RESEARCH ARTICLE OPEN ACCESS

Combined Influence of Dental Caries and Periodontal Disease on Ischemic Stroke Risk

Stefanie Wood,[1] Lawson Logue,[1] Jaclyn Meyer,[1] Kevin Moss,[2] James D. Beck,[3] Michelle C. Johansen,[4] Wayne D. Rosamond,[5] and Souvik Sen[1]

Neurol Open Access 2025;1:e000036. doi:10.1212/WN9.0000000000000036

Correspondence
Dr. Sen
souvik.sen@uscmed.sc.edu

Abstract

Background and Objectives

Periodontal disease (PD) and dental caries are prevalent chronic oral inflammatory conditions associated with systemic health outcomes. Individually, both have been linked to an increased risk of ischemic stroke, a leading cause of morbidity and mortality. However, few studies have examined the combined effect of PD and dental caries on stroke, stroke subtypes, and major adverse cardiovascular events (MACEs) within US cohorts. We aimed to evaluate the individual and joint associations of PD and dental caries with incident ischemic stroke, stroke subtypes, and MACEs and assess the relationship between regular dental care utilization and oral disease status.

Methods

We analyzed data from participants in the Atherosclerosis Risk in Communities study who completed dental assessments during Visit 4 (1996–1998). Participants with previous ischemic stroke, coronary heart disease (CHD), or dental caries without PD were excluded. Oral health status was categorized as good oral health, PD only, or PD with(+) caries. Incident ischemic stroke and MACEs (ischemic stroke, myocardial infarction, or fatal CHD) were identified using adjudicated records through 2019. Cox proportional hazard models estimated hazard ratios (HRs) for outcomes, adjusting for demographics and vascular risk factors. The association of regular dental care with oral disease status was analyzed using logistic regression.

Results

Among 5,986 participants (mean age 63 ± 5.6 years; 52% female), 1,640 had good oral health, 3,151 had PD only, and 1,195 had PD + caries. The incidence of ischemic stroke was 4.1%, 6.9%, and 10.0% across groups, respectively. In fully adjusted models, PD + caries was associated with increased risk of ischemic stroke (HR 1.86; 95% CI 1.32–2.61) and MACEs (HR 1.36; 95% CI 1.10–1.69). Elevated risk was observed for thrombotic (HR 2.27; 95% CI 1.22–4.24) and cardioembolic (HR 2.58; 95% CI 1.27–5.26) strokes. Regular dental care was associated with lower odds of PD (odds ratio [OR] 0.71; 95% CI 0.58–0.86) and PD + caries (OR 0.19; 95% CI 0.15–0.25).

Discussion

Co-occurring PD and dental caries were independently associated with increased risk of ischemic stroke and MACEs. Regular dental care may reduce this risk by improving oral health. Limitations include reliance on one-time dental assessment and residual confounding.

RELATED ARTICLE

Editorial
Taking Care of Mouth Health to Prevent Cerebrovascular Diseases
Page e000042

MORE ONLINE

Supplementary Material

[1]Department of Neurology, School of Medicine, University of South Carolina, Columbia, SC; [2]Department of Biostatistics and Health Data Science, School of Medicine, Indiana University, Indianapolis, IN; [3]Department of Periodontology, Endodontics, and Dental Hygiene, Adams School of Dentistry, University of North Carolina, Chapel Hill, NC; [4]Department of Neurology, School of Medicine, Johns Hopkins University, Baltimore, MD; and [5]Department of Epidemiology, Gillings School of Public Health, University of North Carolina, Chapel Hill, NC.

The Article Processing Charge was funded by University of South Carolina.

Glossary

AA = African American; **ARIC** = Atherosclerosis Risk in Community; **BMI** = body mass index; **CHD** = coronary heart disease; **DARIC** = Dental ARIC; **HDL** = high-density lipoprotein; **HR** = hazard ratio; **LDL** = low-density lipoprotein; **MACE** = major adverse cardiovascular event; **MI** = myocardial infarction; **OR** = odds ratio; **PD** = periodontal disease; **REGARDS** = REasons for Geographic and Racial Differences in Stroke.

Introduction

Both periodontal disease (PD) and dental caries are highly prevalent, both worldwide and in the United States. They are independently associated with incident ischemic stroke[1-3] and represent pathologically distinct entities. PD is a chronic inflammatory disease caused by bacterial colonization that affects the soft and hard structures that support the teeth.[4] Dental caries, also a common chronic infectious and inflammatory condition, stems from cariogenic bacteria adhering to teeth. These bacteria metabolize sugars, leading to acid production that gradually demineralizes tooth structure.[5] Poor oral hygiene is a contributor to both PD and caries; thus, oral hygiene is a potential means of modifying the stroke risk. An increase in tooth brushing frequency decreases the concentration of systemic inflammatory marker levels in serum.[6] It has been reported that regular dental care was associated with 23% lower rates of incident ischemic stroke compared with episodic dental care users.[2]

