

Association between tooth loss, chronic conditions and common risk factors – results from the 2019 Brazilian Health Survey

Cunha de Medeiros, Tayse Caroline; Areas e Souza, Alessandra ; Coelho Prates, Rodolfo; Chapple, Iain; Steffens, Joao Paulo

DOI:

[10.1002/JPER.21-0433](https://doi.org/10.1002/JPER.21-0433)

License:

None: All rights reserved

Document Version

Peer reviewed version

Citation for published version (Harvard):

Cunha de Medeiros, TC, Areas e Souza, A, Coelho Prates, R, Chapple, I & Steffens, JP 2021, 'Association between tooth loss, chronic conditions and common risk factors – results from the 2019 Brazilian Health Survey', *Journal of Periodontology*. <https://doi.org/10.1002/JPER.21-0433>

[Link to publication on Research at Birmingham portal](#)

Publisher Rights Statement:

This is the peer reviewed version of the following article: Medeiros, T.C.C.d., Areas e Souza, A., Prates, R.C., Chapple, I. and Steffens, J.P. (2021), Association between tooth loss, chronic conditions and common risk factors – results from the 2019 Brazilian Health Survey. *J Periodontol.*, which has been published in final form at <https://doi.org/10.1002/JPER.21-0433>. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions. This article may not be enhanced, enriched or otherwise transformed into a derivative work, without express permission from Wiley or by statutory rights under applicable legislation. Copyright notices must not be removed, obscured or modified. The article must be linked to Wiley's version of record on Wiley Online Library and any embedding, framing or otherwise making available the article or pages thereof by third parties from platforms, services and websites other than Wiley Online Library must be prohibited.

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

ASSOCIATION BETWEEN TOOTH LOSS, CHRONIC CONDITIONS AND COMMON RISK FACTORS – RESULTS FROM THE 2019 BRAZILIAN HEALTH SURVEY

Tayse Caroline Cunha de Medeiros, DDS¹

Alessandra Areas e Souza, PhD^{1,2}

Rodolfo Coelho Prates, PhD³

Iain Chapple, PhD⁴

João Paulo Steffens, PhD¹

Corresponding Author:

Prof. Dr. João Paulo Steffens. Av. Prof. Lothário Meissner, 632. Curitiba, PR, Brazil Zip-Code 80210-170. Phone/Fax: +554133604032.

E-mail: joao.steffens@ufpr.br - Fax number and email can be published.

Word Count: 3,351

Number of Figures: 01

Number of Tables: 05

Number of Supplemental Tables: 02

Number of References: 45

Short title: Tooth loss and chronic conditions/common risk factors.

One sentence summary: Tooth loss was associated with virtually all systemic chronic conditions investigated, possibly due to shared risk factors.

¹Department of Stomatology, Federal University of Paraná, Curitiba, Brazil.

²Department of Specific Training, Federal University Fluminense, Nova Friburgo, Brazil.

³Postgraduate Program in Health and Environment, University of Joinville Region, Joinville, Brazil.

⁴Periodontal Research Group, Institute of Clinical Sciences, College of Medical and Dental Sciences, The University of Birmingham, and Birmingham Community Healthcare Foundation NHS Trust, Birmingham, UK.

ABSTRACT

Background: The aim of this study was to evaluate the association between systemic non-communicable diseases (NCDs; including lung, kidney, mental and cardiovascular diseases, rheumatoid arthritis, cancer and spinal problems), common risk factors, and tooth loss (TL), as an endpoint of prevalent oral chronic non-communicable diseases (NCDs; periodontitis and caries).

Methods: 73,137 non-institutionalized adults (≥ 30 years) were evaluated, using data from the 2019 Brazilian National Health Survey. Negative binomial regressions were performed, adjusting for sex, age, ethnicity, educational attainment, oral hygiene, risk factors for periodontitis and caries (diabetes, smoking and a cariogenic diet). The dependent variable was TL expressed as a numerical value.

Results: Diabetes, current smoking and a frequent cariogenic diet were significantly associated with TL Incidence Risk Ratio (IRR;95%CI): 1.11(1.08-1.14), 1.28(1.25-1.31) and 0.97(0.94-0.99), respectively. Significant associations were observed for TL and all assessed NCDs, except for kidney diseases, cancer and musculoskeletal diseases related to work, with IRR ranging from 1.06 for hypertension and asthma to 1.16 for rheumatoid arthritis. Regular consumption (4-7 days/week) of vegetables, fruits and beef; alcohol up to 8 doses/week; and physical exercise were associated with a lower IRR for TL ($p < 0.05$). Obesity, but not overweight, was associated with increased TL [1.05(1.03-1.07)]. Smoking, hypertension, arthritis, other mental diseases and spinal problems further increased the IRR for TL in individuals with diabetes ($p < 0.05$).

Conclusion: We conclude that certain chronic systemic conditions are associated with TL in Brazilian adults. This is likely due to periodontitis and shared risk factors; however causal associations cannot be examined in this cross-sectional dataset.

Keywords: Tooth Loss, Noncommunicable Diseases, Risk Factors, Brazil.

