UNIVERSITY OF LEEDS

This is a repository copy of Association between central obesity and tooth loss in the non-obese people: Results from the continuous National Health and Nutrition Examination Survey (NHANES) 1999–2012.

White Rose Research Online URL for this paper: http://eprints.whiterose.ac.uk/142657/

Version: Accepted Version

Article:

Kang, J orcid.org/0000-0002-2770-1099, Smith, S, Pavitt, S et al. (1 more author) (2019) Association between central obesity and tooth loss in the non-obese people: Results from the continuous National Health and Nutrition Examination Survey (NHANES) 1999–2012. Journal of Clinical Periodontology, 46 (4). pp. 430-437. ISSN 0303-6979

https://doi.org/10.1111/jcpe.13091

© 2019 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd. This is the peer reviewed version of the following article: Kang, J , Smith, S, Pavitt, S et al. (1 more author) (2019) Association between central obesity and tooth loss in the non-obese people: Results from the continuous National Health and Nutrition Examination Survey (NHANES) 1999–2012. Journal of Clinical Periodontology, 46 (4). pp. 430-437. ISSN 0303-6979, which has been published in final form at https://doi.org/10.1111/jcpe.13091. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions.

Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



Title: Association between central obesity and tooth loss in the non-obese people: results from the continuous national health and nutrition examination survey (NHANES) 1999-2012

Authors: Jing Kang¹, Scott Smith², Sue Pavitt², and Jianhua Wu^{2,3}

- 1. Division of Oral Biology, School of Dentistry, University of Leeds, UK
- Division of Applied Health and Clinical Translation, School of Dentistry, University of Leeds, UK
- 3. Leeds Institute for Data Analytics, University of Leeds, UK

Correspondence: Jianhua Wu

DentCRU, Division of Applied Health and Clinical Translation, School of Dentistry, Worsley Building, Level 6, Clarendon Way, University of Leeds, LS2 9LU, UK.

Email: <u>J.H.Wu@Leeds.ac.uk</u>

Tel: 0044 (0)113 343 3431

Conflict of Interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

ORCID

Jianhua Wu http://orcid.org/0000-0001-6093-599X

Abstract

OBJECTIVES

This study is to investigate the association between central obesity and tooth loss in non-obese population.

MATERIAL AND METHODS

This national cross-sectional study included 19436 participants, aged 19-74 years with body mass index(BMI) 18.5-29.9 kg/m², from the national health and nutrition examination survey(NHANES) 1999-2012. Tooth loss was measured by the number of teeth missing. Central obesity was defined by a categorised 3-level waist circumference according to the WHO recommendation. A zero-inflated negative binomial model was used to investigate the association between tooth loss and central obesity. All models were adjusted for demographic, socioeconomic status, lifestyles, medical conditions, and inflammatory biomarkers.

RESULTS: For an overweight person with central obesity, the prevalence of tooth loss increased by 31% (Prevalence ratio [PR]:1.31, 95% CI:1.20-1.44) compared with a person with similar BMI but no central obesity, and increased by 40% (PR:1.40, 95% CI:1.26-1.56) if compared with a normal-weight person without central obesity. There was a clear stepwise association between tooth loss and central obesity.

CONCLUSION

The results reveal that central obesity is significantly associated with tooth loss in the non-obese population, which suggests that non-obese individuals with central

obesity may represent an important target population for oral health preventive strategies.

Key words: Obesity, Tooth loss, Body Mass Index, Central obesity, Periodontal disease, Dental health survey

Clinical Relevance

Scientific rationale for the study: Studies showed that the risk of tooth loss is increased in obese individuals, but the association is unclear in non-obese individuals. The current study investigated the association between central obesity and tooth loss in a non-obese population of 19,436 participants from a large national health survey.

Principal findings: The study showed that central obesity was significantly associated with tooth loss in a clear stepwise relationship in the non-obese population.

Practical implications: Given the evidence of the significant association between central obesity and tooth loss in non-obese population, clinicians should consider non-obese individuals with central obesity in oral health preventive strategies.

Introduction

General obesity (hitherto referred to simply as "obesity") is defined by body mass index (BMI) \geq 30 kg/m², in contrast central obesity is measured by waist-to-hip ratio

(WHR) and waist circumference (WC). Both general and central obesity are wellestablished factors for systemic inflammatory diseases, such as type II diabetes, hypertension and cardiovascular disease (Falagas and Kompoti, 2006, Chrysant and Chrysant, 2013). Studies have shown that obesity could induce chronic low-grade inflammation that reduce individual's immune threshold making obese individual more susceptible to dental caries, periodontal disease, and tooth loss (Tilg and Moschen, 2006, Flink et al., 2008, De Marchi et al., 2012, Nascimento et al., 2015, Suvan et al., 2015, Nascimento et al., 2016). C-reactive protein (CRP) is a nonspecific inflammatory biomarker linked to many inflammatory conditions including infection, periodontitis, cardiovascular disease, diabetes and obesity. The elevated levels of C-reactive protein, observed in obesity, is hypothesised to contribute to the development of periodontitis which along with other dental diseases, inflammatory and environmental factors could eventually lead to tooth loss, or more severely edentulism (Linden et al., 2008, Chaffee and Weston, 2010, Meisel et al., 2014). A mutual relationship might exist among CRP, obesity and periodontitis/tooth loss (Chaffee and Weston, 2010).

