# From Pathogens to Practice: Bridging the Gap Between Dentistry and Medicine

Joint Effort:

Sara Izadi, Vivian Huth, Rishika Sharma

Capstone Project

April 17, 2025

Interdisciplinary Medical Sciences

Schulich School of Medicine and Dentistry

Western University

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# Executive Summary

Periodontal disease (PD) and cardiovascular disease (CVD) are two of the most prevalent non-communicable diseases worldwide. Both conditions are considered 'wicked problems' due to their complex, multifactorial nature, with interwoven social, economic, and environmental determinants. Chronic periodontal inflammation contributes to systemic inflammatory responses that are implicated in the progression of atherosclerosis, endothelial dysfunction, and cardiovascular events. Despite plentiful recorded associations between the two diseases, the current healthcare landscape often falls short of fostering optimal, patient-centred care. Fragmented systems within dental and medical practices result in missed opportunities for early detection, prevention, and comprehensive treatment, particularly for patients who exhibit risk factors for both conditions. This disconnect underscores the need for systemic change to address gaps in collaboration, communication, and integrated care delivery.

Through a comprehensive review of peer-reviewed literature, this research synthesizes biological mechanisms linking PD to CVD and analyzes the systemic and behavioral risk factors that exacerbate both conditions. The findings reveal that patients presenting with periodontal pocket depths ≥4 mm, clinical attachment loss, persistent gingival inflammation, smoking, older age, and comorbidities such as diabetes are at increased risk of cardiovascular complications. These indicators serve as the foundation for a proposed screening checklist designed for use by dental professionals to identify high-risk individuals and initiate timely referrals to medical practitioners.

The project further outlines actionable strategies to bridge the gap between dentistry and medicine, including the development of standardized referral protocols, shared electronic health records, and interprofessional education initiatives. By implementing these systemic changes, healthcare providers can shift from reactive to preventive models of care that recognize the interconnected nature of oral and systemic health. The ultimate goal is to reduce the burden of CVD by improving early detection, promoting interdisciplinary communication, and integrating oral health into the broader continuum of patient-centered care. This work contributes to an emerging framework that supports collaborative, efficient, and equitable healthcare delivery. Collectively, these efforts aim not only to improve early detection and management of cardiovascular risk in dental settings but also to demonstrate how systemic and interdisciplinary changes can be implemented to address broader, complex health challenges.

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# Introduction

## i) Background Information

Periodontal disease (PD) refers to a group of chronic inflammatory conditions that damage the supporting structures of the teeth, including the alveolar bone, gingiva, and periodontal ligament.[1] PD progresses from gingivitis, an early stage characterized by reversible inflammation of the gingiva.[2] The transition to periodontitis is characterised by irreversible destruction of the alveolar bone and periodontal ligament, leading to tooth loss.[2]

In PD, bacterial biofilms primarily originate from the existing oral microbiome, where a shift towards dysbiosis — rather than the introduction of new pathogens — drives an exaggerated immune response that contributes to chronic inflammation and tissue destruction. Bacterial colonization in the periodontal pocket invokes an immune response which provokes neutrophils and macrophages to release pro-inflammatory cytokines and proteolytic enzymes.[3] These enzymes include matrix metalloproteinases (MMPs), which are produced by the host's immune cells, and certain bacterial enzymes, which contribute to the degradation of tissue.[4,5] Despite the host immune cells' attempts to eliminate bacterial invasion, there are chances of dysregulation. This can lead to excessive enzyme and cytokine production, further exacerbating tissue destruction.

Cardiovascular disease (CVD) encompasses a wide range of conditions that impact the heart and blood vessels. These diseases are predominantly driven by atherosclerosis - a process marked by the accumulation of inflammatory cells and fibrous tissue within arterial walls and lipids.[6] This accumulation forms plaque, which can rupture, leading to acute events such as stroke and myocardial infarction.[7] Some primary mechanisms that drive the development of CVD include thrombosis, oxidative stress, chronic inflammation and endothelial dysfunction.[6] These mechanisms impair oxygen delivery and blood flow to vital organs, increasing the risk of systemic complications. Chronic periodontal infections further exacerbate systemic inflammation and endothelial dysfunction by releasing inflammatory mediators and periodontal pathogens into the bloodstream, accelerating atherogenesis and promoting thrombus formation.[8] Such dysfunction is further worsened by prolonged inflammation, metabolic imbalances, and oxidative stress which can contribute to arterial stiffening and increased cardiovascular risk.[6] CVDs are influenced by an amalgamation of environmental factors, genetic predisposition, with severe, yet modifiable risk factors like hyperlipidemia, smoking, diabetes, hypertension, sedentary lifestyle, and obesity.[9] Even with advanced treatments like antihypertensives, lipid-reducing therapies, and interventional methods, CVDs remain a primary cause of global mortality and morbidity.[10]

## ii) PD and CVD as Non-Communicable Diseases

Non-communicable diseases (NCDs) are chronic conditions caused by a combination of genetic predispositions, behavioural patterns and environmental factors rather than being transmitted between individuals. NCDs like CVDs, cancers, and diabetes are a primary cause of mortality worldwide.[11] In Canada, NCDs are responsible for approximately 90% of all deaths, with cancers, diabetes and CVD resulting in about 67% of this total.[12] Likewise, advanced periodontitis impacts 11% of the global population and is labelled as the sixth most prevalent human disease.[13] The complex and interconnected nature of NCDs presents a significant challenge for healthcare systems, especially concerning diagnosis and prevention.[14] Some conditions like PD and CVD are thought to demonstrate a directional relationship, where one condition can exacerbate the progression of the other. This can be exemplified by systemic inflammation originating from PD but contributes to atherosclerosis, a primary driver of CVD. Addressing this interplay necessitates a shift towards an integrated interdisciplinary approach to prevent one condition from resulting in the progression of another.

Although there is evidence of a biological link between PD and CVD, the lack of integration between dental and medical disciplines remains a critical barrier to effective management. Despite shared inflammatory pathways, overlapping risk factors, and evidence of a bidirectional relationship between these conditions, healthcare systems continue to operate in fragmented silos. This disjointed approach limits early diagnosis and coordinated treatment exacerbating preventable health disparities, leaving patients vulnerable to worsening outcomes.[15]

## iii) Biological Relationship Between PD and CVD

The relationship between PD and CVD is a multifaceted healthcare challenge rooted in biological, social, and systemic complexities. As such, risk factors for these diseases are diverse and can be challenging to minimize. Common risk factors for both PD and CVD include an individual's age, sex, family history, smoking frequency, and educational level.[16–18] Given the diversity of these risk factors, an interdisciplinary approach is required for effective mitigation.

The biological relationship between PD and CVD, however, has been studied before. Periodontal pathogens, specifically *Porphyromonas gingivalis,* can enter systemic circulation through either a direct or indirect pathway (Figure 1). Once in systemic circulation, these pathogens trigger inflammatory cascades.[19] These inflammatory mediators include C-reactive protein (CRP), interleukin-6 (IL-6), and tumour necrosis factor-α (TNF-a), all of which contribute to endothelial dysfunction. Pathogens like *P. gingivalis* and *Aggregatibacter actinomycetemcomitans, A. actinomycetemcomitans,* have been identified within atheromatous plaques, suggesting their potential role in plaque formation, progression, or instability.[20] These pathogens activate monocytes and other immune cells, leading to the overproduction of proinflammatory cytokines, which drive vascular inflammation and destabilise plaque.

