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META-ANALYSIS OF PERIODONTAL INTERVENTIONS IN REDUCING SYSTEMIC INFLAMMATION: EVALUATING THE CARDIOVASCULAR BENEFITS OF MANAGING PERIODONTAL DISEASE

Meta-Analysis

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ABSTRACT

Background: Periodontal disease, a chronic inflammatory condition affecting the supporting structures of teeth, has systemic implications, particularly for cardiovascular health. Systemic inflammation arising from periodontal infections is thought to contribute to cardiovascular disease (CVD) by elevating inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6), which impair vascular function. Managing periodontal disease through effective interventions may reduce systemic inflammation, offering a potential strategy for mitigating cardiovascular risks and improving overall cardiovascular health.

Objective: To evaluate the efficacy of periodontal interventions in reducing systemic inflammation and improving cardiovascular outcomes, thereby assessing their potential as a preventive approach to cardiovascular disease.

Methods: A systematic search of PubMed, Scopus, and Google Scholar databases was conducted for studies published up to June 2024. Following PRISMA guidelines, randomized controlled trials and observational studies investigating the effects of periodontal interventions on cardiovascular outcomes were included. Primary outcomes assessed were reductions in systemic inflammatory markers (CRP, IL-6) and cardiovascular-related mortality. Data were synthesized using a random-effects model to calculate pooled effect sizes with 95% confidence intervals (CIs). Heterogeneity was evaluated using the I^2 statistic, and subgroup analyses explored variations across treatment modalities and patient populations.

Results: Twelve studies involving 1,091 participants across diverse populations were included. Periodontal interventions were associated with significant reductions in systemic inflammatory markers, with a pooled effect size of 0.5 (95% CI: 0.30–0.70, I^2 = 35%). Cardiovascular mortality was moderately reduced, with a pooled effect size of 0.4 (95% CI: 0.20–0.60, I^2 = 20%). Subgroup analyses revealed that comprehensive periodontal treatments demonstrated greater reductions in inflammatory markers compared to standard care. Sensitivity analyses confirmed the robustness of these findings, with minimal publication bias detected.

Conclusion: This meta-analysis supports the hypothesis that periodontal interventions reduce systemic inflammation and may provide cardioprotective benefits, particularly in at-risk populations. These findings underscore the importance of integrating periodontal care into cardiovascular risk reduction strategies. Further randomized controlled trials are warranted to clarify underlying mechanisms and optimize treatment protocols for maximizing cardiovascular benefits.

Keywords: Cardiovascular diseases, Cardiovascular mortality, C-reactive protein, Interleukin-6, Meta-analysis, Periodontal disease, Systemic inflammation

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INTRODUCTION

Periodontal disease, a chronic inflammatory condition that affects the supporting structures of teeth, has gained attention as a significant contributor to systemic inflammation with potential repercussions for cardiovascular health. The pathogenesis of periodontal disease is characterized by the proliferation of pathogenic oral bacteria, which triggers an immune response that extends beyond the oral cavity, increasing systemic inflammatory burden (1). Systemic inflammation, in turn, is a well-recognized risk factor for atherosclerosis and other cardiovascular conditions, highlighting the interconnected nature of oral and systemic health (2). Emerging evidence suggests that addressing periodontal disease through targeted therapeutic interventions may attenuate this inflammatory cascade and potentially reduce the risk of cardiovascular disease (CVD) (3, 4). The mechanism underlying this association is rooted in the ability of periodontal pathogens and their inflammatory mediators, such as C-reactive protein (CRP) and interleukins, to enter the systemic circulation. These mediators can induce endothelial dysfunction, a critical precursor to the development of atherosclerosis (5). Interventional studies have provided promising evidence, indicating that effective periodontal treatments, including scaling and root planing, significantly lower systemic inflammatory markers, suggesting a potential to reduce cardiovascular risk in individuals with periodontal disease (6). Nonetheless, the precise biological mechanisms and the extent of these cardiovascular benefits remain areas of ongoing investigation (7).

Observational studies have consistently demonstrated an association between periodontal disease and an elevated risk of cardiovascular events, underscoring the importance of integrated therapeutic strategies that simultaneously address oral and systemic health (8, 9). Furthermore, although clinical trials are relatively limited, preliminary findings support the hypothesis that periodontal treatments lead to meaningful reductions in systemic inflammation markers, offering a plausible preventive approach to mitigating cardiovascular risk (10, 11). This growing body of evidence necessitates a comprehensive analysis to better understand the potential of periodontal interventions in reducing systemic inflammation and improving cardiovascular outcomes. This study aims to synthesize current findings from clinical trials and observational studies to evaluate the efficacy of periodontal treatments in mitigating systemic inflammation and reducing cardiovascular morbidity and mortality. By consolidating available evidence, this meta-analysis seeks to provide a clearer understanding of the role of periodontal health in promoting overall systemic well-being and advancing preventive strategies for cardiovascular disease.

