situation, hypoalbuminemia, and high fasting blood glucose level) factors.

Inverse probability weighting (IPW) was used to adjust for selection bias due to the loss to follow-up (Hernan et al. 2004). Weights were calculated using baseline characteristics; number of teeth, sex, use of regular dental care, annual household income, years of school education, and smoking status.

All statistical analyses were performed using commercially available software (STATA version 14.2; StataCorp., College Station, TX). All p-values were calculated using two-tailed tests with  $p < 0.05$  considered statistically significant.

## **Results**

At baseline, 45 individuals (44 edentulous and 1 with incomplete data) from the 600 participants in the original Niigata study population were excluded, leaving 554 eligible

participants, of whom 180 were lost to follow-up over a period of 6 years. Subsequently, our final cohort comprised 374 individuals with 7,157 teeth. Of these, 6,443 teeth were available for risk analyses of the tooth-specific periodontitis incidence or progression. At the follow-up examination, 587 (8.2%) of the 7,157 teeth were lost. Additionally, incidence or progression of periodontitis was observed to involve 19.0% (1,226/6,443) of the teeth. The process of selection of the respondents is described in detail in the online Supplementary Material.

Among the 374 study participants, 306 (81.8%) were non-smokers, 289 (77.3%) were physically active, 265 (70.9%) maintained a healthy BMI, and 165 (44.1%) had a high-quality diet intake at baseline (Table 1).

Table 2 shows the baseline characteristics of the study population and their teeth according to the baseline healthy lifestyle score. The median number of teeth in the entire cohort was 22 (interquartile range, 13–26), and 201 (53.7%) of the participants were men. The baseline healthy lifestyle score was 0–1 for 41 (11.0%) participants, 2 for 94 (25.1%), 3 for 151 (40.4%), and 4 for 88 (23.5%).

Participants with a lower baseline healthy lifestyle score were more likely to be men, had a greater mean CAL, and were less likely to visit dentists for regular check-ups. On the contrary, none of the tooth-based factors were found to associate with healthy lifestyle scores.

Physically active individuals tended to be non-smokers and had diverse, high-quality diets (Appendix Table 2).

Associations of baseline person-based and tooth-based factors with the risk of periodontitis and tooth loss are presented in Table 3. Among person-based factors, male sex was associated with significantly higher odds for periodontitis

incidence/progression, while regular dental check-ups, tooth brushing  $\geq 2$  times daily, and the use of interdental cleaning devices were associated with significantly lower odds for tooth loss. Among tooth-based factors, filled teeth, posterior teeth, maxillary teeth, abutment teeth, and a higher CAL were all associated with significantly higher odds for periodontitis incidence/progression. Decayed, filled, posterior, maxillary, and abutment teeth, as well as a higher CAL were associated with significantly higher odds for tooth loss.

The effects of individual healthy lifestyle factors on the risk of periodontitis incidence or progression and tooth loss are presented in Table 4. After applying IPW and adjusting for confounding variables, no smoking was associated with significantly lower odds for periodontitis incidence/progression (adjusted OR [aOR]=0.54; 95% confidence interval [CI]: 0.33–0.89).

The table in Figure 1 displays the risks for tooth-specific periodontitis incidence or progression and tooth loss, respectively, in relation to the baseline combined healthy lifestyle score. The aORs are additionally visualized as a forest plot. Compared to the reference group with the least healthy lifestyle (scores 0–1), the aORs for tooth-specific periodontitis incidence or progression were 0.75 (95% CI: 0.38–1.52), 0.56 (95% CI: 0.27–1.14), and 0.32 (95% CI: 0.16–0.62) for participants with baseline healthy lifestyle scores of 2, 3, and 4, respectively, with a significant trend ( $p < 0.01$ ). The corresponding values for the tooth-specific tooth loss were 0.73 (95% CI: 0.41–1.31), 0.49 (95% CI: 0.28–0.86), and 0.42 (95% CI: 0.23–0.77), respectively, with a significant trend ( $p < 0.01$ ). Results of sex-stratified analyses were similar to those for both sexes combined (Appendix Table 3).

