

Accepted Manuscript

Impaired glucose metabolism is associated with tooth loss in middle-aged adults: The Northern Finland Birth Cohort Study 1966

Toni Similä, Juha Auvinen, Katri Puukka, Sirkka Keinänen-Kiukaanniemi, Jorma I. Virtanen

PII: S0168-8227(18)30381-4

DOI: <https://doi.org/10.1016/j.diabres.2018.05.035>

Reference: DIAB 7396

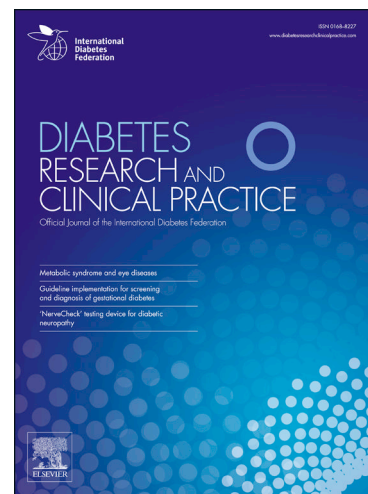
To appear in: *Diabetes Research and Clinical Practice*

Received Date: 9 March 2018

Accepted Date: 22 May 2018

Please cite this article as: T. Similä, J. Auvinen, K. Puukka, S. Keinänen-Kiukaanniemi, J.I. Virtanen, Impaired glucose metabolism is associated with tooth loss in middle-aged adults: The Northern Finland Birth Cohort Study 1966, *Diabetes Research and Clinical Practice* (2018), doi: <https://doi.org/10.1016/j.diabres.2018.05.035>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Impaired glucose metabolism is associated with tooth loss in middle-aged adults: The Northern Finland Birth Cohort Study 1966

Toni Similä ^{a,b,*}, E-mail: toni.simila@oulu.fi

Juha Auvinen ^{b,c}, E-mail: juha.auvinen@oulu.fi

Katri Puukka ^{b,d}, E-mail: katri.puukka@nordlab.fi

Sirkka Keinänen-Kiukaanniemi ^{b,c,e}, E-mail: sirkka.keinanen-kiukaanniemi@oulu.fi

Jorma I. Virtanen ^{a,b}, E-mail: jorma.virtanen@oulu.fi

^a Research Unit of Oral Health Sciences, Faculty of Medicine, University of Oulu, P.O. Box 5000, Oulu, 90014, Finland

^b Medical Research Center Oulu, Oulu University Hospital, P.O. Box 5000, Oulu, 90029, Finland

^c Center for Life Course Health Research, University of Oulu, P.O. Box 5000, Oulu, 90014, Finland

^d NordLab Oulu, Oulu University Hospital, P.O. Box 500, Oulu, 90029, Finland

^e Health Center of Oulu, P.O. Box ???, Oulu, 90100, Finland

*Correspondence:

Toni Similä

Research Unit of Oral Health Sciences

P.O. Box 5000

University of Oulu

90014 Oulu, Finland

E-mail: toni.simila@oulu.fi

Highlights

Tooth loss associates with impaired glucose metabolism in middle-aged adults

Even prediabetic glucose metabolism associates with tooth loss in middle-aged adults

Tooth loss could be used as a simple indicator of impaired glucose metabolism

Abstract

Aim: We investigated the association of impaired glucose metabolism with tooth loss in adults in the Northern Finland Birth Cohort Study 1966 (NFBC1966).

Methods: We examined 4394 participants from the 46-year follow-up of the NFBC1966. Self-reported number of teeth as well as insulin and glucose values, taken during a standard oral glucose tolerance test (OGTT), served as the primary study variables. A multinomial logistic regression model served to analyse (unadjusted, smoking-adjusted and fully adjusted) the association between number of teeth (0–24, 25–27, 28–32) and glucose metabolism in women and men.

Results: Among women, type 2 diabetes – whether previously known or detected during screening – pointed to a higher likelihood of 0–24 teeth (fully adjusted OR=2.99, 95%CI=1.54–5.80) and 25–27 teeth (OR=1.91, 95%CI=1.18–3.08) than did normal glucose tolerance. Similarly, impaired fasting glucose and impaired glucose tolerance together indicated a higher likelihood of 0–24 teeth (OR=1.71, 95%CI=1.09–2.69) than did normal glucose tolerance. A similar, statistically non-significant, pattern emerged among men. Number of teeth associated with OGTT insulin and glucose curves as well as with the Matsuda index in both women and men.

Conclusions: Tooth loss strongly associated with impaired glucose metabolism in middle-aged Finnish women.

Keywords: Prediabetes; Impaired fasting glucose; Impaired glucose tolerance; Tooth loss; Adult

1. Introduction

Tooth loss can substantially impair one's quality of life, causing limited chewing ability, poor dietary intake and functional disorders [1]. Research has shown diabetes and cardiovascular diseases to associate with oral health and tooth loss [2–5], and elevated glucose levels with common periodontal disease [6–8]. Similar finding has been reported between glucose concentration and the number of teeth [8].

Prediabetes is a non-disease condition characterised by elevated fasting or postprandial blood glucose levels. Concurrently, people with diabetes are often obese and suffer from hypertension [9]. Failure to halt the process will lead to prediabetes eventually progressing to diabetes mellitus. Recognising a prediabetic state early on is therefore essential to initiate individual lifestyle changes, focusing on weight control, physical exercise and dietary intake, to postpone or prevent a diabetes diagnosis [10]. In the United States, for instance, 38% of the adult population are estimated to have prediabetes [11].

A follow-up study among Finnish adults investigated whether number of teeth could predict the incidence of cardiovascular diseases, diabetes and all-cause mortality (all confirmed

through national registers) [4]. The capacity of number of teeth to predict emerging diabetes diagnosis was evident: a higher number of missing teeth indicated an elevated risk for diabetes.

Previously, while investigating smoking and tooth loss, the number of missing teeth tended to be higher in subjects with diabetes than in those without [12]. The association between diabetes (self-reported responses combined with information from different registers) and the number of missing teeth, however, showed no statistical significance due to relatively low number of participants in the study.

Although numerous studies have examined diabetes and tooth loss, evidence of a relation with overall glucose metabolism is tenuous. By making use of detailed clinically verified information on different states of diabetes, we aimed to investigate whether even prediabetic glucose metabolism associates with tooth loss in relatively healthy middle-aged Finnish adults.

2. Material and Methods

2.1. Study design

This cross-sectional study used data from the longitudinal Northern Finland Birth Cohort Study 1966 (NFBC1966), which consists of a comprehensive sample of individuals from the two northernmost provinces of Finland (Lapland and Oulu) whose expected year of birth was 1966 (12 068 mothers, 12 231 children, 96.3% of all births in the region) [13]. The cohort members participated in regular monitoring since their mothers' pregnancy. The Ethics Committee of the Northern Ostrobothnia Hospital District in Oulu, Finland approved the

study protocol, which followed the principles of the Declaration of Helsinki. Participation was voluntary and all participants provided their written informed consent. The data were handled on a group level only, and identification codes replaced participants' personal information.

This study used data from the 46-year follow-up (carried out in 2012–2014), which included a mailed survey and a comprehensive in-person clinical health examination. The questionnaires and invitations to health examinations were mailed to all who lived in Finland and whose addresses were known at the beginning of 2012 ($n = 10\,321$). In all, 5950 participants provided self-reported information on number of teeth, and 5120 participants on their diabetic state (defined by previously known and OGTT diagnoses).

