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SYSTEMATIC REVIEW

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Are periodontitis and dental caries associated? A systematic review with meta-analyses

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Abstract

Aim: The epidemiological relationship between periodontitis and caries remains controversial, and evidence synthesis is currently lacking. Therefore, this systematic review was designed to answer the following PECO question: 'In human adults (P), do subjects suffering from periodontitis (E) have higher presence/number of untreated carious lesions and caries experience (O) than subjects not suffering from periodontitis (C)?'.

Materials and Methods: Observational studies that met specific inclusion criteria established to answer to the PECO question were included. Two review authors independently searched for eligible studies, screened the titles and abstracts, carried out the full text analysis, extracted the data and performed the risk of bias assessment. In case of disagreement, a third review author took the final decision during ad hoc consensus meetings. Data synthesis was carried out through random-effects meta-analyses.

Results: A total of 18 studies on 21 cohorts, involving 135,018 participants, were included. Meta-analyses showed a significant association between periodontitis and the presence of at least one tooth with either untreated carious lesions (odds ratio [OR] = 1.63; 95% confidence interval [CI]: 1.32–2.01; p <.00; $I^2 = 83.0\%$) or caries experience (decayed and filled teeth ≥ 1) (OR = 1.27; 95% CI: 1.01–1.59; p = .038; $I^2 = 90.0\%$). Moreover, subjects with periodontitis exhibited a higher number of surfaces (difference in means [MD] = 0.86; 95% CI: 0.46–1.27; p <.001; $I^2 = 0.0\%$) and teeth (MD = 0.35; 95% CI: 0.28–0.42; p <.001; $I^2 = 69.6\%$) with untreated carious lesions, as well as a higher number of teeth with caries experience (standardized difference in means [SMD] = 1.46; 95% CI: 0.15–2.78; p = .029; $I^2 = 98.9\%$) compared with those without periodontitis. Sensitivity analyses focusing on severe periodontitis as exposure mostly showed consistent results. Estimates for caries experience were only slightly attenuated in adjusted models compared with crude models. Subgroup analyses by caries location also indicated that periodontitis was associated only with root caries, while it was not with caries affecting the anatomical crown.

Conclusions: Periodontitis was found to be associated with the presence and number of treated/untreated root carious lesions. Therefore, caries-specific preventive measures (e.g., fluorides) should be considered for individuals with periodontitis.

KEYWORDS
dental caries, epidemiology, European Federation of Periodontology (EFP), European Organization for Caries Research (ORCA), periodontal diseases

Clinical Relevance

Scientific rationale for study: Epidemiological studies have reported conflicting results on the association between periodontitis and dental caries; no systematic reviews have been conducted to date to summarize the available evidence on this topic.
Principal findings: Periodontitis was found to be associated with the presence and the number of treated/untreated root carious lesions.
Practical implications: Caries-specific preventive measures should be considered for individuals with periodontitis.

1 | INTRODUCTION

Periodontitis and dental caries are the most common oral diseases affecting humans worldwide. An estimated 2.3 billion people (95% uncertainty interval [UI], 2.1–2.5 billion) are affected by untreated caries in permanent teeth, while severe periodontitis affects 796 million people (95% UI, 671–930 million) (GBD 2017 Oral Disorders Collaborators et al., 2020), resulting, respectively, in the first and sixth most prevalent human diseases (Kassebaum et al., 2014, 2015, 2017; Morales et al., 2022). They also represent the main causes of tooth loss, posing a significant oral health burden on humankind (Frencken et al., 2017; Jepsen et al., 2017; Tonetti et al., 2017).

These two chronic, complex diseases share some common risk factors and social determinants, which may contribute to their co-occurrence in the same individual (Jepsen et al., 2017). However, it is a common clinical finding that severe forms of dental caries and periodontitis specifically affect different individuals, possibly due to specific microbial signatures within their respective dental-associated biofilms (Sanz et al., 2017). Epidemiological studies examining the relationship between periodontitis and caries have indeed yielded conflicting results (Albandar et al., 1995; Baima et al., 2023; Kinane et al., 1991; Mattila et al., 2010; Sewón et al., 1988).

As already highlighted during the 2016 joint workshop of the European Federation of Periodontology (EFP) and the European Organization for Caries Research (ORCA), no systematic reviews have been conducted to date to summarize the available evidence on the association between periodontitis and dental caries. This information would be relevant for both clinicians and policymakers for improving preventive measures that are, at least partially, disease-specific (e.g., fluorides) (Jepsen et al., 2017).

Therefore, this systematic review was designed to answer the following PECO question: 'In human adults (P), do subjects suffering from periodontitis (E) have higher presence/number of untreated carious lesions and caries experience (O) than subjects not suffering from periodontitis (C)?'.

2 | MATERIALS AND METHODS

This systematic review adheres to the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) 2020 (Page et al., 2021) and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) (Stroup et al., 2000) guidelines. A comprehensive protocol was developed and registered on PROSPERO (CRD42021288402) before starting the review process.

2.1 | Inclusion and exclusion criteria

The inclusion criteria of this systematic review were formulated according to the PECOS acronym.

(P) Population: adult human subjects (≥18 years of age).
(E) Exposure: presence of periodontitis.
(C) Comparison: absence of periodontitis.
(O) Outcome measures: presence/number of untreated carious lesions and caries experience.
(S) Study design: cross-sectional studies.

No studies were excluded based on language, date of publication or publication status.

2.2 | Search methods for study identification

Two review authors (PR and MR) performed in duplicate a systematic search in three electronic databases (Medline via PubMed, Scopus, Web of Science) and in grey literature (OpenGrey; www.opengrey.eu), without language restrictions, from inception until 7 September 2023. The complete search strategies for all electronic databases and grey literature are detailed in Appendix S1.

In addition, two review authors (PR and WGR) hand-searched in duplicate the following seven key dental journals from 1 January 2010 to 11 September 2023: *Journal of Clinical Periodontology*, *Journal of Dental Research*, *Journal of Dentistry*, *Journal of Periodontology*, *Journal of Periodontal Research*, *Caries Research* and *Community Dentistry and Oral Epidemiology*. Finally, the same two review authors also searched within the bibliographies of all the included studies. All studies identified by at least one review author were considered in the next phase (study selection).