## Discussion

In this longitudinal study among community-dwelling older adults, we investigated the combined effects of healthy lifestyle factors on the risk of oral diseases, specifically development of new periodontitis or progression of existing periodontitis and tooth loss. Compared with the least healthy lifestyle (scores 0–1) at baseline, the healthiest lifestyle (score 4) was significantly associated with a lower risk of incidence or progression of periodontitis and tooth loss over 6 years. There was also a significant linear trend between increasingly healthier lifestyle scores and decreased odds for periodontitis incidence or progression as well as for tooth loss.

Our findings are in agreement with previous findings from the cross-sectional study of 12,110 US adults participating in the third National Health and Nutrition Examination Survey that reported participants engaging in a combination of three health-enhancing behaviours (healthy BMI, good physical activity levels, and a high-quality diet) had a lower prevalence of periodontitis compared to those who did not (Al-Zahrani et al., 2005b).

A unique strength of the current study is the longitudinal design. To our knowledge, this is the first study to examine the temporal association between four simultaneous healthy lifestyle factors and the risk of periodontitis incidence or progression and tooth loss in older adults.

Another distinction is our adjustment of the multilevel analyses for tooth-based factors. Both person-based and tooth-based factors were significantly associated with risks of oral disease incidence. Our findings that periodontitis incidence or progression occurs significantly more often among molars and in the maxilla agree with a recent study (Teles et al., 2017). The longitudinal association between the combined healthy



lifestyle score and the risk of incidence or progression of periodontitis and tooth loss remained significant after adjusting for these person-based and tooth-based factors.

The observed association between an overall healthy lifestyle, measured by the combined 4 factors, and oral diseases appears biologically plausible. The underlying mechanisms likely involve multiple pathways, including those of inflammation and immune function. Each healthy lifestyle factor investigated in the current study is believed to play a role in the amelioration of inflammation (Sotos-Prieto et al., 2016, Ertek and Cicero, 2012) and the maintenance of immune function (Kohut and Senchina, 2004, Milner and Beck, 2012, Wardwell et al., 2008, Sopori and Kozak, 1998).

Inflammation and immune function have been suggested to play a key role in the pathogenesis of periodontal disease (Cekici et al., 2014). Overall, a healthy lifestyle can prevent periodontitis by reducing inflammation and maintaining healthy immune function. Second, a healthy lifestyle can minimize the risk of physical disability (Jacob et al., 2016), a risk factor for oral disease (Avlund et al., 2001, Jette et al., 1993, Hatipoglu et al., 2016). Compared with participants with a higher healthy lifestyle score, those with lower scores were less likely to visit the dentist for regular check-ups. A non-significant trend was also observed between the healthy lifestyle score and interdental cleaning habits ( $p=0.09$ ). These findings suggest an association between a healthy lifestyle and oral health behaviour, as indicated previously (Sakki et al., 1998). However, the observed association between combined healthy lifestyle factors and oral diseases was independent of oral health behaviour. This suggests that a healthy lifestyle involves positive effects other than good oral health behaviour, which may promote reduced inflammation and maintain healthy immune function as discussed above.

A study investigating causes of tooth extractions in Japan revealed that periodontitis

was the leading cause among individuals aged  $\geq 65$  years (Aida et al., 2006). A healthy lifestyle may contribute to a decreased risk of tooth loss by lessening the risk of periodontitis. Unfortunately, a limitation of our study is the unavailability of the reason for tooth loss.

Several other study limitations should be acknowledged. First, lifestyle factors other than BMI were self-reported. We confirmed that no study participant was diagnosed with dementia. Nonetheless, the healthy lifestyle score used in this study was subject to recall bias and misclassification. Second, only baseline information was available for generating the healthy lifestyle score and we therefore could not take into account subsequent lifestyle changes. Similarly, only information on smoking habits at baseline was collected, and thus, past smoking habits were not taken into account. Third, because the present study population only included Japanese adults aged 70 years at baseline, the results may not be generalizable to other populations. Fourth, the healthy lifestyle score used in this study did not include all possible lifestyle factors. Although each factor has been studied in terms of its association with oral diseases (Saito et al., 1998, Al-Zahrani et al., 2005a, Johnson and Hill, 2004, Moynihan and Petersen, 2004, Bawadi et al., 2011, Merchant et al., 2003, Jenzsch et al., 2009), other factors such as alcohol consumption (Tezal et al., 2001) and sleep duration (Romandini et al., 2017) are also possibly associated with disease risk. Furthermore, the healthy lifestyle factors investigated in this study can be measured and scored in multiple different ways. For example, quality of diet can be measured in terms of total calories or by sugar consumption. Overnutrition is associated with chronic inflammation (Lionetti et al., 2009), which can contribute to periodontitis. With regard to the risk of tooth loss, excessive sugar consumption can have significant effects as an essential risk factor for