Studies have suggested a positive association between tooth loss and obesity (Jimenez et al., 2012, Ostberg et al., 2012, Jiang et al., 2013, Meisel et al., 2014, Keller et al., 2015, Nascimento et al., 2016). These studies focused on either comparing tooth loss between obese individuals and non-obese individuals, or between those individuals with central obesity and those with normal waist

circumference alone. Few studies adjusted for inflammatory biomarkers such as CRP or the association is often negligible after adjustment (Meisel et al., 2014, Keller et al., 2015, Nascimento et al., 2016).

Measures of central obesity by WC or WHR may provide further information in addition to BMI, and a combination of BMI and central obesity might have a better prognostic value in predicting mortality (Wormser et al., 2011, Coutinho et al., 2013, Sahakyan et al., 2015). Such analysis using both BMI and central obesity, however, requires relatively large sample size to achieve robust results to allow for subgroup analyses and has not been used to date to study the association between non-obese individual with central obesity and tooth loss. National health surveys, such as National Health and Nutrition Examination Survey (NHANES, 2015), are crosssectional survey conducted continuously on a two-year cycle to collect detailed anthropometric and health-related data on a large scale. These surveys provide reliable health, dental measures, and the inflammatory biomarker CRP level, and can be sufficiently large if several surveys are combined.

This study hypothesised that non-obese individuals with central obesity might have a higher risk of tooth loss compared with those non-obese individuals with normal waist circumference. We investigated the risk of tooth loss associated with central adiposity in non-obese individuals using a large national health survey, and assessed the robustness of the association by adjusting for a comprehensive lists of covariate variables and potential confounders.

Material & Methods

Study design and participants

This study is reported in accordance with the STROBE guidelines. This national cross-sectional study included participants from National Health and Nutrition Examination Survey (NHANES). NHANES is a national survey designed to assess the health and nutritional status for the non-institutionalised US population using a stratified, multistage, probability sampling design. NHANES has been using the same survey structure and conducting data collection in two-year cycle since 1999/2000, and consisted of extensive anthropometric, socioeconomic, health and dental related examinations and questionnaires, as well as laboratory testing for biomarkers. Height, weight and waist circumference were measured onsite by trained examiners; dental-related measures were taken by a trained dental survey staff and quality controlled by a second "gold standard" examiner. The methods and design for the survey are available elsewhere (NHANES, 2015).

We extracted data from seven NHANES surveys between 1999 and 2012. The surveys after 2012 did not include dental outcome and were excluded. In total, 33,107 adults aged between 19 and 74 years had BMI and waist circumference available. We restricted our analysis to non-obese individuals (BMI between 18.5 and 29.9 kg/m²) and those with validated tooth loss records. The resulting sample from NHANES was 19,436 participants (9,987 men and 9,449 women).

Exposure and outcome variables

Central obesity was characterised by waist circumference. Waist circumference was measured by a trained examiner or nurse with a measuring tape positioned at the high point of the iliac crest. Waist circumference was categorised into 3 levels (normal, high, and very high) for men (<=94 cm, 94-102 cm, and >102 cm) and women (<=80 cm, 80-88 cm; >88 cm) in accordance to World Health Organization

(WHO) cut-off points recommendations for the increased risk of metabolic complications.(WHO, 2008) Central obesity was defined as those men or women with very high waist circumference. The 3-level categorised waist circumference (normal, high and very high) in combination with 2-level BMI (normal-weight, 18.5≤BMI≤24.9kg/m² and overweight, 25 ≤BMI≤29.9kg/m²) was used as the main exposure in this study.

The teeth for each participant was examined by trained and calibrated health technologists. The status of each tooth was reported as follows: sound, missing due to dental disease, missing due to dental disease but replaced, missing due to other causes, tooth with surface conditions, and unerupted. The tooth was classified as missing if it was reported as missing due to dental disease or missing due to dental disease but replaced. For each participant, the number of teeth missing due to dental disease was between 0 (full dentition) and 32 (edentulous) and was used as the primary outcome. The individuals with tooth loss due to traumatic injuries were excluded in the analysis.

