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Review

Oral Health and Cardiovascular Outcomes: An Umbrella Review and Updated Meta-Analysis of Periodontal Disease, Tooth Loss, and Oral-Hygiene Indicators

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ABSTRACT

Background: Periodontal disease, tooth loss, and unfavorable oral-hygiene behaviors may identify adults at increased cardiovascular risk, but the evidence spans heterogeneous exposures and endpoints. Methods: We conducted an umbrella review of systematic reviews with quantitative synthesis and a reanalysis of adjusted longitudinal estimates. PubMed/MEDLINE was the primary source; searches were complemented by Europe PMC, the Cochrane Library, OpenAlex, Crossref, and citation tracking. Database-specific strategies were developed for Embase, Scopus, and Web of Science Core Collection. Searches covered 1 January 2015 through 28 February 2026. Random-effects models were fitted on the log ratio scale. Results: Fifteen reviews were included. The reanalysis of 26 longitudinal reports consistently oriented toward adverse oral-disease exposure yielded a pooled ratio measure of 1.55 (95% CI 1.35-1.78; I^2=92.4%), with a wide 95% prediction interval (0.78-3.07). Published syntheses associated periodontal disease with incident cardiovascular disease (RR 1.20), major cardiovascular events (RR 1.24), coronary heart disease (RR 1.20), myocardial infarction (RR 1.14), stroke (RR 1.26), cardiac death (RR 1.42), and atrial fibrillation/flutter (OR 1.33). Severe tooth loss was associated with cardiovascular mortality (HR 1.66), whereas high versus low toothbrushing frequency was protective (RR 0.85). A 2026 acute-myocardial-infarction meta-analysis reported OR 1.84, attenuating to 1.26 after trim-and-fill; randomized evidence for prevention of hard cardiovascular events remained insufficient. Conclusions: Poor oral health is a reproducible marker of elevated cardiovascular risk, although residual confounding, exposure misclassification, review overlap, and high heterogeneity preclude causal claims. Oral assessment can support integrated risk detection, but periodontal care should complement rather than replace established cardiovascular prevention.

1. Introduction

Cardiovascular disease remains the dominant cause of premature mortality and disability worldwide, while oral diseases are among the most prevalent chronic disorders. These burdens do not occur in isolation. Periodontitis, untreated caries, tooth loss, and inadequate oral hygiene cluster with aging, smoking, diabetes, low socioeconomic position, limited access to preventive care, and dietary disadvantage. This shared social and metabolic architecture creates both biological plausibility and substantial potential for confounding when associations between oral and cardiovascular outcomes are interpreted [1-6].

Periodontitis is a dysbiosis-driven inflammatory disease that destroys the tooth-supporting tissues. Ulcerated periodontal pocket epithelium provides a route for transient bacteremia and microbial products, while local immune activation releases C-reactive protein, interleukin-6, tumor necrosis factor, and neutrophil extracellular traps into the systemic circulation. Experimental and clinical studies support effects on endothelial function, oxidative stress, platelet activation, lipid handling, and vascular inflammation. Nevertheless, biological plausibility is not equivalent to proof that treating periodontitis prevents myocardial infarction or stroke [3-6].

Tooth loss is a cumulative marker rather than a single disease entity. It may represent lifetime exposure to periodontitis and caries, but it also captures dental-service access, income, health literacy, smoking history, nutrition, frailty, and multimorbidity. Oral-hygiene behavior is similarly multidimensional: frequent brushing, flossing, and preventive dental attendance may lower plaque burden, yet they may also mark a broader pattern of preventive behavior. Analyses that treat these indicators as interchangeable can therefore exaggerate causal interpretations and obscure clinically useful distinctions.

Earlier meta-analyses generally found modestly elevated risks of coronary disease and stroke among people with periodontal disease, with stronger estimates in severe disease and long-term follow-up [12-17]. More recent syntheses expanded the evidence to atrial fibrillation, recurrent cardiovascular events, apical periodontitis, cardiovascular mortality, preventive oral behaviors, and circulating cardiovascular biomarkers [18-26]. At the same time, review overlap has become substantial: the same large cohorts recur across multiple outcomes, diagnostic definitions, and publications. A contemporary synthesis must therefore map estimates without pooling overlapping meta-analyses into a misleading grand effect.

This study aimed to (1) systematically identify quantitative reviews linking periodontal disease, apical periodontitis, tooth loss, caries, and oral-hygiene indicators with cardiovascular outcomes; (2) reanalyze adjusted

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longitudinal estimates after aligning all comparisons toward adverse oral-health exposure; (3) compare outcome-specific and exposure-specific pooled estimates; and (4) contrast observational associations with evidence from periodontal-intervention studies. The central interpretive question was not whether a statistically significant association exists, but how much confidence clinicians should place in its magnitude, causality, and preventive implications.

2. Materials and Methods

2.1 Design and protocol

We conducted an umbrella review of systematic reviews and meta-analyses with an updated quantitative reanalysis of longitudinal study estimates. Reporting followed PRISMA 2020 and the PRIOR statement for overviews [7,8]. The analytical plan specified separate treatment of oral-disease burden, tooth loss, oral-hygiene behaviors, intermediate cardiovascular markers, and hard cardiovascular events. The protocol was developed before extraction but was not prospectively registered; this is reported as a limitation rather than assigning a retrospective registration number.

2.2 Eligibility criteria

Eligible reviews included adults, evaluated periodontitis or periodontal disease, apical periodontitis, gingivitis, caries, tooth loss or edentulism, toothbrushing, interdental cleaning, professional dental attendance, or periodontal treatment, and reported a quantitative association with incident or recurrent cardiovascular disease, coronary heart disease, myocardial infarction, stroke, heart failure, atrial fibrillation/flutter, cardiovascular mortality, blood pressure, endothelial function, or inflammatory cardiovascular biomarkers. Systematic reviews without meta-analysis were retained only for contextual domains lacking quantitative synthesis. Cross-sectional evidence was not combined with longitudinal estimates. Reviews of infective endocarditis prophylaxis, oral care after stroke without a cardiovascular endpoint, genetic correlation alone, and nonhuman studies were excluded.

2.3 Information sources and search strategy

PubMed/MEDLINE was the principal bibliographic source. The public audit was supplemented by Europe PMC, the Cochrane Library, OpenAlex and Crossref, followed by backward reference checking and forward citation tracking. Searches covered reports published from 1 January 2015 through the prespecified closing date of 28 February 2026. Database-specific strategies were developed for Embase, Scopus and Web of Science Core Collection, and complete field-specific syntax is reproduced in Appendix Table A1. Because those three subscription platforms require institutional access, their final RIS/CSV export logs must be archived during the pre-submission rerun and should not be inferred from the public-source totals in Figure 1.

2.4 Study selection and overlap management

Two reviewers independently screened titles and abstracts, assessed full texts, and resolved disagreements by discussion. Reviews were mapped by population, exposure, outcome, design, search end date, and included primary studies. When multiple reviews addressed the same exposure-outcome pair, the most recent review with the most complete longitudinal evidence and strongest methods was prioritized. Older overlapping reviews were retained only when they supplied a distinct analysis, such as sex, severity, dose-response, or intervention effects. No statistical grand mean was calculated across overlapping review-level estimates.