caries (Bernabe et al., 2016), the second leading cause of tooth extraction among older adults in Japan (Aida et al., 2006). However, we were unable to obtain information regarding individual nutrients, nor were we able to assess the caries status at baseline or caries incidence during the study. Finally, even though our analyses were adjusted for various potential confounding variables evaluated, residual confounding due to unmeasured variables, such as history of cigarette smoking and depression, or due to unexpected confounding, may exist. Our findings should therefore be verified in future studies that include collection of such data and be conducted in other geographic areas and age groups.

Within its limitations, our study demonstrates that a healthy lifestyle—defined as simultaneous adherence to the four healthy lifestyle factors: not smoking, a good physical activity level, a healthy BMI, and a high-quality diet—is associated with a lower risk of incidence or progression of periodontitis, and tooth loss over 6 years in elderly Japanese men and women. These findings validate the general expectations of positive effects of modifying risk factors for periodontitis and tooth loss. To prevent oral diseases and promote oral health in older adults, the public health community, clinicians, and other stakeholders should place more emphasis on comprehensive approaches to enhance simultaneous adherence to multiple healthy lifestyle components for the benefit of both oral and general health – and ultimately to enhance quality of life.

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**Table 1.** Distribution of healthy lifestyle scores at baseline for Japanese participants aged 70 years (N=374)

Healthy Lifestyle Score	Number (%) Participants
Smoking	
0 (current smoker)	68 (18.2)
1 (non-smoker)	306 (81.8)
Physical activity	
0 (<10 MET-h/week)	85 (22.7)
1 ( $\geq$ 10 MET-h/week)	289 (77.3)
BMI	
0 (<18.5 or $\geq$ 25 kg/m <sup>2</sup> )	109 (29.1)
1 (18.5–25 kg/m <sup>2</sup> )	265 (70.9)
Diet	
0 ( $\leq$ 6 [group median for DVS])	209 (55.9)
1 (>6 [group median for DVS])	165 (44.1)

BMI, body mass index; DVS, dietary variety score; MET, metabolic equivalent

**Table 2.** Baseline characteristics of the study population (N=374) and their teeth (N=7,157) by baseline healthy lifestyle score

	Total	Healthy Lifestyle Score				p <sup>*</sup>
		0–1	2	3	4	
Person-based factors	N=374 100%	n=41 11.0%	n=94 25.1%	n=151 40.4%	n=88 23.5%	
Number of teeth, median (IQR)	22 (13–26)	19 (8–26)	20 (12–25)	23 (12–26)	23 (15–27)	0.15
Denture use, n (%)	200 (53.5)	21 (51.2)	53 (56.4)	77 (51.0)	49 (55.7)	0.81
Mean CAL (mm), median (IQR)	2.9 (2.3–3.5)	3.2 (2.9–4.0)	3.2 (2.5–3.7)	2.6 (2.2–3.3)	2.8 (2.3–3.3)	<0.01
Men, n (%)	201 (53.7)	34 (82.9)	63 (67.0)	67 (44.4)	37 (42.1)	<0.01
Regular dental check-ups $\geq$ 1/year, n (%)	76 (20.3)	2 (4.9)	15 (16.0)	36 (23.8)	23 (26.1)	0.02
Tooth brushing frequency, $\geq$ 2 times/day, n (%)	255 (68.2)	25 (61.0)	60 (63.8)	102 (67.6)	68 (77.3)	0.16
Use of devices for interdental cleaning, n (%)	137 (36.6)	8 (19.5)	34 (36.2)	58 (38.4)	37 (42.1)	0.09
Annual household income, <2,000,000 JPY, n (%)	49 (13.1)	5 (12.2)	13 (13.8)	22 (14.6)	9 (10.2)	0.80
Years of education, $\leq$ 9 years, n (%)	156 (41.7)	21 (51.2)	40 (42.6)	62 (41.1)	33 (37.5)	0.53
Living alone, n (%)	33 (8.8)	4 (9.8)	8 (8.5)	12 (8.0)	9 (10.2)	0.94
Hypoalbuminemia, n (%)	24 (6.4)	3 (7.3)	10 (10.6)	7 (4.6)	4 (4.6)	0.25
High fasting blood glucose level, n (%)	51 (13.6)	4 (9.8)	14 (14.9)	19 (12.6)	14 (15.9)	0.76