In the United States, stroke remains more common in the southeastern states, referred to as the Stroke Belt.[7] The REasons for Geographic and Racial Differences in Stroke (REGARDS) study specifically investigated participants aged 45–64 years residing in the Stroke Belt.[8] Approximately 40% of the excess stroke risk in the Stroke Belt was attributable to traditional stroke risk factors while the rest was unexplained. In the region, the study found that tooth loss (a surrogate of PD and dental caries) was more common among African American (AA) individuals compared with White individuals and was associated with a higher risk of stroke and prevalence of stroke risk factors. Given this result, REGARDS study investigators postulated that PD and caries, both contributors to tooth loss, may contribute to the higher risk of stroke in the Stroke Belt.[8]

Several studies have examined the relationship between PD and cardiovascular outcomes, including major adverse cardiovascular events (MACEs). Meta-analyses of prospective cohort studies have found that individuals with PD have a 20%–35% increased risk of cardiovascular events, including myocardial infarction (MI) and stroke, even after adjusting for traditional risk factors.[9] More recent imaging studies using Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (FDG-PET/CT) have shown that periodontal inflammation is associated with increased arterial inflammation and predicts future cardiovascular events independent of other risk factors.[10] While fewer studies have focused on dental caries, emerging evidence suggests that untreated or severe caries may also be associated with stroke and all-cause mortality, although the associations with MACEs are less consistent.[11] To date, few studies have evaluated the combined impact of PD and caries on cardiovascular risk. Given their high co-prevalence and shared contributions to chronic inflammation and systemic infection, understanding their joint role in vascular outcomes is increasingly important.

While PD and caries have each been individually linked to cardiovascular outcomes, few studies have evaluated their combined effect on MACE or stroke. To date, no large prospective analyses have examined whether co-occurrence of PD and caries confers additional cardiovascular risk beyond each condition alone. Furthermore, these conditions often co-occur, and their interplay may contribute additional cardiovascular risk beyond their individual effects. Previous studies have not consistently accounted for PD severity, which may confound observed associations. Given that stroke is a heterogeneous condition with distinct subtypes, examining ischemic stroke subtypes may offer insight into differential vascular mechanisms. In this study, we evaluate the joint and individual associations of PD and dental caries with MACEs as well as ischemic stroke subtypes. We hypothesize that the co-occurrence of PD and dental caries is associated with a greater risk of MACEs and ischemic stroke compared with either condition alone, independent of PD severity or traditional vascular risk factors.

Methods

Study Population

The Atherosclerosis Risk in Communities (ARIC) study, launched in 1987, aimed to investigate atherosclerosis and its outcomes. Participants were recruited from 4 US regions: Forsyth County, NC; Jackson, MS; Minneapolis, MN; and Washington County, MD.[12] The baseline dental examination occurred during Visit 4 (1996–1998), with follow-up data censored on December 31, 2019. However, for Jackson participants, follow-up ended in 2017 because of delays in accessing hospital records. Vascular risk factors were assessed at Visit 4, and hospital records were collected for any hospitalizations during the median 21-year follow-up. Annual contact with participants was used to assess stroke and related events. Informed consent was obtained from all participants, and ethical approval was granted by the study's field centers and coordinating center.

At Visit 4, 11,656 participants were assessed. Of these, 6,744 were offered and accepted a dental examination as part of the Dental ARIC (DARIC) study. Exclusions included 1,317 who refused, 1,895 with medical contraindications, 1,619 who were edentulous, 55 of other races, and 26 with dental implants.[13] Ultimately, 6,066 participants without previous coronary heart disease (CHD) or ischemic stroke completed a full-mouth periodontal assessment and dental examination. Excluded individuals were older, had a higher proportion of women, were more likely to be AA, and had higher body mass index (BMI) and waist-to-hip ratios.[3] The final analysis included 5,986 participants, excluding 80 with caries but no PD. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) diagram is illustrated in Figure 1.

Standard Protocol Approvals, Registrations, and Patient Consents

The ethical (institutional) review boards of all ARIC study field centers' participating institutions:the Universities of Mississippi, Minnesota, and North Carolina; Wake Forest University; and Johns Hopkins Universityas well as the coordinating center at University of North Carolina approved the study. All participants provided written informed consent. The research was conducted in accordance with the principles described in the Declaration of Helsinki.

Assessment of Dental Caries and PD

Participants underwent full-mouth oral assessments at Visit 4 using modified Radike[14] criteria. Modifications included using a tongue blade for a more visual examination. Coronal and root carious lesions were recorded separately. Tooth status was classified as sound, decayed, filled, missing, restored with a crown, a decayed or sound root fragment, or implant. Decayed or filled teeth were coded as caries, and root caries were identified by well-defined cavitation and discoloration. Tooth fractures, erosion, and abrasions were not recorded as caries. Participants with lesions but no frank caries were further examined for pit, fissure, and smooth surface lesions. The presence of PD was also assessed, with periodontal profile classes ranging from PPC-A (health) to PPC-G (severe PD).[15] The primary exposures of interest were coronal caries and PD, classified into binary groups (oral health, PD with/without caries) to test the hypothesis that no grading systems combine both.

Assessment of Dental Care Utilization

Dental care utilization was categorized based on participants' responses to the dental history questionnaire they completed. Participants were divided into 2 groups: regular users, who sought routine dental care, and episodic users, who sought dental care only when experiencing symptoms.

