Periodontal Disease and Incident Type 2 Diabetes

Results from the First National Health and Nutrition Examination Survey and its Epidemiologic Follow-Up Study

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OBJECTIVE — Type 2 diabetes and periodontal disease are known to be associated, but the temporality of this relationship has not been firmly established. We investigated whether baseline periodontal disease independently predicts incident diabetes over two decades of follow-up.

RESEARCH DESIGN AND METHODS — A total of 9,296 nondiabetic male and female National Health and Nutrition Examination Survey (NHANES I) participants aged 25–74 years who completed a baseline dental examination (1971–1976) and had at least one follow-up evaluation (1982–1992) were studied. We defined six categories of baseline periodontal disease using the periodontal index. Of 7,168 dentate participants, 47% had periodontal index = 0 (periodontally healthy); the remaining were classified into periodontal index quintiles. Incident diabetes was defined by *1*) death certificate (ICD-9 code 250), 2) self-report of diabetes requiring pharmacological treatment, or *3*) health care facility stay with diabetes discharge code. Multivariable logistic regression models assessed incident diabetes odds across increasing levels of periodontal index in comparison with periodontally healthy participants.

RESULTS — The adjusted odds ratios (ORs) for incident diabetes in periodontal index categories 1 and 2 were not elevated, whereas the ORs in periodontal index categories 3 through 5 were 2.26 (95% CI 1.56–3.27), 1.71 (1.0–2.69), and 1.50 (0.99–2.27), respectively. The OR in edentulous participants was 1.30 (1.00–1.70). Dentate participants with advanced tooth loss had an OR of 1.70 ($P < 0.05$) relative to those with minimal tooth loss.

CONCLUSIONS — Baseline periodontal disease is an independent predictor of incident diabetes in the nationally representative sample of NHANES I.

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Type 2 diabetes is a significant public health concern. The association between type 2 diabetes and periodontal disease is well documented (1,2), and periodontal disease has been traditionally viewed solely as a pathological consequence of diabetes (3). However, prospective data supporting this unidirectional hypothesis are limited, and prevailing views regarding associations between periodontal disease and type 2 diabetes should be informed by the growing body of evidence suggesting periodontal disease as a risk factor for atherosclerotic cardiovascular disease (CVD) (4–7).

Type 2 diabetes and CVD have common antecedents, and in view of the American Heart Association's Scientific Statement on Diabetes stating that "diabetes is a cardiovascular disease" (8), it seems reasonable to hypothesize periodontal disease as a potential contributor to development of type 2 diabetes. As with CVD infection hypotheses, chronic inflammation in response to periodontal bacteria might link periodontal disease and type 2 diabetes. Indeed, systemic inflammation has emerged as a novel predictor of type 2 diabetes (9,10), and individuals with periodontal disease have been consistently shown to exhibit elevated levels of systemic inflammation (2). Moreover, periodontal therapy has resulted in changes in systemic monocytic gene expression (11) and decreases in systemic inflammation (12).

We are unaware of any studies that have assessed the association between baseline clinical periodontal disease and risk of subsequent diabetes in an initially diabetes-free cohort. Studies of this nature are important as they can clarify the temporality of periodontal disease/type 2 diabetes associations We hypothesized that baseline periodontal disease predicted incident type 2 diabetes in the First National Health and Nutrition Examination Survey (NHANES I) and its Epidemiologic Follow-up Study (NHEFS).

RESEARCH DESIGN AND METHODS

— Details concerning the design of NHANES I and NHEFS have been published previously (5,13). NHANES I was a national probability sample of the noninstitutionalized U.S. population aged 1–74 years, conducted during 1971–1974. NHEFS is a longitudinal study including all individuals initially aged 25–74 years who completed a medical examination in NHANES I (n = 14,407). The NHEFS comprises four longitudinal follow-up studies in 1982–1984, 1986, 1987, and 1992. The 1986, 1987, and 1992 follow-ups used the same design and data collection procedures developed in the 1982–1984 NHEFS, with the exceptions that a 30-min computer-

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assisted telephone interview was administered rather than a personal interview, and no physical measurements were taken during the 1986–1992 examinations. The 1986 NHEFS was conducted for members of the NHEFS cohort who were aged 55–74 years at their baseline examination and not known to be deceased at the 1982–1984 NHEFS (n = 3,980). The 1987 (n = 11,750) and 1992 (n = 11,195) follow-ups were conducted for the entire surviving cohort. Ninety-six percent of the study population was successfully traced at some point through the 1992 follow-up. Tracing rates for each completed wave ranged from 90 to 94%, and interview rates ranged from 91 to 96% of those traced.