Tooth-based factors	N=7,157 100%	n=697 9.7%	n=1,701 23.8%	n=2,965 41.4%	n=1,794 25.1%	
<b>Tooth status, n (%)</b>						
Sound	3,320 (46.4)	324 (46.5)	786 (46.2)	1,389 (46.9)	821 (45.8)	0.11
Filled	3,729 (52.1)	362 (51.9)	876 (51.5)	1,540 (51.9)	951 (53.0)	
Decayed	108 (1.5)	11 (1.6)	39 (2.3)	36 (1.2)	22 (1.2)	
<b>Tooth type, n (%)</b>						
Anterior	3,407 (47.6)	335 (48.1)	897 (52.7)	1,423 (48.0)	845 (47.1)	0.92
Posterior	3,750 (52.4)	362 (51.9)	804 (47.3)	1,542 (52.0)	949 (52.9)	
<b>Jaw, n (%)</b>						
Maxilla	3,389 (47.4)	319 (45.8)	778 (45.7)	1,419 (47.9)	873 (48.7)	0.26
Mandible	3,768 (52.6)	378 (54.2)	923 (54.3)	1,546 (52.1)	921 (51.3)	
<b>Used as an abutment, n (%)</b>						
For fixed bridge	790 (11.0)	69 (9.9)	174 (10.2)	359 (12.1)	188 (10.5)	0.11
For a removable denture	658 (9.2)	67 (9.6)	173 (10.2)	255 (8.6)	163 (9.1)	0.34
Highest CAL (mm), median (IQR)	4 (3–4)	4 (3–4)	4 (3–4)	4 (3–4)	4 (3–4)	0.09

CAL, clinical attachment loss; IQR, interquartile range; JPY, Japanese Yen

\*p-value for comparisons among groups

**Table 3.** Risk of periodontitis incidence or progression and tooth loss by baseline person-based and tooth-based factors

Predictors	OR (95% CI) <sup>†</sup>	
	Tooth-specific periodontitis incidence/ progression (N=6,443 teeth)	Tooth-specific tooth loss (N=7,157 teeth)
<b>Person-based factors</b>		
Male sex (versus female sex)	<b>1.97 (1.38–2.81)</b>	1.42 (0.94–2.15)
Regular dental check-ups $\geq 1$ /year*	0.67 (0.45–1.01)	<b>0.47 (0.28–0.79)</b>
Brushing frequency $\geq 2$ times/day*	0.69 (0.47–1.02)	<b>0.64 (0.41–0.99)</b>
Use of devices for interdental cleaning*	0.75 (0.52–1.07)	<b>0.48 (0.31–0.74)</b>
Annual household income <2,000,000 JPY*	0.70 (0.43–1.13)	1.13 (0.66–1.93)
Years of school education $\leq 9$ years*	1.10 (0.76–1.58)	1.15 (0.77–1.74)
Living alone*	0.61 (0.36–1.04)	1.40 (0.78–2.51)
Hypoalbuminemia*	1.64 (0.75–3.59)	1.21 (0.47–3.11)
High fasting blood glucose level*	1.83 (0.87–3.84)	1.49 (0.83–2.67)
<b>Tooth-based factors</b>		
Tooth status (versus sound)		
Decayed	1.78 (0.99–3.18)	<b>7.50 (3.96–14.19)</b>
Filled	<b>1.83 (1.54–2.18)</b>	<b>4.75 (3.49–6.46)</b>
Tooth type (versus anterior)		
Posterior	<b>1.36 (1.15–1.59)</b>	<b>2.47 (1.88–3.24)</b>
Tooth position (versus mandible)		
Maxilla	<b>1.72 (1.40–2.12)</b>	<b>1.37 (1.04–1.81)</b>
Use as an abutment		
For fixed bridge*	<b>1.61 (1.24–2.10)</b>	<b>1.84 (1.26–2.67)</b>
For removable denture*	<b>1.93 (1.43–2.60)</b>	<b>4.53 (3.26–6.29)</b>
Greatest CAL (per 1 mm increase)	<b>1.15 (1.08–1.24)</b>	<b>1.71 (1.58–1.85)</b>

\*Versus no/not.