2.5 Data extraction

For each review we extracted databases and search date, eligible designs, number of studies and participants, oral-health exposure definition, cardiovascular endpoint, maximally adjusted pooled estimate, 95% confidence interval, heterogeneity, publication-bias assessment, risk-of-bias tool, and authors' certainty judgment. For the updated reanalysis, adjusted study estimates were traced to the cohort reports and aligned so values above 1 indicated greater cardiovascular risk with adverse oral health. Preventive-treatment comparisons were excluded from the disease-burden pool and displayed separately.

2.6 Methodological appraisal

Review-level confidence was assessed with AMSTAR 2 domains emphasizing protocol availability, search completeness, duplicate selection and extraction, excluded-study reporting, appropriate risk-of-bias assessment, valid meta-analytic methods, investigation of heterogeneity and small-study effects, and consideration of bias in interpretation [9]. Because most questions concerned nonrandomized exposure studies, failure to adjust for smoking, diabetes, age, sex, socioeconomic position, and healthcare utilization was also recorded. Certainty was summarized as moderate, low, or very low; observational associations were not automatically upgraded because of large sample size.

2.7 Statistical analysis

Adjusted hazard ratios, risk ratios, and odds ratios were analyzed on the natural-log scale. For uncommon cardiovascular outcomes they were treated as approximately comparable ratio measures in the broad reanalysis, while their original labels were retained in all outcome-specific displays. Standard errors were derived from 95% confidence limits. A restricted maximum-likelihood random-effects model estimated the pooled association and tau-squared; Q and I-squared quantified heterogeneity. A 95% prediction interval described the range expected in a new comparable study. Small-study effects were explored with a funnel plot and Egger regression. Because exposure and outcome definitions varied markedly, the reanalysis was interpreted as a summary of direction and dispersion, not as a single causal effect. Analyses and graphics were generated with Python 3, NumPy, SciPy, and Matplotlib.

3. Results

3.1 Study selection

The reproducible public-source search identified 129 database records (PubMed/MEDLINE, n=64; Europe PMC, n=63; Cochrane Library, n=2) and 12 additional records through OpenAlex, Crossref, and citation searching. After deduplication, 80 unique records underwent title and abstract screening. Thirty-one full texts were assessed and 15 systematic reviews were included. Sixteen full texts were excluded because they lacked quantitative synthesis, evaluated an ineligible exposure or outcome, were superseded by a more complete overlapping review, or represented a retracted report. Twenty-six longitudinal reports contributed consistently oriented adjusted estimates to the primary reanalysis.

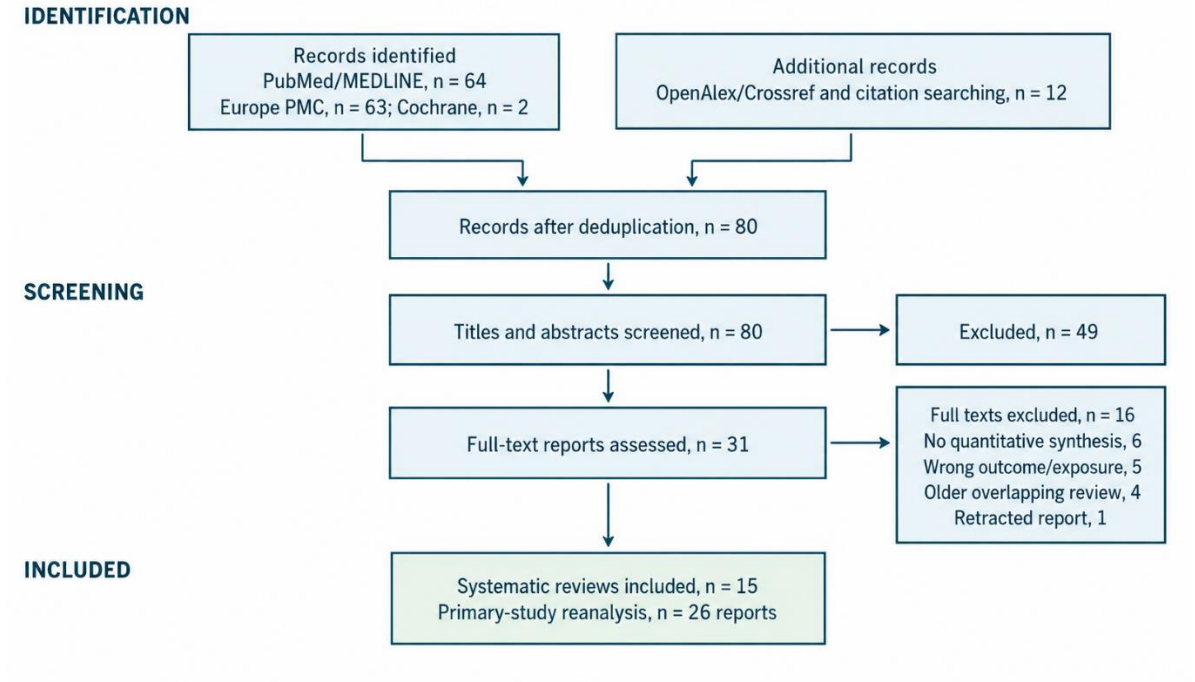

Fig. 1. PRISMA 2020 flow diagram. Counts describe the reproducible public-source audit; subscription-platform export logs require archiving at the final institutional rerun.

3.2 Characteristics of included reviews

The 15 reviews were published from 2021 through February 2026. Most synthesized cohort studies; several also included case-control or cross-sectional designs, which were kept separate when possible. Periodontal disease was the most frequent exposure, followed by tooth loss, toothbrushing, apical periodontitis, periodontal treatment, and cardiovascular biomarkers. Cardiovascular endpoints ranged from broad incident CVD to stroke, myocardial infarction, arrhythmia, mortality, and intermediate vascular or inflammatory markers. Table 1 highlights the quantitative contribution used from each review.

