

REVIEW ARTICLE

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PERIODONTITIS AND SYSTEMIC DISEASE: HOW MUCH MORE EVIDENCE DO WE NEED?

Erida Çela^{1,*}, Ardita Koçi¹

¹Department of Dentistry, Faculty of Dental Medicine, Western Balkans University, 1001 Tirana, Albania

*Corresponding author: E-mail: e.cela22@wbu.edu.al

Abstract

Periodontitis is not just a condition of the mouth. It is a chronic inflammatory disease with potential effects on numerous organ systems of the body. The periodontopathic bacteria, such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, can enter the systemic circulation from the periodontal pocket and have an impact on the body's organs distant from the oral cavity. To review the links between periodontitis and nine systemic disease domains, distinguishing mechanistic, observational, interventional, and causal evidence. This narrative review was supported by a systematic search of PubMed/MEDLINE, the Cochrane Library, and Scopus between January and June 2026. The majority of the reviews used in this paper are peer-reviewed journal articles published between 2016 and 2026. These articles include review articles, evidence-based studies such as Mendelian randomization studies, umbrella reviews, and reviews from professional organizations such as the European Federation of Periodontology, the World Heart Federation, and WONCA Europe. The evidence is strongest for diabetes mellitus, where the relationship (as explained later on) is bidirectional and periodontal treatment reduces HbA1c by 0.43% at 3–4 months. For cardiovascular disease, associations are consistent, but treatment trials with cardiovascular events are lacking. Mendelian randomization findings are mixed, and the links with pregnancy outcomes and neurological conditions remain conflicting or mainly mechanistic. Additionally, a relatively new concept in the fields of immunology and inflammation is discussed, namely the phenomenon of trained immunity and myelopoiesis as a potential explanation for the systemic inflammatory effects of periodontitis even after the periodontal infection has resolved. The evidence presented in this paper indicates that periodontitis is a disease with multiorgan system involvement that merit a place within the medical disciplines beyond dentistry alone, most clearly in endocrine (especially for diabetes patients) and cardiovascular care, while trials with clinical endpoints are still needed for most other domains.

Keywords: Periodontitis, oral health, systemic inflammation, cardiovascular diseases, diabetes mellitus, bidirectional relationship

1. Introduction

1.1. Background and Context of the Research

In the body, few diseases are local in their effects. The human body functions as one system, and the effect of any disease or inflammation is reflected throughout the body in various ways [1,2]. Periodontal disease, one of the most common forms of chronic infection of the body, took decades to reveal its relationship to the remainder of the body and centuries for us to understand.

1.2. Problem Statement

Let's consider a relatively simple fact about periodontal disease. Periodontitis is a wound, and *not* a wound in the metaphorical sense, but one in the literal sense of the body. Within the ulcerated pocket epithelium of periodontitis is a wound that can open to a vascularized surface of between 8 and 20 cm², which sits in constant contact with one of the densest microbial ecosystems within the human body [3]. Unlike almost any other wound in the human body, the periodontal wound persists for years with direct access to the bloodstream. Thus, *the periodontal wound* does not remain a quiet wound that heals in the body unnoticed by its host; rather, it communicates with the body's systems and organs through the language of the body's inflammatory response.

1.3. Aim and Objectives of the Research

Periodontitis has historically been treated as a local disease within the body, as it was thought to affect the soft and hard tissues of the periodontium, leading to tooth loss [4]. However, as will be discussed within this paper, the links between periodontitis and other systemic diseases in the body date back to the 1990s when it was discovered that individuals with periodontitis had higher rates of cardiovascular mortality than those without the disease [5]. Since then, numerous diseases have been linked to periodontitis, with many communicable and non-communicable diseases linked to the periodontal condition [6]. The molecular biology and genetics of these diseases have been explored, but perhaps most importantly, the use of Mendelian randomization has helped to test causation between periodontitis and numerous other diseases, with mixed results.

1.4. Research Questions and Hypotheses

Within this paper, the links between periodontitis and numerous systemic diseases will be explored. The purpose of this paper is to show that the links between periodontal disease and the systems of the human body are rooted in biology, genetics, and medicine, and, therefore, impact the discussion of how the disease should be treated. For each systemic domain, the evidence is examined to distinguish mechanistic plausibility, observational association, interventional evidence, and causal evidence. Periodontal disease is not only a dental problem; rather, its impact on the body impacts the discussion of medicine as a whole.

