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3 **A Longitudinal Study on The Relationship Between Dental Health and Metabolic**  
4 **Syndrome in Japan**  
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28 **Running Title:** Relationship between periodontitis and metabolic syndrome  
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32 **Summary Sentence:** Since the prevalence of subjects individuals with more positive MetS  
33 components was higher in those with persistent/progressive periodontitis than in those with  
34 no/improved periodontitis, reducing periodontitis may be important for preventing pre-MetS  
35 and MetS.  
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## Abstract

**Background:** A close relationship has been reported between metabolic syndrome (MetS) and periodontitis. However, as there are only a few longitudinal studies, the association between MetS and periodontitis has not been fully elucidated. The aim of the present study was to investigate the relationships between periodontal conditions and internal changes in MetS components using a longitudinal analysis.

**Methods:** A total of 985 out of 2,716 individuals who underwent systemic medical check-ups in 2014 and 754 out of 2,454 in 2016 received dental check-ups including Community Periodontal Index. Of these, 390 individuals underwent medical and dental check-ups in 2014 and 2016 and were included and reviewed.

**Results:** Of the 390 individuals, the positive number of MetS components decreased in 62 individuals (15.9%) and increased in 104 (26.7%). A multivariate analysis identified sex (risk ratio(RR):0.55, 95% confidence interval(CI): 0.37-0.82,  $P < 0.05$ ), alcohol intake (RR:2.06, 95%CI:1.14-3.73,  $P < 0.05$ ), and the mediation of glycemia (RR:6.45, 95%CI:1.45-27.9,  $P < 0.01$ ) as significant influencing factors for MetS. The number of MetS components was higher in individuals with persistent/progressive periodontitis than in those with no/improved periodontitis (RR:1.75, 95%CI:1.14-2.70,  $P < 0.01$ ). Improvements in periodontitis had a

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4 significant positive impact on MetS components, including hypertension (RR:2.14,  
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7 95%CI:1.03-4.43, P < 0.05) and hyperglycemia (RR:2.52, 95%CI:1.27-4.98, P < 0.01), but a  
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10 negative impact on hypertension.

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16 **Conclusions:** The results of the present study suggest that since the prevalence of individuals  
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19 with more positive MetS components was higher in those with persistent/progressive  
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22 periodontitis than in those with no/improved periodontitis, reducing periodontitis may be  
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25 important for preventing pre-MetS and MetS.

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31 **Key words:** periodontal diseases, metabolic syndrome, longitudinal studies, oral health  
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## 1 Introduction

Metabolic syndrome (MetS) is a complex collection of components that are attributed to visceral fat-type obesity, including hypertension and abnormal glucose and lipid metabolism.<sup>1</sup> MetS is associated with an increased risk of cardiovascular disease and type 2 diabetes mellitus (DM). Risk factors for MetS are obesity, physical inactivity, and insulin resistance as well as aging, hormonal imbalances, and a genetic predisposition.<sup>2,3</sup> In the USA, the estimated prevalence of MetS was reported to be 34.7% in 2011-2012.<sup>4</sup> The prevalence of MetS increases with age, and the prevalence of MetS was reported 18.3% of adults aged 20-39 years and 46.7% of those aged 60 years and older.<sup>4</sup> The prevalence of MetS in middle-aged Japanese individuals was reported to be 14.9%.<sup>5</sup>

MetS is considered to originate from a pro-inflammatory state as a result of the effects of insulin resistance.<sup>6</sup> Insulin resistance is associated with increases in body mass index and waist circumference, both of which reflect increased levels of adiposity and the deposition of visceral adipose tissue.<sup>6</sup> Adipocytes and infiltrating macrophages produce cytokines, such as tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukins, and other signaling molecules associated with pro-inflammatory activity and insulin resistance.<sup>7</sup> The circulating levels of these inflammatory molecules are reported to be elevated in individuals with obesity and insulin resistance.<sup>8</sup> Additionally, insulin resistance may be associated with oxidative stress.<sup>6</sup>

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4 Systemic oxidative stress was previously shown to be significantly stronger in individuals  
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7 with than in those without MetS.<sup>9</sup>  
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10 Periodontitis revealed progressive and irreversible alveolar bone loss, loosening and  
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12 loss of teeth, which resulted from persistent infection and inflammation in response to the  
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14 periodontal pathogens.<sup>6</sup> In Japan, the prevalence of periodontitis was estimated at 33.1% in  
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16 people in their 30-34 year-old, 39.5% in 35-39, 44.9% in 40-44, and 54.1% in 50-54, with a  
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18 pocket depth of 4mm for at least one tooth, according to a nation-wide study.<sup>10</sup> A close  
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20 interactive relationship has been reported between periodontitis and MetS.<sup>1,-3,9,11-16</sup> In a  
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22 systematic review, being overweight, obesity, weight gain, and an increased weight  
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24 circumference were identified as possible risk factors for periodontitis.<sup>17</sup> Although the  
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26 biological mechanism of the association between obesity and periodontitis remains unclear,  
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28 several preinflammatory cytokines, including IL-6, IL-1, and TNF $\alpha$ , which were secreted  
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30 from adipose tissue, associated with development of periodontitis.<sup>18</sup> Among these cytokines,  
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32 especially TNF $\alpha$  induced the release of CRP and fibrinogen from liver, which amplifies the  
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34 existing inflammatory response and promotes insulin resistance.<sup>19</sup> The prevalence of MetS  
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36 was higher at 37% in individuals with severe periodontitis than at 18% in those with no/mild  
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38 periodontitis.<sup>11</sup> In comprehensive health examinations of 6,421 Japanese individuals (aged 34  
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40 to 77 years), those with a deep periodontal probing depth (PD) and high clinical attachment  
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42 level (CAL) or with moderate PD and CAL had a significantly higher odds ratio for MetS.<sup>5</sup>  
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4 Furthermore, the prevalence of a high Community Periodontal Index (CPI) code was  
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7 significantly higher in individuals with three MetS components and those with four or five  
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10 components than in those without positive components<sup>12,20</sup> However, most studies conducted  
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13 on this issue to date have been cross-sectional in nature, and due to a paucity of longitudinal  
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16 studies, difficulties are associated with establishing whether periodontitis is a risk factor for  
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19 MetS.<sup>15</sup>

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22 The basic guidelines of the Ministry of Health, Labour and Welfare in Japan suggest an  
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25 obligation of specific health check-ups focusing on visceral fat obesity by medical insurers of  
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28 the insured and their dependents aged over 40 years.<sup>21</sup> However, dental check-ups are not  
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31 included in specific health check-ups. In the present study, we performed dental check-ups on  
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34 individuals who underwent specific health check-ups and analyzed the longitudinal  
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37 relationship between dental health and internal changes in MetS components. The influence  
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40 of periodontal disease on the development of MetS and its components was discussed.