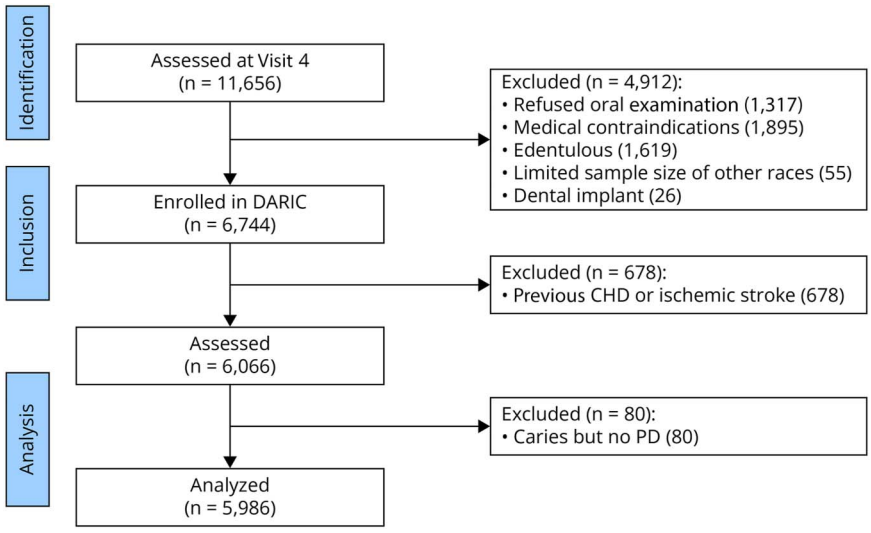
Assessment of Incident Ischemic Stroke and Subtypes

Stroke cases were identified through annual (before 2012) and semiannual (after 2012) phone visits, along with hospital discharge records. Definite or probable strokes were confirmed using ICD-9 codes (430–437), hospital records, and neuroimaging. Ischemic strokes and stroke subtypes were classified by a computer algorithm and physician review, with discrepancies resolved by a second physician. Follow-up data extended to 2019. All strokes were categorized as definite, probable, or suspected, with incident ischemic strokes and subtypes after Visit 4 included in the analysis.[16]

Other Variables of Interest

Age, sex, race, and vascular risk factors (BMI, waist-to-hip ratio, education, diabetes, smoking, alcohol use, hypertension, lipid profile) were assessed during the fourth ARIC study visit (1996–1998).[12] A race/ethnicity variable (Black or White) and ARIC field center accounted for ethnic, regional, and examiner differences.[13] BMI was calculated from weight and

Figure 1 STROBE Diagram



height. Hypertension was defined as systolic blood pressure (BP) ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg, or medication use. Diabetes was defined by fasting glucose ≥126 mg/dL or nonfasting ≥200 mg/dL, or self-reported diagnosis/medication. Participants also reported education, smoking status, and alcohol use.

Statistical Analysis

The cohort consisted of 5,986 participants assessed for oral health and PD ± caries at Visit 4. Demographics and covariates, including age, sex, race, BMI, hypertension, diabetes, waist-to-hip ratio, education, smoking status, alcohol use, and lipid panel, were assessed using analysis of variance for continuous variables and a χ^2 test for categorical variables. Triglycerides and serum C-reactive protein (CRP) are not normally distributed and were assessed using a nonparametric Kruskal-Wallis test. The Gray test was run to determine differences in the time-to-event distribution of incident ischemic stroke as well as MACEs between the oral health, PD only, and PD + caries groups, with all-cause mortality being the competing risk of interest. The proportional hazard assumption was assessed using interaction terms between time measures and covariates in the model. Cox proportional hazard models were then used to assess crude ratios, followed by adjusted hazard ratios (adj. HR), and 95% CIs for incident ischemic stroke, MACEs, and stroke subtypes from the initial dental assessment. Four models were used in this analysis: Model 1 assessed crude HR; Model 2 assessed adj. HR for age, sex, and race; Model 3 assessed adj. HR for age, sex, race, and PD severity; and Model 4 assessed adj. HR for age, race, sex, BMI, hypertension, diabetes, education, smoking status, current alcohol use, and low-density lipoprotein (LDL). The cross-sectional association between regular dental care use and rate of PD with and without caries was tested using binary logistic regression and presented as odds ratio (OR) (95% CI). IBM SPSS Statistics for Windows, Version 29.0 (Armonk, NY), was used for all statistical analyses.

Data Availability

The ARIC investigators are willing to share the data used in this article with a researcher for the purpose of reproducing the results, subject to completion of a data use agreement ensuring appropriate protection of the confidentiality of ARIC participants' data.