2.3 | Study selection

The titles and abstracts (if available) of all identified studies were independently screened by two review authors (PR and WGR). If the articles appeared to meet the inclusion criteria or if there was insufficient data in the title and abstract, the full report was obtained. The selected full texts were then analysed in duplicate by two review authors (PR and CM) to make the final decision regarding their inclusion in the systematic review. Any disagreement during the study selection process was solved through ad hoc consensus meetings in the presence of a third reviewer (MR). The reasons for study exclusion following full text evaluation were recorded. The inter-reviewer agreement (percentage of agreement) of the screening and full text analysis phases was calculated. Multiple publications comprising the same population were included if they presented different analyses in terms of exposures/outcomes; otherwise, only one article was included, and the selection was based on the inclusion criteria and on the adjustments applied to the models reporting the estimates of interest. All included studies underwent data extraction and assessment of risk of bias.

2.4 | Data extraction and management

Data from the included studies were extracted independently and in duplicate by two review authors (PR and CM) using predefined data extraction forms. Any disagreement was solved through discussion, and a third reviewer (MR) made the final decision when necessary. The first three included studies were used for calibration purposes of the data extraction phase. In case of studies reporting on more than one cohort, the data were extracted separately for each cohort. When necessary, the primary study authors were contacted for clarification or missing information.

For each study, the following data were recorded:

- General information. First author, year of publication, country/region of origin and source of the study sample;
- Population (analysed). Inclusion/exclusion criteria, sample size, age (range/mean), men/women (number/percentage), smokers/non-smokers (number/percentage), dental care exposure and socio-economic status;
- Exposure(s) and comparison(s). Periodontitis assessment methods, periodontitis case definition(s) and number of subjects with and without periodontitis;
- Outcome(s). Dental caries assessment methods, dental carious lesion case definition(s) and prevalence and mean number (tooth and surfaces) of untreated carious lesions and caries experience;
- Results. 'Crude' and 'best-adjusted' odds ratios (ORs) with 95% confidence intervals (CIs) for periodontitis versus no periodontitis as exposure/comparison (outcomes: presence of untreated carious lesions and cumulative caries experience) and 'crude' and 'best-adjusted' difference in means (MDs) with standard errors (SEs) for periodontitis versus no periodontitis as exposure/comparison (outcomes: mean number of teeth/surfaces affected by untreated carious lesions and cumulative caries experience), variables adjusted for in the selected 'best-adjusted' models, and subgroup analyses for caries location (coronal/interproximal vs. root caries);
- Risk of bias (see the next section).

When a study reported more than one estimate according to different periodontitis case definitions, the one closest to the EFP's sensitive case definition for epidemiological studies was considered as periodontitis, while the one closest to its specific case definition was considered as severe periodontitis (Tonetti & Claffey, 2005). Otherwise, the study was categorized as reporting about either periodontitis or severe periodontitis according to the same criteria.

If an included study reported more than one estimate according to different untreated carious lesion case definitions, the one closest to the International Caries Detection and Assessment System (ICDAS) ≥1 was considered as untreated carious lesion, while the one closest to ICDAS ≥4 was considered as untreated cavitated dentinal carious lesion (Pitts, Ekstrand, & ICDAS Foundation, 2013). Otherwise, the study was categorized as reporting about either untreated carious lesion or untreated cavitated dentinal carious lesion, according to the same criteria.

Caries experience was defined as the presence of decayed (i.e., untreated carious lesions), missing due to caries, filled teeth/surfaces (DMFT/DMFS) or decayed/filled teeth/surfaces (DFT/DFS) (World Health Organization, 2013).

'Best-adjusted' models were selected as models adjusted for known common risk factors of periodontitis and dental caries (i.e., socio-economic status, smoking, uncontrolled diabetes, obesity, hyposalivation, rheumatoid arthritis, dental care exposure, lack of plaque control, fermentable carbohydrates intake; Chapple et al., 2017), but not for unjustified variables (i.e., variables that are not recognized as possible risk factors for both the diseases).

2.5 | Assessment of risk of bias in the included cohorts

The risk of bias assessment was conducted in duplicate as part of the data extraction process, developing and then applying an ad hoc modification of the Newcastle-Ottawa scale (NOS; Herzog et al., 2013; Wells et al., 2011) for cross-sectional studies specifically designed for the purposes of this systematic review (reported in the Appendix S2). Briefly, each study (or cohort, in case of multiple populations analysed in the same manuscript) was assessed based on study sample selection (two items, one star each), assessment of exposure/outcome variables (two items, two stars each) and confounding factors (two items, maximum of three total stars) criteria. Overall risk of bias was evaluated as follows: low (≥7 stars), moderate (4–6 stars) or high (<4 stars).

2.6 | Data analysis

Whenever necessary (e.g., when dealing with raw numbers), the corresponding estimates (OR/MD with 95% CI/SE) were calculated from the primary studies.

When at least two studies/cohorts were available, meta-analyses were conducted using an ad hoc statistical software (STATA BE, version 17.1, Stata Statistical Software, College Station, TX: StataCorp LP) employing the Der Simonian and Laird random-effects model (DerSimonian & Kacker, 2007). For meta-analytical purposes, incidence risk ratios (IRRs) were merged with ORs (Higgins et al., 2016; Romandini et al., 2021). In cases where a study reported only subgroup analyses for both 'coronal caries' and 'root caries' as outcomes, only the former was considered for the overall meta-analyses. The same rule was also applied for studies reporting results from both 'adjusted' and 'crude' models. Meta-analytical estimates were expressed as OR/MD with 95% CIs. However, results from meta-analyses on caries experience combining DFT/DMFT indices were presented as standardized difference in means (SMD) with 95% CI.