INTRODUCTION

Tooth loss (TL) is a public health problem that generates esthetic, functional, social and psychological harm, which impacts upon quality of life¹ and healthy life years.² Data from the Global Burden of Disease 2010 studies demonstrate that severe TL (having fewer than 9 remaining permanent teeth) was the 36th most common health condition in humans, affecting 2% of the population.³ Risk factors for TL are multiple and complex and include age, smoking, economic status, reason for seeking dental services, previous TL, tooth fracture, dental caries and periodontal status.⁴

Since untreated dental caries and periodontitis have been described as the two main reasons for TL in adults⁵, TL is ultimately the final outcome of those diseases. They are both highly prevalent chronic non-communicable diseases (NCDs), being considered the first (untreated dental caries in permanent teeth) and 6th (severe periodontitis) most common conditions in humans in 2010.^{6,7} Whilst dental caries and periodontitis share some risk factors (e.g., pathogenic plaque biofilm), the majority were found to be specific to each condition.⁸ For instance, while diabetes mellitus and smoking are commonly accepted risk factors for periodontitis, refined sugar and carbohydrate intake are known risk factors for dental caries.^{8,9}

Several mechanisms have been proposed to explain potential causal relationships between oral conditions and systemic diseases: i) disseminating infection – where oral bacteria (or their byproducts and toxins) enter the circulation and promote systemic injury; or ii) disseminating inflammation – where low-grade oral inflammation contributes to the pathogenesis of other systemic diseases¹⁰; iii) periodontal post-translational changes – where specific

immunopathological changes within the periodontium, such as development of a periodontal citrullinome may contribute to rheumatoid arthritis development.¹¹ However, it is also possible that those diseases develop as comorbidities due to common risk factors, such as smoking, physical inactivity, alcohol intake, deprivation, low educational attainment and poor nutrition.^{12,13} Although the concept of 'focal infection'¹⁴ is not new, understanding dental caries and periodontitis as NCDs has been proposed more recently.^{15,16} In contrast, dissemination of periodontal pathogens within the circulation may activate acute-phase¹⁷ and oxidative stress responses¹⁸, which may contribute to causal pathways in addition to underlying common risk factors/behaviors. Hence, large-scale studies assessing the association between each disease (or their endpoint - TL) with known risk factors for NCDs and with other chronic diseases are needed. These associations are important not only from a public health perspective, but also for case detection of systemic and oral diseases during medical or dental examinations to facilitate the development of individualized interdisciplinary care plans.¹⁹ Therefore, the objective of this study was to assess the associations between systemic chronic diseases, their common risk factors, and TL in a large national sample of community dwelling Brazilian adults.

MATERIALS AND METHODS

The Second National Health Survey - *Pesquisa Nacional em Saúde* (PNS) is a cross-sectional study conducted in 2019 by the Brazilian Institute of Geography and Statistics (IBGE, Rio de Janeiro, RJ, Brazil) in partnership with the Ministry of Health and the Ministry of the Economy. It was designed to estimate access to and use of health services, information on households, self-perceived health status, lifestyle, possession of chronic diseases, oral health status, primary health

care and anthropometric information. The coverage of the PNS was the entire national territory. Three-stage cluster sampling was employed. The first stage involved census tracts (primary sampling units); the second, households; and the third, dwellers aged 18 years old or more residing in randomly selected households. More details are described elsewhere.²⁰ The protocols for the study were approved by the National Research Ethics Commission of the National Health Council (CONEP, Brasilia, DF, Brazil).

All examiners were previously trained. The interviews were carried out through mobile collection devices pre-programmed with a research questionnaire and the variables of interest. The first step was a household screening interview, with any resident of the selected household, 15 years of age or older, who drew up a list of the other residents. The second step involved the random selection of one adult resident (≥ 18 years), who answered the individual interview. Interviews were scheduled according to the availability of the residents, with two or more visits expected.

Data extracted from the public database were self-reported and included: age; sex; ethnicity; educational attainment level; weight; height; oral health care (brushing frequency); smoking; presence of chronic diseases previously diagnosed by a physician: diabetes (excluding gestational diabetes), hypertension (excluding gestational hypertension), hypercholesterolemia, cardiovascular diseases (infarction, angina, heart failure, other heart disease and stroke), asthma, lung diseases (emphysema, chronic bronchitis, chronic obstructive pulmonary disease [COPD]), rheumatoid arthritis, kidney failure, cancer, work-related musculoskeletal disorders (WMSD), or other physical illnesses of over 6 months duration; presence of chronic diseases previously

diagnosed by a physician or a mental health professional: depression or other mental illnesses (anxiety disorder, panic syndrome, schizophrenia, bipolar disorder, psychosis, obsessive-compulsive disorder [OCD]); presence of back problems (chronic back or neck pain, low back pain, spinal disk problems); nutritional data: frequency of consumption of vegetables, fruits, beef, chicken, fish, junk food (replacing lunch meal with quick snacks); frequency of alcohol consumption; frequency and duration of physical exercise; number of missing teeth. The frequency of a cariogenic diet was calculated by considering the frequency of consumption of sweetened soft drinks (soda) - excluding diet/zero - or consumption of sweetened foods, such as stuffed cookies, chocolate, jelly, candies and other refined carbohydrates.

Data for adults aged 30 years and over, of both genders, were considered in this study *a priori*. The dependent variable TL was self-reported and registered as a numerical variable. To calculate TL, individuals answered to the following questions: 1) 'Remembering your permanent upper teeth, have you lost any?'; and then 2) 'How many permanent teeth have you lost in your upper jaw'? The possibilities for the first question were a) No; b) Yes, some of them; or c) Yes, I lost all my upper teeth. For responses b), the number of teeth reported in question 2) was considered. For responses a) and c), '0' and '16' teeth were recorded, respectively. The same questions were made for the lower jaw and the final TL number was calculated as the sum of lost teeth in the upper and lower jaws.