Results

Of the 5,986 patients assessed at Visit 4, 1,640 were found to have good oral health, 3,151 were found to have PD only, and 1,195 were found to have PD + caries. The different oral health statuses were compared with each other and analyzed (Table 1). Several baseline characteristics and laboratory values were found to be significant. Participants in the oral health group were more likely to be female. The proportion of women in the oral health, PD only, and PD + caries groups was 68%, 52%, and 49%, respectively, while the proportion of men was 32%, 48%, and 51%, respectively ($p < 0.001$). The oral health data revealed that the White race comprised 97%, 86%, and 50% of the PD only, PD + caries, and oral health groups, respectively, while the African American (AA) group accounted for 3%, 14%, and 50% in those same groups, respectively ($p < 0.001$). The oral health group was more likely to have advanced education, with 5%, 42%, and 53% of participants having basic, intermediate, and advanced education, respectively ($p < 0.001$). Conversely, compared with the PD + caries group, the percentages of participants with basic, intermediate, and advanced education were 28%, 40%, and 32%, respectively ($p < 0.001$). The oral health group was more likely to be current alcohol consumers, with 15%, 21%, and 64% of participants classified as never, former, and current alcohol consumers, respectively ($p < 0.001$). Conversely, compared with the PD + caries group, the percentages of never, former, and current alcohol consumers were 29%, 33%, and 39%, respectively ($p < 0.001$). The oral health group was found to have higher high-density lipoprotein (HDL) cholesterol levels, with mean ± SD values of 55 ± 17, 50 ± 16, and 50 ± 16 mg/dL for oral health, PD only, and PD + caries groups, respectively ($p < 0.001$). The PD only group was found to be older, with mean ages of 62 ± 5.4, 63 ± 5.6, and 62 ± 5.6 years in oral health, PD only, and PD + caries groups, respectively ($p < 0.001$). The PD + caries group was more likely to be current smokers, with the percentages of never, former, and current smokers being 46%, 37%, and 17%, respectively ($p < 0.001$). Conversely, compared with the oral health group, the percentages of never, former, and current smokers were 55%, 39%, and 6%, respectively ($p < 0.001$). The PD + caries group was found to have a higher BMI, with mean ± SD values of 27.3 ± 4.8, 28.7 ± 5.3, and 29.9 ± 6.0 for oral health, PD only, and PD + caries groups, respectively ($p < 0.001$). LDL cholesterol values tended to be lower in the oral health and PD only groups compared with the PD + caries group, with mean values of 121 ± 32, 122 ± 33, and 124 ± 36, respectively ($p = 0.061$). The PD + caries group was found to have a higher waist-to-hip ratio, with mean ± SD values of 0.92 ± 0.8, 0.95 ± 0.07, and 0.96 ± 0.07 for oral health, PD only, and PD + caries groups, respectively ($p < 0.001$). The PD + caries group was also found to have higher rates of hypertension and diabetes. For hypertension, the percentages were 25%, 33%, and 42% for oral health, PD only, and PD + caries groups, respectively ($p < 0.001$), and for diabetes, the percentages were 8%, 13%, and 18%, respectively ($p < 0.001$). Finally, the PD + caries group was found to have higher levels of high-sensitivity CRP, with the values of 2.4 (0.9–6.1), 2.7 (0.9–7.1), and 3.3 (1.3–7.9) for oral health, PD only, and PD + caries groups, respectively ($p < 0.001$).

During a median of a 21-year follow-up period, 67 of the 1,640 patients (4.1%) in oral health had incident stroke events, 216 of the 3,151 patients with PD only (6.9%) had incident stroke events, and 119 of the 1,195 with PD + caries (10%) had incident stroke events. Cumulative incidence curves for ischemic stroke revealed a clear gradient by oral health status, with the highest cumulative incidence observed in participants with PD + caries, followed by

Table 1 Baseline Characteristics and Laboratory Values

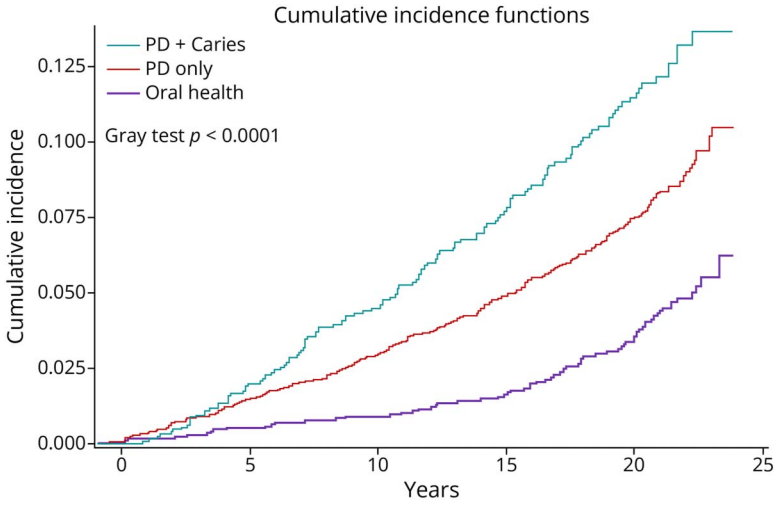
Oral health status				
	Oral health (n = 1,640)	**PD only (n = 3,151)**	**PD + caries (n = 1,195)**	***p* Value**
Age, y[a]	62 ± 5.4	63 ± 5.6	62 ± 5.6	<0.001
Sex, %				
Female	1,114 (68)	1,633 (52)	585 (49)	<0.001
Male	526 (32)	1,518 (48)	610 (51)	
Race, %				
African American	50 (3)	452 (14)	592 (50)	<0.001
White	1,590 (97)	2,699 (86)	603 (50)	
Body mass index[a]	27.3 ± 4.8	28.7 ± 5.3	29.9 ± 6.0	<0.001
Waist-to-hip ratio[a]	0.92 ± 0.08	0.95 ± 0.07	0.96 ± 0.07	<0.001
Hypertension, %	418 (25)	1,026 (33)	497 (42)	<0.001
Diabetes, %	132 (8)	415 (13)	221 (18)	<0.001
Education, %				
Basic	76 (5)	327 (11)	335 (28)	<0.001
Intermediate	686 (42)	1,421 (45)	477 (40)	
Advanced	876 (53)	1,400 (44)	382 (32)	
Smoking, %				
Never	894 (55)	1,413 (45)	545 (46)	<0.001
Former	638 (39)	1,325 (42)	440 (37)	
Current	107 (6)	406 (13)	199 (17)	
Alcohol, %				
Never	254 (15)	553 (18)	343 (29)	<0.001
Former	335 (21)	828 (26)	395 (33)	
Current	1,051 (64)	1770 (56)	457 (39)	
Cholesterol, mg/dL[a]	204 ± 35	201 ± 35	201 ± 39	0.002
LDL, mg/dL[a]	121 ± 32	122 ± 33	124 ± 36	0.061
HDL, mg/dL[a]	55 ± 17	50 ± 16	50 ± 16	<0.001
Triglycerides, mg/dL[b]	125 (89–172)	124 (89–172)	111 (82–163)	<0.001
High-sensitivity CRP[b]	2.4 (0.9–6.1)	2.7 (0.9–7.1)	3.3 (1.3–7.9)	<0.001