*P.gingivalis* releases virulence factors like lipopolysaccharides (LPS), which disrupts endothelial integrity, leading to endothelial dysfunction. Endothelial dysfunction impairs nitric oxide bioavailability, promotes vascular inflammation, and increases permeability and deposition

of low-density lipoprotein (LDL) particles in the arterial intima.[21] These LDL particles oxidise and then attract macrophages that transform into foam cells to create the basis of atherosclerotic plaques.[22]

Increased CRP levels are another key biomarker of systemic inflammation which is a well-established indicator of CVD risk and has been detected at higher levels in patients with advanced periodontal disease.[23] CRP levels remained elevated in patients with subclinical atherosclerosis and PD, even post-adjustment of risk factors like diabetes and smoking. Inflammatory mediators such as IL-6, TNF-α, are also significantly heightened in individuals with concurrent CVD and PD.[19] While considerable evidence supports the PD-CVD connection, the lack of integration and communication between dental and medical disciplines creates significant barriers to effective management.

This literature review aims to synthesise current evidence on shared biological mechanisms but also other crucial factors underlying the relationship between PD and CVD, while identifying the systemic barriers that prevent interdisciplinary collaboration. By addressing these gaps, the review seeks to advocate for a more integrated and holistic approach to managing these interconnected diseases. Ultimately, such an approach has the potential to improve patient outcomes, enhance preventative care, and contribute to reducing the global burden of non-communicable diseases by aligning strategies across disciplines.

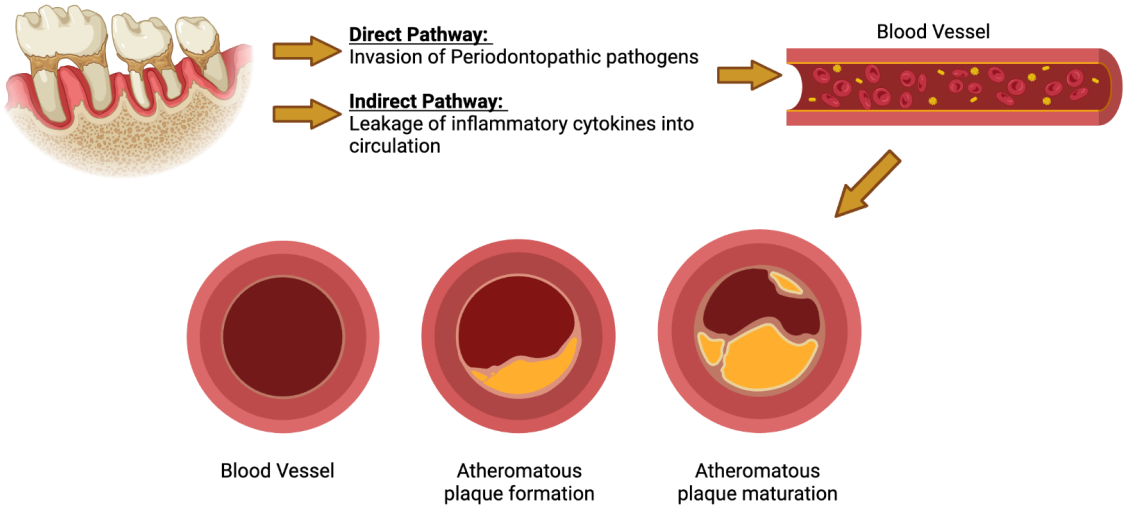


**Figure 1.** An infographic created using BioRender Premium, illustrates the direct and indirect mechanisms by which bacterial pathogens linked to periodontal disease contribute to atherosclerotic plaque formation

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# Methods

This review follows a scoping review methodology, which is well-suited for mapping key concepts, summarizing current knowledge, and identifying gaps in research across broad or complex topics - such as the interplay between PD and CVD. For this review, PubMed was chosen as the sole database for literature retrieval. PubMed is a leading repository for biomedical and clinical research, offering access to MEDLINE-indexed journals, which ensures a high standard of peer-reviewed articles relevant to dentistry, cardiology, and systemic disease interactions. Additionally, PubMed provides advanced search functionalities, including Medical Subject Heading terms, Boolean operators, and filters, which allow for a precise and targeted literature search. Since this review prioritizes depth of analysis over exhaustive breadth, a single-database search is appropriate. To enhance rigor, we employed structured search terms related to PD, CVD, and their risk factors, ensuring that the most relevant studies were captured.

To assess the unilateral relationship between PD and CVD we created the following search string, which is shown in table 1. The search string was constructed using Boolean logic and concept grouping to reflect five distinct but interrelated thematic categories relevant to the relationship between periodontal disease (PD) and cardiovascular disease (CVD). The first group includes terms such as "periodontal disease," "periodontitis," and "oral health" to broadly capture literature related to oral inflammatory conditions and their classification. The second group comprises terminology for cardiovascular outcomes, such as "CVD," "coronary heart disease," and "myocardial infarction," which allowed for the identification of studies linking oral and cardiac conditions. The third grouping focuses on pathophysiological mechanisms—such as "inflammatory response," "pro-inflammatory cytokines," and "endothelial dysfunction"—to capture studies that investigate biological pathways connecting PD and CVD. The fourth group includes association-related terms like "risk factor," "link," and "comorbidity," which are commonly used in epidemiological and observational studies to describe relationships between conditions. Lastly, the fifth grouping introduces known shared risk factors and modifiers, including "diabetes," "smoking," and "socioeconomic status," to account for confounding variables that may influence both oral and cardiovascular health. These thematic clusters were deliberately chosen to ensure a comprehensive yet focused literature retrieval strategy, enabling the review to map the full spectrum of biological, clinical, and epidemiological insights into the PD-CVD connection.

**Table 1.** Overview of the search string developed and executed in PubMed. The search string incorporates various stages and conditions of periodontal and cardiovascular disease, along with their hypothesized shared risk factors.

| Category of Search | Search Query |
|---|---|
| **Periodontal Disease and Oral Health Status** | ("periodontal disease" OR "periodontitis" OR "periodontal infection" OR "oral health") |
| **Cardiovascular Disease Spectrum** | ("cardiovascular disease" OR "CVD" OR "heart disease" OR "coronary heart disease" OR "atherosclerosis" OR "myocardial infarction") |
| **Biological Mechanisms Linking Oral and Cardiovascular Disease** | ("etiology" OR "pathophysiology" OR "inflammatory response" OR "systemic inflammation" OR "pro-inflammatory cytokines" OR "oxidative stress" OR "bacterial biofilm" OR "plaque" OR "dental plaque" OR "pathogenic bacteria" OR "matrix metalloproteinases" OR "vascular inflammation" OR "gingivitis" OR "gum disease" OR "endothelial dysfunction") |
| **Health Associations and Systemic Implications** | ("risk factor" OR "association" OR "link" OR "connection" OR "complications" OR "outcomes" OR "systemic disease" OR "comorbidity") |
| **Epidemiological and Lifestyle Risk Factors** | ("diabetes" OR "smoking" OR "risk factors" OR “socioeconomic status” OR "epidemiology") |

As seen in figure 2, this search produced 810 results, which were then placed through a Title and Abstract screening. A consistent set of exclusion criteria was applied across both stages of screening; this included articles that focused on diseases that do not directly link to ones that are within the scope of the project, such as arthritis or stroke.. Review articles were excluded from extraction as they fell beyond the scope of this literature review, which aims to synthesize primary research findings rather than provide a broad summary of existing literature. However, meta-analyses were retained due to their rigorous statistical analyses and ability to integrate data from multiple studies, offering valuable insights that align with the objectives of this review.