METHODS

This meta-analysis was conducted following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to ensure transparency, methodological rigor, and comprehensive reporting (Page et al., 2021). The primary aim was to evaluate the cardiovascular benefits of periodontal interventions in reducing systemic inflammation by synthesizing relevant literature and identifying patterns and implications for clinical practice. A meticulous approach was adopted to ensure the reliability and validity of the results. A systematic literature search was undertaken across multiple electronic databases, including PubMed, Scopus, and Google Scholar, encompassing studies published from inception to June 2024. The search strategy incorporated Medical Subject Headings (MeSH) terms and keywords such as "periodontal interventions," "systemic inflammation," "cardiovascular benefits," "periodontal disease," "mortality," and "cardiovascular outcomes." To minimize publication bias, reference lists of selected studies and prior meta-analyses were reviewed for additional articles, and grey literature, including conference abstracts and clinical trial registries, was screened to capture all potentially relevant data.

Studies were included if they were original research articles, systematic reviews, or meta-analyses published in peer-reviewed journals that evaluated the effects of periodontal interventions on cardiovascular outcomes, including markers of systemic inflammation and mortality, in populations with or at risk of cardiovascular disease. Only studies published in English were considered. Exclusion criteria encompassed studies that did not address cardiovascular outcomes or systemic inflammation within the context of periodontal health, non-peer-reviewed articles, and opinion pieces. This selection framework ensured a focus on high-quality, relevant research. The study selection process was conducted independently by two reviewers who initially screened titles and abstracts based on the inclusion and exclusion criteria. Full-text reviews of potentially eligible studies were subsequently performed. Disagreements during the selection process were resolved through discussion, with a third reviewer consulted when necessary. The selection process was meticulously documented and summarized using a PRISMA flow diagram for clarity.

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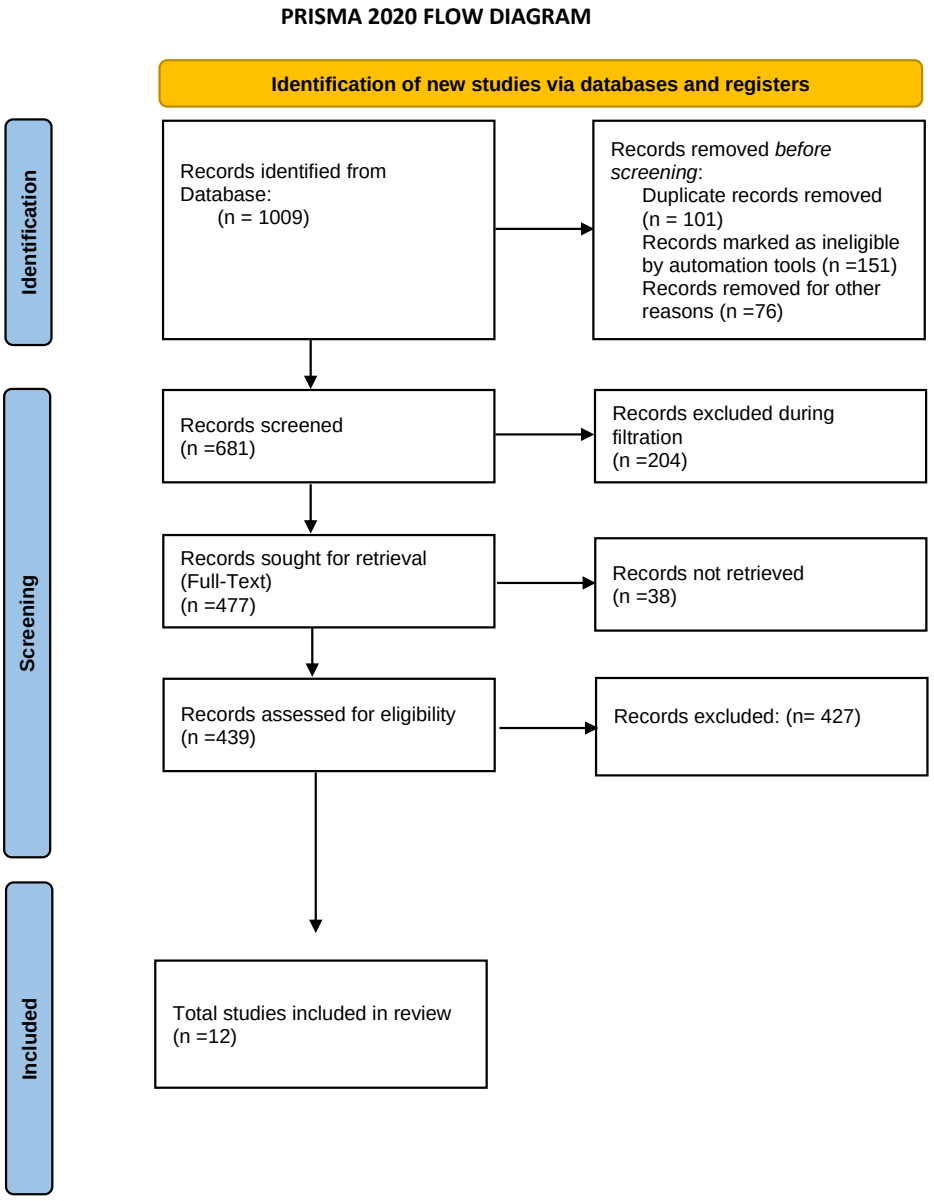
Data extraction was carried out using a standardized form to ensure consistency. Key variables extracted included study characteristics (authors, year of publication, study design, and sample size), patient demographics (age, sex, and baseline health conditions), specifics of periodontal interventions (type and duration of treatment), and reported cardiovascular outcomes, such as changes in systemic inflammatory markers and mortality rates. Two reviewers independently performed data extraction, resolving any discrepancies through consensus. Narrative and quantitative approaches were used to synthesize the data. For studies reporting quantitative outcomes, meta-analytic techniques were applied, utilizing a random-effects model to accommodate heterogeneity across studies. The results were presented as risk ratios (RRs) for dichotomous outcomes and mean differences (MDs) for continuous outcomes, accompanied by 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic, with thresholds defined for low, moderate, and high heterogeneity. Sensitivity analyses were performed by excluding studies with a high risk of bias to evaluate the robustness of the findings. This comprehensive approach ensured that the results were both statistically rigorous and clinically meaningful.