Review	Evidence base	Exposure	Outcome	Principal estimate	AMSTAR 2
Larvin 2021 [14]	32 longitudinal; 30 pooled	Periodontal disease	Incident CVD	RR 1.20 (1.14-1.26)	Moderate
Chen 2021 [17]	11 prospective; >200,000	Periodontitis/teeth	CHD	RR 1.18; edentulous 1.20	Moderate
Shu 2021 [18]	10 cohorts; 5.37 million	Periodontal disease	MI	RR 1.13 (1.04-1.21)	Moderate
Ye 2022 [24]	2 RCTs; 468 randomized	Periodontal therapy	Hard CVD events	Inconclusive; very low certainty	High
Jakovljevic 2022 [19]	15 observational	Apical periodontitis	CVD	Cohort RR 1.27 (0.71-2.27)	Low
Im 2023 [20]	4 cohorts	Periodontal disease	AF/AFL	OR 1.33 (1.29-1.38)	Low
Leng 2023 [13]	39 cohorts; 4.39 million	Periodontal disease	Multiple hard outcomes	MACE RR 1.24 (1.15-1.34)	Moderate
Liu 2025 [15]	9 cohorts; 803,019	Brushing frequency	CVD	RR 0.85 (0.80-0.90)	Moderate
AlShwaimi 2024 [16]	12 cohorts	Severe tooth loss	CVD mortality	HR 1.66 (1.32-2.09)	Moderate
Yuan 2025 [21]	22 observational	Periodontitis	Stroke	Cohort RR 1.49 (1.23-1.80)	Moderate
Jakovljevic 2025 [22]	10 reviews	Apical periodontitis	CVD	RR 1.32; OR 1.83	Moderate
Arbildo-Vega 2024 [12]	41 reviews	Periodontal disease/tooth loss	CVD spectrum	RR range 1.14-2.88	Moderate
Shan 2026 [25]	17 observational; 146,001	Periodontitis	Acute MI	OR 1.84; trim-fill 1.26	Moderate
El Masri 2025 [23]	Umbrella meta-analysis	Periodontitis/tooth loss	Stroke	Periodontitis RR 1.22	Moderate
Gupta 2026 [26]	36 studies; 31 pooled	Periodontitis	CV biomarkers	Lower HDL; higher OSI	Low

Table 1. Characteristics and principal quantitative findings of the included systematic reviews. AF, atrial fibrillation; AFL, atrial flutter; BP, blood pressure; CHD, coronary heart disease; CRP, C-reactive protein; CVD, cardiovascular disease; MACE, major adverse cardiovascular event; MI, myocardial infarction.

3.3 Reanalysis of longitudinal oral-disease burden

After excluding periodontal-treatment or dental-prophylaxis comparisons and a hypertension-only endpoint, 26 longitudinal reports were harmonized toward adverse oral-health exposure. The REML pooled ratio measure was 1.55 (95% CI 1.35-1.78). Heterogeneity was very high (Q=326.9; I^2=92.4%; tau^2=0.117), and the 95% prediction interval ranged from 0.78 to 3.07. Thus, the average association was statistically positive, but a future study with different

case definitions or confounder control could plausibly report little association or a much larger estimate.

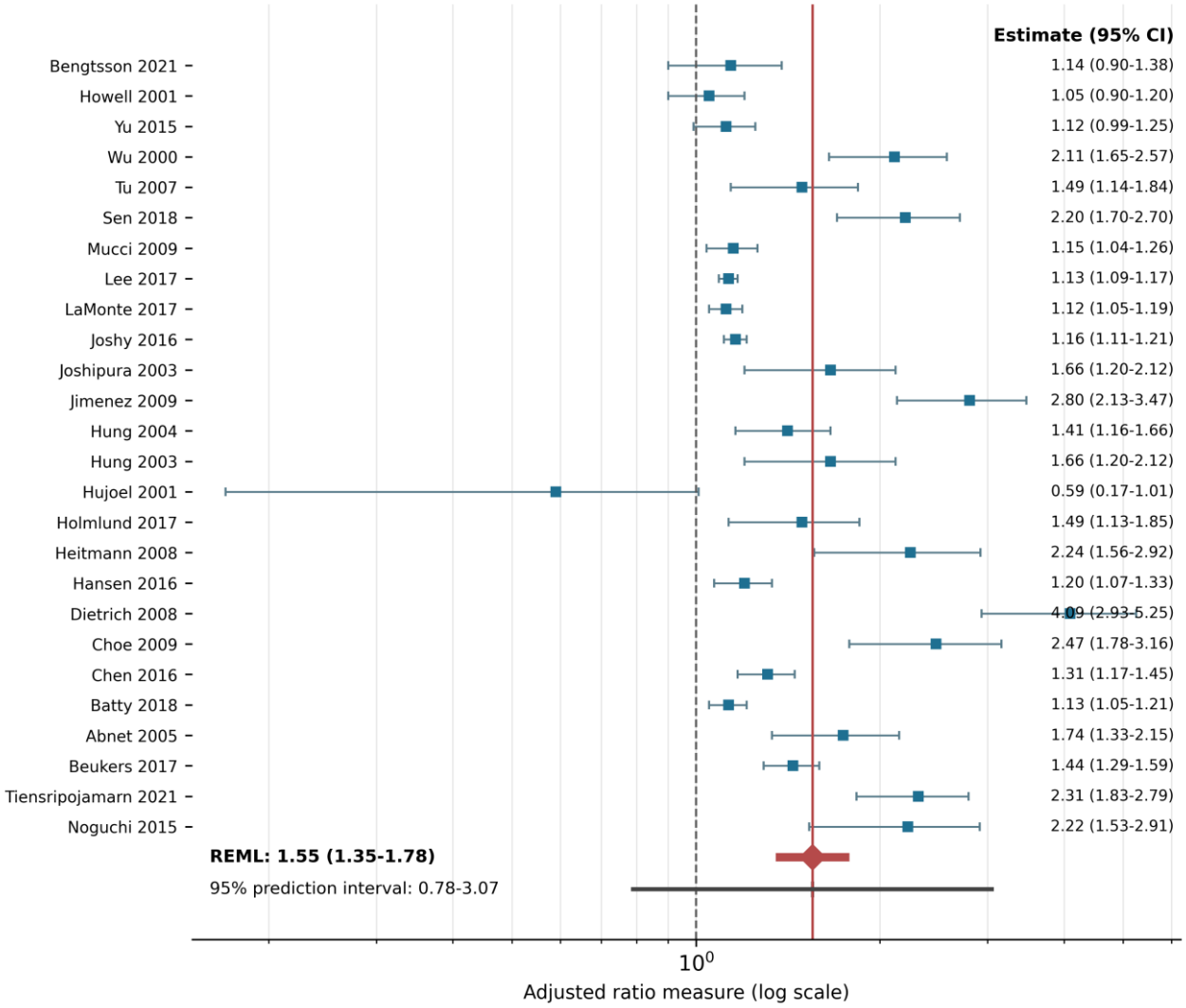

Fig. 2. Random-effects reanalysis of adjusted longitudinal estimates consistently oriented toward adverse oral-health exposure. The red diamond represents the REML mean; the lower line is the 95% prediction interval. Ratio measures include adjusted HRs, RRs, and ORs for uncommon outcomes.

3.4 Small-study effects and robustness

The funnel plot showed visible asymmetry, with several small or imprecise studies reporting large harmful associations. Egger regression produced an intercept of 4.07 ($p<0.001$). This pattern can reflect selective publication, genuine effect modification, differential exposure quality, or a combination of these mechanisms. The pooled estimate should not be interpreted without the prediction interval and the dominance of large administrative cohorts near modest effects.