Additionally, studies were removed if they were not accessible through institutional accounts or were retracted. Articles that failed to examine the association between PD and CVD, particularly those focused exclusively on one condition without addressing their interrelationship, were also excluded. This review focuses specifically on the unidirectional relationship between risk factors — namely, how PD contributes to the development or

exacerbation of CVD. While bidirectional interactions are important and documented in the literature, they introduce interpretive complexities that extend beyond the intended scope of our results. Nevertheless, studies discussing bidirectional relationships were still reviewed and recorded to inform the discussion and recommendations sections, particularly when identifying areas for future research and systemic integration.

A total of 403 articles proceeded to the full-text screening stage, from which 142 were approved and selected for data extraction based on relevance and study design.

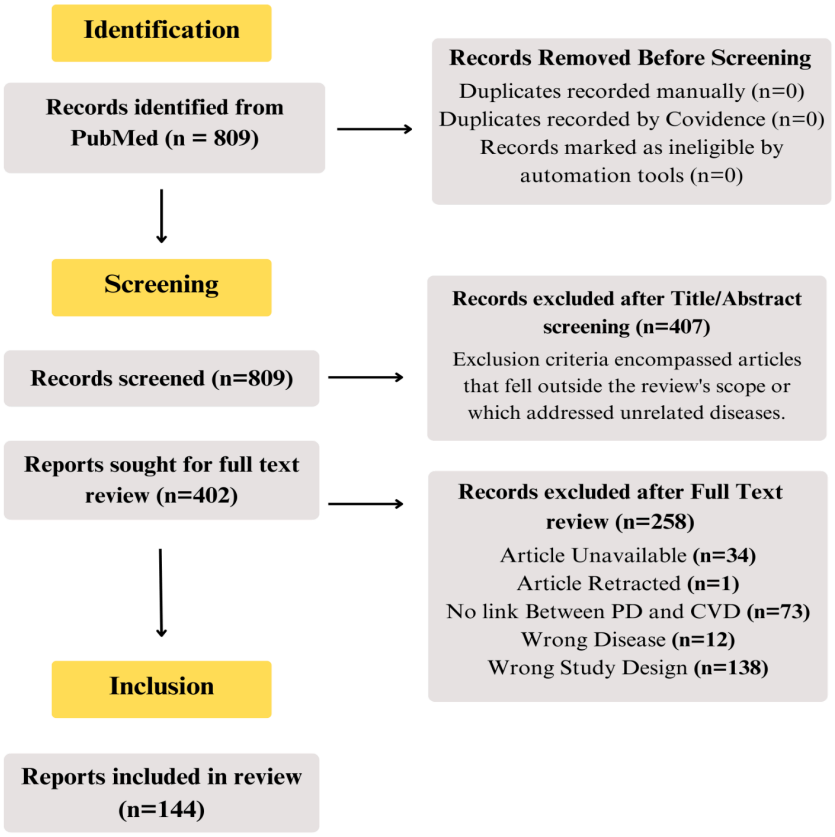


**Figure 2.** A PRISMA chart illustrating the inclusion and exclusion criteria applied to select the 144 articles included in this review.

# Results

Examining the association between PD and CVD requires consideration of key risk factors such as sex, age, and socioeconomic status (SES) which y influence one's disease risk, disease progression, and ability to access care. These factors are critical for understanding how population-level patterns influence the link between PD and CVD and for shaping targeted interventions. While substantial evidence supports the connection, limited research has explored which groups are most vulnerable to the progression of shared risk factors to PD andCVD. Identifying these patterns can guide prevention and policy efforts . Several studies identified sex, age, and SES as key risk factors contributing to the severity and progression of both PD and CVD. Older individuals were more likely to exhibit advanced clinical attachment loss and reported a higher incidence of cardiovascular events. Male patients were frequently reported to have more severe presentations of PD. Studies that included SES-related variables found that lower socioeconomic status was associated with decreased access to routine dental care and higher rates of periodontal inflammation. However, not all studies assessed these variables uniformly; some limited their scope to avoid the influence of confounding factors or due to data availability constraints. These Reported associations between these risk factors and disease outcomes varied depending on study design and population characteristics.

## i) Geographic Distribution of Research

Of the articles analysed in this literature review, 40% of the studies that determined an association between PD and CVD were conducted in or included data from the United States, 35% were based in European countries, 20% from Asian countries, including India, Korea and Japan, and 5% from other regions including those that were international collaborations. These statistics demonstrate the need for Canadian involvement with research regarding the systemic impacts of periodontal health and CVD, fostering an interdisciplinary approach to healthcare promoting improved patient health outcomes.

## ii) Risk Factor Considerations

Risk factors often overlap across varying non communicable diseases.[16] CVD and PD, in particular, share several potential risk factors. Studies examiningPD and its causes often consider a patient's age, sex, ethnicity, smoking behaviours, educational level, and presence of diabetes.[17] When examining CVD, researchers often make note of similar risk factors such as age, sex, frequency of smoking, and diabetes diagnosis, as well as educational and occupational level.[17,18,24] Our review identified twenty one studies reporting greater susceptibility to CVD in male populations, while only 6 studies found similar significant results for females.[25–30] There was substantial variation in sample sizes across the included studies. For instance, one article[31] had a study sample of just 9 participants, which is insufficient to draw meaningful conclusions about sex-specific trends. Additionally, many studies in our extractions exclusively

focused on male populations, likely to control for potential confounding effects related to sex or gender differences.[10,32–39] Conversely, only two studies [40,41] exclusively examined female populations.

Race was considered in twenty studies, though categorization methods varied widely. Many studies used broad classifications such as "white" and "non-white,"[25,42–45] with limited further granularity. In several cases, studies focused exclusively on one racial group due to sample limitations—such as cohorts composed entirely of Japanese or Indian participants[27,29,30,46–49] —while others included racially diverse populations but did not analyze race as a variable of interest. Some studies included race as a covariate in their statistical models, often adjusting for racial differences in cardiovascular or periodontal outcomes.[50–52] A few studies provided stratified analyses by race or ethnicity, noting distributions such as Hispanic, African American, and non-Hispanic white groups.[50,53–57] Despite this variability, no study reported a significant association between race and the PD–CVD link. Overall, while race was inconsistently measured and analyzed, it did not emerge as a significant modifying factor in the association between periodontal and cardiovascular disease across the reviewed literature.

Thirty studies reported a proportional relationship between increasing age and higher PD/CVD risk, while three studies identified significant associations in younger populations. However, the design of some studies may have contributed to these findings, as studies with younger populations often exclude older participants to minimize the confounding effects of age-related comorbidities. For instance, certain articles [28,58] excluded participants over the ages of 85 and 75, respectively, citing comorbidities as a confounding factor. The same article by Morrison et al,[58] with a large sample size of approximately 20,000 participants aged 35 to 85, found significant associations in participants under 70 but no increased risk in those aged 70–84 with poor dental health. Similarly, Nordendahl et al,[28] found the strongest associations in participants under 65 years. Interestingly, one article observed significant relationships between men under 60 and coronary heart disease (CHD), while older men were more strongly associated with edentulism rather than CVD.

None of the reviewed articles included pregnant women in their study populations (Figure 3). Excluding pregnant individuals follows a common practice in research to minimise confounding factors on systemic inflammatory markers such as CRP, given that pregnancy induces significant physiological changes, including heightened inflammatory responses.