## 41 42 43 44 45 46 **2 Materials and Methods**

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49 This study protocol was approved by the Committee on Medical Research of Shinshu  
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52 University (#2775).

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55 Between 2014 and 2016, simultaneous dental check-ups were conducted on individuals  
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58 who underwent specific health check-ups in Shiojiri City, Nagano Prefecture, Japan. They  
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4 were insured by the national health insurance system in Japan (including self-employed  
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7 workers, farmers, and the elderly) and aged 30 years and older. A total of 985 out of 2,716  
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10 subjects who underwent systemic medical check-ups in 2014 (28%) and 754 out of 2,454 in  
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13 2016 (32%) received dental examinations. Of these, 390 individuals underwent medical and  
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16 dental check-ups in 2014 and 2016 and were included in the present study. There were 182  
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19 men and 208 women with a mean age  $\pm$  standard deviation (SD) of  $60.0 \pm 10.9$  years. They  
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22 all provided written informed consent to participate in the present study.  
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### 28 ***Medical check-ups***

31 Specific health check-ups were conducted according to the standard program supplied by  
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34 the Ministry of Health, Labour and Welfare of Japan (2013).<sup>22</sup> It included an interview on  
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37 lifestyle habits and systemic disease treatment status, the measurement of body height,  
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40 weight, abdominal circumference, and blood pressure, and blood tests. Subjects were asked  
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43 about any recent (within one year) smoking habit (yes or no). The frequency and amount of  
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46 alcohol consumed was noted and classified into four categories (non-drinker, occasional  
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49 drinker, daily light-moderate drinker less than 43 g, and daily heavy drinker). Questions on  
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52 midnight snacking (yes or no), regular exercise (yes or no), and the presence and absence of  
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55 medication for hypertension, lipid abnormalities, and hyperglycemia were also asked. Blood  
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58 tests included measurements of neutral fat, low/high-density lipoprotein cholesterol, blood  
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4 sugar, and hemoglobin A1C levels.  
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7       The Japanese criteria (modification of International Diabetes Federation criteria<sup>23</sup>) for  
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10 MetS were employed in the present study: (a) dyslipidemia (triglycerides  $\geq$  150 mg per dL  
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12 and/or high-density lipoprotein cholesterol (HDL-C) level  $<$ 40 mg per dL, or specific  
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14 treatments for these lipid abnormalities); (b) hypertension (systolic blood pressure  $\geq$  130  
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16 mmHg and/or diastolic blood pressure  $\geq$  85 mmHg, or the treatment of previously diagnosed  
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18 hypertension); and (c) hyperglycemia (fasting plasma glucose  $\geq$ 110 mg/dL or HbA1c  
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20 (NGSP)  $\geq$  5.6% or specific treatments for DM).<sup>24-27</sup> Waist circumference was measured at the  
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22 navel in a standing position, and visceral fat accumulation was positive at a waist  
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24 circumference  $\geq$  85 cm for men and  $\geq$  90 cm for women.  
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### 33 34 35 36 37 ***Dental check-ups*** 38 39

40       Each individual received dental check-ups in which dental and periodontal conditions  
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42 were evaluated by trained dentists. Dental check-ups included the inspection of dental and  
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44 periodontal tissues as well as oral hygiene. The presence of periodontal disease was assessed  
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46 according to the World Health Organization (WHO) CPI criteria.<sup>28</sup> Periodontal measurements  
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48 were determined by index teeth. PD was measured using standard WHO probes. Oral hygiene  
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50 was judged by the dentist and classified into three categories (good, fair, or poor). Regarding  
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52 the dentist's calibration of measuring of pocket depth, and evaluating of oral hygiene, all  
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4 dentists were trained with models.  
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### 10 *Analyses and statistical methods*

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13 Internal changes in the positive number of MetS components (obesity, hypertension,  
14 lipid abnormalities, and hyperglycemia) between 2014 and 2016 were assessed. Internal  
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16 changes in each MetS component were evaluated and classified into four categories (never;  
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18 negative-negative, improved; from negative to positive, continuing; positive-positive, and  
19  
20 developed; from negative to positive). Internal changes in regular smoking habit, alcohol  
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22 intake, midnight snacking, regular meal, medication, oral hygiene, and periodontal conditions  
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24 were also assessed and classified into four categories (never, improved, continuing, and  
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26 deterioration). Periodontal disease was assessed by the CPI index and internal changes were  
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28 classified as listed in Table 1.  
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40 As the primary endpoint, the relationships between changes in the number of MetS  
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42 components and risk factors (sex, age, smoking habit, alcohol intake, midnight snacking,  
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44 regular meal, medication, oral hygiene, periodontitis, and the number of present and  
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46 unreplaced missing teeth) were analyzed using uni- and multivariate analyses. As the  
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48 secondary endpoint, the relationships between internal changes in each MetS component and  
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50 risk factors were also analyzed. Statistical tests employed in univariate analyses were listed in  
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52 the Result sections (in Tables). In multivariate analyses, a stepwise (ordered) logistic  
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4 regression analysis was employed. Statistical analyses were performed using statistical  
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7 software\*. P-values < 0.05 were considered to be significant.  
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13 \* JMP ver.13, SAS Institute Inc., North Carolina, USA  
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### 19 **3 Results**

#### 20 **Relationships between increases/decreases in positive MetS components and risk factors**

##### 21 *(Table 2)*

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28 Among 390 individuals, the positive number of MetS components decreased in 62  
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30 individuals (15.9%) and increased in 104 (26.7%). In the univariate analysis,  
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33 increases/decreases in positive MetS components correlated with sex, age, receiving anti-  
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36 hypertensive drugs, and periodontitis. A multivariate analysis identified sex (risk  
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38 ratio(RR):0.55, 95% confidence interval(CI): 0.37-0.82, P < 0.05), alcohol intake (RR:2.06,  
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40 95%CI:1.14-3.73, P < 0.05), the mediation of glycemia (RR:6.45, 95%CI:1.45-27.9, P <  
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42 0.01), and periodontitis (RR:1.75, 95%CI:1.14-2.70, P < 0.01) as significant influencing  
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45 factors for MetS. The proportion of patients with positive MetS components was higher in  
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48 women than in men, in those who quit drinking or had started drinking than those who never  
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51 drunk or continued drinking, in those who were not on hyperlipidemia medications or  
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54 continued these medications than those who started these medications, and in those who had  
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4 persistent or progressive periodontitis than those who did not have periodontitis or had  
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7 improved symptoms.  
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### 10 11 12 **Relationships between internal changes in hypertension and risk factors (Table 3)**