1.5. Significance of the Research

The work that is presented within this paper began as a conference talk delivered at the International Conference on Medicine and Translational Biosciences (ICMTB 2026) entitled "Periodontitis and Systemic Disease: How Much More Evidence Do We Need?" What follows is an expanded discussion of that conference talk, with more detail and with the most up-to-date literature on the topic of periodontitis and its impact on the human body.

2. Materials and Methods

2.1. Study Design

This study is a narrative literature review, supported by a systematic search strategy, designed to synthesize current evidence on the associations between periodontitis and 9 (nine) categories of systemic disease: cardiovascular disease, diabetes mellitus, chronic kidney disease, non-alcoholic fatty liver disease, respiratory disease, rheumatoid arthritis, adverse pregnancy outcomes, Alzheimer's disease, and oncological conditions. A narrative review design was selected because the clinical and mechanistic terrain under investigation spans multiple medical disciplines and required integrative synthesis rather than

quantitative meta-analytic pooling. A systematic review addresses a single focused question with a common exposure and outcome, whereas each of the nine domains examined here would require a separate protocol, and the outcomes reported across them are not commensurable. The systematic search strategy described in Section 2.2 was therefore adopted to support the narrative synthesis rather than to replace it, ensuring that the evidence base remains transparent and reproducible, in keeping with current guidance for narrative reviews [7]. The review is not presented as a systematic review: no protocol was registered, screening was not performed in duplicate, and methodological quality was appraised against the hierarchy of evidence described in Section 2.5 rather than with a formal risk-of-bias instrument. The review was conducted between January and June 2026.

2.2. Literature Search Strategy

A systematic search of the peer-reviewed literature was conducted across three major biomedical databases: PubMed/MEDLINE, the Cochrane Library, and Scopus. Additional targeted searches were performed using Google Scholar to capture recent preprints, consensus documents, and conference-derived publications not yet indexed in primary databases. Reference lists of included articles were also hand-searched to identify additional relevant sources. The following Boolean search string was used as the primary search framework, with modifications applied for each systemic condition: ("*periodontitis*" OR "*periodontal disease*") AND ("*systemic disease*" OR "*cardiovascular*" OR "*diabetes*" OR "*chronic kidney disease*" OR "*NAFLD*" OR "*MASLD*" OR "*respiratory*" OR "*COPD*" OR "*rheumatoid arthritis*" OR "*pregnancy outcomes*" OR "*Alzheimer's disease*" OR "*cancer*" OR "*oncology*"). Searches were restricted to English-language publications. No strict date restriction was applied at the search stage; however, priority was given to studies published from 2020 onward, to align with the 2017 World Workshop Classification of Periodontal and Peri-Implant Diseases [8] as the definitional baseline for periodontitis. Landmark studies published before 2018 (e.g., Beck et al. [5]) were retained where they represented foundational evidence in their respective domains.

2.3. Inclusion and Exclusion Criteria

Inclusion criteria:

- Peer-reviewed original research articles, systematic reviews, meta-analyses, umbrella reviews, consensus reports, and Mendelian randomization studies
- Studies reporting on the association, epidemiology, pathophysiological mechanisms, or clinical outcomes of the relationship between periodontitis and at least one of the nine systemic conditions under review
- Studies in human populations or, where mechanistic evidence was reviewed, in vitro and animal studies of direct translational relevance

Exclusion criteria:

- Non-peer-reviewed sources, editorials, and opinion pieces without supporting data (except where cited as consensus statements from major professional federations)
- Studies in which periodontitis was not specifically defined or distinguished from other oral conditions
- Duplicate publications reporting on the same dataset
- Studies with unresolvable methodological concerns regarding exposure or outcome definitions

2.4. Materials

The primary materials of this review consisted of published scientific literature. No biological specimens, laboratory equipment, chemical reagents, or human participants were directly involved. The corpus of evidence synthesized includes randomized controlled trials, prospective and retrospective cohort studies, cross-sectional studies, case-control studies, Mendelian randomization analyses, systematic reviews and meta-analyses, umbrella reviews, and international consensus documents co-authored by major professional federations including the European Federation of Periodontology (EFP), the World Heart Federation (WHF), and the World Organization of Family Doctors (WONCA Europe).