2.2. Glucose tolerance and diabetes

Participants underwent a 2-h oral glucose tolerance test (OGTT), carried out as part of the clinical examinations, after an overnight (12 h) fasting period. Exclusion criteria from the OGTT included medication for diabetes or a capillary blood glucose level > 8.0 mmol/l measured immediately before the test. Both serum insulin and plasma glucose levels were measured at baseline and at 30, 60 and 120 min after an intake of 75 g glucose. Plasma glucose was analysed by an enzymatic dehydrogenase method (Advia 1800, Siemens Healthcare Diagnostics, Tarrytown, NY, USA) and serum insulin by a chemiluminometric immunoassay (Advia Centaur XP, Siemens Healthcare Diagnostics, Tarrytown, NY, USA). The samples were analysed in NordLab Oulu, a testing laboratory (T113) accredited by Finnish Accreditation Service (FINAS) (EN ISO 15189).

Glucose tolerance status was classified according to the WHO criteria: (i) normal glucose tolerance (NGT) was defined as a fasting plasma glucose (FPG) level < 6.1 mmol/l and a 2-h

glucose level < 7.8 mmol/l, (ii) impaired fasting glucose (IFG) as an FPG level 6.1–6.9 mmol/l and a 2-h glucose level < 7.8 mmol/l, (iii) impaired glucose tolerance (IGT) as an FPG level < 7.0 mmol/l and a 2-h glucose level 7.8–11.0 mmol/l and (iv) screening-detected diabetes mellitus (ScDM) as an FPG level ≥ 7.0 mmol/l and/or a 2-h glucose level ≥ 11.1 mmol/l. Previously known diabetes (PrDM) was determined by combining and verifying information from numerous sources: participants' self-reported diagnoses and medications, hospital outpatient and inpatient registers, and medication registers from the Social Insurance Institution of Finland. These registers include diagnoses made by doctors.

In addition, we defined insulin sensitivity using the Matsuda index (ISI), defined as $ISI = 10000 / \sqrt{FPG * FSI * (\text{Mean OGTT glucose concentration}) * (\text{Mean OGTT insulin concentration})}$, where sqrt = square root and FSI = fasting serum insulin [14].

2.3. Number of teeth

Subjects reported the number of teeth they had at the age of 46 with no distinction between third molars and other teeth. For our analyses, we converted this measure into an ordinal variable with three categories: 0–24, 25–27 or 28–32 [15].

2.4. Oral health-related factors

The mailed questionnaire enquired about education, smoking, use of oral hygiene products and eating habits. Participants reported their level of education at the age of 46; we used this information to form a three-class ordinal variable: 1) 'basic education' included those who had not graduated from high school and had no formal vocational qualification, 2) 'secondary education' included those who had graduated from high school or vocational school, and 3)

'higher education' included participants with a university degree or who had graduated from a polytechnic or equivalent school.

To define smoking status, we used separate categories for current, former and never smokers. Here, 'current smokers' were those who reported smoking at least occasionally. 'Former smokers' included those who had smoked daily for at least one year, but had quit smoking and were not smokers at the time of the study. 'Never smokers' included all participants who had smoked daily for less than one year in their lifetime and were not smokers at the time of the follow-up.

The question concerning tooth brushing frequency included five answer options, which we dichotomised into: 'at least twice daily' or 'once daily or less' based on the recommendation to brush teeth twice daily [15].

Sugar consumption was derived from the set of questions enquiring about the consumption frequency of different foodstuffs. We considered five products as sources of sugar intake: sweet pastries, ice cream, sugary soft drinks, candies and chocolate. The consumption frequency for each foodstuff included six options: 'less than once a month or not at all', 'once or twice a month', 'once a week', 'twice a week', 'almost daily' or 'once daily or more'. Based on this information, we formed a dichotomised variable for any sugar consumption: 'twice a week or less' or 'almost daily or more'.

We assessed the pattern of dental visits from the questionnaire given to participants during the day of their clinical examination. We dichotomised the available information as 'regularly for check-up' or 'symptom based/never'. For additional analysis, we used the number of self-

reported deliveries among women, taken from the mailed questionnaire, as a dichotomised variable (0 or ≥ 1).

2.5. Statistical analysis

For the descriptive analyses, we cross-tabulated the OGTT diabetes and oral health-related variables against the number of teeth (0–24, 25–27, 28–32) separately for women and men. The chi-squared test served to assess the dependence between the study variables and the ‘number of teeth’ categories.

We used a multinomial logistic regression model to analyse the association of prediabetes and diabetes (along with other study variables) with categorised number of teeth (0–24, 25–27, 28–32) separately for women and men. We calculated unadjusted, smoking-adjusted and fully adjusted odds ratios (OR) with 95% confidence intervals (CI) for each variable in the model and the ‘number of teeth’ categories (28–32 teeth served as the reference).

We drew 2-h OGTT curves (baseline, 30 min, 60 min, 120 min) for insulin and glucose separately for women and men. To facilitate comparison, the same diagram included three curves representing the ‘number of teeth’ categories. The median served as the measure of central tendency for the OGTT time points along the curve. We calculated AUC (area under the curve) values for each ‘number of teeth’ curve and statistically compared the values with the Kruskal-Wallis test.

We drew box plots for women and men to compare the Matsuda index according to the ‘number of teeth’ categories (0–24, 25–27, 28–32). We used the Kruskal-Wallis test to assess the statistical significance of the association.

The statistical package R environment version 3.3.2 served for all statistical analyses [16]. We used the CrossTable function (gmodels package) to run cross-tabulations with the chi-squared test. We used the kruskal.test function (stats package) for the Kruskal-Wallis test, and the multinom function (nnet package) for the multinomial logistic regression modelling.

3. Results

Table 1 presents the categorised study variables according to the number of teeth in women and men. The OGTT revealed that 84% of women had normal glucose tolerance, 3% impaired fasting glucose, 8% impaired glucose tolerance, 2% newly diagnosed diabetes and 3% previously diagnosed diabetes. The corresponding values for men were 73%, 11%, 8%, 4% and 4%. Regarding the number of teeth, 39% of women and 42% of men had fewer than 28 teeth. Education, smoking status, the pattern of dental visits, tooth brushing frequency and diabetes status associated statistically significantly with the number of teeth in both women and men. Among women, the percentages of those with NGT for 'number of teeth' categories 0–24, 25–27 and 28–32 were 75%, 83% and 86%, respectively ($p < 0.001$). The corresponding percentages among men were 68%, 70% and 75% ($p = 0.026$). Sugar consumption associated with number of teeth only in men ($p = 0.020$). In addition, women who had delivered babies were more likely to have fewer teeth than those who had not ($p = 0.045$).

Table 2 presents the results of the multinomial logistic regression analyses of the number of teeth and prediabetes and diabetes in women. Number of teeth associated statistically significantly with prediabetes (IFG/IGT) and diabetes (ScDM/PrDM). ScDM/PrDM pointed to a higher likelihood of 0–24 teeth (fully adjusted OR = 2.99, 95% CI = 1.54–5.80) and 25–27 teeth (OR = 1.91, 95% CI = 1.18–3.08) than did NGT. Similarly, IFG/IGT pointed to a higher likelihood of 0–24 teeth (OR = 1.71, 95% CI = 1.09–2.69) than did NGT. Smoking associated statistically significantly with number of teeth (25–27 teeth: for current smoking, OR = 1.53, 95% CI = 1.20–1.94; for former smoking, OR = 1.35, 95% CI = 1.07–1.71). Education, pattern of dental visits, tooth brushing frequency and sugar consumption also associated with number of teeth.