Inter-study heterogeneity was initially assessed by carefully examining the characteristics of the included studies. Additionally, in each meta-analysis, the extent and impact of heterogeneity were assessed by visually inspecting the forest plots and calculating the I^2 statistics. The main meta-analyses focused on periodontitis as exposure and untreated/treated dental caries as outcomes. Sensitivity meta-analyses were a priori planned considering (i) severe periodontitis as exposure, (ii) cavitated dentinal lesions for untreated dental caries as outcome and (iii) DFT for caries experience as outcome (i.e., excluding studies reporting it as DMFT). Additionally, in the presence of main meta-analyses including at least three studies and exhibiting high heterogeneity (I^2 ≥75%), a 'leave-one-out' sensitivity analysis was conducted to assess the impact of each individual study on the meta-analytical estimate. Subgroup meta-analyses were a priori planned according to the region of origin of the study sample (Europe, America, Asia and others), assessment methods of periodontitis and dental caries (verified clinically, radiographically or both), caries location (only crown, only root, both or not reported), adjustment level (crude, adjusted) and the risk of bias (low, moderate, high).

3 | RESULTS

3.1 | Study selection

The electronic search yielded 6050 entries, of which 3671 were retrieved from Medline (via PubMed), 1164 from Scopus and 1215 from Web of Science. No additional studies were identified in OpenGrey and by hand-searching. Cross-reference checking identified seven additional manuscripts, and one unpublished study from a review author was also identified. After removing duplicates, a total of 4781 entries remained. Of these, 4731 studies were discarded after reviewing the titles and abstracts (agreement = 99.12%). After full text analysis, 40 additional articles were excluded; the reasons for exclusion are reported in Table S1 (agreement = 81.03%) (Figure 1).

Finally, 18 studies, involving 21 cohorts and 135,018 participants met the inclusion criteria and were included in this systematic review (Almoznino et al., 2020; AlQobaly & Sabbah, 2020; Baima et al., 2023; Beklen et al., 2022; Durand et al., 2019; Fadel et al., 2011; Frentzen et al., 1990; Haworth et al., 2018; Hyman & Reid, 2003; Martínez et al., 2021; Mattila et al., 2010; Sewón et al., 1988; Soni et al., 2014; Strauss et al., 2019; Tsai et al., 2022; Vehkalahti & Paunio, 1994; Yu et al., 2021; Zimmermann et al., 2015).

3.2 | Characteristics of the included studies

The general characteristics of the included studies are shown in Table 1, while Tables S2–S4 provide information on participants, exposures/comparisons and analysed outcomes, respectively. Three studies reported on two cohorts each (Haworth et al., 2018; Hyman & Reid, 2003; Yu et al., 2021), while the remaining 15 studies analysed only one cohort. Eight of the analysed cohorts were from Europe, nine were from Asia (Almoznino et al., 2020; Baima et al., 2023; Beklen et al., 2022; Fadel et al., 2011; Haworth et al., 2018; Soni et al., 2014; Tsai et al., 2022; Yu et al., 2021) and four were from America (Durand et al., 2019; Hyman & Reid, 2003; Strauss et al., 2019). Thirteen cohorts reported both periodontitis and severe periodontitis as exposure, six reported only periodontitis (Almoznino et al., 2020; AlQobaly & Sabbah, 2020; Hyman & Reid, 2003; Sewón et al., 1988; Soni et al., 2014; Tsai et al., 2022) and two reported only severe periodontitis (Frentzen et al., 1990; Hyman & Reid, 2003). Periodontitis was clinically assessed in 17 cohorts, radiographically in 1 (Sewón et al., 1988) and both clinically and radiographically in 3 (Beklen et al., 2022; Fadel et al., 2011; Tsai et al., 2022). Dental caries status was clinically assessed in 16 cohorts, radiographically in 1 (Sewón et al., 1988) and both clinically and radiographically in the remaining 4 (Almoznino et al., 2020; Fadel et al., 2011; Frentzen et al., 1990; Haworth et al., 2018). Seven cohorts reported untreated dental caries as an outcome (Hyman & Reid, 2003; Mattila et al., 2010; Soni et al., 2014; Strauss et al., 2019; Vehkalahti & Paunio, 1994; Zimmermann et al., 2015), while six cohorts reported caries experience (AlQobaly & Sabbah, 2020; Haworth et al., 2018; Sewón et al., 1988; Yu et al., 2021) and eight reported both untreated dental caries and caries experience.

