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Diabetes in the dental office: using NHANES III to estimate the probability of undiagnosed disease

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Background and Objective: Recent data have suggested that in the past 15 years there has been a dramatic increase in the incidence of diabetes mellitus in the USA. However, evidence suggests that approximately one-third of diabetes cases remain undiagnosed. Because 60% of Americans see a dentist at least once per year for routine, nonemergent, care, it is reasonable to propose that the dental office can be a healthcare location actively involved in screening for unidentified diabetes.

Material and Methods: This study used NHANES III to develop a predictive equation that can form the basis of a tool to help dentists determine the probability of undiagnosed diabetes by using self-reported data and periodontal clinical parameters routinely assessed in the dental office.

Results: Our analyses reveal that individuals with a self-reported family history of diabetes, hypertension, high cholesterol levels and clinical evidence of periodontal disease bear a probability of 27–53% of having undiagnosed diabetes, with Mexican–American men exhibiting the highest probability and white women the lowest.

Conclusion: These findings suggest that the dental office could provide an important opportunity to identify individuals unaware of their diabetic status.

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The incidence of type 2 diabetes in the USA has dramatically increased in the past 15 years (1,2). However, although data are only available from 1988, evidence suggests that ≈30% of diabetes cases may be undiagnosed (2–5). This estimate remained unchanged from 1999 to 2005 (2,5). Whether as a result of more stringent diagnostic criteria and/or an increase in obesity or a sedentary lifestyle, this increase has resulted in a major public health challenge. The most recently available data indicate that some 20.8 million people in the USA have diabetes, which represents 7% of the population (5). Diabetes is associated with significant morbidity and mortality, and is the leading cause of blindness and end-stage renal disease. Nearly two-thirds of patients with diabetes die of cardiovascular or cerebrovascular disease (6–8). In addition, the financial burden that results from diabetes is enormous; in 2002, the cost of diabetes care in the USA was estimated at $132 billion (5).

Previous studies have examined the performance of predictive models for diabetes screening in medical settings using a mix of self-reported and objective characteristics (9–11). Moreover, data from the American Dental Association suggests that more than 60% of Americans see a dentist at least once per year (12). Many of these visits are for routine, nonemergent, care. As studies suggest a two-way relationship between diabetes and periodontitis, with more pronounced periodontal destruction in people with diabetes, but also a poorer metabolic control of diabetes in subjects with periodontitis (13–17), it is reasonable to propose that the dental office can be a healthcare location actively involved in

screening for unidentified diabetes. Thus, this study developed a predictive model as a tool to help dentists determine the probability of undiagnosed diabetes, by using self-reported information readily obtained during an individual's medical history interview and findings from a clinical periodontal examination.

Material and methods

The data for this study came from the NHANES III public-use files. This survey assessed the health status of a nationally representative sample of the civilian noninstitutionalized US population, selected through a stratified multistage probability sampling design. Full descriptions of the sample design in NHANES III have been reported previously (18,19). NHANES III yielded a sample of 20,050 persons, 17 years of age or older. However, this analysis was limited to records of participants who were 20 years and older [for consistency with most national studies (1–3)], had their blood drawn during a morning examination, reported being told by a doctor or healthcare provider that they do not have diabetes and, if female, were not pregnant at the time of the examination ($n = 7231$). Furthermore, this analysis was limited to those who fasted between 08:00 h and 24:00 h and received a complete periodontal examination ($n = 4830$).

The outcome of interest for this study was identifying patients with undiagnosed diabetes, defined as having a fasting plasma glucose level of ≥126 mg/dL, among those who responded negatively to the question 'Have you ever been told by a doctor that you have diabetes? To estimate the conditional probability of having undiagnosed diabetes, several individual characteristics and self-reported health conditions, routinely asked during the medical history at the dental office, were selected. Specifically, the following variables were included in the analysis: age at interview (continuous), sex (male/female), race/ethnicity (non-Hispanic white, non-Hispanic black or African–American, Mexican–American and other), family history of diabetes, self-reported hypertension and self-reported hypercholesterolemia. From hereafter, non-Hispanic blacks and whites will be referred to as African–Americans and whites, respectively. The question 'Including living and deceased, were any of your blood relatives (parents, siblings) ever told by a doctor that they had diabetes?' was used to assess whether there was a family history of diabetes. Self-reported hypertension was determined through the question 'Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?' Similarly, a history of hypercholesterolemia was collected through the question: 'Have you ever been told by a doctor that your cholesterol levels were high?' The information corresponding to these conditions was recorded dichotomously.