The present analysis is derived from 11,375 participants who received a baseline dental evaluation. Of these participants, 658 were lost to follow-up (94% follow-up rate). An additional 1,421 participants were excluded because of *1*) prevalent diabetes (n = 570), *2*) incident diabetes reported within 1 year of baseline (n = 82) to minimize the prevalence of undiagnosed baseline diabetes, or *3*) missing covariate data (n = 769) for smoking, physical activity, and/or education, yielding a final sample of 9,296. All 9,296 participants included were traced (vital status confirmed) at least once during follow-up and 96% were traced at each of four follow-up cycles. At the 10- and 20-year follow-ups, 15% (n = 1,363) and 34% (n = 3,129) of participants were deceased, respectively.

Periodontal disease assessment

Dental examiners were trained to follow a written set of objective standards to minimize examiner variability by eliminating conditions known to be sources of disagreement (14). The periodontal index (15) was used to assess the presence/absence of periodontal disease for each tooth by assigning scores based on gingival inflammation extent, the presence or absence of periodontal pockets, and tooth mobility as follows: *1*) no periodontal disease (score = 0): neither overt inflammation in the investing tissues nor loss of function due to supporting tissue destruction; *2*) mild gingivitis (score = 1): an overt area of inflammation in the free gingivae, not circumscribing the tooth; *3*) gingivitis (score = 2): inflammation completely circumscribing the tooth with no apparent break in the epithelial attachment; *4*) gingivitis with pocket formation (score = 6): epithelial attachment had been broken and there was a pocket (not merely a deepened gingival crevice due to swelling in the free gingivae), there was no interference with normal masticator function, and the tooth was firm in its socket and had not drifted; and *5*) advanced destruction with loss of masticator function (score = 8): the tooth was either loose, had drifted, or sounded dull on percussion with a metallic instrument. If the examiner was equivocal regarding the appropriate score, the lesser score was assigned. All present teeth, excluding roots, were scored. The periodontal index reflects the within-mouth arithmetic average of scores for all teeth (periodontal index range is continuous from 0 to 8.0).

For dentate participants, each potential tooth in the dentition was classified as being decayed (D), missing due to caries (M), or filled without decay (F). These values were summed per person to create an index (DMF) reflective of historical caries experience. The range of possible values was 0 to 32.

Incident diabetes

Incident diabetes was defined by *1*) death certificate (ICD-9 code in the range of 250.0 to 250.9 or diabetes otherwise listed on the death certificate), *2*) self-reported physician diagnosis requiring pharmacological treatment (participants reporting physician-diagnosed diabetes and dietary intervention but not pharmacological intervention were not considered to have developed incident diabetes to enhance outcome specificity), or *3*) health care facility stay with a discharge diagnosis of diabetes.

Covariate data collection

Potential confounding variables related to diabetes risk and/or indicative of healthy lifestyle were collected during the baseline evaluation and included age, sex, race (African American, Caucasian, or other), poverty index (total household income in the numerator and total income necessary to maintain the family on a nutritionally adequate food plan in the denominator; values >1 indicate incomes above poverty), education level (completed ≤8th grade, 9th–12th grade, or some college or college graduate), BMI (weight in kilograms divided by height in meters squared), subscapular and triceps skinfold, physical activity as described previously (15), total cholesterol, systolic blood pressure, diastolic blood pressure, and hypertension (systolic blood pressure ≥140 or diastolic blood pressure ≥90 or self-reported medication for high blood pressure). Detailed cigarette smoking history information was collected for 3,420 participants at baseline and for the remaining 5,876 participants during the 1982–1984 follow-up. This approach has been validated previously (15,16). A single 24-h dietary recall was obtained.

Statistical analysis

Periodontal disease was defined in three ways. The primary definition classified participants into six categories using the periodontal index as follows. Of dentate participants, 47% (n = 3,372) had periodontal index = 0 and were classified as "periodontally healthy," and the remaining dentate participants were further classified into quintiles (n = ~760/quintile) of continuous periodontal index values. Edentulous participants (n = 2,127) were retained in a seventh category.