Covariate variables

Demographic, socioeconomic status (SES), life-style and medical history variables were taken through onsite interview and questionnaires. Age (years) was used as a continuous variable. Education level was dichotomised into those having college degree or above and into those having high school degree or below. Ethnicity was dichotomised as White or other races. Household income was divided into five equivalised quintiles. BMI (kg/m²) was used a continuous variable (rounded to 0.1 kg/m²) and was also dichotomised into normal-weight (18.5 \leq BMI \leq 24.9 kg/m²) and overweight (25 \leq BMI \leq 29.9 kg/m²).

Life style variables such as alcohol intake, smoking status and physical activity were collected through self-completed questionnaires. Participants were defined as alcohol drinker if they had at least 12 alcohol drinks in the past year. Smoking status was dichotomised as ever smoker (current or past) and non-smoker. Participants were assessed as physically active (yes or no) if they have done any moderate-intensity sports, fitness or recreational activities that cause a small increase in breathing or heart rate for at least 10 minutes continuously each day. Participants had reported the time of last dental visit (within 1 year or over 1 year) and the condition of oral hygiene (good/fair or poor). Medical conditions such as cardiovascular disease and diabetes were recorded only if they were confirmed as doctor-diagnosed.

A nonfasting blood sample was drawn from participants who consented to take blood sample, and a 9-hour fasting was required for those participants attending the morning session examinations. CRP was determined in serum by particle-enhanced immunonephelometry (hsCRP kit, Dade Behring) with a test sensitivity of 0.1 mg/L. To account for the possible nonlinear relationship, CRP was categorised into 3 levels (<1.0 mg/L; 1.0-3.0 mg/L; and >3.0 mg/L) according to CDC/AHA recommendations. (Pearson et al., 2003)

Statistical analysis

Descriptive statistics were reported for demographic, socioeconomic, life style, anthropometric, medical conditions and laboratory variables stratified by normalweight and overweight according to BMI and gender as well. Continuous variables were presented as mean (SD) or median (interquartile range) and categorical variables were reported as frequency (%).

Tooth loss was quantified by the number of teeth missing excluding third molars (range 0-28). To account for the higher proportion of zero-missing tooth (Figure 1), a zero-inflated negative binomial model (Preisser et al., 2012) was used to investigate the association between the severity of tooth loss and central obesity measured by a combination of BMI and WC (normal-weight and low WC, normal-weight and high WC, normal-weight and very high WC, overweight and low WC, overweight and high WC, overweight and very high WC). The model included the 6-level measure of central obesity, demographic (age, education level, ethnicity and marital status), SES, life style (alcohol intake, smoking status, dental visit, oral hygiene and physical activity), medical conditions (Cardiovascular diseases and diabetes), and a 3-level CRP as covariates. Backward model selection was used to eliminate covariate variables from the adjusted model using the Akaike information criterion (AIC). The final model contained only exposure variable and covariates that were significant at a significance level of 0.05. Odds ratio (OR) and its 95% confidence interval were reported for the logistic part of the model, corresponding to no tooth loss. Prevalence ratio (PR) and its 95% confidence interval were reported for the truncated negative binomial part of the model, corresponding to the severity of tooth loss. After the final models were established, prevalence ratios were estimated with the estimated model parameters for different combinations of BMI and WC. We explored the fitting of alternative models such as negative binomial model and zero-inflated Poisson model, while zero-inflated negative binomial model provided the best fit of the data in comparison to the alternative models.

A sensitivity analysis was performed by including third molars in the tooth loss to test the impact of the extraction of wisdom teeth. International guidelines also use a 2level cut-off of waist circumference (\geq 102 cm for men or \geq 88 cm for women) to define

central obesity (Yu and Kuo, 2008, NCEP, 2002), therefore we also performed a sensitivity analysis using the 2-level waist circumference (low and high) to examine the robustness of the association by the different cut-off points. Tooth loss due to dental disease was less prevalent in the younger individuals, therefore a subgroup analysis was performed for the stratified age (19-40 and 41-74 years). A mediation analysis was performed to investigate the mediational effect of CRP in the association between central obesity and tooth loss for the study population and age subgroups.

To minimize bias caused by a small proportion of the missing data in the covariate variables, multiple imputation by chained equations was used to produce 10 imputed data sets. Pooled modelling estimates and accompanying 95% CIs were generated according to Rubin's rules.(Rubin and Schenker, 1991). We reported all regression models using the multiply imputed datasets, and we also performed the same analyses on the dataset with complete cases as a sensitivity analysis.

NHANES were collected through complex survey design that were meant to be representative of the general population in US, therefore the descriptive statistics and all models in the study were adjusted for sampling weights and incorporated with clustering and stratification factors to obtain unbiased estimates and robust variance.

Data management and analyses were performed in R version 3.4.1 (https://cran.rproject.org/). R code was presented in Supplement material to demonstrate how to conduct zero-inflated negative binomial model with complex survey design. An alpha level of 0.05 was used to determine statistical significance.