2.5. Data Extraction and Quality Assessment

Data were extracted from each included source according to a standardized framework capturing the following elements: study design, population size and characteristics, exposure definition (how periodontitis was diagnosed or operationalized), outcome measures, confounding variables accounted for, and key findings. For mechanistic studies, the biological pathway under investigation and the level of evidence (in vitro, animal model, or human) were additionally recorded.

The methodological quality of included studies was informally assessed using the following hierarchy of evidence: Mendelian randomization analyses and randomized controlled trials were considered the highest level of causal evidence; systematic reviews and meta-analyses of observational studies were considered high-quality epidemiological evidence; individual prospective cohort studies were ranked above cross-sectional and retrospective designs. Consensus documents from major international bodies were treated as high-authority clinical summaries rather than primary evidence.

2.6. Variables and Analytical Framework

Given the narrative design of this review, formal statistical analyses were not performed. The independent variable across all sections is the presence and severity of periodontitis, defined per the 2017 World Workshop Classification. The dependent variables are the clinical outcomes and disease associations specific to each systemic domain, including cardiovascular endpoints (e.g., myocardial infarction, arterial plaque formation, atrial fibrillation), metabolic endpoints (e.g., HbA1c levels, insulin resistance), renal endpoints (e.g., glomerular filtration rate decline, CKD progression), and oncological endpoints (e.g., cancer incidence and mortality). Where quantitative effect estimates are cited from included studies (e.g., odds ratios, relative risks, HbA1c reductions), these are reported directly from the source publications and were not recalculated.

2.7. Synthesis Method

Included evidence was synthesized thematically, organized by organ system and clinical domain. For each domain, evidence is presented in the following sequence: (1) epidemiological foundation, (2) proposed mechanistic pathways, and (3) clinical and interventional implications. Where evidence from multiple study designs was available for the same association, findings were cross-referenced, and areas of convergence or conflict were discussed. The principal studies for each domain are summarized in Table 1, and the strength of evidence across domains is compared in Section 4.1.

2.8. Ethical Considerations

As this study is a narrative literature review that synthesizes only previously published data from peer-reviewed sources, no ethical approval, institutional review board clearance, or informed consent was required. No human participants, biological materials, or identifiable personal data were involved at any

stage. All cited sources are acknowledged in accordance with Vancouver referencing guidelines, and the intellectual property rights of cited authors and publishers have been respected throughout.

3. Results

3.1. Cardiovascular Disease

The cardiovascular link is the oldest and the best documented with periodontal disease. Beck et al. [5] were among the first to report higher cardiovascular mortality among individuals with periodontitis, and three decades of subsequent work have moved the finding from observation toward mechanism. The EFP consensus report of Sanz et al. [9] confirms links between periodontitis and atherosclerosis and myocardial infarction, with more limited evidence for atrial fibrillation and heart failure, identifying endothelial dysfunction, repeated bacteraemia, and elevated CRP and fibrinogen as plausible mediating pathways. The EFP/WONCA Europe consensus [10] carried these conclusions into general medical practice. Epidemiological consistency is supported by an umbrella review [11] and by a meta-analysis demonstrating that the association holds independent of sex, although with very low certainty of evidence [12], while imaging and genetic data [13] supply a layer of evidence that observational designs alone cannot provide. Mendelian randomization has extended the relationship to cerebrovascular outcomes, with Ma et al. [14] reporting a potential causal effect of chronic periodontitis on cardioembolic stroke.

3.2. Diabetes Mellitus

Diabetes is the domain in which the relationship is most fully characterised, and it is the clearest example of bidirectionality in the whole human system. Stöhr et al. [15], pooling 427,620 participants, found a 26% increased risk of diabetes mellitus (predominantly type 2) among individuals with periodontitis. In the opposite direction, hyperglycaemia increases periodontal susceptibility through the accumulation of advanced glycation end products and their receptor-mediated inflammatory signalling [16,17], while periodontal inflammation may impair insulin signalling through TNF- α pathways [18]. The interventional evidence is also strongest here: the Cochrane review by Simpson et al. [19] found moderate-certainty evidence that periodontal treatment reduces HbA1c by 0.43% at 3–4 months, which makes periodontal therapy one of very few dental interventions with a measurable metabolic endpoint.