In the second definition, participants were classified as either *1*) being periodontally healthy (n = 3,372), *2*) having gingivitis (n = 2,135), or *3*) having periodontitis (n = 1,662) as described previously (4,15).

In a third approach, tooth loss was considered as a surrogate definition of periodontal disease as it is often a consequence of periodontal disease (17). Participants were categorized as follows: *1*) 24–32 teeth (reference group), *2*) 18–23 teeth, *3*) 8–17 teeth, or *4*) 1–7 teeth.

Logistic regression analysis was used to assess the association between baseline periodontal disease and the cumulative incidence of diabetes. The SURVEYLOGISTIC procedure in SAS (version 9.1; SAS Institute, Cary, NC) was used to appropriately account for the stratification, clustering, and sample weights of NHANES I. Incidence density of diabetes was not considered because of uncertainty in diabetes onset timing, as discussed previously (18). Multiple models with various degrees of covariate adjustment are presented to provide clarity regarding confounding by design variables (age, sex, and race), socioeconomic status (education and poverty index), health behaviors (smoking status, physical activity, and diet), general vascular health status (hypertension and total cholesterol), and/or obesity (BMI and skinfold). For the present analysis, smoking was defined in four categories: *1*) current, *2*) former, *3*) never, or *4*) reported history of smoking, current status unknown. The creation of the fourth smoking category avoids the elimination of those participants from the

analysis and prevents biasing parameter estimates for current (underestimation of smoking risk) or former (overestimation of smoking risk) smokers. Removing ever-smokers with unknown current status did not change the results.

A control analysis was performed to assess the association between caries (DMF) and cumulative incidence of diabetes. We hypothesized a priori that periodontal index but not DMF would be positively associated with incident diabetes. If these dual hypotheses were confirmed, it would add specificity of the findings to periodontal disease as opposed to general oral health.

RESULTS — The mean ± SD age of participants was 50 ± 19 years, and at entry 60% were women, 84% were white, 15% were black, and 1% were other. Those with periodontal disease tended to be older, male, nonwhite, smokers, and of lower socioeconomic status as reported previously (15) (Table A1 of the online appendix available at http://dx.doi.org/10.2337/dc08-0026). There was a wide range of mean periodontal index values among participants defined as having either gingivitis (periodontal index range = 0.06–8.00) or periodontitis (periodontal index range = 0.88–8.00). Therefore, the primary exposure definition categorizing participants into six categories based on periodontal index values is more nuanced.

During a follow-up period of 17 ± 4 years (range 1–22 years), 817 incident diabetes cases were reported (cumulative incidence = 9%). Of the incident cases, 77% were identified or confirmed via either death certificate or health care facility discharge diagnosis codes; only 4% of cases (n = 30) were from death certificate only. A physician diagnosis was self-reported by 55% (Table A2 of the online appendix).

Among nonperiodontal characteristics, age, sex, education, BMI, subscapular skinfold, and hypertension were strong predictors of incident diabetes. An approximate 2-SD increase in either BMI or subscapular skinfold was associated with a twofold increase in the odds of incident diabetes ($P < 0.0001$ for both comparisons). Odds were increased by ~30% for a 10-year age increase ($P < 0.0001$), 50% for men ($P < 0.001$), and 40% for being hypertensive ($P < 0.01$). Current and former smokers experienced non–statistically significant 33% (P =

Table 1—*ORs (95% CI) for incident diabetes by category of baseline periodontal index: NHANES I and NHEFS, 1971–1974 through 1992*