Table 3 shows corresponding findings in men. All OR values suggested a slightly higher likelihood of lower number of teeth for IFG/IGT and ScDM/PrDM than did NGT (not statistically significant). Smoking associated statistically significantly with 0–24 teeth (for current smoking, OR = 1.79, 95% CI = 1.23–2.60; for former smoking, OR = 1.38, 95% CI = 0.95–2.01) and, similarly, for 25–27 teeth. Education, pattern of dental visits, tooth brushing frequency and sugar consumption also associated with number of teeth.

Figure 1 incorporates diabetes status on a continuous scale by illustrating the association between number of teeth and OGTT insulin and glucose curves by gender. Among both women and men, insulin and glucose values followed similar patterns according to the number of teeth: 0–24 teeth suggested the highest values for insulin and glucose, whereas 28–32 teeth associated with the lowest values throughout the measurement period. Calculated AUC values confirmed these observations ($p < 0.01$ for all comparisons).

Figure 2 presents the Matsuda index, which summarises information on OGTT insulin and glucose values according to the ‘number of teeth’ categories by gender. A higher number of teeth indicated a higher Matsuda index value among both women and men ($p < 0.001$).

4. Discussion

The strong association of tooth loss with impaired glucose metabolism in middle-aged Finnish women is a novel finding: a lower number of teeth indicated a higher likelihood of prediabetes and diabetes. We observed a similar pattern in men, but the association was not statistically significant. Analysis of continuous insulin and glucose values derived from the OGTT supported these findings.

In Finland, the incidence of type 2 diabetes among men has increased in recent decades [17]. Saaristo et al. [18] reported that the total prevalence of the disease (based on WHO criteria) in 2004–2005 among 45- to 54-year-old men and women was around 9% and 5%, respectively. Moreover, the estimated prevalence of abnormal glucose tolerance among 45- to 54-year-old men and women was as high as 26.4% and 20.5%, respectively. In our study of 46-year-olds, all observed figures resembled these previously reported estimates, except for a slightly higher number of NGT (84%) in women.

Diabetes is known to associate with oral health. Studies have suggested a bidirectional connection between, for example, diabetes and periodontal disease (a chronic inflammatory condition of supporting tissues of the teeth); periodontal disease is a complication of diabetes that plays an important role in poorly controlled diabetes [19]. Moreover, recent studies have reported an association between impaired glucose metabolism and periodontal disease [6,8]. On the other hand, evidence to support an association between diabetes and dental caries (decaying of teeth) in adults is scarce [19]: a recent Korean study reported type 2 diabetes as a possible risk indicator for untreated caries [20].

Most previous studies have used self-reported diagnosed diabetes as the assessment method for the disease in studies of its association with tooth loss, but few studies have focused on prediabetes and tooth loss. A study using data from the National Health and Nutrition Examination Survey (NHANES) found self-reported diabetes to associate with edentulousness and number of missing teeth in those 50 years and older in the U.S., indicating diabetes as a possible risk factor for tooth loss [21]. Another study of U.S. residents investigated this association between self-reported diabetes and number of missing teeth due to ‘tooth decay’ or ‘gum disease’ in adults who had visited a dentist ‘within the past year’ [22]. Interestingly, the authors found that the association between diabetes and tooth loss was stronger in younger age groups than in the oldest one (65 years and older).

Using population-based survey data from the Finnish FINRISK 1997 Study, with its 13-year follow-up among 25- to 74-years-olds, Liljestrand et al. [4] demonstrated that tooth loss could be a predictor of diabetes. Even a few missing teeth indicated increased risk for diabetes; the statistical significance of the finding became evident with higher numbers of missing teeth.

That study, however, used register-based information to identify diabetes in study subjects without considering glucose measurements. Our study, in contrast, included OGTT, which could identify IGT and IFG cases in addition to those with diabetes. Moreover, we were able to include the Matsuda index, which is defined by OGTT measurements, to analyse insulin sensitivity on a continuous scale. Nevertheless, our findings on the association of tooth loss with diabetes in the ScDM/PrDM group of the NFBC1966 resembled those reported with data from the FINRISK 1997 Study.

Jung et al. [8] investigated the association of number of teeth and periodontal disease with prediabetes and diabetes, defined by fasting blood glucose and HbA1c levels, in a cross-sectional study of adult Koreans aged 50 and older. Although based on older participants, the findings of that study were reasonably similar to ours: those with diabetes and prediabetes tended to have fewer remaining teeth than those with normoglycaemia status (the association was stronger for diabetes status). In contrast to that study, we assessed the level of glucose tolerance with OGTT rather than HbA1c and fasting glucose measure.

Our findings suggest that the strength of the association between tooth loss and impaired glucose metabolism varies by gender. To our knowledge, this is the first study to investigate the gender difference of this association, although some studies have raised the possibility that the association is stronger in women than in men [23,24]. Similarly, we found that the association between number of teeth and impaired glucose metabolism was stronger in women than in men. On the other hand, on a continuous scale using the Matsuda index and OGTT glucose and insulin values, this association showed no difference between women and men. One possible explanation for this gender variation could be the lower participation rate

of men than women in the follow-up. In any case, this finding requires further investigation in other study populations, preferably with a prospective study design.

Some studies have suggested an important role for the dental office in diabetes diagnosis and management [19,25]. Lalla et al. [25], for instance, suggested a simple method for how oral health care professionals could screen for prediabetes and diabetes in dental patients. Similarly, the findings of our study suggest number of teeth as a simple and easily determined indicator of impaired glucose metabolism. This measure, along with common risk factor assessment and chairside-determined HbA1c level, could be an effective and convenient method for identifying prediabetes and diabetes in the dental office [26].

The level of oral health in this study population is good mostly thanks to subsidised dental care and preventive services since childhood [12]. Roughly 75% of women and 50% of men followed the recommended oral health behaviour practices of 'brushing teeth at least twice daily' and 'regularly visiting the dental office'. Moreover, overall sugar consumption was low in both women and men. Despite the obedience to recommended practices, these middle-aged participants suffered tooth loss. An earlier study identified smoking history (intensity and duration) as a contributing behavioural factor related to tooth loss [12]. An interesting finding was that women who had given birth were at slightly greater risk for losing teeth (echoing an old proverb that says a mother loses a tooth each time she gives birth to a child). This finding is in line with those of previous American and Korean studies on parity and tooth loss in women [27,28]. This association warrants further investigation along with gestational diabetes and its possible effect on tooth loss.

Our comprehensive study population represents the middle-aged Finnish population well [12]. Moreover, the prevalence of prediabetes and diabetes in this study resembled earlier findings in the middle-aged Finnish population [18]. An important strength of our study was the detailed information available on diabetic state. Data on medications and previous diagnoses were assessable from various registers, but using 2-h OGTT with four measurement points enabled us to define the participants' diabetic state in detail through continuous insulin and glucose measurements. Thus, to our knowledge, this was the first study on diabetes and tooth loss to use comprehensive information on diabetes. Because the data collection during the follow-up on 46-year-olds was extensive, we were able to incorporate reliable information on all relevant confounders to strengthen the cogency of our findings.

