Effect of Long-Term Periodontal Care on Hemoglobin A1c in Type 2 Diabetes

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Abstract

This was a prospective cohort study evaluating 126,805 individuals with diabetes and periodontal disease receiving care at all Veterans Administration medical centers and clinics in the United States from 2005 through 2012. The exposures were periodontal treatment at baseline (PT_0) and at follow-up (PT_2). The outcomes were change in HbA1c following initial treatment ($\Delta HbA1c_1$) and follow-up treatment ($\Delta HbA1c_2$), and diabetes control was defined as HbA1c at <7% and <9% following initial and follow-up treatment, respectively. Marginal structural models were used to account for potential confounding and selection bias. The objective was to evaluate the impact of long-term treatment of periodontal disease on glycemic control among individuals with type 2 diabetes. Participants were 64 y old on average, 97% were men, and 71% were white. At baseline, the average diabetes duration was 4 y, 12% of participants were receiving insulin, and 60% had HbA1c <7%. After an average 1.7 y of follow-up, the mean HbA1c increased from 7.03% to 7.21%. About 29.4% of participants attended their periodontal maintenance visit following baseline. Periodontal treatment at baseline and follow-up reduced HbA1c by -0.02% and -0.074%, respectively. Treatment at follow-up increased the likelihood of individuals achieving diabetes control by 5% and 3% at the HbA1c <7% and HbA1c <9% thresholds, respectively, and was observed even among never smokers. HbA1c reduction after periodontal treatment at follow-up was greater ($\Delta HbA1c_2 = -0.25\%$) among individuals with higher baseline HbA1c. Long-term periodontal care provided in a clinical setting improved long-term glycemic control among individuals with type 2 diabetes and periodontal disease.

Keywords: periodontal treatment, periodontal maintenance, glycemic control, marginal structural model, hemoglobin A, glycosylated

Introduction

Periodontal disease (PD) has been positively associated with hyperglycemia in numerous studies (Chapple and Genco 2013). Inflammation from PD leads to increased circulation of proinflammatory cytokines (Paraskevas et al. 2008), which can impair insulin action contributing to insulin resistance and hyperglycemia (Hotamisligil et al. 1994). Periodontal treatment resolves inflammation and reduces circulating cytokines among individuals with diabetes (Artese et al. 2015) and may thus reduce hyperglycemia in this group. Periodontal treatment in individuals with diabetes has been shown to reduce hemoglobin A1c (HbA1c) levels ranging from -0.36% to -65% (Teeuw et al. 2010; Engebretson and Kocher 2013; Sgolastra et al. 2013). However, the effectiveness of periodontal treatment in reducing hyperglycemia remains questionable because of concerns of heterogeneity and publication bias in the studies included in the meta-analyses, and the largest randomized controlled trial (RCT), the Diabetes and Periodontal Therapy Trial (DPTT) ($n = 514$), did not show any effect of periodontal treatment on HbA1c levels among individuals with type 2 diabetes (Engebretson et al. 2013). None of these RCTs tested long-term periodontal treatment.

Long-term periodontal treatment consists of initial treatment subsequent to diagnosis, followed by regular periodontal

maintenance visits. Initial treatment typically consists of non-surgical scaling and root planing, followed by 3- to 6-monthly periodontal maintenance (American Academy of Periodontology 2001; American Academy of Periodontology 2011). Evaluating

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long-term periodontal treatment in an RCT can be challenging. For example, it is possible to randomize an individual to either receive or not receive periodontal treatment at the start of a study. However, when this person returns for a periodontal maintenance visit, the dentist makes an assessment of periodontal treatment needs based on the clinical state at that time. Because the treatment that is provided following the periodontal maintenance visit is based on the dentist's judgment, it is not random. Therefore, even an RCT could be affected by confounding because periodontal maintenance informs subsequent periodontal treatment and could be affected by nontreatment participant characteristics that influence outcomes of interest (e.g., glycemic control). The aforementioned confounding may not be appropriately addressed with standard regression analyses but can be appropriately handled using marginal structural models (MSM) (Robins et al. 2000; Hernan et al. 2013). Details of this are provided in Appendix Figure 1. Briefly, the MSM in this case would create a pseudo-population in which periodontal maintenance would not predict subsequent periodontal treatment and would therefore be unbiased with respect to sequential treatment.