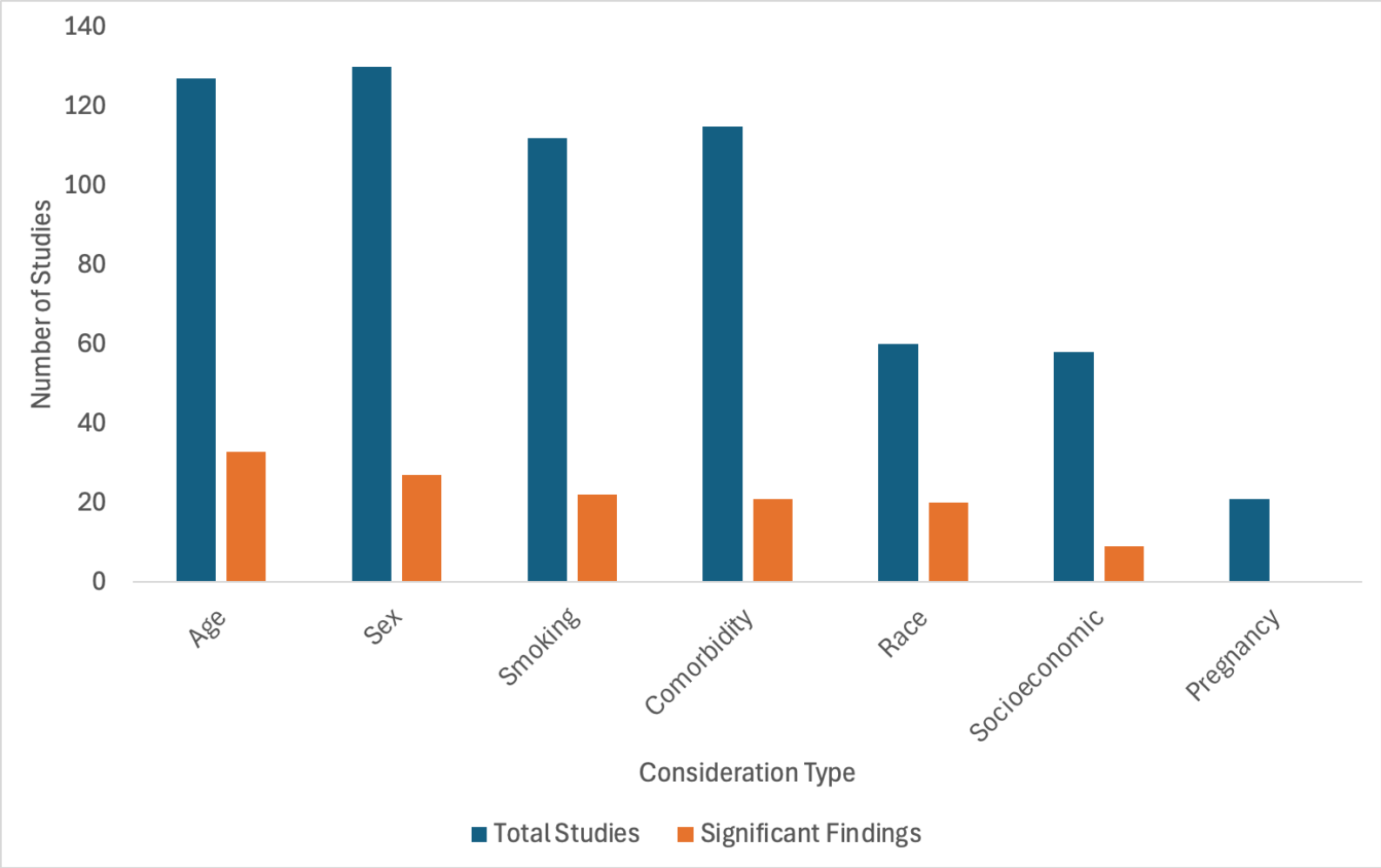


**Figure 3.** Bar graph illustrating the number of studies which generated significant findings related to specific considerations. The considerations analysed in this literature review are those related to age, sex, smoking, comorbidities, race, socioeconomic status, and pregnancy.

Smoking considerations are crucial in exploring the relationship between PD and CVD, with twenty one studies reporting statistically significant findings when comparing smoking and non-smoking populations. However, two studies noted differential effects in non-smoking populations that warrant further investigation. Dorn et al.,[59] found that the association between periodontal disease and recurrent cardiovascular events was significant only in never-smokers. Specifically, the adjusted hazard ratio (HR) for recurrent cardiovascular events associated with mean clinical attachment loss in never-smokers was 1.43 (95% CI: 1.09–1.89), indicating a 43% increased risk per millimeter increase in attachment loss. In contrast, no significant associations were found in ever-smokers. Similarly , Romandini et al,[60] reported that non-smoking females with normal HDL levels exhibited the strongest association between severe periodontitis and elevated platelet count. Individuals with severe periodontitis showed an adjusted increase of

13,048.93 platelets/μL (95% CI: 3,296.26–22,801.61; p = 0.009) compared to those without, suggesting an inflammatory link that may be especially relevant in CVD risk stratification.

Socioeconomic considerations were addressed in relatively few studies, with only nine (6.33%) finding a significant association between SES and the associations between PD and CVD.[51,53,54,61–66] Most studies assessed SES using education level as a proxy, with lower educational attainment linked to worse periodontal outcomes and increased cardiovascular risk. Income-related disparities in oral health outcomes were supported across three studies. Konopka et al.[66] found that individuals in the lowest income group exhibited significantly worse periodontal health compared to higher income groups, with mean values of 2.75 for the Community Periodontal Index, 1.94 for plaque index, and 1.55 for bleeding on probing — all markers of active periodontal inflammation and disease severity. These clinical measures progressively improved with increasing income levels, indicating a strong income gradient in periodontal status. A study by De Angelis et al.[65] reported that participants with lower income were more likely to have a higher number of missing teeth, a marker associated with long-standing untreated periodontitis. Individuals with more than 18 missing teeth had an odds ratio of 2.5 (95% CI: 1.1–6.6) for cardiovascular disease compared to those with fewer missing teeth, even after adjusting for confounding factors. The final article[64] found that lower socioeconomic status — measured through household income, maternal education, and economic class — was significantly associated with increased “Initial Periodontitis,” and this association was mediated by heightened systemic inflammatory burden (standardized coefficient = –0.022).

Comorbidity considerations were a significant focus in twenty one studies,[22,32,34,37,45,49,51,62,64,67–78] which found notable associations between PD and CVD in populations with one or more comorbid conditions, primarily diabetes, hypertension, and hyperlipidemia. Franek et al.[22] investigated type 2 diabetic patients with varying periodontal statuses and found that individuals with gingivitis or periodontitis were more than five times more likely to have increased carotid intima-media thickness (IMT ≥ 0.8 mm) — a surrogate marker of atherosclerosis — compared to periodontally healthy patients (OR = 5.25; 95% CI: 1.1–25). A study from Japan[32] found that among patients with CVD, those with poorly controlled diabetes (HbA1c ≥ 7.0%) had notably worse periodontal status, including greater clinical attachment loss and higher bleeding on probing rates.