One limitation of our study was its cross-sectional design with follow-up data on 46-year-olds, which rendered impossible any examination of causal association between tooth loss and diabetic state. Moreover, we were unable to assess various age groups, thus limiting the generalisation of our findings to younger or older age groups. Furthermore, we used self-reported number of teeth to measure tooth loss, despite the availability of a parallel clinical measure [12], in order to maintain a higher number of participants for the analyses [15].

In conclusion, the findings of this study indicate that the number of teeth strongly associates with prediabetes in women. Tooth loss could also serve as an early indicator of diabetes diagnosed at a later age, which implies that slightly enhanced standard check-up operations in dental offices could enable dentists to effectively and conveniently identify previously undiagnosed prediabetes and diabetes in their patients.

Author contributions

TS designed the study, performed the statistical analyses and wrote the manuscript. JA designed the study and wrote the manuscript. KP participated in data collection, performed the laboratory analyses and edited the manuscript. SKK designed the study and wrote the manuscript. JV designed the study and wrote the manuscript. All authors revised the draft critically and approved the final version of the manuscript.

Acknowledgements

We thank the late professor Paula Rantakallio (launch of NFBC1966), the participants in the 46-year follow-up study and the NFBC project center. NFBC1966 received financial support from University of Oulu Grant no. 24000692, Oulu University Hospital Grant no. 24301140, ERDF European Regional Development Fund Grant no. 539/2010 A31592.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

None.

Availability of data and materials

Data is available from the Northern Finland Birth Cohort (NFBC) for researchers who meet the criteria for accessing confidential data. Please, contact NFBC project center (NFBCprojectcenter@oulu.fi) and visit the cohort website (<http://www.oulu.fi/nfbc/>) for more information.

References

1. Gerritsen AE, Allen PF, Witter DJ, Bronkhorst EM, Creugers NH. Tooth loss and oral health-related quality of life: a systematic review and meta-analysis. *Health Qual Life Outcomes* 2010;8:126. doi: 10.1186/1477-7525-8-126.
2. Dörfer C, Benz C, Aida J, Campard G. The relationship of oral health with general health and NCDs: a brief review. *Int Dent J* 2017;67:14–8. doi: 10.1111/idj.12360.
3. Vedin O, Hagström E, Budaj A, Denchev S, Harrington RA, Koenig W, et al. Tooth loss is independently associated with poor outcomes in stable coronary heart disease. *Eur J Prev Cardiol* 2016;23:839–46. doi: 10.1177/2047487315621978.
4. Liljestrang JM, Havulinna AS, Paju S, Männistö S, Salomaa V, Pussinen PJ. Missing Teeth Predict Incident Cardiovascular Events, Diabetes, and Death. *J Dent Res* 2015;94:1055–62. doi: 10.1177/0022034515586352.
5. Borgnakke WS, Ylöstalo PV, Taylor GW, Genco RJ. Effect of periodontal disease on diabetes: systematic review of epidemiologic observational evidence. *J Clin Periodontol* 2013;40:S135–52. doi: 10.1111/jcpe.12080.
6. Hong JW, Noh JH, Kim DJ. The Prevalence and Associated Factors of Periodontitis According to Fasting Plasma Glucose in the Korean Adults: The 2012-2013 Korea National Health and Nutrition Examination Survey. *Medicine (Baltimore)* 2016;95:e3226. doi: 10.1097/MD.0000000000003226.
7. Demmer RT, Jacobs DR Jr, Singh R, Zuk A, Rosenbaum M, Papapanou PN, et al. Periodontal Bacteria and Prediabetes Prevalence in ORIGINS: The Oral Infections, Glucose Intolerance, and Insulin Resistance Study. *J Dent Res* 2015;94:201S–11S. doi: 10.1177/0022034515590369.

8. Jung YS, Shin MH, Kweon SS, Lee YH, Kim OJ, Kim YJ, et al. Periodontal disease associated with blood glucose levels in urban Koreans aged 50 years and older: the Dong-gu study. *Gerodontology* 2015;32:267–73. doi: 10.1111/ger.12107.
9. He YH, Jiang GX, Yang Y, Huang HE, Li R, Li XY, et al. Obesity and its associations with hypertension and type 2 diabetes among Chinese adults age 40 years and over. *Nutrition* 2009;25:1143–9. doi: 10.1016/j.nut.2009.04.003.
10. American Diabetes Association. Standards of medical care in diabetes – 2017. *Diabetes care* 2017;40(Suppl 1).
http://care.diabetesjournals.org/content/diacare/suppl/2016/12/15/40.Supplement_1.DC1/DC_40_S1_final.pdf. [accessed 9 March 2018].
11. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and Trends in Diabetes Among Adults in the United States, 1988-2012. *JAMA* 2015;314:1021–9. doi: 10.1001/jama.2015.10029.
12. Similä T, Virtanen JI. Association between smoking intensity and duration and tooth loss among Finnish middle-aged adults: The Northern Finland Birth Cohort 1966 Project. *BMC Public Health* 2015;15:1141. doi: 10.1186/s12889-015-2450-6.
13. Conference on Epidemiological Birth Cohort Studies. Paula Rantakallio Memorial Symposium, 2014.
http://www oulu.fi/sites/default/files/Rantakallio_conference_2014_abstract_book.pdf. [accessed 9 March 2018].
14. Matsuda M, DeFronzo RA. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. *Diabetes Care* 1999;22:1462–70.

15. Similä T, Auvinen J, Timonen M, Virtanen JI. Long-term effects of smoking on tooth loss after cessation among middle-aged Finnish adults: The Northern Finland Birth Cohort 1966 Study. *BMC Public Health* 2016;16:867. doi: 10.1186/s12889-016-3556-1.
16. The R Project for Statistical Computing. <http://www.r-project.org>. [accessed 9 March 2018].
17. Abouzeid M, Wikström K, Peltonen M, Lindström J, Borodulin K, Rahkonen O, et al. Secular trends and educational differences in the incidence of type 2 diabetes in Finland, 1972-2007. *Eur J Epidemiol* 2015;30:649–59. doi: 10.1007/s10654-015-0008-7.
18. Saaristo TE, Barengo NC, Korpi-Hyövälti E, Oksa H, Puolijoki H, Saltevo JT, et al. High prevalence of obesity, central obesity and abnormal glucose tolerance in the middle-aged Finnish population. *BMC Public Health* 2008;8:423. doi: 10.1186/1471-2458-8-423.
19. Lamster IB, Lalla E, Borgnakke WS, Taylor GW. The relationship between oral health and diabetes mellitus. *J Am Dent Assoc* 2008;139:19S–24S.
20. Song IS, Han K, Park YM, Ryu JJ, Park JB. Type 2 diabetes as a risk indicator for dental caries in Korean adults: the 2011-2012 Korea national health and nutrition examination survey. *Community Dent Health* 2017;34:169–75. doi: 10.1922/CDH_4113Song07.
21. Patel MH, Kumar JV, Moss ME. Diabetes and tooth loss: an analysis of data from the National Health and Nutrition Examination Survey, 2003-2004. *J Am Dent Assoc* 2013;144:478–85.
22. Kapp JM, Boren SA, Yun S, LeMaster J. Diabetes and tooth loss in a national sample of dentate adults reporting annual dental visits. *Prev Chronic Dis* 2007;4:A59.
23. Ide R, Hoshuyama T, Wilson D, Takahashi K, Higashi T. Periodontal disease and incident diabetes: a seven-year study. *J Dent Res* 2011;90:41–6. doi: 10.1177/0022034510381902.