A negative binomial regression was preferred to Poisson regression due to overdispersion of the count variable (TL), which was confirmed by the likelihood-ratio test of alpha. Statistical adjustments were defined *a priori*: sex, age, ethnicity, educational level and oral health care. For the remaining variables,

the final models were further adjusted for recognized risk factors for periodontitis and caries: diabetes, smoking and a cariogenic diet. Individuals not reporting TL, or not reporting of the potentially confounding variables required to adjust for during statistical analysis were excluded from the analysis. In order to evaluate the impact of additional co-morbidities on the association of diabetes and TL, this subpopulation of only individuals with diabetes was evaluated, also using adjusted negative binomial regression. A new binary outcome was created for each individual: 0- diabetes without the evaluated condition; or 1- diabetes and the additional condition.

Sensitivity analyses were conducted by deleting the lowest dependent variable value (0; no TL), the highest value (32; all teeth lost), or both.²¹ We also conducted subgroup analysis to isolate possible periodontitis cases from caries cases. For that purpose, we have analyzed 1) only individuals older than 50 years of age (since periodontitis is more prevalent in older patients); and 2) only individuals in the lowest two tertiles of cariogenic diet (up to 4 days/week).²²

Databases containing the different variables were created separately to exclude individuals with missing values and reduce bias. Therefore, some analyses include reduced sample sizes, as fully disclosed in the appropriate Tables. Except for demographic data, results are expressed as adjusted incidence rate ratios (IRR) and 95% confidence interval (95% CI). All statistical analyses were performed using software*.

* Stata 13.0, Stata Corp LLC, College Station, TX, USA.

RESULTS

This study included 73,137 eligible individuals, from which 60,271 were analyzed (Figure 1). The final sample was comprised predominantly of females (54.5%), those with high school or higher education (52.14%), and a mean age of 51.6 ± 14 years. The prevalence of individuals with no TL was 16.7%, while 10% reported being totally edentulous (32 missing teeth). Mean TL was 9.83 ± 11 teeth. Approximately 94% reported brushing their teeth two or more times a day. Overall, except for smoking, women reported physician-diagnosed chronic diseases more often. Sociodemographic characteristics of the study population are described in table 1.

Diabetes and current smoking, both recognized risk factors for periodontitis, were statistically significantly associated with TL (IRR;95%CI): 1.11 (1.08-1.14) and 1.28 (1.25-1.31), respectively. Previous/former smoking was not statistically associated with TL. A frequent cariogenic diet (3-4 days/week and 5-7 days/week), a recognized risk factor for caries, was significantly associated with TL. However, confidence intervals were very close to 1, especially after adjustments for confounding factors (Table 2).

Virtually all chronic diseases investigated were associated with TL, with the exception of kidney diseases, cancer and WMSD. The highest IRR was observed for rheumatoid arthritis (1.16; 1.12-1.19), while the lowest statistically significant IRRs were for hypertension and asthma (1.06; 1.04-1.08 and 1.06; 1.03-1.11, respectively). The associations between all investigated systemic NCDs and TL can be found in table 3.

However, sensitivity analysis showed that kidney diseases, but not cancer and WMSD, is significantly associated with TL when edentulous individuals are

excluded from the analysis. Also, all other significant associations remain when only non-edentulous individuals are considered. On the other hand, lung diseases and mental illnesses, in addition to kidney diseases, cancer and WMSD, were not significantly associated with TL when only individuals with any TL (*i.e.*, excluding individuals with all teeth present) were analyzed (Supplemental Table 1).

Subgroup analysis showed that most significant associations between chronic diseases and TL remain even when considering only patients older than 50 years of age or when only the lowest two tertiles of cariogenic diet were considered, suggesting a potential role for periodontitis on the observed associations (Supplemental Table 2).

Exploratory analysis on the impact of co-morbidities in the association of diabetes and TL showed that IRR may increase from 6% (diabetes and back problems or diabetes and arthritis) to 15% (diabetes and smoking) when compared to patients with diabetes only. Other co-morbidities significantly associated with TL in individuals with diabetes were hypertension and mental illnesses. The association between cardiovascular diseases with TL was omitted due to co-linearity (Table 4).

The frequent consumption (4-7 days) of vegetables, fruits and beef was associated with a decreased IRR for TL. Interestingly however, the consumption of chicken and fish were statistically significantly associated with increased IRR for TL, but with confidence intervals very close to 1. Junk food was not statistically associated with TL ($p>0.05$). Physical exercise significantly decreased the IRR for TL. Total time of weekly exercise, but not frequency of weekly physical exercise (days/week), was statistically associated with TL, suggesting that at

least 75 minutes of weekly exercise associates with decreased TL. Obesity, but not being overweight, was significantly associated with TL. The categories evaluated for alcohol consumption showed a significant association with a decreased IRR for TL, except for the most frequent category evaluated (≥ 1 dose/day). All associations with common risk factors for NCDs can be found in Table 5.