Results

Study population consisted of 19,436 individuals with BMI between 18.5 and 29.9 kg/m², 8,874 (45.7%) of whom were normal-weight individuals (Table 1). Comparing with normal-weight individuals, overweight individuals were slightly older (mean age: 46.5 vs 42.0 years); had lower education level (47.4% vs 53.4%); had higher inflammatory CRP level (median: 1.8 vs 1.0 mg/L); and had higher proportion of diabetes (8.4% vs 4.7%). Central obesity distributed differently between normal-weight and overweight individuals (Table 1).

The distribution of tooth loss excluding third molars is shown in Figure 1. 45% of the study population did not have any tooth loss, and percentage decreased exponentially as the number of teeth missing increased (Supplementary Table 1). If third molars were included in tooth loss, only 18% people had the full 32 dentitions; nearly a quarter of participants had 4 missing teeth, 80% of which were wisdom teeth (Supplementary Figure 1).

The results of the zero-inflated negative binomial model demonstrated that central obesity was associated with the severity of tooth loss for those individuals with missing teeth (supplementary Table 2). Based on the results from the model, we estimated the prevalence ratios for tooth loss attributed to central obesity in comparison with other groups.

Individual comparisons for different combinations of BMI, waist circumference, and tooth loss are presented in Table 2. Overweight participants with central obesity (profile 6) had a higher risk of tooth loss than participants with any other combinations of BMI and waist circumference. Specifically, an overweight person with central obesity had an 31% higher risk of tooth loss than a person with similar BMI but no central obesity (profile 4; PR = 1.31, 95% CI: 1.20-1.44, for profile 6 vs. 4,

Table 2). Similarly, the risk of tooth loss increased by 16% for a normal-weight person with central obesity compared with a person with similar BMI but no central obesity (PR = 1.16, 95% CI: 1.04-1.30, for profile 3 vs. 1, Table 2). There was a clear stepwise association between the risk of tooth loss and the combinations of BMI and WC (Figure 2).

In the sensitivity analysis, if third molars were included in tooth loss, the prevalence ratio for comparing profile 6 vs. 4 was reduced from 1.31 to 1.20 (supplementary Table 2 and 3). If the 2-level waist circumference was used in the model, an overweight person with central obesity had 20% higher risk of tooth loss than an overweight person but no central obesity (PR = 1.20, 95% CI: 1.13-1.27, for profile 4 vs. 3, Table 3 and supplementary Table 5). Analyses of the dataset with complete cases showed similar results as the multiply imputed dataset (Supplementary Table 4). Interestingly, the association between household income and tooth loss was reversed in the logistic part of the model when third molars were included in tooth loss (Supplementary Table 3 and 6).

Subgroup analysis for stratified age groups showed similar trend and magnitude of effect in the association between central obesity and tooth loss (Supplementary Table 7-8), although some categories for age group 19-40 years were not statistically significant due to smaller number of teeth missing in these categories.

In the fully adjusted models, CRP showed significant effects in both parts of the models (Supplementary Table 2-6), indicating that CRP was associated with the probability of tooth loss and increased the severity of tooth loss as well. However, mediation analysis for CRP revealed that the mediational effect of CRP was only significant for age 41-74 years but not for age 19-40 years (Supplementary Table 9).

Discussion

Our analyses showed that central obesity in non-obese people is significantly associated with tooth loss. There was a clear stepwise association between tooth loss and central obesity in this non-obese population.

Our study expanded previous findings of tooth loss in obese versus non-obese people by addressing the value of combining measures of body mass index together with abdominal obesity to predict the risk of tooth loss (Meisel et al., 2012, Jiang et al., 2013, Meisel et al., 2014). Previous studies showed only a weak or negligible association using BMI alone as exposure variable with incomplete adjustment for confounders (Ojima et al., 2007, Jiang et al., 2013). Our study, however, has shown that after stratifying BMI into normal and overweight categories, central obesity is an important and significant predictor for tooth loss in the respective categories. Considering nearly one third of the non-obese population is centrally obese, our findings may have significant clinical implications as non-obese individuals with central obesity were often not considered as a priority population for prevention programs by guideline developers. For example, the 2013 AHA/ACC Obesity Management Guidelines (Jensen et al., 2014) recommend measuring waist circumference only in individuals with elevated BMI thereby implying that people with normal BMI are free of any particular adiposity-related risk.

Our study showed that inflammatory biomarker CRP was significantly associated with the probability of tooth loss and increased the severity of tooth loss in both parts of the model. Mediation analysis of CRP indicated that CRP played a more important role in mediating the association between central obesity and tooth loss in older individuals than in young individuals possibly due to lower and shorter exposure of

systemic inflammation in the young individuals. Previous studies also showed that CRP might be an important mediator between obesity and tooth loss or periodontal disease. (Linden et al., 2008, Buchwald et al., 2013, Meisel et al., 2014) Central obesity is closely related to systemic inflammation as characterised by higher CRP levels (Cartier et al., 2009, Meisel et al., 2012), while the general overweight individuals also had higher CRP levels as shown in Table 1. There may be a combined effect of general overweight and central obesity in relation to the level of systemic inflammation. Therefore, central obesity measures such as waist circumference in combination with BMI may contain additional information in predicting tooth loss.

