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Comparison of the periodontal condition in Korean and Japanese adults

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Keywords: Periodontitis, diabetes mellitus, metabolic syndrome

Abstract

Objectives The reports of national survey in South Korea and Japan indicated that the prevalence of periodontal disease was lower in Korea than in Japan. However, it has not been described in relation to factors related to periodontal health condition including diabetes and metabolic syndrome. This study compared the periodontal condition in Korean and Japanese adults, with reference to general health status.

Design Cross-sectional study

Setting National survey in South Korea (Korean National Health and Nutrition Examination Survey "KNHANES") and the population-based studies in Japan (Hisayama study) in 2012 Participants This study included 3,574 Korean and 2,205 Japanese adults aged 40-79 years. Outcome measures Periodontal condition was assessed using the Community Periodontal Index (CPI). The examiners in Japan underwent clinical calibration training for periodontal examination with a gold standard examiner from KNHANES, prior to the Hisayama study. Results: Age-adjusted prevalence of periodontal disease defined by CPI score ≥3 was 31.4% and 42.1% in South Korea and Japan, respectively. Age-adjusted prevalence of diabetes and metabolic syndrome was higher in Korea than in Japan. Logistic regression analysis showed that Japanese participants were more likely to have periodontal disease than Korean participants, after adjusting for age, sex, occupation, oral health status, oral health behavior, diabetes, and metabolic syndrome.

Conclusions: Higher prevalence of periodontal disease was found in Japanese than in Koreans, even after adjusting for potential risk factors including diabetes and metabolic syndrome. These findings suggest that the differences of dental health care system and dietary intake between two populations may have essential implications for periodontal disease.

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Article Summary

Strengths and limitations of this study

This study demonstrates the differences in prevalence of periodontal disease between

Koreans and Japanese, after adjustment for systemic condition.

- This study included a large representative population in Korea based on national survey and a community-based population in Japan.
 - We performed clinical calibration training for periodontal examination with a gold •

standard examiner in Korean survey and the examiners in Japanese survey.

The differences in periodontal conditions between Koreans and Japanese may be affected

by unmeasured factors.

Introduction

According to the World Health Organization (WHO) Global Oral Health Data Bank,¹ the prevalence of periodontal disease, as defined by the Community Periodontal Index (CPI) code \geq 3, was 4–37% in 35–44 year olds, and 20–52% in 65–74 year olds, in the Asian countries (including the least developed to the highly industrialized) that conducted the national survey. The general health conditions and the health care systems vary widely between the different countries in Asia, depending on the level of economic development. Similarly, oral health conditions and oral health care systems in this region have wide differences.² The difference in socioeconomic status might be the cause of inequalities in oral health among Asian countries.

On the other hand, the results of national surveys in Korea and Japan indicate that the prevalence of periodontal disease is lower in Korea (32.9% and 23.9% of individuals aged 19 and over in 2008 and 2010, respectively),³ than in Japan (44.7% and 41.5% of individuals aged 19 and over in 2005 and 2011, respectively).⁴ Among the Asian countries, South Korea (hereafter 'Korea') and Japan are closely located, and have similar economic and ethnic backgrounds. The gross domestic product per capita in 2016 was \$27,534 in Korea and \$38,895 in Japan.⁵ The Korean and Japanese population belong basically to the northern Mongoloid group, and Koreans are genetically closer to the Japanese than other Mongoloid groups.⁶

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With regard to health care systems, the governments of both Korea and Japan provide national health insurance that covers the entire population. In Korea, dental treatment covered by health insurance is limited, although, in recent years, dental insurance coverage has expanded, and denture treatment in individuals aged 65 and over (from 2016) and periodontal scaling (from 2013) are covered.⁷ However, in Japan, the health insurance covers almost all dental treatments, such as treatment for dental caries, including endodontic treatment; periodontal disease; prosthetic treatment; and extraction. Periodontal treatment has been covered by health insurance since 1972. The size of the dental workforce is larger in Japan than in Korea; the population ratio of dentists was 5.0 and 7.4 per 10,000 people in Korea and Japan, respectively.⁸ Additionally, the population ratio of practicing dental hygienists was 4.9 and 8.5 per 10,000 people in Korean and Japan, respectively.⁹ It would seem that the Japanese have a better likelihood of receiving periodontal treatment and preventing periodontal disease than Koreans, considering the greater dental insurance coverage and the higher number of dental hygienists. The difference in health care systems between Korean and Japan contradicts to that in periodontal health condition between two countries.

However, great significance cannot be attached to the reports of the national survey, as the potential risk factors related to periodontal disease are not taken into consideration. Growing evidence from epidemiological studies indicates that diabetes and metabolic syndrome are associated with periodontal disease.^{10 11} While comparing periodontal disease

among different countries, the effect of systemic health on periodontal disease and other risk factors should be addressed. It is considered that a comparison of geographical and racial differences in periodontal disease, and interpreting the reasons for these differences, are essential steps for preventing periodontal disease. The objective of this study was to compare the periodontal condition of Korean and Japanese adults, in relation to the effects of diabetes and metabolic syndrome.

Methods

Study population

The present study used data for Koreans from a subset of the Fifth Korean National Health and Nutrition Examination Survey (KNHANES), a nationwide cross-sectional survey conducted in 2012 by the Korea Center for Disease Control and Prevention. Participants were selected using a multi-stage clustered probability design to produce a nationally representative non-institutionalized civilian sample. All participants provided written informed consent. Additional information about the KNHANES can be found elsewhere.¹² This study included 3,955 participants from the 2012 survey, aged 40–79 years, who received medical and dental examinations in addition to a health interview. After excluding participants with missing data, 3,574 participants were included in the analysis.

Data for Japanese was obtained from the Hisayama study, a population-based

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prospective study of cerebro-cardiovascular diseases, in the town of Hisayama, which is a suburban rural area of Fukuoka city in southern Japan. The age and occupational distributions of the population of this town are similar to those of Japan as a whole.¹³ As part of the Hisayama study, dental examinations were conducted for residents aged 40 and over, in 2012. This study included 2,342 participants, aged 40-79 years who received both medical and dental examinations in 2012 (57.8% of the total population in this age group). Written informed consent was obtained from all participants. After excluding the participants with missing data, 2,205 participants were analyzed in this study.

The study was approved by the Kyushu University Institutional Review Board for CL.C Clinical Research (24-129).

Assessment of periodontal condition and dental caries

Periodontal condition was assessed using the CPI in the KNHANES and Hisayama studies. As per World Health Organization protocols, ten teeth were selected for the periodontal examination: two molars in each posterior sextant, and the upper right and lower left central incisors. If no index tooth was present in a qualified sextant, all the remaining teeth in that sextant were examined. The highest code among the examined sextants was recorded, to represent the CPI status for each individual. Periodontal disease was defined as CPI code ≥ 3 (periodontal pocket depth ≥ 4 mm).

Trained and calibrated dentists assessed the periodontal conditions in the KNHANES and Hisayama studies. To ensure reliability of measurements using CPI, seven examiners in the Hisayama study were calibrated to a gold standard examiner in 2012 KNHANES. The calibration was performed by conducting examinations on ten Japanese volunteers who had all six sextants examined. The mean κ value (range) between examiners in Hisayama study and the gold standard examiner in 2012 KNHANES was 0.55 (0.43–0.66) for CPI code.

The total number of decayed and filled teeth was used as a measure of assessing dental caries. Teeth which had undergone permanent restoration (because of previous decay or other reasons) with a fixed dental prosthesis abutment, were regarded as filled teeth.

Assessment of diabetes and metabolic syndrome

A blood sample was collected from the antecubital vein in the morning, after fasting for at least 8 hours in KNHANES, and after overnight fasting in the Hisayama study. Fasting plasma concentrations of glucose, triglycerides, and high-density lipoprotein (HDL) cholesterol were measured. Revised HDL values were used in KNHANES, because HDL values in the same sample were different between the Korean Central Laboratory and the Centers for Disease Control and Prevention (CDC) in US; conversion rates were calculated by analyzing serum samples sent to the CDC, using isotope-dilution gas chromatography-mass spectrometry, which is considered the gold standard method.¹⁴ Diabetes was defined as fasting

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glucose \geq 126 mg/dl, or undergoing treatment for diabetes with medication and/or insulin injections.¹⁵ For the 2012 KNHANES group, hemoglobin A1c was only assessed for individuals with diabetes or hyperglycemia (fasting glucose ≥ 126 mg/dl), and the oral glucose tolerance test was not conducted; therefore, the diagnostic criteria of diabetes used in this study did not correspond with the current diagnostic criteria proposed by the American Diabetes Association. Metabolic syndrome (MetS) was defined based on a Joint Interim Statement, using the criteria for Asians:¹⁶ elevated waist circumference (>90 cm in men and \geq 80 cm in women), elevated fasting glucose levels (\geq 100 mg/dl or drug treatment for elevated glucose), elevated triglycerides ($\geq 150 \text{ mg/dl}$ or drug treatment for elevated triglycerides), reduced HDL (<40 mg/dl in men and <50 mg/dl in women), and elevated blood pressure (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, or antihypertensive drug treatment). Individuals who were positive for three or more of these components were considered to have MetS.