24. Demmer RT, Jacobs DR Jr, Desvarieux M. Periodontal disease and incident type 2 diabetes: results from the First National Health and Nutrition Examination Survey and its epidemiologic follow-up study. *Diabetes Care* 2008;31:1373–9. doi: 10.2337/dc08-0026.
25. Lalla E, Kunzel C, Burkett S, Cheng B, Lamster IB. Identification of unrecognized diabetes and pre-diabetes in a dental setting. *J Dent Res* 2011;90:855–60. doi: 10.1177/0022034511407069.
26. Bossart M, Calley KH, Gurenlian JR, Mason B, Ferguson RE, Peterson T. A pilot study of an HbA1c chairside screening protocol for diabetes in patients with chronic periodontitis: the dental hygienist's role. *Int J Dent Hyg* 2016;14:98–107. doi: 10.1111/idh.12140.
27. Han K, Kim I, Park YG, Park JB. Associations between the number of natural teeth and the maternal age at childbirth or history of parity in postmenopausal women: The 2010-2012 Korea national health and nutrition examination survey. *Adv Clin Exp Med* 2017;26:627–33. doi: 10.17219/acem/62832.
28. Russell SL, Ickovics JR, Yaffee RA. Exploring potential pathways between parity and tooth loss among American women. *Am J Public Health* 2008;98:1263–70. doi: 10.2105/AJPH.2007.124735.

Table 1 Characteristics of the study variables by the ‘number of teeth’ categories among the 46-year olds.

Number of teeth

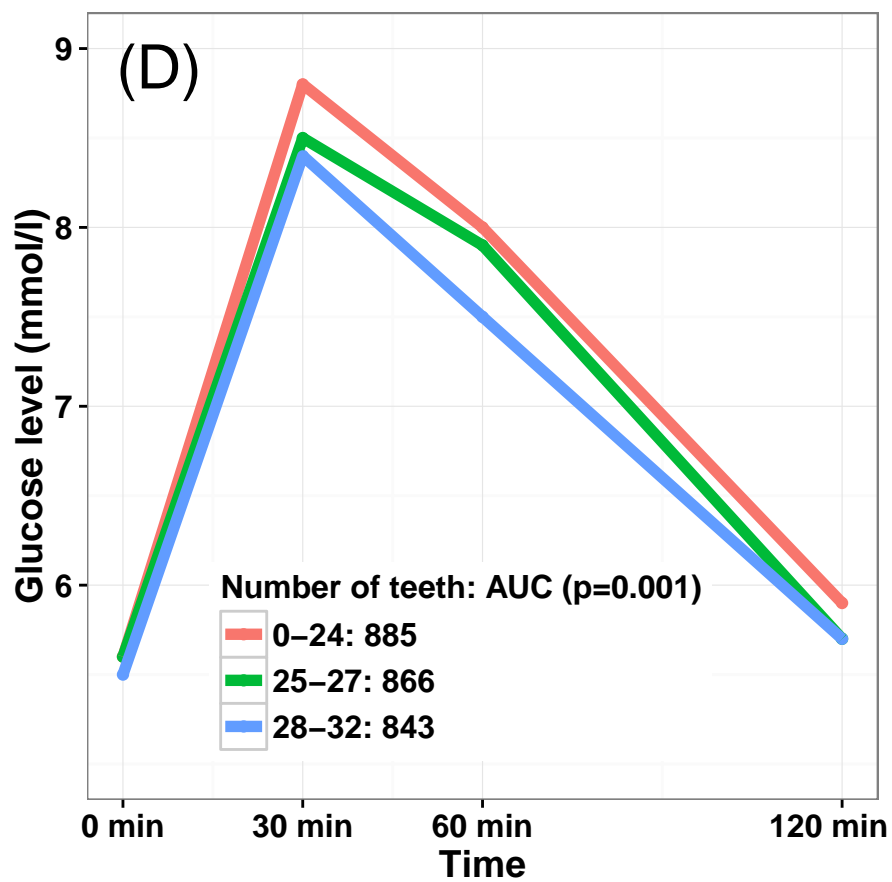
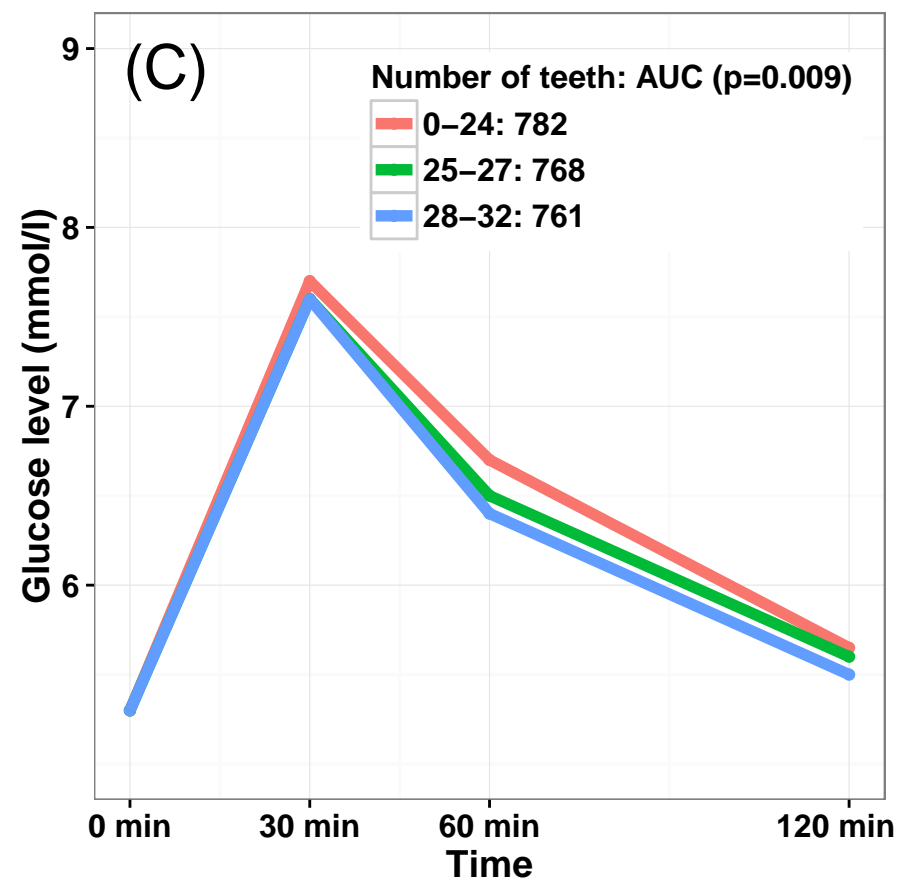
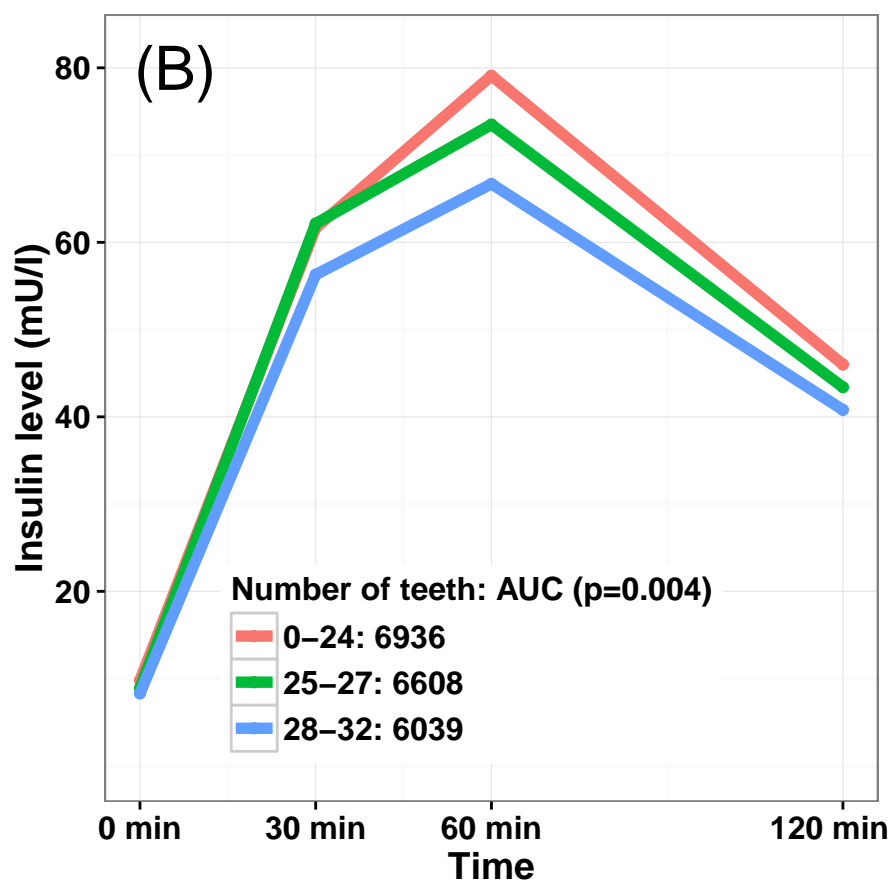
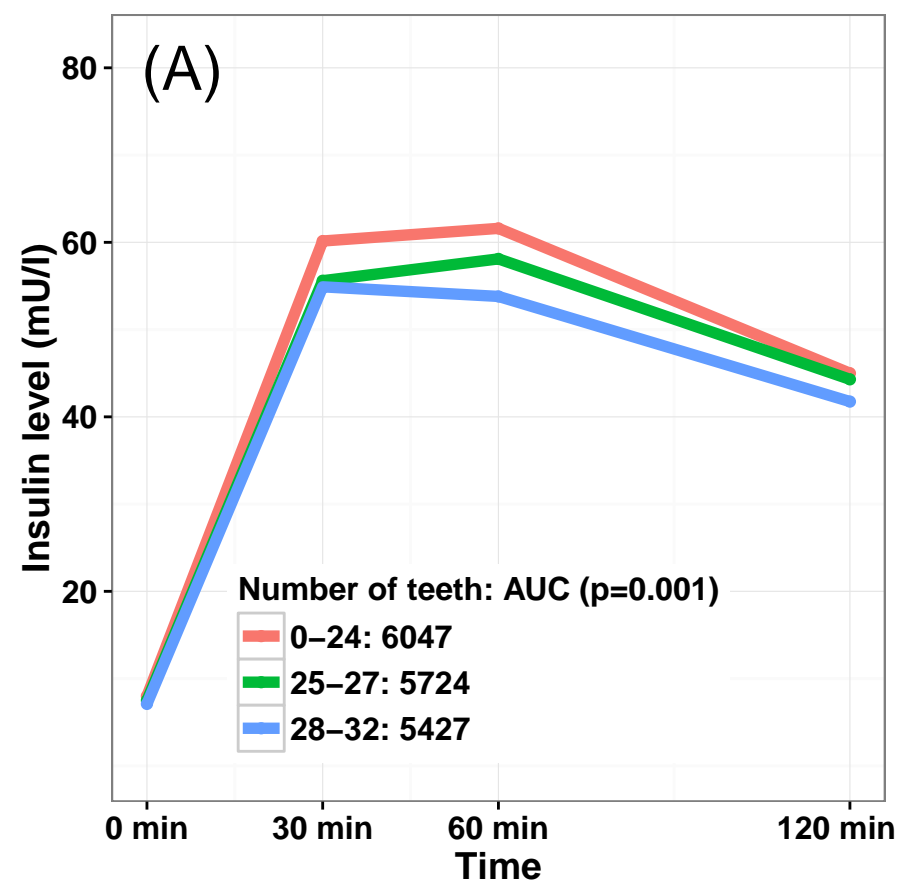
Table 1 Characteristics of the categorised study variables by the ‘number of teeth’ categories among the 46-year olds.