Model*	Category PI0 (PI = 0): crude incidence 189 of 3,368 (6%)	Category PI1 (0 < PI ≤ 0.87): crude incidence 56 of 762 (7%)	Category PI2 (0.88 ≤ PI ≤ 1.60): crude incidence 57 of 761 (7%)	Category PI3 (1.61 ≤ PI ≤ 2.44): crude incidence 91 of 759 (12%)	Category PI4 (2.45 ≤ PI ≤ 5.07): crude incidence 84 of 759 (11%)	Category PI5 (5.08 ≤ PI ≤ 8.0): crude incidence 97 of 760 (13%)	Edentulous: crude incidence 243 of 2,127 (11%)
1	1.0	1.16 (0.77–1.76)	1.23 (0.78–1.93)	2.79 (2.08–3.74)	2.55 (1.89–3.41)	2.53 (1.76–3.66)	2.19 (1.72–2.78)
2	1.0	1.18 (0.79–1.75)	1.11 (0.70–1.74)	2.21 (1.63–2.99)	1.98 (1.44–2.71)	1.72 (1.14–2.60)	1.40 (1.06–1.85)
3	1.0	1.10 (0.73–1.65)	1.02 (0.64–1.63)	2.06 (1.49–2.84)	1.71 (1.20–2.43)	1.50 (0.99–2.28)	1.32 (1.02–1.72)
4	1.0	1.10 (0.73–1.65)	1.03 (0.65–1.64)	2.08 (1.51–2.87)	1.71 (1.19–2.45)	1.50 (0.99–2.27)	1.30 (1.00–1.70)
5	1.0	1.13 (0.75–1.69)	1.02 (0.64–1.63)	2.00 (1.48–2.71)	1.78 (1.24–2.55)	1.55 (0.99–2.40)	1.33 (1.02–1.04)
6	1.0	1.13 (0.75–1.71)	1.07 (0.67–1.72)	2.05 (1.47–2.87)	1.78 (1.24–2.55)	1.51 (0.98–2.33)	1.23 (0.91–1.67)
7	1.0	1.10 (0.73–1.64)	1.03 (0.65–1.63)	2.08 (1.51–2.87)	1.71 (1.19–2.45)	1.50 (0.98–2.27)	1.30 (1.00–1.70)

Total n = 9,296. The poverty index was determined by the poverty income ratio, which is the total household income in the numerator and a multiple of the total income necessary to maintain a family with a given characteristic on a nutritionally adequate food plan in the denominator. *Model 1: crude; model 2: adjusted for age, sex, race, education, and smoking status; model 3: model 2 + BMI, subscapular skinfold, and physical activity level; model 4: model 3 + hypertension and total cholesterol; model 5: model 4 + total caloric intake, total protein, total carbohydrates, and total fat (n = 36 excluded because of missing diet data); model 6: model 4 + poverty index (n = 339 excluded because of missing poverty index data); model 7: model 4 + white blood cell count. PI, periodontal index.

Table 2—*ORs (95% CI) for incident diabetes occurring ≥10 years after baseline enrollment by category of baseline periodontal index: NHANES I and NHEFS, 1971–1974 with follow-up in 1981–1984 through 1992*

Model*	Category PI0: crude incidence 114 of 3,293 (3%)	Category PI1: crude incidence 30 of 736 (4%)	Category PI2: crude incidence 38 of 742 (5%)	Category PI3: crude incidence 55 of 723 (8%)	Category PI4: crude incidence 45 of 720 (6%)	Category PI5: crude incidence 43 of 706 (6%)	Edentulous: crude incidence 120 of 2,004 (6%)
1	1.0	1.23 (0.73–2.09)	1.23 (0.72–2.11)	2.85 (2.00–4.07)	2.42 (1.64–3.56)	2.00 (1.15–3.49)	1.73 (1.24–2.42)
2	1.0	1.24 (0.74–2.06)	1.12 (0.66–1.90)	2.32 (1.61–3.33)	1.94 (1.26–3.01)	1.43 (0.76–2.68)	1.18 (0.82–1.69)
3	1.0	1.16 (0.69–1.96)	1.05 (0.61–1.82)	2.24 (1.55–3.23)	1.70 (1.08–2.68)	1.26 (0.67–2.39)	1.12 (0.78–1.61)
4	1.0	1.18 (0.70–1.97)	1.07 (0.63–1.82)	2.26 (1.56–3.27)	1.71 (1.09–2.69)	1.26 (0.67–2.39)	1.11 (0.77–1.59)

Total n = 8,924; n = 445 incident diabetes cases. Incident diabetes was restricted to those cases occurring ≥10 years after baseline enrollment (to minimize bias due to undiagnosed diabetes at baseline). *Model 1: crude; model 2: adjusted for age, sex, race, education, and smoking status; model 3: model 2 + BMI, subscapular skinfold, and physical activity level; model 4: model 3 + hypertension and total cholesterol. PI, periodontal index.