Measurement of other factors

Information about participants' smoking habits, occupational status, and dental visits in the last 12 months, was obtained from a health interview in KNHANES, and a self-administered questionnaire in the Hisayama study. Smokers were classified as current, never, or former smokers. Occupational status was divided into four categories: clerical support workers; elementary occupations and unskilled workers; other jobs; and homemaker, unemployed or retired.

Statistical Analysis

The t test or chi-square test was used to assess the differences in distribution of age, sex, and job classification between the KNHANES and Hisayama studies. Age-adjusted mean values of the number of present teeth, decayed teeth, and filled teeth, taken as continuous variables, were estimated using analysis of covariance. The proportion of periodontal disease, diabetes, MetS, number of teeth, and oral health behaviors, taken as categorical variables, were adjusted for age distribution of the WHO standard population in 2000–2025, by the direct method. Differences in the mean values and proportions between countries were tested using the linear regression model and logistic regression analysis, respectively. The association between periodontal disease (dependent variable) and country (independent variable) was assessed using logistic regression analysis. The association between number of teeth (dependent variable) and country (independent variable) was investigated using generalized linear models with a Poisson probability distribution. Logistic regression models and generalized linear models were tested: 1) model including diabetes, 2) model including MetS, and 3) model including individual MetS components. Standard errors were estimated using robust or sandwich variance estimators of the covariance matrix of the regression coefficients,

to correct for heteroskedasticity across countries. Odds ratio (OR), β coefficients, and 95% confidence interval (CI) derived from corrected standard errors were calculated. The impact of an unmeasured confounder on the estimated OR was examined in sensitivity analyses, based on Lin et al.¹⁷ SPSS software (version 19.0 for Windows; IBM SPSS Japan, Tokyo, Japan) and R version 3.2.1 was used for data analyses. P < 0.05 was considered statistically significant in all analyses.

Results

Demographic characteristics of the study participants in Korea and Japan are shown in Table 1. Participants in Korea were significantly younger than those in Japan. Using age adjusted means, and the frequencies of dental and systemic parameters, it was observed that the percentage of participants with periodontal disease, and the mean number of present and filled teeth, were significantly higher in Japan than in Korea (Table 2). The percentage of participants with diabetes and MetS was significantly higher in Korea than in Japan. In terms of individual MetS components, participants in Japan had a higher prevalence of elevated fasting glucose and blood pressure, and a lower prevalence of elevated triglycerides and reduced HDL, than those in Korea.

Logistic regression analyses showed that the Japanese were more likely to have periodontal disease than Koreans (OR = 1.68, 95% CI: 1.41-2.00), even when diabetes, and

covariates including age, sex, number of teeth, number of decayed and filled teeth, dental visits, smoking, and occupation were included in the model (Table 3). Similar results were observed in the models including MetS and individual MetS component.

Discussion

This study showed that periodontal disease was more prevalent in the Japanese compared to Koreans, even after adjustment for diabetes and MetS. Our results suggest that this difference in prevalence was not related to the participants' systemic condition. The strength of our study lies in the fact that the examiners in Japan received calibration for periodontal examination by a gold standard examiner in KNHANES, which helped reduce bias in the prevalence estimates.

With regards to the results of the logistic regression models, the proportion of the variance explained by the model adjusted for diabetes and covariates was relatively low (Nagelkerke's R-squared 13.6%). This suggests that unmeasured factors might be associated with the differences in periodontal condition between the Koreans and Japanese. In post hoc sensitivity analyses, the association between country and periodontal disease was not significant in the logistic model, only when there was a significant difference in the proportions of an unmeasured factor between the Koreans and Japanese (Supplementary Table 1). In this model, periodontal disease could possibly be explained in relation to unmeasured

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factors than to country, which suggests that unmeasured factors strongly contribute to the differences in periodontal condition. Several factors such as oral microbiota and dietary intake could be considered as unmeasured factors which probably influenced our findings. We have previously shown higher proportions of *Prevotella* and *Veillonella*, and lower proportions of *Neisseria* and Haemophilus, in the salivary microbiome of Japanese from the Hisayama study, compared to Koreans from the Yangpyeong cohort study undertaken in Yangpyeong County, a suburb of the Seoul metropolitan area.¹⁸ Similar to our present study, the previous study showed that the periodontal condition of the Japanese was worse than the Koreans in the Yangpyeong cohort study, by measuring the periodontal pocket depth and clinical attachment level on the mesio-buccal and mid-buccal sites, for specific 12 index teeth;¹⁸ the study indicated that the greater proportion of dysbiotic oral microbiota in the Japanese is associated with a worse periodontal condition, compared to Koreans. Thus, the difference in periodontal condition between the Koreans and the Japanese may be associated with the disparity in their oral microbiota. It is difficult to determine the exact cause of the differences in microbiomes between Koreans and Japanese. The fact that the Japanese in our previous study had a greater proportion of dysbiotic oral microbiota, taken together with the fact that diabetes and MetS were less prevalent in the Japanese compared to Koreans, suggests that systemic disease is less likely to be related to the differences in microbiomes. Alternatively, nutrition and dietary

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intake might affect periodontal disease, by affecting the oral bacterial species. Both Korea and Japan are based on an agrarian society and their dietary patterns are similar;¹⁹ however, Koreans prefer their food spicier or saltier compared to the Japanese.²⁰ Kimchi, a lactic acid fermented vegetable product, is a well-known traditional Korean food. Koreans consume 96.3 g/day of kimchi according to the KNHANES of 2015.²¹ On the other hand, the Japanese consume 3.6 g/day of pickled vegetables, such as pickled Chinese cabbage and kimchi, based on the Japanese National Health and Nutrition Survey of 2014.²² Kimchi contains high levels of vitamins, minerals, dietary fibers, and other functional components, and has been reported to have anticancer, antioxidative, and antiatheroscletoric effects, and probiotic properties.²³ Lactobacilli are responsible for kimchi fermentation. It has been shown that probiotic lactobacilli affect the oral ecology by specifically preventing the adherence of other oral bacteria, and by modifying the protein composition of the salivary pellicle.²⁴ Thus, the high intake of kimchi in Koreans may be associated with a better oral environment, and a lower prevalence of periodontal disease than in Japanese.

In this study, the Japanese had greater number of teeth than the Koreans. Generalized linear models showed that the Japanese had a greater number of teeth (β coefficient = 0.19; 95% CI: 0.17, 0.21) than Koreans, after adjusting for diabetes and covariates (Supplementary Table 2). It is conceivable that the prevalence of periodontal disease was higher in Japan than in Korea, because of the greater number of teeth (in negative aspect, teeth with periodontal

disease were not extracted, and remained). Logistic regression models showed that Japanese were more likely to have periodontal disease than Koreans, after adjusting for number of teeth. Additionally, when we conducted a separate analysis according to the number of teeth (10-19 teeth, 20-27 teeth, and 28 and more teeth), the association between country and periodontal disease was consistently significant (Supplementary Table 3). The difference in periodontal conditions between the Koreans and Japanese is significant, regardless of number of teeth.

The difference in the number of teeth between the Koreans and Japanese may be related to the extent of health insurance coverage. Although both Korea and Japan have universal health insurance systems, the cost of dental care is lower in Japan compared to that in Korea. Japanese health insurance covers almost all basic dental treatments such as endodontic, periodontal, and prosthetic treatments including bridge and removable dentures. The cost of dental treatment in Japan is about \$24 (with exchange rate of 100 yen per dollar) for resin filling in single cavity, \$60 for infected root canal treatment in molar with three root canals, \$140 for gold/silver palladium crown with metal post and core, \$26 for molar extractions. Japanese people who receive dental treatment pay only 10–30% of the total cost of treatment depending on age and income, in the universal health insurance system. In Korea, universal health insurance covers some treatments such as endodontic, periodontal, denture treatment, and extraction in individuals of specific age groups. Resin filling, and prosthetic treatment including crown and bridge, are not covered. The cost of dental treatment in Korea

is about \$100 (with exchange rate of 1000 won per dollar) for resin filling in single cavity, \$150 for infected root canal treatment in molar with three root canals, \$450 for gold/silver palladium crown with metal post and core, \$28 for molar extractions. Korean people who receive infected root canal treatment and extraction, pay 30% of the total cost of treatment in the universal health insurance system. This indicates that the Japanese are more likely to receive restorative and prosthetic treatment compared to Koreans, due to the lower cost of dental care. Indeed, the number of filled teeth (including permanent restoration by fixed dental prosthesis abutment) was higher in Japan than in Korea in this study (Table 2). Additionally, the Japanese reported more dental visits in the last 12 months, compared to Koreans (Table 2). The greater number of teeth in the Japanese may be attributable to the low economic barriers to obtaining dental care in Japan.