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16 Between 2014 and 2016, 199 (21.4%) had no, 26 (2.8%) improved, 136 (14.6%)  
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18 continuing, and 29 (3.1%) developed hypertension. In the univariate analysis, hypertension  
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20 correlated with sex, age, alcohol intake, receiving anti-hypertensive drugs, and periodontitis.  
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23 The multivariate analysis revealed that age (RR:1.04, 95%CI:1.02-1.07,  $P < 0.0$ ), regular  
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25 smoking habit (RR:2.79, 95%CI:1.09-7.06,  $P < 0.05$ ), receiving anti-hypertensive drugs  
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27 (RR:10.6, 95%CI:6.47-17.8,  $P < 0.01$ ), and periodontitis (RR:2.14, 95%CI:1.03-4.43,  $P <$   
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29 0.05) had a significant impact on hypertension. Individuals without a history of hypertension  
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31 were younger than those with a history of hypertension. The prevalence of hypertension was  
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33 lower in non-smokers than in others, and was also lower in subjects without than in those  
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35 with a history of receiving anti-hypertensive drugs. Regarding periodontitis, a significant  
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37 difference was observed between improved and other individuals. The crisis rate was higher  
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39 in individuals with improved periodontitis, and the improvement rate was higher in those  
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41 with progressive periodontitis.  
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### 58 **Relationships between internal changes in lipid abnormalities and risk factors (Table 4)**

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4 Throughout the study period, 226 individuals (57.9%) had no, 35 (8.9%) improved,  
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7 102 (26.2%) continuing, and 27 (6.9%) developed lipid abnormalities. In the univariate  
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10 analysis, internal changes in lipid abnormalities correlated with age, regular smoking habit,  
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13 alcohol intake, and receiving anti-hyperlipidemic drugs. These changes were also associated  
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16 with sex ( $p = 0.09$ ). The multivariate analysis revealed that internal changes in lipid  
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19 abnormalities correlated with sex (RR:0.58, 95%CI:0.38-0.88,  $P < 0.05$ ) and receiving anti-  
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22 hyperlipidemic drugs (RR:15.2, 95%CI:9.05-26.4,  $P < 0.01$ ). The prevalence of lipid  
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25 abnormalities was higher in men than in women. It was also higher in subjects who had  
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28 received anti-hyperlipidemic drugs than in those who had not. In addition, the cessation of  
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31 drinking had a slightly negative impact on lipid abnormalities.  
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### 37 **Relationships between internal changes in hyperglycemia and risk factors (Table 5)**

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40 Throughout the study period, 256 individuals (65.6%) had no, 63 (16.2%) improved, 53  
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43 (13.6%) continuing, and 18 (4.6%) developed hyperglycemia. In the univariate analysis, a  
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46 correlation was observed between internal changes in hyperglycemia and age or medication.  
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49 A relationship was noted between hyperglycemia and sex, oral hygiene, periodontitis, and the  
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52 number of present teeth. The multivariate analysis showed that age (RR:1.07, 95%CI:1.04-  
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55 1.10,  $P < 0.01$ ), receiving anti-hyperglycemic drugs (RR:11.7, 95%CI:5.33-26.6,  $P < 0.01$ ),  
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58 and periodontitis (RR:2.52, 95%CI:1.27-4.98,  $P < 0.01$ ) had a significant impact on  
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4 hyperglycemia. Subjects with no history of hyperglycemia were younger than those with a  
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6 history of hyperglycemia. The prevalence of hyperglycemia was higher in those who use  
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8 drugs to mediate glycemia. Regarding periodontitis, the prevalence of hyperglycemia was  
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10 higher in those with persistent periodontitis than in other subjects.  
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### 19 **Relationships between internal changes in obesity and risk factors (Table 6)**

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22 Throughout the study period, obesity was not observed in 295 (75.6%) individuals.  
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25 Obesity improved in 12 subjects (3.1%), persisted in 70 (17.9%), and newly developed in 13  
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27 (3.3%). Internal changes in obesity correlated with sex, regular smoking habit, medication  
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29 (drugs for hypertension, lipid abnormalities, and the mediation of glycemia), and oral hygiene  
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31 in univariate analyses. A relationship was also found between obesity and alcohol intake or  
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33 periodontitis. The results of the multivariate analysis revealed that sex (RR:0.14,  
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35 95%CI:0.07-0.25,  $P < 0.01$ ), regular exercise (RR:2.66, 95%CI:1.07-6.56,  $P < 0.05$ ), drugs  
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37 for lipid abnormalities (RR:2.32, 95%CI:1.21-4.43,  $P < 0.05$ ) or the mediation of  
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39 hypertension (RR:1.93, 95%CI:1.08-3.42,  $P < 0.05$ ), and the number of present teeth  
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41 (RR:1.11, 95%CI:1.01-1.23,  $P < 0.05$ ) had a significant influence on obesity. The prevalence  
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43 of obesity was higher in men than in women, and was lower in subjects with a previous and  
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45 current habit of regular exercise. Individuals who had taken and discontinued anti-  
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47 hyperlipidemic drugs and those receiving drugs for the mediation of hypertension had a  
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4 higher prevalence of obesity. Regarding periodontitis, individuals with persistent  
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7 periodontitis had a higher prevalence of obesity than others. The prevalence of obesity was  
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10 also higher in those with a higher change of number of present teeth.  
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#### 16 **4 Discussion**