Remaining characteristics, number (proportion %), χ^2 test.
[a] Mean±SD, analysis of variance (ANOVA).
[b] Median (25%ile-75%ile range), Kruskal-Wallis test.

those with PD only, and the lowest incidence among individuals with good oral health (Gray test $p < 0.0001$) (Figure 2). Similarly, cumulative incidence curves demonstrated a graded association between oral health status and risk of MACEs, with individuals with both PD + caries experiencing the highest cumulative incidence over time, followed by those with PD only, and the lowest incidence observed among individuals with good oral health (Gray test $p < 0.0001$) (Figure 3).

Individuals with poor oral health, particularly those in the PD + caries group, had significantly higher risks of MACEs and ischemic stroke when compared with individuals with good oral health (Table 2). In crude analyses (Model 1), PD only was associated with a 47% increased risk of MACEs (HR 1.47; 95% CI 1.25–1.73) while PD + caries showed a nearly two-fold elevated risk (HR 1.88; 95% CI 1.56–2.26). These associations remained statistically significant in partially adjusted models but were attenuated after full adjustment for

Figure 2 Cumulative Incidence Functions for 3 Measures of Oral Health Associated With Ischemic Stroke



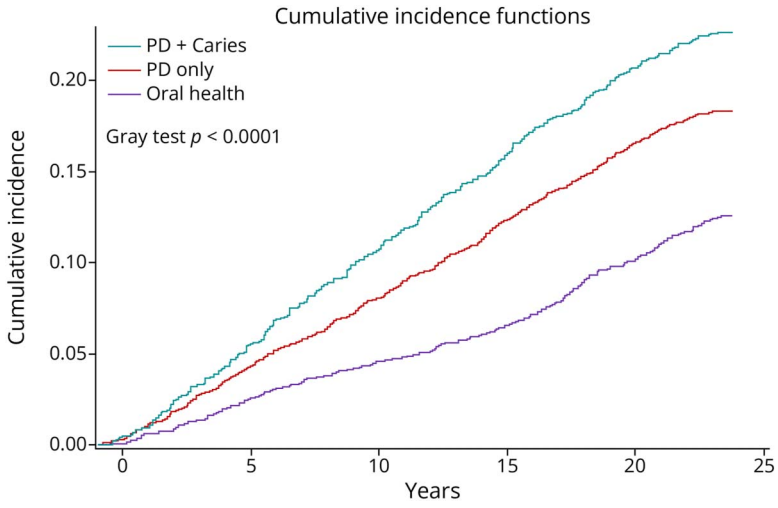
confounders including age, sex, race, diabetes, hypertension, smoking status, LDL levels, alcohol use, and BMI. In the fully adjusted model (Model 4), PD + caries remained independently associated with MACEs (HR 1.36; 95% CI 1.10–1.69) whereas PD only was not statistically significant (HR 1.17; 95% CI 0.99–1.39).

For ischemic stroke, the associations were stronger. In fully adjusted models, PD only was associated with a 44% increased risk of ischemic stroke (HR 1.44; 95% CI 1.09–1.91), and the combination of PD + caries yielded an even higher risk (HR 1.86; 95% CI 1.32–2.61) (Table 2). Subtype analysis revealed particularly elevated risks of thrombotic stroke, with an HR of 1.81 (95% CI 1.05–3.10) for PD only and 2.27 (95% CI 1.22–4.24) for PD with caries. Similarly, for cardioembolic stroke, adjusted HRs were 1.82 (95% CI 1.00–3.33) and 2.58 (95% CI 1.27–5.26), respectively. No statistically significant associations were observed between oral health status and lacunar or "other" ischemic stroke subtypes in fully adjusted models.

Upon these results, we found that regular dental care utilization lowered the chance of PD (OR 0.71 [95% CI 0.58–0.86]; $p < 0.001$) and PD + caries (OR 0.19 [95% CI 0.15–0.25]; $p < 0.001$), thus lowering the risk of incident ischemic strokes.

Additional data provided in eTable 1 show that PD and PD + caries did not significantly interact with the vascular risk factors listed, suggesting lack of effect modification.