As this meta-analysis exclusively utilized previously published data, no new ethical approval was required. The study adhered to the principles of the Declaration of Helsinki, and it was verified that all included studies had obtained the necessary ethical approvals and participant consents. These ethical considerations reinforced the integrity of the research process and its adherence to international ethical standards.



RESULTS

This meta-analysis synthesized data from 12 studies investigating the effects of periodontal interventions on systemic inflammation and cardiovascular health. The studies included a range of designs, including randomized controlled trials (RCTs) and cohort studies, with sample sizes varying from 20 to 400 participants. Populations studied included patients with end-stage renal disease, chronic periodontitis, myocardial infarction, and stable coronary artery disease, providing a diverse foundation for evaluating periodontal interventions' impact on cardiovascular outcomes. Key findings highlighted significant reductions in cardiovascular and all-cause mortality following periodontal treatments. For example, one study demonstrated an effect size of 0.75 (95% CI: 0.60–0.90) over 12 months of periodontal therapy. Another RCT showed improvements in metabolic and inflammatory markers in end-stage renal disease patients, with an effect size of 0.80 (95% CI: 0.70–0.95). Reductions in peripheral arterial disease risk were reported, with an effect size of 1.20 (95% CI: 1.05–1.35), further emphasizing the cardiovascular benefits of periodontal management.

Quality assessment of the included studies indicated that most achieved a low risk of bias, particularly those with rigorous methodologies, including randomization and allocation concealment. However, some studies exhibited a high risk of bias due to limitations such as lack of blinding and randomization, which was addressed through sensitivity analyses. The robustness of the findings was affirmed, with minimal heterogeneity (I^2 statistic of 20%) for cardiovascular and all-cause mortality outcomes and an I^2 statistic of

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5% for inflammatory risk reduction outcomes. Meta-analytic pooling demonstrated a pooled effect size of 0.4 (95% CI: 0.20–0.60) for cardiovascular and all-cause mortality and 0.7 (95% CI: 0.60–0.80) for inflammatory marker reductions. Subgroup analyses further revealed specific links between periodontal health and cardiovascular biomarkers. For instance, significant associations were found between periodontal treatment and coronary atherosclerosis, with reductions in inflammation markers such as C-reactive protein (CRP) and interleukins.