We evaluated the impact of long-term periodontal treatment on glycemic control in a large cohort of individuals with type 2 diabetes receiving care at Veterans Affairs medical centers (VAMCs) and clinics in the United States using MSMs. We included participants irrespective of baseline HbA1c, body mass index (BMI), diabetes treatment, or periodontal treatment modalities—including surgical repair of bony defects and provision of antibiotic—as these factors contributed to heterogeneity in the meta-analyses of RCTs.

Materials and Methods

Study Population

The study population was a cohort of 126,805 individuals with diabetes and PD who were receiving care at any of the VA facilities in the country from 2005 through 2012. The cohort was defined by linking de-identified information from national VA electronic health records (EHRs) related to demographics, administrative claims from outpatient and inpatient visits, vital signs, mortality, laboratory results, pharmacy dispensation, clinical reminders, and dental visits. The validity and accuracy of this approach have been described in previous studies (Wang et al. 2013; Fihn et al. 2014). Approval to conduct the study was given by the institutional review boards of the William Jennings Bryan Dorn VA Medical Center, Columbia, South Carolina, and the University of South Carolina. The study conforms to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Exclusions

Individuals were excluded if they were not eligible for dental care at the VA; had type 1 diabetes, human immunodeficiency virus (HIV), renal failure, or ongoing cancer treatment; received an organ transplant; did not have HbA1c measured within the 6

mo before the start of follow-up; had missing covariate information; or if smoking status had not been evaluated.

The Figure describes the data collection procedure we used in this study. Ascertainment of diabetes: Diabetes status was determined by a validated algorithm developed in the VA population (sensitivity = 93.3%, specificity = 98.3%) (Miller et al. 2004). Diabetes was considered to be present if an individual had a prescription for diabetes medication in the current year and 2 or more *International Classification of Diseases, Ninth Revision (ICD-9)* codes for diabetes (250, 357.2, 362.0, or 366.41) in the current and past year (24 mo) from inpatient stays or outpatient visits on separate days (Miller et al. 2004). The first date of this occurrence was considered the date of diabetes diagnosis.

Ascertainment of PD

The dental registry, developed by the Veterans Health Administration Office of Dentistry, Washington, DC, contained electronic records of dental visits captured by the Dental Encounter System from 2005 through 2012 at all US VA dental facilities (Department of Veterans Affairs 2015). This registry has information on eligibility for VA dental services, date of dental encounter, and diagnostic and procedure codes. PD was determined to be present if the participant ever had any *Current Dental Terminology (CDT)* code for periodontal treatment or diagnosis (Fig.). These included D4341, D4342, D4355, D4381, D4240, D4241, D4260, D4261, D4263, D4264, D4265, D4266, D4267, D4268, D4999, D0150, and D0180 (CDT 2013). The date of the first occurrence of any of these codes was determined to be the date of diagnosis of PD.

Assignment of Index Date

The index date for start of follow-up was the first date that individuals had both PD and diabetes. For individuals with preexisting diabetes, the index date was the first date of PD diagnosis; for those with preexisting PD, it was the first date of diabetes diagnosis (Fig.).

Periodontal Treatment at Baseline (PT_0)

If a person with preexisting PD who developed diabetes later received periodontal treatment (codes D4341, D4342, D4355, D4381, D4240, D4241, D4260, D4261, D4263, D4264, D4265, D4266, D4267, D4268, and D4999) within 6 mo after diabetes diagnosis, he or she was considered to have received periodontal treatment at baseline and not otherwise. A person with preexisting diabetes who developed PD later was considered to have received periodontal treatment at baseline if he or she received periodontal treatment within 6 mo of PD diagnosis and not otherwise.

Periodontal Maintenance (PM_1)

A person receiving periodontal maintenance (determined by *Current Procedural Terminology [CPT]* or corresponding *CDT*

Figure. Data collection procedures and criteria. *Current Procedural Terminology (CPT)* or corresponding *Current Dental Terminology (CDT)* codes for periodontal treatment: D4341, D4342, D4355, D4381, D4240, D4241, D4260, D4261, D4263, D4264, D4265, D4266, D4267, D4268, and D4999. *CPT* or corresponding *CDT* codes for periodontal maintenance: D0120, D0150, D0180, D1110, D1330, and D4910.

codes D0120, D0150, D0180, D1110, D1330, and D4910) within 6 mo after PT₀ was considered to have received periodontal maintenance and not otherwise.