Figure 3 Cumulative Incidence Functions for 3 Measures of Oral Health Associated With MACE



MACE = major adverse cardiovascular event.

Table 2 Crude and Adjusted Hazard Ratios for Oral Health, PD, and PD + Caries Groups

	Model 1	Model 2	Model 3	Model 4
	MACE (MI, fatal CHD, and ischemic stroke)			
Oral health	Reference	Reference	Reference	Reference
PD	1.47 (1.25–1.73)	1.28 (1.08–1.51)	1.18 (0.83–1.48)	1.17 (0.99–1.39)
PD + caries	1.88 (1.56–2.26)	1.63 (1.33–2.01)	1.39 (1.03–1.88)	1.36 (1.10–1.69)
	Ischemic stroke			
Oral health	Reference	Reference	Reference	Reference
PD	1.86 (1.41–2.44)	1.56 (1.18–2.06)	1.45 (0.92–2.28)	1.44 (1.09–1.91)
PD + caries	2.96 (2.19–3.99)	2.28 (1.64–3.16)	2.10 (1.31–3.36)	1.86 (1.32–2.61)
	Ischemic stroke subtype: thrombotic			
Oral health	Reference	Reference	Reference	Reference
PD	2.46 (1.45–4.18)	2.00 (1.17–3.42)	2.33 (1.07–5.06)	1.81 (1.05–3.10)
PD + caries	4.27 (2.44–7.46)	2.85 (1.55–5.25)	3.13 (1.40–7.00)	2.27 (1.22–4.24)
	Ischemic stroke subtype: cardioembolic			
Oral health	Reference	Reference	Reference	Reference
PD	2.25 (1.25–4.04)	1.88 (1.04–3.41)	1.33 (0.48–3.68)	1.82 (1.00–3.33)
PD + caries	3.29 (1.72–6.28)	2.68 (1.34–5.37)	1.98 (0.70–5.63)	2.58 (1.27–5.26)
	Ischemic stroke subtype: lacunar			
Oral health	Reference	Reference	Reference	Reference
PD	1.06 (0.64–1.74)	0.94 (0.57–1.56)	1.22 (0.51–2.92)	0.87 (0.52–1.46)
PD + caries	1.64 (0.92–2.93)	1.52 (0.81–2.85)	1.87 (0.75–4.62)	1.26 (0.65–2.43)
	Ischemic stroke subtype: Others			
Oral health	Reference	Reference	Reference	Reference
PD	1.54 (0.99–2.41)	1.45 (0.92–2.28)	1.25 (0.52–3.01)	1.30 (0.82–2.07)
PD + caries	1.74 (1.00–3.02)	1.62 (0.90–2.94)	1.35 (0.53–3.44)	1.63 (0.88–3.01)

Model 1 = crude hazard ratio (95% CI).
Model 2 = adjusted for age, race, and sex (95% CI).
Model 3 = adjusted for age, race, sex, and PD severity (95% CI).
Model 4 = adjusted for age, race, sex, diabetes, hypertension, current smoking status, alcohol use, LDL levels, education, and BMI (95% CI).

Discussion

This study examined the relationships among PD, dental caries, MACEs, ischemic stroke and its stroke subtypes, and regular dental care in a US cohort. While PD and caries have each been individually linked to cardiovascular outcomes, few studies have evaluated their combined effect on MACE or stroke. Baseline characteristics showed that participants without PD or caries were more likely to be female, be White, have higher education, consume alcohol, and have higher HDL cholesterol. By contrast, the PD + caries group was more likely to be male, be AA, and have higher BMI, higher waist-to-hip ratio, hypertension, diabetes, and lower education, as well as higher CRP levels. The PD only and PD + caries groups had a significantly higher cumulative incidence of ischemic stroke and MACEs compared with the oral health group (Gray test $p < 0.0001$). After adjusting for key covariates, the risk of ischemic stroke was nearly doubled in the PD + caries group, further supported by eTable 1.

A previous analysis of the DARIC study found comparable results regarding the association between PD and stroke.[2] Participants were classified by PD grade into groups described in the Methods section. The study also showed that regular dental care utilization was associated with lower adjusted stroke risk (HR of 0.77; 95% CI 0.63–0.94).[2] Our study supports this notion as we also found that regular dental care utilization lowered the chance of PD (OR 0.71 [95% CI 0.58–0.86]; $p < 0.001$) and PD + caries (OR 0.19 [95% CI 0.15–0.25]; $p < 0.001$), thus lowering the risk of incident ischemic strokes.

Using the same DARIC population, the association between dental caries and increased risk of stroke was investigated and reported previously.[3] Participants with ≥1 dental caries had an increased risk of stroke (adj. HR 1.40 [95% CI 1.10–1.79]) and death (adj. HR 1.13 [95% CI 1.01–1.26]), but not of CHD events (adj. HR 1.13 [95% CI 0.93–1.37]). The association of dental caries with ischemic incident stroke was significantly higher in the AA subgroup when compared with the White subgroup (interaction term $p = 0.0001$). Our study found supporting results as the PD + caries group was more likely to be of AA race (50%, $p < 0.001$).