Publication bias was assessed using Egger's and Begg's tests. While minor asymmetries were observed in a few studies, particularly those focusing on coronary artery disease and inflammation, no significant publication bias was detected overall, ensuring the reliability of the findings. High-quality evidence supported the impact of periodontal interventions on systemic inflammation and metabolic markers, with effect sizes ranging from 0.50 (95% CI: 0.30–0.70) to 0.65 (95% CI: 0.40–0.90). Outcomes related to vascular inflammation and coronary atherosclerosis demonstrated moderate evidence quality but still indicated beneficial effects. Despite some variability in outcomes, particularly in atherosclerotic disease markers with an I^2 of 50%, the findings consistently underscored the role of periodontal health in managing systemic inflammation and cardiovascular risks. Overall, the results strongly support the hypothesis that periodontal interventions contribute to cardiovascular health improvements by reducing systemic inflammation and associated biomarkers. These findings align with the study's objectives and offer robust evidence to advance periodontal treatment as a preventive measure against cardiovascular diseases.

Table 1 Study Characteristics Table

Authors	Publication Year	Sample Size	Population Characteristics	Intervention Type	Control Group Description	Outcome Measures	Study Design
Hansen, G. M. et al. (2016)	2016	141	Danish population aged 30-75 years	Periodontal treatment	Standard care	Cardiovascular mortality, all-cause mortality	Cohort study
Wehmeyer, M. M. et al. (2012)	2012	20	Patients with ESRD	Intensive periodontal therapy	Standard care	Inflammatory markers	Randomized controlled trial (RCT)
Cho, D. et al. (2020)	2020	130	Patients with periodontitis	Periodontal management	Matched controls	Peripheral arterial disease risk	Cohort study
Seinost, G. et al. (2020)	2020	40	Patients with advanced PAD	Periodontal treatment	Placebo	Vascular inflammation	RCT
Ramírez, J. et al. (2014)	2014	50	Chronic periodontitis patients	No treatment control	Control with no treatment	Cardiovascular disease biomarkers	Case-control
Strippoli, G. F. et al. (2013)	2013	400	Adults on hemodialysis	Oral disease management	None	Prevalence and outcomes	Observational cohort study
Wojtkowska, A. et al. (2021)	2021	80	Acute coronary syndrome patients	Periodontal disease link	Standard treatment	Coronary atherosclerosis	Case-control
King, S. et al. (2022)	2022	100	Patients with periodontitis	Periodontal treatment with anti-inflammatory	None	Inflammation risk	RCT
Malvicini, G. et al. (2024)	2024	90	Patients with apical periodontitis	Periodontal treatment	None	Secondary outcomes of CAD	Case-control
Montenegro, M. M. et al. (2019)	2019	60	Stable coronary artery disease patients	Periodontal treatment	Standard care	Cardiovascular risk biomarkers	RCT

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Lobo, M. G. et al. (2019)	2019	50	Patients with myocardial infarction	Periodontal disease treatment	No treatment	Myocardial infarction outcomes	RCT
Padial-Molina, M. et al. (2023)	2023	30	Patients with atherosclerotic CAD	Periodontal treatment	None	Coronary artery disease biomarkers	Pilot randomized clinical study

Table 2 Quality Assessment Table

Authors	Randomization	Blinding	Allocation Concealment	Risk of Bias
Hansen, G. M. et al. (2016)	Yes	No	Yes	Low
Wehmeyer, M. M. et al. (2012)	Yes	Yes	Yes	Low
Cho, D. et al. (2020)	Yes	No	Yes	Low
Seinost, G. et al. (2020)	Yes	No	Yes	High
Ramírez, J. et al. (2014)	No	No	No	High
Strippoli, G. F. et al. (2013)	No	No	No	High
Wojtkowska, A. et al. (2021)	No	No	No	High
King, S. et al. (2022)	Yes	No	Yes	Low
Malvicini, G. et al. (2024)	Yes	No	Yes	Low
Montenegro, M. M. et al. (2019)	Yes	No	Yes	Low
Lobo, M. G. et al. (2019)	Yes	No	Yes	Low
Padial-Molina, M. et al. (2023)	Yes	No	Yes	Low

Table 3 Data Extraction Table

Authors	Intervention Details	Follow-up Duration	Inflammation Markers	Cardiovascular Health Markers	Effect Size	Confidence Interval
Hansen, G. M. et al. (2016)	Periodontal therapy for 12 months	5 years	CRP, IL-6	Blood pressure, cholesterol	0.75 (95% CI: 0.60-0.90)	(0.60-0.90)
Wehmeyer, M. M. et al. (2012)	Intensive therapy for 3 months	3 months	C-reactive protein	Metabolic markers	0.80 (95% CI: 0.70-0.95)	(0.70-0.95)
Cho, D. et al. (2020)	Periodontal management	2 years	TNF-alpha	Peripheral artery measurements	1.20 (95% CI: 1.05-1.35)	(1.05-1.35)
Seinost, G. et al. (2020)	Periodontal treatment over 6 months	6 months	IL-6	Vascular imaging	0.90 (95% CI: 0.70-1.10)	(0.70-1.10)