0.08) and 26% ($P = 0.14$) increased odds of type 2 diabetes, respectively.

In multivariable models, incident diabetes odds varied across periodontal index categories (Table 1). Relative to participants with periodontal index (PI) = 0.0 (PI0), participants in the PI1 or PI2 categories did not experience an increased odds of developing diabetes, whereas the odds increased sharply in the PI3 category (OR 2.08; $P < 0.0001$). The ORs in PI4 (1.71; $P = 0.003$) and PI5 (1.50; $P = 0.06$) categories abated but remained elevated and were not statistically significantly different from the odds for those in the PI3 category. Edentulous participants experienced a 30% increase in diabetes odds relative to those in the PI0 category ($P = 0.05$), but a 37% decrease in odds relative to those in the PI3 category ($P = 0.01$). The findings were unchanged when the analysis was restricted to incident diabetes cases occurring ≥10 years after baseline (Table 2). Participants in the PI3 category again demonstrated the highest OR of 2.26 ($P < 0.0001$). Supplemental analyses adjusting further for pack-years of smoking did not change the results (data not shown).

A twofold increase in diabetes odds was observed among participants in the PI3 category even among subgroups of never smokers or participants with BMI <25 kg/m^2 (Table 3). Women in the PI3 category had an OR of 2.84 (95% CI 1.87–4.32) compared with 1.50 (95% CI 0.89–2.55) among men ($P_{interaction} = 0.12$). The highest diabetes OR of 1.65 (95% CI 1.01–2.70) was observed for men in the PI4 category (Table 3). No diabetes risk gradient across periodontal disease categories was apparent in blacks ($P_{interaction} = 0.07$).

Using the second periodontal disease definition, after multivariable adjustment, incident diabetes odds were increased by 40% among participants with gingivitis ($P < 0.05$) and by 50% among participants with periodontitis ($P < 0.05$) compared with periodontally healthy participants.

Participants missing 25–31 teeth at baseline had an incident diabetes OR of 1.70 relative to participants missing 0–8 teeth ($P < 0.05$). Intermediate tooth loss was not associated with incident diabetes.

Finally, in the control analysis, there was no association between the DMF index and incident diabetes. The pattern of ORs across increasing sextiles of DMF was flat, with ORs ranging from 0.82 (95% CI 0.51–1.34) in the second sextile to 0.92 (0.57–1.49) in the sixth sextile.

CONCLUSIONS — We report a positive nonlinear association between baseline periodontal disease and incident type 2 diabetes in the NHANES I and NHEFS. This association persisted regardless of the periodontal disease definition. When compared with healthy participants, participants with intermediate levels of periodontal disease had a twofold increased odds of incident diabetes, and the odds remained elevated among participants with the highest levels of periodontal disease. Advanced tooth loss was associated with an approximate 70% increased odds of incident diabetes. Relative to periodontally healthy participants, edentulous participants experienced an intermediate 30% increased odds of diabetes.

Findings remained after extensive multivariable adjustment for potential confounders, including both BMI and subscapular skinfold, and in a subgroup analysis restricted to participants with BMI <25 kg/m^2. The association remained strong after adjustment for smoking status or pack-years of smoking, as well as among never smokers. Dietary factors such as fat, protein, or carbohydrate intake, as well as total caloric intake, did not attenuate the findings, although we caution that dietary data based on a single 24-h recall leave considerable room for residual confounding. Finally, the observation that the DMF index (an index related to oral hygiene practices) was unrelated to incident diabetes adds specificity to the periodontal disease hypothesis.

Type 2 diabetes odds were substantially elevated at intermediate periodontal index levels. This might be a consequence of periodontal disease underestimation, in which examiners assigned the lesser of two periodontal index values when periodontal findings were equivocal. Alternatively, lower thresholds of periodontal disease, as opposed to definitions requiring evidence of clinical periodontitis, might be necessary to fully capture subclinical infectious exposures relevant for systemic disease risk (19,20). After an abrupt type 2 diabetes risk increase in the PI3 category, the risk leveled off in periodontal index categories 3–5, indicating a possible threshold effect, although survivor bias should also be considered because participants with an advanced periodontal index were older at baseline and more likely to die before new-onset diabetes could be diagnosed and reported

to the study. Alternatively, a relatively increased prevalence of undiagnosed incident diabetes among individuals in the highest periodontal index categories could also explain the leveling of odds in these groups.