Additionally, salivary counts of *Porphyromonas gingivalis* were more than five times higher in the uncontrolled diabetes group (median $8.9 \times 10^4$ CFU/mL) compared to the well-controlled group ($1.7 \times 10^4$ CFU/mL). Yamazaki et al.[34] further demonstrated that a tailored dental health education intervention in Japanese adults with at least two cardiometabolic risk factors (obesity, hypertension, dyslipidemia, or hyperglycemia) resulted in measurable reductions in cardiovascular risk. Specifically, the intervention group experienced a decrease in systolic blood pressure (–3.7 ± 12.5 mmHg) compared to an increase in the non-intervention group (+4.0 ± 15.9 mmHg), and a significant reduction in waist circumference (–1.6 ± 3.2 cm). These improvements coincided with decreased periodontal pocket depth and bleeding on probing, and increased interdental cleaning behavior. The findings suggest that even non-surgical periodontal interventions targeting behavioral change may yield systemic cardiovascular benefits, particularly in patients with existing comorbidities. These findings align with the expected trend that comorbidities amplify the link between PD and CVD, likely due to

shared inflammatory biomarkers and overlapping clinical parameters.[79] However, many studies within the broader literature opted to exclude patients with comorbidities in an effort to minimise confounding variables,[80] limiting the generalizability of their findings. Articles such as the ones exemplified above provide valuable insight into how comorbid conditions may interact with oral and cardiovascular health, reinforcing the need to study these diseases in the context of real-world, multimorbid populations.

## iii) Reported Barriers and Enablers to Integration of Oral and Cardiovascular Care

The reviewed articles presented a range of strategies to bridge the gap between medicine and dentistry, addressing the interconnected risks of PD and CVD. Several emphasised integrating oral health into broader CVD prevention and management strategies. Articles by Bazile et al,[81] D'Aiuto et al,[82] and Wożakowska-Kapłon et al,[83] proposed incorporating periodontal care into CVD risk assessments and prevention programs, while Belinga et al,[84] advocated for raising awareness among healthcare providers and the public about the link between PD and CVD. Larvin et al,[85] called for public health interventions targeting shared risk factors such as poor oral hygiene, smoking, and stress. Similarly, articles by Rutger Persson et al,[86] and Mustapha et al,[87] stressed the importance of referring high-risk patients with evidence of bone loss or bacterial exposure to both medical and periodontal examinations to mitigate systemic inflammation and reduce CVD risk.

Specific recommendations included the prioritizing gingival inflammation management as a strategy to reduce coronary artery disease risk and the integration of periodontal care into CVD prevention programs.[81,82] Petersen et al, [88] highlighted that, should further studies confirm a causal link between endodontic treatment and aortic atherosclerotic burden, endodontic therapies could achieve an entirely new status in the secondary prevention of CVD. Two articles underscored the necessity of multidisciplinary approaches and effective communication between dental and medical professionals,[89,90] one emphasised the synergistic effect of periodontitis and systemic inflammation on mortality.[89] These shared recommendations collectively suggest a pathway with potential to reduce the burden of PD and CVD through enhanced collaboration, targeted interventions, and the integration of dental and medical care frameworks.

## iv) Study of CVD and PD Biomarkers

Various biomarkers were examined across the 142 studies. CRP was the most researched biomarker with 47 of the studies naming CRP as a focus (Figure 4). Other highly studied biomarkers included lipid profiles and clinical markers (Figure 4). The lipid profile variable encompasses studies which examined the patients' HDL, LDL, triglyceride, or total cholesterol levels. Clinical markers included Gingival Index, number of teeth remaining excluding third molars, attachment level, bleeding on probing,as well as periodontal pocket depth. Seventeen studies examined Interleukins, the most prominent interleukins were IL-6, IL-23, and IL-1B. Antibodies were the focus of 8 studies, while multiple antibodies were

examined IgG was mentioned the most frequently. 93 of the 142 studies (65.49%) evaluated, examined more than one biomarker, 30 (21.13%) of the studies focused on only one type of biomarker, and 19 (13.38%) of the studies did not rely on any biomarkers to develop their findings (Figure 5). The 19 that did not rely on gathering biomarker data in their procedures to develop their findings were either meta-analyses which generated conclusions by examining the findings of pre-existing papers, or they collected their data primarily by means of a questionnaire which examined self reported confounding factors and or behaviours.

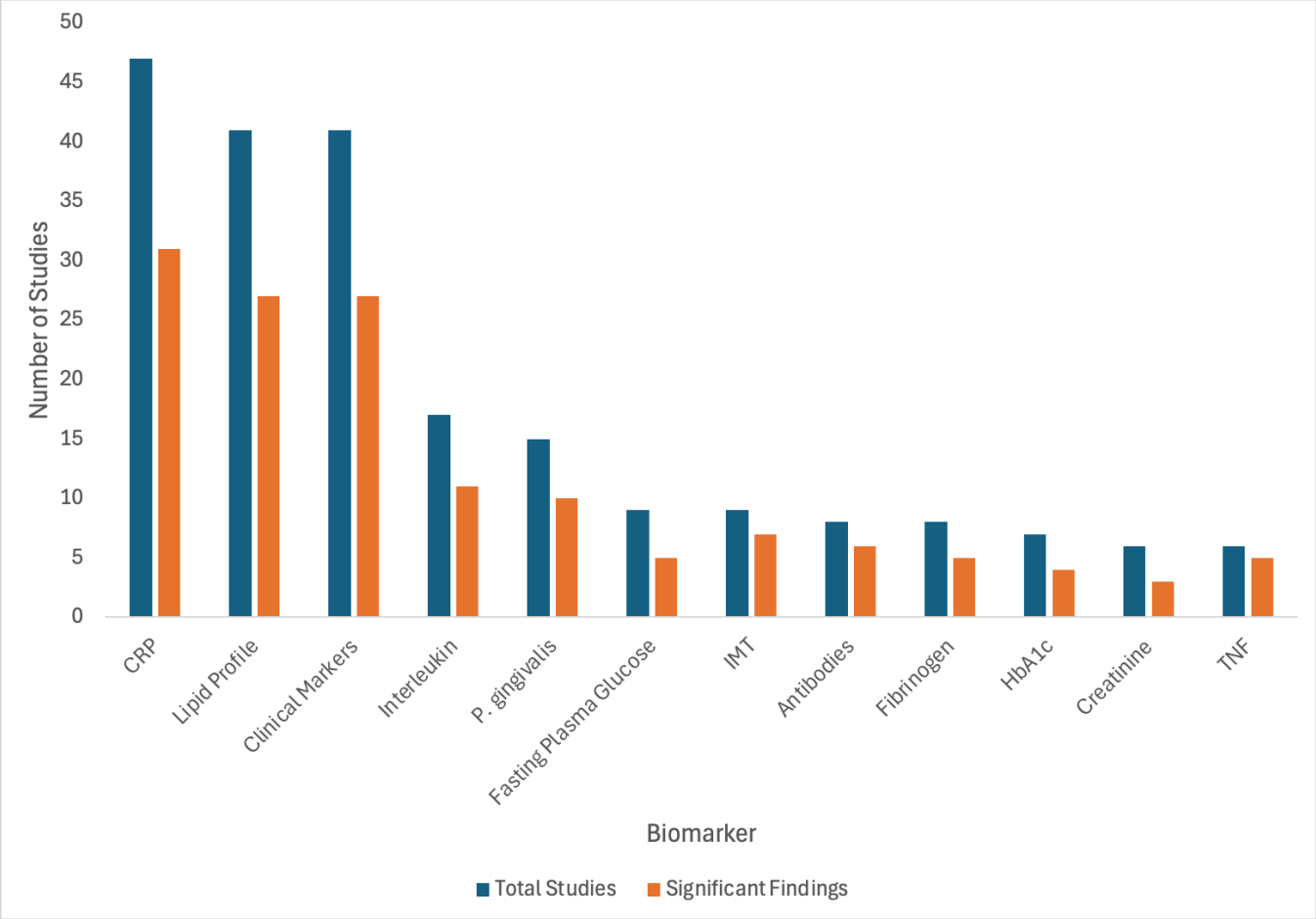


**Figure 4.** Bar graph illustrating the number of studies which focus on specific PD-CVD biomarkers. Lipid profile refers to any study which conducted a full lipid profile or examined LDL, HDL, triglycerides, and or total cholesterol levels.