In addition, the sensitivity analysis showed that the association between tooth loss and central obesity was robust despite of extensive adjustment of covariates and confounders, including third molars or using different cut-off points for central obesity. Adding third molars in tooth loss reduced the association. Removal of third molars may not be related to symptoms or pathology, but rather to prevent future problems.(Cunha-Cruz et al., 2014, Ghorbani and Peres, 2015) This was evident that socioeconomic status was negatively associated with tooth loss in the logistic part of the model when third molars were included in tooth loss (Supplementary table 2 and 5). People in the higher socioeconomic status were more likely to remove their third molars to prevent future problems, therefore the association between tooth loss and central obesity could be confounded by the unmeasured factors.

The strengths of our study include first, the use of a large representative national population of participants. Second, a zero-inflated model was used to model the effect of central obesity on tooth loss (ordinary logistic model) and quantify the prevalence if there was tooth loss (negative binomial model) separately. Third,

adjustment of a comprehensive list of covariate variables, including inflammatory biomarkers and lifestyle factors, reduced the potential confounding bias. However, several limitations of the study should be acknowledged, including some that are intrinsic to the national surveys. This cross-sectional study could not prove a causeand-effect association between central obesity and tooth loss or could not establish the direction of the association. A reverse causation of tooth loss causing central obesity may be possible, because masticatory inefficiency due to tooth loss can consequently change dietary choices with reduced intake of vegetables, fruits and dietary fibres, which can lead to general or central obesity. (Zhu and Hollis, 2015) This cross-sectional study could not investigate the mediational effect of periodontitis in the association between central obesity and tooth loss as the mediational effect of periodontitis leading to tooth loss would have happened before the data collection. Moreover, information on comorbidities (cardiovascular disease, diabetes), dental visits, alcohol intake, smoking status, physical activities, oral hygiene, were selfreported by participants, which potentially can lead to errors. Although a 'raised' waist circumference is a useful indicator of excess abdominal adiposity, we cannot exclude misclassification related to measurement errors.

Conclusion

The study shows that the risk of tooth loss is substantially increased in non-obese people with central obesity. The findings reveal that the impact of central obesity on tooth loss in non-obese population is significant and suggest that non-obese individuals with central obesity may represent an important target population for oral health prevention strategies and guideline development.

Acknowledgement

The research is supported by the National Institute for Health Research (NIHR) infrastructure at Leeds. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

References

- Buchwald, S., Kocher, T., Biffar, R., Harb, A., Holtfreter, B. & Meisel, P. (2013) Tooth loss and periodontitis by socio-economic status and inflammation in a longitudinal population-based study. J Clin Periodontol **40**, 203-211. doi:10.1111/jcpe.12056.
- Cartier, A., Cote, M., Lemieux, I., Perusse, L., Tremblay, A., Bouchard, C. & Despres, J. P. (2009) Sex differences in inflammatory markers: what is the contribution of visceral adiposity? Am J Clin Nutr 89, 1307-1314. doi:10.3945/ajcn.2008.27030.
- Chaffee, B. W. & Weston, S. J. (2010) Association between chronic periodontal disease and obesity: a systematic review and meta-analysis. J Periodontol **81**, 1708-1724. doi:10.1902/jop.2010.100321.
- Chrysant, S. G. & Chrysant, G. S. (2013) New insights into the true nature of the obesity paradox and the lower cardiovascular risk. J Am Soc Hypertens **7**, 85-94. doi:10.1016/j.jash.2012.11.008.
- Coutinho, T., Goel, K., Correa de Sa, D., Carter, R. E., Hodge, D. O., Kragelund, C., Kanaya, A. M., Zeller, M., Park, J. S., Kober, L., Torp-Pedersen, C., Cottin, Y., Lorgis, L., Lee, S. H., Kim, Y. J., Thomas, R., Roger, V. L., Somers, V. K. & Lopez-Jimenez, F. (2013) Combining body mass index with measures of central obesity in the assessment of mortality in subjects with coronary disease: role of "normal weight central obesity". J Am Coll Cardiol 61, 553-560. doi:10.1016/j.jacc.2012.10.035.
- Cunha-Cruz, J., Rothen, M., Spiekerman, C., Drangsholt, M., McClellan, L., Huang,
 G. J. & Northwest Practice-Based Research Collaborative in Evidence-Based,
 D. (2014) Recommendations for third molar removal: a practice-based cohort study. Am J Public Health **104**, 735-743. doi:10.2105/AJPH.2013.301652.
- De Marchi, R. J., Hugo, F. N., Hilgert, J. B. & Padilha, D. M. (2012) Number of teeth and its association with central obesity in older Southern Brazilians. Community Dent Health **29**, 85-89.
- Falagas, M. E. & Kompoti, M. (2006) Obesity and infection. Lancet Infect Dis **6**, 438-446. doi:10.1016/S1473-3099(06)70523-0.
- Flink, H., Bergdahl, M., Tegelberg, A., Rosenblad, A. & Lagerlof, F. (2008) Prevalence of hyposalivation in relation to general health, body mass index and remaining teeth in different age groups of adults. Community Dent Oral Epidemiol 36, 523-531. doi:10.1111/j.1600-0528.2008.00432.x.
- Ghorbani, Z. & Peres, K. G. (2015) Is the association between socioeconomic status and nonreplaced extracted teeth mediated by dental care behaviours in adults? Community Dent Oral Epidemiol **43**, 532-539. doi:10.1111/cdoe.12178.
- Jensen, M. D., Ryan, D. H., Apovian, C. M., Ard, J. D., Comuzzie, A. G., Donato, K. A., Hu, F. B., Hubbard, V. S., Jakicic, J. M., Kushner, R. F., Loria, C. M., Millen, B. E., Nonas, C. A., Pi-Sunyer, F. X., Stevens, J., Stevens, V. J., Wadden, T. A., Wolfe, B. M., Yanovski, S. Z., American College of Cardiology/American Heart Association Task Force on Practice, G. & Obesity,