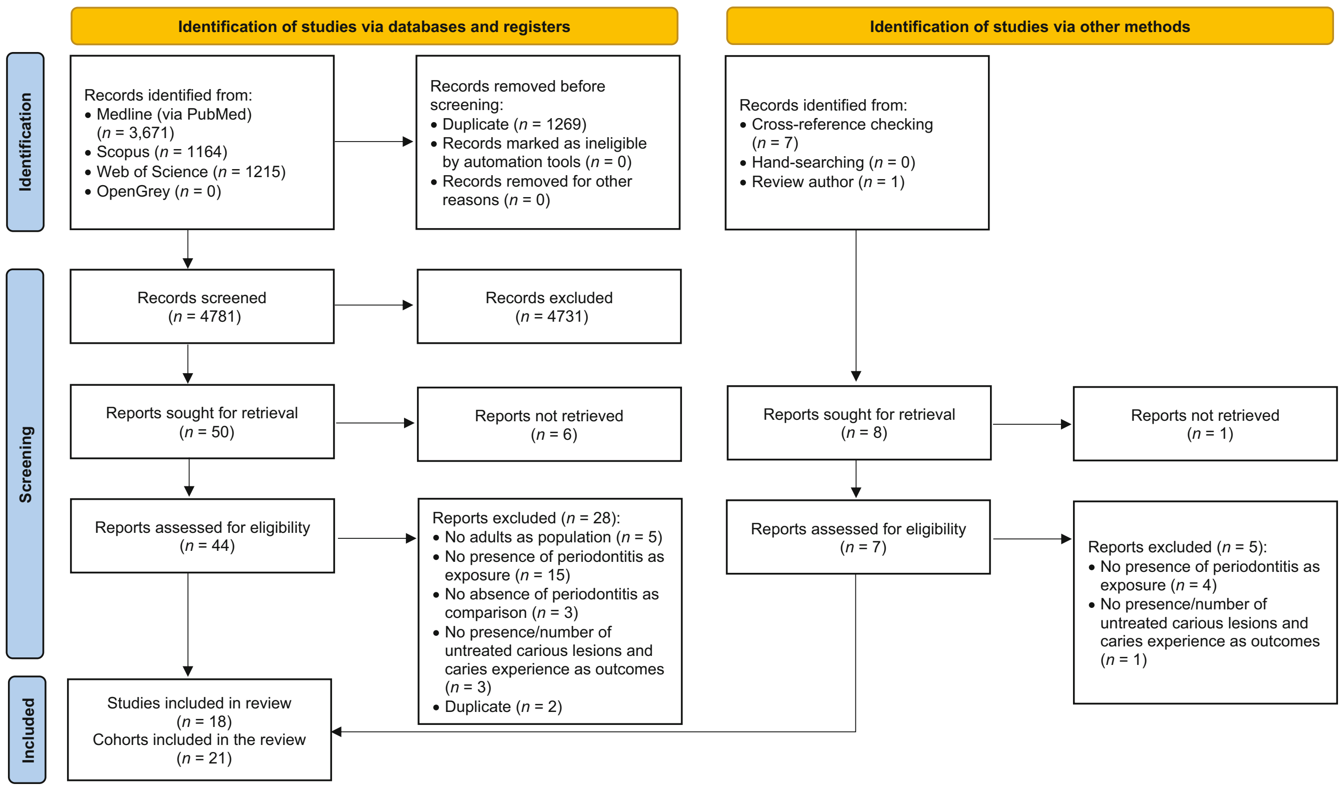

FIGURE 1 PRISMA 2020 flow diagram for study selection.

Table S5 reports the risk of bias assessment of the included cohorts. Three analysed populations were considered to have a low risk of bias (AlQobaly & Sabbah, 2020; Haworth et al., 2018; Strauss et al., 2019), nine had a moderate risk (Baima et al., 2023; Haworth et al., 2018; Hyman & Reid, 2003; Martínez et al., 2021; Mattila et al., 2010; Vehkalahti & Paunio, 1994; Yu et al., 2021) and the remaining nine had a high risk.

3.3 | Periodontitis and untreated dental caries

Fifteen cohorts reported results on the association between periodontitis and untreated caries (Almoznino et al., 2020; Baima et al., 2023; Beklen et al., 2022; Durand et al., 2019; Fadel et al., 2011; Frentzen et al., 1990; Hyman & Reid, 2003; Martínez et al., 2021; Mattila et al., 2010; Soni et al., 2014; Strauss et al., 2019; Tsai et al., 2022; Vehkalahti & Paunio, 1994; Zimmermann et al., 2015). Specifically, three of them reported on the presence of at least one untreated carious lesion (Martínez et al., 2021; Soni et al., 2014; Vehkalahti & Paunio, 1994), nine reported on the number of teeth/surfaces with untreated carious lesions and the remaining three reported on both (Baima et al., 2023; Mattila et al., 2010; Strauss et al., 2019).

3.3.1 | Periodontitis and presence of at least one untreated carious lesion

Table S6 shows the results from the included cohorts on the association between periodontitis and the presence of at least one untreated carious lesion. Meta-analyses indicated a significant association between periodontitis and the presence of at least one untreated carious lesion ($n = 6$ cohorts; 39,961 subjects; OR $= 1.63$; 95% CI: 1.32–2.01; $p < .001$; $I^2 = 83.0\%$) (Figure 2a). The sensitivity meta-analysis using severe periodontitis as the exposure also showed consistent results ($n = 5$ cohorts; 39,561 subjects; OR $= 1.66$; 95% CI: 1.26–2.19; $p < .001$; $I^2 = 86.8\%$). No sensitivity meta-analysis was possible using untreated cavitated dentinal carious lesions as outcome as it was never reported. Leave-one-out sensitivity analyses showed consistent results (Figure S1a). When feasible, subgroup meta-analyses demonstrated results mostly consistent with the main analyses (Table S7).

3.3.2 | Periodontitis and number of untreated carious lesions

Table S8 presents the results from the included cohorts on the association between periodontitis and the number of untreated carious lesions. Four cohorts reported on the number of surfaces (Durand et al., 2019; Frentzen et al., 1990; Hyman & Reid, 2003), seven reported on teeth and one reported on both (Baima et al., 2023).

Five cohorts were not included in the meta-analyses. Three of them indeed reported the outcome through different categorizations instead of continuous values (Hyman & Reid, 2003; Strauss et al., 2019) and two did not report any measure of dispersion of the estimates (Frentzen et al., 1990; Zimmermann et al., 2015). Meta-analyses indicated that individuals with periodontitis have a higher

TABLE 1 Overview of the included studies.