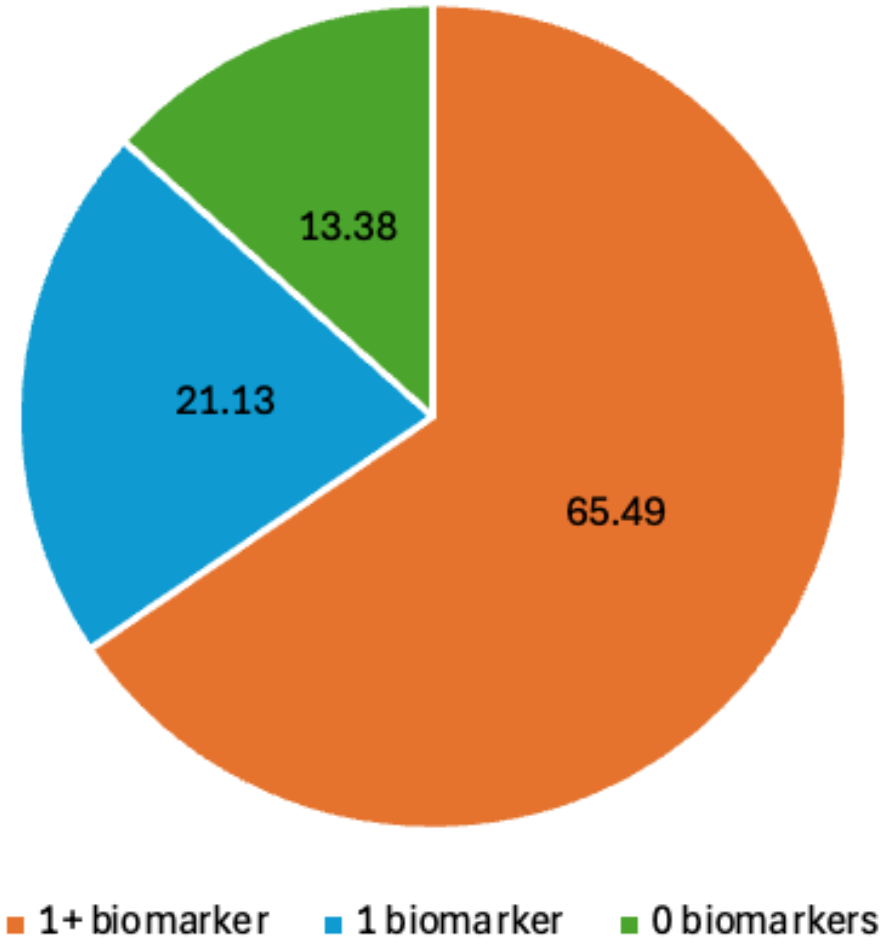


**Figure 5:** Pie chart illustrating the percentage of studies which relied on the examination of more than one, only one, and zero biomarkers in their research.

Emerging research emphasises the interplay between PD and CVD, with a significant focus on identifying direct causal and broader associative patterns. Notably, these studies arise from regions outside Canada, pointing to a discrepancy in localised research in this vital area of public health.

## v) Direct Causal Links Between PD and CVD

Out of the analysed articles, 5 provided strong evidence [29,87,91–93] for direct causal mechanisms linking periodontal pathogens to cardiovascular outcomes. A controlled experimental study[91] observed that *P. gingivalis*, a primary periodontal pathogen, plays a key role in facilitating atherosclerotic processes through CD36/SR-B2-TLR2 dependent pathways. This interaction is crucial because it promotes the invasion and sustenance of *P.gingivalis* in

arterial walls leading to inflammation and atheroma formation. *P.gingivalis* utilises these receptor pathways to heighten lipid uptake by foam cells, a characteristic of atherosclerotic plaque formation. By binding to CD36, a receptor on macrophages, *P. gingivalis* promotes oxidative stress and inflammatory cytokine production via the Toll-like receptor 2 (TLR2). These molecular occurrences result in the activation of the NF-κB signalling pathway, which increases the inflammatory responses within vascular tissues and leads to plaque instability. This mechanistic link was observed in an experimental study in the US[91] , revealing that a *P. gingivalis* infection contributes to significant heightening of the development of atherosclerotic lesions. Such a finding was exemplified by a 175% in lesion development in males and 225% in females who were exposed to the bacterial pathogen.

Additionally, a 10-year retrospective follow-up study conducted in Korea[29] observed chronic exposure to periodontal pathogens, which significantly increased in acute myocardial infarction (AMI) incidence, whereas severe periodontal disease raised AMI risk by 11% over a span of 10 years. A multivariable Cox regression analysis validated individuals with pathogen induced severe PD to reveal a significantly increased risk of developing AMI. The epidemiological results emphasised a clear relationship between the severity of PD and the risk of AMI, which is quantified through adjusted hazard ratios that account for traditional CV risks like age, smoking status, diabetes and hypertension. Such adjustment ensures that the increased risk observed in affiliation with PD is independent of other common CV risk factors. These findings by Cho et al,[29] underscored the potential of periodontal bacteria to actively partake in the atherogenic process.

## vi) Associative Links Supporting Direct Causal Relationship

Systemic markers of bacterial exposure from PD were significantly associated with an increased risk of CVD. One article[87] recorded a summary odds ratio of 1.75 for coronary heart disease associated with periodontal disease indicating a statistically significant predictive relationship between periodontal bacterial burden and cardiovascular risk. Additionally, another study observed that all markers of periodontitis and systemic inflammation were significantly associated with heightened CVD and all-cause mortality.[68] Each standard deviation increase in clinical attachment level (CAL) was associated with a hazard ratio of 1.205 (95% CI: 1.097–1.323) for all-cause mortality and 1.225 (95% CI: 1.042–1.439) for CVD mortality. Similarly, the inflammation score showed a hazard ratio of 1.358 (95% CI: 1.210–1.523) for all-cause mortality and 1.385 (95% CI: 1.141–1.681) for CVD mortality. Interaction models on the additive scale indicated substantial excess mortality risks when both periodontitis and inflammation were elevated, with relative excess risks due to interaction (RERI) suggesting an 18.9% and 27.8% increase in all-cause and CVD mortality, respectively. These observations reveal the critical role of systemic inflammation in connecting periodontal health to CV outcomes.

## Discussion

In this scoping we aimed to synthesize existing information on shared biological mechanisms and crucial factors contributing to the relationship between PD and CVD by examining relevant primary research studies and meta-analyses. This synthesis also allowed us to identify systemic barriers preventing interdisciplinary collaborations between medical and dental professionals. Geographically, we found that the United States was the largest contributor to research concerning the PD-CVD link. A range of overlapping risk factors such as age, sex, smoking behaviours, comorbidity diagnosis, and socioeconomic status, were considered, with age showing the highest number of significant associations. Many of the studies examined at least one biomarker to draw conclusions. Clinical markers, however, including but not limited to gingival index, number of teeth remaining excluding third molars, attachment level, and periodontal pocket depth were also thoroughly studied to examine the PD-CVD link.