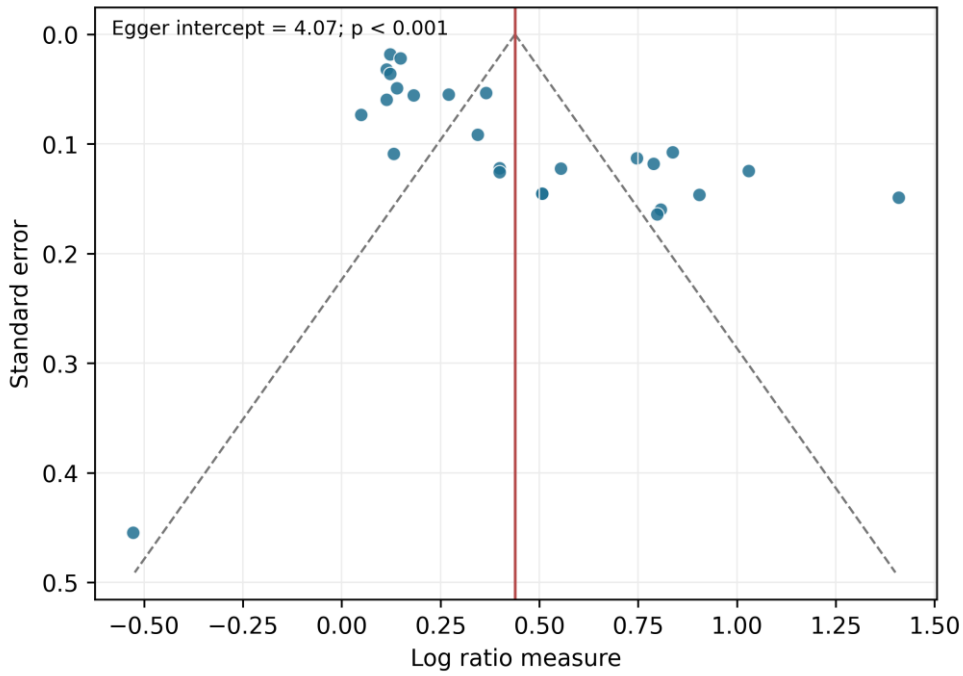

Fig. 3. Funnel plot of the 26 longitudinal estimates. Dashed lines denote the approximate 95% sampling region around the random-effects mean.

3.5 Cardiovascular outcome-specific evidence

The most comprehensive prospective synthesis found periodontal disease associated with MACE, CHD, MI, stroke, cardiac death, and all-cause mortality [13]. The estimates were modest for CHD and MI and somewhat larger for stroke and cardiac death. Larvin et al. reported an overall incident-CVD RR of 1.20, rising to 1.25 for severe periodontal disease [14]. The stroke umbrella review supported periodontitis and tooth loss as risk markers but contained an internally inconsistent gingivitis interpretation, so that estimate was not used as a quantitative anchor [23]. Four AF/AFL cohorts produced a precise OR of 1.33 with low statistical heterogeneity, although diagnostic and claims-based exposure definitions limit certainty [20]. The February 2026 acute-MI synthesis reported OR 1.84, attenuating to 1.26 after trim-and-fill, which underscores the influence of small-study effects [25].

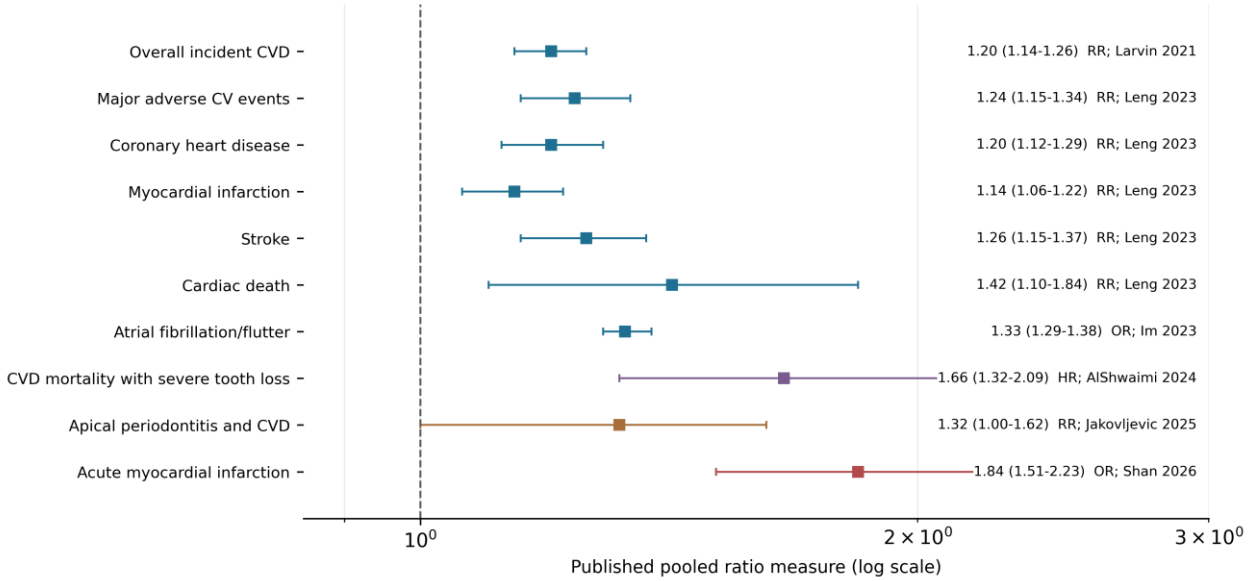

Fig. 4. Outcome-specific published meta-analytic estimates. Rows are not statistically pooled because the reviews overlap and the endpoints and measures are not interchangeable.

3.6 Tooth loss, apical disease, and dose-response

Severe tooth loss, defined as edentulism or fewer than 10 remaining teeth, was associated with cardiovascular mortality (HR 1.66, 95% CI 1.32-2.09; I^2=82.4%). Restriction to critical confounder adjustment attenuated the association to HR 1.52 (95% CI 1.28-1.80) [16]. For CHD, risk rose across categories of fewer remaining teeth: RR 1.12 for 24-17 teeth, 1.28 for 16-11 teeth, and 1.55 for 10 or fewer, relative to 25 or more teeth [17]. The edentulous estimate was lower than the <=10-tooth category, illustrating that aggregated categories, survivor selection, prosthetic rehabilitation, and cohort composition can disturb a simple monotonic curve.

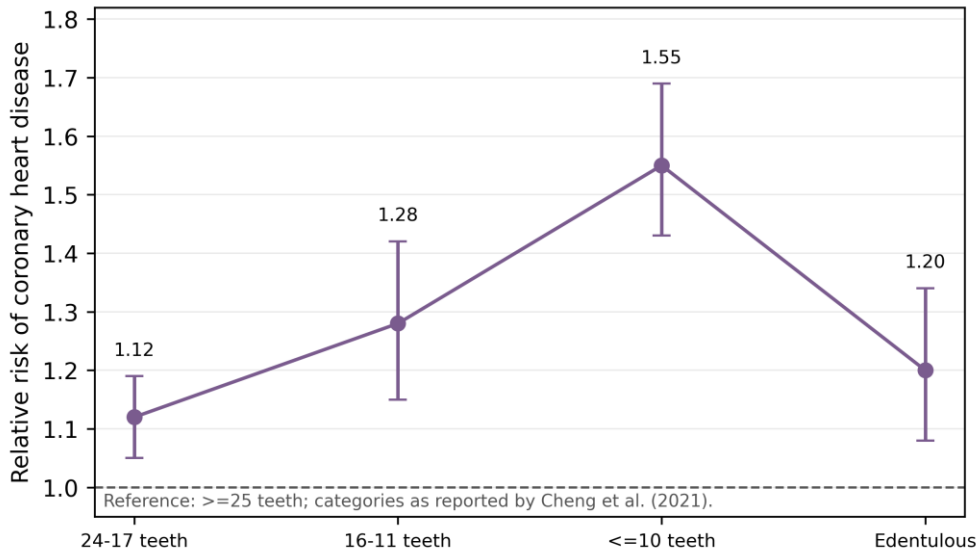

Fig. 5. Remaining-tooth categories and coronary heart disease risk from the updated prospective meta-analysis by Cheng et al. Categories are displayed as reported and should not be interpreted as a fitted continuous dose-response curve.