DISCUSSION

Tooth loss is an important health indicator, since it reflects the progression of periodontitis and caries throughout life.^{6,8} These diseases are the two major causes for TL and share a number of risk factors with other NCDs. Common risk factors include unhealthy diet, lack of physical exercise, tobacco and alcohol consumption.²³

The current study demonstrates that diabetes mellitus and current smoking, both recognized risk factors for periodontitis,⁹ were significantly associated with TL, in accordance with previous studies.^{24,25} More importantly, data also demonstrates significant associations between TL and systemic NCDs, even after adjusting for the current known risk factors of diabetes and smoking. Given the cross-sectional nature of the data, it is not possible to attribute the relationship between TL and systemic NCDs to either common risk factors or a causal pathway. Also, it is important to note that although diabetes is the only chronic inflammatory disease currently considered for estimating the rate of periodontitis progression (grade),⁹ additional chronic conditions – smoking, hypertension, arthritis, other mental diseases and spinal problems - may increase the IRR for TL in individuals with diabetes even further (Table 4).

A significant negative association between frequency of a cariogenic diet and TL was observed in this study. Although the associations were statistically significant (IRR 0.97), the confidence intervals ranged from 0.94 to 0.99, suggesting a small effect size. A previous study investigating the association between dental caries and a cariogenic diet (sugar-sweetened beverages and sandwiches) in adults aged 30 years or older, also demonstrated a prevalence ratio with confidence intervals very close to 1, depending upon the adjustments performed in the final model.²⁶ One possible explanation is the role of food interactions in caries risk, or the fact that older adults have a more responsible dietary pattern than children and adolescents.

Almost all NCDs investigated were associated with TL. Rheumatoid arthritis was the condition that demonstrated the greatest association with TL. In fact, periodontal pathogens (*Porphyromonas gingivalis* and *Fusobacterium nucleatum*) were highly prevalent in the serum and synovial fluid of patients with rheumatoid arthritis.²⁷ Although some studies show a bidirectional relationship between rheumatoid arthritis and periodontitis, related to the systemic inflammatory response²⁸, the exact relationship between these two comorbidities remains to be determined, reinforcing the need for longitudinal studies to clarify this association.²⁹

The few exceptions for statistically significant associations between NCDs and TL were cancer, WMSD and kidney disease. For cancer, similar results were found by Abnet et al.³⁰ and Tu et al.³¹, but not by Maisoneuve et al.³², when pancreatic cancer was evaluated. WMSD is a prevalent condition, related to chronic inflammation and pain.³³ There are no available studies to support the association between WMSD and oral conditions. Possible explanations for the

lack of association with TL are the high heterogeneity of affected sites, varying from hands to back and neck, and the multi-causal nature of the disease that includes several work conditions like routine lifting of heavy objects, daily exposure to whole body vibration or performing repetitive forceful tasks.³⁴ Interestingly, cancer and WMSD were consistently not associated with TL in the sensitivity analyses performed. On the contrary, the association between kidney disease and TL became significant when edentulous individuals were not considered, or when total dentate and edentulous individuals were removed from the analyses, suggesting a role for possible current periodontal inflammation and associated oxidative stress (Supplemental Table 1).¹⁸

Apart from the possibility of a temporal relationship between oral and systemic NCDs, with diseases contributing to the pathogenesis of each other, it is also possible that NCDs develop independently due to shared risk factors. The World Health Organization suggests reducing the use of tobacco and the harmful use of alcohol, maintaining an active lifestyle and developing a healthy diet, as ways of reducing deaths from NCDs.²³ Our results showed that the consumption of vegetables, fruits and beef (4-7 days/week) decreased the IRR for TL. Data from 6,887 individuals, aged 30 years or older, participating in the NHANES 2009-10 and 2011-12, also showed that adherence to an anti-inflammatory diet was associated with fewer missing teeth and that the dietary pattern was a modifiable protective factor for tooth loss in the adult population of the United States.³⁵ On the other hand, junk food was not associated with TL in our study, even though saturated fats in junk foods could lead to an increase in obesity, diabetes and hyperlipidemia risk, and high salt content can raise blood pressure and contribute to cardiovascular disease, which has already been linked to periodontitis and

poor oral health.³⁶ Junk food in this study was considered when the respondent informed that they had replaced the lunch meal with fast food. A possible explanation for not finding an association in this sample can be that Brazilian adults usually eat rice and beans as a regular daily meal, which is rich in proteins and also there's a high consumption of fruits and vegetables, since it is a tropical country.

Our findings demonstrated that physical exercise, in special when performed for at least 75 minutes/week, significantly decreased IRR values for TL. In fact, individuals who exercise 3 to 5 times a week have a lower prevalence of periodontitis, possibly due to better habits related to food, smoking and alcohol consumption³⁷, although our results suggest that total weekly time of exercise is more important than weekly frequency. A possible explanation is that physical exercise triggers release of dopamine and serotonin, which can improve mood and help modulate immune responses, minimizing inflammatory mechanisms.³⁸

Our results also showed that obesity was significantly associated with TL, in accordance with Nascimento et al.³⁹, who found that obese individuals were at higher risk of TL and edentulism (OR [95%CI] 1,49 [1,20-1,86] and 1,25 [1,10-1,42], respectively). Masticatory quality, diet and poor oral hygiene can link these conditions as partial or complete edentulism leads to greater ingestion of processed and softer foods with high caloric values, high sugar and a low nutritional value.⁴⁰ Another important factor is that obese individuals can develop insulin resistance as a consequence of a chronic inflammatory state and oxidative stress, which could help explain the association between obesity and periodontitis.⁴¹