The mechanism linking PD and caries to increased stroke risk is still being studied. PD is associated with higher systemic inflammation due to chronic exposure to Gram-negative bacteria.[17,18] Periodontitis may increase risk of ischemic stroke and MACEs through inflammatory pathways.[8] Dental caries, on the contrary, involves bacteria metabolizing sugars to produce acids that demineralize teeth, leading to infection and inflammation.[19,20] These inflammatory mediators trigger a chronic systemic inflammatory response, contributing to atherosclerosis.[21] PD pathogens have been found in atheromatous plaques in the carotid and coronary arteries while *Streptococcus mutans*, the main dental caries pathogen, has been detected in heart valve and atheromatous plaques.[22,23] Together, these factors likely explain the higher ischemic stroke risk in the PD + caries group.

These findings demonstrate that poor oral health, particularly the presence of both periodontitis and dental caries, is significantly associated with elevated risks of MACEs and ischemic stroke, with especially strong associations observed for thrombotic and cardioembolic stroke subtypes. Even after accounting for a wide range of demographic and clinical covariates, the presence of both PD and caries remained an independent predictor of adverse vascular outcomes. This supports the growing body of evidence linking oral-systemic inflammation to atherosclerotic disease and cerebrovascular pathology.

The stronger associations observed for thrombotic and cardioembolic subtypes suggest potential pathophysiologic mechanisms through which chronic oral infection and inflammation may promote prothrombotic states, endothelial dysfunction, or embolic phenomena. While lacunar stroke did not demonstrate significant associations, likely because of differing etiologies and smaller sample sizes, the consistent trends across multiple models lend support to a systemic link between oral health and vascular disease.

These results highlight the importance of integrating oral health assessments into cardiovascular risk profiling, particularly in populations with a high burden of PD. Future prospective studies and randomized trials of periodontal interventions may further clarify whether improving oral health can directly reduce cardiovascular and cerebrovascular events.

The observed association between regular dental care and reduced stroke risk may reflect not only a potential biological effect—through the reduction of periodontal inflammation and systemic immune activation—but also broader behavioral and sociodemographic factors. Individuals who engage in routine dental visits may also adhere to healthier lifestyles, have better access to medical care, and demonstrate greater health-seeking behaviors overall. While we adjusted for a range of cardiovascular and socioeconomic confounders, the possibility of residual confounding by general health behavior cannot be excluded. Thus, dental care may function both as a proxy for preventive health engagement and as a modifiable exposure with potential biological relevance. Further studies using causal inference frameworks or randomized trials of periodontal treatment will be needed to more definitively determine the etiologic role of dental care in stroke prevention.

Our study had a few limitations. Participants were younger, with lower BMI, lower rates of hypertension and diabetes, and higher education than those excluded, likely because of the exclusion of older individuals in poor health or with tooth loss. Residual and unmeasured confounding may persist despite statistical controls. In addition, the study relied on a single dental assessment and used education level as a proxy for socioeconomic status. However, the study benefits from a large, community-based cohort; long follow-up; rigorous outcome adjudication; and thorough assessment of confounding factors.

A previous case-control study found poorer dental health among patients with acute MI compared with controls, without separately analyzing caries and PD, but considering them collectively.[24] This association remained significant after adjusting for factors such as age, social class, smoking, lipid levels, and diabetes. Beyond this study, research on the combined effect of PD and caries on cardiovascular health is limited.

Our findings suggest that the co-occurrence of PD and dental caries is independently associated with an increased risk of MACEs and ischemic stroke, particularly thrombotic and cardioembolic subtypes. These results underscore the importance of comprehensive oral health as a modifiable factor in cardiovascular and cerebrovascular disease prevention. Integrating dental care into routine medical risk assessment and promoting preventive oral hygiene practices may offer a novel strategy to reduce vascular risk at the population level.

Acknowledgment

The authors thank the staff and participants of the ARIC study for their important contributions.

Author Contributions

S. Wood: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or

interpretation of data. L. Logue: drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. J. Meyer: analysis or interpretation of data. K. Moss: study concept or design; analysis or interpretation of data. J.D. Beck: study concept or design; analysis or interpretation of data. M.C. Johansen: drafting/revision of the manuscript for content, including medical writing for content. W.D. Rosamond: study concept or design; analysis or interpretation of data. S. Sen: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data.

Study Funding

The ARIC study (Atherosclerosis Risk in Communities) was funded in whole or in part with federal funds from the National Heart, Lung, and Blood Institute, NIH, Department of Health and Human Services, under contract numbers 75N92022D00001, 75N92022D00002, 75N92022D00003, 75N92022D00004, and 75N92022D00005. The Dental ARIC study was funded by NIH/National Institute of Dental and Craniofacial Research (44R01-DE021418 and R01-DE021986) and NIH/National Center for Research Resources (UL1-TR001111).

Disclosure

The authors report no relevant disclosures. Go to Neurology.org/OA for full disclosures.

Publication History

Received by *Neurology® Open Access* March 24, 2025. Accepted in final form August 26, 2025. Submitted and externally peer reviewed. The handling editor was Amy Kunchok, MBBS, MMed, FRACP, PhD.