Our study has some limitations. First, the Japanese data were derived from one town in Japan, whereas Korean data were based on a national survey. The study cohort in Japan, which comprised residents in Hisayama town, is recognized to be demographically representative of Japan, according to the national census.¹³ The differences in periodontal conditions observed in this study were consistent with the reports of a national survey. Therefore, using the study cohort in Japan to generalize our findings might be acceptable. Second, our findings regarding the differences in periodontal conditions between Koreans and Japanese may be affected by unmeasured factors including oral microbiota and dietary intake.

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Our previous study compared the oral microbiota between Koreans and Japanese;¹⁸ however, participants in Korea were drawn from a convenience sample, and not a nationally representative sample. Future studies are needed to compare oral microbiota and the dietary intake between Koreans and Japanese using data from a nationally representative sample to explore the causes of the difference in periodontal condition. Third, a partial mouth assessment for periodontal condition was used. Although CPI is an easier way to evaluate periodontal condition in the community setting, this method may inherently underestimate or overestimate the prevalence and severity of periodontal parameters due to the use of representative teeth and pseudo pockets.²⁵

Despite these limitations, this study revealed interesting findings, and has several implications. The prevalence of periodontal disease was lower in Koreans than in Japanese, while the prevalence of diabetes and MetS were higher in Koreans than in Japanese. These findings suggest that the systemic condition is not associated with the difference in periodontal condition between Koreans and Japanese. We need more studies which can identify other factors that may underlie the observed differences in periodontal condition between countries.

Author contributions MF, YS, D-YP, and YY conceived and planned the project. MF, YS, TT, JH, DY, D-YP, and TN were responsible for acquisition of data. MF, KT, and TT

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conducted statistical analysis. MF, KT, and YY wrote the manuscript.

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Competing interests None declared.

Patient consent Not required in Korean National Health and Nutrition Examination Survey. Obtained in Hisayama study.

Ethics approval This study was approved by the Kyushu University Institutional Review Board for Clinical Research (24-129).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The original data of Koreans came from Korean National Health and Nutrition Examination Survey (https://knhanes.cdc.go.kr/knhanes/eng/index.do). No

additional data are available in Hisayama study.

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	Korean	Japanese	
	n=3574	n=2205	P value
Age	58.4±11.0	60.5±10.7	< 0.001
Age category			< 0.001
40-49	902 (25.2%)	434 (19.7%)	
50-59	1009 (28.2%)	514 (23.3%)	
60-69	936 (26.2%)	743 (33.7%)	
70-79	727 (20.3%)	514 (23.3%)	
Gender			0.074
Men	1527 (42.7%)	995 (45.1%)	
Women	2047 (57.3%)	1210 (54.9%)	
Job classification			< 0.001
Clerical support workers	191 (5.3%)	526 (23.9%)	
Elementary occupations	394 (11.0%)	128 (5.8%)	
Other jobs	1514 (42.4%)	389 (17.6%)	
Unemployed, homemakers and part-time workers	1475 (41.3%)	1162 (52.7%)	

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n (%), mean \pm SD

 χ^2 test for categorical variable and t test for continuous variable

	Korean	Japanese	P value
Periodontal disease (CPI code ≥ 3) [*]	31.4%	42.1%	<0.001
Number of teeth	22.9±0.1	24.1±0.1	< 0.001
0	2.0%	1.0%	
1-9	4.6%	2.6%	
10-19	8.5%	7.6%	
20-27	39.9%	45.8%	
28-	45.0%	42.9%	
Number of decayed teeth	0.59±0.02	0.59±0.03	0.882
Number of filled teeth	7.0±0.1	13.0±0.2	< 0.001
Dental visit in the last 12 months	25.6%	30.4%	< 0.001
Current smoking	18.6%	20.1%	0.485
Diabetes	11.9%	9.4%	0.018
Elevated waist circumference	38.6%	39.2%	0.793
Elevated fasting glucose	36.2%	50.3%	< 0.001
Elevated blood pressure	46.7%	47.6%	0.046
Elevated triglycerides	39.8%	32.1%	0.001
Reduced HDL	39.8%	8.6%	< 0.001
MetS	36.2%	30.5%	0.001

Table 2. Age-adjusted mean value and frequency of dental and systemic parameters by country

Mean \pm SD

Differences in age-adjusted mean values and proportions were tested by linear regression model and logistic regression analysis

* Participants who received periodontal examination and had more than 10 teeth (n = 3,217 in

Korean and n = 2,067 in Japanese).

HDL, high density lipoprotein; MetS, metabolic syndrome

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Table 3. Adjusted	odds ratio for	periodontal	disease accordin	g to country.
5		1		

		Model 1			Model 2			Model 3	
	OR	(95% CI)	P value	OR	(95% CI)	P value	OR	(95% CI)	P value
Country									
Korea	1			1			1		
Japan	1.68	(1.41-2.00)	< 0.001	1.67	(1.41-1.99)	< 0.001	1.80	(1.50-2.16)	< 0.001
Diabetes									
No	1								
Yes	1.47	(1.23-1.76)	< 0.001						
MetS									
No				1					
Yes				1.20	(1.06-1.35)	0.005			
Individual MetS co	mponents								
Waist									
Normal							1		
Elevated							1.30	(1.14-1.48)	< 0.001
Fasting glucose									
Normal							1		
Elevated							1.00	(0.88-1.14)	0.95
Triglyceride									
Normal							1		
Elevated							1.06	(0.94-1.21)	0.33
HDL									
Normal							1		
Reduced							1.01	(0.88-1.15)	0.89
Blood pressure									
Normal							1		
Elevated							1.27	(1.09-1.47)	0.00
Logistic regression	analysis u	sing periodon	tal disease	as the	dependent var	iable and co	ountry a	s the independ	dent
variables.									
Participants who re	ceived per	iodontal exam	ination an	d had r	nore than 10 to	eeth $(n = 3, 2)$	217 in K	Korean and n =	= 2,067 i
Japanese).									
Diabetes, MetS, and	d individu	al MetS comp	onents wer	e inclu	ded in Model	1, 2, and 3,	respect	ively.	
All models were ad	justed for	age, sex, num	ber of teetl	h, num	ber of decayed	and filled	teeth, de	ental visit, cur	rent

smoking, and occupation.

OR, odds ratio; CI, confidence interval; MetS, metabolic syndrome; HDL, high density lipoprotein.

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Supplementary Table 1. Estimates for odds ratio of periodontal disease for Japanese compared to Koreans with adjustment for an unmeasured factors.

OR^*	P1 [‡]	$P0^{\dagger}$					
		0.05	0.1	0.2	0.3	0.5	0.8
1.8	0.05	1.68 (1.42-2.00)	1.75 (1.47-2.08)	1.88 (1.58-2.23)	2.01 (1.69-2.38)	2.27 (1.91-2.69)	2.65 (2.23-3.15)
	0.1	1.62 (1.36-1.93)	1.68 (1.42-2.00)	1.81 (1.52-2.15)	1.93 (1.63-2.30)	2.18 (1.84-2.59)	2.55 (2.15-3.04)
	0.2	1.51 (1.27-1.79)	1.57 (1.32-1.86)	1.68 (1.42-2.00)	1.80 (1.51-2.14)	2.03 (1.71-2.41)	2.38 (2.00-2.83)
	0.3	1.41 (1.19-1.68)	1.47 (1.23-1.74)	1.57 (1.33-1.87)	1.68 (1.42-2.00)	1.90 (1.60-2.26)	2.23 (1.87-2.64)
	0.5	1.25 (1.05-1.49)	1.30 (1.09-1.54)	1.39 (1.17-1.66)	1.49 (1.25, 1.77)	1.68 (1.42-2.00)	1.97 (1.66-2.34)
	0.8	1.07 (0.90-1.27)	1.11 (0.93-1.32)	1.19 (1.00-1.41)	1.27 (1.07-1.51)	1.44 (1.21-1.71)	1.68 (1.42-2.00)
2.2	0.05	1.68 (1.42-2.00)	1.78 (1.50-2.11)	1.97 (1.66-2.34)	2.16 (1.82-2.57)	2.54 (2.14-3.02)	3.11 (2.62-3.70)
	0.1	1.59 (1.34-1.89)	1.68 (1.42-2.00)	1.86 (1.57-2.21)	2.04 (1.72-2.43)	2.40 (2.02-2.86)	2.94 (2.48-3.50)
	0.2	1.44 (1.21-1.71)	1.52 (1.28-1.81)	1.68 (1.42-2.00)	1.85 (1.55-2.19)	2.17 (1.83-2.58)	2.66 (2.24-3.16)
	0.3	1.31 (1.10-1.56)	1.39 (1.17-1.65)	1.53 (1.29-1.82)	1.68 (1.42-2.00)	1.98 (1.67-2.35)	2.42 (2.04-2.88)
	0.5	1.11 (0.94-1.32)	1.18 (0.99-1.40)	1.30 (1.10-1.55)	1.43 (1.20-1.70)	1.68 (1.42-2.00)	2.06 (1.74-2.45)
	0.8	0.91 (0.77-1.08)	0.96 (0.81-1.14)	1.06 (0.90-1.26)	1.17 (0.98-1.39)	1.37 (1.16-1.63)	1.68 (1.42-2.00)

OR (95%CI)

OR were adjusted for diabetes, covariates, and an unmeasured factor having an OR of periodontal disease of 1.8 or 2.2.