For the dental examination, dentists trained in the survey examination protocol conducted the periodontal examinations (19). Briefly, the periodontal examination included two sites per tooth, midbuccal and mesiobuccal line angle, in two randomly chosen quadrants, one maxillary and one mandibular, on the assumption that these would be representative of the whole mouth. Third molars were excluded because of their frequent extraction in young adulthood, so a maximum of 14 teeth and 28 sites per individual were examined. For this analysis, periodontitis was defined as at least two sites with clinical attachment level of ≥6 mm and at least one site with a pocket depth of ≥5 mm in one of these sites (20). This is a modification of a definition originally used in a large population-based study (21). We also used definitions based on pocket depth measurements alone: at least two sites with a pocket depth of ≥5 mm, or at least one site with a pocket depth of ≥4, ≥5, ≥ 6 or ≥7 mm. These case definitions are easier to employ in a clinical setting because they do not include attachment level assessments.

Statistical analysis

Descriptive statistics for selected covariates were performed. To determine statistical significance of differences, chi-square analyses (discrete variables) and *t*-tests (continuous variables) were used.

Logistic regression was used to estimate the conditional probability of having undiagnosed diabetes, given selected characteristics such as age, sex, race/ethnicity, family history of diabetes, self-reported hypertension, hypercholesterolemia and periodontitis. To estimate a prediction equation (see Appendix I), two sets of analyses were conducted using different definitions of periodontitis, as defined above. After obtaining the estimates from the logistic regression models, the beta coefficients were used to calculate the conditional probability of having undiagnosed diabetes. Because of the complexity of the confidence interval calculations for the probabilities, and because our interest is not to make inferences, the confidence interval for the probabilities are not presented. In addition, because the individual characteristics for which the predictions will be calculated will vary, the use of confidence intervals does not have practical meaning in this context. The analysis was further adjusted for the number of teeth present. To facilitate interpretation, the probabilities are presented by sex and race/ethnicity. Because of the small sample size for the racial/ethnic group identified as 'Other' ($n = 192$), analyses are presented for African–Americans, Mexican–Americans and whites only. The analyses presented here use the full sample size ($n = 4830$) to develop the prediction equations.

All data management procedures were carried out with SAS (22), and the statistical analyses were conducted using SUDAAN (23). SUDAAN takes into account the complex sample design used in NHANES III. In the tables, the samples sizes are unweighted. However, estimates for means, proportions, standard errors and coefficients used to calculate the probabilities are weighted.

Results

Table 1 displays the distribution of selected characteristics of adults 20 years and older, included in this analysis, by race/ethnicity and sex. In

Table 1. Distribution of selected characteristics in the study population by race/ethnicity and sex: NHANES III[a]