3.3. Chronic Kidney Disease

Chapple et al. [20], reviewing the interplay between the two conditions, describe periodontitis as an independent risk factor for chronic kidney disease. The shared substrate is chronic low-grade inflammation, oxidative stress, and endothelial injury, with the additional consideration that renal impairment itself alters host response and wound healing in the periodontium. As in diabetes, the relationship appears to run in both directions rather than in one.

3.4. Hepatic Disease

Tan et al. [21], using a two-sample Mendelian randomization design, reported genetic evidence suggesting a causal link between chronic periodontitis and non-alcoholic fatty liver disease. The proposed pathway is the translocation of bacterial lipopolysaccharide into the portal circulation, activation of TLR-4 on hepatic cells, and downstream TGF- β /SMAD signalling driving fibrogenesis. Because the liver receives the portal drainage of the gastrointestinal tract, it is anatomically positioned to receive whatever the periodontal wound releases into the swallowed and circulating burden, which makes the hepatic association mechanistically coherent rather than incidental.

3.5. Respiratory Disease

Gomes-Filho et al. [22], in a systematic review with meta-analysis, reported higher odds of pneumonia, COPD, and asthma in patients with periodontitis. Here the route is not primarily haematogenous but rather aspirational: oral pathogens colonising the periodontal pocket are aspirated into the lower airway, where they act on already compromised respiratory epithelium. Respiratory disease was included alongside cardiovascular disease and diabetes in the EFP/WONCA Europe consensus [10], which places it among the associations considered established enough to warrant attention in general practice.

3.6. Rheumatoid Arthritis

The link with rheumatoid arthritis is mechanistically the most specific of all the domains reviewed. *P. gingivalis* is the best-known prokaryote to express peptidylarginine deiminase (PAD), the enzyme that citrullinates host arginine residues. Citrullinated peptides are the antigenic target of anti-cyclic citrullinated peptide (anti-CCP) antibodies, the serological hallmark of rheumatoid arthritis, and PAD-mediated citrullination has therefore been proposed as central to connecting oral infection with autoimmune activation [23]. This gives the oral-systemic link in RA a molecular candidate rather than only a shared inflammatory burden. The interventional evidence is consistent with the connection: an overview and meta-analysis of 18 primary studies found that non-surgical periodontal treatment produced a significant reduction in disease activity from baseline to up to three months after treatment, with a mean difference in DAS28 of -0.76 (95% CI -1.07 to -0.44), alongside decreases in C-reactive protein and erythrocyte sedimentation rate [24], although these data derive mainly from before-and-after comparisons.

3.7. Adverse Pregnancy Outcomes

Raju and Berens [25] review the evidence connecting periodontal status with adverse pregnancy outcomes, principally preterm birth and low birthweight. The proposed mechanism combines haematogenous spread of periodontal pathogens to the fetoplacental unit with the systemic elevation of inflammatory mediators, particularly PGE2 and IL-6, which participate directly in the initiation of labour. However, the evidence for this association remains not fully understood.

3.8. Neurodegenerative Disease

Periodontal pathogen-derived lipopolysaccharide has been proposed to contribute to neuroinflammation and to amyloid aggregation, with amyloid precursor protein processing and blood-brain barrier permeability as the intermediate steps. Oxidative stress has been proposed as the unifying link between periodontitis and Alzheimer's disease, and *P. gingivalis* and its gingipains have been identified in post-mortem brain tissue [26]. This remains the domain where mechanistic plausibility currently outruns the strength of the clinical evidence.

3.9. Oncological Conditions

Xiong et al. [27], in a Mendelian randomization analysis of 20 cancer types, found weak, but not in-existent associations of periodontitis with head and neck cancer, and oropharyngeal cancer in particular, but none with the other cancers, and proposed *F. nucleatum* as a possible mediator in that relationship. Higham and Scannapieco [28] review the epidemiological associations across a wider range of malignancies. The proposed mechanisms are chronic inflammation, oxidative DNA damage, and the direct pro-tumorigenic activity of periodontal pathogens, with oxidative stress markers also linking periodontitis to breast cancer.