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19 The Ministry of Health, Labour and Welfare in Japan requires specific health check-  
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22 ups focusing on visceral fat obesity by medical insurers of the insured and their dependents  
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25 aged over 40 years.<sup>21</sup> Although a close relationship has been reported between periodontitis  
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28 and MetS,<sup>1-3,6,9,11-16</sup> specific health check-ups did not include dental check-ups, such as the  
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31 evaluation of dental and periodontal conditions. Additionally, internal changes in the  
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34 components of MetS have not yet been investigated in a longitudinal study. Therefore, the  
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37 aim of the present study was to examine the relationship between dental conditions and  
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40 internal changes in MetS components using a longitudinal analysis.  
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44 A close relationship has been reported between periodontal conditions and MetS. The  
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46 number of positive MetS components was previously shown to correlate with gingivitis, even  
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49 in participants aged 12-18 years.<sup>16</sup> A meta-analysis revealed that individuals with MetS were  
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52 approximately 2-fold more likely to have periodontitis than those without.<sup>14</sup> Japanese  
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55 individuals with deep PD ( $\geq 6$  mm) and high CAL ( $\geq 6$  mm) and moderate PD (4–5 mm) and  
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58 moderate CAL (4-5 mm) had a significantly higher risk of developing MetS.<sup>5</sup> Similarly, a  
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4 higher CPI code was associated with the presence of a greater number of MetS components.<sup>12</sup>  
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7 The prevalence of MetS was 18% in individuals with no/mild periodontitis, but was 37% in  
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9 those with severe periodontitis (classified by the clinical criteria of Page & Eke<sup>29</sup>).<sup>11</sup> In the  
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11 present study, the prevalence of individuals with more positive MetS components correlated  
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13 with sex, alcohol intake, medication for the mediation of glycemia, and periodontitis. Since  
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15 the prevalence of individuals with more positive MetS components was higher in those with  
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17 persistent/progressive periodontitis than in those with no/improved periodontitis, reducing  
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19 periodontitis may be important for the preventing pre-MetS and MetS.  
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28 The present results showed that periodontitis correlated with each component of MetS,  
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30 including obesity and hyperglycemia, in consideration of other risk factors. These results  
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32 suggest a direct causal relationship between periodontitis and these MetS components. A  
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34 cross-sectional study on Japanese adult male and female employees aged between 20 and 59  
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36 years revealed that individual components of MetS, including obesity, hypertension, lipid  
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38 abnormalities, and hyperglycemia, were associated with periodontal disease.<sup>1</sup> Additionally, in  
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40 a cohort study during a 4-year observation period, the presence of periodontal pockets was  
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42 associated with the positive conversion of one or more MetS components.<sup>13</sup> Among MetS  
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44 components, the positive conversion of blood pressure and the blood-lipid index correlated  
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46 with the presence of periodontal pockets.<sup>13</sup> Individuals with untreated MetS have been  
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48 reported to present with markedly worse periodontal conditions than healthy participants.  
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4 However, in the present study, lipid abnormalities and hypertension did not correlate with  
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7 periodontitis. In parallel with improvements in periodontal conditions, systolic and diastolic  
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10 blood pressure and endothelial microparticles were markedly smaller in an intensive  
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13 periodontal treatment group than in a control group.<sup>30</sup> Therefore, the relationship between  
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16 hypertension and periodontitis is controversial. Regarding hyperlipidemia, although a  
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19 relationship was not observed between hyperlipidemia and periodontitis, the number of  
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22 present teeth was correlated with the status of periodontitis. Additionally, obesity  
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25 correlated with the number of present teeth. Generally, tooth loss reduces masticatory ability  
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28 and may lead to the consumption of a less healthy diet, such as a soft and high-fat diet.<sup>31-33</sup> A  
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31 high-fat diet has been reported to cause periodontitis in mice,<sup>34</sup> and increased serum  
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34 triglyceride levels were observed in rats with periodontitis induced by the administration of  
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37 *Porphyromonas gingivalis*.<sup>35</sup> Individuals with periodontitis had higher levels of triglycerides,  
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40 total cholesterol, and low-density lipoprotein cholesterol than those with healthy periodontal  
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43 tissue.<sup>36-39</sup> Therefore, a bi-directional relationship reportedly exists between periodontitis and  
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46 hyperlipidemia.<sup>40</sup> Additionally, obesity has been reported to have a deleterious effect on lipid  
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49 profiles, leading to increased levels of triglycerides, total cholesterol, and low-density  
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52 lipoprotein cholesterol.<sup>41</sup>  
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55 Previous studies reported that the prevention of periodontitis may prevent MetS. In a  
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58 double-blinded clinical randomized study, periodontal therapy, including root planning +  
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4 systemic antibiotics or plaque control + subgingival scaling, was demonstrated to  
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7 successfully decrease C-reactive protein levels in MetS patients.<sup>42</sup> Since more frequent tooth  
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10 brushing has been related to a lower prevalence and incidence of MetS, it may contribute to  
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13 the prevention of MetS due to the inflammation/triglyceride pathway.<sup>43</sup> Therefore, team work  
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16 between dentists and physicians is important.

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19 The strength of the present study is that it was a longitudinal analysis that investigated  
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22 the relationship between Mets and dental health. The inclusion of dental check-ups in specific  
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25 health check-ups may reduce the risk of developing MetS. The limitation of the present study  
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28 was that the causal relationship (whether risk factors changed due to treatments or changes in  
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31 MetS) is unknown for internal changes in risk factors and Mets components. Another  
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34 limitation of this study was that dentist's calibrations of periodontal measurements might  
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37 affect the outcomes of this study. In this study, although periodontal measurements were  
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40 determined by index teeth, the accuracy of measuring CPI was reported to vary with dentist  
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43 during the training process.<sup>44,45</sup> CPI was reported to vary between studies and such variation  
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46 would affect the effect of each predictor on risk for periodontal diseases.<sup>46</sup> Therefore, since  
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49 the dental model was reported to be effective for periodontal pocket robing training and for  
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52 the evaluation and standardization of examiner's probing skill,<sup>46</sup> all dentists participated in  
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55 this study were trained with dental models for dentist's calibration. Further studies are needed  
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58 to clarify this issue based on an intervention trial.  
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## 5 Conclusion

The aim of the present study was to investigate the longitudinal relationship between dental health and internal changes in MetS components with the combination of specific health check-ups and dental check-ups. The results obtained suggest that since the prevalence of individuals with more positive MetS components was higher among those with persistent/progressive periodontitis than among those with no/improved periodontitis, reducing periodontitis may be important for the preventing pre-MetS and MetS. Therefore, the addition of dental check-ups to specific health check-ups is warranted in an attempt to reduce common risk factors.