Characteristics	African–American ($n = 1336$)		Mexican–American ($n = 1492$)		White ($n = 1810$)	
	Women ($n = 606$)	Men ($n = 730$)	Women ($n = 777$)	Men ($n = 715$)	Women ($n = 855$)	Men ($n = 955$)
Undiagnosed diabetes (%)	2.4 (0.58)[b]	3.3 (0.60)	3.1 (0.66)	2.6 (0.49)	2.6 (0.53)	1.4 (0.38)
Age, year	37.4 (0.6)	37.2 (0.6)	34.8 (0.5)	34.6 (0.5)	42.1 (0.8)	40.0 (0.7)
Family history of diabetes (%)[c]	32.2 (1.9)	25.2 (1.6)	32.5 (1.2)	27.1 (1.8)	18.1 (1.6)	21.0 (1.6)
Hypertension (%)[c]	24.3 (1.4)	21.0 (1.8)	15.6 (1.4)	11.0 (1.5)	19.1 (1.2)	18.4 (1.7)
Hypercholesterolemia (%)[c]	7.0 (0.9)	12.2 (1.7)	14.1 (1.6)	25.1 (1.2)	9.6 (1.5)	25.3 (1.8)
Mean number of teeth	23.5 (0.2)	24.0 (0.2)	25.6 (0.1)	26.1 (0.1)	25.2 (0.1)	25.3 (0.1)
Mean pocket depth, mm	1.57 (0.1)	1.78 (0.1)	1.45 (0.1)	1.64 (0.1)	1.32 (0.1)	1.48 (0.1)
Mean clinical attachment level, mm	0.92 (0.1)	1.31 (0.1)	0.74 (0.1)	0.95 (0.1)	0.87 (0.1)	1.01 (0.1)
Periodontal disease (defined as ≥ 2 sites with clinical attachment level ≥ 6 mm and ≥ 1 site with pocket depth ≥ 5 mm) (%)	2.9 (0.9)	6.4 (1.2)	0.5 (0.3)	2.2 (0.6)	1.4 (0.4)	3.0 (0.6)

[a]All chi-square and *t*-tests comparing racial/ethnic groups were statistically significant at $p < 0.05$ with the exception of undiagnosed diabetes.
[b]Numbers in parentheses represent standard errors.
[c]Self-reported information.

Table 2. Predicted probability of having undiagnosed diabetes for a 45-years-old individual, given selected characteristics, by race/ethnicity and sex: NHANES III

Characteristics	African–American ($n = 1336$)		Mexican–American ($n = 1492$)		White ($n = 1810$)	
	Women ($n = 606$)	Men ($n = 730$)	Women ($n = 777$)	Men ($n = 715$)	Women ($n = 855$)	Men ($n = 955$)
No risk factor	0.01	0.01	0.01	0.01	0.01	0.01
Family history of diabetes[a]	0.02	0.03	0.02	0.03	0.01	0.02
Family history of diabetes and hypertension[a]	0.05	0.07	0.06	0.08	0.03	0.03
Family history of diabetes, hypertension and hypercholesterolemia[a]	0.25	0.29	0.26	0.32	0.13	0.16
Family history of diabetes, hypertension, hypercholesterolemia[a] and periodontal disease [b]	0.44	0.50	0.46	0.53	0.27	0.32

[a]Self-reported information.
[b]Defined as a combination of at least two sites with clinical attachment level ≥ 6 mm and at least one site with pocket depth ≥ 5 mm.

this population, the percentage of individuals with undiagnosed diabetes (i.e. those who responded negatively to the question 'have you ever been told by a doctor that you have diabetes?' but had a fasting plasma glucose of ≥126 mg/dL) ranged from 1.4 to 3.3, depending on the race/ethnicity and sex group. In general, women were older, more likely to report having hypertension and less likely to report being told they have high levels of cholesterol than men, regardless of race/ethnicity. African–American and Mexican–American women were more likely to report having someone in their family with diabetes than were white women. With regard to the periodontal assessments, women exhibited lower means of clinical attachment level and pocket depth than men, regardless of their race/ethnicity. However, men had a higher mean number of teeth than women. As expected, women exhibited a lower prevalence of periodontal disease than men, regardless of the case definition used and their race/ethnicity.