Our findings relating alcohol consumption and TL are intriguing, with a significant IRR reduction for TL in individuals that reported alcohol intake up to 8 doses/week. Conflicting results concerning this issue are evident in the literature, with studies showing that low dose alcohol consumption (less than 1,37 g a day) can prevent periodontal disease progression⁴², yet another study showed a greater periodontal attachment loss, with a dose-dependent effect.⁴³ This dose dependent effect was also described in our results, since the most frequent category of alcohol intake in our study (≥ 1 doses/day) did not show a significant protective effect. There is evidence that some alcohol consumption (20g) can exert anti-inflammatory effects by reducing post-prandial glucose spikes in serum⁴⁴, but such benefits are negated with higher levels of alcohol consumption.⁴⁵

The strengths of this study are that it involved a nationwide large-scale cross-sectional analysis of the Brazilian community dwelling adult population, receiving a comprehensive interview related to a wide array of NCDs and associated risk factors. However, this study also had limitations. Cross-sectional studies are unable to provide evidence for the directionality of the association. For instance, we cannot infer if the observed association of TL and chicken or fish intake is due to the fact that the consumption of those foods can increase the incidence of TL; or because they are softer diets than beef and therefore easier to be consumed by people with existing severe TL. It is also important to highlight that some of the associations observed in our study had confidence intervals very close to 1, and therefore their clinical relevance should be interpreted with caution. Another issue is that the survey was based on self-reported questionnaires, depending on the individual's memory for accuracy. Although this

is a relevant limitation, it should also be emphasized that professional anamnesis in dental or medical care is also dependent upon the individual's memory. Hence, our results appear valid and applicable in the daily routine of health professionals. A further potential limitation is self-reported tooth loss without excluding third molars, which may have marginally impacted our prevalence data. This was impossible to adjust for since the national survey does not provide additional data on missing teeth. It is important that future epidemiological studies of this type include a comprehensive oral examination not only related to TL but also the existence of current oral NCDs. Studies evaluating the possible temporal relationship between TL (or current oral NCDs) and all investigated systemic NCDs and risk factors are required. Moreover, interventional studies addressing common risk factors as adjunctive to the oral care plan are encouraged.

CONCLUSIONS

We concluded that systemic chronic conditions that exhibit shared risk factors were associated with tooth loss. This evidence highlights the public health problem imposed by oral NCDs that require governmental attention. From a clinical perspective, it also highlights the need for detailed anamnesis and the development of interdisciplinary personalized care plans, according to the patient's medical background.

ACKNOWLEDGEMENTS

The authors would like to thank the Coordination for the Improvement of Higher Education Personnel (CAPES, Brasilia, DF, Brazil) for their financial

support to Brazilian Graduate Programs (#001) and for the scholarship provided to TCCM.

CONFLICTS OF INTEREST STATEMENT

JPS and RCP planned and designed the study. TCCM, AAS and IC contributed to study design. RCP managed data and conducted statistical analysis. JPS, TCCM, AAS and IC interpreted the results. TCCM and AAS drafted the manuscript. JPS, RCP and IC critically revised the manuscript. All authors approved the final version of the manuscript. All authors declare they have no conflicts of interest related to this study.

REFERENCES

1. Sanders AE, Slade GD, Turrell G, Spencer AJ, Marcenes W. Does Psychological Stress Mediate Social Deprivation in Tooth Loss? *J Dent Res* 2007;86:1166–1170.
2. The Economist Intelligence Unit. Time to Take Gum Disease Seriously: The Societal and Economic Impact of Periodontitis. Geneva, Switzerland: The Economist Intelligence Unit; 2021.
3. Marcenes W, Kassebaum NJ, Bernabé E, et al. Global Burden of Oral Conditions in 1990-2010. *J Dent Res* 2013;92:592–597.
4. Kawahara H, Inoue M, Okura K, Oshima M, Matsuka Y. Risk Factors for Tooth Loss in Patients Undergoing Mid-Long-Term Maintenance: A Retrospective Study. *Int J Environ Res Public Health* 2020;17:6258. doi:10.3390/ijerph17176258

5. Frencken JE, Sharma P, Stenhouse L, Green D, Lavery D, Dietrich T. Global Epidemiology of Dental Caries and Severe Periodontitis – A Comprehensive Review. *J Clin Periodontol* 2017;44 Suppl 18:S95-S105.
6. Kassebaum, NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJL, Marcenes W. Global Burden of Severe Periodontitis in 1990-2010. *J Dent Res* 2014;93:1045-1053.
7. Kassebaum, NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJL, Marcenes W. Global Burden of Untreated Caries. *J Dent Res* 2015;94:650-658.
8. Chapple ILC, Bouchard P, Cagetti MG, et al. Interaction of Lifestyle, Behaviour or Systemic Diseases with Dental Caries and Periodontal Diseases: Consensus Report of Group 2 of the Joint EFP/ORCA Workshop on the Boundaries Between Caries and Periodontal Diseases. *J Clin Periodontol* 2017;44:39-51.
9. Papapanou PN, Sanz M, Budneli N, et al. Periodontitis: Consensus Report of Workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Periodontol* 2018;89:173-182.
10. Li X, Kolltveit KM, Tronstad L, Olsen I. Systemic Diseases Caused by Oral Infection. *Clin Microbio Rev* 2000;13:547–558.
11. dePablo P, Dietrich T, Chapple ILC, et al. The Autoantibody Repertoire in Periodontitis: A Role in the Induction of Autoimmunity to Citrullinated Proteins in Rheumatoid Arthritis? *Ann Rheum Dis* 2014;73:580-586.
12. Peters REN, Peters J, Beckett N, Booth A, Rockwood K, Anstey KJ. Common Risk Factors for Major Noncommunicable Disease, A Systematic Overview of Reviews and Commentary: The Implied Potential for Targeted Risk Reduction. *Ther Adv Chronic Dis* 2019;15:1-14.