S. (2014) 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. J Am Coll Cardiol **63**, 2985-3023. doi:10.1016/j.jacc.2013.11.004.

- Jiang, Y., Okoro, C. A., Oh, J. & Fuller, D. L. (2013) Sociodemographic and healthrelated risk factors associated with tooth loss among adults in Rhode Island. Prev Chronic Dis **10**, E45. doi:10.5888/pcd10.110285.
- Jimenez, M., Hu, F. B., Marino, M., Li, Y. & Joshipura, K. J. (2012) Prospective associations between measures of adiposity and periodontal disease. Obesity (Silver Spring) **20**, 1718-1725. doi:10.1038/oby.2011.291.
- Keller, A., Rohde, J. F., Raymond, K. & Heitmann, B. L. (2015) Association between periodontal disease and overweight and obesity: a systematic review. J Periodontol 86, 766-776. doi:10.1902/jop.2015.140589.
- Linden, G. J., McClean, K., Young, I., Evans, A. & Kee, F. (2008) Persistently raised C-reactive protein levels are associated with advanced periodontal disease. J Clin Periodontol **35**, 741-747. doi:10.1111/j.1600-051X.2008.01288.x.
- Meisel, P., Holtfreter, B., Volzke, H. & Kocher, T. (2014) Sex Differences of Tooth Loss and Obesity on Systemic Markers of Inflammation. J Dent Res **93**, 774-779. doi:10.1177/0022034514535604.
- Meisel, P., Wilke, P., Biffar, R., Holtfreter, B., Wallaschofski, H. & Kocher, T. (2012) Total tooth loss and systemic correlates of inflammation: role of obesity. Obesity (Silver Spring) **20**, 644-650. doi:10.1038/oby.2011.218.
- Nascimento, G. G., Leite, F. R., Conceicao, D. A., Ferrua, C. P., Singh, A. & Demarco, F. F. (2016) Is there a relationship between obesity and tooth loss and edentulism? A systematic review and meta-analysis. Obes Rev **17**, 587-598. doi:10.1111/obr.12418.
- Nascimento, G. G., Leite, F. R., Do, L. G., Peres, K. G., Correa, M. B., Demarco, F. F. & Peres, M. A. (2015) Is weight gain associated with the incidence of periodontitis? A systematic review and meta-analysis. J Clin Periodontol 42, 495-505. doi:10.1111/jcpe.12417.
- NCEP (2002) National Cholesterol Education Program. Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III Final Report). National Institutes of Health. p. II-17.
- NHANES (2015) National Health and Nutrition Examination Survey. Atlanta, GA: National Center for Health Statistics. In: Accessed at <u>http://www.cdc.gov/nchs/nhanes/survey_methods.htm</u> on 13 July 2016.
- Ojima, M., Hanioka, T., Tanaka, K. & Aoyama, H. (2007) Cigarette smoking and tooth loss experience among young adults: a national record linkage study. BMC Public Health **7**, 313. doi:10.1186/1471-2458-7-313.
- Ostberg, A. L., Bengtsson, C., Lissner, L. & Hakeberg, M. (2012) Oral health and obesity indicators. BMC Oral Health **12**, 50. doi:10.1186/1472-6831-12-50.
- Pearson, T. A., Mensah, G. A., Alexander, R. W., Anderson, J. L., Cannon, R. O., 3rd, Criqui, M., Fadl, Y. Y., Fortmann, S. P., Hong, Y., Myers, G. L., Rifai, N.,

Smith, S. C., Jr., Taubert, K., Tracy, R. P., Vinicor, F., Centers for Disease, C., Prevention & American Heart, A. (2003) Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation **107**, 499-511.