Predicted probabilities of undiagnosed diabetes were calculated for each risk factor and by using a step-down accumulation of risk factors. With the exception of self-reported history of high cholesterol levels, the probability of having undiagnosed diabetes associated with a single risk factor was very low after adjusting for other risk factors, regardless of race/ethnicity and sex (data not shown). The order in which the variables were entered into the model was based on the way that information on demographic characteristics and medical history is usually collected in the dental office. Table 2 shows that, in the example of a 45-year-old individual, as the presence of reported risk factors increases, the probability of having undiagnosed diabetes increases, with men exhibiting higher probabilities than women. Specifically, men and women who reported having a family history of diabetes, being told they have hypertension and high cholesterol levels bear a probability of having undiagnosed diabetes of between 13 and 32%, with Mexican–Americans exhibiting the highest probabilities. Furthermore,

when periodontal disease (defined as a combination of clinical attachment level and pocket depth) was included in the model, the probabilities increase even further, with Mexican–American men exhibiting the highest (53%), and white women the lowest (27%). A similar pattern was observed for the probabilities using a definition of at least two sites with pocket depth of ≥ 5 mm, or when we included the risk factors in a different order (data not shown).

Figure 1 displays the probability of undiagnosed diabetes for African–American, Mexican–American and white adults aged 45, 50, 55 or 60 years, with and without periodontal disease (defined as a combination of clinical attachment level and pocket depth), by sex and after adjusting for family history of diabetes, self-reported hypertension and hypercholesterolemia. Clearly, the probability of having undiagnosed diabetes increased with age for both men and women. However, this increase was greater for those with periodontal disease, regardless of their race/ethnicity. Mexican–American men exhibited the highest increase at each age category.

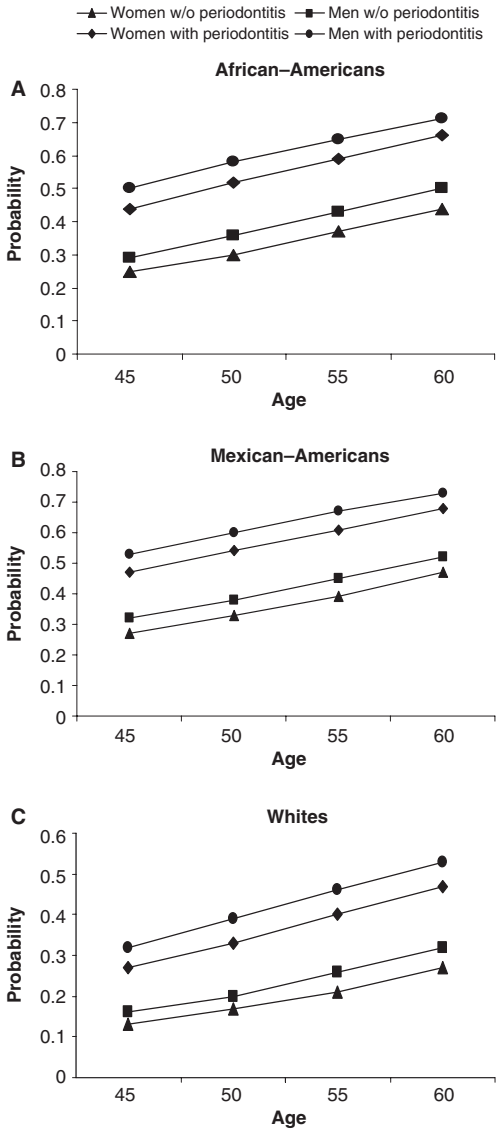

Fig. 1. Predicted probability of having undiagnosed diabetes for 45–60-year-old individuals by race/ethnicity and according to sex and periodontal status. NHANES III. Probabilities adjusted for family history of diabetes, self-reported hypertension and hypercholesterolemia. Periodontitis is defined as at least two sites with clinical attachment level of ≥ 6 mm and at least one site with pocket depth of ≥ 5 mm. w/o, without.