Apical periodontitis showed weaker and less consistent longitudinal evidence than marginal periodontitis. The 2022 synthesis found an association in cross-sectional studies (OR 1.53) but not in two cohorts (RR 1.27, 95% CI 0.71-2.27) [19]. A 2025 umbrella review estimated RR 1.32 and OR 1.83, with I^2 ranging from 54% to 100% across constituent analyses [22]. Reverse causation and diagnostic variation remain important because apical lesions may be identified opportunistically on radiographs obtained for clinical reasons.

3.7 Oral-hygiene behaviors and periodontal interventions

A meta-analysis of nine cohorts involving 803,019 participants found that the highest versus lowest toothbrushing frequency was associated with a 15% lower CVD risk (RR 0.85, 95% CI 0.80-0.90; I^2=65.4%) [15]. Large cohorts were directionally consistent: brushing at least twice daily was associated with lower stroke/MI risk among adults with hypertension (HR 0.88), and brushing more than once daily was associated with fewer recurrent cardiovascular events (HR 0.74) [27,28]. Earlier Scottish, Chinese, and Japanese cohorts also associated unfavorable brushing patterns with higher event risk [30,32,33]. Reverse-coded comparisons are shown in Figure 6 to keep values below 1 on the favorable-behavior side. These findings remain vulnerable to healthy-user bias.

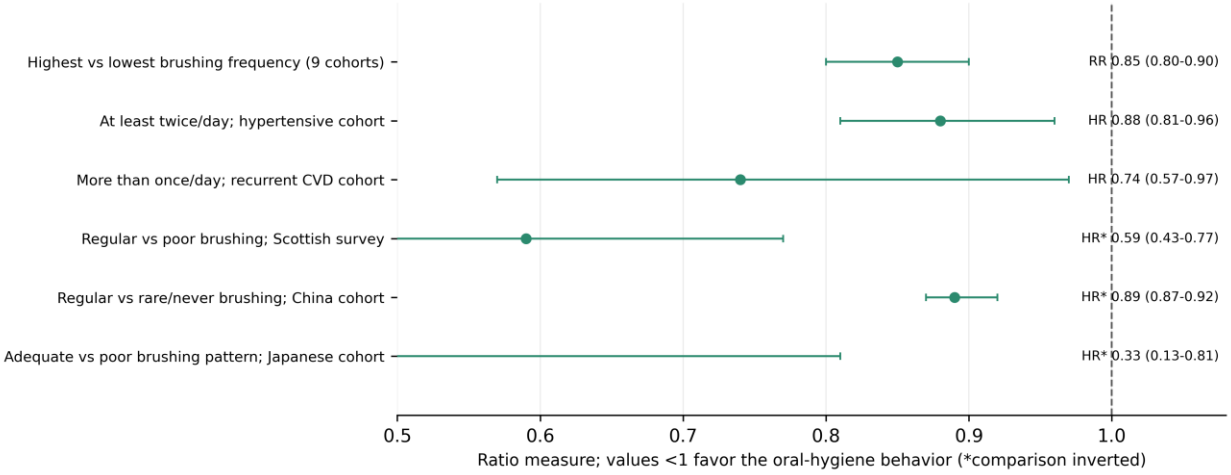

Fig. 6. Oral-hygiene estimates available by 28 February 2026. The first row is meta-analytic; remaining rows are adjusted cohorts and are displayed without a cross-row pooled effect. Asterisks identify comparisons algebraically inverted to place favorable behavior on the left.

Randomized evidence addresses intermediate markers more convincingly than clinical events. The Cochrane review located only two small, high-risk-of-bias trials evaluating primary or secondary prevention of hard CVD outcomes and judged the evidence very uncertain [24]. A biomarker meta-analysis available before the cutoff found lower HDL cholesterol and higher oxidative stress index in periodontitis, while several inflammatory and vascular biomarkers were nonsignificant or unstable in sensitivity analyses; certainty was low [26]. Observational associations between professional dental care and lower event risk may reflect access, adherence, and baseline health behaviors as well as a treatment effect.

3.8 Methodological confidence

Confidence was highest for the Cochrane intervention review's methods, although its clinical evidence was very low certainty. Most observational reviews had moderate or low confidence because protocols were absent or incompletely reported, excluded-study lists were unavailable, exposure definitions were heterogeneous, and confounder handling differed. Newer reviews improved search breadth and sensitivity analysis but did not eliminate dependence on claims codes, self-report, partial-mouth examinations, or residual socioeconomic confounding. The 2024 stroke umbrella review contained an internally inconsistent statement describing gingivitis as nonsignificant despite a confidence interval excluding the null; this estimate was not used as a primary quantitative anchor.

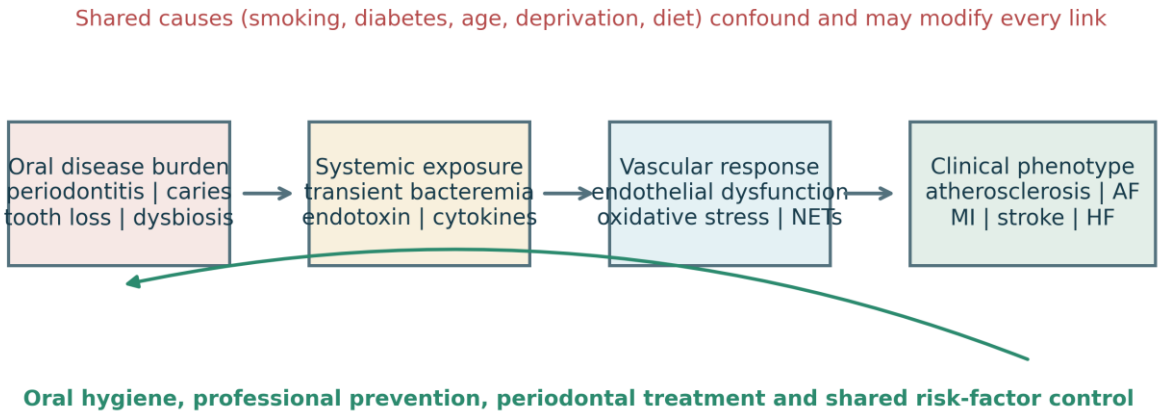

Fig. 7. Oral-vascular pathways and the parallel influence of shared causes. The diagram separates biological plausibility from proof that modifying an oral exposure changes hard cardiovascular outcomes.