3.10. A Cross-Cutting Mechanism: Trained Immunity and Clonal Haematopoiesis

One proposed mechanism cuts across all nine domains and deserves separate statement. Romandini et al. [3] describe maladaptive trained immunity and clonal haematopoiesis of indeterminate potential (CHIP) as mechanisms of the oral-systemic link. Persistent periodontal inflammation can reprogram haematopoietic progenitors in the bone marrow toward a hyper-inflammatory myeloid phenotype. The clinical significance of this is considerable: it explains why the systemic inflammatory consequences of periodontitis can persist after the periodontal infection itself has been resolved. If confirmed, it reframes periodontitis not only as a source of ongoing inflammatory input but as a condition capable of leaving an inflammatory imprint on the immune system.

Table 1. Summary of principal studies by systemic domain, study design, and key finding

Author(s) & Year	Domain	Design	Key Finding
Beck et al. (1996) [5]	Cardiovascular	Cohort	Higher cardiovascular mortality in periodontitis
Sanz et al. (2020) [9]	Cardiovascular	Consensus report	Periodontitis linked to MI and atherosclerosis; limited evidence for heart failure
Stöhr et al. (2021) [15]	Diabetes	Meta-analysis (n = 427,620)	26% increased risk of diabetes (mainly type 2)
Simpson et al. (2022) [19]	Diabetes	Cochrane review of RCTs	Periodontal treatment reduces HbA1c by 0.43% at 3–4 months
Chapple et al. (2025) [20]	Renal	Review	Periodontitis an independent risk factor for chronic kidney disease
Tan et al. (2024) [21]	Hepatic	Mendelian randomization	Genetic evidence suggesting a causal link to NAFLD
Gomes-Filho et al. (2020) [22]	Respiratory	Systematic review & meta-analysis	Higher odds of pneumonia, COPD, and asthma
Raju and Berens (2021) [25]	Pregnancy	Review	Association with preterm birth and low birthweight; evidence conflicting
Xiong et al. (2024) [27]	Oncology	Mendelian randomization	Weak, near-null association with head and neck/oropharyngeal cancer only
Romandini et al. (2026) [3]	Multi-systemic	Mechanistic review	Trained immunity and CHIP as mechanisms

MI: myocardial infarction; NAFLD: non-alcoholic fatty liver disease; CHIP: clonal haematopoiesis of indeterminate potential; RCT: randomized controlled trial.

4. Discussion

4.1. Comparing the Strength of the Evidence

While studies keep reporting associations, they differ in design strength, and this difference matters more than the sheer number of publications. Mendelian randomization studies [14,21,27] offer stronger causal evidence than observational designs because genetic instruments are less subject to the reverse causation and residual confounding that trouble cross-sectional work on oral health, although their results in this review were mixed. Interventional trials [19] provide the most direct clinical evidence of all, since they demonstrate that changing the exposure changes the outcome. But, read against this hierarchy, and the nine domains do not stand equal: diabetes is supported at every level from mechanism to intervention; cardiovascular disease is supported at every level except trials with cardiovascular events as endpoints; hepatic disease has causal-genetic support but little interventional data; oncological disease has largely null genetic findings; chronic kidney disease, respiratory disease, rheumatoid arthritis, and adverse pregnancy outcomes rest mainly on observational evidence; and neurodegenerative disease rests principally on mechanistic plausibility.

4.2. Periodontal Treatment as Systemic Intervention

Periodontal treatment is not only a dental procedure, as it can have measurable systemic effects. Numerous studies have examined its effects in patients with cardiovascular disease, diabetes, renal disease, rheumatoid arthritis, and pregnancy complications: reduction in CRP and IL-6 with improved endothelial function [9], whereas the evidence on pregnancy outcomes remains conflicting [25]. Taken together, this body of interventional evidence has little parallel elsewhere in dentistry, although it rests mainly on surrogate markers rather than hard clinical endpoints.