Reference	Region	Sample size (analysed)	RoB	Main estimates provided (periodontitis vs. non-periodontitis)[a]			
				Presence of at least one untreated carious lesion, OR (95% CI)	Number of untreated carious lesions, MD (SE)	Presence of caries experience, OR (95% CI)	Number of teeth/surfaces with caries experience, MD (SE)
Almoznino et al. (2020)	Israel	162	High	-	Teeth: MD = −0.82 (SE = 0.33)	-	Teeth: MD = 2.90 (SE = 1.04)
AlQobaly and Sabbah (2020)	England, Northern Ireland and Wales	4738	Low	-	-	IRR = 1.03 (95% CI: 1.01–1.05)	Teeth: MD = 1.51 (SE = 0.22)
Baima et al. (2023)	South Korea	23,405	Moderate	OR = 1.96 (95% CI: 1.66–2.32)	Teeth: MD = 0.36 (SE = 0.07) Surfaces: MD = 0.82 (SE = 0.21)	OR = 1.02 (95% CI: 0.79–1.31)	Teeth: MD = −0.11 (SE = 0.15) Surfaces: MD = 0.17 (SE = 0.53)
Beklen et al. (2022)	Turkey	2364	High	-	Teeth: MD = 0.30 (SE = 0.12)	-	Teeth: MD = 5.60 (SE = 0.20)
Durand et al. (2019)	Canada	94	High	-	Surfaces: MD = 1.67 (SE = 0.89)	-	Surfaces: MD = 11.80 (SE = 4.64)
Fadel et al. (2011)	Saudi Arabia	112	High	-	Teeth: MD = −0.82 (SE = 0.77)	OR = 1.17 (95% CI: 0.25–5.50)	-
Frentzen et al. (1990)	Germany	2200	High	-	Surfaces[b]: MD = −0.41 (SE = NR)	-	Teeth[b]: MD = −11.26 (SE = NR)
Haworth et al. (2018)	Sweden	28,691	Low	-	-	-	Teeth: IRR = 1.03 (95% CI: 1.02/1.04) Surfaces: IRR = 1.05 (95% CI: 1.04–1.06)
	South Korea	33,831	Moderate	-	-	-	Teeth: IRR = 0.95 (95% CI: 0.93–0.97) Surfaces: IRR = 0.97 (95% CI: 0.94–1.00)
Hyman and Reid (2003)	USA	8208	Moderate	-	Surfaces: 1–2: OR = 1.44 (95% CI: 0.66–3.16) 3–6: OR = 1.66 (95% CI: 0.67–4.11) ≥7: OR = 10.82 (95% CI: 4.78–24.51)	-	-
		4117	Moderate	-	Surfaces[b]: 1–2: OR = 1.10 (95% CI: 0.60–2.01) 3–7: OR = 1.49 (95% CI: 0.70–3.14) ≥8: OR = 2.92 (95% CI: 1.39–6.10)	-	-
Martínez et al. (2021)	Spain	5130	Moderate	OR = 1.1 (95% CI: 0.9–1.3)	-	OR = 1.4 (95% CI: 0.9–2.2)	Teeth: MD = 0.6 (SE = 0.2)
Mattila et al. (2010)	Finland	5255	Moderate	OR = 1.65 (95% CI: 1.45–1.88)	Teeth: MD = 0.40 (SE = 0.05)	-	-
Sewón et al. (1988)	Finland	416	High	-	-	-	Teeth: MD = 5.22 (SE = NR)
Soni et al. (2014)	India	400	High	OR = 2.22 (95% CI: 1.42–3.47)	-	-	-
Strauss et al. (2019)	Chile	994	Low	OR = 2.31 (95% CI: 1.46–3.66)	Teeth: 1: OR = 1.24 (95% CI: 0.77–2.0) 2: OR = 1.36 (95% CI: 0.84–2.20) 3–4: OR = 1.77 (95% CI: 1.14–2.74) ≥5: OR = 2.47 (95% CI: 1.66–3.67)	-	-
Tsai et al. (2022)	Taiwan	1289	High	-	Teeth: MD = 0.30 (SE = 0.08)	-	Teeth: MD = 0.12 (SE = 0.26)
Vehkalahti and Paunio (1994)	Finland	4777	Moderate	OR = 1.34 (95% CI: 1.10–1.61)	-	-	-

TABLE 1 (Continued)

Reference	Region	Sample size (analysed)	RoB	Main estimates provided (periodontitis vs. non-periodontitis)[a]: Presence of at least one untreated carious lesion, OR (95% CI)	Number of untreated carious lesions, MD (SE)	Presence of caries experience, OR (95% CI)	Number of teeth/surfaces with caries experience, MD (SE)
Yu et al. (2021)	China	4407	Moderate	-	-	OR = 1.44 (95% CI: 1.26–1.64)	Teeth: MD = 0.60 (SE = 0.09)
		4117	Moderate	-	-	OR = 1.63 (95% CI: 1.36–1.95)	Teeth: MD = 0.83 (SE = 0.17)
Zimmermann et al. (2015)	Germany	311	High	-	Teeth: MD = 0.52 (SE = NR)	-	-

Abbreviations: CI, confidence interval; IRR, incidence rate ratio; MD, difference in means; NR, not reported; OR, odds ratio; RoB, risk of bias; SE, standard error.
[a]In cases where a study reported only subgroup analyses for both 'coronal caries' and 'root caries' as outcomes, only the former is reported; the same rule was also applied for studies reporting results from both 'adjusted' and 'crude' models.
[b]Severe periodontitis.

number of surfaces ($n = 2$ cohorts; 23,499 subjects; MD = 0.86; 95% CI: 0.46–1.27; p <.001; $I^2 = 0.0\%$) and teeth ($n = 6$ cohorts; 32,587 subjects; MD = 0.35; 95% CI: 0.28–0.42; p <.001; $I^2 = 69.6\%$) with untreated carious lesions, compared with those without periodontitis (Figure 2b,c).

The sensitivity meta-analysis using severe periodontitis as the exposure showed similar results, although statistical significance was not reached for the number of surfaces (surfaces: $n = 2$ cohorts; 23,499 subjects; MD = 1.71; 95% CI: −1.28 to 4.71; $p = .262$; $I^2 = 88.9\%$) and teeth (teeth: $n = 3$ cohorts; 25,881 subjects; MD = 0.20; 95% CI: −0.01 to 0.42; $p = .066$; $I^2 = 39.2\%$). No sensitivity meta-analysis was possible using untreated cavitated dentinal carious lesions as outcome, as it was never reported. When feasible, subgroup meta-analyses generally showed results consistent with the main analyses (Table S9).

3.4 | Periodontitis and caries experience

Fourteen cohorts reported results on the association between periodontitis and caries experience (Almoznino et al., 2020; AlQobaly & Sabbah, 2020; Baima et al., 2023; Beklen et al., 2022; Durand et al., 2019; Fadel et al., 2011; Frentzen et al., 1990; Haworth et al., 2018; Martínez et al., 2021; Sewón et al., 1988; Tsai et al., 2022; Yu et al., 2021). Specifically, one of them reported on the presence of caries experience (Fadel et al., 2011), eight reported on the number of teeth/surfaces with caries experience (Almoznino et al., 2020; Beklen et al., 2022; Durand et al., 2019; Frentzen et al., 1990; Haworth et al., 2018; Sewón et al., 1988; Tsai et al., 2022) and the remaining five reported on both.