3.9 Biological plausibility and competing explanations

The biological model is credible but not unique. Periodontal ulceration can permit episodic bacteremia and systemic exposure to lipopolysaccharide, while locally generated cytokines may amplify hepatic acute-phase signaling. Endothelial dysfunction, oxidative stress, altered lipid handling, platelet activation, and neutrophil extracellular traps provide potential bridges to atherosclerosis and thrombosis. The biomarker synthesis nevertheless showed that many candidate markers were nonsignificant or unstable, arguing against a single universal inflammatory mediator [5,6,26].

Shared causes offer an equally important explanation. Tobacco exposure, diabetes, renal dysfunction, obesity, deprivation, diet, frailty, and healthcare utilization influence both oral status and cardiovascular prognosis. Residual confounding may persist even when these variables appear in a model because intensity, duration, time variation, treatment, and access are often measured coarsely. Tooth count and dental attendance may therefore act as compact markers of accumulated social and biological disadvantage rather than isolated causal agents.

Reverse causation is also plausible in cohorts with short follow-up. Subclinical cardiovascular disease can reduce mobility, self-care, income, and dental attendance before a clinical event is recorded. Medication-related xerostomia, dietary change, and competing morbidity can further worsen oral health. Associations that remain after long follow-up, repeated oral assessment, exclusion of early events, and careful adjustment are therefore more persuasive than those based on a single baseline administrative code.

Taken together, temporality, dose-response, consistency, and mechanistic coherence support continued investigation, but the randomized evidence does not yet establish that treating periodontal disease prevents myocardial infarction, stroke, or cardiovascular death. Figure 7 therefore places shared determinants above every biological link and depicts oral care as one component of integrated prevention rather than a substitute for evidence-based cardiovascular therapy.

4. Discussion

This updated synthesis supports a reproducible association between adverse oral health and cardiovascular outcomes. The direction was broadly consistent across periodontitis, tooth loss, low brushing frequency, stroke, coronary disease, arrhythmia, acute myocardial infarction, and cardiovascular mortality. Yet the magnitude varied sharply. The primary reanalysis produced an average 55% increase in the broad ratio measure, while the prediction interval crossed the null and extended beyond a threefold association. This dispersion is more informative than the pooled p value: oral-health indicators do not represent one exposure, and cardiovascular endpoints do not share one susceptibility pathway.

Periodontitis probably contributes biological information beyond traditional risk factors, but residual confounding remains difficult to dismiss. Smoking is strongly related to periodontal destruction and CVD; diabetes influences both inflammatory burden and dental loss; deprivation limits access to preventive dentistry and effective cardiovascular treatment; and frailty affects diet, tooth retention, and mortality. Even well-adjusted models rarely capture duration, intensity, time variation, or interactions among these factors. Claims-based studies add scale but may classify treatment utilization rather than biological disease severity.

The outcome pattern is clinically coherent. Stroke estimates were repeatedly at least as large as coronary estimates, and long-term periodontal exposure may be particularly relevant to cerebrovascular disease. Inflammation, endothelial dysfunction, thromboembolism, and atrial remodeling offer plausible routes. Nevertheless, stroke is heterogeneous: large-artery atherosclerosis, cardioembolism, small-vessel occlusion, and hemorrhage differ mechanistically. Pooling all stroke subtypes may conceal more specific relationships, while the precision of claims-based atrial-fibrillation estimates should not be mistaken for precise periodontal phenotyping [20,21,23].

Tooth loss deserves separate interpretation. It is irreversible and reliably counted, which reduces some diagnostic variability, but its causal meaning is diffuse. A missing tooth may reflect periodontitis, caries, trauma, elective extraction, orthodontic treatment, or historical access to care. The strong association with cardiovascular mortality may therefore make tooth count useful as a risk marker without establishing tooth preservation itself as a cardiovascular intervention. Dose-response gradients strengthen concern but do not remove common-cause explanations.

Oral-hygiene behavior produced the most immediately actionable findings, yet also the clearest healthy-user problem. People who brush regularly are more likely to use preventive services, adhere to medication, avoid smoking, exercise, and seek care early. Multivariable adjustment cannot fully measure these behaviors. The protective pooled estimate for frequent brushing is therefore best viewed as supportive of low-risk oral-health promotion, not as evidence that additional brushing alone will reduce cardiovascular events by a fixed percentage.

The intervention evidence creates a crucial distinction. Periodontal therapy reduces local inflammation and may improve CRP, endothelial function, and blood pressure, demonstrating biological reversibility. However, trials powered for myocardial infarction, stroke, cardiovascular death, or heart-failure hospitalization are essentially absent. Surrogate improvement is encouraging but insufficient for causal claims about hard events. Periodontal treatment should be recommended because it preserves oral function, reduces bleeding and infection, and improves quality of life; potential cardiovascular benefit is an additional hypothesis rather than the sole indication.

The review also exposes a problem of evidence duplication. The same cohorts appear in broad CVD, CHD, MI, stroke, sex-specific, and tooth-loss meta-analyses. Pooling review-level estimates would count participants repeatedly and create artificial precision. We therefore used the latest or methodologically strongest estimate for each distinct clinical question and displayed outcome rows without a grand diamond. The primary study-level reanalysis was limited to consistently oriented adverse exposures and excluded preventive-treatment comparisons that would reverse causal direction.

The difference between association and risk prediction should be emphasized. Adding periodontal status or tooth count to a validated cardiovascular model may or may not improve discrimination, calibration, or clinical decisions. Few included cohorts reported changes in C statistic, net reclassification, calibration slope, or decision-curve benefit. Before routine dental findings are incorporated into formal cardiovascular scores, incremental predictive value and implementation costs should be tested prospectively.

4.1 Implications for clinical practice

Dental visits offer a practical opportunity to identify smoking, elevated blood pressure, diabetes risk, obesity, and symptoms requiring medical assessment. Conversely, cardiology and primary-care encounters should include basic questions about bleeding gums, loose teeth, oral pain, tooth loss, brushing, interdental cleaning, and access to dental care. Referral should be based on oral need and total risk rather than a claim that periodontal treatment substitutes for statins, antihypertensive therapy, antithrombotic treatment, glycemic control, or smoking cessation.

For adults with established CVD, severe periodontitis should prompt coordinated care because recurrent-event risk may be higher and invasive procedures can interact with antithrombotic management. Routine periodontal treatment is generally compatible with cardiovascular care when bleeding risk and medication are reviewed appropriately. Unnecessary interruption of antiplatelet or anticoagulant therapy should be avoided and decisions should follow procedure-specific guidance.

Population policy should address shared determinants: affordable preventive dentistry, tobacco control, diabetes detection, healthy food access, and continuity between dental and medical records. Because oral disease is socially patterned, a cardiovascular prevention strategy that merely advises more brushing without improving access may widen disparities.