To explore the role of pocket depth measurements only, the analyses were repeated using definitions of at least one site with pocket depth ≥ 4 mm, ≥ 5 mm, ≥ 6 mm and ≥ 7 mm (Fig. 2). Women and men, regardless of their race/ethnicity, exhibited an increased probability of undiagnosed diabetes if they had at least one site with a pocket depth of ≥ 5 mm, concurrent with a family history of diabetes, having been told they have hypertension, and high cholesterol. Although the probability of undiagnosed diabetes increased with the presence of at least one site with pocket depth ≥ 4 mm, ≥ 5 mm, ≥ 6 mm and ≥ 7 mm, regardless of sex and race/ethnicity, this increase was of lower magnitude among white women. We repeated all the analyses, adjusting for the number of teeth present, and the results remained nearly identical. In addition, we repeated the analyses using similar cut-off points for clinical attachment level (≥ 4 mm, ≥ 5 mm, ≥ 6 mm or ≥ 7 mm); the results showed less monotonic positive patterns than those observed for definitions using pocket depth measurements. However, the probabilities of undiagnosed diabetes were the highest with the presence of at least one site with clinical attachment level of ≥ 5 mm, regardless of age, sex and race/ethnicity (data not shown). Finally, to assess the sensitivity of our models, we repeated the analyses in SAS to obtain the weighted estimated area under the receiver operator curve. The estimated area under the curve was 0.76 for the predicted models including periodontal disease as a covariate ranging from 0.81 for African–Americans to 0.77 for Mexican–Americans. These estimates cannot be calculated in SUDAAN. Therefore, they are weighted, but do not account for the sampling clustering.

Discussion

Informed by the guidelines set forth by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus for diabetes testing in asymptomatic, undiagnosed individuals (7), we have developed an approach to risk assessment for diabetes that is readily