3.4.1 | Periodontitis and presence of caries experience

Table S10 shows the results from the included cohorts on the association between periodontitis and the presence of caries experience. Meta-analyses indicated that periodontitis is associated with the presence of caries experience ($n = 6$ cohorts; 41,909 subjects; OR = 1.27; 95% CI: 1.01–1.59; $p = .038$; $I^2 = 90.0\%$) (Figure 3a). Sensitivity meta-analysis using severe periodontitis as exposure showed consistent results ($n = 5$ cohorts; 37,171 subjects; OR = 1.34; 95% CI: 1.04–1.73; $p = .024$; $I^2 = 55.7\%$). Similarly, a sensitivity meta-analysis using only DFT as outcome for caries experience (i.e., excluding studies expressing it as DMFT) showed similar results ($n = 4$ cohorts; 32,041 subjects; OR = 1.36; 95% CI: 1.11–1.68; $p = .004$; $I^2 = 66.4\%$). Leave-one-out sensitivity analyses showed mostly consistent results in terms of central estimates; however, statistical significance was lost when either Yu et al. (2021) or Martínez et al. (2021) were removed from the meta-analyses (Figure S1b). Subgroup meta-analyses by caries location indicated that the association was only present for root caries ($n = 4$ cohorts; 13,374 subjects; OR = 1.98;

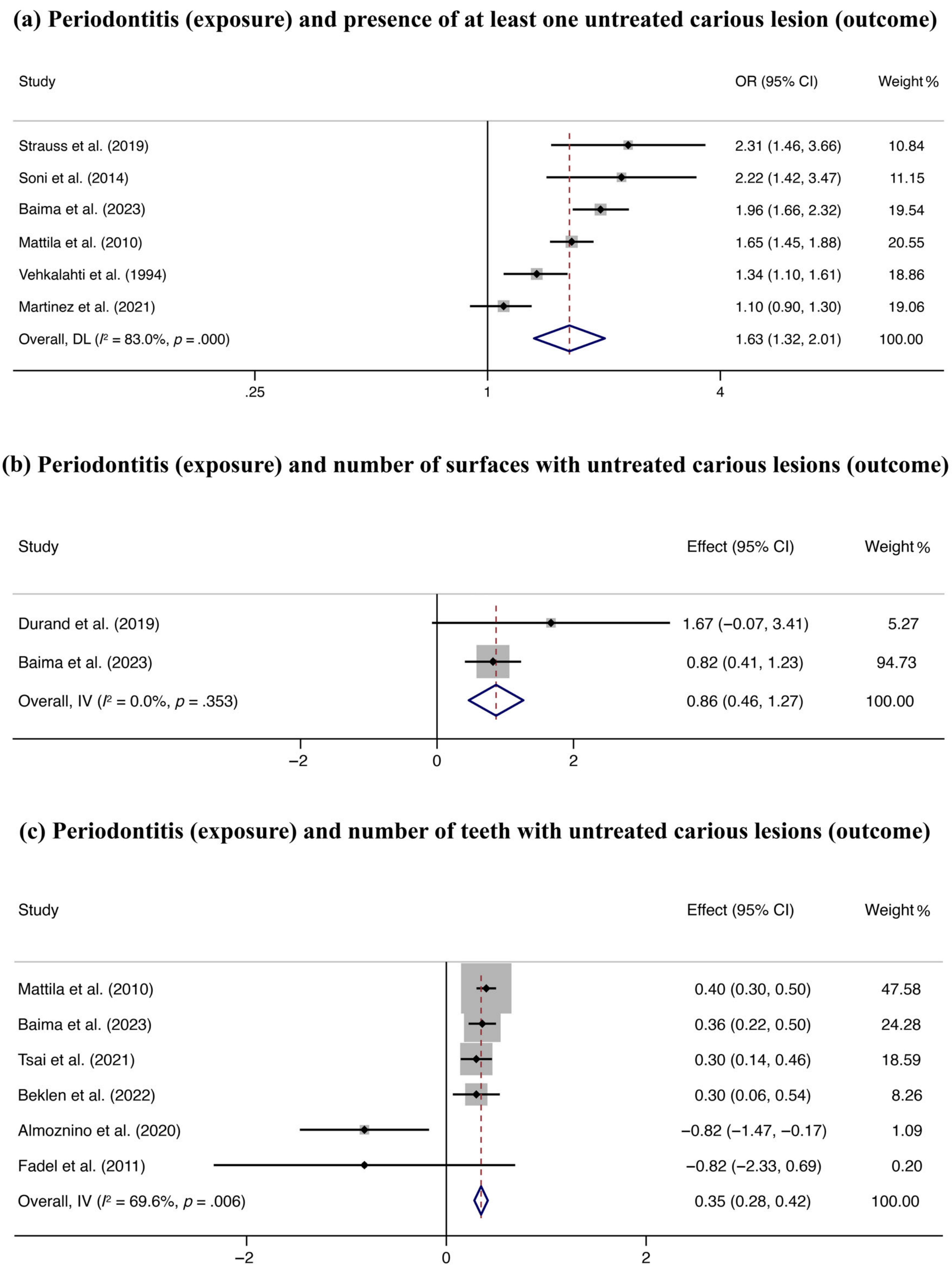

FIGURE 2 Meta-analyses: Periodontitis as exposure and untreated carious lesions as outcome. CI, confidence interval; OR, odds ratio.

95% CI: 1.18–3.32; $p = .010$; $I^2 = 92.7\%$) but not for coronal caries ($n = 4$ cohorts; 13,374 subjects; OR = 1.06; 95% CI: 0.97–1.15; $p = .208$; $I^2 = 46.6\%$). Similarly, adjusted estimates ($n = 3$ cohorts; 33,273 subjects; OR = 1.03; 95% CI: 1.01–1.05; $p = .002$; $I^2 = 0.0\%$) were attenuated but still statistically significant when compared with crude ones ($n = 5$ cohorts; 37,171 subjects; OR = 1.37; 95% CI: 0.86–2.20; $p = .187$; $I^2 = 96.7\%$) (Table S11).