CAL, clinical attachment loss; CI, confidence interval; JPY, Japanese Yen; OR, odds ratio



†Applying inverse probability weighting

**Bold** text highlights statistically significant findings ( $p < 0.05$ ).

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**Table 4.** Risk of periodontitis incidence or progression and tooth loss by the 4 baseline individual healthy lifestyle factors

	Tooth-specific periodontitis incidence/progression (N=6,443 teeth)		
	Number (%) of events	Model 1 <sup>†</sup> OR (95% CI)	Model 2 <sup>‡</sup> OR (95% CI)
<b>Smoking</b>			
0 (current smoker)	342 (31.8)	1	1
1 (non-smoker)	884 (16.5)	<b>0.46 (0.29–0.76)</b>	<b>0.54 (0.33–0.89)</b>
<b>Physical activity</b>			
0 (<10 MET-h/week)	334 (26.6)	1	1
1 (≥10 MET-h/week)	892 (17.2)	<b>0.61 (0.39–0.95)</b>	0.68 (0.43–1.08)
<b>BMI</b>			
0 (<18.5 or ≥25 kg/m <sup>2</sup> )	382 (20.6)	1	1
1 (18.5–25 kg/m <sup>2</sup> )	844 (18.4)	0.83 (0.57–1.20)	0.91 (0.63–1.31)
<b>Diet</b>			
0 (≤6 [group median for DVS])	669 (19.5)	1	1
1 (>6 [group median for DVS])	557 (18.5)	0.94 (0.66–1.33)	0.90 (0.64–1.27)
<b>Tooth-specific tooth loss (N=7,157 teeth)</b>			
	Number (%) of events	Model 1 <sup>†</sup> OR (95% CI)	Model 2 <sup>‡</sup> OR (95% CI)
<b>Smoking</b>			
0 (current smoker)	145 (11.7)	1	1
1 (non-smoker)	442 (7.5)	<b>0.53 (0.31–0.90)</b>	0.68 (0.43–1.07)
<b>Physical activity</b>			
0 (<10 MET-h/week)	166 (11.3)	1	1
1 (≥10 MET-h/week)	421 (7.4)	0.65 (0.39–1.08)	0.80 (0.52–1.23)
<b>BMI</b>			
0 (<18.5 or ≥ 25 kg/m <sup>2</sup> )	181 (8.7)	1	1
1 (18.5–25 kg/m <sup>2</sup> )	406 (8.0)	0.84 (0.55–1.30)	0.82 (0.56–1.18)
<b>Diet</b>			
0 (≤6 [group median for DVS])	350 (9.1)	1	1

1 (>6 [group median for DVS])      237 (7.2)      0.67 (0.45–1.00)      0.80 (0.57–1.13)

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BMI, body mass index; CI, confidence interval; DVS, dietary variety score; MET, metabolic equivalent; OR, odds ratio

**Bold** text highlights statistically significant findings ( $p < 0.05$ ).

<sup>†</sup>Model 1: Applying inverse probability weighting and adjusting for all listed healthy lifestyle factors.

<sup>\*</sup>Model 2: Additionally adjusting for tooth status, tooth type, tooth location, abutment tooth, highest clinical attachment loss, sex, use of regular dental care, brushing frequency, use of devices for interdental cleaning, annual household income, years of school education, living situation, hypoalbuminemia, and high fasting blood glucose level.

## Figure legend

**Figure 1.** Risk of periodontitis incidence or progression (A) and tooth loss (B) over 6 years by baseline combined healthy lifestyle score for Japanese participants who were aged 70 years at baseline (N = 374).

The healthy lifestyle score showed a significant linear relation with the odds for the tooth-specific incidence or progression of periodontitis and tooth loss. The adjusted odds ratios for the tooth-specific incidence or progression of periodontitis were 1 (reference), 0.75 (95% confidence interval [CI]: 0.38–1.52), 0.56 (95% CI: 0.27–1.14), and 0.32 (95% CI: 0.16–0.62) for individuals with a baseline healthy lifestyle score of 0–1, 2, 3, and 4, respectively ( $p_{\text{trend}} < 0.01$ ). The adjusted ORs for the tooth-specific incidence of tooth loss were 1 (reference), 0.73 (95% CI: 0.41–1.31), 0.49 (95% CI: 0.28–0.86), and 0.42 (95% CI: 0.23–0.77) for individuals with a baseline healthy lifestyle score of 0–1, 2, 3, and 4, respectively ( $p_{\text{trend}} < 0.01$ ).