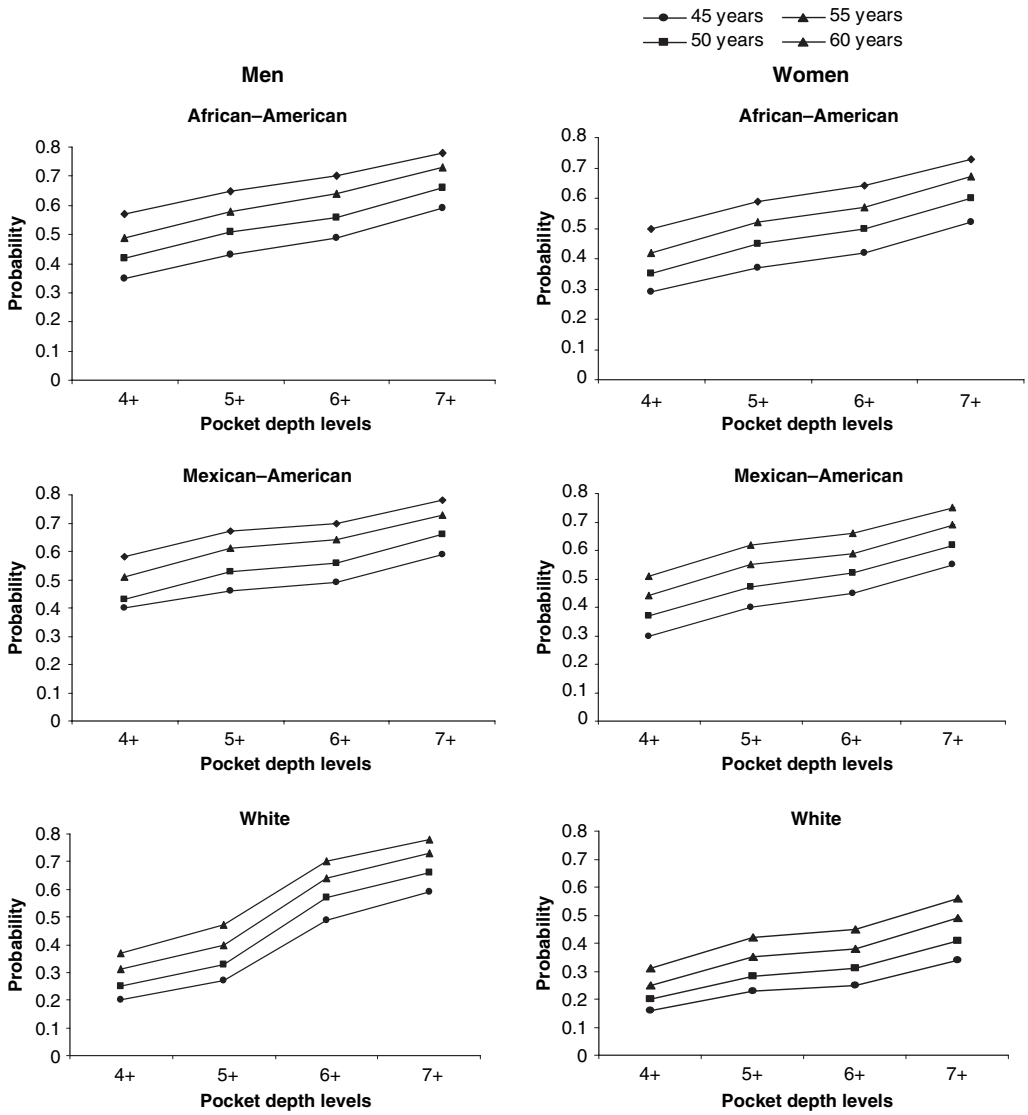

Fig. 2. Predicted probability of having undiagnosed diabetes for 45–60-year-old individuals by race/ethnicity and according to sex and periodontal status. NHANES III. Probabilities adjusted for family history of diabetes, self-reported hypertension and hypercholesterolemia. Periodontitis is defined as at least one site with a pocket depth of ≥4 mm, ≥5 mm, ≥6 mm, or ≥7 mm. PD, pocket depth.

carried out in the dental office. The Expert Committee's guidelines use detailed definitions for factors such as hypertension (blood pressure ≥140/90 mmHg) and hyperlipidemia (low high-density lipoprotein cholesterol: ≥35 mg/dL) and/or high triglyceride level (≥ 250 mg/dL); however, in this study we used patient-reported information obtained via use of a standard health history, coupled with findings from a periodontal examination in the dental office. We used these straightforward self-reported measures to assess the level of risk associated with the presence of these risk factors in white, African–American, and Mexican–American men and women.

Our findings demonstrate that periodontal measurements, coupled with simple patient-reported demographic and medical information, can be used to measure the risk for diabetes in a quantifiable manner. Using different 'case-definitions' of periodontitis in our analyses, we illustrate that assessing clinical attachment levels is especially useful towards achieving this, but that evaluation of the periodontal status, by simply identifying deep pockets via probing depth measurements, also appears to be beneficial. Notable in our findings is the synergistic impact of a relatively small number of risk factors. In the example of a 45-year-old individual in Table 2, the presence of one or two risk factors does not signify risk for diabetes in any of the subpopulations examined, whereas the addition of risk factors three and four occasions a noticeable jump in the level of risk for diabetes. Such results are not necessarily surprising, for they illustrate that a person's risk level is a complex entity in which individual risk factors build upon each other, occasioning spurts in the level of risk. In a report by Dallo & Weller (24), the authors point out that the risk

of diabetes for a 45-year-old white person is comparable to the risk of a 34-year-old African–American and a 31-year-old Mexican–American. Similarly, our findings suggest that the probability of undiagnosed diabetes may be higher among minorities than among whites of the same age (Fig. 1). Without the ability to quantify risk, it is likely that risk assessment, left alone to the clinician, is an uncertain decision-making process.

Previous studies have examined the performance of predictive models for diabetes screening in other healthcare settings; these studies have included a mix of self-reported and objective characteristics in the models (9–11). For example, Baan *et al.* (9), using information on age, sex, use of antihypertensive medication, body mass index, physical inactivity and family history of diabetes, predicted an area under the curve of 0.74. We used information readily available to the dentist (age, sex, race/ethnicity, family history of diabetes, self-reported hypertension, self-reported hypercholesterolemia and signs of periodontal disease) and were able to predict an area under the curve of 0.76. Thus, despite the differences in variables included in the models, our estimated area under the receiver operator curve curve (i.e. the ability to distinguish diabetic from nondiabetic individuals) was very similar to those of previous studies (9,10), which supports the validity of the use of such measures to develop the prediction equation.