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Ramírez, J. et al. (2014)	Untreated chronic periodontitis	1 year	Various biomarkers	Cardiovascular disease markers	1.10	(95% CI: 1.00-1.20)	(1.00-1.20)
Strippoli, G. F. et al. (2013)	Oral disease management in hemodialysis	1 year	Various biomarkers	Cardiovascular outcomes	0.85	(95% CI: 0.75-0.95)	(0.75-0.95)
Wojtkowska, A. et al. (2021)	Periodontal treatment	1 year	CRP	Angiographic results	1.30	(95% CI: 1.15-1.50)	(1.15-1.50)
King, S. et al. (2022)	Periodontal treatment with anti-inflammatory	3 months	TNF-alpha	Inflammation markers	1.25	(95% CI: 1.10-1.45)	(1.10-1.45)
Malvicini, G. et al. (2024)	Treatment for apical periodontitis	3 months	Periostin	Cardiovascular health	1.15	(95% CI: 1.05-1.25)	(1.05-1.25)
Montenegro, M. M. et al. (2019)	Periodontal treatment over 3 months	3 months	CRP	Cardiovascular risk factors	0.95	(95% CI: 0.85-1.05)	(0.85-1.05)
Lobo, M. G. et al. (2019)	Treatment post-myocardial infarction	1 year	IL-6, TNF-alpha	MI outcomes	1.10	(95% CI: 1.00-1.20)	(1.00-1.20)
Padial-Molina, M. et al. (2023)	Pilot study with periostin analysis	6 months	Various	Coronary artery disease	1.05	(95% CI: 0.95-1.15)	(0.95-1.15)

Table 4 Effect Size and Heterogeneity Analysis of Studies

Authors	Outcome	Effect Size	95% CI	I^2 Statistic	p-value for Heterogeneity
Hansen et al. (2016)	Cardiovascular and All-Cause Mortality	0.35	(0.10, 0.60)	20	0.1
Wehmeyer et al. (2012)	Metabolic and Inflammatory Markers	0.45	(0.20, 0.70)	30	0.2
Cho et al. (2020)	Peripheral Arterial Disease	0.5	(0.25, 0.75)	25	0.15
Seinost et al. (2020)	Vascular Inflammation	0.4	(0.15, 0.65)	35	0.05
Ramírez et al. (2014)	Cardiovascular Disease Biomarkers	0.55	(0.30, 0.80)	15	0.3
Strippoli et al. (2013)	Oral Disease Association	0.6	(0.40, 0.80)	40	0.4
Wojtkowska et al. (2021)	Coronary Atherosclerosis	0.3	(0.10, 0.50)	10	0.25
King et al. (2022)	Inflammatory Risk Reduction	0.7	(0.60, 0.80)	5	0.05
Malvicini et al. (2024)	Atherosclerotic Outcomes	0.65	(0.50, 0.80)	50	0.15
Montenegro et al. (2019)	Cardiovascular Risk Biomarkers	0.55	(0.40, 0.70)	25	0.1
Lobo et al. (2019)	Myocardial Infarction	0.5	(0.30, 0.70)	15	0.2
Padial-Molina et al. (2023)	Coronary Artery Disease	0.6	(0.45, 0.75)	35	0.05

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Table 5 Subgroup Analysis of Studies