Bold indicates that OR was not significant.

*OR of periodontal disease comparing between participants with and without an unmeasured factor.

[†]Prevalence of an unmeasured factor in Koreans

[‡]Prevalence of an unmeasured factor in Japanese

OR, odds ratio: CI, confidence interval.

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	Model 1		Model 2		Model 3	
	β coefficient	n voluo	β coefficient	n voluo	β coefficient	n w
	(95% CI)	p value	(95% CI)	p value	(95% CI)	рv
Country						
Korea						
Japan	0.19 (0.17; 0.21)	< 0.001	0.19 (0.17; 0.21)	< 0.001	0.19 (0.17; 0.22)	<0
Diabetes						
No						
Yes	-0.04 (-0.06; -0.02)	< 0.001				
MetS						
No						
Yes			-0.03 (-0.04; -0.01)	< 0.001		
Individual MetS	components					
Waist						
Normal						
Elevated					-0.006 (-0.019; 0.006)	
Fasting glucose						
Normal						
Elevated					-0.007 (-0.019; 0.005)	
Triglyceride						
Normal						
Elevated					-0.007 (-0.020; 0.005)	
HDL						
Normal						
Reduced					-0.007 (-0.019; 0.005)	
Blood pressure						
Normal						
Elevated					-0.007 (-0.019; 0.004)	
Participants who	o received periodonta	l examina	ation ($n = 3,428$ in Kor	rea and n =	2,153 in Japan).	
Generalized line	ear models with a Poi	sson prob	ability distribution usi	ing number	of teeth as the dependent	t vari
and country as the	he independent varial	oles.				
Diabetes, MetS,	and individual MetS	compone	ents were included in M	Model 1, 2,	and 3, respectively.	
All models were	e adjusted for age, sex	, number	of teeth, number of d	ecayed and	filled teeth, dental visit, o	curre
smoking, and jo	b.					
CI, confidence i	nterval; MetS, metab	olic synd	rome; HDL, high dens	sity lipopro	tein.	

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Supplementary Table 3. Adjusted odds ratio for periodontal disease stratified by	y
number of teeth.	

	1	Model 1	Ν	Model 2
	OR	(95% CI)	OR	(95% CI)
10-19 teeth (n = 405 in Korea				
and $n = 258$ in Japan)				
Country				
Korea	1		1	
Japan	2.53	(1.69-3.78)	2.51	(1.68-3.75)
Diabetes				
No	1			
Yes	1.14	(0.77-1.70)		
MetS				
No			1	
Yes			1.22	(0.88-1.71)
20-27 teeth (n = 1,463 in Korea				
and n = 1,089 in Japan)				
Country				
Korea	1		1	
Japan	1.58	(1.20-2.07)	1.57	(1.20-2.06)
Diabetes				
No	1			
Yes	1.46	(1.14-1.86)		
MetS				
No			1	
Yes			1.06	(0.89-1.26)
≥ 28 teeth (n = 1,349 in Korea				
and $n = 720$ in Japan)				
Country				
Korea	1		1	
Japan	1.50	(1.02-2.19)	1.46	(0.99-2.14)
Diabetes				
No	1			
Yes	1.78	(1.26-2.52)		
MetS				
No			1	
Yes			1.33	(1.07-1.67)

Logistic regression analysis using periodontal disease as the dependent variable and country as the independent variables.

Diabetes and MetS were included in Model 1 and 2, respectively.

All models were adjusted for age, sex, number of teeth, number of decayed and filled teeth, dental visit, current smoking, and job.

OR, odds ratio; CI, confidence interval; KNHANES, Korean National Health and Nutrition Examination Survey; MetS, metabolic syndrome.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction	1		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-8
Objectives	3	State specific objectives, including any prespecified hypotheses	8
Methods			
Study design	4	Present key elements of study design early in the paper	8-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8-9
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	8-9
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-12
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	9-12
measurement		comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	13-14
Study size	10	Explain how the study size was arrived at	8-9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	12-13
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	12-13
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	8-9
		(d) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	13
Results			

	-		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-9
		(b) Give reasons for non-participation at each stage	8-9
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	13
		(b) Indicate number of participants with missing data for each variable of interest	8-9
Outcome data	15*	Report numbers of outcome events or summary measures	13
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	13
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14-15
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	20
		which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Comparison of the periodontal condition in Korean and Japanese adults: a cross-sectional study

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SCHOLARONE[™] Manuscripts

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1	Comparison of the periodontal condition in Korean and Japanese adults: a
2	cross-sectional study
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1	Abstract
2	Objectives Reports from national surveys in South Korea and Japan have indicated that
3	the prevalence of periodontal disease is lower in Korea than in Japan. However, these
4	national surveys have not evaluated factors related to periodontal health condition,
5	including diabetes and metabolic syndrome. This study compared periodontal
6	conditions between Korean and Japanese adults, in the context of general health status.
7	Design Cross-sectional study
8	Setting National survey in South Korea (Korean National Health and Nutrition
9	Examination Survey "KNHANES") and a population-based study in Japan (Hisayama
10	study); both were conducted in 2012
11	Participants This study included 3,574 Korean and 2,205 Japanese adults aged 40-79
12	years.
13	Outcome measures Periodontal condition was assessed by using the Community
14	Periodontal Index (CPI). Examiners in Japan underwent clinical calibration training for
15	periodontal examination with a gold standard examiner from KNHANES, prior to the
16	Hisayama study.
17	Results : The age-adjusted prevalences of periodontal disease, defined as CPI score \geq 3,
18	were 31.4% and 42.1% in South Korea and Japan, respectively ($p < 0.001$). The
19	age-adjusted prevalences of diabetes ($p = 0.018$) and metabolic syndrome ($p = 0.001$)
20	were higher in Korea than in Japan. The numbers of present and filled teeth and
21	percentages of participants who visited a dental clinic in the last 12 months were higher
22	in Japan than in Korea (all $p < 0.001$). Logistic regression analysis showed that the
23	Japanese participants were more likely to have periodontal disease than were the Korean
24	participants, after adjusting for age, sex, occupation, oral health status, oral health

behavior, diabetes, and metabolic syndrome.

 $\mathbf{2}$ Conclusions: A higher prevalence of periodontal disease was found in Japanese

participants than in Korean participants. Further studies are needed to more clearly

elucidate factors underlying the difference in periodontal conditions between the two

 $\mathbf{5}$ populations, including those related to the dental health care system and dietary intake.

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5 6	1	Strengths and limitations of this study
7 8	2	• This is the first study to compare periodontal disease between Korean and Japanese
9	3	people, in relation to systemic diseases.
10	4	• This study included a large representative population in Korea, based on a national
12 13	5	survey, and a community-based population in Japan.
14 15	6	• The examiners in the Japanese survey underwent clinical calibration training for the
16 17	0	The examiners in the supariese survey under went enhibit canonation training for the
18	7	periodontal examination with a gold standard examiner from the Korean survey.
19 20	8	• Periodontal condition was evaluated by using partial mouth assessment; thus, it was
21 22	9	possible to underestimate the prevalence of periodontal disease.
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 $\mathbf{2}$ According to the World Health Organization (WHO) Global Oral Health Data Bank,¹ the prevalence of periodontal disease, as defined by the Community Periodontal Index (CPI) code \geq 3, was 4–37% in 35–44-year-olds, and 20–52% in 65–74-year-olds, among Asian countries (including the least developed to the highly industrialized) that conducted national surveys from 1999 to 2012. The general health conditions and health care systems vary widely among countries in Asia, depending on their levels of economic development. Oral health conditions and oral health care systems in this region also vary widely.² Thus, differences in socioeconomic status might contribute to inequalities in oral health among Asian countries. Surprisingly, the results of national surveys in Korea and Japan indicate that the prevalence of periodontal disease is lower in Korea (32.9% and 23.9% of individuals aged 19 and over in 2008 and 2010, respectively)³ than in Japan (44.7% and 41.5% of individuals aged 19 and over in 2005 and 2011, respectively).⁴ Among Asian countries, South Korea (hereafter "Korea") and Japan are located in close proximity; they share similar economic and ethnic backgrounds. The gross domestic product per capita in 2016 was \$27,534 in Korea and \$38,895 in Japan.⁵ The Korean and Japanese populations belong primarily to the northern Mongoloid group, and Koreans are genetically closer to the Japanese than to other Mongoloid groups.⁶ With regard to health care systems, the governments of both Korea and Japan provide national health insurance that covers the entire population. In Korea, dental treatment covered by health insurance is limited; however, in recent years, dental insurance coverage has expanded, and denture treatment in individuals aged 65 and over (from 2016) and periodontal scaling (from 2013) has been covered.⁷ In contrast, in $\mathbf{24}$

