




Review article

# Association between cardiovascular diseases and apical periodontitis: An umbrella review with stratification of evidence and sensitivity analysis

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## Abstract

### Objectives

To systematically evaluate epidemiological evidence regarding cardiovascular disease (CVD) and apical periodontitis (AP) associations through umbrella review methodology.

### Data

Ten systematic reviews were synthesized, including five meta-analyses encompassing 1108–673,083 participants. Meta-analytical effect sizes demonstrated relative risks ranging from 1.20 to 1.38, odds ratios of 1.53 to 2.94, with substantial between-study heterogeneity ( $I^2 = 54\% - 100\%$ ). The pooled estimates of RR studies were 1.32[1.0 to 1.62;  $p = 0.007$ ] and for Odds ratio 1.83[1.33 to 2.53;  $P < 0.001$ ]. Evidence stratification revealed significant heterogeneity in effect magnitudes, methodological approaches, and study quality assessments.

[Sources](#)[Cite](#)

Comprehensive searches of PubMed/MEDLINE, Scopus, EBSCO Host, and multiple grey-literature repositories were conducted from database inception to February 2025, using optimized strategies that integrated Medical Subject Headings, Boolean logic, truncation, and proximity operators.

## Study selection

Dual independent reviewer screening identified systematic reviews examining CVD-AP associations. Following duplicate removal and consensus resolution, 10 systematic reviews were included from 7472 initially screened articles.

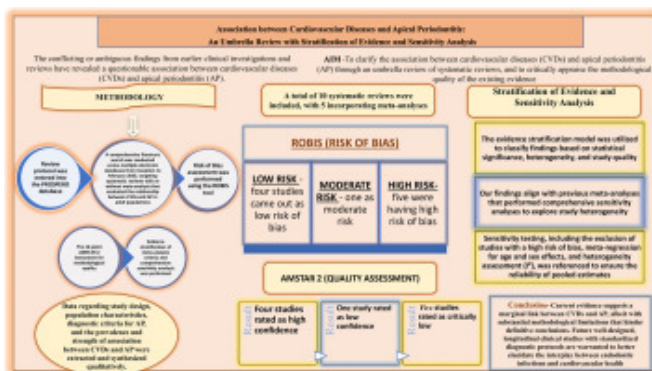
## Conclusion

This umbrella review of ten systematic reviews—including five meta-analyses spanning 1108 to 673,083 participants—demonstrates a consistent, moderately elevated cardiovascular risk associated with apical periodontitis. Pooled estimates showed a 32 % increase in relative risk (RR = 1.32, 95 % CI = 1.00–1.62;  $p = 0.007$ ) and an 83 % higher odds of cardiovascular disease (OR = 1.83, 95 % CI = 1.33–2.53;  $p < 0.001$ ). However, substantial between-study heterogeneity ( $I^2 = 54 - 100 %$ ) and variability in diagnostic criteria temper causal inference.

## Clinical Significance

Collectively, the evidence supports AP as an independent, clinically important marker of cardiovascular vulnerability, justifying intensified prevention and management of endodontic infection within cardiometabolic risk reduction strategies. Future large, prospective cohorts employing standardized AP definitions and rigorous confounder control are needed to clarify dose-response patterns and underlying mechanisms.

## Graphical abstract



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## Introduction

Apical Periodontitis (AP) arises from a complex interplay between endodontic microorganisms, their virulence factors, and host immunity, culminating in periapical granuloma, abscess, or cyst formation [1]. Beyond local tissue destruction, AP has been implicated in systemic disorders, most notably diabetes [2,3] and cardiovascular diseases (CVDs) [4,5], a spectrum that includes coronary, cerebrovascular, and peripheral arterial disease as well as rheumatic and congenital heart disease, deep-vein thrombosis, and pulmonary embolism [6]. CVDs remain the leading global cause of death, accounting for 17.9 million annual fatalities [6].