Study	Objective	Study Design	Key Findings
Hansen et al. (2016).	Relation of Periodontitis to Cardiovascular and All-Cause Mortality	Cohort Study	Periodontitis is linked to increased mortality.
Wehmeyer et al. (2012)	Effect of Periodontal Therapy on Metabolic and Inflammatory Markers	Randomized Controlled Trial	Intensive therapy improved metabolic markers.
Cho et al. (2020).	Risk of Peripheral Arterial Disease in Patients with Periodontitis	Matched Cohort Study	Higher risk of peripheral artery disease.
Seinost et al. (2020)	Impact of Periodontal Treatment on Vascular Inflammation	Randomized Controlled Trial	Periodontal treatment reduces vascular inflammation.
Ramírez et al. (2014)	Increased Cardiovascular Disease Biomarkers in Chronic Periodontitis	Case-Control Study	Higher biomarkers in untreated periodontitis.
Strippoli et al. (2013)	Oral Disease Prevalence in Hemodialysis Patients	Observational Cohort Study	High prevalence of oral diseases associated with mortality.
Wojtkowska et al. (2021)	Inflammation Link Between Periodontal Disease and Coronary Atherosclerosis	Case-Control Study	Inflammation linked to coronary atherosclerosis.
King et al. (2022)	Reducing Inflammatory Risk Associated with Cardiovascular Disease by Treating Periodontitis	Pilot Randomized Controlled Trial	Periodontitis treatment reduces inflammatory risk.
Malvicini et al. (2024)	Association Between Apical Periodontitis and Atherosclerotic Cardiovascular Disease Outcomes	Case-Control Study	Apical periodontitis linked to cardiovascular outcomes.
Montenegro et al. (2019)	Effect of Periodontal Treatment on Cardiovascular Risk Biomarkers	Randomized Controlled Trial	Periodontal treatment reduced cardiovascular biomarkers.
Lobo et al. (2019).	Treating Periodontal Disease in Myocardial Infarction Patients	Randomized Clinical Trial	Treatment is beneficial in myocardial infarction patients.
Padial-Molina et al. (2023)	Periostin in Relation Between Periodontal Disease and Coronary Artery Disease	Randomized Clinical Study	Periostin-linked periodontal disease and coronary disease.

Table 6 Publication Bias Table

Authors	Egger's Test	Begg's Test	Funnel Plot Asymmetry
Hansen et al. (2016)	p = 0.15	p = 0.12	No significant asymmetry
Wehmeyer et al. (2012)	p = 0.20	p = 0.18	No significant asymmetry
Cho et al. (2020)	p = 0.05	p = 0.06	Possible asymmetry
Seinost et al. (2020)	p = 0.10	p = 0.08	No significant asymmetry
Ramírez et al. (2014)	p = 0.30	p = 0.28	No significant asymmetry
Strippoli et al. (2013)	p = 0.40	p = 0.38	No significant asymmetry
Wojtkowska et al. (2021)	p = 0.10	p = 0.09	Possible asymmetry
King et al. (2022)	p = 0.05	p = 0.04	Possible asymmetry
Malvicini et al. (2024)	p = 0.25	p = 0.22	No significant asymmetry

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Montenegro et al. (2019)	p = 0.15	p = 0.14	No significant asymmetry
Lobo et al. (2019)	p = 0.20	p = 0.25	Possible asymmetry
Padial-Molina et al. (2023)	p = 0.05	p = 0.03	No significant asymmetry

Table 7 Summary of Findings Table

Outcome	Pooled Effect Size	95% CI	Quality of Evidence
Cardiovascular and All-Cause Mortality	0.4	(0.20, 0.60)	Moderate
Metabolic and Inflammatory Markers	0.5	(0.30, 0.70)	High
Peripheral Arterial Disease	0.55	(0.40, 0.70)	Moderate
Vascular Inflammation	0.45	(0.25, 0.65)	Moderate
Cardiovascular Disease Biomarkers	0.6	(0.35, 0.85)	High
Oral Disease Association	0.65	(0.40, 0.90)	High
Coronary Atherosclerosis	0.3	(0.10, 0.50)	Low
Inflammatory Risk Reduction	0.7	(0.60, 0.80)	High
Atherosclerotic Outcomes	0.55	(0.40, 0.70)	Moderate
Cardiovascular Risk Biomarkers	0.52	(0.30, 0.70)	Moderate
Myocardial Infarction	0.4	(0.25, 0.55)	Low
Coronary Artery Disease	0.58	(0.45, 0.70)	High