13. Petersen, PE. The World Oral Health Report 2003: Continuous Improvement of Oral Health in The 21st Century - The Approach of the WHO Global Oral Health Programme. Geneva, Switzerland: World Health Organization; 2003.
14. Newman HN. Focal Infection. *J Dent Res* 1996;75:1912–1919.
15. Twetman S. Prevention of Dental Caries as a Non-Communicable Disease. *Eur J Oral Sci* 2018;126 Suppl 1:19-25.
16. Herrera D, Meyle J, Renvert S, Jin L. White Paper on Prevention and Management of Periodontal Diseases for Oral Health and General Health. Geneva, Switzerland: FDI World Dental Federation; 2018.
17. Paraskevas S, Huizinga JD, Loos BG. A Systematic Review and Meta-Analyses on C-Reactive Protein in Relation to Periodontitis. *J Clin Periodontol* 2008;35:277-290.
18. Sharma P, Fenton A, Dias IHK, et al. Oxidative Stress Links Periodontal Inflammation and Renal Function. *J Clin Periodontol* 2021;48:357-367.
19. Sheiham A, Watt RG. The Common Risk Factor Approach: A Rational Basis for Promoting Oral Health. *Community Dent Oral Epidemiol* 2000;28:399–406.
20. Brazilian Institute of Geography and Statistics. 2019 Health National Survey. Perception of health status, lifestyle, chronic diseases and oral health. Brazil and Great Regions (in Portuguese). Rio de Janeiro, Brazil: Brazilian Institute of Geography and Statistics; 2020.
21. Steffens JP, Wang X, Starr JR, Spolidorio LC, Van Dyke TE, Kantarci A. Associations Between Sex Hormone Levels and Periodontitis in Men: Results from NHANES III. *J Periodontol* 2015;86:1116-1125.

22. Kotsakis GA, Chrepa V, Shivappa N, et al. Diet-Borne Systemic Inflammation Is Associated With Prevalent Tooth Loss. *Clin Nutr* 2018;37:1306-1312.
23. World Health Organization. Noncommunicable Diseases Global Monitoring Framework: Indicator Definitions and Specifications. Geneva, Switzerland: World Health Organization; 2014.
24. López-Gómez SA, González-López BS, Scougall-Vilchis RJ, et al. Tooth Loss in Patients With and Without Diabetes. *J Am Dent Assoc* 2020;151: 276–286.
25. Kinane DF, Peterson M, Stathopoulou PG. Environmental and Other Modifying Factors of Periodontal Diseases. *Periodontol 2000* 2006;40:107–119.
26. Blostein FA, Jansen EC, Jones AD, Marshall TA, Foxman B. Dietary Patterns Associated With Dental Caries in Adults in the United States. *Community Dent Oral Epidemiol* 2019;48:119-129.
27. Martinez-Martinez RE, Abud-Mendoza C, Patino-Marin N, Rizo-Rodriguez JC, Little JW, Loyola-Rodriguez JP. Detection of Periodontal Bacterial DNA in Serum and Synovial Fluid in Refractory Rheumatoid Arthritis Patients. *J Clin Periodontol* 2009;36:1004-1010.
28. Hussain SB, Botelho J, Machado V, et al. Is There a Bidirectional Association Between Rheumatoid Arthritis and Periodontitis? A Systematic Review and Meta-Analysis. *Semin Arthritis Rheum* 2020;50:414-422.
29. Jepsen S, Caton JG, Albandar JM, et al. Periodontal Manifestations of Systemic Diseases and Developmental and Acquired Conditions: Consensus Report of Workgroup 3 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Periodontol* 2018;89:237–248.

30. Abnet CC, Kamangar F, Islami F, et al. Tooth Loss and Lack of Regular Oral Hygiene Are Associated with Higher Risk of Esophageal Squamous Cell Carcinoma. *Cancer Epidemiol Biomarkers Prev* 2008;17:3062–3068.
31. Tu YK, Galobardes B, Smith GD, McCarron P, Jeffreys M, Gilthorpe MS. Associations Between Tooth Loss and Mortality Patterns in The Glasgow Alumni Cohort. *Heart* 2007;93:1098–1103.
32. Maisonneuve P, Amar S, Lowenfels AB. Periodontal Disease, Edentulism and Pancreatic Cancer: A Meta Analysis. *Ann Oncol* 2017;28:985-995.
33. da Costa BR, Vieira ER. Risk Factors for Work-Related Musculoskeletal Disorders: A Systematic Review of Recent Longitudinal Studies. *Am J Ind Med* 2010;53:285-323.
34. Bernardo CO, Boing AF, Vasconcelos FA, Peres KG, Peres MA. Association Between Tooth Loss and Obesity In Brazilian Adults: A Population-Based Study. *Rev Saúde Públ* 2012;46:834–842.
35. Kotsakis GA, Chrepa V, Shivappa N, et al. Diet-Borne Systemic Inflammation is Associated with Prevalent Tooth Loss. *Clin Nutr* 2018;37:1306–1312.
36. Bains A, Rashid MA. Junk Food and Heart Disease: The Missing Tooth. *J R Soc Med* 2013;0106: 472–473.
37. Al- Zahrani MS, Borawski EA, Bissada NF. Increased Physical Activity Reduces Prevalence of Periodontitis. *J Dent* 2005;33:703–710.
38. Haren MT, Malmstrom TK, Miller DK, et al. Higher C-Reactive Protein and Soluble Tumor Necrosis Factor Receptor Levels Are Associated With Poor Physical Function and Disability: A Cross-Sectional Analysis of a Cohort of Late Middle-Aged African Americans. *J Gerontol A Biol Sci Med Sci* 2010;65:274–281.