The diverse and overlapping risk-factor considerations - such as such as sex, age, smoking, SES, and comorbidities—reveal the challenges of addressing these conditions within existing healthcare frameworks. As mentioned, only two studies[27,28] exclusively examined female populations, illustrating an imbalance in research design for sex and gender based analysis (SGBA+). The disproportionate impact on male populations highlights the importance of considering sex-specific biological and social determinants in shaping disease progression. Similarly, age-related trends show that older populations typically exhibit higher risk, while younger populations generally show lower risk, with significant associations occurring less frequently. This gradient reflects the difficulty of isolating specific causal pathways amidst competing health risks and comorbidities. One possible explanation for this finding is that younger populations may have fewer competing health risks,[97] allowing the relationship between PD and CVD to emerge more clearly in statistical analyses. These findings suggest that while age is generally proportional to PD/CVD risk, younger populations might also demonstrate unique patterns of association, partly due to study design limitations or exclusions that simplify the analysis of age-related trends.

Smoking, while a well-established risk factor, shows variability in its influence. Some studies find significant associations even in non-smokers, which points to unexplored mechanisms or limitations in study designs.This anomaly suggests that other unidentified mechanisms may contribute to the PD/CVD link in non-smoking populations, particularly when traditional risk factors such as abnormal HDL are absent.

Race was mentioned in twenty studies, but most categorised participants simply as "white" or "non-white," resulting in limited granularity. Despite its inclusion, race was not identified as a significant factor in the association between PD and CVD in these studies. While race is a social construct, it is known to be tied to various health disparities, with BIPOC populations often facing higher rates of chronic disease and premature deaths.[98] One review article conducted by Macias-Konstantopoulos et. al,[99] found that these health disparities caused by race lead to a higher prevalence of NCDs such as hypertension and type 2 diabetes mellitus. Both hypertension and type 2 diabetes mellitus are highlighted in this review as CVD risk factors. This suggests that the role of race in the context of the association between PD and CVD is inadequately explored.[100] This lack of detailed analysis highlights a potential gap in the

literature that warrants further investigation to determine whether race plays a meaningful role in shaping susceptibility to these conditions.

SES, though less frequently studied, highlights inequities in healthcare access and preventive practices which disproportionately affect vulnerable populations. As per the World Health Organization,[101] health and illness follow a social gradient where a lower socioeconomic position correlates to worse health. In countries with privatised dental care, for example, individuals with lower SES may see a dental practitioner less frequently—if at all.[102] These intertwined risk factors illustrate the systemic and interdisciplinary challenges in managing PD and CVD, reinforcing the need for integrated healthcare models that address biological, behavioural, and social determinants of health.[103,104] Without such an approach, the fragmented nature of current models of care will continue to hinder effective prevention, early diagnosis, and management. As a result, these interconnected conditions will continue to be perpetuated as enduring healthcare challenges.

As demonstrated in this review, biomarkers and pathogens are not the only means of studying the PD-CVD connection. We found that 13.38% of the papers reviewed did not use biomarkers at all, choosing instead to either analyse pre-existing data or collect data in the form of a questionnaire. Questionnaires offer unique insights into the patients' health by examining various confounding factors. These included the patients' family history of NCDs, their use of prescription medications, education level, and exercise behaviours. Examining these factors can allow researchers to develop context for biomarker findings. For example, while biomarkers such as CRP, lipid profiles, and *P. gingivalis* give objective measures of biological processes in response to disease,[105] information provided by clinical markers and questionnaires can help the researcher determine social determinant patterns which also play a crucial role in population health.[106] Using both methods of research together will allow the researcher to ensure that their results capture the full extent of the disease in their participants. As mentioned, the PD-CVD connection is multifaceted, and as such the research methods must consider all contributing factors to bridge gaps in the research.

When analysing the articles to discern the associations, which involved shared pathways, and/or confounding risk factors between PD and CVD, certain limitations were noted. A primary limitation was the lack of direct mechanistic links found within the research between these two diseases. This limitation prevents wicked problem identification and results in a broad spectrum of solutions that do not reach the root of the concern, and/or omit critical contributing factors. In extension, many of the articles did not comprehensively assess either PD or CVD regarding potential association. For example, one study included participants with coronary heart disease, a type of CVD, and examined the role of TNF-α in PD. The primary focus of this article was the inflammatory markers of PD, and although CHD was mentioned, a rigorous effect assessment remained absent. This interdisciplinary field of research suffers from a lack of clinical trials. As a result, there is a lack of data which attests to the PD-CVD wicked problem in a clinical setting. Lack of vital data from clinical trials also leads to delayed medical findings, bias and inequality in patient care and outdated public health policies, and underrepresentation of certain populations.[107,108]

As previously mentioned, out of a total of 142 articles only 20 appropriately accounted for race and ethnicity considerations; 27 considered differences based in sex; 9 adjusted for socioeconomic factors and 0 considered pregnancy. In Canada, this lack of research is a

prominent concern. Only 1 research paper—out of the total 142—was performed in Canada as a collaboration with the University of Alberta. This means that the Canadian population is underrepresented in this area of research. This disparity in research could be a result of the extremely limited number of dental schools in Canada,[109] limiting the amount of potential research facilities. Further, as of 2023, Statistics Canada reported that only 65% of Canadians had seen a dental professional in the 12 months prior to 2022.[110] This 65% of Canadians consisted of only 49% of the lowest income quintile and 79% of those in the highest income quintile.[110] These statistics illustrate the limited granularity of Canadian dental patients. As a result, Canadian dental research may be limited due to challenges in recruiting a sufficiently diverse population to limit bias. As researchers in Canada, this underrepresentation limits our ability to propose evidence based solutions that account for unique demographic characteristics and regional health disparities. Canadians, however, can benefit from accessible and applicable research conducted in other nations. For example, global studies that record and report information on their patient demographics can produce findings that can be applied to areas in Canada with similar patient populations.

Applicability of research from other countries to the Canadian landscape, however, does not resolve the lack of communication between Canadian medical and dental systems. This segregation of medicine and dentistry, due to discrepancies in privatisation, creates a lack of communication between the disciplines. This fragmentation perpetuates a siloed perspective on healthcare as a whole, preventing the development of a cohesive approach to address the intercorrelated nature of PD and CVD.

Our results emphasise the relevance of addressing these gaps, particularly through therapeutic interventions tailored to specific risk groups. For instance, if men are found to be more at risk for both PD and CVD, targeted interventions aimed at male populations could be developed. Similarly, if low socioeconomic status is identified as a significant risk factor, healthcare and oral health practitioners could collaborate to design accessible interventions for underserved communities. For example, understanding the underrepresentation of confounding factors like race and ethnicity, SGBA+, and SES, allows us to contextualise problems within the current Canadian healthcare landscape that warrant more research.

## Conclusion

This scoping review has synthesised ample evidence supporting a direct relationship between PD and CVD. To the best of our knowledge, however, no previous research has explicitly proposed the implementation of interventions designed to bridge the communication gaps between healthcare and oral health disciplines. While some recommendations in the existing body of research highlight the importance of interdisciplinary collaboration, a specific plan or protocol has not been proposed. This gap underscores a significant opportunity for advancing integrated care strategies that could improve outcomes for high-risk patients with PD.

# Recommendations

A growing body of evidence highlights the need for a preventive, interdisciplinary approach when managing patients with PD who may also be at risk for CVD. While we have confirmed the association between the progression of PD to systemic dysregulation and a heightened CVD risk, the siloed nature of dental and medical care often hinders timely interventions for at-risk patients.[111] To address this gap, we propose a systematic screening tool for dental practitioners to use during routine periodontal evaluations. The overarching goal is to identify patients who present with specific risk factors, both periodontal and systemic, and to foster streamlined communication between general dental practitioners (GDPs) and general medical practitioners (GPs). By recognizing and referring high-risk individuals early, dental teams can help prevent or mitigate the progression of CVD, in turn improving patient health outcomes.[112]

## i) Checklist for Dental Practitioners

A successful screening protocol must be grounded in practical, evidence-based criteria which captures both periodontal status and modifiable cardiovascular risk factors. Common findings from the literature indicate that certain clinical periodontal measurements, such as periodontal pocket depth beyond 4 mm, severe attachment loss, and bleeding on probing, often show a stronger association with systemic inflammatory markers linked to CVD.[113] These markers are further amplified by specific patient attributes most notably including smoking frequency, older age, and comorbid conditions such as diabetes.[114] Based on patterns observed through the data extraction process, the proposed screening checklist identifies five categories of risk.