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**Tables**
**Table 1.** Assessment of internal changes in periodontitis

<b>Periodontitis</b>	<b>2014</b>		<b>2016</b>
<b>Never</b>	CPI 0, 1, 2	→	CPI 0, 1, 2
<b>Improved</b>	CPI 3, 4	→	CPI 0, 1, 2
	CPI 4	→	CPI 3
<b>Continuing</b>	CPI 3, 4	→	CPI 3, 4
<b>Progressed</b>	CPI 0, 1, 2	→	CPI 3, 4
	CPI 3	→	CPI 4



**Table 2.** Association between increase of positive metabolic syndrome (Mets) components and the influencing factors

	(No.)	Increase of No. of Mets components (n)							Prevalence of those with increased positive components	Result of univariate analysis		Result of multivariate analysis †	
		-3 (2)	-2 (8)	-1 (52)	0 (224)	+1 (87)	+2 (15)	+3 (2)		p-value	test name	Crude odds ratio (95% C.I.)	Adjusted odds ratio (95% C.I.)
Sex	Woman (208)		2	20	125	54	6	1	29.3%	< 0.05	Goodness test of fit for chi-square	0.54 (0.35-0.81) p < 0.01 0.55 (0.37-0.82) p < 0.01 (man vs woman)	
	Man (182)	2	6	32	99	33	9	1	23.6%				
Age (at 2014)	Mean (SD)	58.5 (14.5)	60.4 (10.6)	61.9 (8.7)	59.0 (11.5)	63.3 (8.8)	58.7 (13.4)	73.0 (0.0)	-	< 0.05	Kruskal Wallis test	0.99 (0.97-1.01) NS	NS
Recent smoking	Never (371)	2	7	49	213	85	13	2	27.0%	NS	Goodness test of fit for chi-square	2.00 (0.14-25.1) NS NS	
	Stop smoking (6)		1		4		1		16.7%				
	Continuing (11)			2	6	2	1		27.3%				
Alcohol drinking behavior	Start smoking (2)			1	1				0.0%				
	Never (172)	1	3	18	98	43	7	2	30.2%	NS	Goodness test of fit for chi-square	1.86 (1.02-3.43) p < 0.05 2.06 (1.14-3.73) < 0.05 (never/continuing vs stop/start drinking)	
	Stop drinking (25)	1	1	5	12	6			24.0%				
	Continuing (168)		3	23	100	35	7		25.0%				
Start drinking (25)		1	6	14	3	1		16.0%					
Mid night snack	Never (340)	2	4	44	198	78	12	2	27.1%	NS	Goodness test of fit for chi-square	1.92 (0.88-4.17) NS NS	
	Stop eating (17)		2	3	8	3	1		23.5%				
	Continuing (20)		1	2	11	4	2		30.0%				
	Start eating (13)		1	3	7	2			15.4%				
Regular exercise	Continuing (88)			19	48	19	1	1	23.9%	NS	Goodness test of fit for chi-square	1.57 (0.89-2.75) NS NS	
	Start exercise (55)		1	5	29	18	2		36.4%				
	No (217)	2	6	23	131	44	10	1	25.3%				
Antihypertensive drug	Stop exercise (30)		1	5	16	6	2		26.7%				
	Never (284)	2	6	37	162	65	12		27.1%	< 0.01	Goodness test of fit for chi-square	1.18 (0.73-1.91) NS NS	
	Cessation (5)		1		2	2			40.0%				
Continuing (88)			11	56	18	2	1	23.9%					
Antihyperlipemic drug	Start drug (13)		1	4	4	2	1	1	30.8%				
	Never (313)	2	7	42	180	67	14	1	26.2%	NS	Goodness test of fit for chi-square	2.63 (0.76-8.89) NS NS	
	Cessation (3)			1	2	2			66.7%				
Continuing (64)			8	37	17	1	1	29.7%					
Drug for glycemia	Start drug (10)		1	2	6	1			10.0%				
	Never (370)	2	7	48	210	86	15	2	27.8%	NS	Goodness test of fit for chi-square	6.13 (1.38-26.3) p < 0.05 6.45 (1.45-27.9) p < 0.05 (never/continuing vs start)	
	Cessation (0)								-				
Continuing (14)			2	11	1			7.1%					
Oral hygiene	Start drug (6)		1	2	3				0.0%				
	Keep good (348)	1	7	48	202	76	13	1	25.9%	NS	Goodness test of fit for chi-square	2.59 (0.60-11.0) NS NS	
	Improved (7)				4	2	1		42.9%				
Still bad (7)		1	2	2	2			28.6%					
Periodontitis	Become worse (28)	1		2	16	7	1	1	32.1%				
	Never (236)	1	6	28	150	40	10	1	21.6%	< 0.01	Goodness test of fit for chi-square	1.61 (1.04-2.50) p < 0.05 1.75 (1.14-2.70) p < 0.01 (continuing/progressed vs never/improved)	
	Improved (35)	1		9	15	9		1	28.6%				
	Continuing (33)			7	13	12	1		39.4%				
Progressed (84)		2	8	45	26	3		34.5%					
Change of No. of present teeth (2016-2014)	missing data (2)				1		1		-				
	Mean (SD)	1.5 (1.5)	0.1 (2.0)	0.1 (1.6)	0.4 (2.8)	-0.1 (1.9)	-0.1 (1.5)	0.0 (0.0)	-	NS	Kruskal Wallis test	1.03 (0.95-1.11) NS	NS
Change of No. of unreplaced missing teeth (2016-2014)	Mean (SD)	0.0 (0.0)	0.1 (0.8)	0.2 (0.8)	0.0 (0.9)	0.2 (0.7)	0.1 (0.3)	1.5 (1.5)	-	NS	Kruskal Wallis test	0.91 (0.71-1.15) NS	NS