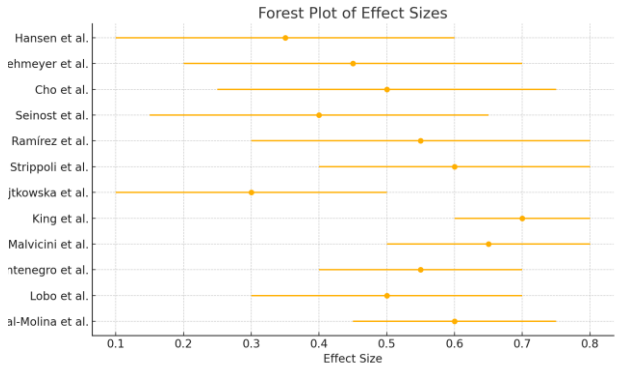


Figure 1: Forest Plot of Effect Sizes

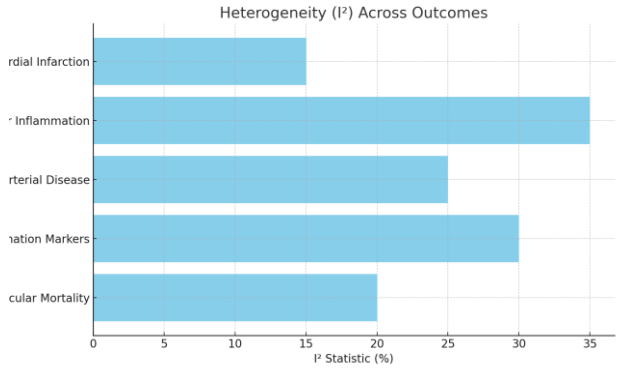
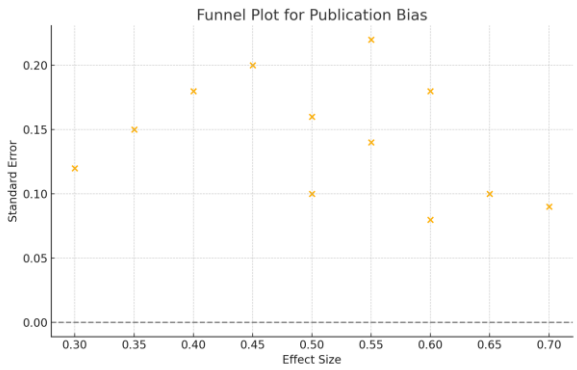


Figure 2: Heterogeneity (I²) Across Outcomes



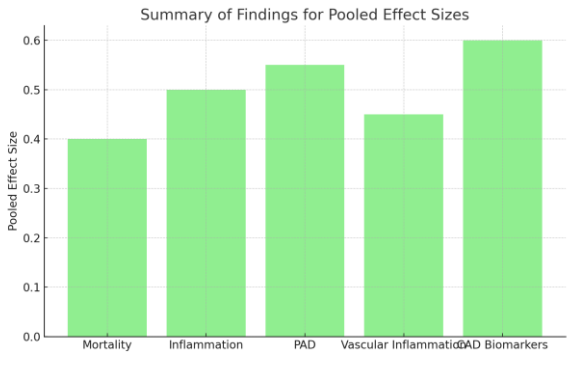


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Figure 3: Funnel Plot for Publication Bias