- Preisser, J. S., Stamm, J. W., Long, D. L. & Kincade, M. E. (2012) Review and recommendations for zero-inflated count regression modeling of dental caries indices in epidemiological studies. Caries Res **46**, 413-423. doi:10.1159/000338992.
- Rubin, D. B. & Schenker, N. (1991) Multiple imputation in health-care databases: an overview and some applications. Stat Med **10**, 585-598.
- Sahakyan, K. R., Somers, V. K., Rodriguez-Escudero, J. P., Hodge, D. O., Carter, R. E., Sochor, O., Coutinho, T., Jensen, M. D., Roger, V. L., Singh, P. & Lopez-Jimenez, F. (2015) Normal-Weight Central Obesity: Implications for Total and Cardiovascular Mortality. Ann Intern Med **163**, 827-835. doi:10.7326/M14-2525.
- Suvan, J. E., Petrie, A., Nibali, L., Darbar, U., Rakmanee, T., Donos, N. & D'Aiuto, F. (2015) Association between overweight/obesity and increased risk of periodontitis. J Clin Periodontol. doi:10.1111/jcpe.12421.
- Tilg, H. & Moschen, A. R. (2006) Adipocytokines: mediators linking adipose tissue, inflammation and immunity. Nat Rev Immunol **6**, 772-783. doi:10.1038/nri1937.
- WHO (2008) World Health Organization. Waist Circumference and Waist-Hip Ratio. Geneva, Switzerland.
- Wormser, D., Kaptoge, S., Di Angelantonio, E., Wood, A. M., Pennells, L., Thompson, A., Sarwar, N., Kizer, J. R., Lawlor, D. A., Nordestgaard, B. G., Ridker, P., Salomaa, V., Stevens, J., Woodward, M., Sattar, N., Collins, R., Thompson, S. G., Whitlock, G. & Danesh, J. (2011) Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. Lancet **377**, 1085-1095. doi:10.1016/S0140-6736(11)60105-0.
- Yu, Y. H. & Kuo, H. K. (2008) Association between cognitive function and periodontal disease in older adults. J Am Geriatr Soc 56, 1693-1697. doi:10.1111/j.1532-5415.2008.01847.x.
- Zhu, Y. & Hollis, J. H. (2015) Associations between the number of natural teeth and metabolic syndrome in adults. J Clin Periodontol 42, 113-120. doi:10.1111/jcpe.12361.

	18.5≤BMI≤	24.9 kg/m²	25≤BMI≤2	25≤BMI≤29.9 kg/m²	
Characteristic	Women	Men	Women	Men	
n	4740	4134	4709	5853	
Age in years, mean (SD)	41.8 (15.7)	42.3 (16.3)	45.7 (15.6)	47.1 (15.1)	
Ethnicity, races other than white	2257 (47.6)	2330 (56.4)	2764 (58.7)	3233 (55.2)	
Education, College or above	2775 (58.7)	1957 (47.4)	2251 (47.8)	2751 (47.0)	
BMI (kg/m²), mean (SD)	22.3 (1.7)	22.7 (1.7)	27.4 (1.4)	27.5 (1.4)	
Waist circumference					
Normal	2138 (46.4)	3587 (89.0)	111 (2.4)	1561 (27.4)	
High	1787 (38.8)	408 (10.1)	913 (19.9)	2516 (44.2)	
Very high	683 (14.8)	35 (0.9)	3558 (77.7)	1610 (28.3)	
CRP (mg/l), median [IQR]	1.1 [0.5, 2.9]	0.9 [0.4, 2.1]	2.5 [1.1, 5.1]	1.5 [0.7, 3.1]	
Categorised CRP					
<1.0 mg/l	1730 (45.2)	1685 (52.5)	798 (20.8)	1669 (35.0)	
1.0-3.0 mg/l	1179 (30.8)	955 (29.8)	1412 (36.9)	1896 (39.8)	
>3.0 mg/l	916 (23.9)	568 (17.7)	1620 (42.3)	1203 (25.2)	
Equivalised household income					
Top quintile	1334 (31.2)	870 (23.4)	938 (22.2)	1450 (27.5)	
2 nd quintile	897 (21.0)	744 (20.0)	952 (22.5)	1178 (22.3)	
3 rd quintile	908 (21.3)	896 (24.1)	978 (23.1)	1244 (23.6)	
4 th quintile	580 (13.6)	608 (16.3)	701 (16.6)	767 (14.5)	
Bottom quintile	552 (12.9)	602 (16.2)	657 (15.5)	637 (12.1)	
Last dental visits > 1 year	948 (36.1)	1281 (54.1)	1011 (39.6)	1461 (46.4)	
Poor dental hygiene	405 (10.5)	506 (15.0)	474 (12.0)	593 (12.1)	
Alcohol intake	2807 (66.5)	3176 (83.4)	2500 (59.0)	4647 (85.9)	
Ever smoker	1794 (37.9)	2414 (58.4)	1728 (36.7)	3259 (55.7)	
Physically active	2428 (51.6)	1825 (44.5)	2095 (44.9)	2644 (45.5)	
Diabetes	171 (3.6)	240 (5.9)	354 (7.6)	522 (9.0)	
Cardiovascular disease	165 (3.5)	261 (6.3)	246 (5.2)	453 (7.7)	