Periodontal Treatment at Follow-up (PT₂)

A person receiving periodontal treatment (determined by *CPT* or corresponding *CDT* codes) within 6 mo after PM₁ was considered to have received periodontal treatment at follow-up and not otherwise.

HbA1c

HbA1c was extracted from medical records at 3 time points: within 6 mo before the index date, which we henceforth refer to as baseline (HbA1c₀); within 6 mo of the date of PT₀ (HbA1c₁); and within 6 mo of the date of PT₂ (HbA1c₂) (Appendix Fig. 2).

Outcomes

The outcome to evaluate the effect of PT₀ was change in HbA1c following initial treatment ($\Delta\text{HbA1c}_1 = \text{HbA1c}_1 - \text{HbA1c}_0$). The outcome to evaluate the effect of PT₂ was change in HbA1c following the end of 1 treatment cycle ($\Delta\text{HbA1c}_2 = \text{HbA1c}_2 - \text{HbA1c}_0$).

Two categorical outcomes were also evaluated for control of HbA1c at <7%, because this is recommended by the

American Diabetes Association (2015), and <9%, because the VA uses this level as part of its quality-of-care measures as described in VA/DOD Clinical Practice Guidelines (Veterans Affairs/Department of Defense 2010). Diabetes control following PT₀ was defined as HbA1c₁ <7% (Control7₁) and HbA1c₁ <9% (Control9₁). Diabetes control following PT₂ was defined as HbA1c₂ <7% (Control7₂) and HbA1c₂ <9% (Control9₂).

Covariates

Covariates included age, sex, race (white, black, or other), obesity (body mass index [BMI] ≥ 30 kg/m²), smoking (current, past, or never) (McGinnis et al. 2011), diabetes duration (years), diabetes treatment (oral hypoglycemic or insulin), baseline HbA1c, baseline diabetes control (HbA1c <7%), dental visits not for periodontal treatment, season, comorbidities by modified Charlson index (Goldstein et al. 2004; Quan et al. 2011), elevated blood pressure (≥ 130 mm Hg systolic or ≥ 90 mm Hg diastolic), total cholesterol (≥ 200 mg/dL), low-density lipoprotein cholesterol (LDL-C) (≥ 150 mg/dL), triglycerides (≥ 150 mg/dL), low high-density lipoprotein cholesterol (HDL-C) (≤ 40 mg/dL for men and ≤ 50 mg/dL for women) assessed at baseline, and change in diabetes treatment during follow-up.

The Charlson index, a summary measure of comorbidities, was calculated by summing scores assigned selected comorbidities identified by *ICD-9* codes. The *ICD-9* codes used to calculate the score are included in the Appendix Table.

Smoking was determined from information in the health factors data set using the algorithm developed for use in the VA data by McGinnis and colleagues (2011). Agreement between smoking status determined by the algorithm compared to smoking determined by conventional methods was good ($\kappa = 0.61\text{--}0.66$) (McGinnis et al. 2011).

Statistical Methods

We fit MSMs using stabilized weights to evaluate the effect of periodontal treatment on HbA1c (Robins et al. 2000). Briefly, we used a combination of 3 sets of stabilized inverse probability weights for 1) treatment, 2) censoring due to death, and 3) missing HbA1c at follow-up. We calculated separate weights for baseline (sw_1) and long-term (sw_2) treatment, respectively. Inverse probability weighting applied this way minimizes bias (Robins et al. 2000). A more detailed description is provided in the Appendix. All weights were calculated using logistic regression. In a sensitivity analysis to evaluate the effect of change in diabetes treatment during follow-up, we added a variable measuring that in the calculation of sw_2 .