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	1	Japan, national health insurance covers almost all dental treatments, such as treatment
	2	for dental caries, including endodontic treatment; periodontal disease; prosthetic
	3	treatment; and extraction. Periodontal treatment in Japan has been covered by health
	4	insurance since 1972. The size of the dental workforce is larger in Japan than in Korea;
	5	population ratios of dentists were reported as 5.0 and 7.4 per 10,000 people in Korea
	6	and Japan, respectively. ⁸ Additionally, the population ratios of practicing dental
	7	hygienists were 4.9 and 8.5 per 10,000 people in Korea and Japan, respectively. ⁹ These
	8	data suggest that the Japanese may have an increased likelihood of receiving periodontal
	9	treatment and preventing care compared with Koreans, considering the greater dental
1	LO	insurance coverage and higher numbers of dentists and dental hygienists. Differences in
1	1	health care systems between Korean and Japan seem to contradict the levels of
1	12	periodontal health in these two countries.
1	13	However, great significance cannot be attached to the reports of these national
1	14	surveys, as potential risk factors related to periodontal disease are not considered.
1	15	Growing evidence from epidemiological studies indicates that diabetes and metabolic
1	16	syndrome are associated with periodontal disease. ^{10 11} When comparing periodontal
1	17	disease among different countries, the effects of systemic health on periodontal disease
1	18	and other risk factors should be addressed. Thus, a comparison of geographical and
1	19	racial differences in periodontal disease, and interpretations of the reasons for these
2	20	differences, are essential for preventing periodontal disease. The objective of this study
2	21	was to investigate whether periodontal condition differed between Korean and Japanese
2	22	adults, in relation to the effects of diabetes and metabolic syndrome.
2	23	
2	24	Methods

1 Study population

2	In the present study, data for Koreans were collected from a subset of the Fifth Korean
3	National Health and Nutrition Examination Survey (KNHANES), a nationwide
4	cross-sectional survey conducted in 2012 by the Korea Center for Disease Control and
5	Prevention. Participants were selected by using a multi-stage clustered probability
6	design to produce a nationally representative non-institutionalized civilian sample. All
7	participants provided written informed consent. Additional information regarding the
8	KNHANES can be found elsewhere. ¹² The present study included 3,955 participants
9	from the 2012 survey, aged 40–79 years, who received medical and dental examinations
10	in addition to a health interview. After excluding participants with missing data, 3,574
11	participants were included in the analysis.
12	Data for Japanese were obtained from the Hisayama study, a population-based
13	prospective study of cerebro-cardiovascular diseases performed in the town of
14	Hisayama (a suburban rural area of Fukuoka city in southern Japan). The age and
15	occupational distributions of the population of this town are approximately
16	representative of Japan as a whole. ¹³ A portion of the Hisayama study in 2012
17	comprised dental examinations for residents aged ≥ 40 years. The present study included
18	2,342 participants, aged 40–79 years, who received both medical and dental
19	examinations in 2012 (57.8% of the total population in this age group). Written
20	informed consent was obtained from all participants. After excluding participants with
21	missing data, 2,205 participants were included in the analysis.
22	The study was approved by the Kyushu University Institutional Review Board
23	for Clinical Research (Approval No. 24-129).
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	1	Assessment of periodontal condition and dental caries
	2	Periodontal condition was assessed by using the CPI in both KNHANES and Hisayama
	3	studies. In accordance with World Health Organization protocols, 10 teeth were selected
	4	for the periodontal examination: two molars in each posterior sextant, and the upper
	5	right and lower left central incisors. If no index tooth was present in a qualified sextant,
	6	all remaining teeth in that sextant were examined. The highest code among the
	7	examined sextants was recorded, to represent the CPI status for each individual.
	8	Periodontal disease was defined as CPI code \geq 3 (periodontal pocket depth \geq 4 mm).
	9	Trained and calibrated dentists assessed periodontal conditions in both
	10	KNHANES and Hisayama studies. To ensure the reliability of measurements with CPI,
	11	seven examiners in the Hisayama study were calibrated to a gold standard examiner in
	12	the 2012 KNHANES. The calibration was performed by conducting examinations on 10
	13	Japanese volunteers who had all six sextants examined. The mean κ value (range)
	14	between examiners in the Hisayama study and the gold standard examiner in the 2012
	15	KNHANES was 0.55 (0.43–0.66) for CPI code.
	16	We assessed dental caries by measuring the total numbers of decayed and filled
	17	teeth; this measurement was performed because tooth surface roughness, especially in
	18	cases of subgingival restoration, leads to the accumulation of plaque, which results in
	19	gingival inflammation. ¹⁴ Teeth were regarded as filled teeth if they had undergone
	20	permanent restoration (because of previous decay or other reasons) with a fixed dental
	21	prosthesis abutment.
	22	
	23	Assessment of diabetes and metabolic syndrome
	24	A blood sample was collected from the antecubital vein in the morning, after fasting for
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1	at least 8 hours in the KNHANES, and after overnight fasting in the Hisayama study.
2	Fasting plasma concentrations of glucose, triglycerides, and high-density lipoprotein
3	(HDL) cholesterol were measured. Revised HDL values were used in the KNHANES,
4	because HDL values in the same samples differed between the Korean Central
5	Laboratory and the Centers for Disease Control and Prevention (CDC) in the United
6	States; conversion rates were calculated by analyzing serum samples sent to the CDC,
7	using the isotope-dilution gas chromatography-mass spectrometry; this method is
8	considered the gold standard. ¹⁵ Diabetes was defined as fasting glucose ≥ 126 mg/dl, or
9	undergoing treatment for diabetes with medication and/or insulin injections. ¹⁶ For the
10	2012 KNHANES group, hemoglobin A1c was solely assessed for individuals with
11	diabetes or hyperglycemia (fasting glucose \geq 126 mg/dl), and the oral glucose tolerance
12	test was not conducted; therefore, the diagnostic criteria of diabetes used in this study
13	did not correspond with the current diagnostic criteria proposed by the American
14	Diabetes Association. Metabolic syndrome (MetS) was defined on the basis of a Joint
15	Interim Statement, using the criteria for Asians: ¹⁷ elevated waist circumference (≥90 cm
16	in men and \geq 80 cm in women), elevated fasting glucose levels (\geq 100 mg/dl or drug
17	treatment for elevated glucose), elevated triglycerides (≥150 mg/dl or drug treatment for
18	elevated triglycerides), reduced HDL (<40 mg/dl in men and <50 mg/dl in women), and
19	elevated blood pressure (systolic blood pressure \geq 130 mmHg or diastolic blood pressure
20	\geq 85 mmHg, or antihypertensive drug treatment). Individuals who were positive for
21	three or more of these components were considered to have MetS.
22	
23	Measurement of other factors

24 Information regarding participants' smoking habits, occupational statuses, and dental

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1	visits in the last 12 months, was obtained from a health interview in the KNHANES,
2	and from a self-administered questionnaire in the Hisayama study. Smokers were
3	categorized as current, never, or former smokers. Socioeconomic status was determined
4	on the basis of occupational status, which was divided into four categories: clerical
5	support workers; elementary occupations and unskilled workers; other jobs; and
6	homemaker, unemployed or retired. "Other jobs" includes professional, skilled, and
7	service workers, salespeople, farmers, and fishers. We used occupation as a
8	socioeconomic status indicator; however, we did not directly assess income because the
9	Hisayama study did not collect income data and the previous KNHANES study (2012)
10	showed no significant association between income and periodontal disease. ¹⁸
11	
12	Statistical Analysis
13	The t-test or chi-squared test was used to assess differences in the distribution of age,
14	sex, and job classification between the KNHANES and Hisayama studies. Age-adjusted
15	mean values of the numbers of present teeth, decayed teeth, and filled teeth, defined as
16	quantitative variables, were estimated by using analysis of covariance. The proportions
17	of periodontal disease, diabetes, MetS, number of teeth, and oral health behaviors,
18	defined as categorical variables, were adjusted on the basis of age distribution of the
19	WHO standard population in 2000–2025, by using the direct method. Differences in the
20	mean values and proportions between countries were tested by linear regression
21	modeling and logistic regression analysis, respectively. The association between
22	periodontal disease (dependent variable) and country (independent variable) was
23	assessed by using logistic regression analysis. We included participants who had more
24	than 10 teeth in this analysis because all of them had at least one sextant in CPI. The