Table 1. Characteristics of study population, stratified by BMI and gender.

Data are presented as frequency (%) unless specified; SD: standard deviation; IQR: interquartile range; CRP, C-reactive Protein. Numbers may not sum to totals due to missing values; percentage may not sum to 100 due to rounding.

Table 2. Prevalence ratios and 95% confidence interval for the severity of tooth loss as estimated by the zero-inflated negative binomial model. Third molars were excluded in tooth loss, and a 3-level waist circumference was used. To interpret the prevalence ratio, select an intersection of two anthropometric profiles of interest (BMI and WC). The group of interest (i) relative to reference (j) is labelled as "i vs. j" in the cells. For example, to compare an overweight and centrally obese individual (profile 6) to an overweight individual with normal WC (profile 4), the cell in row 4 and column 6 would be used (denoted as 6 vs. 4 with PR = 1.31 and 95% CI: 1.20 to 1.44).

1. Normal-	2 vs. 1	3 vs. 1	4 vs. 1	5 vs. 1	6 vs. 1
weight	1.13	1.16	1.07	1.17	1.40
and low WC	(1.05-1.22)	(1.04-1.30)	(0.96-1.18)	(1.06-1.28)	(1.26-1.56)
1 vs. 2	2. Normal-	3 vs. 2	4 vs. 2	5 vs. 2	6 vs. 2
0.88	weight	1.03	0.94	1.03	1.24
(0.82-0.95)	and high WC	(0.92-1.15)	(0.85-1.05)	(0.94-1.13)	(1.13-1.36)
1 vs. 3	2 vs. 3	3. Normal-weight and very high WC	4 vs. 3	5 vs. 3	6 vs. 3
0.86	0.97		0.92	1.01	1.21
(0.77-0.96)	(0.87-1.09)		(0.81-1.05)	(0.89-1.13)	(1.07-1.36)
1 vs. 4	2 vs. 4	3 vs. 4	4 .	5 vs. 4	6 vs. 4
0.94	1.06	1.09	Overweight	1.10	1.31
(0.85-1.04)	(0.95-1.18)	(0.96-1.24)	and low WC	(1.00-1.20)	(1.20-1.44)
1 vs. 5	2 vs. 5	3 vs. 5	4 vs. 5	5. Overweight and high WC	6 vs. 5
0.86	0.97	0.99	0.91		1.20
(0.78-0.94)	(0.88-1.06)	(0.88-1.12)	(0.83-1.00)		(1.13-1.28)
1 vs. 6	2 vs. 6	3 vs. 6	4 vs. 6	5 vs. 6	6. Overweight
0.71	0.81	0.83	0.76	0.83	and very high
(0.64-0.79)	(0.73-0.89)	(0.74-0.93)	(0.69-0.84)	(0.78-0.89)	WC

Table 3. Prevalence ratios and 95% confidence interval for the severity of tooth loss as estimated by the zero-inflated negative binomial model. Third molars were excluded in tooth loss, and a 2-level waist circumference was used.

1. Normal-weight and not centrally obese	2 vs. 1	3 vs. 1	4 vs. 1
	1.08	1.06	1.27
	(1.01-1.19)	(0.98-1.20)	(1.16-1.39)
1 vs. 2	2. Normal-weight and centrally obese	3 vs. 2	4 vs. 2
0.92		0.98	1.18
(0.84-0.99)		(0.88-1.10)	(1.05-1.32)
1 vs. 3	2 vs. 3	3. Overweight and not centrally obese	4 vs. 3
0.94	1.02		1.20
(0.87-1.02)	(0.91-1.14)		(1.13-1.27)
1 vs. 4	2 vs. 4	3 vs. 4	4. Overweight and centrally obese
0.79	0.85	0.83	
(0.72-0.86)	(0.76-0.95)	(0.79-0.89)	

Figure legend

Figure 1. Distribution of tooth loss excluding third molars.

Figure 2. Prevalence ratio and 95% CI for the severity of tooth loss by the combinations of BMI and waist circumference.