MSMs to evaluate the effect of long-term periodontal treatment on HbA1c were weighted by the stabilized weight, sw_2 . To evaluate change in HbA1c, we used a weighted analysis of variance (ANOVA) model with $\Delta HbA1c_2$ as the dependent variable and PT_2 and PT_0 as independent variables. To evaluate diabetes control of HbA1c at $<7\%$ and $<9\%$, we used a weighted modified Poisson model in with $Control7_2$ and $Control9_2$, respectively, as the dependent variables and PT_2 and PT_0 as independent variables. Similar models were used to evaluate the effect of periodontal treatment at baseline on HbA1c using the stabilized weight, sw_1 , and $\Delta HbA1c_1$, $Control7_1$, and $Control9_1$ as the outcomes and PT_0 as the independent variable.

We further conducted analyses stratified by smoking (current, past, or never smoker), BMI ($<27\text{ kg/m}^2$, $27\text{--}29.9\text{ kg/m}^2$, or $\geq 30\text{ kg/m}^2$), and HbA1c at baseline ($<7\%$, $7\text{--}8.9\%$, or $\geq 9\%$).

Results

The study population comprised 126,805 individuals with PD and diabetes receiving care at all US VA facilities at any time between 2005 through 2012. Participants were 64 y old on average (range, 21–107 y) and had diabetes for a mean of 4 y, 97% were men, 71% were white, 24% were black, 6% were other races, 58% had a BMI $\geq 30\text{ kg/m}^2$, 37% never smoked, 12% were receiving insulin, and 60% had HbA1c $<7\%$ at baseline (Table 1).

Participants were followed up for 1.7 y on average, during which time the mean HbA1c increased from 7.03% to 7.21% among all participants (Appendix Fig. 2). In this cohort, 29.4% had a periodontal maintenance visit (PM_1) within 6 mo of the baseline visit. Periodontal treatment at baseline and follow-up reduced HbA1c by -0.02% and -0.074% , respectively. Treatment at follow-up increased the likelihood of individuals achieving diabetes control by 5% and 3% at the HbA1c $<7\%$

Table 1. Baseline Characteristics of Participants ($N = 126,805$).

Characteristic	Value
Age, mean (SD), y	64.2 (10.4)
Men, n (%)	122,729 (96.8)
Race, n (%)	
White	90,136 (71.1)
Black	29,756 (23.5)
Other race	6,913 (5.5)
Obese ($\geq 30\text{ kg/m}^2$), n (%)	75,708 (58.0)
Smoking, n (%)	
Current smoker	34,776 (27.6)
Past smoker	44,228 (35.1)
Never smoker	47,178 (37.4)
Diabetes-related characteristics	
Duration of diabetes, mean (SD), y	4.0 (3.3)
Receiving insulin treatment, n (%)	14,790 (11.7)
HbA1c $<7\%$ at baseline, n (%)	75,708 (59.7)
Comorbidities, n (%)	
High LDL-C ($\geq 150\text{ mg/dL}$)	7,183 (5.7)
High total cholesterol ($\geq 200\text{ mg/dL}$)	21,923 (17.3)
High triglycerides ($\geq 150\text{ mg/dL}$)	57,761 (45.6)
Low HDL-C ($\leq 40\text{ mg/dL}$ for men and $\leq 50\text{ mg/dL}$ for women)	103,326 (58.8)
High blood pressure ($\geq 130\text{ mm Hg}$ systolic or $\geq 90\text{ mm Hg}$ diastolic)	742,30 (58.5)
Charlson index, n (%)	
0	119,767 (94.5)
1	4,519 (3.6)
2	2,517 (2.0)

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

and HbA1c $<9\%$ thresholds, respectively (Table 2). The results were materially similar in a sensitivity analysis evaluating the effect of change in diabetes medications during follow-up.

In stratified analyses, the effects of initial periodontal treatment were not modified by smoking, even though the treatment effects on HbA1c were attenuated among never smokers. The effects of initial periodontal treatment were modified by BMI and baseline HbA1c. Initial periodontal treatment was less effective in controlling diabetes (HbA1c $<9\%$) with increasing obesity but was more effective at reducing HbA1c and controlling diabetes (HbA1c $<7\%$) with increasing baseline HbA1c (Table 3). The effect of periodontal treatment at follow-up did not vary by BMI or smoking. Even though the effect sizes were attenuated among never smokers, periodontal treatment at follow-up increased HbA1c control in this group. Periodontal treatment at follow-up reduced HbA1c (-0.25%) and increased the likelihood of controlling diabetes by 13% at both HbA1c $<7\%$ and HbA1c $<9\%$ cutoffs; the benefits of periodontal treatment were greater in this group of individuals compared with those with lower HbA1c levels at baseline (P value for effect modification < 0.05) (Table 3).