**Figure 1. Risk of periodontitis incidence or progression (A) and tooth loss (B) over 6 years by baseline combined healthy lifestyle score\* for Japanese participants who were aged 70 years at baseline (N = 374)**

(A)	Tooth-specific periodontitis incidence/progression (N = 6,443 teeth)		
	Number (%) of events	Model 1 <sup>†</sup> ORs (95% CI)	Model 2 <sup>‡</sup> ORs (95% CI)
Healthy lifestyle score			
0-1	163 (27.7)	1	1
2	402 (27.0)	0.80 (0.40-1.60)	0.75 (0.38-1.52)
3	468 (17.2)	<b>0.53 (0.26-1.10)</b>	0.56 (0.27-1.14)
4	193 (11.7)	<b>0.30 (0.15-0.59)</b>	<b>0.32 (0.16-0.62)</b>
<i>P</i> <sub>trend</sub> <sup>§</sup>		<0.01	<0.01

(B)	Tooth-specific tooth loss (N = 7,157 teeth)		
	Number (%) of events	Model 1 <sup>†</sup> ORs (95% CI)	Model 2 <sup>‡</sup> ORs (95% CI)
Healthy lifestyle score			
0-1	90 (12.9)	1	1
2	184 (10.8)	0.76 (0.38-1.51)	0.73 (0.41-1.31)
3	204 (6.9)	<b>0.33 (0.17-0.63)</b>	<b>0.49 (0.28-0.86)</b>
4	109 (6.1)	<b>0.31 (0.15-0.61)</b>	<b>0.42 (0.23-0.77)</b>
<i>P</i> <sub>trend</sub> <sup>§</sup>		<0.01	<0.01

**Bold text highlights statistically significant findings (*P* < 0.05).**

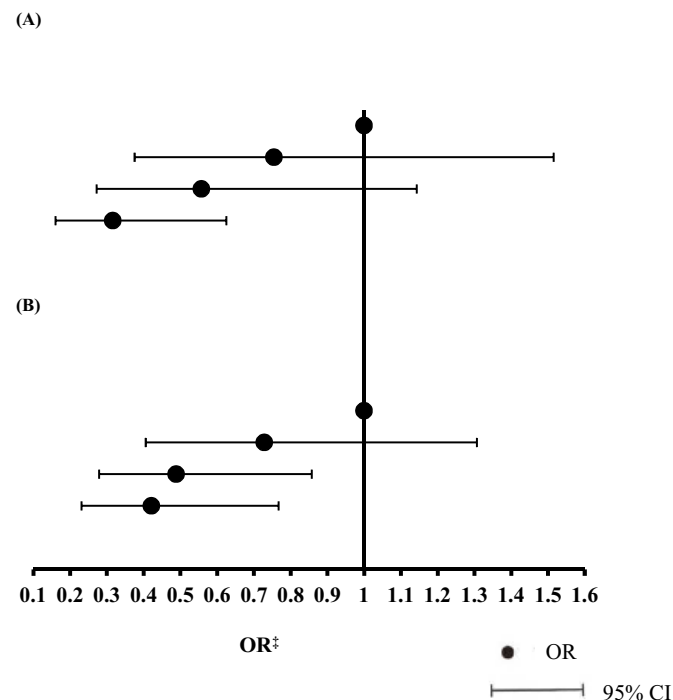
CI, confidence interval; OR, odds ratio

\*Four lifestyle factors (cigarette smoking, physical activity, relative weight, and dietary quality) were allocated a score of healthy (1 point) or unhealthy (0 points). The healthy lifestyle score (0-4 points) was generated by adding the individual scores for the four factors.

<sup>†</sup>Applying inverse probability weighting.

<sup>‡</sup>Applying inverse probability weighting and adjusting for tooth status, tooth type, tooth location, abutment tooth, highest clinical attachment loss, sex, use of regular dental care, brushing frequency, use of devices for interdental cleaning, annual household income, years of school education, living situation, hypoalbuminemia, and high fasting blood glucose level.

<sup>§</sup>*P*-values for a linear trend



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