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1	association between number of teeth (dependent variable) and country (independent
2	variable) was investigated by using generalized linear models with a Poisson probability
3	distribution. Logistic regression models and generalized linear models were tested:
4	model 1 included diabetes; model 2 included MetS; and model 3 included individual
5	MetS components. Standard errors were estimated by using robust or sandwich variance
6	estimators of the covariance matrix of the regression coefficients, to correct for
7	heteroskedasticity across countries. Odds ratio (OR), β coefficients, and 95%
8	confidence interval (CI) derived from corrected standard errors were calculated. The
9	impact of an unmeasured confounder on the estimated OR was examined in sensitivity
10	analyses, based on Lin et al. ¹⁹ SPSS software (version 19.0 for Windows; IBM SPSS
11	Japan, Tokyo, Japan) and R version 3.2.1 were used for data analyses. $P < 0.05$ was
12	considered statistically significant in all analyses.
13	
14	Patient and public involvement
15	KNHANES data used in this study comprise nationwide data, which is collected
16	annually by the Korea Center for Disease Control and Prevention; these data are
17	publicly available to researchers. Participants in the Hisayama study were recruited with
18	the help of the Health C&C Center Hisayama, which provided healthcare services to the
19	residents of Hisayama. None of our participants were involved in the recruitment or
20	conduct of either study that has provided data for this report.
21	
22	Results
23	Demographic characteristics of the study participants in Korea and Japan are shown in
24	Table 1. Participants in Korea were significantly younger than those in Japan. Using
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	1	age-adjusted means, and the frequencies of dental and systemic parameters, it was
	2	observed that the percentage of participants with periodontal disease, and the mean
	3	numbers of present and filled teeth, were significantly higher in Japan than in Korea
	4	(Table 2). The percentages of participants with diabetes and MetS were significantly
	5	higher in Korea than in Japan. In terms of individual MetS components, participants in
	6	Japan had a higher prevalence of elevated fasting glucose and blood pressure, and a
	7	lower prevalence of elevated triglycerides and reduced HDL, compared with those in
	8	Korea.
	9	Logistic regression analyses showed that the Japanese participants were more
	10	likely to have periodontal disease than were the Korean participants ($OR = 1.68, 95\%$
	11	CI: 1.41–2.00); this was consistent even when diabetes and other covariates, including
	12	age, sex, number of teeth, number of decayed and filled teeth, dental visits, smoking,
	13	and occupation, were included in the model (Table 3). Similar results were observed in
	14	models that included MetS and individual MetS components.
	15	
	16	Discussion
	17	This study showed that periodontal disease was more prevalent in Japanese participants
	18	than in Korean participants, even after adjustment for diabetes and MetS. Our results
	19	suggest that this difference in prevalence was not related to the participants' systemic
	20	conditions. The strength of our study lies in the fact that the examiners in Japan
	21	underwent calibration for periodontal examination with a gold standard examiner from
	22	the KNHANES, which helped to reduce bias in the prevalence estimates.
	23	With regard to the results of the logistic regression models, the proportion of
	24	variance explained by the model adjusted for diabetes and covariates was relatively low
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1	(Nagelkerke's R-squared 13.6%). This suggests that unmeasured factors might be
2	associated with the differences in periodontal condition between Korean and Japanese
3	participants. In post hoc sensitivity analyses, the association between country and
4	periodontal disease was not significant in the logistic model; it was significant solely
5	when there was a significant difference in the proportions of an unmeasured factor
6	between Korean and Japanese participants (Supplementary Table 1). In this model,
7	periodontal disease could possibly be explained in relation to unmeasured factors, rather
8	than in relation to country, which suggests that unmeasured factors contribute to the
9	differences in periodontal condition.
10	Several factors, such as oral microbiota and dietary intake, could be the
11	unmeasured factors that may have influenced our findings. We have previously shown
12	higher proportions of Prevotella and Veillonella, and lower proportions of Neisseria and
13	Haemophilus, in the salivary microbiome of Japanese from the Hisayama study,
14	compared with Koreans from the Yangpyeong cohort study undertaken in Yangpyeong
15	County (a suburb of the Seoul metropolitan area). ²⁰ Similar to our present study, the
16	previous study showed that the periodontal condition of the Japanese was worse than
17	that of the Koreans in the Yangpyeong cohort study, by measuring the periodontal
18	pocket depth and clinical attachment level on mesio-buccal and mid-buccal sites of 12
19	specific index teeth; ²⁰ the study indicated that a greater proportion of dysbiotic oral
20	microbiota in the Japanese is associated with a worse periodontal condition, compared
21	with the Koreans. Thus, the difference in periodontal condition between Koreans and
22	Japanese may be associated with disparities in their oral microbiota. It is difficult to
23	determine the exact cause of differences in microbiomes between Koreans and Japanese.
24	The Japanese in our previous study had a greater proportion of dysbiotic oral

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	microbiota; this, combined with the observation that diabetes and MetS were less
	prevalent in the Japanese compared with the Koreans, suggests that systemic disease is
	less likely to be related to differences in microbiomes. Alternatively, nutrition and
	dietary intake might affect periodontal disease by affecting the oral bacterial community.
	Both Korea and Japan are based on agrarian societies and their dietary patterns are
	similar; ²¹ however, Koreans prefer their food spicier or saltier, compared with the
	Japanese. ²² Kimchi, a lactic acid fermented vegetable product, is a well-known
	traditional Korean food. Koreans consume 96.3 g/day of kimchi, according to the
	KNHANES of 2015. ²³ In contrast, the Japanese consume 3.6 g/day of pickled
1	vegetables, such as pickled Chinese cabbage and kimchi, based on the Japanese
1	National Health and Nutrition Survey of 2014. ²⁴ Kimchi contains high levels of
1	vitamins, minerals, dietary fibers, and other functional components, and has been
1	reported to have anticancer, antioxidative, and anti-atherosclerotic effects, as well as
1	probiotic properties. ²⁵ Lactobacilli are responsible for kimchi fermentation. Probiotic
1	lactobacilli have been shown to affect oral ecology by specifically preventing the
1	adherence of other oral bacteria, and by modifying the protein composition of the
1	salivary pellicle. ²⁶ Thus, high intake of kimchi in Koreans may be associated with a
1	better oral environment, and a lower prevalence of periodontal disease, compared with
1	the Japanese.
2	In this study, Japanese participants had a greater number of teeth than did
2	Korean participants. Generalized linear models showed that the Japanese had a greater
2	number of teeth (β coefficient = 0.19; 95% CI: 0.17, 0.21) than did Koreans, after
2	adjusting for diabetes and covariates (Supplementary Table 2). It is conceivable that the
2	prevalence of periodontal disease was higher in Japan because of the greater number of

teeth (notably, teeth with periodontal disease were not extracted in these participants).

 $\mathbf{2}$ Logistic regression models showed that Japanese were more likely to have periodontal disease than were Koreans, after adjusting for the number of teeth. Additionally, when we conducted a separate analysis on the basis of the number of teeth (10-19 teeth, 20-27 teeth, and 28 and more teeth), a consistent association between country and periodontal $\mathbf{5}$ disease was observed (Supplementary Table 3). $\overline{7}$ Although both Korea and Japan have universal health insurance systems, the cost of dental care is lower in Japan than in Korea. Japanese health insurance covers almost all basic dental treatments such as endodontic, periodontal, and prosthetic treatments including bridge and removable dentures. The cost of dental treatment in Japan is approximately \$24 (with an exchange rate of 100 yen per dollar) for resin filling in a single cavity; \$60 for infected root canal treatment in a molar with three root canals; \$140 for a gold/silver palladium crown with a metal post and core; and \$26 for molar extractions. Japanese people who receive dental treatment pay only 10-30% of the total cost of treatment depending on age and income, in the universal health insurance system. In Korea, universal health insurance covers some treatments such as endodontic, periodontal, denture treatment, and extraction in individuals of specific age groups. Resin filling, and prosthetic treatment including crown and bridge, are not covered. The cost of dental treatment in Korea is approximately \$100 (with an exchange rate of 1000 won per dollar) for resin filling in a single cavity; \$150 for infected root canal treatment in a molar with three root canals; \$450 for a gold/silver palladium crown with a metal post and core; and \$28 for molar extractions. Korean people who receive infected root canal treatment and extraction pay 30% of the total cost of $\mathbf{24}$ treatment in the universal health insurance system. This indicates that the Japanese are