**Periodontitis severity indicators** encompass pocket depths of 3 mm or more, clinical attachment loss, and notable gum recession.[3,115] Studies [94,114] have found that deeper periodontal pockets often indicate heightened systemic inflammation, as periodontal pathogens and inflammatory cytokines may enter the bloodstream more readily.[116] Although individual articles vary in defining “severe” PD, pocket depths consistently stand out as a key metric to highlight. Dental practitioners could incorporate a simple threshold - for example, any pocket measuring 5 mm or greater — which would flag the patient as needing further medical consultation, especially if other risk factors are present.

**Medical risk factors and patient histories** would serve as another risk category. Smoking is an especially salient factor within this category, as numerous studies have linked tobacco use with both periodontal deterioration, as well as a pronounced risk of atherosclerotic changes.[117,118] Thus, it would be preferential for GDPs to inquire patients about their smoking status (current, former, or never), smoking frequency, and duration of tobacco usage. Patients who report moderate-to-heavy smoking could be flagged for referral, given the synergy between smoking, periodontal inflammation, and endothelial dysfunction.[119] Similarly, pre-existing conditions such as hypertension or diabetes should be flagged in the patient’s dental record as

research suggests that even when these conditions are considered well-managed**,** PD worsens systemic inflammation and thus, CVD risk for these individuals is compounded.[120,121]

**Demographic considerations** may also serve as a risk category. For example, older adults generally face an increased burden of PD and CVD.[122,123] Several of the extracted articles noted that individuals over 65 show more severe alveolar bone loss and a higher rate of cardiovascular complications. Although the correlation is not exclusively age-dependent, age-based screening thresholds may help prioritize patient follow-up. It is worth acknowledging that certain studies also highlight sociodemographic factors such as lower socioeconomic status and limited access to routine care. While Canadian seniors have recently been awarded dental benefits through the novel Dental Care Plan, many still remain under-insured, as this program is only intended to cover basic dental costs.[124,125] These circumstances further justify the value of a straightforward screening tool that captures the most at-risk segments of the population.

Another screening category may include **race considerations.** While race is not consistently accounted for in health-centred literature, some studies do highlight that racialized communities often face disparities in access to both dental and medical care.[126,127] These disparities are often driven by socioeconomic and structural factors rather than inherent biological differences. In regions with pronounced health inequities, racial and ethnic considerations can intersect with reduced continuity of care, delayed diagnoses, and unaddressed comorbidities such as diabetes, which is an established risk factor for both periodontal disease and CVD.[128]

Finally, **additional periodontal or systemic markers** may be the last category for consideration. Dental teams can collect information on key indicators such as the frequency of gum bleeding and recurrent periodontal abscesses, both of which can signal persistent periodontal disease.[129] While these factors may not be as quantifiable as periodontal severity indicators, they provide valuable clinical insights into ongoing inflammation. When cross-referenced with known cardiovascular risk markers—such as a family history of heart disease or abnormal cholesterol levels (if disclosed by the patient)—these observations can help GDPs make more informed referral decisions. Although most dental offices do not routinely assess systemic biomarkers such as CRP, inquiring about recent medical test results that indicate elevated inflammatory markers may provide useful contexts. Integrating such discussions into dental assessments could strengthen the link between oral and systemic health, supporting timely medical referrals when necessary.[130]

## ii) The Urgent Need for Streamlined Interprofessional Communication

Recognizing high-risk patients without robust mechanisms for referral and follow-up is insufficient. Research on interprofessional communication has revealed that time constraints and a lack of established referral pathways often prevent GDPs and GPs from collaborating effectively.[130] Similarly, resources from the National Academy of Medicine highlight the importance of effective communication, collaboration, referral processes, navigation, and feedback between providers and patients as key strategies for bridging the gap between medical and dental care.[131] This is especially relevant for high-need individuals who may not

otherwise see a physician, as the dentist's role becomes a gateway for broader health assessment.

## iii) Approaches to Implementing a Dental-Medical Referral Network

Much like referrals between optometrists and GPs or physiotherapists and GPs, a streamlined, standardized referral form could be the anchor for effective cross-specialty communication. This form, integrated into the dental practice's workflow, would capture the critical details of the patient's periodontal status—especially any indicators from the screening checklist—along with relevant notes on systemic health factors (e.g., "Patient is a heavy smoker with periodontal pocket depths >5 mm; strong suspicion of elevated cardiovascular risk"). The goal is to ensure GPs have concise documentation of the patient's oral health context and over time, as these forms become standardized, it will reduce guesswork and improve acceptance rates for referrals.

Such a referral process should be initiated as soon as a patient identified as high-risk presents with periodontal disease, whether during a routine dental visit or an initial assessment. This step is particularly important at the first presentation, as early intervention can greatly influence cardiovascular outcomes. Beyond the initial visit, regular follow-ups—such as periodontal maintenance appointments—can help reinforce the referral process. These follow-ups offer an opportunity to update medical records and track disease progression. Any changes in the patient's periodontal status or overall health should be communicated to their general practitioner, ensuring coordinated and timely care. Ideally, the referral system becomes a seamless part of the patient's long-term care continuum.

Additionally, we suggest the creation of a shared electronic health record channel for GPs and GDPs. Universal electronic health records are still rare in many regions, but local pilot programs or partnerships (e.g., between large dental clinics and nearby family practices) could create shared portals. Kaiser Permanente and HealthPartners in the United States illustrate the effectiveness of integrating medical and dental records: unified digital platforms allow providers to see real-time updates of patients' medical history, medication lists, and lab results.[131] Even if a fully integrated approach is not immediately feasible in every Canadian jurisdiction, partial solutions—such as a secure messaging platform or a regionally shared database—can facilitate timely communication.

Although dentistry in Canada frequently operates as a privatized service, certain groups—such as seniors or those enrolled in specific provincial programs—can access subsidized care.[132] The targeted approach of a PD–CVD screening tool is therefore especially valuable for these populations, where age or socioeconomic factors might compound risk. By integrating referrals in such contexts, a subset of patients who frequently interact with dentists (e.g., for denture adjustments or re-care visits) could be directed to comprehensive medical assessments that they would otherwise miss. In turn, GPs can monitor or adjust antihypertensive or hypoglycemic regimens with greater context of the patient's oral inflammatory status, acknowledging that persistent gum infection may negatively influence cardiovascular health.

## iv) Future Directions

Beyond the immediate objectives of risk identification and referral, additional research in Canada is needed to validate whether an integrated PD–CVD screening model measurably decreases cardiovascular incidence or severity. Longitudinal studies, such as multi-center trials or province-wide retrospective reviews, could evaluate whether early referral from dentists correlates with lower rates of myocardial infarction, stroke, or costly interventions. Parallel work might investigate health outcomes among subpopulations, considering how factors like smoking, advanced age, and poor oral hygiene interact with the screening tool's predictive value. Ultimately, this research could yield more refined, evidence-based tools that hone in on the best combination of periodontal metrics and systemic indicators.

Schulich
MEDICINE & DENTISTRY

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