3.4.2 | Periodontitis and number of teeth/surfaces with caries experience

Table S12 presents the results from the included cohorts on the association between periodontitis and the number of surfaces/teeth with caries experience. Two cohorts reported on the number of surfaces (Durand et al., 2019; Frentzen et al., 1990),

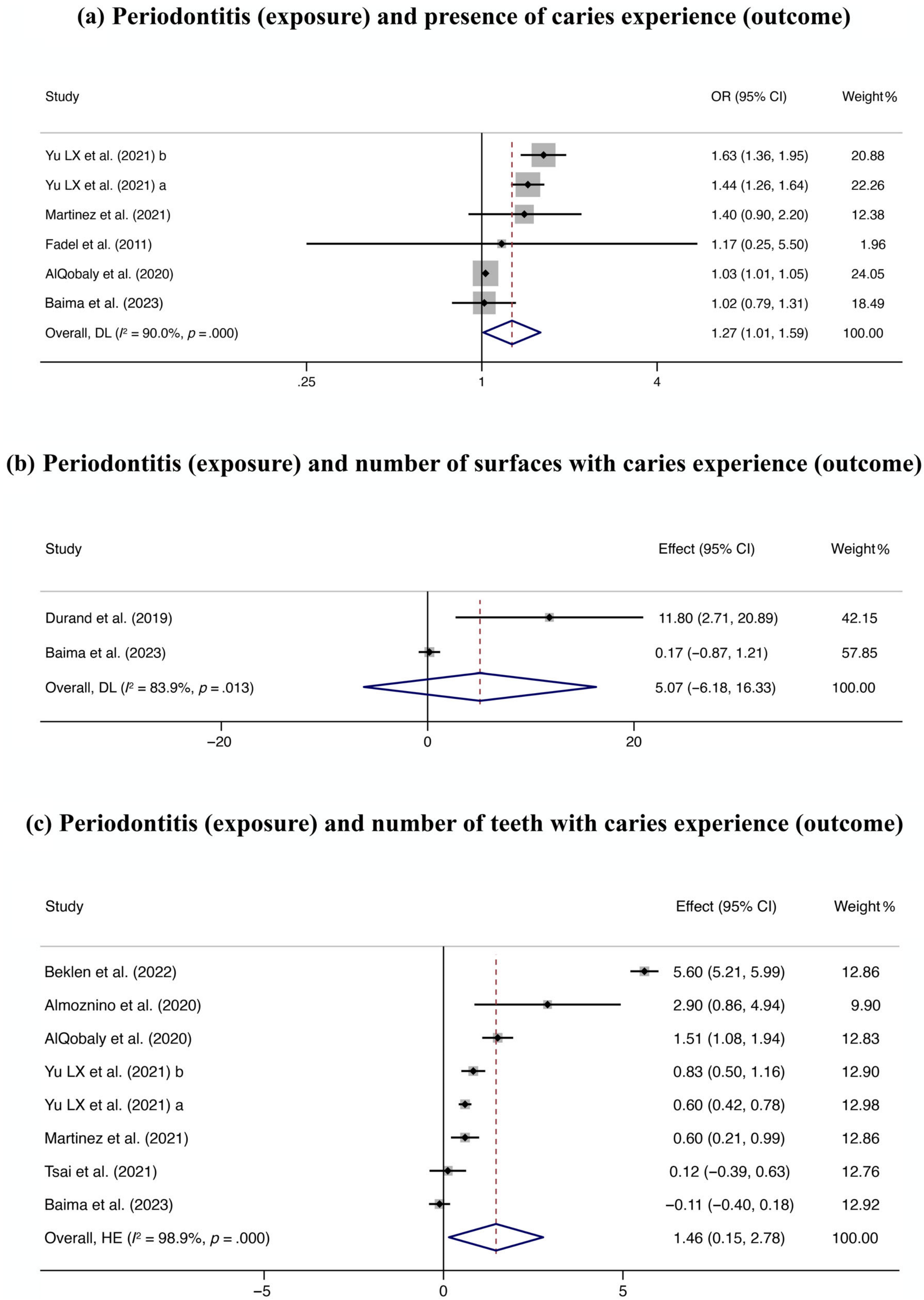

FIGURE 3 Meta-analyses: Periodontitis as exposure and caries experience as outcome. CI, confidence interval; OR, odds ratio.

eight reported on the number of teeth and the remaining three reported on both (Baima et al., 2023; Haworth et al., 2018).

Four cohorts were not included in the meta-analyses. Two of them reported the outcome only through incidence risk ratios instead of continuous values (Haworth et al., 2018) while two did not report any measure of dispersion of the estimates (Frentzen et al., 1990; Sewón et al., 1988). Meta-analyses indicated that periodontitis subjects have a higher number of surfaces ($n = 2$ cohorts; 23,499 subjects; MD = 5.07; 95% CI: −6.18 to 16.33; $p = .377$; $I^2 = 83.9\%$) and teeth ($n = 8$ cohorts; 45,612 subjects; SMD = 1.46; 95% CI: 0.15–2.78; $p = .029$; $I^2 = 98.9\%$) with caries experience compared with non-periodontitis subjects, although the former did not reach statistical significance (Figure 3b,c).

The sensitivity meta-analysis using severe periodontitis as exposure showed comparable results (surfaces: $n = 2$ cohorts; 23,499 subjects; MD = 3.33; 95% CI: −6.16 to 12.82; $p = .491$; $I^2 = 69.9\%$) (teeth: $n = 5$ cohorts; 39,423 subjects; SMD = 1.52; 95% CI: −0.30 to 3.34; $p = .102$; $I^2 = 99.1\%$). A sensitivity meta-analysis excluding missing teeth was feasible only for DFT and resulted in an attenuated estimate ($n = 3$ cohorts; 31,929 subjects; MD = 0.44; 95% CI: −0.06 to 0.94; $p = .080$; $I^2 = 90.7\%$). Leave-one-out sensitivity analyses were possible only for the number of teeth with caries experience and they mostly showed consistent results in terms of the direction of association; however, statistical significance was lost when either Almoznino et al. (2020) or AlQobaly and Sabbah (2020) was removed from the meta-analyses (Figure S1c). When feasible, subgroup meta-analyses generally showed attenuated estimates for adjusted (vs. crude) estimates and for studies with moderate (vs. high) risk of bias. Subgroup meta-analysis by caries location indicated that the association was statistically significant only for root caries ($n = 4$ cohorts; 18,392 subjects; SMD = 0.52; 95% CI: 0.25–0.78; $p < .001$; $I^2 = 97.7\%$) (Table S13).