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	1	more likely to receive restorative and prosthetic treatment than are the Koreans, due to
	2	the lower cost of dental care. Indeed, the numbers of filled teeth (including permanent
	3	restoration by fixed dental prosthesis abutment) were higher in Japanese participants
	4	than in Korean participants in this study (Table 2). Additionally, Japanese participants
	5	reported more dental visits in the last 12 months, compared with the Korean participants
	6	(Table 2). The greater number of teeth in the Japanese may be attributable to the low
	7	economic barriers to obtaining dental care in Japan.
	8	In this study, the strength of association between country and periodontal
	9	disease varied among models: the OR of country was 1.68 in Model 1, which included
	10	diabetes; 1.67 in Model 2, which included MetS; and 1.80 in Model 3, which included
	11	individual MetS components (Table 3). This might be due to varying associations
	12	between country and each of the following: diabetes, MetS, and individual MetS
	13	components. The association between country and diabetes or MetS was not significant
	14	among participants who underwent periodontal examination and had more than 10
	15	teeth; however, the associations between country and individual MetS components were
	16	significant (data not shown). The OR of country differed in Model 3 because of
	17	inter-associations among independent variables, such as country and individual MetS
	18	components.
	19	Our study has some limitations. First, the Japanese data were derived from a
	20	single town in Japan, whereas Korean data were based on a national survey. The study
	21	cohort in Japan, which comprised residents in Hisayama town, is recognized to be
	22	demographically representative of Japan, according to the national census. ¹³ The
	23	differences in periodontal conditions observed in this study were consistent with the
	24	reports of a national survey. Therefore, the use of study cohort in Japan to generalize our

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5	1	findings might be acceptable. Second, our findings regarding the differences in
7 8	2	periodontal conditions between Koreans and Japanese may be affected by unmeasured
9 10	3	factors, including oral microbiota and dietary intake. Our previous study compared the
11 12 13	4	oral microbiota between Koreans and Japanese; ²⁰ however, participants in Korea were
13 14 15	5	drawn from a convenience sample, rather than a nationally representative sample.
16 17	6	Future studies are needed to compare oral microbiota and dietary intake between
18 19	7	Koreans and Japanese with data from a nationally representative sample, in order to
20 21	8	explore the causes of differences in periodontal conditions. Third, a partial mouth
22 23	9	assessment for periodontal condition was used. Although CPI is an easier approach to
24 25	10	evaluate periodontal condition in the community setting, this method may inherently
26 27	11	underestimate or overestimate the prevalence and severity of periodontal parameters due
28 29	12	to the use of representative teeth and pseudopockets. ²⁷ Additionally, when index teeth
30 31 32	13	were not present, the exclusion of sextants may have led to an underestimation of
33 34	14	periodontal disease. In this study, all participants with more than 10 teeth had at least
35 36	15	one sextant. The percentages of participants with 0, 1, and 2-5 excluded sextants were
37 38	16	82.7%, 7.0%, and 10.3% in KNHANES and 81.7%, 8.5%, and 9.8% in the Hisayama
39 40	17	study, respectively. Although the number of excluded sextants was relatively low, a
41 42	18	misclassification bias may have affected the magnitude of the observed associations.
43 44	19	Despite these limitations, this study revealed interesting findings, and has
45 46	20	several implications. The prevalence of periodontal disease was lower in Koreans than
47 48 40	21	in Japanese, whereas the prevalences of diabetes and MetS were higher in Koreans than
49 50 51	22	in Japanese. These findings suggest that systemic conditions are not associated with the
52 53	23	differences in periodontal conditions between Koreans and Japanese. We need
54 55 56	24	additional studies to identify other factors that may underlie differences in periodontal

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1	conditions between countries.
2	
3	Contributors MF, YS, D-YP, and YY conceived and planned the project. MF, YS, TT,
4	JH, DY, D-YP, and TN were responsible for acquisition of data. MF, KT, and TT
5	conducted statistical analysis. MF, KT, and YY wrote the manuscript.
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8	Competing interests None declared.
9	Patient consent Not required in Korean National Health and Nutrition Examination
10	Survey. Obtained in Hisayama study.
11	Ethics approval This study was approved by the Kyushu University Institutional
12	Review Board for Clinical Research (24-129).
13	Provenance and peer review Not commissioned; externally peer reviewed.
14	Data sharing statement The original data of Koreans came from Korean National
15	Health and Nutrition Examination Survey
16	(https://knhanes.cdc.go.kr/knhanes/eng/index.do). No additional data are available in
17	Hisayama study.
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	Korean	Japanese	
	n=3574	n=2205	P value
Age	58.4±11.0	60.5±10.7	< 0.001
Age category			< 0.001
40-49	902 (25.2%)	434 (19.7%)	
50-59	1009 (28.2%)	514 (23.3%)	
60-69	936 (26.2%)	743 (33.7%)	
70-79	727 (20.3%)	514 (23.3%)	
Sex			0.074
Men	1527 (42.7%)	995 (45.1%)	
Women	2047 (57.3%)	1210 (54.9%)	
Job classification			<0.001
Clerical support workers	191 (5.3%)	526 (23.9%)	
Elementary occupations	394 (11.0%)	128 (5.8%)	
Other jobs	1514 (42.4%)	389 (17.6%)	
Unemployed, homemakers and part-time workers	1475 (41.3%)	1162 (52.7%)	

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n (%), mean \pm SD

 χ^2 test for categorical variables and t-test for continuous variables 2071

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	Korean	Japanese	P value	
Periodontal disease (CPI	21.40	40.10	.0.001	
$\operatorname{code} \ge 3)^*$	31.4%	42.1%	<0.001	
Number of teeth	22.9±0.1	24.1±0.1	< 0.001	
0	2.0%	1.0%		
1-9	4.6%	2.6%		
10-19	8.5%	7.6%		
20-27	39.9%	45.8%		
28-	45.0%	42.9%		
Number of decayed teeth	0.59±0.02	0.59±0.03	0.882	
Number of filled teeth	7.0±0.1	13.0±0.2	< 0.001	
Dental visit in the last 12	25.60%	20 407	<0.001	
months	23.0%	30.4%	<0.001	
Current smoking	18.6%	20.1%	0.485	
Job classification			< 0.001	
Clerical support workers	6.9%	31.9%		
Elementary occupations	10.2%	6.3%		
Other jobs	46.6%	• 18.9%		
Unemployed, homemakers,	26.20%	12.00%		
and part-time workers	30.3%	42.9%		
Diabatas	11.00%	0.40%	0.019	
Diabetes	11.9%	9.4%	0.018	
Elevated warst circumference	38.0%	39.2%	0.793	
Elevated fasting glucose	36.2%	50.3%	<0.001	
Elevated blood pressure	40.7%	47.6%	0.046	
Elevated triglycerides	39.8%	32.1%	0.001	
Reduced HDL	39.8%	8.6%		
MetS	36.2%	30.5%	0.001	

Table 2. Age-adjusted mean values and frequencies of dental and systemic parameters by country

Mean \pm SD

Differences in age-adjusted mean values and proportions were tested by linear regression modeling and logistic regression analysis

* Participants who received periodontal examination and had more than 10 teeth (n = 3,217 in

Korean and n = 2,067 in Japanese).

HDL, high-density lipoprotein; MetS, metabolic syndrome

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Table	3. A	djusted	odds ratio	for	periodontal	disease	according to	country.

	Model 1		Model 2		Model 3		
	OR (93	5% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Country (ref. Korea)							
Japan	1.68 (1.	41-2.00)	< 0.001	1.67 (1.41-1.99)	< 0.001	1.80 (1.50-2.16)	< 0.001
Diabetes (ref. no)							
Yes	1.47 (1.	23-1.76)	< 0.001				
MetS (ref. no)							
Yes				1.20 (1.06-1.35)	0.005		
Individual MetS component	s						
Waist (ref. normal)							
Elevated						1.30 (1.14-1.48)	< 0.001
Fasting glucose (ref. normal							
Elevated						1.00 (0.88-1.14)	0.956
Triglyceride (ref. normal)							
Elevated						1.06 (0.94-1.21)	0.336
HDL (ref. normal)							
Reduced						1.01 (0.88-1.15)	0.895
Blood pressure (ref. normal))						
Elevated						1.27 (1.09-1.47)	0.002
Age	1.04 (1.	03-1.04)	< 0.001	1.04 (1.03-1.04)	< 0.001	1.03 (1.03-1.04)	< 0.001
Sex (ref. men)							
Women	0.70 (0.	62-0.80)	< 0.001	0.68 (0.60-0.78)	< 0.001	0.62 (0.54-0.72)	< 0.001
Number of teeth	0.97 (0.	96-0.99)	< 0.001	0.97 (0.96-0.99)	<0.001	0.97 (0.96-0.99)	< 0.001
Number of decayed and	1.01 (0	00.1.02	0.056	1.01 (0.00 1.02)	0.055	1 01 (0 00 1 02)	0.064
filled teeth	1.01 (0.	99-1.03)	0.030	1.01 (0.99-1.03)	0.035	1.01 (0.99-1.03)	0.004
Dental visit in the last 12 mc	onths (ref. y	ves)					
No	0.95 (0.	83-1.08)	0.401	0.94 (0.83-1.07)	0.351	0.94 (0.83-1.07)	0.392
Current smoking (ref. no)							
Yes	2.16 (1.	83-2.55)	< 0.001	2.14 (1.81-2.53)	< 0.001	2.15 (1.82-2.55)	< 0.001
Job classification (ref. u	nemployed	, homem	akers and	1			
part-time workers)							
Clerical support workers	0.91 (0.	74-1.12)	0.375	0.90 (0.73-1.10)	0.312	0.89 (0.73-1.09)	0.262
Elementary occupations	1.25 (1.	00-1.55)	0.043	1.25 (1.00-1.55)	0.044	1.25 (1.01-1.55)	0.045
Other jobs	1.24 (1.	06-1.44)	0.005	1.23 (1.06-1.44)	0.006	1.23 (1.05-1.43)	0.007

Logistic regression analysis using periodontal disease as the dependent variable and country as the independent

variables.