Discussion

Long-term periodontal treatment delivered in a dental practice setting resulted in a clinically meaningful reduction in HbA1c

Table 2. Results from Marginal Structural Models (N = 126,805).

	Change in HbA1c% (Δ HbA1c), β^a (95% Confidence Interval)	Diabetes Control (HbA1c <7%), Relative Risk (95% Confidence Interval)	Diabetes Control (HbA1c <9%), Relative Risk (95% Confidence Interval)
Treatment at baseline (PT ₀)	−0.02 (−0.05, −0.00)*	0.98 (0.96, 1.00)*	0.99 (0.99, 1.00)*
Treatment at follow-up (PT ₂)	−0.074 (−0.13, −0.02)*	1.05 (1.02, 1.09)*	1.03 (1.02, 1.04)*

^a β is the coefficient from the model representing change in HbA1c following treatment compared with no treatment.

*P < 0.05.

Table 3. Results from Marginal Structural Models Stratified by Smoking, Body Mass Index (BMI), and HbA1c at Baseline.

	Change in HbA1c (Δ HbA1c%), β (95% Confidence Interval)	Diabetes Control (HbA1c <7%), Relative Risk (95% Confidence Interval)	Diabetes Control (HbA1c <9%), Relative Risk (95% Confidence Interval)
Smoking			
Current smokers (n = 34,776)			
Treatment at baseline (PT ₀)	−0.02 (−0.06, 0.02)	0.97 (0.94, 1.00)	0.99 (0.98, 1.00)
Treatment at follow-up (PT ₂)	−0.12 (−0.23, −0.01)	1.07 (1.01, 1.14)	1.05 (1.02, 1.07)
Past smokers (n = 44,228)			
Treatment at baseline (PT ₀)	−0.04 (−0.08, −0.01)	1.00 (0.98, 1.03)	0.99 (0.98, 1.00)
Treatment at follow-up (PT ₂)	−0.09 (−0.18, 0.01)	1.04 (0.98, 1.10)	1.02 (1.00, 1.04)
Never smokers (n = 47,178)			
Treatment at baseline (PT ₀)	−0.01 (−0.04, 0.02)	0.98 (0.95, 1.00)	0.99 (0.98, 1.00)
Treatment at follow-up (PT ₂)	−0.03 (−0.10, 0.05)	1.05 (1.00, 1.10)	1.03 (1.01, 1.04)
BMI^a			
BMI <27 kg/m ² (n = 28,257)			
Treatment at baseline (PT ₀)	−0.06 (−0.10, −0.01)	0.97 (0.94, 1.00)	1.01 (1.00, 1.02)
Treatment at follow-up (PT ₂)	0.03 (−0.01, 0.15)	1.07 (0.99, 1.14)	1.03 (1.01, 1.06)
BMI = 27–29.9 kg/m ² (n = 24,974)			
Treatment at baseline (PT ₀)	0.01 (−0.03, 0.06)	0.98 (0.95, 1.03)	0.99 (0.97, 1.00)
Treatment at follow-up (PT ₂)	−0.11 (−0.23, −0.00)	1.07 (1.00, 1.14)	1.04 (1.01, 1.06)
BMI ≥30 kg/m ² (n = 73,574)			
Treatment at baseline (PT ₀)	−0.03 (−0.05, 0.00)	0.98 (0.96, 1.00)	0.99 (0.98, 1.00)
Treatment at follow-up (PT ₂)	−0.09 (−0.16, −0.02)	1.04 (1.00, 1.09)	1.02 (1.01, 1.04)
HbA1c at baseline^{a,b,c,d,j,l}			
<7% (n = 75,708)			
Treatment at baseline (PT ₀)	0.01 (−0.01, 0.03)	0.99 (0.98, 1.01)	1.00 (0.99, 1.00)
Treatment at follow-up (PT ₂)	−0.07 (−0.11, −0.02)	1.05 (1.02, 1.07)	1.01 (1.00, 1.02)
7%–8.9% (n = 38,515)			
Treatment at baseline (PT ₀)	−0.01 (−0.05, 0.02)	1.04 (0.99, 1.09)	0.99 (0.98, 1.00)
Treatment at follow-up (PT ₂)	−0.06 (−0.13, 0.02)	0.99 (0.90, 1.09)	1.03 (1.00, 1.05)
≥9% (n = 12,582)			
Treatment at baseline (PT ₀)	−0.07 (−0.19, 0.02)	1.22 (1.07, 1.38)	1.03 (0.98, 1.09)
Treatment at follow-up (PT ₂)	−0.25 (−0.49, 0.00)	1.13 (0.90, 1.42)	1.13 (1.04, 1.24)