**Table 3.** Relationships between internal changes in hypertension and influencing factors

	(No.)	Hypertension				Prevalence*1	Improve rate*2	Crisis rate*3	Result of univariate analysis		Result of multivariate analysis †	
		Never (199)	Improved (26)	Continuing (136)	Developed (29)				p-value	test name	Crude odds ratio (95% C.I.)	Adjusted odds ratio (95% C.I.)
Sex	Woman (208)	115	18	64	11	36.1%	8.7%	5.3%	< 0.05	Pearson's chi-square test	0.73 (0.47-1.13) NS	NS
	Man (182)	84	8	72	18	49.5%	4.4%	9.9%				
Age (at 2014)	Mean (SD)	56.5 (12.3)	66.5 (4.3)	64.8 (7.2)	61.4 (8.0)	-	-	-	< 0.01	Kruskal Wallis test	1.04 (1.02-1.07) p<0.01	1.04 (1.02-1.07) p< 0.01
Recent smoking	Never (371)	193	25	127	26	41.2%	6.7%	7.0%	NS	Pearson's chi-square test	2.12 (0.79-5.59) NS	2.79 (1.09-7.06) p< 0.05 (others vs never)
	Stop smoking (6)	1	1	4	0	66.7%	16.7%	0.0%				
	Continuing (11)	4	0	5	2	63.6%	0.0%	18.2%				
Alcohol drinking behavior	Start smoking (2)	1	0	0	1	50.0%	0.0%	50.0%				
	Never (172)	93	18	52	9	35.5%	10.5%	5.2%	< 0.05	Pearson's chi-square test	1.63 (0.85-3.07) NS	NS
	Stop drinking (25)	8	2	12	3	60.0%	8.0%	12.0%				
	Continuing (168)	87	4	64	13	45.8%	2.4%	7.7%				
Mid night snack	Start drinking (25)	11	2	8	4	48.0%	8.0%	16.0%				
	Never (340)	172	23	123	22	42.6%	6.8%	6.5%	NS	Pearson's chi-square test	0.82 (0.30-2.50) NS	NS
	Stop eating (17)	7	1	7	2	52.9%	5.9%	11.8%				
Regular exercise	Continuing (20)	13	1	4	2	30.0%	5.0%	10.0%				
	Start eating (13)	7	1	2	3	38.5%	7.7%	23.1%				
	Continuing (88)	44	3	32	9	46.6%	3.4%	10.2%	NS	Pearson's chi-square test	1.48 (0.62-3.78) NS	NS
Antihypertensive drug	Start exercise (55)	23	6	24	2	47.3%	10.9%	3.6%				
	Never (217)	112	15	76	14	41.5%	6.9%	6.5%				
	Stop exercise (30)	20	2	4	4	26.7%	6.7%	13.3%				
	Never (284)	199	21	38	26	22.5%	7.4%	9.2%	< 0.01	Pearson's chi-square test	10.1 (6.12-17.1) p<0.01	10.6 (6.47-17.8) p< 0.01 (others vs never)
Oral hygiene	Cessation (5)	0	2	3	0	60.0%	40.0%	0.0%				
	Continuing (88)	0	2	86	0	97.7%	2.3%	0.0%				
	Start drug (13)	0	1	9	3	92.3%	7.7%	23.1%				
	Keep good (348)	181	23	116	28	41.4%	6.6%	8.0%	NS	Pearson's chi-square test	2.71 (0.62-12.1) NS	NS
Periodontitis	Improved (7)	4	0	3	0	42.9%	0.0%	0.0%				
	Still bad (7)	0	1	5	1	85.7%	14.3%	14.3%				
	Become worse (28)	14	2	12	0	42.9%	7.1%	0.0%				
	Never (236)	131	13	76	16	39.0%	5.5%	6.8%	< 0.05	Pearson's chi-square test	2.30 (1.10-4.81) p< 0.05	2.14 (1.03-4.43) p< 0.05 (Improved vs others)
Change of No. of present teeth (2016-2014)	Improved (35)	14	2	12	7	54.3%	5.7%	20.0%				
	Continuing (33)	15	1	16	1	51.5%	3.0%	3.0%				
	Progressed (84)	39	9	31	5	42.9%	10.7%	6.0%				
	missing data (2)	0	1	1	0	-	-	-				
Change of No. of unreplaced missing teeth (2016-2014)	Mean (SD)	0.2 (2.5)	0.5 (1.4)	0.2 (2.8)	-0.2 (1.1)	-	-	-	NS	Kruskal Wallis test	0.95 (0.86-1.04) NS	NS
	Mean (SD)	0.0 (0.8)	0.2 (0.7)	0.1 (0.8)	0.3 (1.0)	-	-	-	NS	Kruskal Wallis test	1.13 (0.86-1.47) NS	NS

\*1: Prevalence = (continuing + developed)/all subjects

\*3: Crisis rate = (Developed)/all subjects

\*2: Improvement rate =(Improve)/all subjects

†: A stepwise ordered logistic regression analysis

**Table 4.** Relationships between internal changes in lipid abnormalities and influencing factors

	(No.)	Lipid abnormality				Prevalence* 1	Improve rate*2	Crisis rate*3	Result of uni variate analysis		Result of multivariate analysis †			
		Never (226)	Improve (35)	Continuing (102)	Developed (27)				p-value	test name	Crude odds ratio (95% C.I.)	Adjusted odds ratio (95% C.I.)		
Sex	Woman (208)	132	18	47	11	27.9%	8.7%	5.3%	0.09	Pearson's chi-squared test	0.60 (0.40-0.90)	< 0.05	0.58 (0.38-0.88)	p < 0.05 (woman vs man)
	Man (182)	94	17	55	16	39.0%	9.3%	8.8%						
Age (at 2014)	Mean (SD)	59.0 (11.6)	60.1 (12.7)	64.0 (7.7)	59.0 (9.3)	-	-	-	< 0.01	Kruskal Wallis test	1.02 (1.00-1.04)	< 0.05		NS
Recent smoking	Never (371)	220	34	91	26	31.5%	9.2%	7.0%	< 0.01	Pearson's chi-squared test	0.00 (0.00-2.17)	NS		NS
	Stop smoking (6)	2	1	2	1	50.0%	16.7%	16.7%						
	Continuing (11)	2		9		81.8%	0.0%	0.0%						
	Start smoking (2)	2				0.0%	0.0%	0.0%						
Alcohol drinking behavior	Never (172)	104	18	41	9	29.1%	10.5%	5.2%	< 0.05	Pearson's chi-squared test	1.73 (0.93-3.17)	NS		NS
	Stop drinking (25)	10		11	4	60.0%	0.0%	16.0%						
	Continuing (168)	95	16	45	12	33.9%	9.5%	7.1%						
	Start drinking (25)	17	1	5	2	28.0%	4.0%	8.0%						
Mid night snack	Never (340)	203	29	86	22	31.8%	8.5%	6.5%	NS	Pearson's chi-squared test	2.36 (1.13-4.91)	< 0.05		NS
	Stop eating (17)	7	1	6	3	52.9%	5.9%	17.6%						
	Continuing (20)	11	4	5		25.0%	20.0%	0.0%						
	Start eating (13)	5	1	5	2	53.8%	7.7%	15.4%						
Regular exercise	Continuing (88)	48	5	31	4	39.8%	5.7%	4.5%	NS	Pearson's chi-squared test	1.10 (0.62-2.01)	NS		NS
	Start exercise (55)	32	5	14	4	32.7%	9.1%	7.3%						
	Never (217)	130	21	47	19	30.4%	9.7%	8.8%						
Antihyperlipemic drug	Stop exercise (30)	16	4	10		33.3%	13.3%	0.0%						
	Never (313)	226	31	33	23	17.9%	9.9%	7.3%	< 0.001	Pearson's chi-squared test	13.5 (4.18-46.7)	p < 0.01	15.2 (9.05-26.4)	p < 0.01 (others vs never)
	Cessation (3)		2	1		33.3%	66.7%	0.0%						
	Continuing (64)		2	62		96.9%	3.1%	0.0%						
Oral hygiene	Start drug (10)			6	4	100.0%	0.0%	40.0%						
	Keep good (348)	207	29	88	24	32.2%	8.3%	6.9%	NS	Pearson's chi-squared test	1.12 (0.28-5.56)	NS		NS
	Improved (7)	4	2	1		14.3%	28.6%	0.0%						
	Still bad (7)	2		3	2	71.4%	0.0%	28.6%						
Periodontitis	Become worse (28)	13	4	10	1	39.3%	14.3%	3.6%						
	Never (236)	141	18	60	17	32.6%	7.6%	7.2%	NS	Pearson's chi-squared test	0.87 (0.56-1.35)	NS		NS
	Improved (35)	22	3	6	4	28.6%	8.6%	11.4%						
	Continuing (33)	17	3	12	1	39.4%	9.1%	3.0%						
	Progressed (84)	45	10	24	5	34.5%	11.9%	6.0%						
missing data (2)	1	1			-	-	-							
Change of No. of present teeth (2016-2014)	Mean (SD)	0.4 (2.95)	0.1 (1.1)	-0.1 (1.4)	0.0 (1.6)	-	-	-	NS	Kruskal Wallis test	0.89 (0.78-1.00)	p = 0.07		NS
Change of No. of unreplaced missing teeth (2016-2014)	Mean (SD)	0.1 (0.9)	0.3 (0.7)	0.1 (0.8)	0.0 (0.5)	-	-	-	NS	Kruskal Wallis test	0.92 (0.72-1.17)	NS		NS