Among the strengths of our study are the use of a nationally representative data set and the large sample size, which allows the inclusion of several covariates. Findings based on the NHANES III data set are necessarily limited by the accuracy of the variables included in the survey. NHANES III provides a single fasting plasma glucose measurement which we used to 'diagnose' diabetes, whereas a clinical diagnosis involves confirmation with a second test on the following day (7,8). Although the fasting plasma glucose test has replaced the oral glucose tolerance test as the diagnostic standard, if used, the two-step, two-test method could be expected to result in fewer classification errors. Thus, we recognize that the use of a single fasting plasma glucose test may result in a nondifferential misclassication, leading to an over- or under-estimation of our results. Moreover, although our analyses are restricted to people with a complete periodontal examination, our low prevalence of undiagnosed diabetes is consistent with studies using NHANES data (2,3). The self-reported nature of the information collected in the medical history, is another limitation. However, self-reported data have been shown to be highly correlated with physician's records (25–27). Therefore, if any difference in reporting these conditions were to occur, it would have been nondifferential, underestimating the study's results. Furthermore, a limitation inherent in NHANES' periodontal data is the use of partial-mouth recording examining only two sites (mesiobuccal and midfacial) in two randomly selected quadrants, under the assumption that these measurements are representative of the full mouth (28,29). The latest European Workshop on Periodontology addressed the issue of a lack of uniformity in the literature with respect to the criteria used for case definitions for periodontitis (30), and suggested a definition based on interproximal attachment loss measurements. This definition could not be adopted in the present study, as NHANES methodology utilizes midbuccal and mesiobuccal line angle measurements only. However, we did use more than one definition of disease, and the consistency of our findings throughout the different analyses attests to the validity of the predictive equation generated with the selected variables. Finally, because people with diagnosed diabetes were excluded from our analyses, the prevalence of periodontal disease reported here is lower than that observed in other studies, using NHANES data (31).

The quantification of risk level for diabetes brings with it attendant clinical responsibilities for the dentist practitioner, for example, how are various risk levels to be described to the patient in terms of their implications for necessary medical follow-up, referral for screening and diagnosis as well as an emphasis on prudent oral healthcare recommendations? What are the implications for the dentist him/herself regarding treatment planning? It is well established that early detection and appropriate metabolic management of affected individuals can significantly delay the development of most complications (6,32,33). In this regard, the early identification and diagnosis of diabetes has been the focus of efforts from the American Diabetes Association (7), and the medical (34) and public health communities, for many years (35). The findings of this study, although not definitive, afford the opportunity to test this model in the dental clinic and validate the results with laboratory diagnostic testing. This will provide the dental professional with a tool to directly involve himself/herself in the healthcare of the patients seen in the dental office, particularly in the identification of undiagnosed patients with diabetes. Specifically, the dental provider should be able to refer at-risk patients (e.g. those presenting with a clustering of medical risk factors), in addition to signs of periodontal disease, to their primary care physician for blood glucose testing to establish diagnosis. The approach taken here also has the capacity to quantify the level of patient risk for undiagnosed diabetes, making it possible to tailor or target the message given to the patient, including the possible recommendation for further consultation with the patient's physician. With a growing body of knowledge suggesting that oral infection, and associated tissue inflammation, may adversely affect diseases and conditions at distinct sites (cerebrovascular/cardiovascular disease, pregnancy outcomes, respiratory disease and metabolic control in diabetes) (36–39), there needs to be an increased emphasis on the interplay of oral diseases, their management and treatment, and the systemic health of patients seen in the dental office.

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Appendix I

The equation below was used to calculate the probability of undiagnosed diabetes:

$$\Pr(D|\sum x_i) = \frac{1}{1 + e^{-\alpha + \sum_{i=1}^{k} \beta_i x_i}},$$

where

$$\sum_{i=1}^{k} \beta_i x_i$$

represents the covariates included in the models: age, sex, race/ethnicity, family history of diabetes, self-reported hypertension, hypercholesterolemia and periodontal disease.