The implications run deep into how care gets delivered. A periodontist treating a type 2 diabetic with severe periodontitis is not managing a side effect of diabetes, but rather, they are intervening directly in that patient's glycaemic trajectory, and that's why we need to insist on being more keen on treatment of periodontal disease. An obstetrician managing a high-risk pregnancy should screen for periodontal disease as part of antenatal care, not as a courtesy referral to dentistry, although evidence that treatment improves birth outcomes is still lacking. A cardiologist facing unexplained elevated CRP should consider periodontal assessment as a normal part of the inflammatory workup to make up for all of the evidence discussed until now. Periodontal disease should be treated as guilty until proven otherwise.

4.3. The Multidisciplinary Model

Romandini et al. [3], in arguably the most comprehensive current statement of the oral-systemic paradigm, propose treating periodontal management as a preventive strategy against multimorbidity rather than an isolated dental task. They call for restructured care pathways in which periodontists, cardiologists, endocrinologists, rheumatologists, nephrologists, pulmonologists, neurologists, and obstetricians are routinely consulted on periodontal management for patients at systemic risk. None of this requires an infrastructural overhaul. Concretely, it means adding a periodontal status field to standard medical history forms outside dental settings; building referral pathways between general physicians and periodontists for patients with diabetes, CKD, RA, or cardiovascular disease; and including periodontal screening in preconception and antenatal care for high-risk obstetric populations.

4.4. What Treating Periodontitis Achieves Systemically

Pulling the interventional findings together: in cardiovascular disease, periodontal treatment reduces circulating CRP, IL-6, and fibrinogen [9] and improves endothelial function, with a meta-analysis of fourteen randomized controlled trials reporting significant improvement in flow-mediated dilation within three months, but no significant difference at six months [29]. A separate meta-analysis found that non-surgical periodontal treatment also improves flow-mediated dilation and carotid intima-media thickness, but not pulse wave velocity, a measure of arterial stiffness [30]. In diabetes, it produces a clinically meaningful 0.43% HbA1c reduction at 3–4 months [19]. In rheumatoid arthritis, it lowers DAS28 by a mean difference of 0.76 together with CRP and erythrocyte sedimentation rate, based mainly on before-and-after comparisons [24]. In pregnancy, the evidence remains conflicting [25], and a reduction in preterm birth and low birthweight has not been established. These effects concern mainly surrogate markers measured over short follow-up periods, so to further understand periodontal disease in these patients, as understood more studies are needed, which cannot be done without the certain amount of awareness which makes you question: “How much more evidence do we need?”.

4.5. Limitations and Research Gaps

Despite growing evidence, several gaps remain. Most studies establish association rather than causation, and large-scale randomized controlled trials testing periodontal treatment as a systemic intervention are

scarce across most disease domains. The mechanisms linking periodontitis to Alzheimer's disease and to cancer are not yet completely characterized and thus not fully understood. Several considerations should be taken into account when interpreting these findings. The breadth of this review, which spans nine disease domains that differ in biological mechanisms, outcome measures, and maturity of evidence, precluded quantitative pooling and limits direct comparison across domains. The included studies also vary in design, ranging from experimental and cross-sectional studies to cohort studies, randomized controlled trials, and Mendelian randomization analyses, and in the case definitions used for periodontitis, which include clinical attachment loss, probing depth, radiographic bone loss, self-report, and the 2017 classification. Systemic outcomes were likewise ascertained using different criteria. Consistent with the narrative design, no protocol was registered, study selection was not performed in duplicate, and the search was limited to English-language publications. Potential publication bias toward positive associations should also be acknowledged. Finally, no formal risk-of-bias assessment was undertaken; for this reason, the evidence for each domain was interpreted according to the hierarchy of study designs described in Section 2.5 and compared in Section 4.1.

5. Conclusions

Periodontitis is a mechanistically integrated contributor to systemic disease across multiple domains, although the strength of the evidence differs considerably between them, mostly due to the methodology of studies used to understand the relationship.