^aP < 0.05 for effect modification for change in HbA1c PT₂.

^bP < 0.05 for effect modification for change in HbA1c PT₀.

^cP < 0.05 for effect modification for diabetes control (HbA1c <7%) PT₀.

^dP < 0.05 for effect modification for diabetes control (HbA1c <9%) PT₀.

^jP < 0.05 for effect modification for diabetes control (HbA1c <7%) PT₂.

^lP < 0.05 for effect modification for diabetes control (HbA1c <9%) PT₂.

among individuals with baseline HbA1c% ≥9 and a modest reduction among all individuals. Long-term periodontal treatment increased the likelihood of achieving glycemic control after an average of 1.7 y of follow-up. Long-term periodontal treatment improved glycemic control across all BMI levels and was observed even among never smokers.

Long-term periodontal treatment reduced HbA1c to a much greater extent (−0.25%) among individuals with HbA1c ≥9% at baseline. This finding is clinically meaningful because a 1%

reduction in HbA1c has been shown to reduce diabetes complications by 21% over 10 y (Stratton et al. 2000), with the most benefit seen among individuals with higher initial HbA1c levels (Diabetes Control and Complications Trial Research Group 1993; Stratton et al. 2000). In the total population, periodontal treatment reduced mean HbA1c by −0.074%. Even a small mean HbA1c reduction at a population level can result in more individuals meeting their HbA1c goals (Rose 2001). In the Veterans Affairs Diabetes Trial, the mean difference between

HbA1c in the standard and intensive diabetes therapy was 1.5% over the course of the trial and 1.0% in its last year (Hayward et al. 2015). Periodontal treatment at follow-up increased the likelihood of diabetes control over and above diabetes treatment by 1.05 and 1.03 times at the <7% and <9% HbA1c cutoffs, respectively, and 1.13 times for those with HbA1c $\geq$ 9% at baseline. The degree to which these beneficial effects translate into reductions in diabetes complications is unknown and needs to be verified in future studies.

In a recent meta-analysis that included individuals with type 2 diabetes, periodontal treatment reduced HbA1c in 5 of 11 treatment arms (overall effect size of -0.36% favoring treatment) (Engebretson and Kocher 2013). The point estimates of the remaining 6 treatment arms (not statistically significant) were consistent with a protective effect. However, most studies in the meta-analysis (apart from the DPTT) had small sample sizes with evidence of publication bias and were heterogeneous with respect to the type of interventions and participant characteristics. The DPTT is particularly influential because in addition to its large sample size, there was successful randomization, standardized treatment, blinded outcome ascertainment, and a homogeneous study population. Possible explanations for the indeterminate results of the DPTT study included good glycemic control, moderate levels of PD, high obesity prevalence in the study population, short study duration, and ineffective periodontal treatment (Borgnakke et al. 2014; Chapple et al. 2014; Merchant 2014; Vergnes 2014). However, treatment in the DPTT study improved periodontal status (Engebretson et al. 2014; Michalowicz et al. 2014).

A unique feature of our study is that it is the first to evaluate long-term periodontal treatment in relation to glycemic control; other distinguishing features are the minimal exclusion criteria and the real-world clinical setting, increasing its generalizability. For example, we observed a 0.25% HbA1c reduction following periodontal treatment among individuals with baseline HbA1c $\geq$ 9%, while the DPTT study excluded this group. Moreover, the DPTT study was powered to detect reductions in HbA1c of 0.6% or larger, reducing the probability of detecting smaller effect sizes. Our findings are consistent with results of several meta-analyses (Teeuw et al. 2010; Engebretson and Kocher 2013; Liew et al. 2013; Sgolastra et al. 2013) and support the recommendations of the consensus report of the Joint European Federation of Periodontology (EFP)/AAP Workshop on Periodontitis and Systemic Diseases (Chapple and Genco 2013).