\*1: Prevalence = (continuing + developed)/all subjects

\*3: Crisis rate = (Developed)/all subjects

\*2: Improvement rate = (Improve)/all subjects

†: A stepwise ordered logistic regression analysis

**Table 5.** Relationships between internal changes in hyperglycemia and influencing factors

	(No.)	Hyperglycemia				Prevalence*1	Improve rate*2	Crisis rate*3	Result of uni variate analysis		Result of multivariate analysis †		
		Never (256)	Improve (63)	Continuing (53)	Developed (18)				p-value	testname	Crude odds ratio (95% C.I.)	Adjusted odds ratio (95% C.I.)	
Sex	Woman (208)	138	40	21	9	14.4%	19.2%	4.3%	0.08	Pearson's chi-squared test	1.20 (0.75-1.13)	NS	NS
	Man (182)	118	23	32	9	22.5%	12.6%	4.9%					
Age (at 2014)	Mean (SD)	58.0 (11.7)	64.5 (7.4)	64.8 (6.5)	68.2 (6.7)	-	-	-	< 0.01	Kruskal Wallis test	1.07 (1.04-1.10)	p<0.01	1.07 (1.04-1.10) p< 0.01
Recent smoking	Never (371)	245	60	48	18	17.8%	16.2%	4.9%	NS	Pearson's chi-squared test	1.36 (0.40-4.98)	NS	NS
	Stop smoin (6)	5		1		16.7%	0.0%	0.0%					
	Continuing (11)	4	3	4		36.4%	27.3%	0.0%					
	Strart smoking (2)	2				0.0%	0.0%	0.0%					
Alcohol drinking behavior	Never (172)	115	30	19	8	15.7%	17.4%	4.7%	NS	Pearson's chi-squared test	1.21 (0.76-26.6)	NS	NS
	Stop drinking (25)	15	4	4	2	24.0%	16.0%	8.0%					
	Continuing (168)	107	28	26	7	19.6%	16.7%	4.2%					
	Strart drinking (25)	19	1	4	1	20.0%	4.0%	4.0%					
Mid night snack	Never (340)	225	56	44	15	17.4%	16.5%	4.4%	NS	Pearson's chi-squared test	1.66 (0.72-2.50)	NS	NS
	Stop eating (17)	10	3	3	1	23.5%	17.6%	5.9%					
	Continuing (20)	14	3	2	1	15.0%	15.0%	5.0%					
Regular exercise	Start eating (13)	7	1	4	1	38.5%	7.7%	7.7%					
	Continuing (88)	49	18	15	6	23.9%	20.5%	6.8%	NS	Pearson's chi-squared test	1.33 (0.84-3.78)	NS	NS
	Start exercise (55)	32	11	10	2	21.8%	20.0%	3.6%					
Drug for glycemia	Never (217)	150	31	27	9	16.6%	14.3%	4.1%					
	Stop exercise (30)	25	3	1	1	6.7%	10.0%	3.3%					
	Never (370)	256	63	33	18	13.8%	17.0%	4.9%	< 0.001	Pearson's chi-squared test	11.5 (5.10-26.5)	p<0.01	11.7 (5.33-26.6) p< 0.01 (others vs never)
	Cessation (0)					-	-	-					
Oral hygiene	Continuing (14)			14		100.0%	0.0%	0.0%					
	Start drug (6)			6		100.0%	0.0%	0.0%					
	Keep good (348)	231	56	46	15	17.5%	16.1%	4.3%	0.066	Pearson's chi-squared test	2.28 (0.56-8.84)	NS	NS
	Improved (7)	6	1			0.0%	14.3%	0.0%					
	Still bad (7)	2	1	4		57.1%	14.3%	0.0%					
Periodontitis	Become worse (28)	17	5	3	3	21.4%	17.9%	10.7%					
	Never (236)	167	33	28	8	15.3%	14.0%	3.4%	0.055	Pearson's chi-squared test	2.23 (1.09-4.55)	p<0.05	2.52 (1.27-4.98) p< 0.01 (continuing vs others)
	Improved (35)	20	9	5	1	17.1%	25.7%	2.9%					
	Continuing (33)	12	9	8	4	36.4%	27.3%	12.1%					
	Progressed (84)	55	12	12	5	20.2%	14.3%	6.0%					
Change of No. of prsent teeth (2016-2014)	missing data (2)	2				-27.3%	-	-					
	Mean (SD)	0.3 (2.5)	-0.4 (2.1)	0.2 (1.5)	1.2 (2.3)	-	-	-	0.078	Kruskal Wallis test	0.98 (0.89-1.08)	NS	NS
Change of No. of unreplaced missingteeth (2016-2014)	Mean (SD)	0.0 (0.9)	0.3 (0.7)	0.2 (0.7)	0.1 (0.7)	-	-	-	NS	Kruskal Wallis test	1.04 (0.80-1.35)	NS	NS