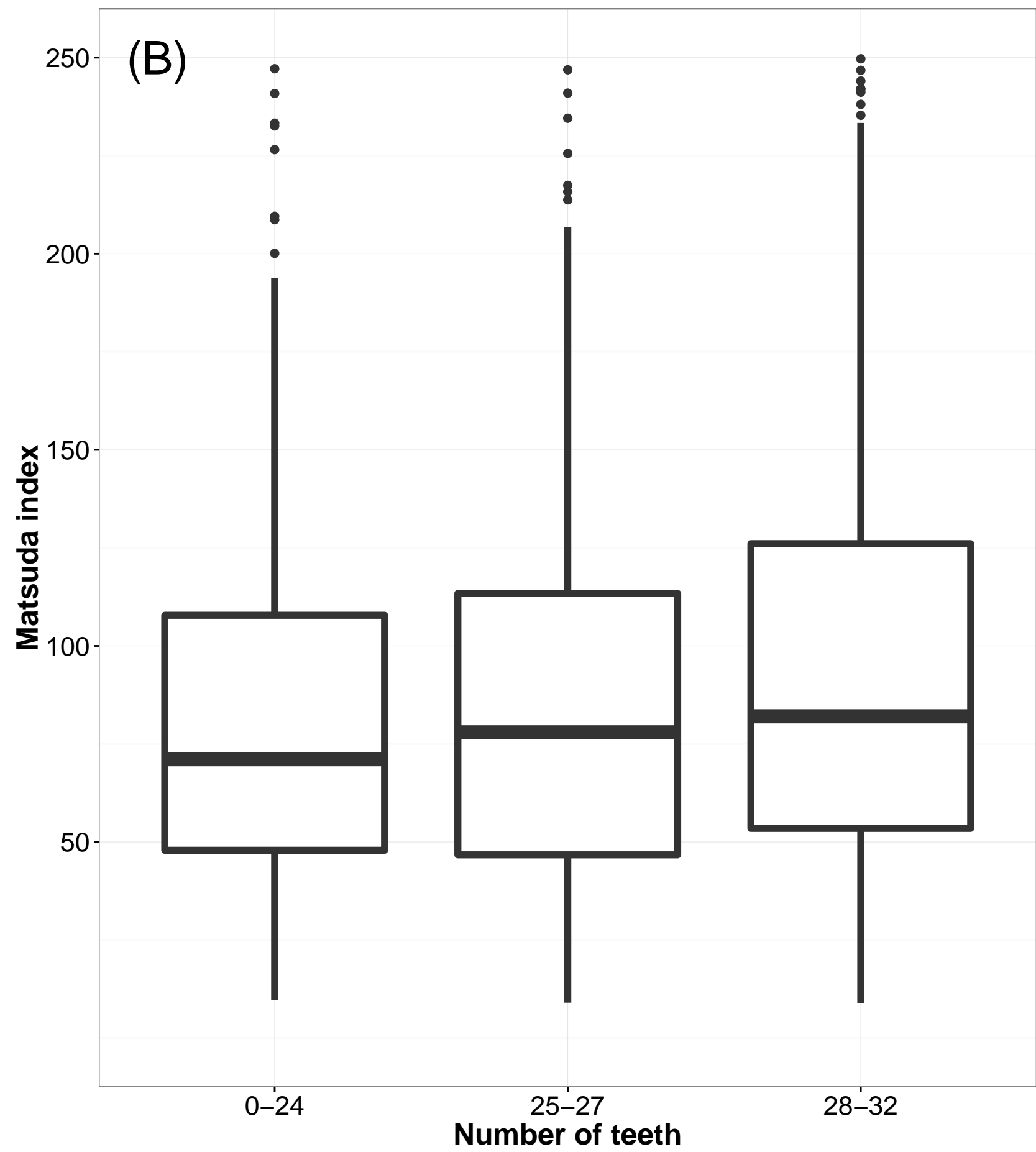
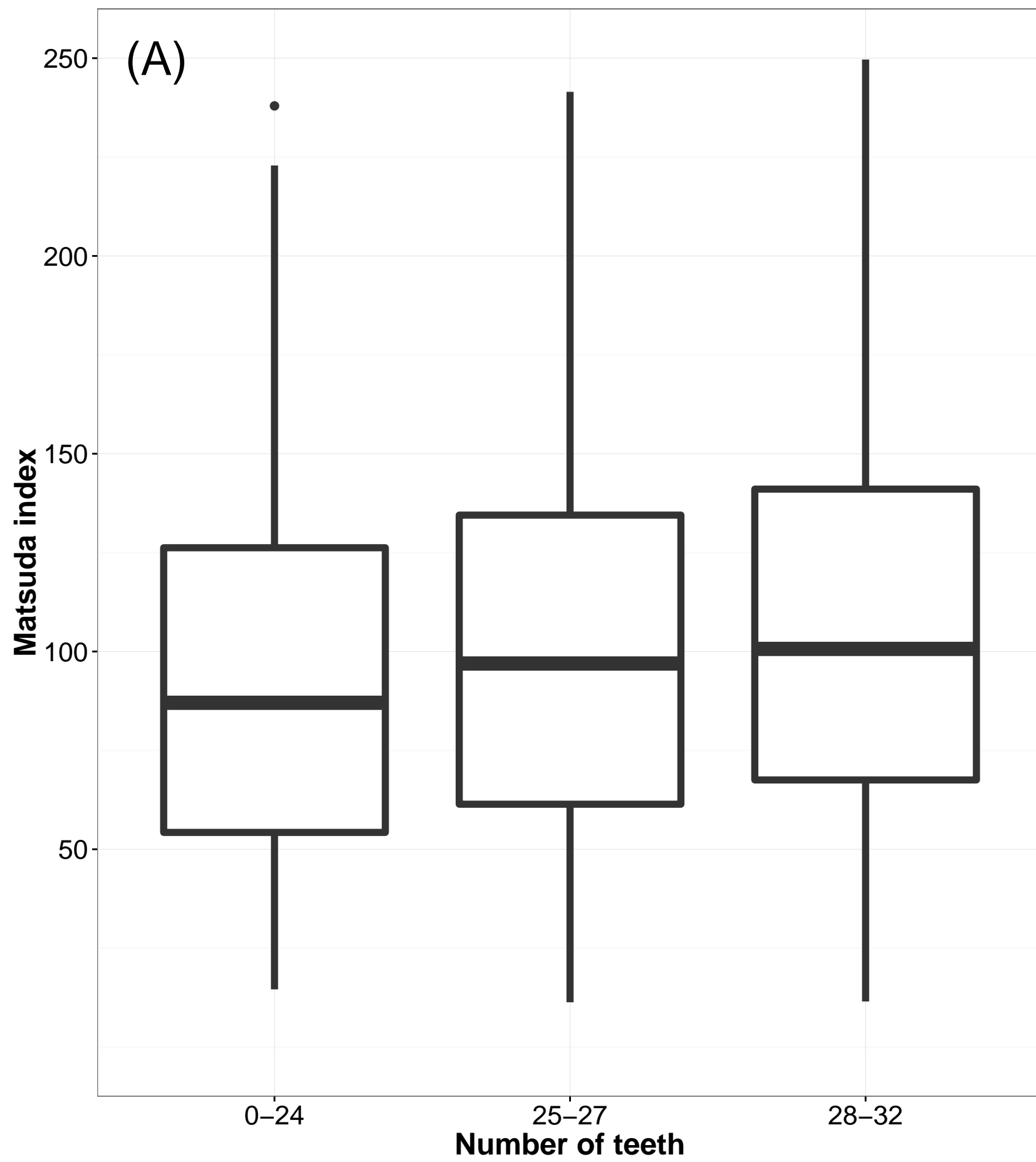
Table 2 Results of the multinomial logistic regression analyses for the association between study variables and number of teeth among women (n=2170).