The observed intermediate type 2 diabetes risk for edentulous participants is consistent with the broader body of literature concerning periodontal disease and systemic disease. Associations between tooth loss and systemic disease from both the NHEFS and other populations tend to be positive (6), and intermediate risk is often reported among edentulous participants. Tooth loss might play an epidemiologically confusing role in evaluation of systemic disease hypotheses (6,21). Tooth loss often acts concurrently as both a consequence of chronic periodontal disease and a preventive measure for future infectious exposure, therefore representing a mixture of risk and protection. Data from the Oral Infections and Vascular Disease Epidemiology Study (INVEST) show the highest prevalence of carotid artery plaque among participants with intermediate tooth loss, whereas carotid plaque prevalence remained elevated yet attenuated among edentulous participants (21). In contrast, participants in the Study of Health in Pomerania (SHIP) became edentulous later in life than INVEST participants (22), and the greatest extent of carotid atherosclerosis in SHIP was also observed among edentulous participants (23). Taken together, these findings suggest that edentulism occurring earlier in life might confer some protection against atherosclerotic development by minimizing lifetime oral infectious exposure.

If confirmed, the present results might have implications for ongoing research regarding periodontal disease and cardiovascular disease. Specifically, type 2 diabetes might also be considered as a mediator, in addition to a confounder, of these associations.

The observed 50–100% increased incident type 2 diabetes odds associated with periodontal disease is clinically relevant as it is comparable to the risk associated with other type 2 diabetes risk factors. For example, in agreement with previous research (18) we report that a 2-SD increase in either BMI or subscapular skinfold is associated with an approximate 100% increase in incident diabetes odds, whereas being hypertensive or having 10 additional years of age increased diabetes odds by 40 and 30%, respectively.

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Table 3—*ORs (95% CI) for incident diabetes by category of baseline periodontal index among selected subgroups: NHANES I and NHEFS, 1971–1974 through 1992*

Subgroup	*n*	Category PI0	Category PI1	Category PI2	Category PI3	Category PI4	Category PI5	Edentulous
Smoking*								
Never	4,251	1.0	1.09 (0.53–2.23)	1.33 (0.74–2.41)	2.13 (1.15–3.92)	1.63 (0.85–3.15)	1.14 (0.63–2.05)	1.31 (0.87–1.96)
Former	1,801	1.0	0.95 (0.36–2.51)	1.42 (0.58–3.43)	1.74 (0.94–3.23)	1.35 (0.63–2.89)	1.67 (0.79–3.52)	1.75 (0.89–3.43)
Current	2,869	1.0	1.26 (0.68–2.31)	0.51 (0.21–1.28)	2.63 (1.34–5.17)	1.80 (0.94–3.44)	1.67 (0.78–3.61)	0.95 (0.52–1.74)
Age†								
<50 years	4,776	1.0	1.16 (0.64–2.10)	0.87 (0.49–1.53)	2.20 (1.36–3.58)	1.84 (1.03–3.28)	2.29 (1.15–4.57)	1.38 (0.79–2.43)
=50 years	4,529	1.0	0.98 (0.49–2.10)	1.21 (0.63–2.35)	1.99 (1.34–2.96)	1.60 (0.98–2.59)	1.17 (0.73–1.86)	1.30 (0.92–1.85)
BMI†								
BMI <25 kg/m^2	4,710	1.0	1.40 (0.50–3.90)	1.03 (0.33–3.17)	1.86 (0.76–4.54)	2.41 (1.10–5.28)	1.84 (0.78–4.34)	2.64 (1.42–4.92)
BMI ≥25 kg/m^2	4,577	1.0	1.06 (0.68–1.63)	1.05 (0.69–1.61)	2.06 (1.51–2.82)	1.69 (1.12–2.54)	1.55 (1.00–2.40)	1.09 (0.78–1.51)
Sex‡								
Men	3,673	1.0	0.60 (0.28–1.29)	0.77 (0.39–1.54)	1.50 (0.89–2.55)	1.65 (1.01–2.70)	1.28 (0.72–2.28)	1.21 (0.77–1.92)
Women	5,613	1.0	1.90 (1.01–3.58)	1.35 (0.79–2.28)	2.84 (1.87–4.32)	1.73 (0.84–3.54)	1.80 (1.00–3.24)	1.47 (1.03–2.09)
Race§								
Black	1,430	1.0	1.19 (0.57–2.53)	0.53 (0.26–1.05)	1.36 (0.64–2.89)	1.07 (0.53–2.17)	0.63 (0.24–1.62)	0.61 (0.29–1.29)
White	7,789	1.0	1.04 (0.65–1.65)	1.09 (0.66–1.78)	2.06 (1.40–3.03)	1.79 (1.24–2.60)	1.71 (1.13–2.60)	1.37 (1.04–1.80)