Regardless, Periodontitis functions as a persistent, chronic inflammatory lesion with effects that may reach many organ systems in the body. Its influence is understood to be, until now, mediated through bacteria, cytokines, trained immune cells, and oxidative metabolites, acting along vascular, respiratory, and enteral routes that cross the disciplinary lines drawn across medicine. The nine systemic domains covered in this review – cardiovascular disease, diabetes, chronic kidney disease, hepatic pathology, respiratory disease, rheumatoid arthritis, adverse pregnancy outcomes, neurodegenerative disease, and cancer risk – may not be nine separate stories. They may be variations on a single underlying inflammatory signal, generated repeatedly from the same source, received by organs not otherwise connected to it.

The evidence supports its inclusion in broader medical frameworks, particularly in endocrinology and cardiology. These findings underline the need for interdisciplinary clinical integration and highlight periodontal management as a potentially important element in improving systemic health outcomes.

The relationship between periodontal disease and the host is mechanistic, bidirectional, interventional, and, in some cases, supported by genetic evidence of causality. Periodontal therapy lowers HbA1c, reduces cardiovascular inflammatory markers, and eases rheumatoid disease activity, whereas its effect on pregnancy outcomes remains poorly defined.

Bringing periodontal assessment into the clinical frameworks of medicine – most clearly endocrinology and cardiology, and potentially nephrology, oncology, rheumatology, and obstetrics – is not simply an interdisciplinary courtesy. It represents a priority that is already evidence-based for diabetes and cardiovascular disease and, for the other fields, awaits long-term trials with clinical endpoints, with consequences for patient outcomes that may extend well beyond the mouth.

So, given this conclusion, how much more evidence do we need? What else is missing before we implement periodontal disease as part of the screenings for these patients? To fully understand one's health is to fully observe it, and without observing oral and periodontal health, no medical professional would be able to do so. Periodontal disease, for the patients who have it, should not be dismissed as a

bystander to their aggravated immune response and decreased quality of life until proven otherwise and treating the patient is the simplest way to find out. Especially because periodontal treatment is safe, well established, and beneficial for oral health in its own right, there is little reason not to put out the fire where we can reach it, in the inflamed periodontium.

Furthermore, with one source of inflammation less, the rest of the body may find it easier to recover, a possibility that is still being investigated, but one that patients should not have to wait for.

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List of Abbreviations

A. actinomycetemcomitans – *Aggregatibacter actinomycetemcomitans*; **AGEs** – Advanced Glycation End Products; **anti-CCP** – Anti-Cyclic Citrullinated Peptide Antibodies; **APP** – Amyloid Precursor Protein; **APP-β** – Amyloidogenic Amyloid Precursor Protein Beta Fragment; **ApoE** – Apolipoprotein E; **BBB** – Blood-Brain Barrier; **CHIP** – Clonal Hematopoiesis of Indeterminate Potential; **CKD** – Chronic Kidney Disease; **COPD** – Chronic Obstructive Pulmonary Disease; **CRP** – C-Reactive Protein; **DAMPs** – Damage-Associated Molecular Patterns; **DAS28** – Disease Activity Score in 28 Joints; **DNMT3A** – DNA Methyltransferase 3 Alpha; **EFP** – European Federation of Periodontology; **F. nucleatum** – *Fusobacterium nucleatum*; **HbA1c** – Glycated Hemoglobin; **IL-1β** – Interleukin-1 Beta; **IL-6** – Interleukin-6; **LDL** – Low-Density Lipoprotein; **LPS** – Lipopolysaccharide; **MASLD** – Metabolic Dysfunction-Associated Steatotic Liver Disease; **NAFLD** – Non-Alcoholic Fatty Liver Disease; **NK cells** – Natural Killer Cells; **P. gingivalis** – *Porphyromonas gingivalis*; **PAD** – Peptidylarginine Deiminase; **PAMPs** – Pathogen-Associated Molecular Patterns; **PGE2** – Prostaglandin E2; **RA** – Rheumatoid Arthritis; **SMAD** – Sma and Mad (Suppressor of Mothers Against Decapentaplegic) proteins; **T. denticola** – *Treponema denticola*; **T. forsythia** – *Tannerella forsythia*; **TGF-β** – Transforming Growth Factor Beta; **TLR-4** – Toll-Like Receptor 4; **TNF-α** – Tumor Necrosis Factor Alpha; **WHF** – World Heart Federation

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