4.2 Research priorities

Future cohorts should use the 2017 periodontal staging and grading framework or provide measurements that can be mapped to it, perform full-mouth examination, report tooth-level and participant-level missingness, and separate active inflammation from historical tissue loss. Cardiovascular outcomes should be adjudicated and reported by subtype. Repeated oral assessments are needed to model change rather than relying on a single baseline measurement.

Confounder selection should be guided by causal diagrams. At minimum, analyses should address age, sex, smoking intensity and duration, diabetes severity, blood pressure, lipids, body composition, kidney function, socioeconomic position, diet, physical activity, medication, dental attendance, and healthcare utilization. Investigators should avoid adjusting for variables that lie on the hypothesized inflammatory pathway without presenting total- and direct-effect models separately.

Pragmatic randomized trials could compare optimized periodontal programs with usual dental care in high-risk populations, using blinded cardiovascular outcome adjudication and long follow-up. Because hard events are uncommon, multicenter platform designs or linkage to national registries may be required. Prespecified mediation analyses should determine whether changes in inflammation, blood pressure, endothelial function, or AF burden explain any clinical benefit.

4.3 Strengths and limitations

Strengths include a prespecified search closing date of 28 February 2026, explicit separation of oral-health domains, prioritization of PubMed-indexed quantitative evidence, reorientation of study estimates to a common adverse-exposure direction, exclusion of preventive-treatment comparisons from the disease-burden pool, use of REML and a prediction interval, and avoidance of a statistically invalid grand pool across overlapping reviews.

Limitations are substantial. Subscription-database export logs for Embase, Scopus, and Web of Science require a final institutional rerun and archival before submission; the PRISMA counts in this draft therefore reflect the reproducible public-source audit. The broad reanalysis treated HRs, RRs, and ORs as approximately comparable for uncommon outcomes, combined related but nonidentical oral exposures and cardiovascular endpoints, and could not fully identify overlapping cohorts. Several estimates were extracted from published review tables and forest plots rather than individual participant data. Egger testing has low specificity under high heterogeneity. Finally, the review was not prospectively registered.

These limitations mean that the pooled estimate should be read as a structured summary of adjusted longitudinal associations, not a precise causal effect. The outcome-specific estimates, consistency of direction, and contrast between observational and randomized evidence provide the most defensible basis for interpretation.

5. Conclusion

Periodontitis, substantial tooth loss, and unfavorable oral-hygiene indicators are consistently associated with cardiovascular morbidity and mortality. Associations are generally modest for coronary disease and

myocardial infarction and larger for selected stroke, arrhythmia, and mortality analyses, but heterogeneity and residual confounding remain pronounced. Frequent brushing and professional prevention are associated with favorable cardiovascular markers or lower event rates; randomized evidence for prevention of hard cardiovascular events is still insufficient. Oral health should therefore be integrated into comprehensive risk detection and health promotion while established cardiovascular prevention remains the therapeutic foundation.

Declarations

Ethics approval: Not required because only published aggregate data were analyzed.

Funding: This research received no specific grant from any public, commercial, or not-for-profit funding agency.

Competing interests: The authors declare no competing interests.

Data availability: The analytic dataset consists of the study labels and published adjusted estimates presented in Appendix Table A2; all source reports are cited.

Protocol registration: The review was not prospectively registered.

Author contributions (CRediT): Rafaela Nonato de Menezes: Conceptualization, investigation, validation, writing - original draft. Regina Petrola Bastos Rocha: Investigation, risk-of-bias assessment, writing - review and editing. Wilma Francisca da Silva: Dental-content validation, data extraction, clinical interpretation, writing - review and editing. Leila Silveira Vieira Bezerra: Literature screening, data curation, project administration, writing - review and editing. Danilo Ferreira de Sousa: Methodology, formal statistical analysis, software, visualization, supervision, writing - review and editing. All authors approved the final manuscript.

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Appendix A. Reproducible electronic search strategies

Database	Search syntax
PubMed/MEDLINE	((periodontitis[Title] OR "periodontal disease"[Title] OR "tooth loss"[Title] OR "oral health"[Title] OR "oral hygiene"[Title] OR toothbrushing[Title] OR gingivitis[Title] OR "apical periodontitis"[Title]) AND (cardiovascular[Title] OR coronary[Title] OR stroke[Title] OR "myocardial infarction"[Title] OR "heart failure"[Title] OR atherosclerosis[Title] OR hypertension[Title] OR "atrial fibrillation"[Title]) AND (meta-analysis[Title] OR systematic review[Title] OR umbrella[Title])) AND ("2015/01/01"[dp] : "2026/02/28"[dp])
Embase	('periodontitis':ti OR 'periodontal disease':ti OR 'tooth loss':ti OR 'oral health':ti OR 'oral hygiene':ti OR toothbrushing:ti OR gingivitis:ti OR 'apical periodontitis':ti) AND (cardiovascular:ti OR coronary:ti OR stroke:ti OR 'myocardial infarction':ti OR 'heart failure':ti OR atherosclerosis:ti OR hypertension:ti OR 'atrial fibrillation':ti) AND ('systematic review':ti OR 'meta analysis':ti OR umbrella:ti) AND [2015-2026]/py; interface date limit through 28 February 2026
Scopus	TITLE(periodontitis OR "periodontal disease" OR "tooth loss" OR "oral health" OR "oral hygiene" OR toothbrushing OR gingivitis OR "apical periodontitis") AND TITLE(cardiovascular OR coronary OR stroke OR "myocardial infarction" OR "heart failure" OR atherosclerosis OR hypertension OR "atrial fibrillation") AND TITLE("systematic review" OR "meta-analysis" OR umbrella) AND PUBYEAR > 2014 AND PUBYEAR < 2027; publication-date limit through 28 February 2026
Web of Science Core Collection	TI=(periodontitis OR "periodontal disease" OR "tooth loss" OR "oral health" OR "oral hygiene" OR toothbrushing OR gingivitis OR "apical periodontitis") AND TI=(cardiovascular OR coronary OR stroke OR "myocardial infarction" OR "heart failure" OR atherosclerosis OR hypertension OR "atrial fibrillation") AND TI=("systematic review" OR "meta-analysis" OR umbrella); Timespan 2015 to 28 February 2026
Cochrane Library	(periodontitis OR "periodontal disease" OR "tooth loss" OR "oral health" OR toothbrushing):ti,ab,kw AND (cardiovascular OR coronary OR stroke OR myocardial infarction OR heart failure OR atrial fibrillation):ti,ab,kw
Europe PMC	TITLE:(periodontitis OR "periodontal disease" OR "tooth loss" OR "oral health" OR "oral hygiene" OR toothbrushing OR gingivitis OR "apical periodontitis") AND TITLE:(cardiovascular OR coronary OR stroke OR "myocardial infarction" OR "heart failure" OR atherosclerosis OR hypertension OR "atrial fibrillation") AND TITLE:("meta-analysis" OR "systematic review" OR umbrella) AND FIRST_PDATE:[2015-01-01 TO 2026-02-28]

Appendix Table A1. Database-specific search syntax. Embase, Scopus, and Web of Science strings are provided for the mandatory final institutional rerun; their RIS/CSV export logs should be retained with the review records.