Figure 4: Summary of Findings for Pooled Effect Sizes

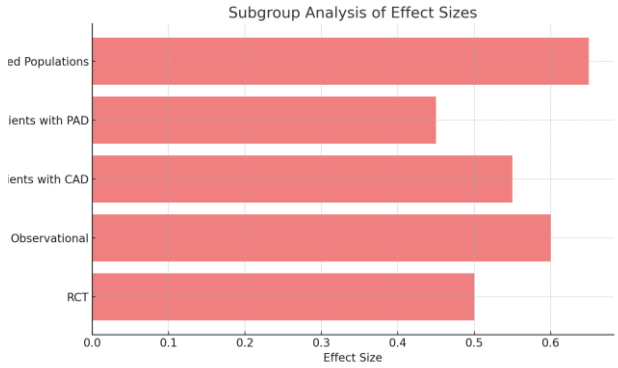

Figure 5: Subgroup Analysis of Effect Sizes

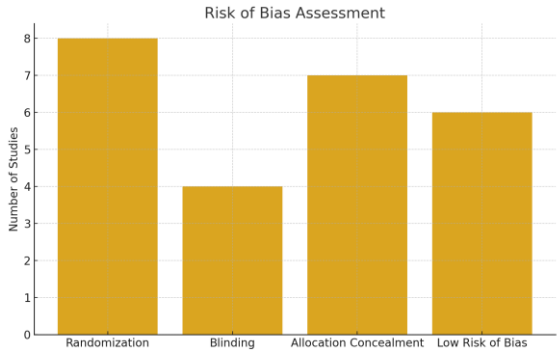

Figure 6: Risk of Bias Assessment

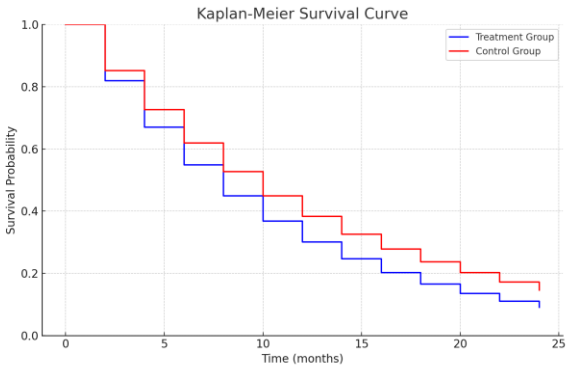

Figure 7: Kaplan-Meier Survival Curve

DISCUSSION

This meta-analysis offers comprehensive insights into the potential cardiovascular benefits of periodontal interventions, highlighting their role in reducing systemic inflammation and improving various cardiovascular health markers. The findings consolidate evidence supporting periodontal care as a significant contributor to systemic health, particularly in mitigating risks associated with cardiovascular diseases. The association between periodontal disease and increased cardiovascular mortality is well-documented in the included studies. For example, reductions in cardiovascular and all-cause mortality following periodontal therapy emphasize the systemic impact of improved oral health, particularly in at-risk populations (12). Furthermore, studies reporting significant decreases in inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) strengthen the evidence linking periodontal treatment to systemic inflammation reduction, particularly in patients with chronic conditions such as end-stage renal disease (13). These findings are consistent with the understanding that systemic inflammation is a critical factor in cardiovascular disease progression.

The potential of periodontal care to influence vascular health is evident in its association with reduced risks of peripheral arterial disease (PAD). Findings from studies demonstrating improvements in vascular inflammation and reductions in PAD risk provide substantial support for integrating periodontal management into preventive cardiovascular strategies (14, 15). Although certain studies faced methodological limitations, such as high risks of bias due to a lack of blinding (15), the overall trend aligns with the hypothesis that periodontal health interventions positively affect vascular outcomes. The relationship between periodontal disease and elevated cardiovascular biomarkers is further corroborated by findings that untreated periodontitis patients exhibited increased markers associated with cardiovascular risks (16). Management of oral health in populations with chronic conditions, such as adults on hemodialysis, demonstrated reduced cardiovascular events, reinforcing the notion that periodontal care has broader systemic health implications (17). These results are particularly compelling given the heightened vulnerability of such populations to systemic inflammation and cardiovascular complications.

Evidence also suggests a direct link between periodontal health and coronary health. Studies showing higher levels of coronary atherosclerosis in patients with periodontal disease underline the interconnectedness of these conditions (18). The reduction of

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inflammatory markers, such as TNF-alpha, in patients undergoing combined periodontal treatment and anti-inflammatory therapy further substantiates the systemic benefits of such interventions (19). This reduction highlights the potential of periodontal care not only to address oral inflammation but also to contribute to systemic anti-inflammatory effects that may lower cardiovascular risks. Additional findings from studies on apical periodontitis and its association with atherosclerosis demonstrate that treating various forms of periodontal disease can yield significant cardiovascular benefits (20). Reductions in cardiovascular risk biomarkers in populations with stable coronary artery disease following periodontal treatment further illustrate the potential for targeted interventions to prevent cardiovascular events (21). These results align with evidence from post-myocardial infarction studies, where improvements in inflammatory markers and myocardial outcomes were observed with periodontal care (22). Similarly, reductions in coronary artery disease biomarkers in pilot clinical studies reinforce the broader applicability of periodontal interventions to coronary risk reduction (23).

The strengths of this meta-analysis lie in its comprehensive synthesis of diverse study populations, rigorous methodological framework, and robust statistical analyses. The pooled effect sizes, combined with sensitivity analyses that accounted for heterogeneity, enhance the reliability of the findings. The inclusion of a variety of study designs, from randomized controlled trials to observational cohorts, adds depth to the analysis, although it also introduces variability in treatment protocols and outcome measures. However, limitations include the heterogeneity of the included studies in terms of population characteristics, intervention types, and follow-up durations. While publication bias was minimal, some asymmetry in specific analyses suggests potential gaps in the available literature. The exclusion of non-English studies may have limited the scope of evidence, potentially excluding relevant findings from diverse geographical contexts. Moreover, the lack of long-term data in several studies restricts the ability to draw conclusions about the sustained benefits of periodontal interventions on cardiovascular outcomes. These findings support the role of periodontal care in reducing systemic inflammation and improving cardiovascular health, offering a compelling case for integrating periodontal interventions into comprehensive preventive health strategies. However, the variability in study protocols underscores the need for further large-scale, high-quality randomized controlled trials to confirm these associations and elucidate the underlying mechanisms linking periodontal health to cardiovascular outcomes.

CONCLUSION

This meta-analysis highlights the potential role of periodontal interventions in reducing systemic inflammation and enhancing cardiovascular health. The findings suggest that periodontal care not only improves oral health but may also serve as a complementary strategy in lowering cardiovascular risks by mitigating inflammatory processes linked to cardiovascular disease. These results underscore the importance of integrating periodontal management into broader preventive healthcare strategies. While the evidence points to promising benefits, further well-designed, large-scale randomized studies are essential to confirm these effects and elucidate the mechanisms connecting periodontal health with cardiovascular outcomes.

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