References

1. Lee HJ, Choi EK, Park JB, Han KD, Oh S. Tooth loss predicts myocardial infarction, heart failure, stroke, and death. *J Dent Res.* 2019;98(2):164-170. doi:10.1177/0022034518814829
2. Sen S, Giamberardino LD, Moss K, et al. Periodontal disease, regular dental care use, and incident ischemic stroke. *Stroke.* 2018;49(2):355-362. doi:10.1161/STROKEAHA.117.018990
3. Sen S, Logue L, Logue M, et al. Dental caries, race and incident ischemic stroke, coronary heart disease, and death. *Stroke.* 2024;55(1):40-49. doi:10.1161/STROKEAHA.123.042528
4. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. *Lancet.* 2005;366(9499):1809-1820. doi:10.1016/S0140-6736(05)67728-8
5. Qin X, Zi H, Zeng X. Changes in the global burden of untreated dental caries from 1990 to 2019: a systematic analysis for the global burden of disease study. *Heliyon.* 2022;8(9):e10714. doi:10.1016/j.heliyon.2022.e10714
6. de Oliveira C, Watt R, Hamer M. Toothbrushing, inflammation, and risk of cardiovascular disease: results from Scottish health survey. *BMJ* 2010;340:c2451. doi:10.1136/bmj.c2451
7. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. *Circulation.* 2015;131(4):e29-e322. doi:10.1161/CIR.0000000000000152
8. You Z, Cushman M, Jenny NS, Howard G.; REGARDS. Tooth loss, systemic inflammation, and prevalent stroke among participants in the reasons for geographic and racial difference in stroke (REGARDS) study. *Atherosclerosis* 2009;203(2):615-619. doi:10.1016/j.atherosclerosis.2008.07.037
9. Guo X, Li X, Liao C, Feng X, He T. Periodontal disease and subsequent risk of cardiovascular outcome and all-cause mortality: a meta-analysis of prospective studies. *PLoS One.* 2023;18(9):e0290545. doi:10.1371/journal.pone.0290545
10. Van Dyke TE, Kholy KE, Ishai A, et al. Inflammation of the periodontium associates with risk of future cardiovascular events. *J Periodontol.* 2021;92(3):348-358. doi:10.1002/JPER.19-0441
11. Ramadhani A, Vianti V, Badruddin IA, Bahar A, Malik NA, Rahardjo A. The association between dental caries and cardiovascular disease: a scoping review. *Eur J Gen Dentistry.* 2024;14(02):122-135. doi:10.1055/s-0044-1793851
12. Wright JD, Folsom AR, Coresh J, et al. The ARIC (atherosclerosis risk in communities) study: JACC focus seminar 3/8. *J Am Coll Cardiol.* 2021;77(23):2939-2959. doi:10.1016/j.jacc.2021.04.035
13. Elter JR, Champagne CM, Offenbacher S, Beck JD. Relationship of periodontal disease and tooth loss to prevalence of coronary heart disease. *J Periodontol.* 2004;75(6):782-790. doi:10.1902/jop.2004.75.6.782
14. Radike A. *Criteria for the Diagnosis of Dental Caries*. American Dental Association; 1968:88.
15. Morelli T, Moss KL, Beck J, et al. Derivation and validation of the periodontal and tooth profile classification system for patient stratification. *J Periodontol.* 2017;88(2):153-165. doi:10.1902/jop.2016.160379
16. Jones SA, Gottesman RF, Shahar E, Wruck L, Rosamond WD. Validity of hospital discharge diagnosis codes for stroke: the atherosclerosis risk in communities study. *Stroke* 2014;45(11):3219-3225. doi:10.1161/STROKEAHA.114.006316
17. Mustapha IZ, Debrey S, Oladubu M, Ugarte R. Markers of systemic bacterial exposure in periodontal disease and cardiovascular disease risk: a systematic review and meta-analysis. *J Periodontol.* 2007;78(12):2289-2302. doi:10.1902/jop.2007.070140
18. Romagna C, Dufour L, Troisgros O, et al. Periodontal disease: a new factor associated with the presence of multiple complex coronary lesions. *J Clin Periodontol.* 2012;39(1):38-44. doi:10.1111/j.1600-051X.2011.01802.x
19. Farges JC, Alliot-Licht B, Renard E, et al. Dental pulp defence and repair mechanisms in dental caries. *Mediators Inflamm.* 2015;2015:230251. doi:10.1155/2015/230251
20. Jain A, Bahuguna R. Role of matrix metalloproteinases in dental caries, pulp and periapical inflammation: an overview. *J Oral Biol Craniofac Res.* 20152015;5(3):212-218. doi:10.1016/j.jobcr.2015.06.015
21. Bartova J, Sommerova P, Lyuya-Mi Y, et al. Periodontitis as a risk factor of atherosclerosis. *J Immunol Res.* 2014;2014:636893. doi:10.1155/2014/636893
22. Pavlic V, Peric D, Kalezic IS, et al. Identification of periopathogens in atheromatous plaques obtained from carotid and coronary arteries. *Biomed Res Int.* 2021;2021:9986375. doi:10.1155/2021/9986375
23. Nakano K, Inaba H, Nomura R, et al. Detection of cariogenic Streptococcus mutans in extirpated heart valve and atheromatous plaque specimens. *J Clin Microbiol.* 2006;44(9):3313-3317. doi:10.1128/JCM.00377-06
24. Mattila KJ, Nieminen MS, Valtonen VV, et al. Association between dental health and acute myocardial infarction. *BMJ.* 1989;298(6676):779-781. doi:10.1136/bmj.298.6676.779