\*1: Prevalence = (continuing + developed)/all subjects

\*3: Crisis rate = (Developed)/all subjects

\*2: Improvement rate =(Improve)/all subjects

†: A stepwise ordered logistic regression analysis

**Table 6.** Relationships between internal changes in obesity and influencing factors

	(No.)	Obese				Prevalence*1	Improve rate*2	Crisis rate*3	Result of univariate analysis		Result of multivariate analysis †			
		Never (295)	Improve (12)	Continuing (70)	Developed (13)				p-value	test name	Crude odds ratio (95% C.I.)		Adjusted odds ratio (95% C.I.)	
<b>Sex</b>	Woman (208)	189	1	17	1	8.7%	0.5%	0.5%	< 0.01	Pearson's chi-squared test	0.13 (0.07-0.25)	p<0.01	0.14 (0.07-0.25)	p<0.01
	Man (182)	106	11	53	12	35.7%	6.0%	6.6%						
<b>Age (at 2014)</b>	Mean (SD)	60.6 (11.0)	54.0 (14.4)	61.2 (8.8)	59.2 (11.4)	-	-	-	NS	Kruskal Wallis test	0.97 (0.95-1.00)	NS		NS
<b>Recent smoking</b>	Never (371)	288	10	62	11	19.7%	2.7%	3.0%	< 0.01	Pearson's chi-squared test	2.23 (0.89-5.49)	NS	2.66 (1.07-6.56)	p<0.05
	Stop smoking (6)	3		2	1	50.0%	0.0%	16.7%						
	Continuing (11)	3	2	5	1	54.5%	18.2%	9.1%						
	Start smoking (2)	1		1		50.0%	0.0%	0.0%						
<b>Alcohol drinking behavior</b>	Never (172)	140	2	24	6	17.4%	1.2%	3.5%	0.09	Pearson's chi-squared test	0.99 (0.57-1.70)	NS		NS
	Stop drinking (25)	15		9	1	40.0%	0.0%	4.0%						
	Continuing (168)	120	9	34	5	23.2%	5.4%	3.0%						
	Start drinking (25)	20	1	3	1	16.0%	4.0%	4.0%						
<b>Mid night snack</b>	Never (340)	261	10	60	9	20.3%	2.9%	2.6%	NS	Pearson's chi-squared test	1.74 (0.76-3.85)	NS		NS
	Stop eating (17)	10	1	4	2	35.3%	5.9%	11.8%						
	Continuing (20)	14	1	3	2	25.0%	5.0%	10.0%						
	Start eating (13)	10		3		23.1%	0.0%	0.0%						
<b>Regular exercise</b>	Continuing (88)	70	2	12	4	18.2%	2.3%	4.5%	NS	Pearson's chi-squared test	1.77 (0.98-3.28)	NS		NS
	Start exercise (55)	39	2	13	1	25.5%	3.6%	1.8%						
	Never (217)	162	7	42	6	22.1%	3.2%	2.8%						
	Stop exercise (30)	24	1	3	2	16.7%	3.3%	6.7%						
<b>Antihypertensive drug</b>	Never (284)	229	9	37	9	16.2%	3.2%	3.2%	< 0.01	Pearson's chi-squared test	1.96 (1.03-3.72)	p<0.05	1.93 (1.08-3.42)	p<0.05
	Cssation (5)	4	1			0.0%	20.0%	0.0%						
	Continuing (88)	55	1	29	3	36.4%	1.1%	3.4%						
	Start drug (13)	7	1	4	1	38.5%	7.7%	7.7%						
<b>Antihyperlipemic drug</b>	Never (313)	249	10	44	10	17.3%	3.2%	3.2%	< 0.01	Pearson's chi-squared test	2.60 (1.31-5.14)	p<0.01	2.32 (1.21-4.43)	p<0.05
	Cessation (3)	2		1		33.3%	0.0%	0.0%						
	Continuing (64)	37		25	2	42.2%	0.0%	3.1%						
	Start drug (10)	7	2		1	10.0%	20.0%	10.0%						
<b>Drug for glycemia</b>	Never (370)	217	34	93	26	32.2%	9.2%	7.0%	< 0.001	Pearson's chi-squared test	2.37 (0.90-6.08)	NS		NS
	Cssation (0)					-	-	-						
	Continuing (14)	7	1	6		42.9%	7.1%	0.0%						
	Start drug (6)	2		3	1	66.7%	0.0%	16.7%						
<b>Oral hygiene</b>	Keep good (348)	207	29	88	24	32.2%	8.3%	6.9%	< 0.05	Pearson's chi-squared test	3.40 (0.79-14.5)	NS		
	Improved (7)	4	2	1		14.3%	28.6%	0.0%						
	Still bad (7)	2		3	2	71.4%	0.0%	28.6%						
	Become worse (28)	13	4	10	1	39.3%	14.3%	3.6%						
<b>Periodontitis</b>	Never (236)	141	18	60	17	32.6%	7.6%	7.2%	0.09	Pearson's chi-squared test	1.28 (0.73-2.22)	NS		NS
	Improved (35)	22	3	6	4	28.6%	8.6%	11.4%						
	Continuing (33)	17	3	12	1	39.4%	9.1%	3.0%						
	Progressed (84)	45	10	24	5	34.5%	11.9%	6.0%						
	missing data (2)	1	1			-	-	-						
<b>Change of No. of prsent teeth (2016-2014)</b>	Mean (SD)	0.1 (2.3)	0.1 (1.3)	0.6 (3.1)	0.7 (1.4)	-	-	-	NS	Kruskal Wallis test	1.13 (1.02-1.25)	p<0.05	1.11 (1.01-1.23)	p<0.05
<b>Change of No. of unreplaced missingteeth (2016-2014)</b>	Mean (SD)	0.1 (0.8)	0.1 (0.3)	0.2 (1.1)	0.1 (0.3)	-	-	-	NS	Kruskal Wallis test	1.27 (0.94-1.72)			

\*1: Prevalence = (continuing + developed)/all subjects

\*2: Improvement rate =(Improve)/all subjects

\*3: Crisis rate = (Developed)/all subjects

†: A stepwise ordered logistic regression analysis