Table 3 Results of the multinomial logistic regression analyses for the association between study variables and number of teeth among men (n=1527).

Figure 1 Median OGTT insulin and glucose curves by gender and number of teeth. Description: (A) Women: insulin (n=2522), (B) Men: insulin (n=1786), (C) Women: glucose (n=2528), (D) Men: glucose (n=1786). Footnote: OGTT, oral glucose tolerance test; AUC, area under the curve. P-values for comparison of AUC values by the ‘number of teeth’ categories (Kruskal-Wallis test).

Figure 2 Distribution of Matsuda index according to the ‘number of teeth’ categories among women (n=2514) and men (n=1780). Description: (A) Women (p<0.001), (B) Men (p<0.001). Footnote: Outliers representing values higher than 250 were omitted from the presentation. P-values for comparison of Matsuda index by the ‘number of teeth’ categories (Kruskal-Wallis test).





		0–24	25–27	28–32	Total	P value ^a
		%	%	%	%	
Women	Education (n=3302)					
	Basic	9	6	3	4	<0.001
	Secondary	36	29	24	27	
	Higher	55	65	73	69	
	Smoking status (n=3103)					
	Never	46	49	58	54	<0.001
	Former	20	23	21	22	
	Current	34	28	21	24	
	Dental visit: pattern (n=2824)					
	Regularly for check-up	59	70	74	71	<0.001
	Symptom based/Never	41	30	26	29	
	Tooth brushing (n=3348)					
	At least twice daily	66	77	81	78	<0.001
	Once daily or less	34	23	19	22	
	Sugar consumption (n=3354)					
	Twice a week or less	59	62	64	63	0.281
	Almost daily or more	41	38	36	37	
	OGTT diabetes (n=2563)					
	NGT	75	83	86	84	<0.001
	IFG	6	3	3	3	
IGT	9	8	7	8		
ScDM	5	2	2	2		
PrDM	5	4	2	3		
Total (n)		100 (317)	100 (982)	100 (2056)	100	
Men	Education (n=2561)					
	Basic	15	9	7	9	<0.001
	Secondary	53	51	37	43	
	Higher	32	40	56	48	
	Smoking status (n=2437)					
	Never	29	38	47	41	<0.001
	Former	28	28	27	28	
	Current	43	34	26	31	
	Dental visit: pattern (n=1940)					
	Regularly for check-up	40	56	55	53	<0.001
	Symptom based/Never	60	44	45	47	
	Tooth brushing (n=2586)					
	At least twice daily	36	45	56	50	<0.001
	Once daily or less	64	55	44	50	
	Sugar consumption (n=2591)					
	Twice a week or less	65	66	70	68	0.020
	Almost daily or more	35	34	30	32	
	OGTT diabetes (n=1831)					
	NGT	68	70	75	73	0.026
	IFG	15	11	9	11	
IGT	7	9	9	8		
ScDM	4	4	4	4		
PrDM	6	6	3	4		
Total (n)		100 (423)	100 (662)	100 (1510)	100	

Abbreviations: OGTT, oral glucose tolerance test; NGT, normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; ScDM, screen detected diabetes mellitus; PrDM, previously known diabetes.