4 | DISCUSSION

As highlighted during the 2016 joint workshop of the EFP and the ORCA, no systematic reviews have been previously conducted summarizing the available evidence on the association between periodontitis and dental caries. The results of this systematic review, including 21 cohorts and a total of 135,018 participants, indicated that periodontitis is associated with root caries but not with caries affecting the anatomical crown. Sensitivity meta-analyses focusing on severe periodontitis as the exposure generally yielded consistent results. Estimates for caries experience were only slightly attenuated in adjusted models compared with crude models.

Pieces of available epidemiological evidence hypothesized that periodontitis and dental caries may co-occur because of common risk factors/determinants, including access to dental care, socio-economic factors, smoking, lack of plaque control and intake of fermentable carbohydrates (Jepsen et al., 2017). Results from our subgroup meta-analyses by adjustment level only partially confirmed this concept. Indeed, the estimates of association were only slightly attenuated in the adjusted models compared with the crude ones. Despite a risk of residual confounding cannot be ruled out, these results therefore suggest the presence of an independent association between periodontitis and dental caries.

Clinical attachment loss due to periodontitis results in an increased tooth surface area exposed to the oral cavity, which confers an intrinsic higher risk for root caries development (Heasman et al., 2017; López et al., 2017). Although the design of the included studies prevents the verification of causality, the findings from our systematic review conceptually align with this notion. Subgroup meta-analyses by caries location indeed indicated that the association is mostly present for root caries, rather than coronal caries. The higher critical pH for demineralization of the cementum compared with enamel may contribute to rendering the root surfaces more vulnerable to dental caries once exposed to the dental biofilm (Hoppenbrouwers et al., 1987). This higher solubility of the root cementum is attributed to the greater content of organic matrix and the content of carbonate and magnesium in hydroxyapatite compared with the enamel (Dung & Liu, 1999). However, it is yet to be determined whether this association may vary after periodontitis treatment and/or depending on whether clinical attachment loss due to periodontitis affects the supra-(recession) or sub-(increased probing pocked depth) gingival environment. Indeed, the root surface exposed to a sub-gingival microenvironment can be colonized by an anaerobic proteolytic biofilm rather than an acidogenic flora characteristic of dental caries, which may influence the reported associations. Similarly, it remains unclear whether an association with dental caries may also exist for gingival recessions not associated with periodontitis, although they affect only a minor proportion of the population (Romandini et al., 2020; Romano et al., 2022; Strauss et al., 2023).

Some limitations should be considered when interpreting the findings from this systematic review. Only 3 out of 21 included cohorts were considered to have a low risk of bias, primarily due to issues related to the assessment of periodontitis. Indeed, while the periodontal status was always clinically and/or radiographically verified, eight cohorts employed partial-mouth examination protocols. On the same line, none of the included studies staged the severity of dental caries, which prevented any evaluation of the notion that severe forms of dental caries and periodontitis may specifically affect different individuals. Furthermore, despite subgroup analyses indicating minimal influence of model adjustments on association estimates, a risk of confounding bias from common risk factors may still exist in some meta-analyses. Owing to the lack of cohort studies, only cross-sectional designs were included, which further limits the ability to evaluate causality and the direction of the association. Finally, most meta-analyses showed moderate to high heterogeneity, possibly due to the inherent differences between the analysed populations and variations in periodontitis assessment methods. Accordingly, despite leave-one-out sensitivity analyses mostly confirming the estimates of association, the results from the meta-analyses should be interpreted cautiously. The reader should, however, also consider that the risk of selection bias in this systematic review was minimized by the comprehensive nature of the search strategy as well as the absence of language restrictions which was achieved thanks to the involvement of native translators working in the field of dentistry for the analysis of manuscripts reported in German, Russian and Persian. Moreover, the inclusion of 14 representative samples of populations from different geographical regions further strengthens the generalizability of the present findings.

5 | CONCLUSIONS

Periodontitis was found to be associated with the presence and number of treated/untreated root carious lesions. However, these results should be evaluated cautiously in light of the low estimates of associations found and considering the above-mentioned limitations, especially the moderate to high risk of bias in most of the included studies and the high heterogeneity observed in most meta-analyses.

5.1 | Implications for practice

Caries-specific preventive measures should be considered for individuals with periodontitis. These measures may include using toothpastes with a high fluoride content, professionally applying fluorides to root surfaces, maintaining effective self-performed oral hygiene and controlling diet. Additionally, patients with periodontitis should undergo thorough examinations for checking the presence of root carious lesions during supportive periodontal care. Indeed, periodontal therapy and supportive care have shown to also play an important role in reducing the development of new and recurrent caries lesions (Axelsson et al., 1991, 2004; Axelsson & Lindhe, 1981).

5.2 | Implications for research

The findings of this systematic review warrant further research. Prospective cohort studies on representative samples are needed to confirm the current findings and verify the temporality of the associations in both directions. These studies should not only focus on the presence of periodontitis and caries but also assess their severity, grade, extent and activity through comprehensive standardized full-mouth examinations and the utilization of clinical and radiographic diagnostic parameters. It is especially relevant to differentiate between root and coronal caries. In addition to patient-level analyses, site-level analyses should be conducted to disentangle the possible clinical and microbiological reciprocal relationships between the two diseases, depending on whether clinical attachment loss affects the supra-(recession) or sub-(increased probing pocket depth) gingival environment. Researchers should take measures to minimize the risk of confounding by collecting detailed data on common risk factors, especially on socio-economic status and exposure to dental care. Furthermore, it is important to also analyse edentulous participants by exploring the causes for tooth loss, as those participants may have had both periodontitis and dental caries despite being systematically excluded from published reports.

AUTHOR CONTRIBUTIONS

Pierluigi Romandini contributed to study conception and design, data acquisition, analysis and interpretation and manuscript drafting. Crystal Marruganti contributed to data acquisition, analysis and critically revised the manuscript. William Giuseppe Romandini contributed to data acquisition and manuscript drafting. Mariano Sanz and Simone Grandini contributed to data interpretation and critically revised the manuscript. Mario Romandini contributed to study conception and design, data acquisition, analysis and interpretation and manuscript drafting.

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CONFLICT OF INTEREST STATEMENT

The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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