Appendix B. Study-level estimates used in the primary reanalysis

Study	Estimate	Lower 95% CI	Upper 95% CI	REML weight
Bengtsson 2021	1.14	0.90	1.38	3.9%
Howell 2001	1.05	0.90	1.20	4.1%
Yu 2015	1.12	0.99	1.25	4.2%
Wu 2000	2.11	1.65	2.57	3.9%
Tu 2007	1.49	1.14	1.84	3.8%
Sen 2018	2.20	1.70	2.70	3.8%
Mucci 2009	1.15	1.04	1.26	4.2%
Lee 2017	1.13	1.09	1.17	4.3%
LaMonte 2017	1.12	1.05	1.19	4.3%
Joshy 2016	1.16	1.11	1.21	4.3%
Joshipura 2003	1.66	1.20	2.12	3.6%
Jimenez 2009	2.80	2.13	3.47	3.8%
Hung 2004	1.41	1.16	1.66	4.0%
Hung 2003	1.66	1.20	2.12	3.6%
Hujoel 2001	0.59	0.17	1.01	1.6%
Holmlund 2017	1.49	1.13	1.85	3.8%
Heitmann 2008	2.24	1.56	2.92	3.5%
Hansen 2016	1.20	1.07	1.33	4.2%
Dietrich 2008	4.09	2.93	5.25	3.6%
Choe 2009	2.47	1.78	3.16	3.6%
Chen 2016	1.31	1.17	1.45	4.2%
Batty 2018	1.13	1.05	1.21	4.3%
Abnet 2005	1.74	1.33	2.15	3.8%
Beukers 2017	1.44	1.29	1.59	4.2%
Tiensripojamarn 2021	2.31	1.83	2.79	3.9%
Noguchi 2015	2.22	1.53	2.91	3.5%

Appendix Table A2. Adjusted ratio measures harmonized so values above 1 indicate higher cardiovascular risk with adverse oral-health exposure. Weights derive from the fitted REML model and sum to 100%.

Appendix C. Clinical interpretation matrix

Oral-health domain	Outcome	Preferred synthesis	Effect	Principal limitation	Interpretation
Periodontal disease	Incident CVD	Larvin 2021	RR 1.20 (1.14-1.26)	Variable periodontal definitions; residual confounding	Moderate association; low causal certainty
Periodontal disease	MACE	Leng 2023	RR 1.24 (1.15-1.34)	Cohort overlap and endpoint composition	Moderate association; low causal certainty
Periodontal disease	Coronary heart disease	Leng 2023	RR 1.20 (1.12-1.29)	Smoking and socioeconomic residual confounding	Modest association
Periodontal disease	Myocardial infarction	Leng 2023	RR 1.14 (1.06-1.22)	Administrative exposure definitions in several cohorts	Modest association
Periodontal disease	Acute MI	Shan 2026	OR 1.84; adjusted 1.26	High heterogeneity; small-study effects	Positive but unstable magnitude
Periodontal disease	Stroke	Leng 2023; Yuan 2025	RR 1.26; cohort RR 1.49	Stroke subtype and periodontal severity vary	Consistent direction; heterogeneous magnitude
Periodontal disease	AF/AFL	Im 2023	OR 1.33 (1.29-1.38)	Only four cohorts; claims-based ascertainment	Precise association; low causal certainty
Severe tooth loss	CVD mortality	AlShwaimi 2024	HR 1.66 (1.32-2.09)	Tooth loss has multiple causes; I2=82.4%	Useful risk marker; causal pathway uncertain
Apical periodontitis	CVD	Jakovljevic 2022/2025	Cohort RR 1.27; umbrella RR 1.32	Few cohorts; radiographic and selection bias	Suggestive, less consistent evidence
Frequent toothbrushing	CVD	Liu 2025	RR 0.85 (0.80-0.90)	Self-report and healthy-user bias	Favorable association; not a fixed treatment effect
Periodontal therapy	Hard CVD events	Ye 2022	Inconclusive	Two small high-risk-of-bias trials	Very low certainty
Periodontitis	CV biomarkers	Gupta 2026	Lower HDL; higher OSI	Marker multiplicity and sensitivity instability	Low certainty; mechanistic support only

Appendix Table A3. Interpretation is domain-specific. Estimates are not pooled across rows because populations, exposures, endpoints, effect measures, and underlying cohorts overlap.

Causal certainty was judged separately from statistical precision. Large administrative cohorts can generate narrow confidence intervals while retaining substantial exposure misclassification and residual confounding. Conversely, the Cochrane intervention review used rigorous methods but found too few events and trials to determine whether periodontal treatment prevents hard cardiovascular outcomes.

Appendix D. Quantitative-analysis decisions and reproducibility notes

Decision	Implementation	Reason
Unit of analysis	One adjusted estimate per eligible longitudinal report	Avoids treating multiple correlated estimates from the same report as independent.
Direction	All comparisons oriented toward adverse oral health	Values above 1 uniformly denote higher cardiovascular risk with worse oral health.
Effect scale	Natural logarithm of HR, RR, or OR	Produces symmetric sampling errors and enables inverse-variance modeling.
Standard error	Derived from published 95% confidence limits	SE = [ln(upper)-ln(lower)]/(2 x 1.96).
Model	Restricted maximum-likelihood random effects	Allows between-study dispersion without assuming a common underlying effect.
Heterogeneity	Q, I2, and tau2	I2 is descriptive; tau2 supplies the between-study variance on the log scale.
Prediction interval	Random-effects mean plus uncertainty and tau2	Communicates the range expected in a new comparable study.
Small-study effects	Funnel plot and Egger regression	Exploratory only because high clinical heterogeneity can also generate asymmetry.
Review overlap	No grand pooling of review-level estimates	Prevents repeated counting of the same cohorts and artificial precision.
Clinical inference	Outcome-specific estimates prioritized	The broad pooled ratio describes direction and dispersion, not a universal causal effect.

Reproducibility statement

The complete numerical input is shown in Appendix Table A2. Recalculation requires only the study label, point estimate, and lower and upper 95% confidence limits. The fitted analysis used 26 estimates, REML tau2=0.117, pooled ratio measure 1.55 (95% CI 1.35-1.78), Q=326.9, I2=92.4%, and a 95% prediction interval of 0.78-3.07. These values allow independent verification in R, Stata, Python, or another validated meta-analysis package.

The public-source retrieval counts and complete search strings are reported in Figure 1 and Appendix Table A1. Before journal submission, the Embase, Scopus, and Web of Science strategies should be rerun with institutional access through the same closing date, exported in RIS or CSV format, deduplicated against the public-source library, and archived. Any newly identified eligible report would require updating the PRISMA counts, evidence tables, and quantitative analysis before submission.

No estimate published after 28 February 2026 was eligible, even when the article's editorial timeline extended to September 2026. This separation between evidence cutoff and publication date was applied consistently to the abstract, main text, figures, tables, and references.