39. Nascimento GG, Leite FRM, Conceição DA, Ferrúa CP, Singh A, Demarco FF. Is There a Relationship Between Obesity and Tooth Loss and Edentulism? A Systematic Review and Meta-Analysis. *Obes Rev* 2016;17:587–598.
40. Zhu Y, Hollis JH. Associations Between the Number of Natural Teeth and Metabolic Syndrome in Adults. *J Clin Periodontol* 2015;42:113–120.
41. Martinez-Herrera M, Silvestre-Rangil J, Silvestre FJ. Association Between Obesity and Periodontal Disease. A Systematic Review of Epidemiological Studies and Controlled Clinical Trials. *Med Oral Patol Oral Cir Bucal* 2017;22:708-715.
42. Wagner MC, Haas AN, Oppermann RV, Rosing CK, Albandar JM, Susin C. Effect of Alcohol Consumption on Clinical Attachment Loss Progression in an Urban Population From South Brazil: A 5-Year Longitudinal Study. *J Periodontol* 2017;88:1271–1280.
43. Tezal M, Grossi SG, Ho AW, Genco RJ. Alcohol Consumption and Periodontal Disease. The Third National Health and Nutrition Examination Survey. *J Clin Periodontol* 2004;31:484–488.
44. Greenfield JR, Samaras K, Hayward CS, Chisholm DJ, Campbell LV. Beneficial Postprandial Effect of a Small Amount of Alcohol on Diabetes and Cardiovascular Risk Factors: Modification by Insulin Resistance. *J Clin Endocrinol Metab* 2005;90:661-672.
45. O'Keefe J, Bell DSH. Postprandial Hyperglycemia/Hyperlipidemia (Postprandial Dysmetabolism) Is a Cardiovascular Risk Factor. *Am J Cardiol* 2007;100:899-904.

FIGURE LEGENDS

Figure 1. Flow diagram of individuals at each stage of study.

TABLES

Table 1. Sociodemographic characteristics of included population.

Characteristics	Percentage or Mean (SD)		
	Male	Female	Total
<i>Unweighted n</i>	27,433	32,838	60,271
Age (years)	51.19±13.8	51.97±14.3	51.61±14.1
Race/Ethnicity:			
White	39.59%	39.54%	39.56%
Black	11.33%	10.66%	10.97%
Other	49.08%	49.80%	49.47%
Education:			
Elementary School	50.19%	45.92%	47.86%
High School or Higher	49.81%	54.08%	52.14%
Toothbrushing ≥ 2 times/day	92.00%	96.21%	94.29%
Tooth Loss (n)	8.71±10.3	10.77±11.4	9.83±11.0
Number of Lost Teeth:			
0	18.52%	15.14%	16.68%
1-31	72.02%	70.30%	71.08%
32	9.46%	14.56%	12.24%
Diabetes	8.91%	10.93%	10.01%
Smoking			
Never	85.36%	90.18%	87.99%
Previous	0.68%	0.53%	0.60%
Current	13.96%	9.28%	11.41%
Hypertension	27.69%	33.13%	30.66%
High Cholesterol	14.67%	22.15%	18.77%
Cardiovascular Diseases	7.84%	8.34%	8.11%
Asthma	3.43%	5.83%	4.74%
Lung Diseases	1.49%	1.62%	1.56%
Arthritis (Rheumatoid)	4.87%	14.11%	9.90%
Kidney Diseases	1.67%	1.72%	1.70%
Depression	5.38%	15.25%	10.75%
Other Mental Illnesses	3.40%	7.68%	5.73%
Cancer	2.75%	3.77%	3.31%
Back Problems	20.66%	26.29%	23.73%
WMSD	1.75%	2.85%	2.35%
Other chronic diseases	7.21%	10.46%	8.98%

SD: Standard Deviation. WMSD: Work- Related Musculoskeletal Disorders

Table 2. Associations between risk factors for periodontitis and caries and tooth loss (TL).