^a From Chi-squared test.

Table 2 Results of the multinomial logistic regression analyses for the association between study variables and number of teeth^a among women (n=2170).

Table 3 Results of the multinomial logistic regression analyses for the association between study variables and number of teeth among men (n=1527).

	n	Unadjusted OR	Adjusted OR ^a	Adjusted OR ^c	Unadjusted OR	Adjusted OR ^b	Adjusted OR ^c
		(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
OGTT diabetes							
NGT (ref.)	1839	1.00	1.00	1.00	1.00	1.00	1.00
IFG/IGT	245	1.83 (1.17–2.86)	1.82 (1.17–2.84)	1.71 (1.09–2.69)	1.16 (0.86–1.56)	1.16 (0.86–1.57)	1.15 (0.85–1.56)
ScDM/PrDM	86	3.40 (1.79–6.44)	3.31 (1.74–6.30)	2.99 (1.54–5.80)	1.92 (1.20–3.09)	1.90 (1.18–3.06)	1.91 (1.18–3.08)
Smoking status							
Never (ref.)	1230	1.00		1.00	1.00		1.00
Former	485	1.15 (0.77–1.74)		1.09 (0.71–1.65)	1.38 (1.09–1.73)		1.35 (1.07–1.71)
Current	455	1.67 (1.14–2.46)		1.39 (0.93–2.09)	1.61 (1.27–2.03)		1.53 (1.20–1.94)
Education							
Higher (ref.)	1524	1.00	1.00	1.00	1.00	1.00	1.00
Secondary	561	2.00 (1.41–2.84)	1.93 (1.36–2.74)	1.72 (1.20–2.46)	1.33 (1.07–1.64)	1.26 (1.01–1.56)	1.24 (0.99–1.54)
Basic	85	4.41 (2.33–8.35)	4.03 (2.10–7.72)	3.29 (1.69–6.39)	2.16 (1.33–3.50)	1.91 (1.17–3.11)	1.86 (1.14–3.04)
Dental visit: pattern							
Regularly for check-up (ref.)	1554	1.00	1.00	1.00	1.00	1.00	1.00
Symptom based/Never	616	1.92 (1.38–2.66)	1.89 (1.35–2.62)	1.67 (1.19–2.34)	1.14 (0.93–1.40)	1.13 (0.92–1.39)	1.10 (0.89–1.36)
Tooth brushing							
At least twice daily (ref.)	1719	1.00	1.00	1.00	1.00	1.00	1.00
Once daily or less	451	2.32 (1.64–3.28)	2.26 (1.60–3.19)	1.80 (1.26–2.57)	1.17 (0.93–1.48)	1.13 (0.89–1.43)	1.04 (0.82–1.32)
Sugar consumption							
Twice a week or less (ref.)	1338	1.00	1.00	1.00	1.00	1.00	1.00
Almost daily or more	832	1.27 (0.92–1.75)	1.34 (0.96–1.85)	1.40 (1.00–1.95)	1.14 (0.94–1.39)	1.20 (0.99–1.46)	1.23 (1.01–1.49)

Abbreviations: OR, odds ratio; CI, confidence interval; OGTT, oral glucose tolerance test; NGT, normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; ScDM, screen detected diabetes mellitus; PrDM, previously known diabetes.

^a 28–32 teeth as reference category.

^b Adjusted for smoking status.

^c Adjusted for other row variables in this table.

	n	Unadjusted OR (95% CI)	Adjusted OR ^b (95% CI)	Adjusted OR ^c (95% CI)	Unadjusted OR (95% CI)	Adjusted OR ^b (95% CI)	Adjusted OR ^c (95% CI)
OGTT diabetes							
NGT (ref.)	1133	1.00	1.00	1.00	1.00	1.00	1.00
IFG/IGT	291	1.32 (0.91–1.91)	1.27 (0.87–1.85)	1.20 (0.82–1.76)	1.33 (0.99–1.78)	1.29 (0.95–1.73)	1.23 (0.91–1.66)
ScDM/PrDM	103	1.63 (0.94–2.83)	1.56 (0.89–2.72)	1.40 (0.79–2.48)	1.43 (0.90–2.28)	1.38 (0.86–2.21)	1.26 (0.79–2.03)
Smoking status							
Never (ref.)	700	1.00		1.00	1.00		1.00
Former	429	1.58 (1.10–2.28)		1.38 (0.95–2.01)	1.45 (1.09–1.93)		1.33 (0.99–1.78)
Current	398	2.35 (1.64–3.36)		1.79 (1.23–2.60)	2.09 (1.57–2.79)		1.81 (1.35–2.44)
Education							
Higher (ref.)	778	1.00	1.00	1.00	1.00	1.00	1.00
Secondary	643	2.45 (1.78–3.38)	2.24 (1.61–3.10)	1.98 (1.41–2.77)	2.04 (1.59–2.61)	1.87 (1.46–2.41)	1.72 (1.33–2.23)
Basic	106	4.55 (2.69–7.70)	3.95 (2.32–6.73)	3.57 (2.07–6.14)	2.31 (1.42–3.76)	2.03 (1.24–3.32)	1.91 (1.16–3.13)
Dental visit: pattern							
Regularly for check-up (ref.)	818	1.00	1.00	1.00	1.00	1.00	1.00
Symptom based/Never	709	1.82 (1.35–2.45)	1.71 (1.26–2.32)	1.62 (1.19–2.21)	0.99 (0.78–1.25)	0.94 (0.74–1.19)	0.90 (0.70–1.14)
Tooth brushing							
At least twice daily (ref.)	787	1.00	1.00	1.00	1.00	1.00	1.00
Once daily or less	740	1.82 (1.35–2.46)	1.68 (1.24–2.28)	1.31 (0.95–1.80)	1.57 (1.24–1.99)	1.46 (1.15–1.86)	1.28 (1.00–1.65)
Sugar consumption							
Twice a week or less (ref.)	1012	1.00	1.00	1.00	1.00	1.00	1.00
Almost daily or more	515	1.43 (1.05–1.94)	1.49 (1.09–2.03)	1.44 (1.05–1.98)	1.32 (1.03–1.69)	1.37 (1.07–1.76)	1.31 (1.02–1.69)

Abbreviations: OR, odds ratio; CI, confidence interval; OGTT, oral glucose tolerance test; NGT, normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; ScDM, screen detected diabetes mellitus; PrDM, previously known diabetes.

^a 28–32 teeth as reference category.

^b Adjusted for smoking status.

^c Adjusted for other row variables in this table.