Epidemiologically, AP imposes a sizable burden: a review of 33 cross-sectional studies (> 300,000 teeth) estimated prevalences of  $\approx 10\%$  for root-filled teeth and  $\approx 5\%$  for AP, roughly two and one lesions per adult, respectively [7]. Despite this ubiquity, AP's contribution to systemic inflammation has been under-recognized. Projections indicate a 10% rise in CVD prevalence and a near-tripling of related healthcare costs within two decades [8]. Atherosclerosis, the pathological substrate of most CVDs, is fundamentally inflammatory [9,10]; T-helper 1 cells and macrophages secrete pro-inflammatory cytokines that drive plaque growth, destabilization, and thrombus formation [9,10]. Microbial colonization of the arterial wall further amplifies local inflammation and adaptive immune responses, fostering atherogenesis [11,12]. Transient bacteremia from AP [13] and its attendant low-grade systemic inflammation [14] may therefore act as triggers or accelerants of CVD.

Multiple systematic reviews/meta-analyses have assessed the AP-CVD link [4,[15], [16], [17], [18], [19], [20], [21], [22], [23], [24]]. Eight early reviews suggested a possible association but called for longitudinal data [15]; González-Navarro et al. confirmed this trend yet highlighted methodological gaps [16]; conversely, Berlin-Broner et al. deemed current evidence insufficient for causality, citing moderate-to-low study quality [4]. Subsequent analyses echoed limited, inconsistent evidence [[17], [18], [19], [20],22], with one report finding no relationship between AP and hypertension [21]. Given these discrepancies, umbrella reviews, systematic syntheses of systematic reviews, have been advocated to resolve conflicting findings and map evidence certainty [24].

Accordingly, the present umbrella review aims to (i) clarify whether AP correlates with CVDs in adults and (ii) delineate persisting knowledge gaps to guide future high-quality longitudinal and interventional research.

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## Section snippets

### Material and methods

The current umbrella review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [25]. The protocol of the current umbrella review was registered in the PROSPERO database (CRD42024558284). The PRIRES (Preferred Reporting Items for Resistance Exercise Studies), which is a checklist developed using an umbrella review of systematic reviews, has been uploaded as a supplementary table. ...

### Literature search process

The PRISMA flow diagram (Fig. 1) sets out the entire literature search process. The total number of articles identified from the four electronic databases was 7472; of these, 5921 were duplicates and were removed. Title and abstract screening identified 1427 studies for exclusion, while 124 studies were selected for full-text retrieval. Out of which, 49 reports' full text was not retrieved and hence excluded. 75 articles in the full text were thoroughly reviewed. 65 studies were excluded after ...

### Discussion

The result of previous systematic reviews are conflicting and unreliable. Epidemiological evidence from primary studies highlights a correlation between AP and the onset of CVDs. In order to improve understanding, remove discrepancies, spot possible knowledge gaps, and gather vital information on the subject of interest into a comprehensive reference publication, an umbrella review assesses and combines the findings of several systematic reviews [27,28]. Therefore, an umbrella review approach ...

### Conclusion

To summarize, we advocate a streamlined, multidisciplinary screening pathway for apical periodontitis in cardiovascular patients that integrates: (1) a focused medical-dental history capturing demographics, CVD phenotype, lifestyle and metabolic risk factors, key medications, and oral-health behaviours; (2) targeted clinical and radiographic evaluation periodontal charting, vitality testing, high-resolution periapicals with PAI scoring, and CBCT only for lesions  $\geq$  PAI 3; (3) optional ...

### CRedit authorship contribution statement

**Adinath Walmik Talekar:** Writing – review & editing, Writing – original draft, Visualization, Software, Resources. **Dax Abraham:** Writing – review & editing, Writing – original draft,

Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Aakansha Puri:** Writing – review & editing, Writing – original draft, Supervision, Software, Resources, Investigation, Funding acquisition, ...

## Declaration of competing interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article. ...

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## Financial support

No financial support was received for conducting this review at any stage. ...

## Registration

The protocol of the current umbrella review was registered in the PROSPERO database (CRD42024558284). ...

## Ethical Approval Statement and Document

Not applicable as this is an umbrella review. ...

## Permission to Reproduce material from other sources

Not Applicable. ...

## Artificial Intelligence

No artificial intelligence tools were used in writing this manuscript. ...

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