

## Effect of Smoking on Periodontitis: A Systematic Review and Meta-regression

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**Context:** The study systematically reviewed articles on the association between tobacco smoking and periodontitis, as it has been hypothesized that smoking affects the course of periodontitis through impairment of immunological and vascular mechanisms.

**Evidence acquisition:** Searches of articles indexed in PubMed, Scopus, and Embase were performed up to and including May 2017. Search strategy included MeSH and free terms: *periodontitis, periodontal diseases, smoking, tobacco use, tobacco, tobacco products, cigarette, pipe, and cigar*. Only original prospective longitudinal studies that investigated the association between smoking and periodontitis incidence or progression were included. Results were shown as combined risk ratio. Meta-regression and subgroup analyses were used to explore potential sources of heterogeneity. Analyses were conducted in August 2017.

**Evidence synthesis:** Twenty-eight studies were included in the review; of these, only 14 presented data that could be included in the meta-analysis. Pooled adjusted risk ratios estimate that smoking increases the risk of periodontitis by 85% (risk ratio=1.85, 95% CI=1.5, 2.2). Meta-regression demonstrated that age explained 54.2% of the variability between studies, time of follow-up explained 13.5%, loss to follow-up 10.7%, criteria used to assess the periodontal status explained 2.1%, and severity of periodontitis explained 16.9%.

**Conclusions:** Smoking has a detrimental effect on the incidence and progression of periodontitis. Tobacco smoking, therefore, is important information that should be assessed along with other risk factors for periodontitis.

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### CONTEXT

Smoking is acknowledged as an important risk factor for noncommunicable chronic diseases. Smoking-related diseases have become one of the leading causes of death in the world.<sup>1,2</sup> Despite a decrease in smoking habits, estimates suggest that in 2020 approximately 10% of all deaths will be related to smoking.<sup>1</sup> Health expenditures attributable to tobacco-related diseases exceed the total tax revenue from tobacco products.<sup>1</sup> Thus, the magnitude of tobacco-related expenditures is a significant burden for both individuals and healthcare systems.

Periodontitis is a chronic destructive inflammatory condition affecting the supporting structures of the teeth and as such, it is listed in the global burden of chronic diseases.<sup>3</sup> In its ultimate stage, periodontitis leads to

tooth loss. Both conditions, periodontitis and tooth loss, affect mastication and speech and have an impact on quality of life and self-esteem.<sup>4</sup> In contrast to the decrease of dental caries, severe periodontitis remains unchanged since 1990.<sup>3</sup> Meta-analysis on the prevalence of severe periodontitis shows that approximately 700 million people are affected worldwide.<sup>3</sup> Given the combination of greater life expectancy and a significant reduction in tooth loss because of dental caries, the burden of periodontitis is expected to increase.

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The association between tobacco smoking and periodontitis is taken for granted. However, most of the evidence originates from cross-sectional studies, which precludes the establishment of temporal relationships. Furthermore, many epidemiologic studies on the topic suffer from important methodologic flaws, like high loss of participants and a short-term follow-up, which lead to conflicting estimates between studies. To date, there is no systematic review on the topic; the only published reviews have focused on the effect of smoking cessation on periodontal healing.<sup>5,6</sup> Additionally, the magnitude of the association of tobacco smoking and the incidence and progression of periodontitis controlling for differences across studies have never been estimated.

Accordingly, this study aimed to systematically review prospective longitudinal studies addressing the association between tobacco smoking and incidence and progression of periodontitis, and to also assess whether methodologic characteristics of the studies influence the variability between estimates by performing meta-regression analysis.

## EVIDENCE ACQUISITION

The report of this systematic review was based on the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) and protocols guidelines.<sup>7</sup> The review question is: Is tobacco smoking associated with the incidence or the progression of periodontitis?

### Eligibility Criteria

**Types of studies.** Original prospective longitudinal studies with  $\geq 12$  months of follow-up that investigated the association between tobacco smoking and periodontitis were considered. Studies evaluating the effect of periodontal healing among smokers, and studies conducted with individuals under supportive periodontal therapy were not considered. Finally, literature reviews, case-control studies, cross-sectional studies, retrospective longitudinal studies, case reports, anthropological studies, in vitro and in situ studies, comments, or conference abstracts were excluded.

**Exposure and outcome measurements.** Studies should present at least two measures of periodontitis (clinical attachment level/probing depth/alveolar bone loss) to fulfill the inclusion criteria. The criteria to monitor the periodontal condition was accepted as stated in the studies.

### Search Strategy

Electronic searches were conducted in PubMed via MEDLINE, Embase, and Scopus. Studies published up to and including May 2017 were included. An initial search was performed on PubMed using the following search strategy: (*Periodontal diseases* [MeSH] OR *Periodontitis* [MeSH] OR *Chronic Periodontitis* [MeSH] OR *Periodontal diseases* [all] OR *Periodontitis* [all] OR *Chronic Periodontitis* [all]) AND (*Smoking* [MeSH] OR *Tobacco Use* [MeSH] OR *Tobacco* [MeSH] OR *Tobacco Products* [MeSH] OR

*Smoking* [all] OR *Tobacco Use* [all] OR *Tobacco* [all] OR *Tobacco Products* [all] OR *Cigarette* [all] OR *Pipe* [all] OR *Cigar* [all]) AND (*Cohort Studies* [MeSH] OR *Longitudinal Studies* [MeSH] OR *Follow-up Studies* [MeSH] OR *Prospective Studies* [MeSH]). No restriction regarding date or language was applied. Search was performed in the reference list of all articles included. Additionally, gray literature was investigated by screening the first 200 hits of a Google Scholar search.

### Studies Selection

The software Endnote, version X8.0.1, was used to manage the references in all stages of the review. Firstly, duplicate references were excluded. Subsequently, titles and abstracts were evaluated independently by two reviewers based on the eligibility criteria. Lists were compared and disagreements were solved by consensus. The same two reviewers assessed the full text of studies with potential to be included in the review based on the aforementioned inclusion and exclusion criteria. Lists were compared and in the event of disagreement, a consensus was reached by discussion. The  $\kappa$  statistic was used to assess the level of agreement between the reviewers along the process.

### Data Extraction

Information extracted from the studies was grouped in the following categories:

1. characteristics of the publication: author and year of publication;
2. characteristics of the study: sample size and main characteristics, geographic location of the study, follow-up period; and
3. characteristics of the exposure and the outcome: definition and criteria used to evaluate periodontitis and smoking, and criteria used to evaluate the change in periodontal status. In addition, information about analytical approach, crude and adjusted results, and confounders were collected.

Data were independently extracted by the same two reviewers. Extracted data were compared and in the event of disagreement, discussions were held to reach consensus. When more than one category of periodontitis or smoking was reported, only the most extreme category of comparison was included in the meta-analysis. This approach was chosen to avoid the inclusion in duplicate of the individuals from the reference category. In studies presenting multiple assessments over time, only the most recent estimate was gathered. Analyses were conducted in August 2017.

### Critical Appraisal

The specific version of the Newcastle–Ottawa scale for cohort studies was used to appraise the quality of the studies included in this review. The scale comprises eight items allocated in three dimensions: (1) selection of study groups, (2) comparability of study groups, and (3) assessment of outcome and adequacy of follow-up. Before the critical appraisal process, both reviewers had a meeting to agree on how each parameter should be evaluated. The reviewers critically appraised the studies independently and in the event of disagreements, consensus was reached by discussion. Critical assessment according to each dimension of the instrument

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