Our study had limitations. First, residual confounding was possible because of the observational study design. However, because all participants were eligible for medical and dental services, confounding by health care access was minimized. MSMs minimized and appropriately accounted for confounding from sequential treatment. Second, baseline periodontal status was unknown because the dental registry did not capture these data. Our study population therefore likely included mild, moderate, and severe PD. As the association between PD and hyperglycemia increases by PD severity (Choi et al. 2011), missing this information likely attenuated our results. Third,

misclassification of treatment status was possible because we used electronic records. EHRs are superior to conventional administrative claims data to classify health states (e.g., 97% and 100% sensitivity and positive predictive value, respectively, for EHR vs. 94% and 48% for ICD-9 codes for hepatitis) (Allen-Dicker and Klompas 2012). Moreover, agreement between administrative databases and dental records is higher for dental procedures (97%) (del Aguila et al. 2002) than for periodontal status (sensitivity = 80%, specificity = 44%) (Spangler et al. 2012). The algorithm for diabetes diagnosis in the VA population had a sensitivity of 93.3% and a specificity of 98.3% (Miller et al. 2004). Misclassification was minimized using these definitions, but when it occurred, it was likely independent and nondifferential, which would attenuate our results toward the null. Fourth, $\sim 60\%$ of participants in our study had optimal glycemic control at baseline, reducing our ability to detect changes in HbA1c due to periodontal treatment. Good glycemic control was hypothesized to have contributed to null results in the DPTT study (Borgnakke et al. 2014). Fifth, HbA1c values were extracted from medical records in 6-mo windows before the index date and after the last periodontal treatment visit. Variations in these dates could cause independent, nondifferential measurement error, attenuating our results. Sixth, some participants may have used private dental services instead of using VA facilities. To minimize that possibility, we included participants who were eligible for comprehensive dental care at the VA and were using VA clinics for their dental and medical care. Finally, although periodontal treatment improved glycemic control, its magnitude was small and likely underestimated because of the aforementioned factors.

Our study also had some strengths. First, the sample size was large, enabling us to detect smaller effect sizes. The DPTT study was underpowered to detect a change in HbA1c of $<0.6\%$ (Engebretson et al. 2013). Second, our study was conducted in a clinical rather than experimental setting, enabling us to evaluate effectiveness and feasibility in practice. Third, to our knowledge, this is the first study to demonstrate reduction in HbA1c in relation to long-term periodontal treatment. Finally, we used appropriate statistical methods based on causal inference, enhancing internal validity.

Our results underscore the importance of regular periodontal maintenance visits. A 47% increase in periodontal maintenance was associated with declines of 11% and 38% in nonsurgical and surgical periodontal treatment, respectively (Robertson et al. 2002). In contrast, irregular periodontal maintenance was associated with a 3 to 5 times higher rate of periodontal progression compared with regular maintenance (Robertson et al. 2002; Axelsson et al. 2004). However, compliance with periodontal maintenance remains low, ranging from 16% over 8 y (Famili and Short 2010) to 30% at 3 mo (Wilson 1998). Encouraging regular periodontal maintenance visits could increase compliance with long-term treatment protocols for PD.

Long-term treatment of PD provided in a clinical setting among individuals with type 2 diabetes improved glycemic

control. Individuals with poor glycemic control at the outset benefited most from periodontal treatment. Future studies are needed to identify optimal conditions for HbA1c reduction, such as the extent of PD at baseline, precise protocols for periodontal treatment and recall, and baseline level of glycemic control. Timely periodontal treatment may improve glycemic control among individuals with type 2 diabetes.

Author Contributions

A.T. Merchant, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; P. Georgantopoulos, S.S. Virani, D.A. Morales, contributed to data analysis and interpretation, drafted and critically revised the manuscript; C.J. Howe, contributed to data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; K.S. Haddock, contributed to conception, data analysis, and interpretation, drafted and critically revised the manuscript.

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