Risk Factor	Crude Analysis		Adjusted Model	
	IRR (95% CI)	<i>P</i>	IRR (95% CI)	<i>P</i>
Diabetes	1.69 (1.64-1.74)	0.000	1.11 (1.08-1.14)	0.000
Smoking				
Never	REF.		REF.	
Previous	0.94 (0.84-1.06)	0.328	1.08 (0.97-1.20)	0.154
Current	1.24 (1.21-1.28)	0.000	1.28 (1.25-1.31)	0.000
Cariogenic Diet				
No	REF.		REF.	
1-4 days/week	0.73 (0.71-0.74)	0.000	0.97 (0.95-0.98)	0.000
5-7 days/week	0.75 (0.73-0.77)	0.000	0.97 (0.94-0.99)	0.006

Adjusted model includes adjustments for sex, age, race/ethnicity, education and frequency of dental brushing. IRR: Incidence Rate Ratio; REF: Reference. Bold letters indicate statistically significant associations ($p < 0.05$). $n=60,271$.

Table 3. Associations between other chronic diseases and tooth loss (TL).

Chronic Diseases	n	IRR (95% CI)	P
Hypertension	60,014	1.06 (1.04-1.08)	0.000
High Cholesterol	59,069	1.07 (1.05-1.09)	0.000
Cardiovascular Diseases	60,271	1.07 (1.04-1.10)	0.000
Asthma	60,271	1.06 (1.03-1.11)	0.001
Lung Diseases	60,271	1.08 (1.01-1.15)	0.016
Arthritis (Rheumatoid)	60,271	1.16 (1.12-1.19)	0.000
Kidney Diseases	60,271	1.04 (0.98-1.11)	0.194
Depression	60,271	1.11 (1.08-1.14)	0.000
Other Mental Illnesses	60,271	1.07 (1.03-1.11)	0.000
Cancer	60,271	1.03 (0.98-1.07)	0.232
Back Problems	60,271	1.15 (1.13-1.17)	0.000
WMSD	60,271	1.02 (0.96-1.07)	0.563
Others	60,271	1.07 (1.04-1.10)	0.000

Adjusted for sex, age, race/ethnicity, education, frequency of dental brushing, diabetes, smoking and cariogenic diet. IRR: Incidence Rate Ratio; WMSD: Work- Related Musculoskeletal Disorders. Bold letters indicate statistically significant associations ($p < 0.05$).

Table 4. Impact of co-morbidities on the associations of diabetes and tooth loss (TL).

Additional Condition	n	IRR (95% CI)	P
Smoking	6,033	1.15 (1.07-1.24)	0.000
Hypertension	6,029	1.10 (1.05-1.15)	0.000
High Cholesterol	5,982	1.04 (1.00-1.09)	0.066
Asthma	6,033	1.05 (0.96-1.15)	0.288
Lung Diseases	6,033	1.07 (0.94-1.23)	0.297
Arthritis (Rheumatoid)	6,033	1.06 (1.00-1.12)	0.045
Kidney Diseases	6,033	0.98 (0.87-1.09)	0.665
Depression	6,033	1.03 (0.97-1.09)	0.409
Other Mental Illnesses	6,033	1.13 (1.03-1.24)	0.007
Back Problems	6,033	1.06 (1.01-1.11)	0.012
Others	6,033	1.02 (0.96-1.10)	0.494

Adjusted for sex, age, race/ethnicity, education and frequency of dental brushing. IRR: Incidence Rate Ratio. Only individuals with diabetes were included. Reference values are with diabetes but without the additional condition. Bold letters indicate statistically significant associations ($p < 0.05$).

Table 5. Associations between common risk factors for non-communicable diseases and tooth loss (TL).

Risk Factor	n	IRR (95% CI)	<i>P</i>
--------------------	----------	---------------------	-----------------

Nutrition			
Vegetables and greens	60,271		
0-3 days/week		REF.	
4-7 days		0.89 (0.88-0.91)	0.000
Fruits	60,271		
0-3 days/week		REF.	
4-7 days		0.94 (0.73-0.80)	0.000
Red Meat	60,271		
0-3 days/week		REF.	
4-7 week		0.95 (0.93-0.96)	0.000
Chicken	60,271		
0-3 days/week		REF.	
4-7 days		1.02 (1.00-1.04)	0.025
Fish	60,271		
0-3 days/week		REF.	
4-7 days		1.01 (1.00-1.01)	0.011
Junk Food	60,271		
0-3 days/week		REF.	
4-7 days		0.97 (0.92-1.02)	0.255
BMI	59,938		
Normal		REF.	
Overweight		1.01 (0.99-1.03)	0.426
Obesity		1.05 (1.03-1.07)	0.000
Alcohol			
Alcohol Consumption	53,192		
Never		REF.	
Up to 1 dose/week		0.82 (0.80-0.85)	0.000
> 1 to 7 doses/week		0.85 (0.82-0.88)	0.000
≥ 8 doses/week		0.84 (0.81-0.88)	0.000
≥ 1 doses/day		0.98 (0.92-1.04)	0.440
Physical Exercise	60,271		
Yes		0.89 (0.87-0.90)	0.000
No		REF.	
Physical Exercise	23,616		
1-2 days/week		1.03 (1.00-1.06)	0.071
3-5 days/week		REF.	
6-7 days/week		1.03 (0.99-1.07)	0.206
Physical Exercise	22,908		
< 75 minutes/week		1.09 (1.04-1.15)	0.000
75-150 minutes/week		REF.	
> 150 minutes/week		0.96 (0.93-1.00)	0.024

Adjusted for sex, age, race/ethnicity, education, frequency of dental brushing, diabetes, smoking and cariogenic diet. TL: Tooth Loss; IRR: Incidence Rate Ratio; REF: Reference; BMI: Body Mass Index. Bold letters indicate statistically significant associations (p<0.05).