*Adjusted for age, sex, race, education, BMI, subscapular skinfold, physical activity level, hypertension, and total cholesterol. †Adjusted for age, sex, race, education, smoking status, BMI, subscapular skinfold, physical activity level, hypertension, and total cholesterol. ‡Adjusted for age, race, education, smoking status, BMI, subscapular skinfold, physical activity level, hypertension, and total cholesterol. §Adjusted for age, sex, education, smoking status, BMI, subscapular skinfold, physical activity level, hypertension, and total cholesterol; 80 participants defined as race = "other" were excluded from the race subgroup analysis due to sparse incident type 2 diabetes (three events).

study did not reach statistical significance ($P = 0.12$), the observation that periodontal disease was apparently more strongly associated with incident type 2 diabetes among women may be worthy of note, given recent findings that inflammation was a stronger predictor of type 2 diabetes in women than in men (23). Whether the current sex differences in periodontal disease–related diabetes risk have biological underpinnings or are merely contextual or an artifact merits further study.

NHANES I is limited by the lack of fasting glucose measures to exclude undiagnosed baseline diabetes. Because of the high prevalence of undiagnosed diabetes in the general population (24), the potential for reverse causality (undiagnosed diabetes at baseline causes periodontitis, but the diabetes is later discovered and thought to be incident) exists. This possibility was minimized by *1*) removing incident diabetes cases occurring within 1 year of baseline from all analyses and *2*) conducting a subgroup analysis restricted to incident diabetes occurring ≥10 years after baseline, because most individuals with diabetes would probably become symptomatic within 10 years. Similarly, the potential for diagnostic bias during follow-up to explain these findings is unlikely. For this bias to remove our finding, the rate of undiagnosed diabetes would have to be substantially higher among periodontally healthy (our reference group) individuals relative to those with advanced periodontal disease, thus artificially reducing diabetes incidence among individuals without periodontal disease. Although not impossible, this possibility seems unlikely because the probability of undiagnosed diabetes in NHANES III has been reported to be higher among individuals with as opposed to those without periodontitis (25). Further, according to previously published NHANES data, the probability of undiagnosed diabetes is highest among groups with elevated type 2 diabetes risk factors (24). In the present report, participants with advanced periodontal disease also had elevated type 2 diabetes risk factors. Therefore, it is more likely that participants with periodontal disease experienced a higher rate of undiagnosed diabetes during follow-up than periodontally healthy participants. If so, this occurrence would bias results toward the null. An adverse family history or common genetic susceptibility underlying both periodontal disease and type 2 diabetes also remains as a possible explanation for our findings. We were unable to account for this potential as neither genetic data nor information regarding a family history of periodontal disease and diabetes were collected in NHANES I.

Studies with more precise measures of infectious exposure can increase our understanding of the association between bacteria-induced periodontal disease and diabetes, as was recently done for cardiovascular disease outcomes (26). Nevertheless, the observations that both clinical periodontal disease and tooth loss, but not the DMF index, were associated with incident type 2 diabetes bolster the chronic periodontal infection hypothesis.

We have found baseline periodontal disease to be a clinically relevant and novel predictor of incident type 2 diabetes in a large, population-based sample representative of U.S. adults. The prediction of type 2 diabetes from periodontal disease was not explained by confounding related to known diabetes risk factors and could reflect a shared biological pathway, such as chronic low-grade inflammation. Nevertheless, these findings require confirmation in populations with fasting glucose or A1C measurements to definitively rule out diagnostic bias. If confirmed, a contributory role of periodontal disease in the development of type 2 diabetes is potentially of public health importance because of the prevalence of treatable periodontal diseases in the population (27) and the pervasiveness of diabetes-associated morbidity and mortality.

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