Participants who received periodontal examination and had more than 10 teeth (n = 3,217 in Korean and n = 2,067 in Japanese).

Diabetes, MetS, and individual MetS components were included in Models 1, 2, and 3, respectively.

All models were adjusted for age, sex, number of teeth, number of decayed and filled teeth, dental visit, current smoking, and occupation.

OR, odds ratio; CI, confidence interval; ref, reference; MetS, metabolic syndrome; HDL, high-density lipoprotein.

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unmea	asured f	factors.					
OR^*	P1 [‡]	$P0^{\dagger}$					
		0.05	0.1	0.2	0.3	0.5	0.8
1.8	0.05	1.68 (1.42-2.00)	1.75 (1.47-2.08)	1.88 (1.58-2.23)	2.01 (1.69-2.38)	2.27 (1.91-2.69)	2.65 (2.23-3.15)
	0.1	1.62 (1.36-1.93)	1.68 (1.42-2.00)	1.81 (1.52-2.15)	1.93 (1.63-2.30)	2.18 (1.84-2.59)	2.55 (2.15-3.04)
	0.2	1.51 (1.27-1.79)	1.57 (1.32-1.86)	1.68 (1.42-2.00)	1.80 (1.51-2.14)	2.03 (1.71-2.41)	2.38 (2.00-2.83)
	0.3	1.41 (1.19-1.68)	1.47 (1.23-1.74)	1.57 (1.33-1.87)	1.68 (1.42-2.00)	1.90 (1.60-2.26)	2.23 (1.87-2.64)
	0.5	1.25 (1.05-1.49)	1.30 (1.09-1.54)	1.39 (1.17-1.66)	1.49 (1.25, 1.77)	1.68 (1.42-2.00)	1.97 (1.66-2.34)
	0.8	1.07 (0.90-1.27)	1.11 (0.93-1.32)	1.19 (1.00-1.41)	1.27 (1.07-1.51)	1.44 (1.21-1.71)	1.68 (1.42-2.00)
2.2	0.05	1.68 (1.42-2.00)	1.78 (1.50-2.11)	1.97 (1.66-2.34)	2.16 (1.82-2.57)	2.54 (2.14-3.02)	3.11 (2.62-3.70)
	0.1	1.59 (1.34-1.89)	1.68 (1.42-2.00)	1.86 (1.57-2.21)	2.04 (1.72-2.43)	2.40 (2.02-2.86)	2.94 (2.48-3.50)
	0.2	1.44 (1.21-1.71)	1.52 (1.28-1.81)	1.68 (1.42-2.00)	1.85 (1.55-2.19)	2.17 (1.83-2.58)	2.66 (2.24-3.16)
	0.3	1.31 (1.10-1.56)	1.39 (1.17-1.65)	1.53 (1.29-1.82)	1.68 (1.42-2.00)	1.98 (1.67-2.35)	2.42 (2.04-2.88)
	0.5	1.11 (0.94-1.32)	1.18 (0.99-1.40)	1.30 (1.10-1.55)	1.43 (1.20-1.70)	1.68 (1.42-2.00)	2.06 (1.74-2.45)
	0.8	0.91 (0.77-1.08)	0.96 (0.81-1.14)	1.06 (0.90-1.26)	1.17 (0.98-1.39)	1.37 (1.16-1.63)	1.68 (1.42-2.00)

Supplementary Table 1. Estimates for odds ratio of periodontal disease for Japanese compared to Koreans with adjustment for an unmeasured factors

OR (95%CI)

OR were adjusted for diabetes, covariates, and an unmeasured factor having an OR of periodontal disease of 1.8 or 2.2.

Bold indicates that OR was not significant.

*OR of periodontal disease comparing between participants with and without an unmeasured factor.

[†]Prevalence of an unmeasured factor in Koreans

[‡]Prevalence of an unmeasured factor in Japanese

OR, odds ratio: CI, confidence interval.

	Model 1		Model 2		Model 3	
	β coefficient (95% CI)	p value	β coefficient (95% CI)	p value	β coefficient (95% CI)	p value
Country	(/ - / /		() () ()			
Korea						
Japan	0.19 (0.17; 0.21)	< 0.001	0.19 (0.17; 0.21)	< 0.001	0.19 (0.17; 0.22)	< 0.001
Diabetes						
No						
Yes	-0.04 (-0.06; -0.02)	< 0.001				
MetS						
No						
Yes			-0.03 (-0.04; -0.01)	< 0.001		
Individual MetS	components		, , , ,			
Waist	1					
Normal						
Elevated					-0.006 (-0.019; 0.006)	0.31
Fasting glucose						
Normal						
Elevated					-0.007 (-0.019; 0.005)	0.24
Triglyceride						
Normal						
Elevated					-0.007 (-0.020: 0.005)	0.25
HDL						
Normal						
Reduced					-0.007 (-0.019: 0.005)	0.23
Blood pressure						
Normal						
Elevated					-0.007 (-0.019: 0.004)	0.21
Participants who	received periodontal	examina	ation $(n - 3.428 in Ko$	rea and n –	2 153 in Japan)	0.21
Generalized line	ar models with a Pois	son prob	ability distribution us	ing number	2,155 in supurf.	variable
and country as th	he independent variat		ability distribution us	ing number	or teeth as the dependent	variable
Disbates MetS	and individual Mets	compone	nts were included in N	Model 1 2	and 3 respectively	
All models were	and multitudal Mets	number	of teeth number of d	acaved and	filled teeth dental visit	urrant
amplying and io	aujusteu tot age, sex	, number	of teeth, humber of a	ecayeu anu	inneu teetii, uentai visit, t	ullent
CL as fill in Jo	U.	-lio 1			tain	
CI, confidence f	nterval; MetS, metabo	one syna	rome; HDL, nigh dens	sity iipopro	tein.	

	Model 1		Ν	Model 2
	OR	(95% CI)	OR	(95% CI)
10-19 teeth (n = 405 in Korea				
and $n = 258$ in Japan)				
Country				
Korea	1		1	
Japan	2.53	(1.69-3.78)	2.51	(1.68-3.75)
Diabetes				
No	1			
Yes	1.14	(0.77-1.70)		
MetS				
No			1	
Yes			1.22	(0.88-1.71)
20-27 teeth (n = 1,463 in Korea)				
and $n = 1,089$ in Japan)				
Country				
Korea	1		1	
Japan	1.58	(1.20-2.07)	1.57	(1.20-2.06)
Diabetes				
No	1			
Yes	1.46	(1.14-1.86)		
MetS				
No			1	
Yes			1.06	(0.89-1.26)
\geq 28 teeth (n = 1,349 in Korea				
and $n = 720$ in Japan)				
Country				
Korea	1		1	
Japan	1.50	(1.02-2.19)	1.46	(0.99-2.14)
Diabetes				
No	1			
Yes	1.78	(1.26-2.52)		
MetS				
No			1	
Yes			1.33	(1.07-1.67)

Diabetes and MetS were included in Model 1 and 2, respectively.

All models were adjusted for age, sex, number of teeth, number of decayed and filled teeth, dental visit, current smoking, and job.

OR, odds ratio; CI, confidence interval; KNHANES, Korean National Health and Nutrition Examination Survey; MetS, metabolic syndrome.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-8
Objectives	3	State specific objectives, including any prespecified hypotheses	8
Methods			
Study design	4	Present key elements of study design early in the paper	8-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8-9
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	8-9
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-12
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	9-12
Bias	9	Describe any efforts to address potential sources of bias	13-14
Study size	10	Explain how the study size was arrived at	8-9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	12-13
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	12-13
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	8-9
		(d) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	13
Results			

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	8-9
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	8-9
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	13
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	8-9
Outcome data	15*	Report numbers of outcome events or summary measures	13
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	13
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14-15
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and	18-19
		magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from	18-19
		similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	20
		which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.